# PREPARATION OF 4-AMINO-1,6-ANHYDRO-4-DEOXY-β-D-GLUCOPYRANOSE. ISOMERIZATION OF 4-AMINO-1,6 : 2,3-DIANHYDRO-4-DEOXY-β-D-MANNOPYRANOSE TO 1,6-ANHYDRO-3,4-DIDEOXY-3,4-EPIMINO-β-D-ALTROPYRANOSE*

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4-Amino-1,6-anhydro-4-deoxy-β-D-glucopyranose (*I*) was prepared by ammonolysis of 1,6 : 3,4-dianhydro-2-O-benzyl-β-D-galactopyranose (*III*) and subsequent catalytic debenzylation. On reaction of 1,6 : 3,4-dianhydro-2-O-*p*-toluenesulfonyl-β-D-galactopyranose (*IV*) with sodium azide in 2-ethoxyethanol 4-azido-2-O-*p*-toluenesulfonyl derivative *X* was obtained which was converted to azido epoxide *XI*. Its catalytic reduction gave 4-amino-1,6 : 2,3-dianhydro-4-deoxy-β-D-mannopyranose (*XXI*) which, when heated with a solution of alkali hydroxide, afforded 1,6-anhydro-3,4-dideoxy-3,4-epimino-β-D-altropyranose (*XXII*) and 4-aminoglucosan *I*.

Amino derivatives of 1,6-anhydro-β-D-hexopyranoses, accessible both by ammonolysis of oxirane derivatives and by hydrogenation of azido derivatives, are promising starting substances for the syntheses of nitrogen containing oligosaccharides[1,2]. In 1,6-anhydrohexoses, the aziridine ring, which is accessible by cyclization of amino derivatives[3] or by isomerization of amino epoxides[4], may also be synthetically useful. Its cleavage extends the possibilities of the synthesis of amino saccharides and their derivatives. In our opinion the study of isomerizations of amino epoxides also represents one of the routes leading to the elucidation of the mechanism of ammonolysis of more complex sulfonyl esters, *e.g.* some 2,4-di-O-*p*-toluenesulfonyl esters of hexopyranoses[5,6].

We devoted the first part of our work to the preparation of 4-amino-1,6-anhydro-4-deoxy-β-D-glucopyranose (*I*), so that we might check definitely the statement[3] that this compound is not one of the main by-products isolated by Jeanloz[5] from the reaction mixture after ammonolysis of 1,6-anhydro-2,4-di-O-*p*-toluenesulfonyl-β-D-glucopyranose (*II*). The starting compound for the preparation of 4-aminoglucosan *I* was 1,6 : 3,4-dianhydro-2-O-benzyl-β-D-galactopyranose (*III*), obtained by two-step synthesis from 1,6 : 3,4-dianhydro-2-O-*p*-toluenesulfonyl-β-D-galacto-

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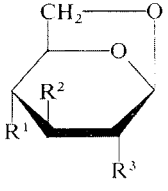
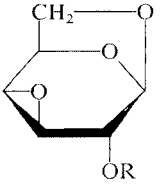
pyranose[7] (*IV*). Detosylation of epoxide *IV* with sodium amalgam[8] gave 1,6 : 3,4-dianhydro-β-D-galactopyranose (*V*), which on subsequent benzylation with benzyl bromide[9] gave epoxide *III*.

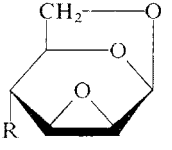
Reaction of compound *III* with ethanolic ammonia at 100°C gave 4-amino-1,6-anhydro-2-O-benzyl-4-deoxy-β-D-glucopyranose (*VI*) in 79% yield. Hydrogenolysis of this derivative on palladium on charcoal in acetic acid led to 4-amino-1,6-anhydro-4-deoxy-β-D-glucopyranose (*I*) which was isolated in the form of hydrochloride *VII*. On acetylation with acetic anhydride in pyridine triacetate *VIII* was prepared.



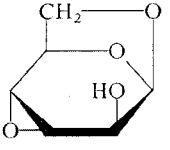
*I*, $R^1 = NH_2$, $R^2$, $R^3 = OH$
*II*, $R^1$, $R^3 = OTs$, $R^2 = OH$
*VI*, $R^1 = NH_2$, $R^2 = OH$, $R^3 = OBn$
*VII*, $R^1 = NH_3Cl$, $R^2$, $R^3 = OH$
*VIII*, $R^1 = NHAc$, $R^2$, $R^3 = OAc$
*X*, $R^1 = N_3$, $R^2 = OH$, $R^3 = OTs$
*XII*, $R^1 = N_3$, $R^2$, $R^3 = OH$
*XIII*, $R^1$, $R^3 = N_3$, $R^2 = OH$
*XIV*, $R^1$, $R^3 = NH_2$, $R^2 = OH$
*XV*, $R^1$, $R^3 = NHAc$, $R^2 = OAc$



