AZIDO DERIVATIVES OF 1,6-ANHYDRO-β-D-HEXOPYRANOSES CORRESPONDING TO 3-DEOXY- AND 4-DEOXY-D-GLUCOSAMINE*

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Nucleophilic substitution of the tosyloxy group in 1,6-anhydro-3-deoxy-2-O-*p*-toluenesulfonyl-β-D-*arabino*-hexopyranose (*II*) with lithium azide gave azido derivative *V* which was acetolysed and deacetylated to 2-azido-2,3-dideoxy-D-*ribo*-hexose (*IX*). The oxirane ring in 1,6 : 2,3-dianhydro-4-deoxy-β-D-*lyxo*-hexopyranose (*XII*) was opened using lithium azide and the mixture of 2- and 3-azido derivatives *XIII* of D-*xylo* and *XIV* of D-*arabino* configuration formed was separated by an extraction procedure after previous selective trimethylsilylation. Azido derivative *XIII* was converted to 2-azido-2,4-dideoxy-D-*xylo*-hexose (*XIX*) on acetolysis and deacetylation. Hydrogenation of azido derivatives *IX* and *XIX* on palladium on charcoal and subsequent N-acetylation gave corresponding 3- and 4-deoxy derivatives of D-glucosamine, *XI* and *XXI*.

In connection with the synthesis of 2-amino-2,4-dideoxy-D-*lyxo*-hexose (4-deoxy-D-mannosamine) elaborated[1] as a contribution to the studies of the inhibition of the biosynthesis of N-acetylneuraminic acid we wished to make other deoxy derivatives of 2-amino-2-decxyhexoses accessible. As suitable derivatives of this type deoxy derivatives of 2-amino-2-deoxy-D-glucose (D-glucosamine) came into consideration, having the hydroxyl group in the position $C_{(3)}$ or $C_{(4)}$ substituted by hydrogen.

Both these derivatives have already been described in literature. 2-Amino-2,3-dideoxy-D-*ribo*-hexose (D-lividosamine), was characterized for the first time in 1971 when an older procedure was reproduced, making use of 4,6-O-benzylidene derivatives of methyl 2-acetamido-2-deoxy-β-D-glucopyranoside[2]. The hydroxyl group on $C_{(3)}$ was mesylated and substituted with thioacetate, and the 3-thio derivative formed was desulfurated with Raney-nickel and thus converted to the corresponding 3-deoxy derivative. The removal of the protecting groups afforded the hydrochloride of D-lividosamine. For the formation of the $C_{(3)}$ methylene group analogous syntheses make use of the reaction of the hydroxyl group on $C_{(3)}$ with sulfuryl chloride and then tributyl stannane[3] or its conversion to mesyl- or tosyl ester, then to iodo derivative,

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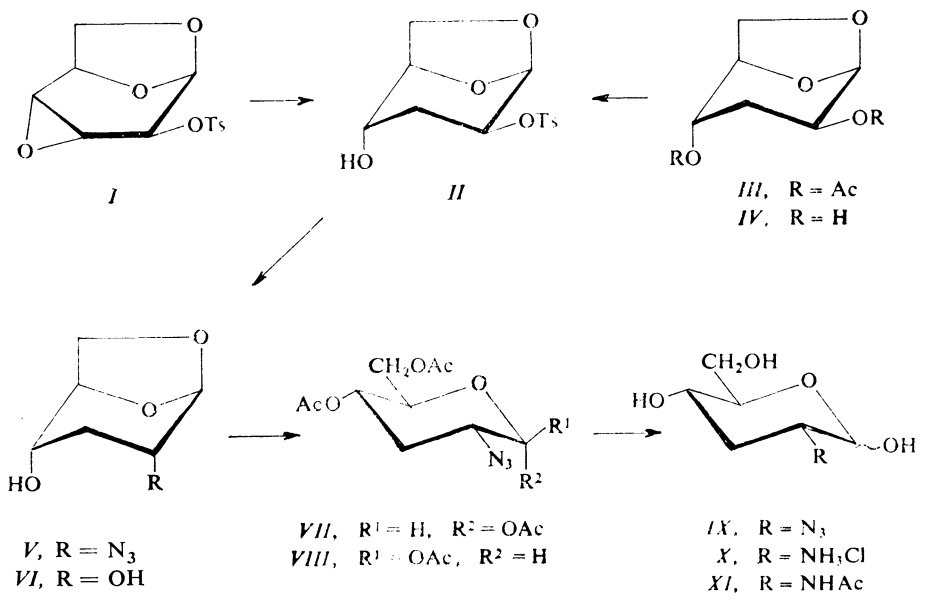
which is eventually reduced with Raney-nickel or tributyl stannane[4-6]. Other methods are based on the reductive splitting off of the acetoxy group in the neighbourhood of oxime, or on the reduction of tosyl hydrazone in the presence of acetamido group[7,8]. The addition of azide ions to ethyl 2,3-dideoxy-α-D-*glycero*-hex-2-enopyranosid-4-ulose[9] takes place with low stereoselectivity. However, some of the mentioned syntheses have been conducted only up to the stage of glycosides[6-8]; two of them concern the L-enantiomer[4,5].

