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ACTION OF AMMONIA ON THE METHYL 2,3-ANHYDRO-D-RIBOFURANOSIDES, AND TREATMENT OF THE PRODUCTS WITH NITROUS ACID*

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ABSTRACT

The reaction between methyl 2,3-anhydro-5-*O*-*p*-nitrobenzoyl-β-D-ribofuranoside (**2**) and ammonia gives mainly the D-*xylo* amine **3**, as previously reported. Azide ion shows similar regioselectivity with methyl 2,3-anhydro-β-D-ribofuranoside (**1**). Ammonia reacts with methyl 2,3-anhydro-5-*O*-*p*-nitrobenzoyl-α-D-ribofuranoside (**11**) to give the D-*arabino* amine **12** and D-*xylo* amine **13** in the ratio 2:1. Both isomers were obtained crystalline after chromatography on Dowex 1 (HO^-) resin. With nitrous acid, **3**, **13**, and **12** each yield the parent epoxide, together with other products. In particular, **12** gives 2-*O*-methyl-D-ribose **14** as the major product; the structure of **14** was proved by synthesis of the enantiomer **21**. Conformational aspects of the deaminations are discussed.

INTRODUCTION

In 1934, Bodycote, Haworth, and Hirst[1] showed that reaction between methyl 2-*O*-toluene-*p*-sulphonyl-β-D-glucopyranoside and ammonia gave methyl 3-amino-3-deoxy-β-D-altropyranoside, probably by way of the *manno* epoxide. The amine was treated with nitrous acid, but the structures of the non-reducing products could not be established by the methods then available. Since that time, many aminodeoxy sugar derivatives have been prepared by epoxide-ring opening[2,3], and their reactions with nitrous acid studied[4]. We have been interested in the deamination of aminodeoxy sugars in which the amino group is attached directly to a furanose ring, a field which has received little attention[4].

In 1958, during work[5,6] related to the antibiotic puromycin, the methyl 2,3-anhydro-D-ribofuranosides **1** and **10** were treated with ammonia. The major product in each reaction was believed to be the 3-amino-3-deoxy-D-*xylo* isomer (**3** and

*Dedicated to the memory of Sir Edmund Hirst, C.B.E., F.R.S.

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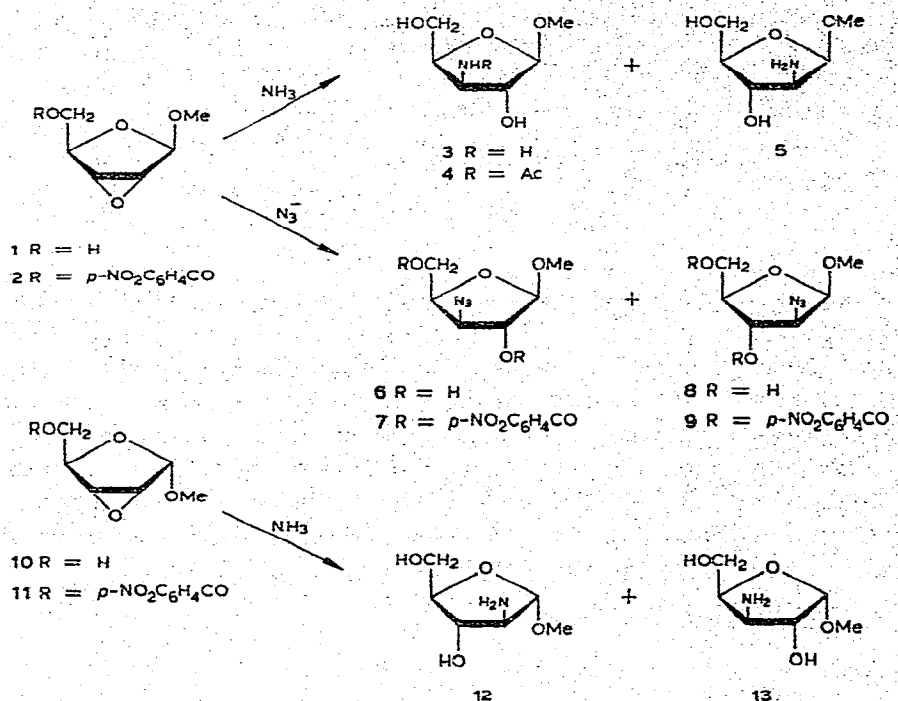
13), but the evidence in the α-series (10→13) was unconvincing. More recently, there have been several examples of preferred nucleophilic attack at C-2 in methyl 2,3-anhydro-α-D-ribofuranoside[7–9] (10) and its derivatives[10–14]. Montgomery and his colleagues[9], in particular, have reinvestigated the ammonolysis of 10 and shown that the 2-amino-2-deoxyarabinoside 12 and the xyloside 13 were produced in the ratio 3:2.



