*Carbohydrate Research*, 76 (1979) 109–119


# NITROUS ACID DEAMINATION OF CONFORMATIONALLY INVERTED AMINODEOXYHEXOPYRANOSES*

TOMÁŠ ELBERT†, MILOSLAV ČERNÝ,
*Department of Organic Chemistry, Charles University, 12840 Prague 2 (Czechoslovakia)*

AND JACQUES DEFAYE
*Centre de Recherches sur les Macromolécules Végétales, C.N.R.S., 53 X, 38041 Grenoble (France)*
(Received March 13th, 1979; accepted for publication, April 3rd, 1979)

## ABSTRACT

Nitrous acid deamination of 2-amino-1,6-anhydro-2-deoxy-β-D-glucopyranose (**1**) in the presence of weakly acidic, cation-exchange resin gave 1,6:2,3-dianhydro-β-D-mannopyranose (**3**) and 2,6-anhydro-D-mannose (**6**), characterized, respectively, as the 4-acetate of **3** and the per-*O*-acetylated reduction product of **6**, namely 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-mannitol, obtained in the ratio of 7:13. Comparative deamination of the 4-*O*-benzyl derivative of **1** led to similar qualitative results. Deamination of 3-amino-1,6-anhydro-3-deoxy-β-D-glucopyranose gave 1,6:2,3- and 1,6:3,4-dianhydro-β-D-allopyranose (**13** and **16**), characterized as the corresponding acetates, obtained in the ratio of 31:69, as well as the corresponding *p*-toluenesulfonates. Deamination of 4-amino-1,6-anhydro-4-deoxy-β-D-glucopyranose and of its 2-*O*-benzyl derivative gave the corresponding 1,6:3,4-D-*galacto* dianhydrides as the only detectable products. 2,5-Anhydro-D-glucose, characterized as the 1,3,4,6-tetra-*O*-acetyl derivative of the corresponding anhydropolyol, was obtained in 39% yield from the same deamination reaction performed on 2-amino-1,6-anhydro-2-deoxy-β-D-mannopyranose (**24**). In 90% acetic acid, the nitrous acid deamination of **24**, followed by per-*O*-acetylation, gave only 1,3,4-tri-*O*-acetyl-2,5-anhydro-α-D-glucoseptanose. In the case of 1,6-anhydro-3,4-dideoxy-3,4-epimino-β-D-altropyranose, only the corresponding glycosene was formed, namely, 1,6-anhydro-3,4-dideoxy-β-D-*threo*-hex-3-enopyranose.

## INTRODUCTION

Nitrous acid deamination of polyfunctional amines is usually a complex

*Part 5 of a series "Nitrous Acid Deamination of Polyfunctional Systems". For part 4, see ref. 1. For a preliminary report, see ref. 2. Results obtained as part of the RCP 529, "Glucides et Glycoconjugués" of the C.N.R.S.

†Visiting research associate, Fellow of the French Government (C.I.E.S. Paris), May–July 1978, C.N.R.S., Grenoble, under the auspices of the exchange programme France–Czechoslovakia.

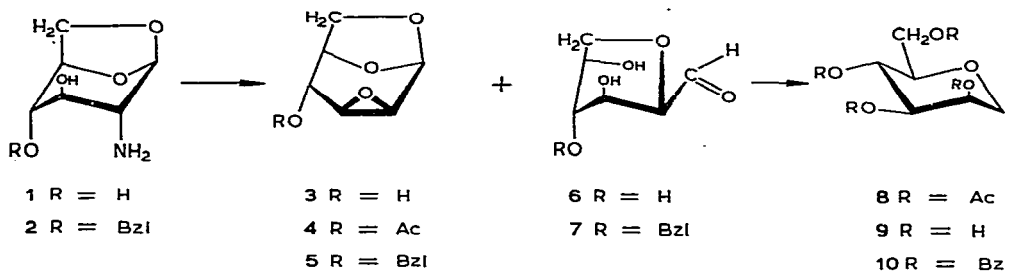
reaction due to the high reactivity of the "hot", poorly solvated carbonium ion that results from the heterolysis of the high-energy precursor diazonium ion. Neighboring-group participations appear to play a preponderant role in acyclic systems, and the outcome of the reaction is usually dependent on the nature of the atom adjacent to the amino group. Thus, deamination of 2-amino-2-deoxyhexonic acids[3] leads to 2,5-anhydrohexonic acids with retention of configuration at C-2, whereas the same reaction performed on 2-amino-2-deoxy-D-glucitol leads to a more complex mixture involving migration to C-2 of either a carbon or a hydrogen atom[4]. The presence of a sulfur-containing group vicinal to the amino group, as in 2-amino-2-deoxyhexose dialkyl dithioacetals, is even more directive and results in most cases in the migration of an alkylthio group to C-2 in a proportion that has been correlated with the steric migratory aptitude of the sulfur substituent, as well as the ionic conditions of the deamination reaction[1,5,6]. Nitrous acid deamination of 1-amino-1-deoxypentitols, which leads exclusively to 1,4- or 2,5-anhydrides together with some of the corresponding alditols[7], represents one example in acyclic systems where correlations have been possible between conformations of these molecules in their initial and transition state and the outcome of the reaction[8]. Furthermore, it is quite apparent that in cyclic systems, at least in six-membered rings, nitrous acid deamination reactions are mainly under the control of the ground-state molecular conformation. Thus, equatorial amines in hexopyranoses series give rise, in most cases, to ring-contraction products involving the migration of the atom *trans* and coplanar to the nitrogen atom in the more favored conformation[9]. Although axial amines in such polyfunctional systems are not well documented, the known examples appear to give rise preponderantly to substitution reactions of a vicinal hydroxyl group. This leads to epoxides, although migration of a coplanar vicinal hydrogen atom, which leads to the generation of a carbonyl group at an adjacent position, may not be excluded[10,11].

