PREPARATION OF METHYL 3-AMINO-3,6-DIDEOXY-β-D-HEXOPYRANOSIDES BY CONDENSATION OF (2*R*, 4*R*)-2-METHOXY-4-METHYL-3-OXAPENTANE-1,5-DIAL WITH NITROMETHANE*

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Condensation of (2*R*,4*R*)-2-methoxy-4-methyl-3-oxapentane-1,5-dial (*II*), formed *in situ* by the reaction of methyl 6-deoxy-β-D-glucopyranoside (*I*) with sodium periodate, with nitromethane in the presence of sodium methoxide gives a mixture of methyl 3,6-dideoxy-3-nitro-β-D-hexopyranosides of *gluco* (*IIIa*), *galacto* (*IVa*), *manno* (*Va*), *talo* (*VIa*), and *ido* (*VIIa*) configurations in a 25 : 6·8 : 6·1 : 1 : 1·5 ratio. This mixture was converted by hydrogenation on Raney nickel under pressure and subsequent reaction with ethoxycarbonyl chloride to a mixture of corresponding methyl 3,6-dideoxy-3-(N-ethoxycarbonyl)amino-β-D-hexopyranosides *IIIc*—*VIIc*. A mixture of substances *IIIc*—*VIIc* when chromatographed and submitted to alkaline hydrolysis afforded individual methyl 3-amino-3,6-dideoxy-β-D-hexopyranosides *IIIb*—*VIIb*. The latter were converted to corresponding N-acetyl derivatives *IIId*—*VIId* and peracetyl derivatives *IIIe*—*VIIe*. After isomerisation of a mixture of nitro sugars *IIIa*—*VIIa* with 1M sodium hydroxide, nitrogalactoside *IVa* prevailed in the reaction mixture. The configurations of single substances were determined on the basis of chemical reactions and PMR spectra. An experiment is described aiming at the explanation of the formation of single nitro sugars *IIIa*—*VIIa* on the basis of the computation of their free energies.

In papers[1–5] we investigated the partial acylation of methyl 3-acetamido-3,6-dideoxy-α-D(L)-hexopyranosides. For the evaluation of some factors which might influence the stereospecificity of acylation it was desirable to compare our earlier results with the results of partial acylation of β-anomers of the mentioned compounds. However, methyl 3-acetamido-3,6-dideoxy-β-D(L)-hexopyranosides have not yet been described and therefore we describe their preparation in this paper.

We chose a procedure that was found suitable in the preparation of methyl 3-acetamido-3,6-dideoxy-α-L-hexopyranosides of *gluco*[1,6,7], *manno*[7], *galacto*[7], and *talo*[7] configurations. These substances were prepared by hydrogenation of the corresponding methyl 3,6-dideoxy-3-nitro-α-L-hexopyranosides in a mixture of methanol and

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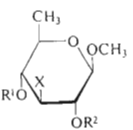
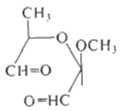
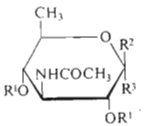
acetic anhydride; the appropriate nitro sugars were obtained by chromatographic separation of the mixtures resulting from the condensation of (2*R*, 4*S*)-2-methoxy-4-methyl-3-oxapentane-1,5-dial. By condensation of (2*R*,4*R*)-2-methoxy-4-methyl-3-oxapentane-1,5-dial (*II*), formed *in situ* by the action of sodium periodate on methyl 6-deoxy-β-D-glucopyranoside[8]* (*I*), with nitromethane in the presence of sodium methoxide we obtained a mixture of five methyl 3,6-dideoxy-3-nitro-β-D-hexopyranosides of *gluco* (*IIIa*), *galacto* (*IVa*), *manno* (*Va*), *talo* (*VIa*) and *ido* (*VIIa*) configurations. In contrast to the condensation of the diastereoisomeric (2*R*,4*S*)-dialdehyde, we were unable to separate this mixture of nitro sugars either by crystallisation or chromatographically on a thin layer or a column of silica gel. On alumina these substances decomposed. Therefore, we converted the mixture to a mixture of corresponding methyl 3-amino-3,6-dideoxy-β-D-hexopyranosides *IIIb* – *VIIb*. Its partial separation was possible only after conversion to a mixture of methyl 3,6-dideoxy-3-(N-ethoxycarbonyl)amino-β-D-hexopyranosides *IIIc* – *VIIc* and chromatography on a silica gel column. In the first chromatographic fraction we obtained the (N-ethoxycarbonyl)amino derivative of *talo* configuration (*VIc*), in the second fraction







I; $R^1 = R^2 = H$, X = OH

IIIa; $R^1 = R^2 = H$, $X = NO_2$

IIIb; $R^1 = R^2 = H$, $X = NH_2$

IIIc; $R^1 = R^2 = H$, $X = C_2H_5OCONH$

IIId; $R^1 = R^2 = H$, $X = CH_3CONH$

IIIe; $R^1 = R^2 = CH_3CO$, $X = CH_3CONH$

IIIh; $R^1 = CH_3SO_2$, $R^2 = CH_3CO$
X = CH_3CONH

IIIi; $R^1 = R^2 = CH_3SO_2$, $X = CH_3CONH$

II

IIIf; $R^1 = CH_3CO$,
$R^2 = CH_3COO$, $R^3 = H$

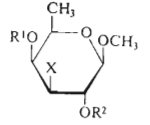
IIIg; $R^1 = CH_3CO$,
$R^2 = H$, $R^3 = CH_3COO$

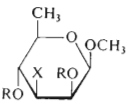
* When preparing hundreds of grams of compound *I* we started from D-glucose which was converted to a mixture of methyl glucosides by a modified procedure according to Hall and Stamm[9]. In the mixture containing approximately 13% of unreacted D-glucose methyl β-D-glucopyranoside prevailed. This mixture was treated with *p*-toluenesulfonyl chloride in pyridine at a low temperature and then acetylated with acetic anhydride to afford crystalline methyl 2,3,4-tri-O-acetyl-6-O-*p*-toluenesulfonyl-β-D-glucopyranoside[10]. This was converted on reaction with sodium iodide in butanone to the corresponding 6-deoxy-6-iodo derivative[10] from which we obtained substance *I* in a 40% overall yield on hydrogenation under pressure and alkaline deacetylation.

a mixture of isomers of *manno* (*Vc*) and *ido* (*VIIc*) configurations, and in the third fraction a mixture of isomers of *gluco* (*IIIc*) and *galacto* (*IVc*) configurations.

Derivative *VIc* was submitted to alkaline hydrolysis that afforded methyl 3-amino-3,6-dideoxy-β-D-talopyranoside (*VIb*) from which we obtained the required methyl 3-acetamido-3,6-dideoxy-β-D-talopyranoside (*VId*) on reaction with acetic anhydride in methanol; on acetylation of the amino derivative *VIb* with acetic anhydride in pyridine we obtained methyl 3-acetamido-2,4-di-O-acetyl-3,6-dideoxy-β-D-talopyranoside (*VIe*). The mixture of derivatives *Vc* and *VIIc* from the second chromatographic fraction was also submitted to alkaline hydrolysis and the resulting mixture of amino derivatives *Vb* and *VIIb* was separated chromatographically after acetylation with acetic anhydride in pyridine. Thus we obtained pure methyl 3-acetamido-2,4-di-O-acetyl-3,6-dideoxy-β-D-mannopyranoside (*Ve*) and the same derivative with *ido* configuration (*VIIe*). Alkaline hydrolysis of the substance *Ve* or *VIIe* gave amino derivatives *Vb* or *VIIb* resp., from which we prepared acetamido derivatives *Vd* and *VIId* on reaction with acetic anhydride in methanol. The mixture of substances *Vb* and *VIIb* may be also separated directly by partition chromatography on silica gel in the system 2-propanol–chloroform–ammonia–water 10 : 10 : 1 : 1, but the above procedure is better from the preparative point of view.