DISCUSSION

Initially, we studied reactions in the β-series. When the crystalline *p*-nitrobenzoate[6] 2 was treated with conc. aqueous ammonia at 100° in a sealed tube, the ester group was removed and two ninhydrin-positive products, in the ratio ~10:1, were detected by paper chromatography. The major product was the D-*xylo* amine 3, and the minor product was, presumably, the D-*arabino* amine 5. *N*-Acetylation of the mixture afforded the known[5,6] crystalline amide 4 in 69% yield, and subsequent alkaline hydrolysis[15] gave the pure amine 3 as a colourless syrup. The minor product was not isolated.

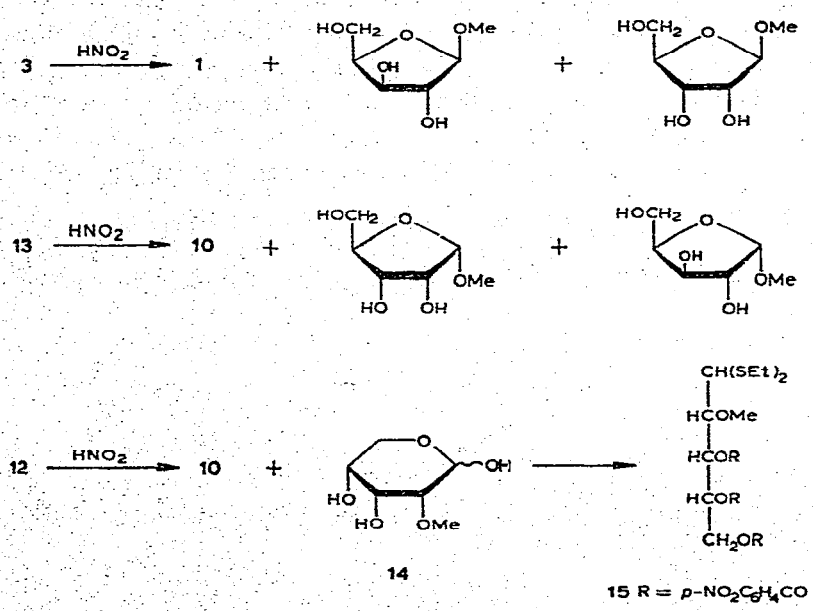
As an alternative route to the aminodeoxypentosides, the epoxide 1 was treated with sodium azide and ammonium chloride in boiling, aqueous 2-methoxyethanol[16]. Two products were detected by t.l.c. and isolated by chromatography on silica gel. The less-polar compound, the crystalline 2-azido-2-deoxyarabinoside 8 (2.5%), was

characterised as the crystalline bis(*p*-nitrobenzoate) **9**. The more-polar isomer, the syrupy 3-azido-3-deoxyxyloside **6** (85%), also gave a crystalline bis(*p*-nitrobenzoate) (**7**). The D-*xylo* structure of the azide **6** was shown by conversion into the known[5,6] acetamide **4** by hydrogenation, followed by *N*-acetylation.