2-Amino-2,4-dideoxy-D-*xylo*-hexose was prepared so far in the form of N-acetyl derivative[3,10] *via* benzyl 2-acetamido-3,6-di-O-acetyl-2-deoxy-α-D-glucopyranoside, accessible from 4,6-O-benzylidene derivatives of benzyl glycoside of α-D-glucosamine. The introduction of the methylene group into the position $C_{(4)}$ was carried out gradually on reaction of the 4-hydroxy group with sulfuryl chloride and tributyl stannane[3] or *via* its tosylate and iodide by dehalogenation with palladium on charcoal[10].

In view of the synthetic possibilities offered by the skeleton of 1,6-anhydrohexopyranoses and the further possible utilization of the intermediates for the synthesis of oligosaccharides, new syntheses have been elaborated, leading *via* 1,6-anhydro-2-azido-2,3-dideoxy-β-D-*ribo*-hexopyranose (*V*) and 1,6-anhydro-2-azido-2,4-dideoxy-β-D-*xylo*-hexopyranose (*XIII*) and the corresponding azido derivatives of free hexoses, *IX* and *XIX*. The derivatives of hexoses with an azido group in the position $C_{(2)}$ are advantageous for α-glycosylation, because the azido group does



I *II* *III*, R = Ac; *IV*, R = H

V, R = N_3; *VI*, R = OH

VII, R^1 = H, R^2 = OAc; *VIII*, R^1 = OAc, R^2 = H

IX, R = N_3; *X*, R = NH_3Cl; *XI*, R = NHAc

SCHEME 1

not participate[11], and further as intermediates for the preparation of 2-amino-2-deoxyhexoses[12–14].

As starting compound for the synthesis of 3-deoxy derivative *IX* (Scheme 1) 1,6 : 3,4-dianhydro-2-O-*p*-toluenesulfonyl-β-D-altropyranose (*I*) was used which was obtained in a 69% yield by a three-step sequence from 1,6 : 3,4-dianhydro-2-O-*p*-toluenesulfonyl-β-D-galactopyranose[15,16]. We assumed that the oxirane ring of epoxide *I* would be cleaved by complex hydrides highly regioselectively, under formation of 1,6-anhydro-3-deoxy-2-O-*p*-toluenesulfonyl-β-D-*arabino*-hexopyranose (*II*). We tested the reaction with lithium tetrahydridoaluminate in tetrahydrofuran, but this reagent also partly attacks the tosyloxy group in position $C_{(2)}$. However, the use of a mixture of sodium tetrahydridoborate and aluminum chloride in diglyme[17] was found suitable, affording a 91% yield. An authentic specimen for identification purposes was prepared from diacetate *III* by deacetylation[18] and subsequent partial tosylation of the 1,6-anhydro-3-deoxy-β-D-*arabino*-hexopyranose (*IV*) formed (using tosyl chloride in pyridine), during which the equatorial hydroxyl group on $C_{(2)}$ reacted preferentially.

The key reaction of the synthesis of azido derivative *IX* was the nucleophilic S_N2 substitution of *endo*-tosyloxy group of deoxy derivative *II* with azide ion. It is known[19] that the substitution on $C_{(2)}$ in aldohexopyranosides, *i.e.* in the neighbourhood of the anomeric centre, generally proceeds only with difficulty and that its preparative utilisation is restricted. In their deoxy derivatives in which a decrease in steric and polar hindrances may be expected, the substitution was successful in several cases, as for example with 1,6-anhydro-3,4-dideoxy-2-O-*p*-toluenesulfonyl-β-D-*threo*-hexopyranose[13] or with 4,6-O-benzylidene derivatives of 3-deoxyhexopyranosides[14]. In our case lithium azide in hexamethylphosphoric triamide at 110°C was used for the substitution of the tosyloxy group in deoxy derivative *II*; under these conditions the reaction took 45 hours. The yield of 1,6-anhydro-2-azido-2,3-dideoxy-β-D-*ribo*-hexopyranose (*V*) was 53%. Its IR spectrum contained characteristic vibrations of the azido group (2 130 cm^{-1}) and hydroxy group (3 580 cm^{-1}). From the parameters of the ^1H NMR spectrum it follows that compound *V* occurs in chloroform solution in the $^1C_4$(D) conformation. The chemical shifts of H-2 (δ = 3·58), H-3eq (δ = 1·92) and H-3ax (δ = 2·15) indicated the presence of an azido group on $C_{(2)}$ and two hydrogen atoms on $C_{(3)}$. The coupling constants $J_{2,3eq} \sim 1{\cdot}7$, $J_{3eq,4} \sim 1{\cdot}7$ and $J_{4,5} \sim 2{\cdot}4$ Hz correspond to the equatorial orientation of H-2, H-3eq and H-4 hydrogens, which is in agreement with the observed constants of the *W* type, $J_{1,3eq} \sim 1{\cdot}7$, $J_{2,4} \sim 0{\cdot}9$ and $J_{3eq,5} \sim 1{\cdot}7$ Hz. The given parameters are in good correlation with the corresponding parameters[20] of 1,6-anhydro-3-deoxy-β-D-*ribo*-hexopyranose (*VI*), as evident from Table I.