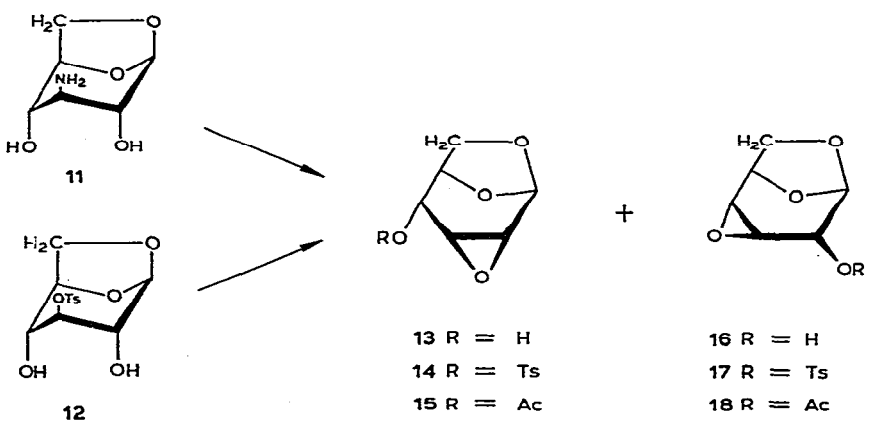
A better stereospecificity in the outcome of nitrous acid deamination reactions may be expected from conformationally more-rigid system. Thus, the preliminary results of Bashford and Wiggins[12] reported the formation of 1,6:3,4-dianhydro-β-D-talopyranose by deamination of 4-amino-1,6-anhydro-4-deoxy-β-D-mannopyranose, and later on 2-amino-1,6-anhydro-2-deoxy-β-D-glucopyranose was found to give the corresponding 2,6-*manno* anhydride under similar conditions[13]. More recently, the deamination of 2-amino-1,6-anhydro-2-deoxy-3-*O*-*p*-tolylsulfonyl-β-D-altropyranose was reported to lead to a 2,5-anhydro-D-allose derivative in excellent yield[14]. In view of the importance of the deamination reaction in the structural analysis of glycosaminoglycans, as well as in preparative carbohydrate chemistry[9,10], a more systematic investigation of inverted-ring aminodeoxy carbohydrate systems was of interest and made possible, owing to the recent availability of a number of aminodeoxy-1,6-anhydrohexopyranose derivatives[15]. The present paper describes the deamination of 2-, 3-, and 4-amino-1,6-anhydro-2-, -3-, and -4-deoxy-β-D-glucopyranose (**1**, **11**, **19**), 2-amino-1,6-anhydro-2-deoxy-β-D-mannopyranose (**24**), 1,6-anhydro-3,4-dideoxy-3,4-epimino-β-D-altropyranose (**30**), and some of their derivatives (**2** and **20**).

## RESULTS AND DISCUSSION

The deaminations were performed in aqueous media with sodium nitrite in the presence of a weakly acidic cation-exchange resin (Amberlite IRC-45, $H^+$) unless otherwise stated. Since the products of deamination are freely soluble in water, the use of the resin markedly reduces the amount of inorganic salts in the reaction mixture and thus facilitates, after evaporation of water, their direct isolation or the preparation of derivatives.

2-Amino-1,6-anhydro-2-deoxy-β-D-glucopyranose[16] (**1**) has both OH-3 and the O-6 ring atom in the favorable, antiperiplanar orientation for participation in the decomposition of a diazonium ion at C-2. If the general concepts for nitrous acid deamination mechanisms in six-membered-ring cyclic systems[9–11] are valid, two possible pathways may lead from **1** either to 1,6:2,3-dianhydro-β-D-mannopyranose (**3**) through participation of OH-3 or to 2,6-anhydro-D-mannose (**6**) through migration of an antiperiplanar C-1–O-6 bond. The latter type of reaction was the only one observed by Micheel *et al.*[13] for **1**. Because of the low stability of this aldehydo-anhydro sugar (which readily gives rise to β-elimination reaction[17] of OH-3), as well as in the hope of obtaining the dianhydride **3** (which is known to undergo readily isomerisation in alkaline medium into 1,6:3,4-dianhydro-β-D-altropyranose[18]), the