The mixture of derivatives *IIIc* and *IVc* was first submitted to alkaline hydrolysis. The mixture of amino derivatives *IIIb* and *IVb* obtained was separated by partition chromatography on silica gel. Pure amino derivatives *IIIb* or *IVb* were converted by reaction with acetic anhydride in methanol to methyl 3-acetamido-3,6-dideoxy-β-D-glucopyranoside (*IIId*) or methyl 3-acetamido-3,6-dideoxy-β-D-galactopyranoside (*IVd*). Reaction of amino derivatives *IIIb* or *IVb* with the same reagent in pyridine led to corresponding peracetyl derivatives *IIIe* or *IVe*.



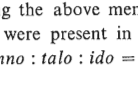


IVa; $R^1 = R^2 = H$, $X = NO_2$
IVb; $R^1 = R^2 = H$, $X = NH_2$
IVc; $R^1 = R^2 = H$, $X = C_2H_5OCONH$
IVd; $R^1 = R^2 = H$, $X = CH_3CONH$
IVe; $R^1 = R^2 = CH_3CO$, $X = CH_3CONH$
IVf; $R^1 = H$, $R^2 = CH_3SO_2$, $X = CH_3CONH$
IVg; $R^1 = CH_3CO$, $R^2 = CH_3SO_2$, $X = CH_3CONH$

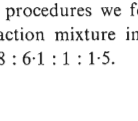
Va; $R = H$, $X = NO_2$
Vb; $R = H$, $X = NH_2$
Vc; $R = H$, $X = C_2H_5OCONH$
Vd; $R = H$, $X = CH_3CONH$
Ve; $R = CH_3CO$, $X = CH_3CONH$

The mentioned method of separation of a mixture of amino sugars *IIIb*–*VIIb* was also modified, so that we first separated the predominant substance *IIIb* and substance *VIIb* from the mixture of substances *IVb*–*VIb*. Both these main chromatographic fractions were then converted to a mixture of the corresponding (N-ethoxycarbonyl)amino derivatives *IIIc* and *VIIc*, or *IVc*–*VIc*, respectively; after their chromatographic separation on silica gel we obtained the individual derivatives *IIIc*–*VIIc*.

The separation of a mixture of amino derivatives *IIIb*–*VIIb* required their conversion to a mixture of (N-ethoxycarbonyl)amino derivatives or peracetyl derivatives and *vice versa*. In order to make sure that the data on the quantitative representation of single amino derivatives in the original mixture are not distorted by an error originating from the enormously different reactivity of some of the amino or (N-ethoxycarbonyl)amino or peracetylamino derivatives we converted each of the five amino glycosides *IIIb*–*VIIb* to corresponding derivatives *IIIc*–*VIIc* or *IIIe*–*VIIe*. We found that the first reaction always took place in an approximately 90% yield, while the second was almost quantitative. As the alkaline hydrolysis of each of the five derivatives *IIIc*–*VIIc* or *IIIe*–*VIIe* to the corresponding amino derivatives *IIIb*–*VIIb* always took place in an approximately quantitative yield, our method of analysis should be sufficiently accurate for the determination of the composition of the original mixture* of the nitro compounds *IIIa*–*VIIa* unless – of course – they are isomerized during the hydrogenation under pressure. As shown below, pure nitro galactoside *IVa* is not isomerized during hydrogenation under pressure to amino derivative *IVb*. Using the above mentioned procedures we found that single configurational isomers were present in the reaction mixture in the following ratio: *gluco* : *galacto* : *manno* : *talo* : *ido* = 25 : 6·8 : 6·1 : 1 : 1·5.



VIa; R = H, X = NO_2
VIb; R = H, X = NH_2
VIc, R = H, X = C_2H_5OCONH
VId; R = H, X = CH_3CONH
VIe; R = CH_3CO, X = CH_3CONH



VIIa, R = H, X = NO_2
VIIb; R = H, X = NH_2
VIIc, R = H, X = C_2H_5OCONH
VIId; R = H, X = CH_3CONH
VIIe; R = CH_3CO, X = CH_3CONH

* We were unable to determine quantitatively simultaneously all five configurational isomers by PMR spectrometry at the stage of derivatives *b*, *d*, *e*; neither were we able to determine them by gas chromatography of derivatives *e* or persilylated substances *b*.

In analogy to other deoxynitro glycosides[11], when the original mixture of nitro glycosides *IIIa*–*VIIa* was treated with sodium hydroxide their isomerization took place, accompanied by a change in optical rotation. When this became constant the isomer with the galacto configuration prevailed in the mixture, *i.e.* substance *IVa* which we were able to isolate in this case in a pure state by crystallisation. The remaining fraction (after crystallising out *IVa*) was analysed in the same manner as above. In the reaction mixture after isomerization single configurational isomers were represented in the following ratio: *gluco* : *galacto* : *manno* : *talo* : *ido* = 7·3 : : 12·6 : 2 : 1 : 1. On hydrogenation of nitro derivative *IVa* under the condition used for the hydrogenation of the mixture of nitro derivatives *IIIa*–*VIIa* we obtained pure amino derivative *IVb*.

As we had correlated the amino sugar for each configuration with its N-acetyl derivative, (N-ethoxycarbonyl)amino derivative and peracetyl derivative, it sufficed – for the determination of the configuration of each of the isomers – to prove the configuration in one of the derivatives mentioned only. The *gluco* configuration of substances *IIIa*–*IIIe* was demonstrated: *a*) by comparing of the properties of substances *IIIb* and *IIIe* with the properties of the same substance obtained by another route[12]; *b*) on acetolysis of substance *IIIe* we obtained 3-acetamido-1,2,4-tri-O-acetyl-3,6-dideoxy-β-D-glucopyranose (*IIIf*) and its α-anomer *IIIg*. The melting points, absolute values of optical rotations and the IR spectra of substances *IIIf* and *IIIg* coincided with the same constants given in the literature[6] for the enantiomers of substances *IIIf* and *IIIg*; *c*) the PMR spectrum of derivative *IIIc* ($J_{1,2}$ = 7·5, $J_{2,3}$ = 7·5, $J_{3,4}$ = 9·4, $J_{4,5}$ = 9·1) confirms the axial arrangement of all hydrogen atoms on the pyranose skeleton. For the proof of the *galacto* configuration in substances *IVa*–*IVe* we made use of *a*) the fact that the substances containing an acetamido group in the *trans* position in the neighbourhood of the mesyloxy group afford under the effect of sodium acetate in aqueous 2-methoxyethanol acetamido alcohols with reversed configuration on the carbon atom initially carrying the methanesulfonyloxy group (see ref.[1–5,13] and other references given therein); we obtained[15] by the mentioned reaction of methyl 3-acetamido-2-O-acetyl-3,6-dideoxy-4-O-methanesulfonyl-β-D-glucopyranoside[15] (*IIIh*) a product identical with substance *IVd*; *b*) the PMR spectrum of glucopyranoside *IVe*. The *manno* configuration in substances *Va*–*Ve* was checked: *a*) by hydrolysis of substance *Vd* which gave a product identical with the hydrochloride of 3-amino-3,6-dideoxy-D-mannose[14]; *b*) by comparing the properties of substances *Vd* and *Ve* with the properties of the same substances obtained by a different route[12]; *c*) by PMR spectrum of derivative *Vc*. The configuration *talo* in substances *VIa*–*VIe* was demonstrated by reaction of methyl-3-acetamido-3,6-dideoxy-2,4-di-O-methanesulfonyl-β-D-glucopyranoside (*IIIi*) prepared from derivative *IIId* on reaction with methanesulfonyl chloride in pyridine, with sodium acetate in aqueous 2-methoxyethanol. This reaction afforded first methyl 3-acetamido-3,6-dideoxy-2-O-methanesulfonyl-β-D-galactopyranoside (*IVf*) which on further reaction with the

same reagent was converted to methyl 3-acetamido-3,6-dideoxy-β-D-talopyranoside identical with compound *IVd*.* We confirmed the structure of the intermediate *IVf* by its conversion to methyl 3-acetamido-4-O-acetyl-3,6-dideoxy-2-O-methanesulfonyl-β-D-galactopyranoside (*IVg*) and comparison of the PMR spectra of compound *IVg* and *IVe*. We found that in the PMR spectrum of substance *IVg* the α-hydrogen signal is shifted by about 0·5 p.p.m. upfield (in comparison with *IVe*), which we also observed in other configurational isomers[15,16]. The configuration *ido* in substances *VIIa–VIIe* follows from the PMR spectrum of substance *VIIe*. Its spectrum differs from the PMR spectra of methyl 3-acetamido-2,4-di-O-acetyl-3,6-dideoxy-β-D-gulopyranoside[17] and methyl 3-acetamido-2,4-di-O-acetyl-3,6-dideoxy-β-D-altropyranoside[17] and also from the spectra of peracetates *IIIe–VIe*; by its simplicity it indicates a symmetrical molecule. The low value of $J_{1,2} < 1{\cdot}5$ excludes a diaxial arrangement of the hydrogen atoms on carbon atoms 1 and 2, *i.e.* a possibility that substance *VIIe*, when in the probable $^4C_1$ conformation, could have the configuration *allo*. The values $J_{2,3} = 8$ and $J_{3,4} = 8$ indicate that substance *VIIe* occurs in a chloroform–acetone mixture 4 : 1 predominantly in $^1C_4$ conformation.