The cleavage of 1,6-anhydro bridge of azido derivative *V* was carried out by acetolysis in a mixture of acetic anhydride and acetic acid under catalysis with sulfuric acid. The mixture of acetylated anomers *VII* and *VIII* formed could be partly sepa-

TABLE I

Parameters of the ^{1}H NMR spectra (200 MHz) of azido derivatives of 1,6-anhydrohexoses and corresponding deoxy derivatives in deuteriochloroform

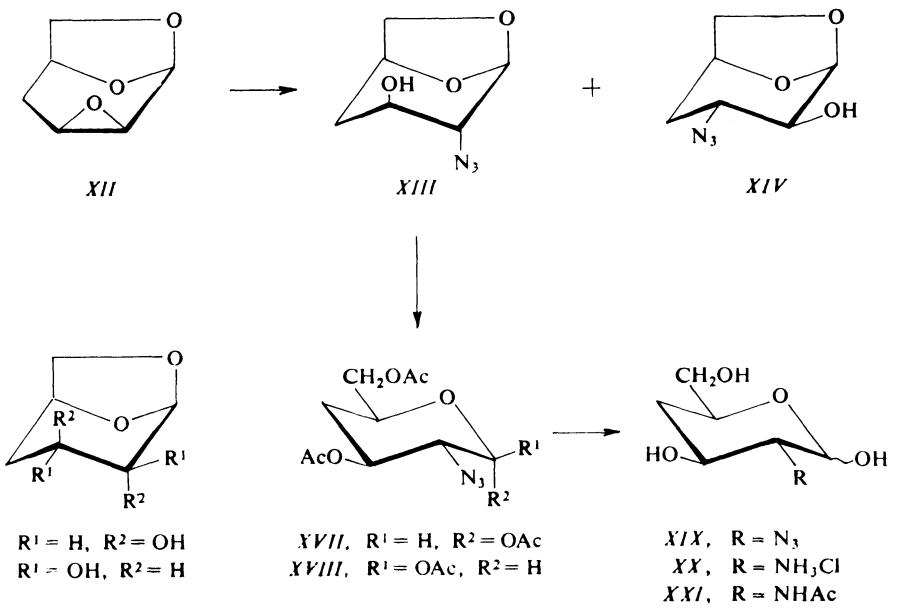
Compound[a]	H-1	H-2	H-3[b]	H-4[b]	H-5	H-6[c]
V[d]	5·42	3·58	2·15 1·92	3·64	4·54	3·83 3·85
VI	5·41	3·66	2·06 1·83	3·75	4·56	3·88 3·91
XIII	5·54	3·31	3·99	2·32 1·84	4·60	4·22 3·76
XIV	5·40	3·54	3·63	1·82 2·04	4·62	3·85
XV	5·47	3·59	3·85	2·31 1·77	4·55	4·20 3·75
XVI	5·37	3·43	3·84	1·83 2·08	4·61	3·80

Compound[a]	$J_{1,2}$	$J_{2,3}$[b]	$J_{3,4}$[b]	$J_{4,5}$[b]	$J_{5,6}$[c]	$J_{6,6}$
V[d]	1·9	5.0 1·7	4·6 1·7	2·4	0·8 5·9	8·1
VI	2·1	4·3 1·8	4·3 1·8	2·7	0·9 5·4	7·8
XIII	0·8	±0	5·3 1·6	4·3 1·6	0·5 5·0	7·1
XIV	1·7	8·5	10·9 6·3	3·2 2·0	2·0 4·2	—
XV	2·0	1·5	5·1 1·6	4·4 1·5	0·4 5·0	7·1
XVI	1·7	7·8	10·6 6·6	3·5 2·2	±0 5·7	—

[a] Parameters of *VI*, *XV*, *XVI* taken from literature[20]. [b] If two values are one above the other, then the upper one refers to the axial and the lower to the equatorial hydrogen of the methylene group. [c] The upper value refers to H-6 endo, the lower to H-6 exo. [d] Parameters of the 400 MHz spectrum. Other parameters of the spectra; *V*: $J_{1,3eq} \sim 1{\cdot}7$, $J_{1,4} \sim 0{\cdot}8$, $J_{2,5} \sim 0{\cdot}6$, $J_{3,3} =$ $= 15{\cdot}6$, $J_{3eq,5} \sim 1{\cdot}7$, OH (2·84 d) $J_{OH,4} = 11{\cdot}2$; *VI*: $J_{1,3eq} = 1{\cdot}6$, $J_{1,4} = 0{\cdot}8$, $J_{2,4} = 1{\cdot}1$, $J_{2,5} = 0{\cdot}7$, $J_{3,3} = 15{\cdot}6$, $J_{3eq,5} = 2{\cdot}2$; *XIII*: $J_{1,3} \pm 0$, $J_{1,4eq} = 0{\cdot}9$, $J_{1,5} \pm 0$, $J_{1,6ex} = 0{\cdot}3$, $J_{2,4eq} = 1{\cdot}5$, $J_{2,5} \pm 0$, $J_{4,4} = 15{\cdot}2$, $J_{4,6ex} = 1{\cdot}7$, OH (2·77 bs); *XIV*: $J_{4,4} = 13{\cdot}6$, $J_{4ax,6en} \pm 0$, $J_{4ax,6ex} \pm 0$, $J_{4eq,6} = 0{\cdot}7$; *XV*: $J_{1,3} = 1{\cdot}6$, $J_{1,4eq} = 1{\cdot}0$, $J_{2,4eq} = 1{\cdot}5$, $J_{3,5} = 1{\cdot}5$, $J_{4,4} =$ $= 15{\cdot}2$, $J_{4ax,6ex} = 1{\cdot}7$; *XVI*: $J_{4,4} = 13{\cdot}6$, $J_{4ax,6ex} \pm 0$; after addition of trichloroacetyl isocyanate: H-6en (4·00 dd), H-6ex (3·87 ddd), $J_{6,6} = 7{\cdot}6$, $J_{6en,5} = 0{\cdot}6$, $J_{6ex,5} = 5{\cdot}0$, $J_{6ex,4ax} =$ $= 1{\cdot}6$ Hz.

