

TRANSFORMATIONS OF DEOXY SugARS*

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6-Deoxyaldoses are known to be more stable in alkaline medium than the corresponding aldoses. They undergo transformations with suitable reagents under appropriate reaction conditions to form the corresponding 6-deoxyhexuloses and $C_{(3)}$ -isomeric 6-deoxyhexuloses. Transformation of 6-deoxy-L-mannose and 6-deoxy-L-galactose affords 5-deoxy-L-arabino-hexulose, 6-deoxy-L-ribo-hexulose, 6-deoxy-L-xylo-hexulose and 6-deoxy-L-lyxo-hexulose.

6-Deoxysaccharides are relatively widespread in the nature; free or O-methyl derivatives are constituents of various heart glycosides or some antibiotics. The substitution of hydrogen at $C_{(6)}$ by a hydroxyl group influences the properties of the whole molecule; investigation of this phenomenon was the aim of this paper. The enolization of 3-deoxysaccharides¹ proceeds more easily than that of saccharides. Moreover, saccharides, in contrast to 3-deoxysaccharides, can isomerize in the first step of enolization from 1,2-enediol to 2,3-enediol; consequently, either 3-ketose or a $C_{(3)}$ -hydroxy epimer can be formed. Thus, D-fructose and D-psicose². Although a like rearrangement of 1,2-enediol to 2,3-enediol can also be anticipated with 6-deoxysaccharides, there is so far no report on this matter.

6-Deoxy-L-mannose and 6-deoxy-L-galactose were the model substances for this investigation. We ascertained that the stability of 6-deoxysaccharides in saturated $Ca(OH)_2$ solution is greater than that of the corresponding saccharides. *E.g.* D-glucose forms with $Ca(OH)_2$ D-fructose in 30–40% yield within 24 h (ref.³). Transformation of 6-deoxy-D-glucose under the same reaction conditions gave 6-deoxy-D-arabino-hexulose (6-deoxy-D-fructose) in *c.* 10% yield only. A partial rearrangement of 1,2-enediol to 2,3-enediol takes place on treatment of D-glucose with $Ca(OH)_2$ (the origination of D-psicose); on the other hand, no formation of 6-deoxy-D-ribo-hexulose (6-deoxy-D-psicose) from 6-deoxy-D-glucose was observed. The effect of triethylamine is comparable with that of $Ca(OH)_2$. The corresponding 2-ketose is formed in approximately 10% yield within 24 h; another ketose cannot be detected. N,N'-Dicyclohexylcarbodiimide was employed as a transformation reagent for preparation

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of D-psicose from D-fructose⁴. Our experiments showed that transformation of 6-deoxy-L-mannose with dicyclohexylcarbodiimide in tert-butanol under a 24 h reflux led to 6-deoxy-L-*arabino*-hexulose in *c.* 15% yield; no isomerization of C₍₃₎-hydroxyl group occurred. The transformation in melt has a more rapid course, nonetheless an epimeric aldose and a C₍₃₎-epimeric ketose were obtained in addition to the corresponding ketose. Thus, transformation of 6-deoxy-L-mannose furnished 6-deoxy-L-*arabino*-hexulose, 6-deoxy-L-*ribo*-hexulose, 6-deoxy-L-glucose and probably 6-deoxy-L-*xylo*-hexulose in a trace amount. The optimum time for transformation of 6-deoxysaccharides in anhydrous pyridine was found to be *c.* 24 h; a longer transformation time was associated with an appearance of degradation products. The reaction course is similar to that of dicyclohexylcarbodiimide in melt.

Although 6-deoxyaldoses are more stable in alkaline medium than the corresponding saccharides, the selection of suitable reaction conditions makes it possible to rearrange 1,2-enediol to 2,3-enediol under formation of an isomeric ketose at C₍₃₎.