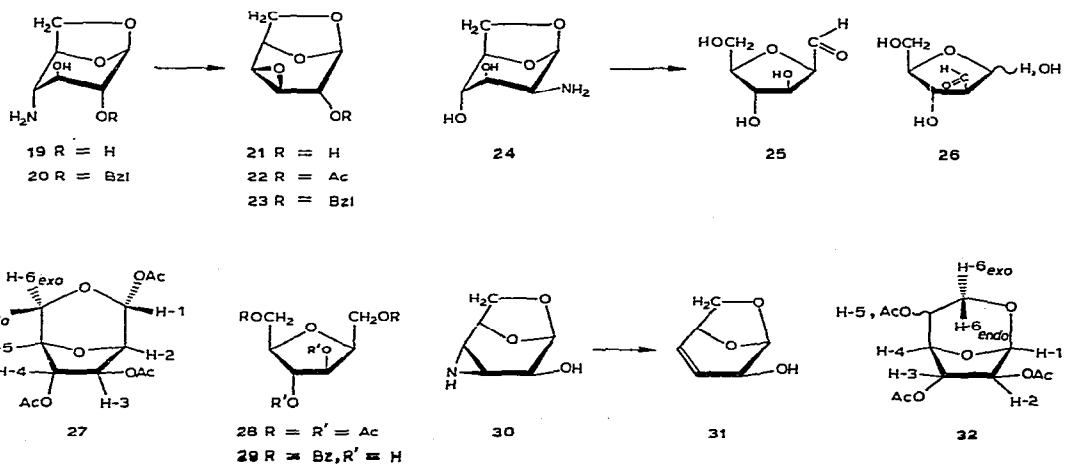


product of the deamination was reduced with sodium borohydride in a buffered medium[19]. After acetylation, two crystalline acetates were obtained in the ratio of 7:13 and characterized, respectively, as the known 4-*O*-acetyl-1,6:2,3-dianhydro-β-D-mannopyranose[20] (**4**) and 1,3,4,5-tetra-*O*-acetyl-2,6-anhydro-D-mannitol [2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-mannitol or tetra-*O*-acetylstyracitol (**8**)]. When the deamination was performed in acetate buffer with the 4-*O*-benzyl derivative[16] **2** of the anhydride **1**, 1,6:2,3-dianhydro-4-*O*-benzyl-β-D-mannopyranose[21] (**5**) was directly isolated from the reaction mixture in 37% yield, together with some 2,6-anhydro-4-*O*-benzyl-D-mannose, obtained in 24% yield in the form of the 2,3,4,6-tetra-*O*-benzoyl derivative of styracitol (**10**)[13] after subsequent reductions and benzoylation.

3-Amino-1,6-anhydro-3-deoxy-β-D-glucopyranose[22] (**11**) may theoretically yield two isomeric epoxides, namely 1,6:2,3-dianhydro-β-D-allopyranose (**13**) and 1,6:3,4-dianhydro-β-D-allopyranose (**16**), which result from the participation of the vicinal *trans*-diaxial OH-2 and OH-4. In fact, both epoxides were formed and characterized as the corresponding *p*-toluenesulfonates **14** and **17** by comparison with authentic samples[23]. The composition of the reaction mixture was estimated by g.l.c. of the corresponding acetates **15** and **18**, obtained in the ratio of 31:69 from the reaction mixture. This result is in good agreement with the SN2 reaction of 1,6-anhydro-3-*O*-*p*-tolylsulfonyl-β-D-glucopyranose (**12**) with sodium hydroxide[24], which gave similarly **13** and **16** in the ratio of 3:7. Furthermore, the isomerisation of **13** and **16** at 100° in acetone by the action of sodium iodide is known[25] to yield **13** and **16** in the ratio of 1:3. Thus, it is interesting to note that the apparent similarity between both sulfonate displacement and deamination reaction in this bridged-ring system presumably reflects the thermodynamic stability of the resulting epoxides **13** and **16**.

Two pathways may be considered for the deamination of 4-amino-1,6-anhydro-4-deoxy-β-D-glucopyranose (**19**): one involves the participation of the *trans*-diaxial OH-3, which would lead to 1,6:3,4-dianhydro-β-D-galactopyranose (**21**), the other



migration of the antiperiplanar $CH_2OH$-6 leading to 4-*C*-hydroxymethyl-D-*xylo*-pentodialdose. When the hydrochloride[26] of **19** was used, t.l.c. of the reaction mixture (obtained after pyridine–acetic anhydride acetylation) showed only one component, which was isolated in 60% yield and identified as the known 2-*O*-acetyl-1,6-3,4-dianhydro-β-D-galactopyranose[20] (**22**). Similarly, a comparative deamination performed in acetate buffer with the 2-*O*-benzyl derivative[26] **20** of **19** gave in 86% yield the 2-*O*-benzyl derivative **23** of **21**, identical with an authentic sample[27].

Nitrous acid deamination of the equatorial $^1C_4$ amine **24** is of special interest in connection with the pioneer results of Levene[28], who noticed unexpectedly that although deamination with nitrous acid of 2-amino-2-deoxy-D-mannose gives D-glucose (result confirmed later on[29,30]), deamination with mercuric oxide gives 2,5-anhydro-D-glucose (**25**). In an attempt to explain this discrepancy between the two oxidative reagents, Shafizadeh[31] in 1958 suggested the possibility of interconversion between the two chair forms of 2-amino-2-deoxy-D-mannose $^4C_1 \rightleftharpoons {}^1C_4$ on heating with mercuric oxide, which would bring $NH_2$-2 into equatorial orientation, leading to an antiperiplanar attack at C-2 by the O-6 ring atom. It should be noticed that, in this perspective, another possible reaction would be the migration of the antiperiplanar C-3–C-4 bond, which would lead to 2-deoxy-2-*C*-formyl-D-arabinose (**26**).

In the present work, the reaction was performed with 2-amino-1,6-anhydro-2-deoxy-β-D-mannopyranose hydrochloride[32] (**24**) under two sets of conditions. When the cation-exchange resin was used, following the usual deamination procedure, the reaction mixture was reduced with sodium borohydride and acetylated, and only one major component was detected and isolated in 39% yield; the structure of 1,3,4,6-tetra-*O*-acetyl-2,5-anhydro-D-glucitol[33] (**28**) was assigned to it mainly on the basis of the n.m.r. spectrum at 250 MHz, which shows the expected four-regions signal-pattern for the ring protons characteristic of this type of structure with well resolved coupling-constants for H-3, -4, and -5, and on the basis of the mass spectrum, which shows the pseudomolecular ion and a fragment at *m/e* 259 resulting from the cleavage of one acetoxyhydroxymethyl exocyclic lateral chain. Conversion of **28** into the known crystalline 2,5-anhydro-1,6-di-*O*-benzoyl-D-glucitol[33] (**29**) is a further proof for the formation of 2,5-anhydro-D-glucose (**25**) from the nitrous acid deamination of **24**.

