AMINO SUGARS. XXVIII.*

PARTIAL ACETYLATION OF METHYL 4-ACETAMIDO-4,6-DIDEOXY-α-D-GLUCOPYRANOSIDE

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Partial acetylation of methyl 4-acetamido-4,6-dideoxy-α-D-glucopyranoside (*I*) with acetyl chloride or acetic anhydride in pyridine gives rise in addition to the 2,3-di-O-acetyl derivative *IV* also to a mixture of the 2-O-acetyl derivative *II* and 3-O-acetyl derivative *III* in a 76 : 24 and 58 : 42 ratio, respectively. From the latter compounds were prepared the mesyl derivatives *V* and *VI*. The reaction of methyl 3,4-anhydro-6-deoxy-2-O-methanesulphonyl-α-D-galactopyranoside (*VII*) with sodium azide gave the azido derivative *VIII* which, after hydrogenation and acetylation with acetic anhydride in pyridine, afforded compound *VI*. The minor product of the azidolysis, compound *IX*, was transformed by hydrogenation and acetylation to methyl 3-acetamido-3,6-dideoxy-2-O-methanesulphonyl-α-D-gulopyranoside (*XI*). From the mesyl derivatives *V* and *VI*, respectively were prepared methyl 4-acetamido-2,3-anhydro-4,6-dideoxy α-D-allopyranoside (*XIII*) and the α-D-mannopyranoside *XIV*, respectively. The mesyl derivative *VI*, when treated with sodium acetate yielded the acetamidoaltroside *XV*, and similarly the mesyl derivative *V* yielded the acetamido derivatives *I* and *XV*.

In previous papers[1–5] we have compared the relative reactivity of the secondary hydroxyl groups in position 2 and 4 on the pyranose skeleton of the methyl 3-acetamido-3,6-dideoxy-α-D(L)-hexopyranosides. Partial acetylation with acetyl chloride leads in all cases preferentially to 2-O-acetyl derivatives, whilst when using acetic anhydride for the acetylation, the ratio of the 2-O- to the 4-O-acetyl derivative depends on the configuration of the acetylated amino sugar. These partial acetylated products, whose free hydroxyl group is *trans* orientated with respect to the acetamido group, gave on mesylation followed by solvolysis of the mesylacetyl derivatives with sodium acetate in aqueous 2-methoxyethanol methyl 3-acetamido-3,6 dideoxy-α-D(L)hexo pyranosides with opposite configuration at the carbon atom which initially was bearing the free hydroxyl group.

In the present paper we are dealing with the partial acetylation of methyl 4-acetamido-4,6-dideoxy-α-D-glucopyranoside[6] (*I*) by action of acetyl chloride as well as acetic anhydride in pyridine. We were interested in the relative reactivity of the hydroxyl groups in position 2 and 3 and also in the possible application of the partial acetylation products for the preparation of methyl 4-acetamido-4,6-dideoxy-α-

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D-hexopyranosides, *i.e.* the N-acetyl derivatives of substances which especially lately are enjoying considerable interest.

Some configurational isomers of 4-amino-4,6-dideoxy-D-hexoses have been found in natural material (the D-gluco[7,8], D-galacto[9,10], and D-manno[11] isomers). Stevens and coworkers described the preparation of derivatives having the *gluco*[12], *galacto*[13], *talo*[14], and *manno*[15] configuration, and by these authors have also been prepared derivatives having the *ido*, *altro*, and *gulo* configuration, as follows from paper[15], but neither the procedure for preparing them nor their properties have up to now been published in the literature. Another procedure for the synthesis of derivatives with *talo* and *manno* configuration has been described by British authors[16,17]. In our laboratory were prepared derivatives having the *talo*[18] and *gluco*[6] configuration.

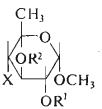
By partial acetylation of the acetamidoglucoside *I* (ref.[6]) with both acetyl chloride and acetic anhydride in pyridine we obtained a mixture of methyl 4-acetamido-2-O-acetyl-4,6-dideoxy-α-D-glucopyranoside (*II*), methyl 4-acetamido-3-O-acetyl-4,6-dideoxy-α-D-glucopyranoside (*III*), and the 2,3-di-O-acetyl derivative[6] *IV*. This mixture was separated by chromatography on silica gel. With both acetylating agents, the hydroxyl group in position 2 is preferentially acetylated, but acetyl chloride reacts more selective (ratio of *II* : *III* = 76 : 24) than acetic anhydride (ratio of *II* : *III* = = 58 : 42). Thus, the acetamidoglucoside *I* behaves on acetylation with both agents very similar to methyl 3-acetamido-3,6-dideoxy-α-L-glucopyranoside[1]. Treatment compounds *II* and *III*, respectively with methane sulphochloride in pyridine afforded the corresponding mesyl derivatives *V* and *VI*, respectively.