EXPERIMENTAL

Melting points were determined on a Kofler block, optical rotation was measured with an automatic polarimeter Perkin-Elmer, model 141. For paper chromatography on Whatman No 1 sheet following solvent systems were used: water-saturated 2-butanone (A), n-butanol-toluene (2 : 1) saturated with water (B). Saccharides were detected with urea and diphenylamine¹ and potassium perchlorate and benzidine⁵. 6-Deoxysaccharides used in transformations were Koch-Light products. Densitometer ERI-10 (Zeiss, Jena) was employed for quantitative evaluation of paper chromatography.

Transformation of 6-Deoxy-L-mannose

a) *By pyridine*: 6-deoxy-L-mannose (3 g) was refluxed in pyridine (30 ml) for 24 h; the solvent was evaporated under diminished pressure, the residue was three times evaporated with ethanol (30 ml each), decoloured with charcoal and crystallized from ethanol (10 ml). The unreacted 6-deoxy-L-mannose was recovered (1.35 g). Paper chromatography showed the following composition of the reaction mixture: 6-deoxy-L-mannose ($R_F = 1$ in (A) and (B)), 6-deoxy-L-*arabino*-hexulose ($R_{rel} = 1.45$ (A), 1.39 (B)), 6-deoxy-L-*ribo*-hexulose ($R_{rel} = 1.86$ (A), 1.70 (B)), 6-deoxy-L-glucose ($R_{rel} = 0.82$ (A), 0.95 (B)) (20 : 65 : 10 : 1). Another compound, which gave colouration with urea and diphenylamine characteristic of ketoses, was found in the reaction mixture in trace amounts. According to comparison of its chromatographic mobility with reference substance one can assume this sugar to be 5-deoxy-L-*xylo*-hexulose ($R_{rel} = 2.05$ (A), 1.88 (B)). The residue after crystallization was chromatographed on cellulose (Whatman, column 4.5 × 60 cm) in system A. Following substances were separated in addition to mixed fractions: 6-deoxy-L-*ribo*-hexulose $[\alpha]_D^{22} + 6.8$ (*c.* 3.1, H₂O), sirup (125 mg), reported⁶ $[\alpha]_D^{20} + 8.2$ (H₂O), amorphous; treatment with phenylhydrazine afforded phenylsazone of 6-deoxy-L-*ribo*-hexulose, m.p. 178–180°C, $[\alpha]_D^{22} + 67.8$ (*c.* 1.5, pyridine), reported⁶ m.p. 179–180°C, $[\alpha]_D^{23} + 66.3$ (pyridine); 6-deoxy-L-*arabino*-hexulose $[\alpha]_D^{22} + 7.3$ (*c.* 5.0, H₂O), sirup (850 mg), reported⁷ $[\alpha]_D - 6$ (H₂O) for the sirupy antipode; reaction with *o*-nitrophenylhydrazine furnished the corresponding hydrazone, m.p. 134–136°C, $[\alpha]_D^{22} - 39.2$ (*c.* 1.1, ethanol), reported⁷ m.p. for the antipode 136–137°C, $[\alpha]_D + 40$ (ethanol); the unreacted 6-deoxy-L-mannose (280 mg), m.p. 92–94°C,

$[\alpha]_D^{22} + 9.2$ (c 2.0, H₂O), reported^{8,9} m.p. 93–94°C, $[\alpha]_D + 10$ (H₂O), 6-deoxy-L-glucose (8.1 mg), m.p. 137–141°C, $[\alpha]_D^{22} - 29.1$ (c 0.4, H₂O). Additional two substances formed during transformation in trace amounts revealed characteristic colouration upon detection with urea and diphenylamine (ketose yellow, 6-deoxyaldoses brown spots). According to their chromatographic mobilities, these compounds might be 6-deoxy-L-*lyxo*-hexulose ($R_{rel} = 1.75$ (A), 1.60 (B)) and 6-deoxy-L-*xylo*-hexulose.

b) By calcium hydroxide: 6-deoxy-L-mannose (1 g) in saturated Ca(OH)₂ solution (10 ml) was allowed to stand at room temperature. The course of this reaction was monitored by paper chromatography. 6-Deoxy-L-*arabino*-hexulose began to form after 3 h, c. 10% was estimated after 24 h, and c. 25% after 5 days. No further ketoses originated.