On the other hand, deamination of **24** in 90% acetic acid gave two products, as shown by t.l.c. Lyophilization of the resulting mixture, followed by pyridine–acetic anhydride acetylation, gave in 40% yield crystalline 1,3,4-tri-*O*-acetyl-2,5-anhydro-α-D-glucoseptanose (**27**). Two other minor components were detected and isolated by column chromatography, but they deteriorated rapidly, and all attempts at characterization failed. Although the methyl glycoside of the branched aldehyde sugar **26** was shown to be stable during nitrous acid deamination[34], there is the possibility that some free **26**, produced during the present deamination process, may undergo elimination in acidic media. The structural proof for **27** results mainly from the chemical-ionisation mass-spectral data, with isobutane as reagent gas, which shows the *quasi*-molecular ion at *m/e* 289, followed by an intense ion at *m/e*

TABLE I

COMPARISON OF THE COUPLING CONSTANTS (Hz) FOR 1,3,4-TRI-*O*-ACETYL-2,5-ANHYDRO-α-D-GLUCOSEPTANOSE (**27**) AND 2,3,5-TRI-*O*-ACETYL-1,6-ANHYDROHEXOFURANOSES[35] (**32**)

| **27** | **32** |
|---|---|
| $J_{1,2}$ 0.5 | |
| $J_{2,3}$ 6.5 | $J_{1,2}$ 3.5–4.5 |
| $J_{3,4}$ 3 | $J_{2,3}$ 1.5–2.7 |
| $J_{4,5}$ 0 | $J_{3,4}$ 0 |
| $J_{5,6endo}$ 1.0[a] | $J_{4,5endo}$[a] 2.0 |
| $J_{5,6exo}$ 2.0[a] | $J_{4,5exo}$[a] 4.4 |
| $J_{6endo,6exo}$[a] 11.5 | $J_{6endo,6exo}$[a] 11.4–14.1 |

[a]The H-$6_{endo}$–H-$6_{exo}$ signals are assigned according to $J_{5,6}$ values.

229 ($MH^+$ −60). The n.m.r. spectrum shows the presence of three acetate groups, and the coupling constants for the ring protons are in close agreement with known data[35] for 2,3,5-tri-*O*-acetyl-1,6-anhydrohexofuranoses (**32**) (Table I). The larger value of $J_{2,3}$ and smaller value of $J_{5,6endo}$–$J_{5,6exo}$ for **27**, compared with the corresponding values $J_{1,2}$ and $J_{4,5endo}$–$J_{4,5exo}$ for **32**, are probably determined by different relative orientations of the oxygen atoms in the 1,3-dioxane (**32**) and 1,4-dioxane ring (**27**). The low value of $J_{1,2}$ for **27** indicates that the 1,4-dioxane ring adopts a chair conformation. Thus, these results lend strong support to the aforementioned findings of Levene[28] and the conformational explanation of Shafizadeh[31].

Epimino compounds are known to give the corresponding, unsaturated derivatives upon deamination, either in the carbohydrate[36,37] or in the steroid field[38,39]. In the case of epimine **30**, it was of interest to examine whether the vicinal free hydroxyl group would influence the course of the reaction. In fact, only one compound was formed, according to t.l.c. of the reaction mixture, and characterized as the known 1,6-anhydro-3,4-dideoxy-β-D-*threo*-hex-3-enopyranose[40] (**31**).

The results just described are in general agreement with the stereochemical rules established for the nitrous acid deamination of six-membered-cyclic systems[9–11]. As expected, the introduction into such molecules of a bridged link, which is known to stabilize one conformation, improves the stereospecificity of the deamination reaction. In most cases, this results in fewer compounds than in the case of non-bridged or conformationally more mobile systems, except when the bridge participates itself in the reaction, as in amine **1**. Axial amine groups usually give epoxides through vicinal-group participation, although this observation cannot be generalized. By contrast, equatorial amine groups (as in **24**) lead mainly to rearranged products. Deamination of epimines leads to the introduction, in fairly good yield, of a double bond, even in the presence of a vicinal hydroxyl group as in **30**.

## EXPERIMENTAL

*General methods.* — Solutions were dried over sodium sulfate or calcium chloride and concentrated *in vacuo* at <40°. Thin-layer chromatography was performed on Silica gel F-254 (Merck) with (*A*), 10:10:1:1 2-propanol–chloroform–ammonia–water; (*B*), 10:1 chloroform–methanol; (*C*), 20:1 benzene–acetone; (*D*), 3:2 ethyl acetate–light petroleum ether; (*E*), 1:1 ether–cyclohexane; and (*F*), 20:1, chloroform–ether, all solvents v/v. The compounds were detected by spraying the plates with 50% sulfuric acid. Column chromatography was performed on Silica gel 60 (Merck, 70–230 mesh) with the aforementioned solvent-systems. Microanalyses were performed by the Service Central de Microanalyse du C.N.R.S., Lyon. Melting points were determined with a Boetius micromelting-point apparatus or with a Leitz heated-block. Optical rotations were measured with Bendix–Ericsson ETL 143 A or Roussel–Jouan "Quick Polarimètre" automatic polarimeters. G.l.c. was performed on a Girdel model 3000 apparatus (flame-ionization detector) with a nitrogen flow rate of 30 mL/min, and a glass column (120 × 0.3 cm) packed as specified. The corresponding, quantitative estimations were obtained with a numerical integrator LTT 2 100 (Paris). I.r. spectra were recorded on chloroform solutions (*c* 0.05–0.07) with a Zeiss–Jena UR 10 spectrophotometer. $^1$H-N.m.r. spectra (250 MHz) were recorded by M. H. Reutenauer at the Laboratoire Grenoblois de Résonance Magnétique Nucléaire, with a Cameca spectrometer (Thomson–CSF) operating in the frequency-sweep mode, with 50% of tetramethylsilane as the lock signal and internal reference; chemical shifts are reported as $\delta$ values. Assignments were usually confirmed by spin decoupling or the INDOR technique. Mass spectra were determined by M. C. Bosso with an A.E.I. MS-30 instrument, coupled with a Varian 100 MS data-acquisition processing system, using either electron impact (e.i.) ionisation mode (70 eV, accelerating voltage 2 kV, electronic current 100 $\mu$A) or chemical ionisation (c.i.) technique (reagent gas isobutane, 270 eV, accelerating voltage 4 kV, electronic current 2.6 mA); in both cases, source temperature was usually 150°.