rated by chromatography on silica gel, and this sufficed for the measurement of the ^{1}H NMR spectrum of pure α-(*VII*) and β-(*VIII*) anomer. Their spectra in deuteriochloroform confirm the presence of three acetoxyl groups in both anomers, and they differ mainly in the region of anomeric protons H-1 (α-anomer: $\delta = 6{\cdot}20$, $J_{1,2} = 3$ Hz; β-anomer: $\delta = 5{\cdot}53$, $J_{1,2} = 3$ Hz; β-anomer: $\delta = 5{\cdot}53$, $J_{1,2} = 8{\cdot}4$ Hz). Other important parameters, primarily the coupling constants, are practically identical for both anomers ($J_{2,3ax} \sim 12$, $J_{2,3eq} \sim 5$, $J_{3ax,4} \sim 11$, $J_{3eq,4} \sim 5$ and $J_{4,5} \sim 10$ Hz) and they demonstrate that they exist in a $^4C_1$(D) conformation.

Deacetylation of a mixture of anomers *VII* and *VIII* with sodium methoxide in methanol gave 2-azido-2,3-dideoxy-D-*ribo*-hexose (*IX*). Its catalytic hydrogenation on palladium on charcoal in dilute hydrochloric acid gave the hydrochloride of 2-amino-2,3-dideoxy-D-*ribo*-hexose (D-lividosamine), which when acetylated in aqueous medium afforded N-acetyl derivative *XI*.



XII *XIII* *XIV*

XV, $R^1 = H$, $R^2 = OH$
XVI, $R^1 = OH$, $R^2 = H$

XVII, $R^1 = H$, $R^2 = OAc$
XVIII, $R^1 = OAc$, $R^2 = H$

XIX, $R = N_3$
XX, $R = NH_3Cl$
XXI, $R = NHAc$

SCHEME 2

In comparison with the above mentioned synthesis of D-lividosamine derivatives the synthesis of 2-azido-2,4-dideoxy-D-*xylo*-hexose (*XIX*) and corresponding amino derivatives *XX* and *XXI* was more difficult (Scheme 2). In this case the cleavage of 2,3-oxirane ring on the 1,6-anhydrohexopyranose skeleton was the key reaction which under normal conditions gives derivatives of the D-gluco series[21]. However, in our case we had to use 1,6 : 2,3-dianhydro-4-deoxy-β-D-*lyxo*-hexopyranose (*XII*)

as the starting compound, in which the polar effects act on the oxirane ring in such a manner, that its anomalous equatorial cleavage is enhanced[22]. In agreement with this, when epoxide *XII* reacts with sodium azide in ethanol, a mixture of 2-azido derivative *XIII* and 3-azido derivative *XIV* is obtained in which the undesired diequatorial isomer *XIV* predominates (21 : 79). We succeeded in reversing this ratio in favour of the diaxial 2-azido derivative *XIII* by using lithium azide in hexamethylphosphoric triamide[23]. Under these conditions the products *XIII* and *XIV* are formed in a 54 : 46 ratio, as determined by gas chromatography. The separation of both products was carried out by partial silylation with N,N-diethyltrimethylsilylamine according to ref.[24] and partitioning between hexane and water. 3-Azido derivative *XIV* with the equatorial hydroxyl was silylated selectively and it passed into hexane, while 2-azido derivative *XIII* did not react and remained in the aqueous phase from which it was extracted with chloroform. For a good separation the elimination of the residual hexamethylphosphoric triamide from the mixture of azides before silylation is important. Extraction with sulfuric acid was found suitable for this purpose. The structure of both azido derivatives was demonstrated by ^{1}H NMR spectroscopy. From the parameters it follows that both compounds are in chloroform in $^1C_4$ (D) conformation. For azide *XIII* the values of the coupling constants $J_{2,3}$ and $J_{3,4}$ are within the 0–5·3 Hz interval, which corresponds to *e*, *e* and *e*, *a* arrangement of the H-2, H-3 and H-4 hydrogens, while for derivative *XIV* this interval is 6·3 – 10·9 Hz, which characterizes the *a*, *e* and *e*, *a* interactions[20]. The spectra can be correlated with the spectra[20] of corresponding 1,6-anhydro-4-deoxy-β-D-hexopyranoses *XV* and *XVI* (Table I).