These results confirm the earlier work[5,6] with regard to ammonolysis of **1** and its preferential reactivity at C-3 towards nucleophiles[3].

When the α-*ribo* epoxide[6] **11** was heated in a sealed tube with conc. aqueous ammonia, two ninhydrin-positive compounds were produced, in the ratio ~2:1. They were readily separated by chromatography[17] on Dowex 1 (HO^-) anion-exchange resin and isolated in crystalline from. The compound (29%) eluted first had m.p. 122–123° and was clearly the 3-amino-3-deoxyxyloside[5,9] **13**; eluted second (62%) was the 2-amino-2-deoxyarabinoside[9] **12**, m.p. 80–81°. These results are in general agreement with those of Montgomery *et al.*[9], but our method gives a much better yield of the pure isomers.

When the amine **3** was treated with nitrous acid in dilute acetic acid, the major product (t.l.c.) was the *ribo*-epoxide **1**, which was isolated as the crystalline *p*-nitrobenzoate **2** in 63% yield. Paper chromatography of the product mixture showed the presence of methyl pentosides (reaction with periodate and Schiff's reagent[18]). When this fraction was isolated by preparative paper chromatography and subjected to acid hydrolysis, ribose and xylose were detected in the ratio ~1:2.



The deamination of the corresponding amine (**13**) in the α-series was studied by paper chromatography. Apart from an unidentified product of high R_F value (reactive

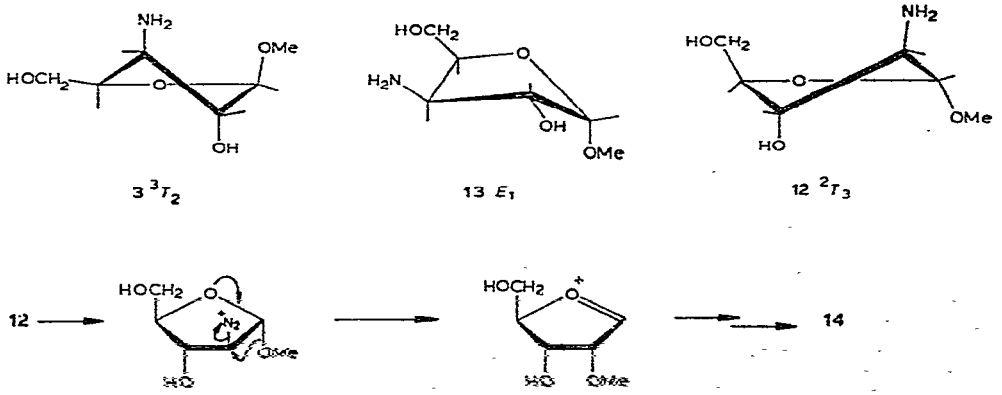
to aniline hydrogen phthalate[19]), the products were analogous to those found in the deamination of 3. The *ribo*-epoxide **10** was a major product, together with a periodate-positive mixture that gave ribose and xylose (3:1) on subsequent hydrolysis with acid.

Deamination of methyl 2-amino-2-deoxy-α-D-arabinofuranoside (**12**) with nitrous acid afforded two products. The minor component (~20%) was identified chromatographically as the *ribo*-epoxide **10**. The major product was 2-*O*-methyl-D-ribose (**14**), identified by chromatographic comparison with a synthetic sample of the enantiomer and by conversion into the tris(*p*-nitrobenzoate) **15** of the diethyl dithioacetal. The synthesis of 2-*O*-methyl-L-ribose (**21**) is described below.

The deamination of carbohydrate amines can follow a number of different courses[4]. It is believed that a diazonium cation is formed as an intermediate whose decomposition is very rapid (energy of activation[20] ~3–5 kcal.mol^{-1}). This energy is less than the barrier[21] for inversion of the pyranose ring (~10 kcal.mol^{-1}), and so the ground-state conformation of the diazonium ion is important. The formation of epoxides by deamination of carbohydrate amines is well known[4], and in the best-authenticated examples[22,23], the hydroxyl and amino groups have a clear diaxial relationship in the ground state of the molecule. A recent example has been the demonstration that 1,2-anhydro-α-D-mannopyranose is an intermediate in the deamination of 2-amino-2-deoxy-D-mannose[4,24].