The chemical shifts of the methyl groups belonging to single O-acetyl and N-acetyl groups are also in agreement with the proposed structures for substances *IIIe–VIIe* (Table I). As it was shown by Lichtenthaler[18] the shift of the methyl of the O-acetyl group in the axial or equatorial position ranges from 2·13–2·20 or 1·98–2·13 p.p.m. respectively, while the methyl group shift of the N-acetyl group in the axial or equatorial position ranges from 1·98–2·13 and 1·90–1·97 p.p.m., respectively.

The nitromethane condensation described by us is so far the first case when the presence of five nitro glycosides was demonstrated in the reaction mixture. This means that in contrast to earlier investigations one of the sodium salts of aci-nitroglycosides formed during nitromethane condensation must have given both nitro glycosides on acidification. The mutual ratio of aci-nitro forms is influenced by too many factors[11] in the kinetically controlled condensation, so that further conclusions cannot be made from the values which we obtained. The formation of this pair of nitro glycosides with the configurations *ido* (*VIIa*) and *talo* (*VIa*), belonging to the sodium salt of methyl 3-aci-nitro-3,6-dideoxy-β-D-*lyxo*-hexopyranoside (*D*), may be explained on the basis of conformational free energies G_{conf} of nitro derivatives *VIa* and *VIIa*. When the sodium salt of aci-nitrohydroxy compound is acidified with an ion exchanger the isomerization on the carbon atom carrying the nitro group is so fast that a thermodynamical equilibrium is established according to the magnitude of the conformational free energies of the corresponding nitro derivative[11,19]. In Table II the values of conformational free energies G_{conf} are given for both chair forms of all eight nitro sugars which may be formed on condensation of dialdehyde

* A gradual exchange of the mesyloxy groups in methyl 3-acetamido-3,6-dideoxy-2,4-di-O-methanesulfonyl-α-L-glucopyranoside was observed by Richardson and McLauchlan[6].

TABLE I

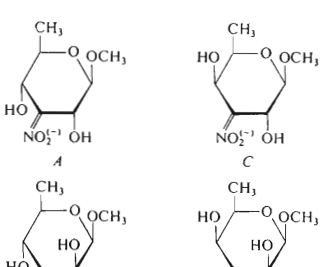
Chemical Shifts Values of O-Acetyl and N-Acetyl Groups in the PMR Spectra of Methyl 3-Acetamido-2,4-di-O-acetyl-3,6-dideoxy-β-D-hexopyranosides (*IIIe*—*VIIe*) in Deuteriochloroform (δ scale, p.p.m.).

Compound	More stable conformer[a]	2-O-acetyl		4-O-acetyl		3-N-acetyl	
		position	δ	position	δ	position	δ
IIIe	$^4C_1$	ekv.	2·06	ekv.	2·06	ekv.	1·89
IVe	$^4C_1$	ekv.	2·06	ax.	2·17	ekv.	1·91
Ve	$^4C_1$	ax.	2·18	ekv.	2·08	ekv.	1·91
VIe	$^4C_1$	ax.	2·18	ax.	2·18	ekv.	1·94
VIIe	$^1C_4$	ekv.	2·09	ekv.	2·07[b]	ekv.	1·94

[a] For compounds *IIIe*, *IVe* and *Ve* it was established[16] that in deuteriochloroform they occur at 37°C in the $^4C_1$ conformation almost exclusively; compound *VIIe* occurs in a 72% proportion in $^1C_4$ conformation, while for compound *VIe* the preferential occurrence of the $^4C_1$ conformation may be assumed on the basis of the analogy with methyl 3-acetamido-2,4-di-O-acetyl-3,6-dideoxy-α-L-talopyranoside for which 97% of the $^4C_1$ conformer were measured[16]; [b] this value cannot be assigned unequivocally to the carbon atom 2; it also might belong to the carbon atom 4 and *vice versa*.

II with nitromethane. The calculation was carried out according to ref.[20] using the values by Angyal[21].* As the values of the 1,3-diaxial interaction of the nitro group with the methyl group (A) or with the methoxyl group (A′) will be substantially higher than the value of the gauche interaction of the nitro group and the hydroxyl group (B), the nitroglycosides with *gluco*, *galacto*, *manno* and *talo* configuration (*IIIa*—*VIa*) should exist exclusively in their $^4C_1$ configuration with the nitro group in the equatorial position. The magnitude of the conformational free energy of the nitro group (2A″) on the cyclohexane skeleton in tert-butyl alcohol was determined to be 1·16 kcal mol^{-1} (ref.[23]); in 95% ethanol it was 0·95 kcal mol^{-1} (calculated from the equilibrium constant[24] of base catalysed isomerization of 4-tert-butyl-1-nitrocyclohexane). It may be supposed that the value 2A″ in methanol will not differ too much from 1 kcal mol^{-1} on tetrahydropyran skeleton either. To our knowledge the value B has not been measured so far; it may be expected that it will be larger than the gauche

* These values of interaction energies were measured in aqueous solutions; the differences between the values measured in methanol, used by us, do not seem — according to the published data (in kcal mol^{-1}) — too high. For example O_a/H_a 0·45 (water)[21] — 0·44 (2-propanol)[22]. Even larger changes in O_1/O_2, $(CH_3)_a/O_a$, or anomeric effect should not change the conclusions of the discussion given.



interaction of two hydroxyl groups, *i.e.* B > 0·35 kcal mol^{-1}. On cyclohexane skeleton and in 95% ethanol the value of gauche interaction of the nitro group and the methoxy group was computed to be 0·8 kcal mol^{-1}.* Hence it seems probable that the value B will not exceed 1 kcal mol^{-1}. This means, of course, (Table II) that also in nitro sugars with (*R*) configuration on the third carbon atom, *i.e.* in methyl 3,6-dideoxy-3-nitro-β-D-*allo*-, -*gulo*-, -*altro*-, and -*ido*-hexopyranoside the conformation $^4C_1$ with the nitro group in axial position should predominate in all instances.

Under these suppositions among all possible conformers that may be formed on acidification of the sodium salt of methyl 3-aci-nitro-3,6-dideoxy-β-D-*ribo*-hexopyranoside (*A*) the conformer $^4C_1$ of the substance *IIIa* has the lowest value of the conformational free energy. In the same manner, among conformers that may be formed on acidification of the sodium salt of methyl 3-aci-nitro-3,6-dideoxy-β-D-*arabino*-hexopyranoside (*B*), or -*xylo*-hexopyranoside (*C*) the $^4C_1$ conformer *IVa*, or *Va*, resp., are energetically most stable. Only in the case of the four conformers which may be formed on acidification of the sodium salt of methyl 3-aci-nitro-3,6-dideoxy-β-D-*lyxo*-hexopyranoside (*D*) the values of the $^4C_1$ conformer of substances *VIa* and *VIIa* are similar to such an extent that the formation of both these nitro sugars may be expected. From the ratio of derivatives *VIa* : *VIIa* = 1 : 1·5 the value

* During base catalysed isomerization of 1-methoxy-1-phenyl-2-nitrocyclohexane in 95% ethanol, 57% of 1-methoxy-*trans*-1-phenyl-2-nitrocyclohexane and 43% of *cis*-derivative were determined in equilibrium state, *i.e.* ΔG = 0·16 kcal mol^{-1} (ref.[24]); under the supposition that both isomers will be substantially more stable in the conformation with the phenyl residue in equatorial position, these derivatives differ only in the 2A″ value and in the gauche interaction of the methoxyl group and the nitro group; this interaction should not differ substantially from a similar interaction with the hydroxy group, *i.e.* from the value B (see[21]). When taking for 2A″ the value 1 kcal mol^{-1} it follows from the equation B + 0·16 = 2A″ that B = 0·84 kcal mol^{-1}.