*III*, R = Bn
*IV*, R = Ts
*V*, R = H



*XI*, R = $N_3$
*XXIII*, R = $NH_3Cl$
*XXIV*, R = NHAc
*XXV*, R = OH



*XXVI*

Bn = $C_6H_5CH_2$
Ts = $p$-$CH_3C_6H_4SO_2$
Ac = $CH_3CO$

The proof of the structure of hydrochloride *VII* is based on the evaluation of the $^1$H-NMR spectrum which confirmed the existence of this compound in $^1C_4$ conformation in a hexadeuteriodimethyl sulfoxide[10] solution. The presence of an amino group on $C_4$ is indicated by the small value of the chemical shift of H-4 (3·13$\delta$). The low coupling constants $J_{1,2} = J_{2,3} = 1{\cdot}3$ Hz, $J_{3,4} = 1{\cdot}5$ Hz and $J_{4,5} \approx 1$ Hz prove the equatorial arrangement of the hydrogens H-2, H-3, H-4, and the values $J_{1,3} \approx 1{\cdot}3$ Hz and $J_{2,4} \approx 1{\cdot}0$ Hz indicate the W-type interactions. (In its parameters the spectrum entirely corresponds to the $^1$H-NMR spectrum of 2-amino-1,6-anhydro-2-deoxy-β-D-glucopyranose hydrochloride[10] (*IX*)). The molecular rotation value of hydrochloride *VII*, $[M]_D$ −127° (water), does not differ much from the rotation range[3] of presently known hydrochlorides of 2- or 3-amino-deoxy derivatives of 1,6-anhydro-β-D-glucopyranose[3,11].

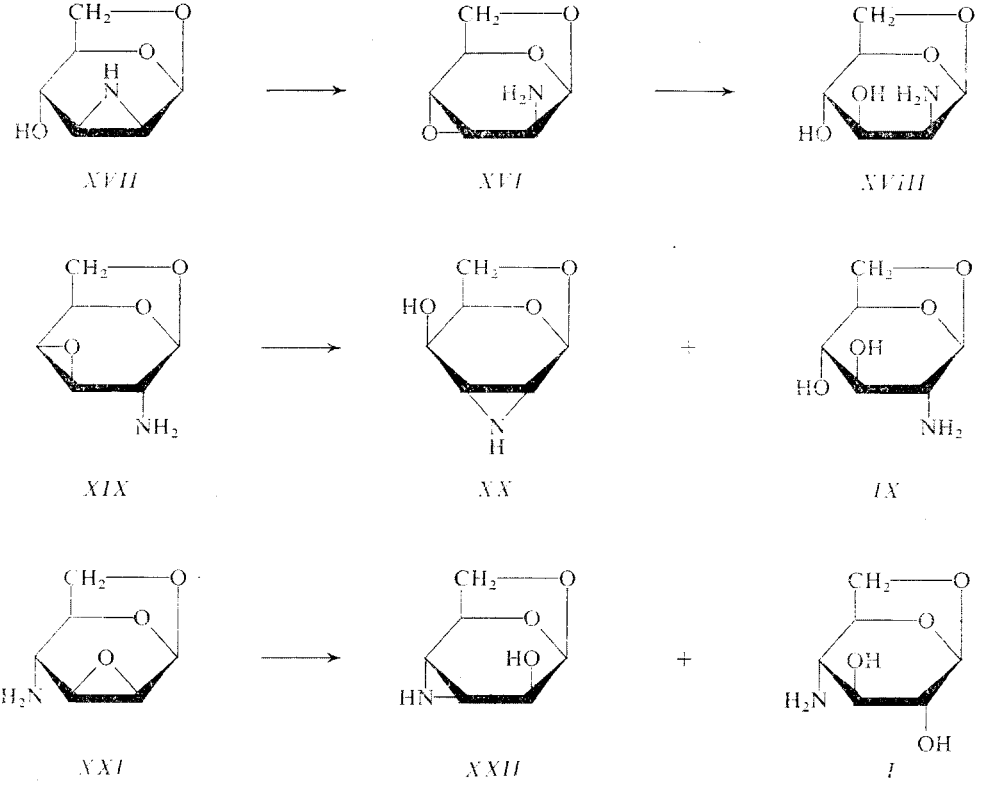
The structure of compound *I* was definitely confirmed by an alternative synthesis from epoxide *IV*. A part of this synthesis was also carried out independently by Paulsen (see preliminary communication[12]). On reaction with sodium azide in boiling aqueous 2-ethoxyethanol and under addition of ammonium chloride epoxide *IV* afforded 1,6-anhydro-4-azido-4-deoxy-2-O-*p*-toluenesulfonyl-β-D-glucopyranose (*X*) in a 62% yield. Its reaction with sodium methoxide in chloroform led to 1,6 : 2,3-dianhydro--4-azido-4-deoxy-β-D-mannopyranose (*XI*) in 72% yield. After alkaline hydrolysis of azido epoxide *XI* 1,6-anhydro-4-azido-4-deoxy-β-D-glucopyranose (*XII*) was obtained which was hydrogenated on palladium on charcoal in ethanol to give the amino derivative *I*. This compound was acetylated to triacetate *VIII* which was identical with the triacetate of 4-aminoglucosan *VIII* prepared from benzyl epoxide *III* by the following reaction sequence: *III* → *VI* → *VII* → *VIII*. Thus, the structure of 4-aminoglucosan *I* may be considered as safely proved. On the basis of the fact that the properties of hydrochloride *VII* and triacetate *VIII* differ substantially from the properties of the corresponding derivatives in the paper by Jeanloz[5], it may be inferred that the structure of the product isolated by Jeanloz and described as 4-amino--1,6-anhydro-4-deoxy-β-D-glucopyranose (*I*) is in fact differrent. It is apparently 4-amino-1,6-anhydro-4-deoxy-β-D-mannopyranose[3].