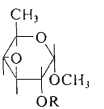
The mesyl derivative *VI*, which is more difficult accessible from the partial acetylation product of compound *I*, we prepared from methyl 3,4-anhydro-6-deoxy-2-O-methanesulphonyl-α-D-galactopyranoside[19] (*VII*). On treating compound *VII* with sodium azide in 2-methoxyethanol in the presence of ammonium chloride a mixture of both azido derivatives *VIII* and *IX* is formed in a 9 : 1 ratio, the separation of which was performed by chromatography on silica gel. From the prevalent syrupy substance *VIII*, we obtained on hydrogenation over platinum the crystalline methyl 4-amino-4,6-dideoxy-2-O-methanesulphonyl-α-D-glucopyranoside (*X*) giving on acetylation with acetic anhydride in pyridine compound *VI*. The minor azidolysis product, *i.e.* the syrupy derivative *IX*, when hydrogenated over platinum, followed by N-acetylation with acetic anhydride in methanol, afforded methyl 3-acetamido-3,6-dideoxy-2-O-methanesulphonyl-α-D-gulopyranoside (*XI*), which we have prepared in our laboratory already earlier[5]. From the identity of the peracetylation product of substance *X* with compound *VI* (and indirectly also from the formation of derivative *IX* from the minor azidolysis product of the anhydro derivative *VII*) follows unambiguously that compound *VI* contains the mesyl group in position 2. Thus, also the position of the O-acetyl groups in the derivatives *II*, *III*, *V*, and *VI* has been proved.

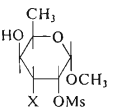
The highly stereospecific cleavage of the oxiran ring in compound *VII* in favour of the azido derivative *VIII* (*i.e.* a cleavage contrary to the Fürst-Plattner rule, if we consider substance *VII* to be more likely in the half-chair *C1* conformation) is in contrast with the azidolysis[6] of un-

substituted methyl 3,4-anhydro-6-deoxy-α-D-galactopyranoside[20] (*XII*), where methyl 3-azido-3,6-dideoxy-α-D-gulopyranoside is formed as the predominant product. In the anhydro derivatives *VII* and *XII* are in the half-chair *C1* conformation the substituents at carbon atoms 2 and 5 situated in a quasi-equatorial position and the methoxy group in an axial position (anomeric effect[21]). Therefore, it is unlikely that in the azidolysis of the anhydro derivative *VII* (in contrast to the anhydro derivative *XII*) will assert itself the *1C* conformer which, in accordance with the Fürst-Plattner rule, would afford the 4-azido derivative *VIII*.* In the azidolysis of the anhydro derivative *VII*, the azide ion approaches preferentially position 4 obviously because position 3 is less advantageous on account of possible steric and polar[22] interactions between the azide ion and the mesyloxy group in position 2.

By treating the mesyl derivative *V* and *VI*, respectively with methanolic sodium methoxide we prepared methyl 4-acetamido-2,3-anhydro-4,6-dideoxy-α-D-allopyranoside (*XIII*) and methyl 4-acetamido-2,3-anhydro-4,6-dideoxy-α-D-mannopyranoside (*XIV*), respectively. Acid hydrolysis of the anhydro derivative *XIV*



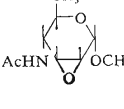


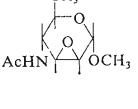


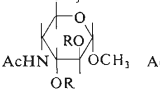
I; $R^1 = R^2 = H$, X = NHAc
II; R^1 = Ac, R^2 = H, X = NHAc
III; R^1 = H, R^2 = Ac, X = NHAc
IV; $R^1 = R^2$ = Ac, X = NHAc
V; R^1 = Ac, R^2 = Ms, X = NHAc
VI; R^1 = Ms, R^2 = Ac, X = NHAc
VIII; R^1 = Ms, R^2 = H, X = N_3
X; R^1 = Ms, R^2 = H, X = NH_2
XVII; R^1 = Ms, R^2 = H, X = NHAc
Ac = CH_3CO— Ms = CH_3SO_2—

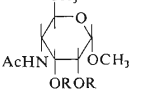
VII, R = Ms
XII, R = H

IX, X = N_3
XI, X = NHAc









XIII *XIV*

XV, R = H
XVI, R = Ac

XVIII, R = H
XIX, R = Ac

* Such considerations applies Stevens[15] in the case of the azidolysis of methyl 3,4-anhydro-6-deoxy-α-D-talopyranoside and its 2-O-benzoyl derivative, where of course the substituent at carbon atom 2 is always situated in an axial position (in the more probable *C1* conformation).

in acetone affords methyl 4-acetamido-4,6-dideoxy-α-D-altropyranoside (*XV*) as the only product. The configuration of derivative *XV* was confirmed by the proton magnetic resonance spectrum of methyl 4-acetamido-2,3-di-O-acetyl-4,6-dideoxy-α-D-altropyranoside (*XVI*), prepared from compound *XV* by acetylation with acetic anhydride in pyridine.