$\Delta G = 0{\cdot}25$ kcal mol^{-1} may be calculated. Under the supposition that $2A'' = 1$ kcal . . mol^{-1} the value 0·65 kcal mol^{-1} for B follows, which is in good agreement with the above calculated value for B on cyclohexane skeleton.

After treatment the original mixture of nitro sugars *IIIa*–*VIIa* with one equivalent of sodium hydroxide nitrogalactoside *IVa* prevailed in the reaction mixture. In the group of methyl 3,6-dideoxy-3-nitro-α-L-hexopyranosides it was found[20] that under the effect of an excess of the base on nitro sugars an equilibrium is attained based on thermodynamical stabilities of aci-nitro forms of single sugars, while when a catalytic amount of the base is used the composition of the mixture formed depends primarily on thermodynamical stabilities of nitro sugars. According to thermodynamical stabilities of sodium salts of methyl 3-aci-nitro-3,6-dideoxy-β-D-hexopyranosides (*A* – *D*) single nitro derivatives should be represented in the sequence (Table II) *talo* + *ido* > *galacto* > *manno* > *gluco*, while according to thermodynamical stabilities of nitro glycosides the sequence should be *gluco* > > *galacto* > *manno* > *talo* + *ido*. In our case, when the isomerization was carried out with one equivalent of the base the resulting sequence *galacto* > *gluco* > *man-*

TABLE II

Values of Conformational Free Energies (G_{conf}) of Methyl 3-Aci-nitro-3,6-dideoxy-β-D-hexopyranosides and the Corresponding Methyl 3,6-Dideoxy-3-nitro-β-D-hexopyranoside

Configuration	G_{conf} in conformation kcal mol^{-1} [a]		Configuration	G_{conf} in conformation kcal mol^{-1} [a]	
	$^4C_1$	$^1C_4$		$^4C_1$	$^1C_4$
ribo	5·35	4·0	*gluco*	1·35 + 2 B	4 + A + A′
			allo	1·35 + 2B + 2 A″	5·35 + 2 B
arabino	4·25	5·30	*manno*	2·25 + 2 B	3·3 + B + A + A′
			altro	2·25 + B + 2 A″	4·65 + 2 B
xylo	3·80	5·40	*galacto*	1·80 + 2 B	3·4 + B + A + A′
			gulo	1·80 + B + 2 A″	4·75 + 2 B
lyxo	3·30	7·30	*talo*	3·30 + 2 B	3·3 + 2 B + A + A′
			ido	3·30 + 2 A″	4·65 + 2 B

[a] For the calculation the following values of the non-bonding interaction energies[21] (kcal mol^{-1}) were used: O_a/H_a 0·45; $(CH_3)_a/H_a$ 0·9; O_a/O_a 1·5; $(CH_3)_a/O_a$ 2·5; O_1/O_2 0·35; $(CH_3)_1/O_2$ 0·45; anomeric effect 1·0 for O(2)H axial, 0·55 for O(2)H equatorial; the interaction of the nitronate grouping with the neighbouring equatorial hydroxy group[20] is 2·0. In the table the following indications are further used for the following nonbonding interactions: A = $(NO_2)_a/(CH_3)_a$; A′ = $(NO_2)_a/CH_3O_a$; A″ = $(NO_2)_a/H_a$; B = $(NO_2)_1/O_2$

no > *talo* + *ido* is evidently determined by the stability of both nitro glycosides and their aci-nitro forms.

EXPERIMENTAL

The melting points were measured on a Kofler block and they are not corrected. Optical rotations were measured on an Opton instrument at 20°C and 0·5—1·0 concentration. The infrared spectra were recorded on a Perkin Elmer 325 apparatus. The PMR spectra were measured, unless otherwise stated, in deuteriochloroform on a Varian EMS-300 and Varian XL-100 instruments, using tetramethylsilane as internal reference; the chemical shifts are given in δ-scale (p.p.m.), the coupling constants J in Hz. The mass spectra were measured on an LKB 9000 spectrometer. Samples for analysis were dried at 20—50°C and 0·05—0·1 Torr. Column chromatographies were carried out on silica gel from Lachema (Brno) 70—200 μ, thin-layer chromatography on silica gel G according to Stahl (Merck, Darmstadt), 10—40 μ, dimensions of the plates 25 × 75 mm, layer thickness 0·2—0·3 mm. Detection was carried out by spraying the plates with 1% cerium(IV) sulfate in 10% sulfuric acid and heating. The solvents were evaporated on a rotatory evaporater in a vacuum (water pump) at a temperature below 50°C. Light petroleum for crystallisation was of the 45—60°C range. When some substances described in this paper were prepared by several methods their melting points and optical rotations were always coincident (within the experimental limits) with the values given for analytical preparations and their identity was always checked by IR spectrophotometry.

Methyl 6-Deoxy-β-D-glucopyranoside (*I*)

To a solution of 360 g of D-glucose in 500 ml of water, dimethyl sulfate (310 ml) and a solution of potassium hydroxide (160 g) in water (260 ml) were added dropwise and under stirring at 30—35°C, keeping the pH of the reaction mixture between 7 and 9. Dimethyl sulfate was added over 1 hour while the potassium hydroxide solution was added as long as the pH value had the tendency to decrease, *i.e.* about 9 hours. The mixture was then stirred for 2 hours, the pH of the solution adjusted to 8·5 with sulphuric acid and the unreacted dimethyl sulfate decomposed with aqueous ammonia. After evaporation of the mixture to dryness (finally twice with 300 ml of ethanol) 841 g of a mixture composed of salts, 13% of D-glucose (determined by the method in ref.[25]), and methyl glucosides were obtained.

Batches of 420 g of this mixture were mixed with 1100 ml of pyridine and 410 g of *p*-toluenesulfonyl chloride* in 700 ml pyridine were added dropwise to the mixture (—30°C) keeping the temperature below —10°C. The temperature was then allowed to rise to 5°C and 800 ml of acetic anhydride were added under cooling. After 10 minutes the acetylation was completed (according to thin-layer chromatography in benzene–ethanol 100 : 6) and the mixture was poured into 10 l of water. The crystalline methyl 2,3,4-tri-O-acetyl-6-O-*p*-toluenesulfonyl-β-D-glucopyranoside began to precipitate after inoculation, it was collected the next day by filtration under suction, and dried. After crystallisation from 700 ml of ethanol 200 g of this compound were obtained, m.p. 155—163°C which was worked up without further purification.

A mixture of 120 g of methyl 2,3,4-tri-O-acetyl-6-O-*p*-toluenesulfonyl-β-D-glucopyranoside, 165 g of sodium iodide, and 900 ml of butanone (distilled from sodium iodide) was refluxed

* This optimum amount of *p*-toluenesulfonyl chloride corresponded to the maximum degree of conversion to mono-6-O-tosyl derivative when a minimum amount of the ditosyl derivative was formed; it was determined by preliminary experiments.

for 4 hours, evaporated to dryness and the residue mixed with 600 ml of chloroform. After washing with water, sodium thiosulfate solution and water the chloroform solution was dried over magnesium sulfate and evaporated to dryness. A syrup (125 g) was thus obtained from which 53 g of methyl 2,3,4-tri-O-acetyl-6-deoxy-iodo-β-D-glucopyranoside precipitated after addition of 50 ml of ethanol; by concentration of the mother liquors another 42 g of the same substance were obtained.