In the reaction of tosyl epoxide *IV* with the azide 1,6-anhydro-2,4-diazido-2,4-dideoxy-β-D-glucopyranose (*XIII*) is formed as a by-product in about 5% yield, which in current solvent systems has identical $R_F$ values as ester *X*. It could be isolated only after conversion of ester *X* to azidoepoxide *XI*. Its hydrogenation on palladium on charcoal in ethanol gave 2,4-diamino-1,6-anhydro-2,4-dideoxy-β-D-glucopyranose (*XIV*) which was acetylated with acetic anhydride and sodium acetate to 2,4-diacetamido-3-O-acetyl-1,6-anhydro-2,4-dideoxy-β-D-glucopyranose (*XV*), the properties of which corresponded to those given in the literature[5].

Further we studied the question of mutual isomerization of *trans*-amino epoxides and *trans*-hydroxy epimines. It is true that 2-amino-1,6 : 3,4-dianhydro-2-deoxy--β-D-altropyranose (*XVI*) has not been proved in literature[3] as a product of isomerization of 1,6-anhydro-2,3-dideoxy-2,3-epimino-β-D-mannopyranose (*XVII*), but the assumption of its transitory formation is an acceptable explanation for the mechanism of alkaline hydrolysis of epimine *XVII*, leading to 2-amino-1,6-anhydro-2-deoxy--β-D-mannopyranose (*XVIII*). The isomerization reaction was also recently followed in the opposite direction[4]; from 2-amino-1,6 : 3,4-dianhydro-2-deoxy-β-D-galactopyranose (*XIX*) 1,6-anhydro-2,3-dideoxy-2,3-epimino-β-D-gulopyranose (*XX*) was formed as a by-product in addition to the product of hydrolysis, *i.e.* 2-amino-1,6--anhydro-2-deoxy-β-D-glucopyranose (*IX*).

We endeavoured to demonstrate that the above mentioned reaction is a general reaction of *trans*-amino epoxides and to find such an amino epoxide in which hydrolysis would compete as little as possible with its isomerization in alkaline medium. In this we succeeded in the case of the isomerization of 4-amino-1,6 : 2,3-dianhydro-4-de-

oxy-β-D-mannopyranose (*XXI*) to 1,6-anhydro-3,4-dideoxy-3,4-epimino-β-D-altropyranose (*XXII*). The starting amino epoxide *XXI* was prepared by hydrogenation of azido epoxide *XI* on palladium on charcoal in ethanol and it was isolated in the form of hydrochloride *XXIII*. Although the hydrogenation was not smooth (traces of substances with $R_F$ corresponding to *altro*-epimine *XXII* and 4-aminoglucosan *I* are formed), hydrochloride *XXIII* was obtained in a 56% yield and characterized as acetyl derivative *XXIV* after acetylation with acetic anhydride in pyridine.




The structure of hydrochloride *XXIII* was confirmed by $^1$H-NMR spectra. The oxirane ring in the position 2,3 is indicated by the high value of $J_{2,3} = 3{\cdot}8$ Hz, and its configuration is determined by the coupling constants $J_{1,2} = 3{\cdot}1$ Hz and $J_{3,5} = 1{\cdot}65$ Hz. The low values of the coupling constants $J_{3,4} = 0{\cdot}7$ Hz and $J_{4,5} = 1{\cdot}1$ Hz are in agreement with the *trans* position of the amino group with respect to the oxirane ring and also to the 1,6-anhydride bridge. In its parameters the spectrum corresponds to that of an oxygen analogue, *i.e.* 1,6 : 2,3-dianhydro-β-D-manno-

pyranose[3] (*XXV*), ($J_{1,2}$ = 3·2 Hz, $J_{2,3}$ = 3·8 Hz, $J_{3,4}$ = 0·6–0·7 Hz, $J_{4,5}$ = 1·1 Hz, $J_{3,5}$ = 1·4 to 1·5 Hz).

The isomerization reaction of the *manno*-epoxide *XXI* was carried out in 5% potassium hydroxide, with respect to the possibility of comparing it with preceding experiments[4]. At room temperature the reaction did not take place, as shown by the analysis of the reaction mixture during the reaction by polarimetry and thin-layer chromatography. In contrast to this, when the reaction was carried out at 100°C the presence of the starting compound *XXI* could no longer be proved after 5 hours. *altro*-Epimine *XXII* was isolated by column chromatography in an 82% yield, together with 11% of hydrolytic products from which acetate of 4-aminoglucosan *VIII* was obtained as the main product after previous acetylation with acetic anhydride in pyridine. Its properties corresponded to those of an authentic sample, prepared from epoxide *III*.