Sugars in which an amino group is attached directly to a furanose ring are of potential interest in deamination studies. In the furanose ring, the barrier to conformational inversion, *i.e.*, pseudorotation[25], is ~3–4 kcal.mol^{-1}, which is about the same as the energy of activation proposed for the decomposition of an alkyldiazonium ion. Therefore, the deamination reaction in the furanose series should be less subject to conformational control. Nevertheless, it is of interest to see whether there is any correlation between the ground-state conformation of the diazonium ion (assuming that it is the same as that of the parent amine) and the nature of the deamination products.

The ^{1}H-n.m.r. spectrum of **3** in D_2O is consistent with the $^3T_2$ conformation[25–29], in which HO-2 and H_2N-3 have a dihedral angle that approaches 180°.



The yield of epoxide **1** from the deamination of **3** was high, in keeping with the idea that the $^3T_2$ conformation was concerned in the reaction.

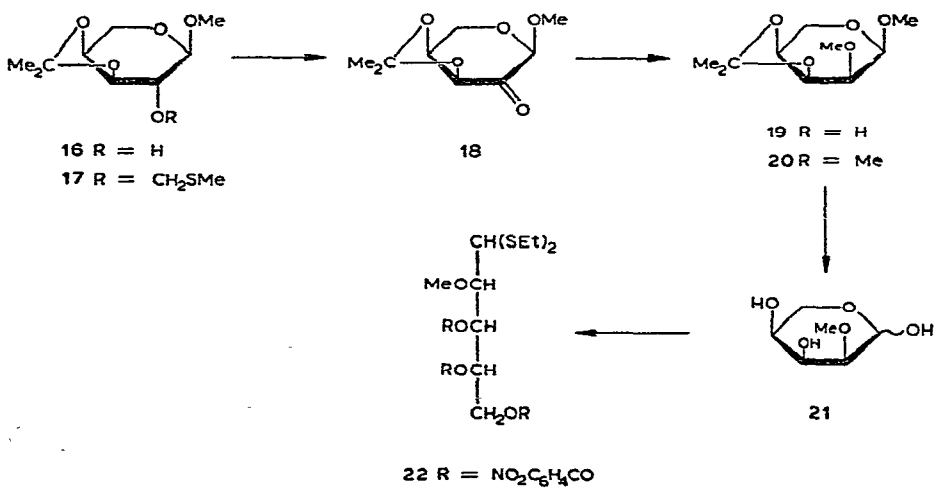
In the ^{1}H-n.m.r. spectrum of **13** in D_2O, the most noticeable feature was a high value (8 Hz) for both $J_{2,3}$ and $J_{3,4}$. Of the possible conformations (E_1, ^2E), the dihedral angle between the hydroxyl and amino groups is ~90–100°. The yield of epoxide **10** from the deamination, estimated chromatographically, was less than in the *β*-series. The formation of the pentosides from deamination of **3** and **13** may be due to hydration of the C-3 carbonium ion or, for the *ribo* products, attack by water on the unstable diazonium intermediate.

The migration of an ether oxygen atom is very common during deamination[4], usually to give a five-membered ring. There are also examples of 1,2-migration of an oxygen atom from C-1 of a glycoside, facilitated by electron-release from the oxygen atom of a pyranose ring[24,30]. The conformational requirements for such a process (see formulae) should resemble those for epoxide formation, and therefore it was of particular interest to study the conformation of the aminoarabinoside **12**.

The ^{1}H-n.m.r. spectrum in D_2O indicates that **12** exists in the $^2T_3$ or E_3 conformation. In either of these conformations, diaxial relationships exist between the C-2 amino group on the one hand, and the glycosidic oxygen and C-3 hydroxyl group on the other. In the deamination of **12**, **10** and **14** were the sole products, **14** being formed in greater amount.