45 g portions of further unpurified methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo-β-D-glucopyranoside were dissolved in 200 ml of methanol, 9 g of diethylamine and 60 ml of Raney nickel were added and the mixture hydrogenated in an autoclave at 90 atm and room temperature for 3 hours. The catalyst was filtered off and the methanolic filtrates of five hydrogenations were combined and evaporated to dryness. The residue was mixed with 700 ml of ether and extracted three times with 200 ml of water. The combined aqueous extracts were extracted with 500 ml of ether. The combined ethereal extracts were dried over magnesium sulfate and evaporated to dryness. The residue was crystallised from methanol and then deacetylated without further purification by treatment with a catalytic amount of sodium methoxide in methanol. The reaction mixture was deionised with Amberlite IR-120 (H^+) and evaporated to dryness. The methyl 6-deoxy-β-D-glucopyranoside (*I*) obtained was recrystallised from ethyl acetate. The aqueous extract after the working up the reaction mixture after hydrogenation was evaporated to dryness, dissolved in pyridine (300 ml), and acetylated by addition of 150 ml of acetic anhydride. After evaporation of this mixture to dryness and extraction with chloroform the extract was washed with water. The dried chloroform solution of methyl 2,3,4-tri-O-acetyl-6-deoxy-β-D-glucopyranoside was evaporated to dryness and deacetylated in the same manner as above. Further amounts of substance *I* were obtained by chromatography of the mother liquors obtained after crystallisation of substance *I* from ethyl acetate. The total yield from 360 g of D-glucose was 133 g (40%) of substance *I*, m.p. 130–132°C, $[\alpha]_D$ −55° (water).

Condensation of Dialdehyde *II* with Nitromethane

To a solution of 20 g of substance *I* in 200 ml of water 48 g of sodium periodate were added over 20 minutes keeping the temperature below 20°C. After 30 minutes the cooling bath was set aside and the reaction mixture stirred for 45 minutes, then neutralized with 9·2 g of sodium hydrogen carbonate, and poured into 1 litre of ethanol. After one hour's standing at 5°C the mixture was filtered, the material on the filter washed twice with 100 ml of cold ethanol, and the filtrate evaporated to dryness. The syrupy residue was dissolved in 200 ml of ethanol, the precipitated salts filtered off under suction and washed three times with 50 ml of ethanol. The ethanolic filtrates were combined and evaporated to dryness. The syrupy residue (21 g) was dissolved in 132 ml of methanol and mixed under cooling with 106 ml of 1M sodium methoxide and 16 ml of nitromethane. The mixture was stirred for 40 minutes at room temperature and neutralized by addition of Amberlite IR-120 (H^+). The resin was filtered off, washed with 100 ml of methanol and 100 ml of 50% methanol. The combined filtrates were evaporated to dryness, the residue dissolved in 100 ml of methanol and filtered with charcoal. After evaporation 26 g of syrup were obtained which was extracted 3× with 150 ml of ether. The combined ethereal filtrates were evaporated to a mixture of derivatives *IIIa*–*VIIa* (22 g) which crystallized on standing. This mixture was dissolved in 200 ml of methanol and hydrogenated for three hours at 90 atm after addition of 70 ml of Raney nickel. The catalyst was filtered off, washed with methanol and the combined filtrates were evaporated to a volume of about 150 ml and filtered with active charcoal. After evaporation of the filtrate 15 g of a crystalline mixture of compounds *IIIb*–*VIIb* were obtained. To a solution of this mixture (15 g) in 300 ml of pyridine ethyl chloroformate (9 ml) was added at 0°C under stirring over 10 minutes. The reaction mixture was stirred for 60

min at 0°C and decomposed with water. After neutralization with sodium hydrogen carbonate it was evaporated to dryness and the residue extracted with several portions of acetone. The combined acetone extracts afforded, when evaporated, 19·5 g of a mixture of (N-ethoxycarbonyl)-amino derivatives *IIIc*—*VIIc* that was fractionated on a silica gel column (600 g). By elution of the column with a benzene–ethanol mixture (100 : 4) four chromatographic fractions were obtained: Fraction *A* (970 mg) was partly crystalline and contained persubstituted derivatives according to IR spectra (absence of OH-group) and mass spectra; this fraction was not further worked up. Fraction *B* (640 mg), a syrup, crystallised on standing. After recrystallisation from a mixture of ethanol–light petroleum 300 mg (1·2 mmol) of pure derivative *VIc* were obtained. Fraction *C* (2·3 g) represented a mixture of substances *Vc* and *VIIc* which after crystallisation from ethanol–light petroleum had m.p. 173—175°C. Fraction *D* (9·6 g) was a crystalline mixture of compounds *IIIc* and *IVc*.

Fraction *C* (2·3 g) was dissolved in 16 ml of water, 2 g of potassium hydroxide were added to it and the mixture was heated at 55°C for 6 hours. After cooling to room temperature it was diluted with 40 ml of water and poured onto a column (80 ml) of Amberlite IR-120 (H^+). The column of the resin was first washed with water in order to eliminate non-basic material and then with 0·5% of ammonia solution. After evaporation of the ammoniacal eluate, 1·65 g of a syrup were obtained which was dissolved in 30 ml of pyridine. After addition of 15 ml of acetic anhydride the mixture was allowed to stand at room temperature for 24 hours, decomposed with water and evaporated to dryness, eventually with toluene. The syrupy product obtained contained according to thin-layer chromatography in benzene–ethanol 10 : 1 two substances. After chromatographic separation on a silica gel column (50 g; benzene–ethanol 100 : 5) 2·220 g (7·32 mmol) of crystalline peracetate *Ve* and 540 mg (1·78 mmol) of crystalline peracetate *VIIe* were obtained.

Fraction *D* was worked up in 2 g portions, by dissolving them in 16 ml of water, adding 2 g of potassium hydroxide and heating at 55°C for 5 hours; in the manner described for fraction *C*, 1·5 g of a mixture of amino derivatives *IIIb* and *IVb* was obtained which was separated on a silica gel column (50 g) with 2-propanol–chloroform–conc.ammonia–water 10 : 10 : 1 : 1 (bottom layer). On combination of the first chromatographic fractions 1 100 mg (6·22 mmol) of pure crystalline amino derivative *IIIb* were obtained, corresponding to 5·28 g (30 mmol) of substance *IIIb* in the total chromatographic fraction *D*. From subsequent chromatographic fractions 300 mg (1·69 mmol) of crystalline derivative *IVb* were obtained which corresponds to a content of 1·44 g (8·15 mmol) of substance *IVb* in the total chromatographic fraction *D*.

Isomerization of the Mixture of Nitro Sugars *IIIa*—*VIIa*

Ten grammes of a mixture of nitro sugars *IIIa*—*VIIa* obtained by the procedure given above were dissolved in 500 ml of 0·1M-NaOH and the isomerization course was followed by measuring the optical rotation of the solution. When the optical rotation assumed the constant value (after 5 hours) the mixture was neutralized with Amberlite IR-120 (H^+), filtered and evaporated to dryness. The residue was extracted with ether, the extract dried and evaporated to give 8·5 g of a crystalline residue. After trituration with 50 ml of ether 2 g (9·65 mmol) of nitro derivative *IVa* were obtained. For analysis nitro derivative *IVa* was crystallised several times from ethyl acetate; m.p. 182—184 °C (change of modification at 155—170°C), $[\alpha]_D$ +33° (water). For $C_7H_{13}NO_6$ (207·2) calculated: 40·58% C, 6·32% H, 6·76% N; found: 40·74% C, 6·47% H, 6·65% N.