The acetamido derivative *XV* we prepared also directly by heating the mesyl derivative *VI* with sodium acetate either in aqueous or anhydrous 2-methoxyethanol. In both instances, solvolysis of compound *VI* takes place in principle by the same reaction sequence: From the mesyl derivative *VI* is split off the O-acetyl group under formation of the mesyl derivative *XVII*, which then affords the anhydro derivative *XIV* from which in turn the acetamido derivative *XV* is formed. In aqueous medium cleavage of the anhydro derivative *XIV* proceeds relatively quickly so that after heating for 8 or 48 hours only the mesyl derivative *XVII* and derivative *XV* were isolated from the reaction mixture. In anhydrous 2-methoxyethanol formation of derivative *XVII* takes probably place in such a manner by which the O-acetyl group of compound *VI* esterifies 2-methoxyethanol. From derivative *XVII* results again the anhydro derivative *XIV* which is presumably cleaved by the acetate anion. The cleavage product (probably the 3-O-acetyl derivative of compound *XV*) is then deacetylated to compound *XV*. In favour of this mechanism speak the following by us performed experiments: *a*) Short heating of the 2,3-di-O-acetyl derivative *IV* with anhydrous sodium acetate in 2-methoxyethanol afforded derivative *I*, and in the reaction mixture was proved the presence of 2-methoxyethyl acetate by means of gas chromatography and mass spectroscopy *b*) after solvolysis of compound *VI* in anhydrous medium compounds *XVII*, *XIV*, and *XV* were isolated from the reaction mixture; *c*) heating the anhydro derivative *XIV* with anhydrous sodium acetate in 2-methoxyethanol in the presence of a little methanesulphonic acid led to the formation of derivative *XV*. In absence of the mentioned acid substance *XIV* does not react. Thus, the reaction of compound *VI* in aqueous medium proceeds similar to that reported by Jeanloz[23] for the solvolysis of methyl 3,4,6-tri-O-benzoyl-2--O-methanesulphonyl-α-D-glucopyranoside. In the endeavour to suppress the deacetylation of compound *VI* and so to increase the probability for the intermolecular S_N2 substitution of the mesyloxy group, we performed the reaction of this substance with sodium acetate in anhydrous dimethylformamide. The only one isolable product, besides about 30% of the starting material *VI*, was again the acetamido derivative *XV*.

The solvolysis of the mesyl derivative *V* in aqueous 2-methoxyethanol proceeds similar to that of substance *VI*. The hydrolysis of the O-acetyl group gives rise to the anhydro derivative *XIII* (in one experiment we have isolated this compound from the reaction mixture), which undergoes a further hydrolytic cleavage into a mixture of the acetamido derivatives *I* and *XV*. Substances *I* and *XV* (in about the same proportion as in the solvolysis of compound *V*) we have also obtained on heating the

anhydro derivative *XIII* in the same medium in which the solvolysis of the mesyl derivative *V* was performed. The solvolysis of substance *V* affords in addition to compounds *I* and *XV* also methyl 4-acetamido-4,6-dideoxy-α-D-allopyranoside (*XVIII*), the structure of which was confirmed by the PMR spectrum of methyl 4-acetamido-2,3-di-O-acetyl-4,6-dideoxy-α-D-allopyranoside (*XIX*) prepared from *XVIII* by acetylation with acetic anhydride in pyridine. The formation of substance *XVIII* is probably due to displacement of sulphonyloxy group at C-3 involving participation of the acetamido group.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured on a polarimeter Opton (with subjective readings) at 21°C in the concentration range of 0·5—1·5. Analytical samples were dried for 8—10 hours at room temperature at 1 Torr. Thin-layer chromatography was performed on silica gel G according to Stahl, grain size 10—40 μ (Merck, Darmstadt), on plates 25 × 75 mm in the solvent system chloroform–ethanol 10 : 1 unless otherwise stated. For detection the chromatograms were sprayed with a solution of 5% ceric sulphate in 10% sulphuric acid followed by heating. Preparative chromatography was carried out on silica gel (Lachema, Brno) of grain size 70—200 μ. The solvents were evaporated on a vacuum rotatory evaporator at a maximum temperature of 50°C in water pump vacuum. The chromatographic fractions were after evaporation always dried at room temperature in a vacuum of 1—2 Torr. For crystallisation was used light petroleum with b.p. 45—60°C. If the substances described in the present paper were prepared by different experiments, their melting points and optical rotations were, within the experimental error, always identical with the data given for the analytical samples, and the identity of the substances was corroborated by comparison of their infrared spectra. The proton magnetic resonance spectra were taken on a Varian HA-100 using tetramethylsilane as internal standard and the infrared spectra were taken on a Perkin-Elmer 325 spectrometer.