Acetolysis of azido derivative *XIII* in a mixture of acetic anhydride and acetic acid under catalysis of sulfuric acid gave a mixture of anomeric acetyl derivatives *XVII* and *XVIII* which could not be separated preparatively on silica gel. Deacetylation of this mixture with sodium methoxide in methanol afforded crystalline 2-azido-2,4-dideoxy-D-*xylo*-hexose (*XIX*). Its ^{1}H NMR spectrum in hexadeuteriodimethyl sulfoxide is complex, but it corresponds to the structure considered. In the region of anomeric protons the doublet at $\delta = 4{\cdot}33$ with the coupling constant $J_{1,2} = 8$ Hz is dominant, which corresponds to the predominance of the β-anomer in solution of compound *XIX*. Azido hexose *XIX* was converted to hydrochloride of 2-amino-2,4-dideoxy-D-*xylo*-hexose (*XX*) by catalytic hydrogenation on palladium (on charcoal) in dilute hydrochloric acid. On subsequent acetylation in aqueous medium corresponding N-acetyl derivative *XXI* was formed, the properties of which were in accord with the literature data[10].

EXPERIMENTAL

The melting points were measured on a micromelting point apparatus Boëtius, optical rotation on a Bendix–Ericsson 143A polarimeter at 23–25°C. The IR spectra were measured on a Zeiss-

-Jena UR-20 spectrophotometer in chloroform, the values of characteristic frequencies are given in cm^{-1}. The ^1H NMR spectra were measured on a Tesla BS 467 (60 MHz) or a Varian XL-200 (200 MHz) instrument; the chemical shifts are given in ppm, δ-scale, the coupling constants J in Hz. As internal references tetramethylsilane (TMS) or sodium 4,4-dimethyl-4-silapentane-1--sulphonate (DSS) were used. Preparative chromatographies were carried out on silica gel columns (Lachema, 60—120 μm), while thin-layer chromatography (TLC) was done on silica gel G (Merck). Detection was carried out by spraying the plates with 50% sulfuric acid and heating, while aminohexoses were also detected specifically using a 0·5% ninhydrin solution in ethanol, and reducing sugars by subsequent spraying with 0·3% silver nitrate in moist acetone and 2% sodium hydroxide in 95% methanol. Gas chromatography was carried out on a Chrom 3 apparatus (Laboratory Apparatus), using nitrogen as carrier gas and FID. Hydrogenations were carried out at normal pressure, using water as sealing liquid. For drying of the solutions anhydrous magnesium sulfate was used. All solutions were evaporated on rotary vacuum evaporators at 40—50°C water bath and 2 kPa pressure. Samples for analysis were dried over phosphorus pentoxide at 13 Pa.

1,6-Anhydro-3-deoxy-2-O-*p*-toluenesulfonyl-β-D-*arabino*-hexopyranose (*II*)

A) Epoxide[15,16] *I* (10 g; 33·5 mmol) was dissolved in diglyme (70 ml) with sodium tetrahydridoborate (4·2 g, 110 mmol) and a solution of anhydrous aluminum trichloride (4·9 g, 36·8 mmol) in diglyme (40 ml) was added to it dropwise and stirred at room temperature for 72 h, when the reaction was terminated according to TLC in chloroform–methanol (20 : 1). After neutralization with 10% sulfuric acid the mixture was extracted with chloroform. The extract was evaporated and eventually dried at 50—60°C/13 Pa. Chromatography on silica gel (50 g column) in benzene–acetone (20 : 1) gave 9·2 g (91%) of deoxy derivative *II*, m.p. 93—95°C (ether–light petroleum), $[\alpha]_D$ −33° (*c* 0·44, chloroform), IR spectrum: 3 600 (—OH), 1 182, 1 197, 1 386 (—O—SO_2). For $C_{13}H_{16}O_6S$ (300·3) calculated: 51·99% C, 5·37% H, 10·67% S; found: 52·29% C, 5·66% H, 10·61% S.

B) A solution of 50 mg of sodium in 5 ml of methanol was added dropwise to a solution of diacetyl derivative[18] *III* (150 mg, 0·65 mmol) in methanol (5 ml) and the mixture was allowed to stand at room temperature for 2 h; TLC chloroform–methanol (10 : 1). After addition of solid carbon dioxide the solution was evaporated and dried. Extraction with acetone (2 × 5 ml) and evaporation gave oily deacetylated product *IV* (100 mg) which was dissolved in pyridine (1 ml) and the solution was cooled to −5°C. At this temperature a solution of *p*-toluenesulfonyl chloride (150 mg; 0·79 mmol) in pyridine (1 ml) was added dropwise and the mixture was allowed to stand for 48 h. Then the reaction mixture contained monotosyl derivative *II* in addition to a small amount of the starting compound, as well as a further minor, less polar component corresponding to the product of tosylation of both hydroxyl groups of the starting diol *IV*; TLC: chloroform–-methanol (20 : 1). Methanol (1 ml) was then added to the solution, which was evaporated. Water was added to the residue and the mixture was extracted with chloroform and the extract was evaporated and dried. Chromatography on a silica gel column (15 g) in chloroform–methanol (100 : 1) afforded 120 mg (61%) of derivative *II*, m.p. 95—96°C, $[\alpha]_D$ −33° (*c* 1·02, chloroform); IR spectrum was identical with the spectrum of the sample prepared under *A*.

