ISOMERIZATION OF 2-AMINO-1,6 : 3,4-DIANHYDRO-2-DEOXY-β-D-GALACTOPYRANOSE TO 1,6-ANHYDRO-2,3-DIDEOXY-2,3-EPIMINO-β-D-GULOPYRANOSE IN ALKALINE MEDIUM*

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2-Amino-1,6 : 3,4-dianhydro-2-deoxy-β-D-galactopyranose (*I*) hydrolyses to 2-amino-1,6-anhydro-2-deoxy-β-D-glucopyranose (*II*) in aqueous 5% potassium hydroxide at elevated temperature under simultaneous partial isomerization to 1,6-anhydro-2,3-dideoxy-2,3-epimino-β-D-gulopyranose (*IV*). The structure of epimine *IV* was demonstrated by mass spectrometry and proton magnetic resonance.

In a recent paper[1] describing the preparation of epimino derivatives of 1,6-anhydro-β-D-hexopyranoses we demonstrated that 1,6-anhydro-2,3-dideoxy-2,3-epimino-β-D-mannopyranose hydrolyses in aqueous alkaline medium to 2-amino-1,6-anhydro-2-deoxy-β-D-mannopyranose. However, it was not reliably proved that the supposed intermediate of this reaction, 2-amino-1,6 : 3,4-dianhydro-β-D-altropyranose, which would originate by isomerization of epimino derivative, was indeed present in the reaction mixture. From the considerations on the isomerization of α-hydroxy epoxides[2,3] and on the different reactivity of the oxirane[4] and the aziridine ring[5,6] we came to the conclusion that α-aminoepoxides should isomerize more easily than α-hydroxyepimines (of course, in both cases the stereoisomers with a three-membered ring *trans* oriented with respect to the hydroxyl or the amino group). Therefore we concentrated our study on the properties of 2-amino-1,6 : 3,4-dianhydro-2-deoxy-β-D-galactopyranose (*I*). This compound was prepared from 2-amino-1,6-anhydro-2-deoxy-β-D-glucopyranose in a described manner[7].

During the study of the reactivity of amino epoxide *I* we determined polarimetrically that this compound does not change even after 24 hours standing in a neutral aqueous solution. In 0·1M-NaOH at room temperature it does not change either, while

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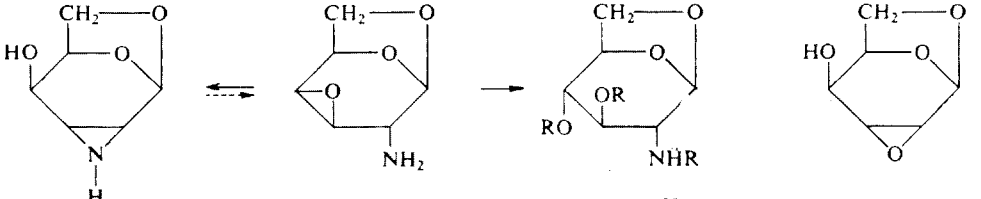
1,6 : 3,4-dianhydro-β-D-galactopyranose (an oxygen analogue of aminoepoxide *I*) isomerizes rapidly under similar conditions to 1,6 : 2,3-dianhydro-β-D-gulopyranose (*V*) under formation of an equilibrium mixture of both dianhydro derivatives[2]. After several hours' heating of amino epoxide *I* in 5% aqueous potassium hydroxide at about 100°C it was possible to demonstrate in the reaction mixture by thin layer chromatography in addition to the starting compound two further ninhydrin positive substances. By chromatography on silica gel 2-amino-1,6-anhydro-2-deoxy-β-D-glucopyranose (*II*) was isolated as the predominant component of the mixture. The structure proof of this compound was carried out after its conversion to 2-acetamido--3,4-di-O-acetyl-1,6-anhydro-2-deoxy-β-D-glucopyranose (*III*) by comparison with an authentic specimen. Chromatographically the by-product 1,6-anhydro-2,3--dideoxy-2,3-epimino-β-D-gulopyranose (*IV*), was also isolated. Its structure was proved on the basis of the PMR spectrum which is similar to the spectrum of 1,6 : 2,3--dianhydro-β-D-gulopyranose (*V*) with the exception of the chemical shifts of $H_{(2)}$ and $H_{(3)}$ and their vicinal $J_{2,3}$. The signals of the —CH_2—O— group confirm that the 1,6-anhydropyranose skeleton remained intact in the molecule. The presence of the hydroxyl group and the imino group are indicated by the signals of two deuterium-exchangeable protons at 3·00 and 5·35 p.p.m.. The position of the aziridine ring follows from the chemical shifts of protons $H_{(2)}$ and $H_{(3)}$ (1·92 or 2·02 p.p.m. resp.), which are substantially more upfield than in 1,6 : 2,3-dianhydro-β-D-gulopyranose (*V*) ($H_{(2)}$ 2·90 and $H_{(3)}$ 2·86 p.p.m.). The increase in the $J_{2,3}$ value (5·5 Hz in epimine *IV* in contrast to 3·9 Hz in epoxy derivative *V*) is also in agreement with the change of the electronegativity of the heteroatom in the three-membered ring. The configuration of the aziridine ring follows from the low value of $J_{1,2} < 1$ and the configuration of the hydroxyl group at $C_{(4)}$ is determined unequivocally by the values of the coupling constants, $J_{3,4} < 1$ and $J_{4,5} = 5$ Hz. According to expectations the value of optical rotation of epimino derivative *IV* ($[\alpha]_D$ +27° in water) is in good agreement with the optical rotation value of 1,6 : 2,3-dianhydro-β-D-gulopyranose (*V*) ($[\alpha]_D$ +30° in water) and the isomerization of α-amino epoxide *I* to α-hydroxyepimine *IV* is accompanied by a shift of optical rotation similar to that met in the isomerization of 1,6 : 3,4-dianhydro-β-D-galactopyranose to 1,6 : 2,3-dianhydro-β-D-gulopyranose[2] (*V*).