The structure of *altro*-epimine *XXII* was confirmed by $^1$H-NMR spectra. The presence of the NH and OH group is indicated by the broad two-proton signal at 2·90$\delta$, which disappeared after addition of deuterated acetic acid. The aziridine cycle in the position 3,4 is indicated by the low values of the chemical shifts of H-3 and H-4 (1·74 and 2·11$\delta$) in comparison with the shift of H-2 (3·51$\delta$), as well as the high value of the coupling constant $J_{3,4} \approx 5$ Hz (which is comparable with the values $J_{2,3}$ = 6·1 Hz of *manno*-epimine *XVII* and $J_{2,3}$ = 5·5 Hz of *gulo*-epimine *XX*). The configuration of the aziridine ring follows from the relatively low values $J_{2,3} \approx \approx 0$ Hz and $J_{4,5}$ = 1·2 Hz when compared with the value $J_{1,2}$ = 3·1 Hz, determining the configuration on $C_{(2)}$. (The coupling constants are comparable with those measured for 1,6 : 3,4-dianhydro-β-D-altropyranose[13] (*XXVI*): $J_{1,2}$ = 2·8 Hz, $J_{2,3}$ = = 0 Hz, and $J_{4,5}$ = 1·5 Hz). The value of optical rotation $[\alpha]_D$ −120° (water) does not differ much from the value $[\alpha]_D$ −113° (water), measured for the oxygen analogue, *i.e. altro*-epoxide *XXVI*.

Amino epoxide *XXI* is isomerized in 5% potassium hydroxide at an elevated temperature to *altro*-epimine *XXII* and simultaneously, to a smaller extent, it is hydrolysed to 4-aminoglucosan *I*. A similar course was also observed in experiments aiming at the isomerization of amino epoxide *XXI* in water. Compound *I* is a product of *trans*-diaxial cleavage of the 2,3-oxiran ring of epoxide *XXI*, and in view of the fact that other products of hydrolysis were not found in higher amounts it may be stated that *altro*-epimine *XXII* is stable in an alkaline medium. In order to check this statement epimine *XXII* was heated with 5% potassium hydroxide at 100°C for 48 hours. Thin-layer chromatography did not show any changes in the reaction mixture. The stability of *altro*-epimine *XXII* distinctly contrasts with the earlier described[3] behaviour of *manno*-epimine *XVII* in alkaline medium, which can be explained[3] by its isomerization to *altro*-epoxide *XVI*.

When the reactivity of epimines *XVII* and *XXII* was compared with the reactivity of the corresponding oxygen-containing derivatives, *i.e.* 1,6 : 2,3-dianhydro-β-D-man-

nopyranose (*XXV*) and 1,6 : 3,4-dianhydro-β-D-altropyranose (*XXVI*), in 5% potassium hydroxide, the higher reactivity of the derivatives having *manno* configuration, *i.e.* of epoxides *XXV* and epimine *XVII* was clearly shown.

Similarly, in the mixture after isomerization of amino *manno*-epoxide *XXI* more of the corresponding epimine could be found after the same time interval than in the case of the isomerization[4] of amino *galacto*-epoxide *XIX*. Under the supposition that the hydrolysis of the oxirane ring takes place in 5% potassium hydroxide at the same rate[14,15] in both derivatives, the higher amount of epimine corresponds to the higher reactivity of amino epoxide during isomerization. Equally, the extent of isomerization in *manno*-epoxide *XXV* is higher[15] than in *galacto*-epoxide *V*.

On the basis of the above-mentioned analogies with oxygen derivatives it may be assumed that the isomerization of *trans*-amino epoxides and also *trans*-hydroxy epimines will take place with increasing willingness in the order of configurations *altro* < *gulo* < *galacto* < *manno*.

## EXPERIMENTAL

The melting points were measured on a micromelting point apparatus Boëtius. Specific rotations were measured on a Bendix-Ericsson ETL 143 A and Perkin-Elmer MC-141 polarimeter at 23 to 25°C. The IR spectra were measured in 3–5% chloroform solutions, unless stated otherwise, on a Zeiss, Jena UR 10 spectrophotometer. The measurement of hydrogen bonds was carried out in tetrachloromethane on a Unicam SP 700 instrument at concentrations lower than $10^{-3}$M. The $^1$H-NMR spectra were measured on a Varian HA-100 instrument and the signals of single protons were assigned by the method of double resonance. Thin-layer chromatography was carried out on silica gel according to Stahl (layer thickness 0·2–0·3 mm) in the following solvent systems: $S_1$ benzene–acetone (10 : 1), $S_2$ chloroform–methanol (10 : 1), and $S_3$ chloroform–propanol-25% ammonia–water–ethanol (20 : 20 : 2 : 2 : 1). Universal detection by mineralization with 50% sulfuric acid was applied. Azido compounds were detected specifically by spraying the plates first with Buchanan's reagent and then with 50% sulfuric acid[3]. Amino hexoses were detected with 0·5% ninhydrin in ethanol. Column chromatographies were carried out on silica gel L 100/250 μ. The solvents were evaporated on a vacuum rotatory evaporator at 40–50°C. Samples for analysis were dried over phosphorus pentoxide at 0·2 Torr.