1,6-Anhydro-2-azido-2,3-dideoxy-β-D-*ribo*-hexopyranose (*V*)

Anhydrous lithium azide (6·0 g, 123 mmol) was added to a solution of tosyl ester *II* (3·0 g, 10 mmol) in hexamethylphosphoric triamide (50 ml) and the mixture was heated at 110 °C for 45 h. After this time the starting compound could no longer be detected in the mixture by TLC in chloroform–methanol (20 : 1). After cooling the mixture was poured into water (200 ml), extracted

with ethyl acetate (3 × 100 ml) and the extract was washed with 10% sulfuric acid (2 × 100 ml). The ethyl acetate solution was dried over potassium carbonate and evaporated. Chromatography of the product (1·2 g) on a silica gel column (50 g) in benzene–acetone (50 : 1) gave 800 mg (53%) of azido derivative *V*, m.p. 80–81°C, $[\alpha]_D$ −75° (*c* 0·16, chloroform). IR spectrum: 3 580 (—OH), 2 130 ($-N_3$). ^{1}H NMR spectrum (400 MHz), see Table I. For $C_6H_9N_3O_3$ (171·2) calculated: 42·11% C, 5·30% H, 24·55% N; found: 42·19% C, 5·21% H, 24·10% N.

1,4,6-Tri-O-acetyl-2-azido-2,3-dideoxy-α-D-*ribo*-hexopyranose (*VII*) and the β-Anomer *VIII*

Azido derivative *V* (0·4 g, 2·34 mmol) was dissolved in acetic anhydride (3 ml) and acetic acid (1·4 ml) was added to it. When the mixture was cooled to 0°C, 96% sulfuric acid (25 µl) was added and the mixture allowed to stand at room temperature for 4 h; TLC: cyclohexane–ethyl acetate–ethanol (6 : 4 : 3). Sodium acetate was added (0·1 g) and the mixture evaporated. The residue was evaporated twice with 25 ml of toluene. The solid residue was extracted with dichloromethane (3 × 10 ml), the solution dried and evaporated. Chromatography on a silica gel column in benzene–acetone (50 : 1) gave 690 mg (94%) of an oily mixture of anomers *VII* and *VIII* in three fractions, of which the first and the last (15 mg each) contained pure α-anomer *VII* and β-anomer *VIII*, respectively. ^{1}H NMR spectrum (60 MHz), deuteriochloroform: α-anomer *VII*, 6·20 d (1 H, H-1, $J_{1,2}$ = 3), 4·90 ddd (1 H, H-4, $J_{3ax,4}$ = 11, $J_{3eq,4}$ = 5, $J_{4,5}$ = 10), 4·20 m (2 H, H-6,6′), 3·60 ddd (1 H, H-5, $J_{4,5}$ = 10, $J_{5,6}$ = 2, $J_{5,6'}$ = 5), 3·52 ddd (1 H, H-2, $J_{1,2}$ = 3, $J_{2\,3ax}$ = 12, $J_{2,3eq}$ = = 5), 2·48 dt (1 H, H-3eq, $J_{2,3eq}$ = 5, $J_{3,3}$ = 12, $J_{3eq,4}$ = 5), 2·19 s (3 H, $OCOCH_3$), 2·05 s (6 H, 2 × $OCOCH_3$), 1·57 bm (1 H, H-3ax, *W* = 40); β-anomer *VIII*: 5·53 d (1 H, H-1, $J_{1,2}$ = = 8·4), 4·81 ddd (1 H, H-4, $J_{3ax,4}$ = 11, $J_{3eq,4}$ = 5, $J_{4,5}$ = 10), 4·20 m (2 H, H-6,6′), 3·76 ddd (1 H, H-5, $J_{5,4}$ = 10, $J_{5,6}$ = 3, $J_{5,6'}$ = 4·5), 3·60 ddd (1 H, H-2, $J_{2,1}$ = 8, $J_{2,3ax}$ = 12, $J_{2,3eq}$ = = 5), 2·55 dt (1 H, H-3eq, $J_{2,3eq}$ = 5, $J_{3,3}$ = 12, $J_{3eq,4}$ = 5), 2·16 s (3 H, $OCOCH_3$), 2·05 s (6 H, 2 × $OCOCH_3$), 1·43 m (1 H, H-3ax, $J_{2,3ax}$ = 12, $J_{3,3}$ = 12, $J_{3ax,4}$ = 11). For $C_{12}H_{17}$. $.N_3O_7$ (315·3) calculated: 45·71% C, 5·44% H, 13·33% N; found: for *VII* ,45·97% C, 5·48% H, 13·06% N; for *VIII*, 45·81% C, 5·37% H, 13·10% N.

2-Azido-2,3-dideoxy-D-*ribo*-hexose (*IX*)

A solution of a mixture of acetyl derivatives *VII* and *VIII* (0·2 g, 0·63 mmol) in methanol (10 ml) was cooled at 0°C and a solution of sodium methoxide in methanol (3 drops of a solution of 200 mg of sodium in 10 ml of methanol) was added to it. After heating to room temperature the solution was allowed to stand for 3 h; TLC: cyclohexane–ethyl acetate–ethanol (6 : 4 : 3). The methoxide was then decomposed with solid carbon dioxide and the solution evaporated, the residue was dissolved in water and deionized on an Amberlite IR 120 column (15 ml) in H^+-form. After washing with water and evaporation 110 mg (92%) of an oily residue were obtained, consisting of azido derivative *IX*, $[\alpha]_D$ +21° (5 min) → +14° (at equilibrium, *c* 1·36, water). For $C_6H_{11}N_3O_4$ (189·2) calculated: 38·09% C, 5·86% H, 22·21% N; found: 38·07% C, 6·09% H, 22·02% N.