IV *I* *II*, R = H; *III*, R = CH_3CO *V*

From the results it follows that 2-amino-1,6 : 3,4-dianhydro-2-deoxy-β-D-galactopyranose (*I*) hydrolyses at elevated temperatures in alkaline medium to 2-amino-1,6-anhydro-2-deoxy-β-D-glucopyranose (*II*) and it also isomerizes simultaneously to 1,6-anhydro-2,3-dideoxy-2,3-epimino-β-D-gulopyranose (*IV*) according to Scheme.

Although we did not prove the isomerization of epimino derivative *IV* to amino-epoxide *I*, we can suppose it on the basis of the behaviour of 1,6-anhydro-2,3-dideoxy-2,3-epimino-β-D-mannopyranose in alkaline medium[1].

Among the products of hydrolysis of amino epoxide *I* and 1,6-anhydro-2,3-dideoxy-2,3-epimino-β-D-mannopyranose[1] substances were found which were probably formed by diaxial cleavage of the oxirane derivatives: in the first case it was 1,6-anhydro-2-amino-2-deoxy-β-D-glucopyranose (*II*) and in the second 1,6-anhydro-2-amino-2-deoxy-β-D-mannopyranose. The products of hydrolysis of the aziridine ring could not be proved reliably in the reaction mixture. This is in agreement with the observation that the aziridine ring is more stable in alkaline medium than the oxirane ring.

EXPERIMENTAL

The melting points were determined on a micromelting point apparatus Boëtius. Optical rotations were measured on an automatic polarimeter Bendix Ericsson ETL, type 143A, at 23–25°C. Thin-layer chromatography was carried out on silica gel G according to Stahl. For detection sulfuric acid (50%) and heating was applied, unless stated otherwise. The solvents were evaporated under reduced pressure at a temperature not exceeding 50°C.