It is interesting that in each of the three aminoglycosides (**3**, **13**, and **12**) studied, the glycosidic methoxyl group has an axial conformation, probably due to the anomeric effect[28].

2-*O*-Methyl-D(or L)-ribose, which was required as a reference compound, was prepared as follows. Methyl α-L-arabinopyranoside[31], prepared by the benzoate ester route[32] previously used in the D series, was converted into the isopropylidene acetal **16** (80%). Oxidation with methyl sulphoxide–acetic anhydride[33] gave the required



ketone **18** (18%) together with the thioether **17** (70%); both products were crystalline. When **18** was reduced with sodium borohydride in ethanol, only the ribopyranoside **19** was formed; none of the arabinoside **16** was detected. Methylation of **19** with methyl iodide and sodium hydride in *N,N*-dimethylformamide gave the ether **20** as a homogeneous syrup (99%). Hydrolysis of **20** with aqueous sulphuric acid gave 2-*O*-methyl-L-ribose (**21**) having chromatographic properties identical to those of the major deamination product of **12**; **21** was converted into the crystalline dithioacetal derivative **22**. The synthesis of **21** has also been reported by Haines and Lundie[34], who used a similar route from benzyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside.

In the β-series, we found that borohydride reduction of methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose was relatively unspecific and gave both *ribo* and *arabino* products. It appears that lithium aluminium hydride[34,35] and catalytic hydrogenation[35] are more specific.

EXPERIMENTAL

Melting points are uncorrected. I.r. spectra were recorded for potassium bromide discs, or for films, with a Hilger and Watts Infrascan spectrophotometer. Mass spectra were recorded with an A.E.I. MS-9 mass spectrometer. N.m.r. spectra were recorded with a Perkin–Elmer R10 spectrometer at 60 MHz or a Bruker KIS HX5 spectrometer at 90 MHz, with tetramethylsilane or sodium 3-trimethylsilylpropane-1-sulphonate as internal standard. Specific rotations were measured with a Bendix–Ericson ETL-NPL 143A automatic polarimeter (path length, 1 cm).

Adsorption chromatography was performed with silica gel (Hopkin and Williams). For t.l.c., Kieselgel G (Merck) was used as adsorbent; carbohydrates were detected with anisaldehyde–sulphuric acid[36], and epoxides with sodium iodide and Methyl Red[37].

Analytical paper chromatography (p.c.) was performed on Whatman No. 1 paper; on a preparative scale, Whatman 3MM paper was used. The descending front technique was used with the following solvents: *A*[38], ethyl acetate–pyridine–water–acetic acid (5:5:3:1) in the trough and ethyl acetate–pyridine–water (40:11:6) in the tank; and *B*, 1-butanol–pyridine–water (3:1:1). Free sugars were detected with aniline hydrogen phthalate[19], glycols with periodate and Schiff's reagent[18], amines with ninhydrin[39], and epoxides with sodium iodide and Methyl Red[37]. Evaporations were performed under reduced pressure below 40° on a rotary evaporator.

*Ammonolysis of methyl 2,3-anhydro-5-*O*-*p*-nitrobenzoyl-β-*D*-ribofuranoside* (**2**). — The epoxide **2** (4.53 g) was heated with conc. aqueous ammonia (45 ml) in a Carius tube at 100° for 17 h. The amber solution was evaporated to dryness and the residue extracted with water (100 ml). The solution was poured through a column of Dowex 1 (HO^-) resin (50 ml), and the combined washings (300 ml) were evaporated to give a syrup (2.48 g, 99%). Paper chromatography (solvent *A*) revealed two ninhydrin-positive compounds, R_{GLCN} 1.65 and 1.55, corresponding to **3** and **5** in the ratio ~10:1.