### 4-Amino-1,6-anhydro-2-O-benzyl-4-deoxy-β-D-glucopyranose (*VI*)

A solution of 3 g of epoxide *III* (ref.[9]) in 60 ml of ethanol saturated with ammonia at 0°C was heated in an autoclave at 100°C for 28 hours. The reaction course was followed by thin-layer chromatography in chloroform–methanol (20 : 1) ($R_F$ of epoxide 0·91, $R_F$ of aminobenzyl derivative 0·09). The mixture was concentrated, mixed with ether and allowed to crystallize. Recrystallization from a mixture of acetone, ethanol and light petroleum gave 2·5 g (79%) of a product, melting at 134–135°C, $[\alpha]_D$ −46° (*c* 0·80, chloroform). For $C_{13}H_{17}NO_4$ (251·3) calculated: 62·14% C, 6·82% H, 5·57% N; found: 62·11% C, 6·86% H, 5·58% N.

### Hydrochloride of 4-Amino-1,6-anhydro-4-deoxy-β-D-glucopyranose (*VII*)

Hydrogenolysis of 1·5 g of derivative *VI* was carried out in 30 ml of acetic acid in the presence of 0·5 g of 5% palladium on charcoal, under normal pressure and at 40–50°C. After 7 hours the

reaction was finished (indicated by thin-layer chromatography in $S_2$), the catalyst was filtered off and the filtrate was concentrated. The residue was dried and dissolved in 20 ml of ethanol, the solution was acidified with 5% ethanolic hydrogen chloride to pH 5 and evaporated.

Crystallization of the residue from ethanol gave 700 mg (58%) of hydrochloride *VII*, m.p. 160–180°C (under decomposition), $[\alpha]_D$ −65° (*c* 0·82, water). For $C_{16}H_{12}ClNO_4$ (197·6) calculated: 36·47% C, 6·12% H, 17·94% Cl, 7·09% N; found: 36·03% C, 6·09% H, 17·97% Cl, 7·10% N. $^1$H-NMR spectrum (in hexadeuteriodimethyl sulfoxide with traces of $CD_3COOD$, and $CDCl_3$ with hexamethyldisiloxane as internal reference, chemical shifts values in $\delta$-scale, corrected for tetramethylsilane, coupling constants *J* in Hz): 5·31 (H-1), 3·38 (H-2), 3·66 (H-3), 3·13 (H-4), 4·70 (H-5), 4·18 (H-$6_{endo}$), 3·65 (H-$6_{exo}$): $J_{1,2}$ = 1·3, $J_{2,3}$ = 1·3. $J_{3,4}$ = 1·5. $J_{4,5}$ = = 1·0, $J_{5,6endo}$ = 0·7, $J_{5,6exo}$ = 5·7, $J_{6,6}$ = 7·3, $J_{1,3}$ = 1·3, $J_{2,4}$ = 0·5.

4-Acetamido-2,3-di-O-acetyl-1,6-anhydro-4-deoxy-β-D-glucopyranose (*VIII*)

*a*) Hydrochloride *VII* (50 mg) was acetylated with 0·5 ml acetic anhydride in 2 ml of pyridine by standing at room temperature for 12 hours and under occasional shaking. After decomposition of excess acetic anhydride with methanol the mixture was evaporated. The residue was dissolved in 2 ml of water and extracted with chloroform. The extract was dried over anhydrous magnesium sulfate, concentrated and the residue crystallized from ether. Yield, 52 mg (73%) of acetate *VIII*, m.p. 135–136°C, $[\alpha]_D$ −29° (*c* 1·53, chloroform), $[\alpha]_D$ 0° (*c* 0·81, methanol). For $C_{12}H_{17}NO_7$ (287·3) calculated: 50·17% C, 5·96% H, 4·88% N; found: 50·32% C, 6·0% H, 4·85% N. IR spectrum 1515 cm$^{-1}$, 1677 cm$^{-1}$ $\nu$(N—C=O); 1752 cm$^{-1}$ $\nu$(O—C=O); 3436 cm$^{-1}$ $\nu$(NH).

*b*) A solution of 100 mg qf *XII* in 5 ml of 96% ethanol was mixed with 100 mg of 10% palladium on charcoal and hydrogenated at normal pressure and at 40–50°C for 10 hours. The reaction was followed by thin-layer chromatography in system $S_2$. The catalyst was filtered off and the solution concentrated to afford 81 mg (94%) of aminoglucosan *I* which was acetylated with 0·7 ml of acetic anhydride in 3 ml of pyridine overnight. After decomposition of excess acetic anhydride with water the mixture was evaporated and the residue purified with charcoal in methanol and then concentrated and crystallized from ether. The yield of acetate *VIII* was 137 mg (89%), m.p. 135–137°C, $[\alpha]_D$ −26° (*c* 0·34, chloroform). Its IR spectrum was identical with that of acetate *VIII* prepared under *a*).