2-Amino-2,3-dideoxy-D-*ribo*-hexose Hydrochloride (*X*)

An aqueous solution of azido derivative *IX* (250 mg, 1·32 mmol in 50 ml) was acidified with 20% hydrochloric acid (0·4 ml) and 10% of palladium on charcoal (50 mg) was added to it. Hydrogenation took 4 h; TLC: chloroform–2-propanol–25% ammonia–water–ethanol (20 : 20 : 2 : 2 : 1). The catalyst was filtered off through celite, the solution was evaporated and the residue dried. The oily product, hydrochloride X (250 mg, 95%) was used directly for N-acetylation. A sample for analysis (50 mg) was dissolved in water, decolorized with charcoal, evaporated and the residue

crystallized from ethanol. M.p. 150–160°C (decomp.), $[\alpha]_D$ +60° (5 min) → +42° (equilibrium, c 1·73, water). For $C_6H_{14}ClNO_4$ (199·7) calculated: 36·10% C, 7·07% H, 17·76% Cl, 7·02% N; found: 36·29% C, 7·16% H, 17·68% Cl, 7·01% N. Literature gives m.p. 150–160°C (decomp.), $[\alpha]_D$ +43° (equilibrium, *c* 0·3, water)[5]; m.p. 132–135°C, $[\alpha]_D$ +73° → +44° (*c* 1·05, water)[2].

2-Acetamido-2,3-dideoxy-D-*ribo*-hexopyranose (*XI*)

A solution of hydrochloride *X* (200 mg, 1 mmol) in water (1 ml) was added to a mixture of Dowex 1X8 (15 ml, 100–200 mesh) in carbonate form and water (5 ml), cooled to 2°C. Acetic anhydride (0·7 ml, 7 mmol) was added dropwise and under stirring at this temperature and the mixture was stirred for 90 min; TLC: ethyl acetate–2-propanol–pyridine–water (7 : 3 : 2 : 2). The ion exchanger was filtered off, washed with water and the combined filtrates were filtered through a column (15 ml) of Amberlite IR 120 in H^+-form. The product was washed with water and 150 mg (73%) of N-acetate *XI* were thus obtained. It would not crystallize, $[\alpha]_D$ +35° (20 min) → 26° (equilibrium, *c* 1·16, water). For $C_8H_{15}NO_5$ (205·2) calculated: 46·81% C, 7·37% H, 6·83% N; found: 46·63% C, 7·28% H, 6·57% N. Literature[2] gives m.p. 151–152°C, $[\alpha]_D$ +54° → +26° (*c* 1·0, water).

1,6-Anhydro-2-azido-2,4-dideoxy-β-D-*xylo*-hexopyranose (*XIII*) and 1,6-Anhydro-3-azido-3,4-dideoxy-β-D-*arabino*-hexopyranose (*XIV*)

A) Lithium azide (6·75 g, 138 mmol) was added to a solution of epoxide[25] *XII* (2·45 g, 19·1 mmol in hexamethylphosphoric triamide (50 ml) and the mixture was heated under stirring to 120°C.) Benzoic acid (2·34 g, 19·2 mmol) was then added gradually to the mixture under stirring, which was continued at the same temperature for 30 min; TLC: benzene–acetone (20 : 1); the reaction mixture was cooled and poured into water (100 ml). The aqueous solution was extracted with ethyl acetate (5 × 50 ml) and the extract was washed with 10% sulfuric acid (2 × 50 ml) and dried over potassium carbonate. After filtration and evaporation 3·5 g (107%) of the crude mixture were obtained in which the ratio of the products was determined by gas chromatography: Gas Chrom Q column, 6·5% OV 101, T_c = 124° C, v_N = 22 ml min^{-1}, t_1 = 4·1 (hexamethylphosphoric triamide), t_2 = 5·2 (*XIII*), t_3 = 5·7 (*XIV*), $h_2 : h_3$ = 54 : 46. The mixture of azides was dissolved in acetone (35 ml) and diethyltrimethylsilylamine (3·8 ml, 20 mmol) was added to it at 0°C, and the mixture was stirred for 45 min. An ice-cold 2% solution of potassium carbonate (35 ml) was added and the mixture extracted with hexane (2 × 35 ml) and chloroform (5 × 35 ml). The hexane solution of the trimethylsilyl ether of 3-azide *XIV* was evaporated, the residue was dissolved in aqueous ethanol and a drop of 10% sulfuric acid was added. After 15 min the mixture was extracted with chloroform (3 × 30 ml), the extract was dried, evaporated and chromatographed on a silica gel column in benzene–acetone (50 : 1). After crystallization from ether 650 mg (20%) of 3-azido derivative *XIV* were obtained, m.p. 40–41°C, $[\alpha]_D$ −167° (*c* 0·24, chloroform). IR spectrum: 3 600 (—OH), 2 120 (—N_3). ^{1}H NMR spectrum (200 MHz) is shown in Table I. For $C_6H_9N_3O_3$ (171·2) calculated: 42·11% C, 5·30% H, 24·55% N; found: 42·17% C, 5·18% H, 24·21% N. The chloroform solution of azide *XIII* was dried, evaporated and chromatographed on a silica gel column, the same as in the case of the isomer *XIV*. Yield, 1·46 g (45%) of 2-azido derivative *XIII*, m.p. 65–67°C (decomp., from ether), $[\alpha]_D$ +27° (*c* 0·23, chloroform). IR spectrum: 3 580 (—OH), 2 120 (—N_3). ^{1}H NMR spectrum (200 MHz) is shown in Table I. For $C_6H_9N_3O_3$ (171·2) calculated: 42·11% C, 5·30% H, 24·55% N; found: 42·31% C, 5·18% H, 24·32% N.