Partial Acetylation of Methyl 4-Acetamido-4,6-dideoxy-α-D-glucopyranoside (*I*)

With acetyl chloride: A mixture of the acetamido derivative *I* (500 mg, 2·28 mmol) in pyridine (10 ml) was treated at −70°C with acetyl chloride (0·22 ml). The reaction mixture was set aside for 24 h at −15°C and afterwards for an additional 24 h at 0°C. Then it was decomposed with water and twice evaporated to dryness with 10 ml of water and finally with toluene. The syrupy residue was chromatographed on a column of silica gel (30 g). From the column were eluted the peracetyl derivative *IV* (290 mg, 42%; chloroform–ethanol 200 : 1), the 3-O-acetyl derivative *III* (71 mg, 11·9%; chloroform–ethanol 100 : 1), the 2-O-acetyl derivative *II* (258 mg, 43·3%; chloroform–ethanol 100 : 3), and the starting material *I* (10 mg, 2%; chloroform–ethanol 100 : : 5—10). The 2-O-acetyl derivative *II* was recrystallised from a mixture of ethyl acetate and light petroleum, m.p. 156—158°C, $[\alpha]_D$ +172 ± 1° (chloroform). For $C_{11}H_{19}NO_6$ (261·3) calculated: 50·58% C, 7·32% N, 5·36% N; found: 50·70% C, 7·41% H, 5·54% N. The 3-O-acetyl derivative *III* was crystallised from the same solvent mixture, m.p. 232—234°C, $[\alpha]_D$ +237 ± 2° (chloroform). For $C_{11}H_{19}NO_6$ (261·3) calculated: 50·58% C, 7·32% H, 5·36% N; found: 50·70% C, 7·22% H, 5·31% N.

With acetic anhydride: A mixture of the acetamido derivative *I* (500 mg, 2·28 mmol) in pyridine (10 ml) was treated at −70°C with acetic anhydride (0·27 ml). By the same procedure as above were obtained the peracetyl derivative *IV* (207 mg, 30%), the 3-O-acetyl derivative *III* (159 mg, 26·7%), 2-O-acetyl derivative *II* (219 mg, 36·8%), and the starting compound *I* (30 mg, 6%).

Deacetylation of compound IV: A mixture of compound *IV* (220 mg), 2-methoxyethanol (10 ml) dried with the molecular sieve Potasit A3, and fused sodium acetate (500 mg) was heated under reflux for 15 min, whereupon by thin-layer chromatography compound *IV* was not any

more detected. The mixture was evaporated to dryness and the distillate redistilled under atmospheric pressure over a column as long as the boiling point did not exceed 125°C. In the residue the presence of 2-methoxyethyl acetate was gas chromatographically established by comparing it with an authentic specimen (gas chromatograph Chrom 3, capillary column coated with tetra-(2-cyanoethoxy)neopentane, 120°C, flow rate 2·5 ml H_2/min, flame-ionisation detection, retention time 5 min). The mass spectrum (LKB-9000 instrument) was identical with that of 2-methoxyethyl acetate published in the catalogue of Eastman Kodak Company Research Laboratories.

Methyl 4-Acetamido-2-O-acetyl-4,6-dideoxy-3-O-methanesulphonyl-α-D-glucopyranoside (*V*)

A mixture of the 2-O-acetyl derivative *II* (341 mg, 1·31 mmol) and pyridine (7 ml) was treated at −70°C with methane sulphochloride (0·15 ml). The reaction mixture, after leaving it at −15°C for 24 h, was decomposed with water and twice evaporated to dryness with 10 ml of water and then twice with toluene. The residue was transferred onto a column of silica gel (7 g) and eluted with benzene–ethanol 100 : 2 to give substance *V* in quantitative yield. Recrystallisation from ethanol yielded 422 mg (95%) of compound *V*, m.p. 198−200°C, $[\alpha]_D$ +147 ± 2° (chloroform). For $C_{12}H_{21}NO_8S$ (339·4) calculated: 42·47% C, 6·24% H, 4·13% N, 9·45% S; found: 42·78% C, 6·41% H, 3·92% N, 9·42% S.