1,6-Anhydro-4-azido-4-deoxy-2-O-*p*-toluenesulfonyl-β-D-glucopyranose (*X*)

A mixture of 10 g of epoxide *IV* (ref.[7]), 10 g of sodium azide, and 50 g of ammonium chloride in 100 ml of 2-ethoxyethanol and 30 ml of water was refluxed for 5 hours. The reaction was followed chromatographically on thin-layer plates in system $S_1$. Ammonium chloride was filtered off and rinsed with 50 ml of chloroform. The combined filtrates were purified with charcoal, extracted with water and the aqueous layer was extracted with chloroform. The extract was added to the original solution which was dried over magnesium sulfate and evaporated. The residual 2-ethoxyethanol was eliminated by distillation with toluene. Purification of 9 g of the product (78%) on a silica gel column, using benzene–acetone (20 : 1) for elution, gave 7·1g (62%) of syrupy *X*, $[\alpha]_D$ −69° (*c* 0·75, chloroform), ref.[12] gives $[\alpha]_D$ −75° (the solvent was not given). For $C_{13}H_{15}N_3O_6S$ (341·3) calculated: 9·39% S; found: 9·51% S. IR spectrum: 1186 cm$^{-1}$, 1200 cm$^{-1}$, 1380 cm$^{-1}$ $\nu$(—$SO_2$—O—); 2100 cm$^{-1}$ $\nu$($N_3$); 3500 cm$^{-1}$, 3600 cm$^{-1}$ $\nu$(OH).

1,6 : 2,3-Dianhydro-4-azido-4-deoxy-β-D-mannopyranose (*XI*) and 1,6-Anhydro-2,4-diazido-2,4-dideoxy-β-D-glucopyranose (*XIII*)

A solution of sodium methoxide (1·1 g of sodium in 30 ml of methanol) was added under stirring and cooling with ice to a solution of 5 g of *X* in 15 ml of chloroform and the mixture was stirred for 90 minutes. Chromatography on thin-layer plate in system $S_1$ demonstrated two substances in the reaction medium, with $R_F$ 0·6 and 0·34. The mixture was extracted with water and the aqueous phase was extracted with chloroform. The combined chloroform solutions were purified with charcoal, dried over magnesium sulfate and evaporated. The residue (2·5 g) was dissolved in benzene and chromatographed on 20 g of silica gel. Benzene–acetone (20 : 1) mixture eluted 2·2 g (88%) of epoxide *XI* of $R_F$ 0·60, which crystallized out after prolonged standing. Recrystallization from an acetone–ether–light petroleum mixture gave 1·8 g (72%) of pure product, m.p. 40—42°C, $[\alpha]_D$ −19° (*c* 1·0, chloroform), ref.[12] gives m.p. 49°C, $[\alpha]_D$ −21° (the solvent was not given). For $C_6H_7N_3O_3$ (169·2) calculated: 42·61% C, 4·17% H, 24·84% N; found: 42·65% C, 4·23% H, 24·53% N. IR spectrum: 2100 $cm^{-1}$ $\nu(N_3)$. Benzene–acetone (10 : 1) mixture eluted 250 mg of derivative *XIII*, $R_F$ 0·34, which after crystallization from ether–light petroleum mixture gave 100 mg of product of m.p. 52—53°C, $[\alpha]_D$ −71° (*c* 0·86, chloroform), literature[12] gives m.p. 49·5°C, $[\alpha]_D$ −72° (the solvent was not given). For $C_6H_8N_6O_3$ (212·2) calculated: 39·61% N; found: 39·63% N. IR spectrum: 2100 $cm^{-1}$ $\nu(N_3)$; 3610 $cm^{-1}$ $\nu$(OH), hydrogen bonds measurement: 3571 $cm^{-1}$ $\nu(OH)_{bonded}$, 3613 $cm^{-1}$ $\nu(OH)_{free}$; this may be compared with 1,6-anhydro-2,4-dideoxy-β-D-*threo*-hexopyranose[16]: 3575 $cm^{-1}$ $\nu(OH)_{bonded}$, 3624 $cm^{-1}$ $\nu(OH)_{free}$.

1,6-Anhydro-4-azido-4-deoxy-β-D-glucopyranose (*XII*)

A suspension of 0·5 g of epoxide *XI* in 10 ml of 5% potassium hydroxide solution was heated in a sealed tube at 100°C for 5 hours under shaking. The reaction course was followed by thin-layer chromatography in $S_2$. After deionization of the solution on a column of Dowex 50 WX8 (20 g) and concentration the residue was chromatographed on a column of silica gel (20 g) with chloroform–methanol (20 : 1) as eluent. Yield, 330 mg (60%) of a product which was crystallized from an acetone–ether mixture to afford 280 mg (51%) of azidohydrin of m.p. 109—110°C, $[\alpha]_D$ −97° (*c* 0·78, methanol). For $C_6H_9N_3O_4$ (187·2) calculated: 38·51% C, 4·85% H, 22·45% N; found: 38·91% C, 5·02% H, 22·30% N. IR spectrum: 2100 $cm^{-1}$ $\nu(N_3)$; 3564 $cm^{-1}$, 3609 $cm^{-1}$ $\nu$(OH).