*Nitrous acid deamination of 2-amino-1,6-anhydro-2-deoxy-β-*D*-glucopyranose* (**1**). — To a solution of **1** (ref. 16, 0.15 g) in water (8 mL) was added Amberlite IRC 50 ($H^+$, 2.5 g). The solution was cooled in ice-water, and sodium nitrite (100 mg) in water (2 mL) was then added dropwise. The reaction mixture was kept for 2 h at 0° with occasional stirring, and then shaken for 4 h at room temperature. The resin was filtered off and thoroughly washed. To the filtrate, sodium borohydride (30 mg) was added in several portions while carbon dioxide[19] was bubbled through the solution in order to keep the pH between 7 and 8. After addition of all borohydride, the mixture was kept for 10 min while bubbling was maintained. The solution was then treated with Amberlite IR 120 ($H^+$) and evaporated to dryness. Boric acid was removed from the residue by three co-evaporations with methanol (10-mL portions). After the last evaporation, the residue was dissolved in pyridine (5 mL), and acetic anhydride (1 mL) added. The mixture was kept overnight, the excess of acetic anhydride removed with methanol, the reaction mixture evaporated, and the

residue thrice treated with toluene (5-mL portions) to remove acetic acid. T.l.c. (*C*) revealed that the syrupy mixture (0.17 g, 65%) consisted of two components ($R_F$ 0.13 and 0.28), which were separated on a column of silica gel (*C*), 1/10th of the reaction mixture being kept for quantitative estimation by g.l.c. The faster-moving component (30 mg after crystallisation), m.p. 55.5–57.5° (ethanol), $[\alpha]_D^{20}$ −63° (*c* 1.06, chloroform) was identified as the dianhydride **4** by comparison with an authentic sample; lit.[20] m.p. 57.5–59.5°, $[\alpha]_D^{20}$ −63° (*c* 0.86, chloroform). To the slower moving component (syrup, 108 mg), structure **8** was assigned; mass spectral data (e.i.): *m/e* 333 ($MH^+$), 273 ($MH^+$ −AcOH), 259 ($MH^+$ −$CH_2OAc$), 230 ($MH^+$ −AcOH−Ac); n.m.r. (chloroform-*d*): δ 2.03, 2.08, 2.13, 2.19 (4s, 3 H, *Me*CO), 3.60 (oct, $J_{4,5}$ 10, $J_{5,6a}$ 5.5, $J_{5,6b}$ 2.25 Hz, H-5), 3.69 (dd, $J_{a,b}$ 13, $J_{1a,2}$ 1.0 Hz, H-1a), 4.07 (dd, $J_{1b,2}$ 2.0 Hz, H-1b), 4.14 (dd, $J_{a,b}$ 12.4, $J_{5,6a}$ 2.25 Hz, H-6a), 4.26 (dd, $J_{5,6b}$ 5.5 Hz, H-6b), 5.06 (q, $J_{2,3}$ 3.7, $J_{3,4}$ 10 Hz, H-3), 5.29 (t, $J_{3,4} = J_{4,5} = 10$ Hz, H-4), and 5.33 (m, H-2).

*O*-Deacetylation of **8** (102 mg) with sodium methoxide gave 1,5-anhydro-D-mannitol (or styracitol, **9**) (38 mg, 76%), m.p. 156–157°, $[\alpha]_D^{20}$ −49.2° (*c* 1.14, water); lit.[41] m.p. 156–157°, $[\alpha]_D$ −50.3° (*c* 1.06, water).

G.l.c. of the mixture of acetates **4** and **8** (SE-30 on glass beads; temperature 80–150°, at a rate of 5°/min, $temp._{inject.}$ 220°, $temp._{detect.}$ 250°, $t_r$ 156 s for **4** and 636 s for **8**) gave a ratio of 7/13 for the components.

*Nitrous acid deamination of 2-amino-1,6-anhydro-4-O-benzyl-2-deoxy-β-D-glucopyranose* (**2**). — To a solution of **2** (ref. 16, 500 mg) in acetate buffer (pH 4.6, 25 mL) was added at 0° a solution of sodium nitrite (1.5 g) in water (15 mL). The mixture was stirred for 20 h at room temperature, and then extracted with chloroform (3 × 10 mL). The combined, dried extracts afforded, after concentration, 1,6:2,3-dianhydro-4-*O*-benzyl-β-D-mannopyranose[21] (**5**, 170 mg, 37%), m.p. 61–63° (ether–petroleum ether), $[\alpha]_D^{20}$ −27° (*c* 0.95, chloroform); lit.[21], m.p. 64°, $[\alpha]_D^{20}$ −27° (chloroform).