Methyl 4-Acetamido-3-O-acetyl-4,6-dideoxy-2-O-methanesulphonyl-α-D-glucopyranoside (*VI*)

a) To a mixture of the 3-O-acetyl derivative *III* (255 mg, 0·98 mmol) in pyridine (4 ml) was added at −70°C methane sulphochloride (0·15 ml). The reaction mixture was left at −15°C for 24 h. By the same procedure as described for compound *V* was obtained the mesyl derivative *VI* (323 mg, 97·5%), which for analysis was crystallised from a mixture of ethanol and light petroleum, m.p. 172−173°C, $[\alpha]_D$ +162·5 ± 1° (chloroform). For $C_{12}H_{21}NO_8S$ (339·4) calculated: 42·47% C, 6·24% H, 4·13% N, 9·45% S; found: 42·39% C, 6·22% H, 4·21% N, 9·69% S.

b) To a solution of compound *X* (102 mg, 0·4 mmol) in pyridine (5 ml) was added acetic anhydride (0·5 ml) and the reaction mixture was left at room temperature overnight. Then it was twice evaporated to dryness with 10 ml of water and afterwards twice with 10 ml of toluene. The crystalline residue (100%), after two crystallisations from a mixture of ethanol and light petroleum, afforded 120 mg (90%) of compound *VI*.

Preparation of Derivatives *X* and *XI* from the Anhydro Derivative *VII*

To a solution of the anhydro derivative *VII* (698 mg; 2·93 mmol) in 2-methoxyethanol (10 ml) and water (0·8 ml) were added sodium azide (800 mg) and ammonium chloride (500 mg). The reaction mixture was refluxed for 4·5 h, then evaporated to dryness, and the residue was chromatographed on a column of silica gel (30 g). Elution with benzene afforded the starting material *VII* (20 mg). With benzene–ethanol (200:1) mixture were eluted the chromatographically uniform syrupy substance *VIII* (654 mg) the infrared spectrum of which showed a strong absorption at 2100 cm^{-1}, a mixture of substances *VIII* and *IX* (14 mg), and the syrupy substance *IX* (58 mg) showing strong absorption at 2100 cm^{-1}. Overall yield 87%. Part of substance *VIII* (540 mg, 1·92 mmol) was dissolved in methanol (10 ml) and hydrogenated at normal pressure and room temperature over PtO_2. The catalyst was then filtered off, washed with methanol and the combined filtrates evaporated to dryness. The residue (100%) was four times crystallised from ethanol–ether mixture to afford the amino derivative *X* (200 mg, 41%), m.p. 176−178°C, $[\alpha]_D$ +98·6 ± 1° (water). For $C_8H_{17}NO_6S$ (255·3) calculated: 37·64% C, 6·71% H, 5·49% N, 12·56% S; found: 37·65% C,

6·68% H, 5·75% N, 12·98% S. The mother liquors from the crystallisation of the amino derivative *X* were evaporated and the residue, after drying, was acetylated with acetic anhydride in pyridine by the same procedure as described above for the preparation of compound *VI*, giving 277 mg of compound *VI*. Thus, the overall yield of the hydrogenation was 83·6%.

Compound *IX* (53 mg), dissolved in methanol (5 ml), was hydrogenated in the same manner as compound *VIII*. The syrupy basic residue remaining after removal the solvent was dissolved in 5 ml of methanol. The solution was treated with acetic anhydride (0·1 ml) and the mixture allowed to stand overnight. Then the solution was evaporated to dryness and the residue twice crystallised from ethyl acetate–light petroleum mixture to afford 45 mg of derivative *XI*, m.p. 193—194°C, $[\alpha]_D$ +80·8° (chloroform). The melting point was undepressed on admixture with an authentic specimen[5] and their infrared spectra (in chloroform) were identical.

Methyl 4-Acetamido-2,3-anhydro-4,6-dideoxy-α-D-allopyranoside (*XIII*)

A solution of the mesyl derivative *V* (146 mg, 0·43 mmol) in methanol (7 ml) containing one drop of Tashiro was treated dropwise at 40°C with 1M methanolic sodium methylate to permanent alkaline reaction (still after 2·5 h). Then the mixture was neutralised with gaseous carbon dioxide and evaporated. The residue was sublimed at 80°C at 0·1 Torr to give 80 mg (92%) of derivative *XIII*, m.p. 183—187°C. For analysis it was crystallised from a mixture of ethyl acetate and light petroleum, m.p. 186—187°C (with sublimation), $[\alpha]_D$ +209·0° (chloroform). For $C_9H_{15}NO_4$ (201·2) calculated: 53·73% C, 7·52% H, 6·96% N; found: 53·59% C, 7·57% H, 7·13% N.

Cleavage of the anhydro derivative XIII: A mixture of the anhydro derivative *XIII* (50 mg), 2-methoxyethanol (5 ml), water (0·5 ml), and sodium acetate trihydrate (500 mg) was heated under reflux for 20 h. Then it was evaporated to dryness and the residue chromatographed on a column of silica gel (3 g). Elution with the same eluents as in the case of the solvolysis of compound *V* afforded 22 mg of compound *XV* and 30 mg of compound *I*.