2,4-Diacetamido-3-O-acetyl-1,6-anhydro-2,4-dideoxy-β-D-glucopyranose (*XV*)

A solution of 170 mg of derivative *XIII* in 15 ml of 96% ethanol was mixed with 200 mg of 10% palladium on charcoal and hydrogenated at normal pressure and at 40—50°C for 6 hours. At two hour intervals the apparatus was rinsed with hydrogen. After control by thin-layer chromatography in $S_3$ the catalyst was filtered off and the filtrate evaporated. The 118 mg (92%) of diamino derivative *XIV* obtained were refluxed in 3 ml of acetic anhydride containing 100 mg of freshly remelted sodium acetate for one hour. Excess acetic anhydride was decomposed with water under cooling with ice and the solution was neutralized with a saturated sodium carbonate solution. After evaporation to dryness the residue was extracted with 50 ml of chloroform in a Soxhlet extractor. The solution was evaporated and the residue crystallized from ethanol–ether to give 158 mg (76%) of acetate *XV*, m.p. 229—230°C (under sublimation), $[\alpha]_D$ −43° (*c* 0·34, methanol, literature[5] gives m.p. 228—230°C, $[\alpha]_D$ −44° (*c* 0·94, methanol). For $C_{12}H_{18}N_2O_6$ (286·3) calculated: 50·35% C, 6·34% H, 9·79% N; found: 50·35% C, 6·53% H, 10·01% N.

Hydrochloride of 4-Amino-1,6 : 2,3-dianhydro-4-deoxy-β-D-mannopyranose (*XXIII*).

A solution of 1 g of epoxide *XI* in 30 ml of 96% ethanol was mixed with 0·5 g of 10% palladium on charcoal and hydrogenated at normal pressure and at 40—50°C. The apparatus was rinsed with hydrogen after each 2 hours reaction time. The reaction course was controlled by thin-layer chromatography in $S_2$. After 12 hours the catalyst was filtered off and the mixture concentrated to 15 ml volume, then acidified with a 5% ethanolic hydrogen chloride solution to pH 5. The solution of hydrochloride *XXIII* was evaporated to half of its volume, ether was added and the mixture allowed to crystallize; yield 0·6 g (56%), m.p. 175—185°C, under decomposition, $[\alpha]_D$ −21° (*c* 1·56, water). For $C_6H_{10}ClNO_3$ (179·6) calculated: 40·13% C, 5·61% H, 19·74% Cl, 7·80% N; found: 40·17% C, 5·69% H, 19·44% Cl, 7·90% N. IR spectrum (nujol): 2967—2850 $cm^{-1}$ $\nu(NH_3^+)$. $^1$H-NMR spectrum (in $CD_3OD$): 5·76 (H-1), 3·58 (H-2), 3·24 (H-3), 3·71 (H-4), 4·57 (H-5), 3·84 (H-$6_{endo}$), 3·74 (H-$6_{exo}$); $J_{1,2} = 3{\cdot}1$, $J_{2,3} = 3{\cdot}8$, $J_{3,4} = 0{\cdot}7$, $J_{4,5} = 1{\cdot}1$, $J_{5,6exo} = 5{\cdot}8$, $J_{5,6endo} = 2{\cdot}9$, $J_{6,6} = 7{\cdot}8$, $J_{2,4} = 0{\cdot}8$, $J_{3,5} = 1{\cdot}65$, $J_{1,5} \neq 0 < 0{\cdot}3$, $J_{1,6endo} \approx 0{\cdot}4$, $J_{1,6exo} \approx 0{\cdot}5$.

4-Acetamido-1,6 : 2,3-dianhydro-4-deoxy-β-D-mannopyranose (*XXIV*)

A solution of hydrochloride *XXIII* in 3 ml of pyridine was allowed to stand with 0·5 ml of acetic anhydride at room temperature for 24 hours. After control by thin-layer chromatography in $S_2$ excess acetic anhydride was decomposed with water and the solution worked up in the manner mentioned for acetate *VIII*, under *a*). After purification with active charcoal in methanol and crystallization from ethanol–ether 60 mg (50%) of *XXIV* were obtained, m.p. 139—143°C (sublimation), $[\alpha]_D$ −26° (*c* 1·22, chloroform). For $C_8H_{11}NO_4$ (185·2) calculated: 51·89% C, 5·99% H, 7·56% N; found: 51·75% C, 5·98% H, 7·70% N. IR spectrum: 1 510 $cm^{-1}$, 1 677 $cm^{-1}$ $\nu$(N—C=O); 3 331 $cm^{-1}$, 3 432 $cm^{-1}$ $\nu$(NH).