B) A mixture of epoxide *XII* (1 g, 7·8 mmol), sodium azide (1·5 g, 23 mmol), ammonium chloride (1·5g, 28 mmol), ethanol (20 ml) and water (5 ml) was refluxed for 24 h; TLC: benzene–

–acetone (20 : 1). The mixture was diluted with water and ethanol was evaporated. The residue was extracted with chloroform and the extract was dried and evaporated. The residue (1·1 g, 82%) was a mixture of azides *XIII* and *XIV*. Gas chromatography: Gas Chrom Q column, 4% OV 210, $T_c = 124°C$, $v_N = 22$ ml min^{-1}, $t_1 = 5·1$, $t_2 = 7·2$ min, h_1 (*XIII*): h_2 (*XIV*) = 21 : 79.

1,3,6-Tri-O-acetyl-2-azido-2,4-dideoxy-α-D-*xylo*-hexopyranose (*XVII*) and its β-Anomer *XVIII*

Azido derivative *XIII* (1·63 g, 9·5 mmol) was dissolved in a mixture of acetic anhydride (12 ml) and acetic acid (5 ml) and 0·1 ml of 96% sulfuric acid was added to it. The mixture was stirred for 3 h; TLC: benzene–acetone (10 : 1). Anhydrous sodium acetate (200 mg) and water were then added and the mixture was extracted with chloroform. The extract was dried, evaporated and chromatographed on a silica gel column (15 g) in benzene–acetone (15 : 1), giving 2·8 g (93%) of a mixture of acetates *XVII* and *XVIII* in the form of an oil, $[\alpha]_D$ +2° (*c* 1·21, chloroform), IR spectrum: 2 100 (—N_3), 1 255, 1 762 (CH_3COO). For $C_{12}H_{17}N_3O_7$ (315·3) calculated: 45·71% C, 5·44% H, 13·33% N; found: 45·58% C, 5·41% H, 12·97% N.

2-Azido-2,4-dideoxy-D-*xylo*-hexose (*XIX*)

A mixture of acetyl derivatives *XVII* and *XVIII* (2·7 g, 8·6 mmol) was dissolved in methanol (50 ml) and a solution of sodium (100 mg) in methanol (5 ml) was added to it. The mixture was allowed to stand at room temperature for 12 h; TLC: benzene–acetone (10 : 1). Working up as in the case of derivative *X* gave 1·5 g (92%) of an oily azido derivative *XIX*, which was used directly for further work. For analytical purposes 170 mg of the product were chromatographed on a silica gel column (15 g) in ethyl acetate–ether (1 : 1). Azide *XIX* (110 mg) was obtained, which crystallized out after prolonged standing, m.p. 130—160°C (decomp.; from ethanol), $[\alpha]_D$ +2·8° (5 min) → +4·7° (equilibrium, water). ^{1}H NMR spectrum (200 MHz, hexadeuteriodimethyl sulfoxide, tetramethylsilane): 7·01 d (1 H, $C_{(1)}$—OH), $J_{OH,1} = 6·8$), 5·25 d (1 H, $C_{(3)}$—OH, $J_{OH,3} = 5·9$), 4·69 t (1 H, $C_{(5)}$—OH, $J_{OH,5} = 5·4$), 4·33 dd (1 H, H-1, $J_{1,OH} = 6·8$, $J_{1,2} = 8·0$), 3·30—3·50 m (4 H, H-3, H-5, H-6,6'), 2·91 dd (1 H, H-2, $J_{2,1} = 8·0$, $J_{2,3} = 9·5$), 1·83 ddd (1 H, H-4eq, $J_{4,4} = -12·6$, $J_{4,3} = 5·1$, $J_{4,5} = 1·3$), 1·24 m (1 H, H-4ax). For $C_6H_{11}N_3O_4$ (189·2) calculated: 38·10% C, 5·86% H, 22·21% N; found: 38·36% C, 5·91% H, 21·88% N.

2-Acetamido-2,4-dideoxy-D-*xylo*-hexose (*XXI*)

20% Hydrochloric acid (0·25 ml) was added to a solution of azido derivative *XIX* (100 mg, 0·53 mmol) in water (30 ml) and 10% palladium on charcoal (50 mg) was added to the mixture, which was then hydrogenated for 6 h and worked up as in the case of derivative *X*. The hydrochloride *XX* formed (120 mg) was dissolved in 10% methanol (2 ml) and N-acetylated as in the case of derivative *XI*. After working up and drying 55 mg of a glassy product were obtained (*XXI*, 51% calculated per azide *XIX*), $[\alpha]_D$ +78° (10 min) → 73° (equilibrium, *c* 1·05, water); literature gives $[\alpha]_D$ +78° (*c* 1·58, water)[3] and $[\alpha]_D$ +80° (*c* 0·6, water)[10].

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