The water phase resulting from the chloroform extraction was treated portionwise with sodium borohydride (100 mg) while carbon dioxide was bubbled through[19]. After 15 min, the solution was freed of cations with Dowex 50 cation-exchange resin ($H^+$), and evaporated, and the residue was dissolved in ethanol (5 mL) and hydrogenated at atmospheric pressure and 40° in the presence of palladium-on-charcoal (10%, 200 mg). After 20 h, the catalyst was filtered off, and the solution concentrated to a syrup that was benzoylated with benzoyl chloride (1.5 mL) in pyridine (10 mL) overnight. An aqueous saturated sodium hydrogencarbonate solution (40 mL) was then added to the pyridine solution, and the product was extracted with chloroform (3 × 10 mL). After being dried, the chloroform solution gave on concentration 1,5-anhydro-2,3,4,6-tetra-*O*-benzoyl-D-mannitol (**10**, 280 mg, 24%), m.p. 142–143° (ethanol), $[\alpha]_D^{20}$ −145° (*c* 0.82, chloroform); lit.[13] m.p. 142°, $[\alpha]_D^{26}$ −147.4° (*c* 1, chloroform).

*Nitrous acid deamination of 3-amino-1,6-anhydro-3-deoxy-β-D-glucopyranose* (**11**). — Deamination of **11** (ref. 22, 100 mg) was performed as described for **1**. T.l.c. (*A*) revealed the presence of two components ($R_F$ 0.5 and 0.6). After evaporation

of the solvent, *p*-toluenesulfonyl chloride (1.5 g) was added to the dried residue (phosphorus pentaoxide overnight) dissolved in pyridine (3 mL). After being kept overnight, the reaction mixture was diluted with ice–water (10 mL) and extracted with chloroform (3 × 5 mL). The extracts gave, after concentration, an oily residue (126 mg, 60%) that showed in t.l.c. (*D*) the presence of two components. By preparative t.l.c. (same eluent), 60 mg of this mixture gave 1,6:2,3-dianhydro-4-*O*-*p*-tolylsulfonyl-β-D-allopyranose (**14**, 21 mg, $R_F$ 0.5), m.p. 146–147° (ethanol), $[\alpha]_D^{20}$ +53.5° (*c* 0.78, chloroform); {lit.[23] m.p. 146–147°, $[\alpha]_D^{20}$ +52° (*c* 1.0, chloroform)} and 1,6:3,4-dianhydro-2-*O*-*p*-tolylsulfonyl-β-D-allopyranose (**17**, 33 mg, $R_F$ 0.35), m.p. 116–117° (ethanol), $[\alpha]_D^{20}$ −97.5 (*c* 0.98, chloroform); lit.[23] m.p. 116–117°, $[\alpha]_D^{20}$ −95° (*c* 0.4, chloroform). The i.r. spectra of both compounds were superposable with those of authentic samples.

For the quantitative estimation of the deamination reaction mixture by g.l.c., another batch of the amine **11** (10 mg) was deaminated according to the aforementioned procedures, and the resulting compounds were converted into acetates **15** and **18** with pyridine–acetic anhydride (7.6 mg, total yield 66%). The g.l.c. column was filled with 3% OV 225 on Chromosorb Q HMDS (80–100 mesh, $temp._{column}$ 120°, $temp._{inject.}$ 200°, $temp._{detect.}$ 240°), and acetates **15** and **18**, prepared from authentic samples[23], were the standards (respective $t_r$ 600 s and 648 s). The reaction mixture consisted of 31% of **15** and 69% of **18**.

*Nitrous acid deamination of 4-amino-1,6-anhydro-4-deoxy-β-*D*-glucopyranose* (**19**). — Compound **19** (ref. 26, 47 mg) was deaminated as described for **1**. According to t.l.c. (*A*), the reaction mixture contained only one product. After evaporation of the solvent, the dried residue was dissolved in pyridine (1 mL), and acetic anhydride (0.15 mL) was added. After being kept overnight, the excess of acetic anhydride was removed with methanol, the reaction mixture evaporated, and the residue thrice treated with toluene to remove acetic acid. The resulting syrup **22** crystallized from ethanol (21 mg, 52%), m.p. 114–116° (sublimation at 113°), $[\alpha]_D^{20}$ −54° (*c* 1.0, chloroform); lit.[20] m.p. 115–117°, $[\alpha]_D^{20}$ −55° (*c* 1.0, chloroform); i.r. spectrum identical with that of an authentic sample. The total yield of crude **22** (60%) was estimated by g.l.c. ($t_r$ 432 s).

*Nitrous acid deamination of 4-amino-1,6-anhydro-2-*O*-benzyl-4-deoxy-β-*D*-glucopyranose* (**20**). — Deamination of **20** (ref. 26, 50 mg) in acetate buffer was performed as described for **2**. The reaction mixture was then extracted with chloroform (3 × 4 mL). Evaporation of the combined extracts gave chromatographically pure 1,6:3,4-dianhydro-2-*O*-benzyl-β-D-galactopyranose (**23**, 40 mg, 86%), m.p. 45–47° (ether–petroleum ether), $[\alpha]_D^{20}$ −53° (*c* 1.16, chloroform); lit.[27] m.p. 47–48°, $[\alpha]_D^{20}$ −55° (chloroform). The i.r. spectra of both compounds were superposable.