The mother liquor after crystallisation of substance *IVa* containing a mixture of nitro derivatives *IIIa*—*VIIa* was hydrogenated under the same conditions as above. Then the mixture of amino sugars (5 g) was separated on 400 g of silica gel with 2-propanol–chloroform–conc.ammonia–water 10 : 10 : 1 : 1 (bottom layer). From the first fractions 2·2 g of a crystalline mixture

of substances *IIIb* and *VIIb* were obtained, from the subsequent fractions 2·8 g of a mixture of amino derivatives *IVb*, *Vb* and *VIb*. The mixtures of amino derivatives *IIIb* and *VIIb*, or *IVb*, *Vb* and *VIb* were dissolved in 50 or 60 ml resp., of pyridine and converted on reaction with ethyl chloroformate (1·2 ml or 1·5 ml resp.) to mixtures of corresponding (N-ethoxycarbonyl)amino derivatives *IIIc* and *VIIc*, or *IVc*, *Vc* and *VIc*, respectively, under the same conditions as above. After chromatographic separation of the mixture of substances *IIIc* and *VIIc* on 100 g of silica gel (benzene–ethanol 100 : 4) 2·50 g (10·1 mmol) of substance *IIIc* and 0·4 g (1·6 mmol) of substance *VIIc* were obtained. In the same manner the second mixture was also separated on 150 g of silica gel. This separation gave 0·4 g (1·6 mmol) of substance *VIc*, 0·8 g (3·2 mmol) of substance *Vc*, and 2·63 g (10·55 mmol) of substance *IVc*.

Preparation of (N-Ethoxycarbonyl)amino Derivatives *IIIc*—*VIIc* from the Corresponding Amino Derivatives *IIIb*—*VIIb*

To a stirred solution of 530 mg of pure amino sugar in 13 ml of pyridine 0·4 ml of ethyl chloroformate were added at 0°C and the stirring continued for another hour at 0°C. After decomposition with water and neutralization with sodium hydrogen carbonate it was evaporated to dryness. The residue was transferred to a column of silica gel (50 g) and the product eluted with benzene–methanol mixture (100 : 4). From each amino derivative (*IIIb*–*VIIb*) about 670 mg (90%; average) of corresponding (N-ethoxycarbonyl)amino derivative were obtained.

Methyl 3,6-*dideoxy*-3-(N-*ethoxycarbonyl*)*amino*-β-D-*glucopyranoside* (IIIc): After crystallisation from a benzene–ethanol–light petroleum mixture the m.p. was 157—159°C, $[\alpha]_D$ −29° (water). For $C_{10}H_{19}NO_6$ (249·3) calculated: 48·19% C, 7·68% H, 5·62% N; found: 48·29% C, 7·76% H, 5·77% N. PMR (D_2O): 1·24 (3 H, triplet, J = 7·1, CH_3CH_2); 1·30 (3 H, doublet, $J_{5,6}$ = 6·1, CH_3—CH); 3·55 (3H, singlet, CH_3O); 4·12 (2H, quartet, J = 7·1, —CH_2—); 4·40 (1 H, doublet, $J_{1,2}$ = 7·5, H — 1); 3·35 (1 H, triplet, $J_{2,3}$ = 7·5, $J_{1,2}$ = 7·5, H — 2); 3·27 (1 H, quartet, $J_{3,4}$ = 9·4, $J_{2,3}$ = 7·5, H — 3); 3·15 (1 H, quartet, $J_{4,5}$ = 9·1, $J_{3,4}$ = 9·4, H — 4); 3·56 (1 H, octet, $J_{5,6}$ = 6·1, $J_{4,5}$ = 9·1, H — 5).

Methyl 3,6-*dideoxy*-3-(N-*ethoxycarbonyl*)*amino*-β-D-*galactopyranoside* (IVc): After recrystallisation from benzene, m.p. 157—158°C, $[\alpha]_D$ +30° (water). For $C_{10}H_{19}NO_6$ (249·3) calculated: 48·19% C, 7·68% H, 5·62% N; found: 48·35% C, 7·74% H, 5·55% N.

Methyl 3,6-*dideoxy*-3-(N-*ethoxycarbonyl*)*amino*-β-D-*mannopyranoside* (Vc): After crystallisation from a mixture of ethanol and light petroleum the m.p. was 174—175°C, $[\alpha]_D$ −95° (water). For $C_{10}H_{19}NO_6$ (249·3) calculated: 48·19% C, 7·68% H, 5·62% N; found: 48·23% C, 8·09% H, 5·36% N. PMR (D_2O): 1·24 (3 H, triplet, J = 6·9, CH_3CH_2); 1·31 (3 H, doublet, $J_{5,6}$ = 6, CH_3—CH); 3·52 (3 H, singlet, CH_3O); 4·12 (2 H, quartet, J = 6·9, —CH_2—); 4·60 (1 H, doublet, $J_{1,2}$ = 1·0, H — 1); 3·94 (1 H, quartet, $J_{2,3}$ = 2·8, $J_{1,2}$ = 1·0, H — 2); 3·65 (1 H, quartet, $J_{3,4}$ = 9·3, $J_{2,3}$ = 2·8, H — 3); 3·30 (1 H, triplet, $J_{3,4}$ = 9·3, $J_{4,5}$ = 9·3, H — 4); 3·50 (1 H, octet, $J_{4,5}$ = 9·3, $J_{5,6}$ = 6·0, H — 5).

Methyl 3,6-*dideoxy*-3-(N-*ethoxycarbonyl*)*amino*-β-D-*talopyranoside* (VIc): After crystallisation from a mixture of ethanol and light petroleum the m.p. was 144—146°C, $[\alpha]_D$ −37° (water). For $C_{10}H_{19}NO_6$ (249·3) calculated: 48·19% C, 7·68% H, 5·62% N; found: 48·10% C, 7·95% H, 5·79% N.

Methyl 3,6-*dideoxy*-3-(N-*ethoxycarbonyl*)*amino*-β-D-*idopyranoside* (VIIc): After crystallisation from a mixture of ethanol and light petroleum the m.p. was 175—177°C, $[\alpha]_D$ −48° (water). For $C_{10}H_{19}NO_6$ (249·3) calculated: 48·19% C, 7·68% H, 5·62% N; found: 48·10% C, 7·46% H, 5·58% N.

Preparation of Amino Derivatives *IIIb*— *VIIb* from Corresponding (N-Ethoxycarbonyl)amino Derivatives *IIIc*— *VIIc* or Peracetyl Derivatives *IIIe*— *VIIe*

A solution of 500 mg of the starting compound in 4 ml of 4M-KOH was heated at 55°C for 4—6 hours, diluted with 10 ml of water, and poured onto a column of 15 ml of Amberlite IR-120 (H^+). The ion exchanger column was first washed with water and then with 0·5% ammonia solution. After evaporation of the ammoniacal eluent the corresponding amino derivative was obtained in almost quantitative yield.

Methyl 3-*amino*-3,6-*dideoxy*-β-D-*glucopyranoside* (IIIb): After crystallisation from ethanol, m.p. 194—196°C, $[\alpha]_D$ −55° (water). For $C_7H_{15}NO_4$ (177·2) calculated: 47·45% C, 8·53% H, 7·90% N; found: 47·64% C, 8·63% H, 7·78% N.

Methyl 3-*amino*-3,6-*dideoxy*-β-D-*galactopyranoside* (IVb): After crystallisation from ethanol, m.p. 192—194°C (at 150° a slow change of crystal modification), $[\alpha]_D$ −15·3° (water). For $C_7H_{15}NO_4$ (177·2) calculated: 47·45% C, 8·53% H, 7·90% N; found: 47·75% C, 8·63% H, 7·75% N.

Methyl 3-*amino*-3,6-*dideoxy*-β-D-*mannopyranoside* (Vb): The product was crystallised from ethanol and then sublimated at 70°C and 0·005 Torr; m.p. 149—151°C, $[\alpha]_D$ −91° (water). For $C_7H_{15}NO_4$ (177·2) calculated: 47·45% C, 8·53% H, 7·90% N; found: 47·46% C, 8·72% H, 7·96% N.

Methyl 3-*amino*-3,6-*dideoxy*-β-D-*talopyranoside* (VIb): Amorphous substance, after sublimation at 100—130°C and 0·01 Torr the m.p. was 85—100°C, it could not be crystallised; $[\alpha]_D$ −52° (water). For $C_7H_{15}NO_4$ (177·2) calculated: 47·45% C, 8·53% H, 7·90% N; found: 47·41% C, 8·54% H, 7·91% N.