c) By triethylamine: 6-deoxy-L-mannose (0.5 g) in triethylamine (2.5 ml; 1 ml of triethylamine, 1 ml of water and 0.5 ml of ethanol) was allowed to stand at room temperature. The transformation was found to proceed a little slower than with calcium hydroxide. Approximately 25% of 6-deoxy-L-*arabino*-hexulose was formed within 7 days. No further ketose was estimated.

d) By N,N'-dicyclohexylcarbodiimide in tert-butanol: 6-deoxy-L-mannose (200 mg) and carbodiimide (1 g) were dissolved in tert-butanol (10 ml) and heated to reflux. Twelve h of reaction produced 6-deoxy-L-*arabino*-hexulose in c. 10% yield. No further ketose was found.

e) By N,N'-dicyclohexylcarbodiimide in melt: a stirred mixture of 6-deoxy-L-mannose (2 g) and carbodiimide (2 g) was heated at 120°C for 5 h; water (15 ml) was added and the solution was extracted with ether (3.5 ml). The aqueous layer was concentrated after purification with charcoal, dissolved in ethanol (5 ml) and crystallized to give the unreacted 6-deoxy-L-mannose (930 mg). Paper chromatography of the reaction mixture revealed the presence of 6-deoxy-L-mannose (20%), 6-deoxy-L-*arabino*-hexulose (60%), 6-deoxy-L-*ribo*-hexulose (10%), 6-deoxy-L-glucose (1%) and a trace amount of a further ketose, which might be 6-deoxy-L-*xylo*-hexulose according to comparison of its chromatographic mobility with those of standards. The substances were quantitatively separated on a cellulose (Whatman) packed column in solvent system A. Following saccharides were obtained in addition to mixed fractions: 6-deoxy-L-*ribo*-hexulose, sirup, $[\alpha]_D^{22} + 7.6$ (c 3.1, H₂O), 76 mg, (3.8% to the starting 6-deoxy-L-mannose), 6-deoxy-L-*arabino*-hexulose (584 mg, 29%), $[\alpha]_D^{22} + 6.9$ (c 2.2, H₂O), unreacted 6-deoxy-L-mannose (162 mg) and 6-deoxy-L-glucose (23 mg, ~1%), $[\alpha]_D^{22} - 29.7$ (c 1.5, H₂O).

Transformation of 6-Deoxy-L-galactose

6-Deoxy-L-galactose (100 mg) in pyridine (2 ml) was refluxed for 24 h, pyridine removed under diminished pressure, the residue dissolved in ethanol (5 ml) and evaporated to dryness (3 times). The product contained after purification with charcoal the unreacted 6-deoxy-L-galactose ($R_{rel} = 0.55$ (A), 0.73 (B), 60%), 6-deoxy-L-*lyxo*-hexulose (30%) and 6-deoxy-L-talose ($R_{rel} = 2.08$ (A), 1.95 (B), trace amount) and a further ketose, which might be 6-deoxy-L-*ribo*-hexulose according to chromatographic mobility. The mixture separated on paper Whatman No 3 in the solvent system A gave: the unreacted 6-deoxy-L-galactose (54.2 mg), m.p. 139–141°C, $[\alpha]_D^{22} - 75.4$, (c 2.0, H₂O), reported¹⁰ m.p. 140–141°C, $[\alpha]_D - 76$ (H₂O); 6-deoxy-L-*lyxo*-hexulose, sirup $[\alpha]_D^{22} + 3.1$ (c 2.1, H₂O), reported¹¹ m.p. 68–69°C, $[\alpha]_D^{22} + 3.4$ (H₂O); *o*-nitrophenylosazone m.p. 160–162°C, $[\alpha]_D - 69.5$ (methanol); 6-deoxy-L-*xylo*-hexulose (4.1 mg), m.p. 84–86°C, $[\alpha]_D^{22} - 28.6$ (c 0.5, H₂O), reported⁶ m.p. 84–85°C, $[\alpha]_D^{22} - 29.8$ (H₂O).

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