Methyl 4-Acetamido-2,3-anhydro-4,6-dideoxy-α-D-mannopyranoside (*XIV*)

To a solution of the mesyl derivative *VI* (808 mg, 2·38 mmol) in methanol (20 ml) was added 1·11M methanolic sodium methylate (3 ml) and the mixture was refluxed for 3·5 h. After cooling down, gaseous carbon dioxide was passed into the methanolic solution, whereupon the solution was evaporated to dryness and the solid residue extracted three times with 25 ml of ethyl acetate. The ethyl acetate extracts were combined and evaporated to dryness. The residue afforded after crystallisation from ether–light petroleum 354 mg (74%) of the anhydro derivative *XIV*, m.p. 134—135°C, $[\alpha]_D$ +113·0 ± 1° (chloroform), and the mother liquor furnished further 75 mg of this derivative (overall yield 90%). For $C_9H_{15}NO_4$ (201·2) calculated: 53·73% C, 7·52% H, 6·96% N; found: 53·94% C, 7·57% H, 6·96% N.

Reaction of the Glucopyranoside *VI* with Sodium Acetate

a) *In aqueous 2-methoxyethanol*: A mixture of the mesyl derivative *VI* (175 mg, 0·517 mmol), 2-methoxyethanol (8 ml), sodium acetate trihydrate (700 mg), and water (0·8 ml) was refluxed for 48 h. Then it was evaporated to dryness, the residue extracted with hot ethyl acetate and the solvent removed by evaporation. The solid residue was recrystallised from ethyl acetate–light petroleum mixture to afford 72 mg of derivative *XV*. The mother liquors (which according to thin-layer chromatography on silica gel in the solvent system ethyl acetate–ethanol 9 : 1 contain the substances *XVII* and *XV*; in the solvent systems chloroform–ethanol 20 : 1, 10 : 1, and 5 : 1 these

substance are not separated) were evaporated to dryness and the residue chromatographed on a column of silica gel (5 g). Elution with ethyl acetate and ethyl acetate–ethanol 100 : 1 respectively afforded 5 mg of the syrupy substance *XVII*, 8 mg of a mixture of the substances *XVII* and *XV*, and 11 mg of substance *XV* (overall yield of substance *XV* 73·5%). In another experiment, where this reaction was performed with 105 mg of the mesyl derivative *VI* but the reaction time was only 8 h, we isolated 23 mg (25%) of the mesyl derivative *XVII*, 8 mg of a mixture of the substances *XVII* and *XV*, and 31 mg (45%) of substance *XV*.

b) *In anhydrous 2-methoxyethanol*: A mixture of the mesyl derivative *VI* (175 mg), 2-methoxyethanol (8 ml, dried with the molecular sieve Potasit A3), and fused sodium acetate (700 mg) was refluxed for 60 h. Then the reaction mixture was evaporated to dryness, the residue extracted with hot ethyl acetate and the solvent removed from the extract by evaporation. The residue, which according to thin layer chromatography contained a mixture of the anhydro derivative *XIV* and compound *XV*, afforded on sublimation at 60—70°C at 0·1 Torr the anhydro derivative *XIV* (53 mg, 51%). The residue after the sublimation was in form of its solution in chloroform–ethanol 100 : 3 filtered through a column of silica gel (3 g), thus giving 51 mg (45%) of the chromatographically pure derivative *XV*. In another experiment, where the mesyl derivative *VI* (144 mg) was heated in anhydrous 2-methoxyethanol (6 ml) with fused sodium acetate (500 mg) for 4·5 h the chromatographic separation (column of 10 g of silica gel, eluent ethyl acetate and ethyl acetate–ethanol 100 : 1, respectively) yielded 5 mg of substance *XIV*, 27 mg of substance *XVII*, 46 mg of a mixture of the substances *XVII* and *XV*, and 25 mg of substance *XV*.

c) *In anhydrous dimethylformamide*. A mixture of the mesyl derivative *VI* (150 mg), anhydrous dimethylformamide (5 ml), and fused sodium acetate (300 mg) was heated under reflux for 76 h. Then the reaction mixture was evaporated to dryness and the residue (which according to thin-layer chromatography consisted of a complex mixture of substances) was twice chromatographed on a column of silica gel. Elution with chloroform–ethanol mixture 100 : 1 to 100 : 5 yielded (after recrystallisation form ethyl acetate–light petroleum) 45 mg of the starting material *VI* and 11 mg of compound *XV*. All other chromatographic fractions were inhomogeneous, yellowish syrupy substances and were not further investigated.