*Nitrous acid deamination of 2-amino-1,6-anhydro-2-deoxy-β-*D*-mannopyranose* (**24**). — *Procedure A*. The hydrochloride of amine **24** (ref. 32, 150 mg) was treated as described for **1**. After acetylation with acetic anhydride–pyridine of the reaction mixture (155 mg), one major and two minor components were detected in t.l.c. (*C*). A chromatographic separation on silica gel (*E*) gave as major component **28** (102 mg,

39% syrup); n.m.r. (chloroform-*d*): $\delta$ 2.086, 2.102, 2.106, 2.122 (4 s, 3 H, $CH_3CO$), 4.07 (oct, $J_{4,5}$ 3.5, $J_{5,6a}$ 6.5, $J_{5,6b}$ 4.5 Hz, H-5), 4.12–4.42 (m, 5 H, H-1a, -1b, -2, -6a, and -6b), 5.01 (q, $J_{3,4}$ 1.4 Hz, H-4), 5.33 (dd, $J_{2,3}$ 4.0 Hz, H-3); m.s. (e.i.): 333 ($MH^+$), 273 ($MH^+$ —AcOH), and 259 ($M^+$ —$CH_2OAc$).

Zemplén *O*-deacetylation of **28** with sodium methoxide, and partial benzoylation according to ref. 33 led to 2,5-anhydro-1,6-di-*O*-benzoyl-D-glucitol (**29**), m.p. 135–138° (begins to sublime at ~130°), $[\alpha]_D^{20}$ +2.6° (*c* 1.75, ethanol); lit.[33] m.p. 135.5–138.5°, $[\alpha]_D^{20}$ +2.31 (*c* 2.0, ethanol).

*Procedure B.* To a cooled solution (ice–water bath) of the free amine **24** (ref. 36, 110 mg) in 90% acetic acid (10 mL) was added, under stirring, a solution of sodium nitrite (150 mg) in water (1 mL). The cooled reaction mixture was stirred for an additional 2 h, and then another batch of sodium nitrite (50 mg) was added, and the reaction mixture stirred for 4 h at room temperature. T.l.c. (*A*) of the reaction mixture showed two components ($R_F$ 0.28 and 0.47), the slower-moving absorbing in the u.v. region. The dried reaction mixture (lyophilisation) was acetylated with acetic anhydride (2 mL) and pyridine (6 mL) overnight. After the usual workup and a preparative chromatography on silica gel (*F*), the faster-moving component (**27**, 78 mg, 40%) was isolated; after crystallisation from ether, it sublimed at 110°, m.p. 114–115°, $[\alpha]_D^{20}$ +22.0° (*c* 1.5, chloroform); n.m.r. (chloroform-*d*); $\delta$ 2.14, 2.16 and 2.18 (3 s, 3 H, $CH_3CO$), 3.77 (dd, $J_{6exo,6endo}$ 11.5, $J_{5,6endo}$ 1 Hz, H-$6_{endo}$), 4.11 (broad s, H-5), 4.21 (dd, $J_{5,6exo}$ 2 Hz, H-$6_{exo}$), 4.40 (d, $J_{2,3}$ 6.5 Hz, H-2), 5.30 (q, $J_{3,4}$ 3 Hz, H-3), 5.34 (d, H-4), and 5.83 (s, $J_{1,2} \leqslant 0.5$ Hz, H-1).

*Anal.* Calc. for $C_{12}H_{16}O_8$: C, 50.00; H, 5.60. Found: C, 49.96; H, 5.59.

*Nitrous acid deamination of 1,6-anhydro-3,4-dideoxy-3,4-epimino-β-D-altropyranose* (**30**). — The epimine **30** (ref. 26, 150 mg) was deaminated as described for **1**. According to t.l.c. (*B*), the reaction mixture contained only one component ($R_F$ 0.60). After evaporation of the solvent, the residue was extracted with chloroform in the presence of dry sodium sulfate. Evaporation of the chloroform extracts afforded **31** (88 mg, 65%), m.p. 63–65° (ether), sublimes at 55°, $[\alpha]_D^{20}$ —35.5° (*c*, 1.07 chloroform); lit.[40] m.p. 65–66.5°, $[\alpha]_D^{20}$ —35.3° (*c* 1.0, chloroform); n.m.r. (chloroform-*d*): $\delta$ 2.22 (OH), 3.75 (q, $J_{6endo,6exo}$ 6.7, $J_{5,6exo}$ 4.0 Hz, H-$6_{exo}$) 3.85 (d, H-$6_{endo}$), 4.34 (broad s, H-2), 4.66 (t, $J_{4,5}$ 4.3 Hz, H-5), 5.52 (t, $J_{1,2} = J_{1,3} = 2.2$ Hz, H-1), 5.72 (dt, $J_{2,3}$ 2.25, $J_{3,4}$ 10 Hz, H-3), and 6.12 (q, $J_{2,4} \leqslant 0.5$ Hz, H-4).

## REFERENCES


1 P. ANGIBEAUD, C. BOSSO, J. DEFAYE, D. HORTON, C. COHEN-ADDAD, AND M. THOMAS, *J. Chem. Soc., Perkin Trans. 1*, (1979) 1583–1592.

2 P. ANGIBEAUD, C. BOSSO, M. ČERNÝ, AND J. DEFAYE, *Journées Chim. Biochim. Glucides (Grenoble)*, 6 (1976); *Actual. Chim. Suppl.*, Sept. 1976, p. 11, Abstr. 34.