Reaction of 2-Amino-1,6 : 3,4-dianhydro-2-deoxy-β-D-galactopyranose (*I*) with Potassium Hydroxide

A solution of 0·20 g of amino epoxide[7] *I* in 2 ml of 5% aqueous potassium hydroxide was bubbled through with nitrogen and heated at 90–110°C for 6 hours in a sealed tube. After this period the presence of 2-amino derivative *II* and epimino derivative *IV* could be demonstrated in the reaction mixture by thin-layer chromatography in chloroform–2-propanol–conc. ammonia–water (10 : 10 : 1 : 1): amino derivative *II* (R_F 0·21), epimine *IV* (R_F 0·61); in paper chromatography on Whatman No 4 paper (descending technique) using the system pyridine–1-butanol–water (6 : 4 : 3) for elution: amino derivative *II* (R_F 0·42), epimine *IV* (R_F 0·62). Detection was carried out with a solution of ninhydrin in acetone and heating at 100°C. The reaction mixture was evaporated under reduced pressure with 0·5 g silica gel and the residue was put on a column of 5 g of silica gel. Epimine *IV* was eluted with a chloroform–methanol (9 : 1) mixture, yield was 40 mg (20%), while amino derivative *II* was eluted with ethanol–conc. ammonia (4 : 1), to afford 180 mg (80%).

Epimino derivative *IV* was purified by decolorizing its ethanolic solution with charcoal and crystallization from ethanol–light petroleum. The product *IV* was obtained (24 mg) melting at 143–145°C (at 90–100°C a change in anisotropy occurred in the polarized light), $[\alpha]_D$ + 27° ± ± 2° (*c* 0·45, water). Paper chromatography on Whatman No 4 paper in water saturated 1-butanol: epimino derivative *IV* (R_F 0·53), amino epoxide *I* (R_F 0·37); detection with ninhydrin in acetone and heating at 100°C. Mass spectrometry (Jeol D 100), for $C_6H_9NO_3$ *m/e* calculated: 143·0582,

found: 143·0518. PMR spectra (measured in hexadeuteriodimethyl sulfoxide on a Varian HA-100 instrument at 100 MHz; chemical shifts (δ) and coupling constants were obtained by first-order analysis with 0·01 p.p.m. or 0·1 Hz accuracy, in the case of epimine *IV* the accuracy of J was approximately 0·5 Hz): Epimino derivative *IV*: $H_{(1)}$ 5·48, $H_{(2)}$ 1·92, $H_{(3)}$ 2·02, $H_{(4)}$ 3·95, $H_{(5)}$ 4·20, $H_{(6)en}$ 4·08, $H_{(6)ex}$ 3·59 p.p.m.; $J_{1,2} < 1·0$, $J_{2,3}$ 5·5, $J_{3,4} < 1·0$, $J_{4,5}$ 5·0, $J_{5,6en}$ 2·0, $J_{5,6ex}$ 6·5, $J_{6en,6ex}$ 7·5 Hz. Dianhydro derivative *V*: $H_{(1)}$ 5·45, $H_{(2)}$ 2·90, $H_{(3)}$ 2·86, $H_{(4)}$ 3·92, $H_{(5)}$ 4·23, $H_{(6)en}$ 3·97, $H_{(6)ex}$ 3·57 p.p.m.; $J_{1,2}$ 0·9, $J_{2,3}$ 3·9, $J_{3,4} \sim 0$, $J_{4,5}$ 4·8, $J_{5,6en}$ 1·9, $J_{5,6ex}$ 6·4, $J_{6en,6ex}$ 7.7 Hz.

3,4-Di-O-acetyl-2-acetamido-1,6-anhydro-2-deoxy-β-D-glucopyranose (*III*)

Amino derivative *II* (150 mg) obtained by hydrolysis of aminoepoxide *I* was dissolved in 1·5 ml of pyridine and acetylated with 0·8 ml of acetic anhydride. After 12 hours' standing at 25°C the mixture was evaporated, the residue dissolved in water and extracted with chloroform. The chloroform solution was dried over calcium chloride and concentrated to a syrup. Yield 140 mg (50%). According to thin-layer chromatography in chloroform–methanol (100 : 1) the syrup contained a small amount of substances with R_F values 0·31 and 0·18 in addition to triacetyl derivative *III* (R_F 0·38). Preparative chromatography on silica gel in the same solvent system and crystallization from a mixture of ethanol–ether–light petroleum gave 75 mg of triacetyl derivative *III* of m.p. 137—139°C, $[\alpha]_D$ — 91° (*c* 0·7, chloroform), the physical constants of which coincided with literature data[7,8]; its IR spectrum was identical with the spectrum of an authentic sample[7] (measured in chloroform on a UR 20 Zeiss, Jena, instrument), and the mixed melting point was undepressed.

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