The syrupy substance *XVII* (23 mg) was dissolved in pyridine (2 ml) and after treating with acetic anhydride (0·2 ml) the reaction mixture was left overnight. Then it was evaporated to dryness first with water and finally with toluene. The residue was crystallised from ethyl acetate–light petroleum mixture to afford 21 mg of compound *VI*. PMR spectrum of compound *XVII* (deuteriochloroform): 1·21 p.p.m. (3 H, doublet, CH_3—); 1·92 p.p.m. (3 H, singlet, O-acetyl); 2·04 p.p.m. (3 H, singlet, N-acetyl); 3·01 p.p.m. (3 H, singlet, CH_3SO_2—); 3·42 p.p.m. (3 H, singlet, CH_3O); 3·69 p.p.m. (1 H, multiplet, $J_{5,CH_3} = 6{\cdot}0$, $J_{5,4} = 9{\cdot}5$ H-5); 3·99 p.p.m. (1 H, quartet, $J_{4,3} = 9{\cdot}5$, $J_{4,5} = 9{\cdot}5$, $J_{4-NH} = 10$, H-4); 4·62 p.p.m. (1 H, doublet of a doublet), $J_{2,1} = 2{\cdot}6$, $J_{2,3} = 9{\cdot}5$, H-2); 4·94 p.p.m. (1 H, doublet, $J_{1,2} = 2{\cdot}6$, H-1); 5·26 p.p.m. (1 H, triplet, $J_{3,2} = 9{\cdot}5$, $J_{3,4} = 9{\cdot}5$, H-3); 5·64 p.p.m. (1 H, broad doublet, NH—). For analysis the acetamido derivative *XV* was crystallised from ethyl acetate–light petroleum mixture, m.p. 152—153°C, $[\alpha]_D$ +170 ± 1° (water). For $C_9H_{17}NO_5$ (219·2) calculated: 49·32% C, 7·82% H, 6·39% N; found: 49·54% C, 7·90% H, 6·58% N.

Reaction of the Glucopyranoside *V* with Sodium Acetate

A mixture of the glucopyranoside *V* (295 mg, 0·87 mmol), 2-methoxyethanol (10 ml), sodium acetate trihydrate (1 g), and water (1 ml) was refluxed for 35 h, then evaporated to dryness and the residue transferred onto a column of silica gel (10 g). Elution the column with chloroform–ethanol 100 : 1 to 100 : 10 gave three fractions: Fraction A (77 mg) containing according to thinlayer

chromatography predominantly the acetamidoaltroside *XV* and in small amount the acetamidoalloside *XVIII*, fraction B (24 mg) containing according to thin-layer chromatography the acetamidoalloside *XVIII* and acetamidoglucoside *I*, and fraction C (71 mg, 37%) containing the chromatographically pure acetamidoglucoside *I*. Fraction A afforded on recrystallisation from ethyl acetate–light petroleum the chromatographically pure derivative *XV* (58 mg, 30·5%). Fraction B, enriched with acetamidoalloside *XVIII* by addition of the mother liquors from fraction A, was combined with similar fractions from other experiments and chromatographed on a column of silica gel. In this way was obtained the chromatographically pure derivative *XVIII* (in a yield of 15 ± 5%), which after recrystallisation from ethyl acetate–light petroleum had m.p. 136 to 137°C, $[\alpha]_D$ +225·1 ± 2° (water). In another experiment a mixture of the mesyl derivative *V* (146 mg, 0·43 mmol), 2-methoxyethanol (5 ml), water (0·5 ml), and sodium acetate trihydrate (500 mg) was heated under reflux for 10 h. The reaction mixture was again evaporated and the residue, dissolved in chloroform–ethanol mixture 10 : 1, was filtered through a column of silica gel (10 g). After evaporating the filtrate, sublimation of the residue at 50—60°C at 0·1 Torr furnished 44 mg (51%) of the anhydro derivative *XIII*. The not sublimed residue contained according to thin-layer chromatography the acetamido derivatives *I*, *XV* and *XVIII* as well as two substances with higher R_F values than that of derivative *XV*.

Cleavage of the Anhydro Derivative *XIV*

a) A solution of the anhydro derivative *XIV* (114 mg, 0·57 mmol) in a mixture of acetone (10 ml) and 1M-H_2SO_4 (1 ml) was heated at 40°C for 75 min (until compound *XIV* had disappeared from the thin-layer chromatogram). The reaction mixture was then neutralised with barium carbonate, filtered and the filtrate evaporated to dryness. After purification of the residue by chromatography (5 g of silica gel, eluent chloroform–ethanol 100 : 3) its recrystallisation from ethyl acetate–light petroleum mixture yielded 88 mg (71%) of compound *XV*.

b) A mixture of the derivative *XIV* (50 mg), over the molecular sieve Potasit A3 dried 2-methoxyethanol (4 mg), and fused sodium acetate (250 mg) was heated under reflux. After refluxing for 25 h, on thinlayer chromatography was detected exclusively derivative *XIV*, whereupon methanesulphonic acid (0·02 ml) was added. Already after 30 min was in the reaction mixture detected derivative *XV*. After heating for 48 h (from the addition of the methanesulphonic acid), the reaction mixture was worked up in the same way as described in the case of the solvolysis of compound *VI*, example *b*, thus affording 12 mg of the starting compound *XIV* and 31 mg of compound *XV*.