Methyl 3-*amino*-3,6-*dideoxy*-β-D-*idopyranoside* (VIIb): After crystallisation from a mixture of ethanol and light petroleum the m.p. was 153—155°C, $[\alpha]_D$ −83° (water). For $C_7H_{15}NO_4$ (177·2) calculated: 47·45% C, 8·53% H, 7·90% N; found: 47·52% C, 8·61% H, 7·80% N.

Preparation of Acetamido Derivatives *IIId*— *VIId* from Amino Derivatives *IIIb*— *VIIb*

To a solution of 585 mg of amino derivative in 23 ml of methanol 1·85 ml of acetic anhydride were added and the mixture allowed to stand overnight at room temperature. It was then evaporated to dryness, eventually twice with 10 ml portions of toluene; yield 85—99%.

Methyl 3-*acetamido*-3,6-*dideoxy*-β-D-*glucopyranoside* (IIId): After crystallisation from ethanol the m.p. was 247—249°C (in a sealed capillary, sublimates from 220°C up), $[\alpha]_D$ −43° (water). For $C_9H_{17}NO_5$ (219·2) calculated: 49·31% C, 7·82% H, 6·39% N; found: 49·08% C, 8·06% H, 6·30% N.

Methyl 3-*acetamido*-3,6-*dideoxy*-β-D-*galactopyranoside* (IVd): After three crystallisations from ethanol, m.p. 246—248°C (in a selaed capillary, at 230° the substance begins to sublimate), $[\alpha]_D$ +48° (water). For $C_9H_{17}NO_5$ (218·2) calculated: 49·31% C, 7·82% H, 6·39% N; found: 49·44% C, 7·93% H, 6·46% N.

Methyl 3-*acetamido*-3,6-*dideoxy*-β-D-*mannopyranoside* (Vd): After crystallisation from ethanol, m.p. 238—240°C (in a sealed capillary), $[\alpha]_D$ −117° (water). For $C_9H_{17}NO_5$ (219·2) calculated: 49·31% C, 7·82% H, 6·39% N; found: 49·35% C, 7·75% H, 6·20% N.

Methyl 3-*acetamido*-3,6-*dideoxy*-β-D-*talopyranoside* (VId): After crystallisation from ethyl acetate, m.p. 111—113·5°C, or 146—148°C (second modification), $[\alpha]_D$ −29° (water). For $C_9H_{17}NO_5$ (219·2) calculated: 49·31% C, 7·82% H, 6·39% N; found: 49·04% C, 7·98% H, 6·25% N.

Methyl 3-*acetamido*-3,6-*dideoxy*-β-D-*idopyranoside* (VIId): After crystallisation from ethanol, m.p. 201—203°C, $[\alpha]_D$ −66° (water). For $C_9H_{17}NO_5$ (219·2) calculated: 49·31% C, 7·82% H, 6·39% N; found: 49·12% C, 7·82% H, 6·32% N.

Preparation of Peracetyl Derivatives *IIIe*—*VIIe* from Corresponding Amino Derivatives *IIIb*—*VIIb*

A mixture of 150 mg of amino derivative, 6 ml of pyridine and 3 ml of acetic anhydride was allowed to stand at room temperature for 24 hours. After decomposition with water it was evaporated to dryness, eventually twice with 10 ml of toluene. In all instances a crystalline product was obtained in a 95—100% yield.

Methyl 3-*acetamido*-2,4-*di*-O-*acetyl*-3,6-*dideoxy*-β-D-*glucopyranoside* (IIIe): After crystallisation from acetone–ether–light petroleum, m.p. 207·5—208·5°C, $[\alpha]_D$ −11° (chloroform). For $C_{13}H_{21}NO_7$ (303·3) calculated: 51·48% C, 6·98% H, 4·62% N; found: 51·76% C, 7·02% H, 4·65% N.

Methyl 3-*acetamido*-2,4-*di*-O-*acetyl*-3,6-*dideoxy*-β-D-*galactopyranoside* (IVe): After crystallisation from ethyl acetate–light petroleum, m.p. 188—189·5° (about 160° change of crystal modification), $[\alpha]_D$ +22° (chloroform). For $C_{13}H_{21}NO_7$ (303·3) calculated: 51·48% C, 6·98% H, 4·62% N; found: 51·74% C, 7·14% H, 4·61% N. PMR data: 1·19 (3 H, doublet, $J_{5,6} = 6·4$, CH_3—CH); 1·91 (3 H, singlet, CH_3CONH); 2·06 (3 H, singlet, CH_3COO—); 2·17 (3 H, singlet, CH_3COO—); 3·49 (3 H, singlet, CH_3O—); 4·40 (1 H, doublet, $J_{1,2} = 7·8$, H — 1); 4·89 (1 H, quartet, $J_{2,3} = 11·0$, $J_{1,2} = 7·8$, H — 2); 4·30 (1 H, octet, $J_{3,4} = 3·0$, $J_{2,3} = 11·0$, $J_{NH,3} = 8·4$, H — 3); 5·17 (1 H, quartet, $J_{4,5} = 1·0$, $J_{3,4} = 3·0$, H — 4); 3·80 (1 H, quartet, $J_{5,6} = 6·4$, $J_{4,5} = 1·0$ H — 5); 5·93 (1 H, doublet, $J_{NH,3} = 8·4$, NH).

Methyl 3-*acetamido*-2,4-*di*-O-*acetyl*-3,6-*dideoxy*-β-D-*mannopyranoside* (Ve): After crystallisation from a mixture of ethyl acetate and light petroleum, m.p. 180—181°C, $[\alpha]_D$ −59° (chloroform). For $C_{13}H_{21}NO_7$ (303·3) calculated: 51·48% C, 6·98% H, 4·62% N; found: 51·33% C, 7·13% H, 4·77% N. Mass spectrum (*m/e*): 303 (M^+), M — 31, M — 60, M — 60 — 43.

Methyl 3-*acetamido*-2,4-*di*-O-*acetyl*-3,6-*dideoxy*-β-D-*talopyranoside* (VIe): After crystallisation from mixture of ethyl acetate and light petroleum, m.p. 204—205°C (under sublimation), $[\alpha]_D$ −28° (chloroform). For $C_{13}H_{21}NO_7$ (303·3) calculated: 51·48% C, 6·98% H; found: 51·45% C, 7·14% H.

Methyl 3-*acetamido*-2,4-*di*-O-*acetyl*-3,6-*dideoxy*-β-D-*idopyranoside* (VIIe): After crystallisation from ethyl acetate, m.p. 188—190°C, $[\alpha]_D$ −72° (chloroform). For $C_{13}H_{21}NO_7$ (303·3) calculated: 51·48% C, 6·98% H, 4·62% N; found: 51·39% C, 7·04% H, 4·54% N. Mass spectrum (*m/e*): 303 (M^+), M — 31, M — 60, M — 60 — 43. PMR data (deuteriochloroform–20% CD_3COCD_3): 1·35 (3 H, doublet, $J_{5,6} = 6·8$, CH_3CH); 1·95 (3 H, singlet, CH_3CONH); 2·08 (6 H, singlet, 2 × CH_3COO), 3·46 (3 H, singlet, CH_3O—), 6·61 (1 H, doublet, $J_{NH,3} = 8·0$, NH); 4·20 (1 H, multiplet, $J_{5,6} = 6·8$, $J_{4,5} = 4·6$, H — 5); 4·92 (1 H, quartet, $J_{4,5} = 4·6$, $J_{3,4} \sim 8$, H — 4), 4·58 (1 H, multiplet, $J_{3,4} \sim 8$, $J_{2,3} \sim 8$, $J_{NH,3} = 8·0$, H — 3); 4·78—4·90 (2 H, multiplet, $J_{2,3} \sim 8$, $J_{1,2} < 1·5$, H — 1, H — 2).