3 P. A. LEVENE AND F. B. LAFORGE, *J. Biol. Chem.*, 20 (1915) 433–434; 21 (1915) 351–359; P. A. LEVENE, *J. Biol. Chem.*, 36 (1918) 89–94; P. A. LEVENE AND E. P. CLARK, *J. Biol. Chem.*, 46 (1921) 19–33; A. B. FOSTER, *Chem. Ind. (London)*, (1955) 627.

4 T. BANDO AND Y. MATSUSHIMA, *Bull. Chem. Soc. Jpn.*, 46 (1973) 593–596.

5 A. E. EL-ASHMAWY, D. HORTON, L. G. MAGBANUA, AND J. M. J. TRONCHET, *Carbohydr. Res.*, 6 (1968) 229–309.

6 J. DEFAYE, T. NAKAMURA, D. HORTON, AND K. D. PHILIPS, *Carbohydr. Res.*, 16 (1971) 133–134.
7 D. D. HEARD, B. G. HUDSON, AND R. BARKER, *J. Org. Chem.*, 35 (1970) 464–467.
8 M. BLANC-MUESSER, J. DEFAYE, AND D. HORTON, *Carbohydr. Res.*, 68 (1979) 175–187.
9 J. DEFAYE, *Adv. Carbohydr. Chem. Biochem.*, 25 (1970) 181–194.
10 J. M. WILLIAMS, *Adv. Carbohydr. Chem. Biochem.*, 31 (1975) 9–79.
11 M. CHÉREST, H. FELKIN, J. SICHER, F. ŠIPOŠ, AND M. TICHÝ, *J. Chem. Soc.*, (1965) 2513–2521.
12 V. G. BASHFORD AND L. F. WIGGINS, *Nature (London)*, 165 (1950) 566.
13 F. MICHEEL, W. NEIER, AND T. RIEDEL, *Chem. Ber.*, 100 (1967) 2401–2409.
14 C.-D. CHANG AND T. L. HULLAR, *Carbohydr. Res.*, 54 (1977) 217–230.
15 M. ČERNÝ AND J. STANĚK, JR., *Adv. Carbohydr. Chem. Biochem.*, 34 (1977) 23–177.
16 M. ČERNÝ, O. JULÁKOVÁ, AND J. PACÁK, *Collect. Czech. Chem. Commun.*, 39 (1974) 1391–1396.
17 M. ČERNÝ AND T. ELBERT, unpublished results.
18 M. ČERNÝ, J. PACÁK, AND J. STANĚK, *Collect. Czech. Chem. Commun.*, 30 (1965) 1151–1157.
19 D. HORTON AND K. D. PHILIPS, *Carbohydr. Res.*, 30 (1973) 367–374.
20 P. DRAŠAR, Thesis, Charles University, Prague, 1972.
21 T. TRNKA AND M. ČERNÝ, *Collect. Czech. Chem. Commun.*, 36 (1971) 2216–2225.
22 T. TRNKA, M. ČERNÝ, M. BUDĚŠÍNSKÝ, AND J. PACÁK, *Collect. Czech. Chem. Commun.*, 40 (1975) 3038–3045.
23 M. ČERNÝ, T. TRNKA, P. BERAN, AND J. PACÁK, *Collect. Czech. Chem. Commun.*, 34 (1969) 3377–3382.
24 M. ČERNÝ, J. STANĚK, JR., AND J. PACÁK, *Collect. Czech. Chem. Commun.*, 34 (1969) 849–856.
25 T. TRNKA AND M. ČERNÝ, to be published.
26 M. ČERNÝ, I. ČERNÝ, AND J. PACÁK, *Collect. Czech. Chem. Commun.*, 41 (1976) 2942–2951.
27 M. PRYSTAŠ, L. KALVODA, AND F. ŠORM, *Collect. Czech. Chem. Commun.*, 41 (1976) 1426–1447.
28 P. A. LEVENE, *J. Biol. Chem.*, 39 (1919) 69–76.
29 N. M. K. NG YING KIN AND J. M. WILLIAMS, *Chem. Commun.*, (1971) 1123–1124.
30 D. HORTON, K. D. PHILIPS, AND J. DEFAYE, *Carbohydr. Res.*, 21 (1972) 417–419.
31 F. SHAFIZADEH, *Adv. Carbohydr. Chem.*, 13 (1958) 9–61.
32 H. VEČERKOVÁ, Thesis, Charles University, Prague, 1978.
33 T. A. W. KOERNER, JR., R. J. VOLL, AND E. S. YOUNATHAN, *Carbohydr. Res.*, 59 (1977) 403–416.
34 B. ERBING, B. LINDBERG, AND S. SVENSSON, *Acta Chem. Scand.*, 27 (1973) 3699–3704.
35 K. HEYNS, W. D. SOLDAT, AND P. KÖLL, *Chem. Ber.*, 104 (1971) 2063–2070; R. U. LEMIEUX AND R. NAGARAJAN, *Can. J. Chem.*, 42 (1964) 1270–1278.
36 R. D. GUTHRIE AND D. KING, *Carbohydr. Res.*, 3 (1966) 128–129.
37 R. D. GUTHRIE AND J. A. LIEBMANN, *J. Chem. Soc., Perkin Trans. 1*, (1974) 650–657.
38 K. PONSOLD, *Chem. Ber.*, 97 (1964) 3524–3528.
39 G. DREFAHL, K. PONSOLD, AND B. SCHÖNECKER, *Chem. Ber.*, 97 (1964) 2014–2017.
40 P. KÖLL, T. SCHULTECK, AND R. W. RENNECKE, *Chem. Ber.*, 109 (1976) 337–344.
41 H. G. FLETCHER, JR., AND H. W. DIEHL, *J. Am. Chem. Soc.*, 74 (1952) 3175–3176.