Methyl 4-Acetamido-2,3-di-O-acetyl-4,6-dideoxy-α-D-altropyranoside (*XVI*)

A mixture of the derivative *XV* (70 mg), pyridine (3 ml), and acetic anhydride (0·3 ml) was left standing overnight. Then it was evaporated to dryness first together with water and finally with toluene to give the chromatographically pure substance *XVI* (96 mg). For analysis it was recrystallised from ethyl acetate–light petroleum, m.p. 169—170°C, $[\alpha]_D$ +122·5 ± 1° (chloroform). For $C_{13}H_{21}NO_7$ (303·3) calculated: 51·48% C, 6·98% H, 4·62% N; found: 51·78% C, 7·05% H, 4·34% N. PMR spectrum (deuteriochloroform, δ values): singlets of the CH_3—CO groups at 1·99 p.p.m., 2·09 p.p.m., and 2·10 p.p.m., and further 1·27 p.p.m. (3 H, doublet, $J_{6,5}$ = = 6·4, CH_3-); 3·35 p.p.m. (3 H, singlet, CH_3O-); 3·95 p.p.m. (1 H, $J_{5,4}$ = 9·6, $J_{5,6}$ = 6·4, doublet of a quartet, H-5); 4·35 p.p.m. (1 H, doublet of a triplet, $J_{4,3}$ = 3·5, $J_{4,5}$ = 9·6, J_{4-NH} = = 9·6, H-4); 4·57 p.p.m. (1 H, broad singlet, $J_{1,2}$ = 1·5, $J_{1,3} \neq 0 < 1$, H-1); 4·85 p.p.m. (1 H,

broad triplet, $J_{3,2} = 3{\cdot}7$, $J_{3,4} = 3{\cdot}5$, $J_{3,1} \neq 0 < 1$, H-3); 4·98 p.p.m. (1 H, doublet of a doublet, $J_{2,1} = 1{\cdot}5$, $J_{2,3} = 3{\cdot}7$, H-5).

Methyl 4-Acetamido-2,3-di-O-acetyl-4,6-dideoxy-α-D-allopyranoside (*XIX*)

A mixture of substance *XVIII* (47 mg), pyridine (3 ml) and acetic anhydride (0·3 ml) was worked up in the same manner as described above in the preparation of compound *XVI*, giving (after recrystallisation from ethyl acetate–light petroleum) 49 mg of derivative *XIX*, m.p. 188—189°C, $[\alpha]_D + 165{\cdot}5 \pm 1°$ (chloroform). For $C_{13}H_{21}NO_7$ (303·3) calculated: 51·48% C, 6·98% H, 4·62% N; found: 51·50% C, 6·98% H, 4·88% N. PMR spectrum of compound *XIX* (deuteriochloroform δ values): singlets of CH_3CO groups at 1·97 p.p.m., 2·04 p.p.m., and 2·14 p.p.m., and further 1·23 p.p.m. (3 H, doublet, $J_{6,5} = 6{\cdot}1$, CH_3-); 3·40 p.p.m. (3 H, singlet, CH_3O-); 3·95 p.p.m. (1 H, doublet of a quartet, $J_{5,6} = 6{\cdot}1$, $J_{5,4} = 9{\cdot}5$, H-5); 4·18 p.p.m. (1 H, doublet of a triplet, $J_{4,3} = 2{\cdot}9$, $J_{4,5} = 9{\cdot}5$, $J_{4-NH} = 9{\cdot}5$, H-4); 4·73 p.p.m. (1 H, broad doublet, $J_{1,2} = 4{\cdot}0$, $J_{1,3} \neq \neq 0 \leqslant 1$, H-1); 4·98 p.p.m. (1 H, triplet, $J_{2,1} = 4{\cdot}0$, $J_{2,3} = 3{\cdot}6$, H-2); 5·39 p.p.m. (1 H, broad triplet, $J_{3,2} = 3{\cdot}6$, $J_{3,4} = 2{\cdot}9$, $J_{3,1} \neq 0 < 1$, H-3), 5·49 p.p.m. (1 H, broad doublet, $J_{NH-4} = = 9{\cdot}5$, NH-).

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* *Note added in proof:* After we had sent our paper to the editor we found that C. L. Stevens and C. P. Bryant (Methods in Carbohydrate Chemistry VI, p. 235. Academic Press, New York 1972) had published the preparation of methyl 4-acetamido-4,6-dideoxy-α-D-allopyranoside from methyl 6-deoxy-2,3-O-isopropylidene-α-D-*ribo*-hexopyranosid-4-ulose oxime.

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