Acetolysis of Methyl 3-Acetamido-2,4-di-O-acetyl-3,6-dideoxy-β-D-glucopyranoside (*IIIe*)

A mixture of 304 mg of substance *IIIe*, 4 ml of acetic anhydride, and 0·2 ml of conc. sulfuric acid was allowed to stand at room temperature for 24 hours, poured onto ice and 8 g of sodium

hydrogen carbonate, and allowed to stand in a refrigerator overnight. After extraction with chloroform the extract was washed with water, dried over magnesium sulfate and evaporated to dryness. The syrupy residue (230 mg) was chromatographed on a column of silica gel (20 g) with benzene–ethanol 100 : 3. Substance *IIIf* (12 mg) was eluted first and after crystallisation from ethanol–light petroleum melted at 234—234·5°C, $[\alpha]_D$ +26° (chloroform). Literature[6] gives for 3-acetamido-1,2,4-tri-O-acetyl-3,6-dideoxy-β-L-glucopyranose m.p. 232—234°C, $[\alpha]_D$ —22·5° (chloroform). From subsequent chromatographic fractions substance *IIIg* (110 mg) was obtained which after crystallisation from a mixture of ethanol and light petroleum had m.p. 197·5—198·5°C, $[\alpha]_D$ +103° (chloroform). Literature[6] gives for 3-acetamido-1,2,4-tri-O-acetyl-3,6-dideoxy-α--L-glucopyranose m.p. 194—195°C, $[\alpha]_D$ —111° (chloroform).

Methyl 3-Acetamido-3,6-dideoxy-2,4-di-O-methanesulfonyl-β-D-glucopyranoside (*IIIi*)

To a mixture of 500 mg of compound *IIId* and 25 ml of pyridine 0·5 ml of methanesulfonyl chloride were added at —70°C and the mixture allowed to stand at —15°C overnight. After decomposition with water it was extracted several times with chloroform. The combined chloroform extracts were washed with water, dilute hydrochloric acid, water, then dried and evaporated. The syrupy residue (800 mg, 93%) crystallised on standing. For analysis compound *IIIi* was crystallised from acetone–light petroleum, m.p. 164—165°C, $[\alpha]_D$ —18° (chloroform). For $C_{11}.H_{21}NO_9S_2$ (375·4) calculated: 35·20% C, 5·14% H, 3·40% N; found: 35·40% C, 5·28% H, 3·66 N.

Reaction of Dimesyl Derivative *IIIi* with Sodium Acetate in Aqueous 2-Methoxyethanol

a) A mixture of 496 mg of compound *IIIi*, 35 ml of 2-methoxyethanol, 2 ml of water and 2·25 g of sodium acetate trihydrate was refluxed for 9 hours, evaporated to dryness, and the residue transferred to a column of silica gel (10 g). Elution with benzene–ethanol 10 : 1 gave 255 mg (69%) of compound *IVf*, which after crystallisation from ethanol had m.p. 154—155°C, $[\alpha]_D$ —1·7° (chloroform). For $C_{10}H_{19}NSO_7$ (297·3) calculated: 40·40% C, 6·44% H; found: 40·47% C, 6·51% H.

b) A mixture of 350 mg of compound *IIIi*, 15 ml of 2-methoxyethanol, 1 ml of water and 1·1 g of sodium acetate trihydrate was refluxed for 67 hours. It was then worked up as under *a*). Yield, 165 mg (84%) of compound *VId*.

Methyl 3-Acetamido-4-O-acetyl-3,6-dideoxy-2-O-methanesulfonyl-β-D-galactopyranoside (*IVg*)

To a solution of 2-O-mesyl derivative *IVf* (28 mg) in 0·6 ml of pyridine 0·3 ml of acetic anhydride were added and the mixture allowed to stand at room temperature overnight. After decomposition with water and evaporation to dryness (eventually with toluene) 30 mg (94%) of compound *IVg* were obtained; after crystallisation from ethanol–light petroleum, m.p. 179—180°C, $[\alpha]_D$ +20·5° (chloroform). For $C_{12}H_{21}NO_8S$ (339·4) calculated: 42·47% C, 6·24% H; found: 42·19% C, 6·46% H. PMR data: 1·19 (3 H, doublet, $J_{5,6} = 6·5$, CH_3CH—); 1·98 (3 H, singlet, CH_3.CONH—); 2·17 (3 H, singlet, axial CH_3COO—); 3·09 (3 H, singlet, CH_3SO_2O—); 3·58 (3 H, singlet, CH_3O—); 4·30—4·50 (3 H, multiplet, H — 1, H — 2, H — 3); 5·30 (1 H, quartet, $J_{3,4} = 2·2$, $J_{4,5} = 1·0$, H — 4); 3·86 (1 H, octet, $J_{5,6} = 6·5$, $J_{4,5} = 1·0$, H — 5); 5·90 (1 H, doublet, $J = 8$, NH).

Hydrolysis of Acetamidomannoside *Vd*

A solution of 112 mg of compound *Vd* in 5 ml of 2M-HCl was refluxed for 2 hours and evaporated to dryness, finally four times with 10 ml of water. The syrupy residue crystallised out on standing in a desiccator over KOH. After crystallisation from ethanol–ether, m.p. 159–161°C, $[\alpha]_D$ −10° (water). Literature[14] gives for 3-amino-3,6-dideoxy-D-mannose hydrochloride m.p. 162°C, $[\alpha]_D$ −11·2 (water).

The analyses were carried out in the Department of Organic Analysis, Central Laboratories, Institute of Chemical Technology, head Dr L. Helešic. The PMR spectra were measured in the Department of NMR Spectroscopy of the same Laboratories, head Prof. V. Dědek, and the mass spectra were measured in the Department of Mass Spectroscopy of the same Laboratories, head Dr V. Kubelka. We thank them all.

REFERENCES

1. Čapek K., Šteffková J., Jarý J.: This Journal *31*, 1854 (1966).
2. Čapek K., Šteffková J., Jarý J.: This Journal *32*, 2491 (1967).
3. Čapek K., Šteffková J., Jarý J.: This Journal *32*, 781 (1968).
4. Čapek K., Šteffková J., Jarý J.: This Journal *33*, 1750 (1968).
5. Čapek K., Šteffková J., Jarý J.: This Journal *35*, 107 (1970).
6. Richardson A. C., McLauchlan K. A.: J. Chem. Soc. *1962* 2499.
7. Baer H. H., Čapek K.: Can. J. Chem. *47*, 99 (1969).
8. Fischer E., Zach K.: Ber. *45*, 3761 (1912).
9. Hall D. M., Stamm O. A.: Carbohydrate Res. *12*, 421 (1970).
10. Compton J.: J. Am. Chem. Soc. *60*, 395 (1938).
11. Baer H. H.: Advan. Carbohydrate Chem. Biochem. *24*, 67 (1969).
12. Staněk J. jr, Čapek K., Jarý J.: This Journal *39*, 1479 (1974).
13. Goodman L.: Advan. Carbohydrate Chem. Biochem. *22*, 109 (1967).
14. Dutcher J. D., Walters D. R., Wintersteiner O.: J. Org. Chem. *28*, 995 (1963).
15. Čapek K., Staněk J. jr, Jarý J.: This Journal, in press.
16. Staněk J. jr, Trška P., Čapek K., Jarý J.: This Journal, in press.
17. Čapek K., Staněk J. jr, Čapková J., Jarý J.: Unpublished results.
18. Lichtenthaler F. W.: Chem. Ber. *102*, 994 (1969).
19. Angyal S. J., Luttrell B. M.: Australian J. Chem. *23*, 1485 (1970).
20. Kovář J., Čapek K., Baer H. H.: Can. J. Chem. *49*, 3960 (1971).
21. Angyal S. J.: Australian J. Chem. *21*, 2737 (1968).
22. Lewin A. H., Winstein S.: J. Am. Chem. Soc. *84*, 2464 (1962).
23. Ouellette R. J., Booth G. E.: J. Org. Chem. *31*, 587 (1966).
24. Bordwell F. G., Yee K. C.: J. Am. Chem. Soc. *92*, 5933 (1970).
25. Jureček M. in the book: *Organická analysa* II. Published by Nakladatelství ČSAV, Prague 1957.

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