1,6-Anhydro-3,4-dideoxy-3,4-epimino-β-D-altropyranose (*XXII*)

*a*) A solution of 3 g of hydrochloride of *XXIII* in 100 ml of a 5% potassium hydroxide solution was heated in an autoclave at 100°C for 5 hours. Chromatography on thin-layer plates in $S_3$ demonstrated the presence of two products of $R_F$ 0·4 and 0·2. The mixture was evaporated with 20 g of silica gel and chromatographed on a silica gel column (100 g). Chloroform–methanol (10 : 1) mixture eluted 1·97 g (82%) of epimine *XXII* of $R_F$ 0·4; recrystallization from ethanol gave 1·47 g (75%) of product, m.p. 147—148°C, sublimating from 140°C, $[\alpha]_D$ −120° (*c* 0·42, water). For $C_6H_9NO_3$ (143·1) calculated: 50·35% C, 6·34% H, 9·79% N; found: 50·48% C, 6·29% H, 9·49% N. Hydrogen bonds measurement: 3 293 $cm^{-1}$ $\nu$(NH), 3 563 $cm^{-1}$ $\nu$(OH). $^1$H-NMR spectrum (in hexadeuteriodimethyl sulfoxide): 5·05 (H-1), 3·51 (H-2), 1·74 (H-3), 2·11 (H-4), 4·56 (H-5), 3·96 (H-$6_{endo}$), 3·66 (H-$6_{exo}$); $J_{1,2} = 3{\cdot}1$, $J_{2,3} = 0$, $J_{3,4} = 5{\cdot}0$, $J_{4,5} = 1{\cdot}2$, $J_{5,6exo} = 4{\cdot}4$, $J_{5,6endo} = 0{\cdot}5$, $J_{6,6} = 7{\cdot}1$, $J_{1,3} = 1{\cdot}7$, $J_{2,4} = 0{\cdot}5$, $J_{3,5} = 0{\cdot}3$. A mixture of chloroform and methanol (5 : 1) eluted 282 mg (11%) of aminoglucosan *I*, $R_F$ 0·2, of which 200 mg were converted by acetylation with acetic anhydride and pyridine to acetate *VIII*. The mixture was evaporated, dissolved in a minimum amount of water and the aqueous solution was extracted with chloroform. Concentration of chloroform solution gave 340 mg of a residue in which in addition to acetate *VIII* of $R_F$ 0·3 an admixture of substances of $R_F$ values 0·2 and 0·06 could also be detected by thin-layer chromatography in $S_2$. Chromatography on silica gel with chloroform–methanol (100 : 1) and fractional crystallization of mixed fractions from ether gave 227 mg (61%) of acetate *VIII*, $R_F$ 0·3, m.p. 135—137°C, $[\alpha]_D$ −29° (*c* 1·71, chloroform). Its infrared spectrum was identical with that of acetate *VIII* prepared from hydrochloride *VII*. In addition

to 54 mg of a mixture of acetates of $R_F$ values 0·3 and 0·2, 7 mg of a syrupy acetate of $R_F$ 0·2 and 27 mg of acetate of $R_F$ 0·06 were also isolated as by-products.

*b*) A solution of 150 mg of hydrochloride *XXIII* in 2·38 ml of a 0·5M-NaOH solution was made up to 3 ml with water, bubbled through with nitrogen, and heated in a glass autoclave at 100°C for 5 hours. When thin-layer chromatography in $S_3$ no longer showed the presence of the starting compound *XXI*, 0·5 ml of 25% ammonia were added and the solution poured onto a column of 5 g of Bio-deminrolite, which was washed with 30 ml of 5% ammonia. The solutions were evaporated and the residue crystallized from ethanol–ether, giving 99 mg (83%) of epimine *XXII*, m.p. 145—147°C, the $[\alpha]_D$ value and the IR spectrum of which were identical with analogous data of epimine *XXII*, prepared under *a*). In the mother liquors aminoglucosan *I* could be proved by thin-layer chromatography in $S_3$.

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*Note added in proof:* A full paper by H. Paulsen and H. Koebernick dealing with the synthesis of aminodeoxy derivatives of 1,6-anhydro-β-D-glucopyranose appeared in Chem. Ber. *109*, 104 (1976), compare Ref. 12.

**REFERENCES**

1. Schmitt, F., Sinaÿ P.: Carbohydrate Res. *29*, 99 (1973).
2. Rabinsohn Y., Acher A. J., Shapiro D.: J. Org. Chem. *38*, 202 (1973).
3. Černý M., Elbert T., Pacák J.: This Journal *39*, 1752 (1974).
4. Černý M., Juláková O., Pacák J., Buděšínský M.: This Journal *40*, 2116 (1975).
5. Jeanloz R. W., Rapin A. M. C.: J. Org. Chem. *28*, 2978 (1963).
6. Černý M., Černý I., Trnka T., Pacák J.: Unpublished results.
7. Černý M., Gut V., Pacák J.: This Journal *26*, 2542 (1961).
8. Höök J. E., Lindberg B.: Acta Chem. Scand. *20*, 2363 (1966).
9. Prystaš M., Šorm F.: This Journal *36*, 1448 (1971).
10. Trnka T., Černý M., Buděšínský M., Pacák J.: This Journal *40*, 3038 (1975).
11. Micheel F., Michaelis E.: Chem. Ber. *96*, 1959 (1963).
12. Paulsen H., Koebernick H., Stenzel W., Köll P.: Tetrahedron Lett. *1975*, 1493.
13. Buděšínský M., Černý M.: Unpublished results.
14. Černý M., Pacák J., Staněk J.: This Journal *30*, 1151 (1965).
15. Trnka T., Černý M.: This Journal *36*, 2216 (1971).
16. Pecka J., Staněk J. jr, Černý M.: This Journal *39*, 1192 (1974).

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