The crude syrup (2.00 g) was dissolved in water (10 ml), and acetic anhydride (1.6 ml) was added with ice-cooling. The solution was warmed at 50° for 10 min and then evaporated to dryness. Trituration of the syrup with ethyl acetate gave impure **4** (1.75 g, 70%), m.p. 98–102°. Recrystallised from ethanol–ethyl acetate, **4** had m.p. 106–108°; lit.[5] m.p. 107–109°, lit.[6] 105–106°.

*Methyl 3-amino-3-deoxy-β-*D*-xylofuranoside* (**3**). — The *N*-acetyl derivative **4** (1.00 g) was heated with saturated, aqueous barium hydroxide (50 ml) at 90–100° for 14 h. The cooled solution was neutralised with solid CO_2, filtered through Hyflo, and evaporated to give a colourless syrup, which was dissolved in water (25 ml). The solution was passed through a column of Amberlite IRC-50 (H^+) resin (70 ml), and methanol–water (1:1, 200 ml) eluted impurities. Elution with 2M ammonia in methanol–water (1:1, 220 ml) afforded **3** as a chromatographically pure, colourless syrup (750 mg, 94%), $[\alpha]_D$ −82.4° (*c* 1.10, ethanol); ν_{max}^{film} 3280 and 3370 cm^{-1} (OH, NH). N.m.r. (90 MHz, D_2O) data: τ 5.13 (s, 1 H, $J_{1,2}$ <0.5 Hz, H-1), 5.65 (m, 1 H, H-4), 5.96 (d, 1 H, $J_{1,2}$ <0.5, $J_{2,3}$ 2.6 Hz, H-2), 6.24 (m, 2 H, H-5,5'), 6.60 (s, 3 H, OMe), 6.63 (dd, 1 H, $J_{2,3}$ 2.6, $J_{3,4}$ 6.0 Hz, H-3).

*Reaction of methyl 2,3-anhydro-β-*D*-ribofuranoside* (**1**) *with azide ion.* — Compound (3.29 g) was dissolved in 2-methoxyethanol (33 ml) and water (11 ml), sodium azide (5.95 g) and ammonium chloride (2.42 g) were added, and the mixture was stirred at the boiling point for 28 h. Evaporation of the solvents *in vacuo*, followed by extraction of the residue with ethyl acetate, yielded a red syrup (4.85 g) which was shown by t.l.c. to contain two products. The mixture was chromatographed on silica gel (130 g); elution with chloroform containing methanol (1.5%) gave a mixture of both components (1.01 g). Subsequent elution with 98:2 chloroform–methanol afforded a homogeneous syrup (2.89 g, 68%), from which a pure sample of methyl 3-azido-3-deoxy-β-D-xylofuranoside (**6**) was obtained by distillation (75–80°/0.01 mmHg); ν_{max}^{film} 3380 (OH) and 2120 cm^{-1} (N_3).

Anal. Calc. for $C_6H_{11}N_3O_4$: C, 38.10; H, 5.84; N, 22.25. Found: C, 38.47; H, 5.80; N, 22.40.

Rechromatography of the first fraction on silica gel (30 g), with elution by benzene–ether (6:4), gave **8** as a homogeneous syrup (107 mg, 2.5%) which distilled at 70–75°/0.05 mmHg, and crystallised on standing; m.p. 77–78; ν_{max}^{KBr} 3400 (OH) and 2128 cm^{-1} (N_3).

Elution with benzene–ether (1:1) gave more of **6** (750 mg, total 85%).

Conventional treatment of **6** with excess of *p*-nitrobenzoyl chloride in pyridine yielded the bis(*p*-nitrobenzoate) **7** (77%), m.p. 103–104° (from methanol), $[\alpha]_D$ +16° (*c* 0.75, chloroform). N.m.r. (60 MHz, $CDCl_3$) data: τ 1.76 (s, 8 H, Ar), 4.49 (br s, 1 H, H-2), 4.81 (s, 1 H, H-1), 5.32 (m, 4 H), and 6.49 (s, 3 H, OMe).

Anal. Calc. for $C_{20}H_{17}N_5O_{10}$: C, 49.30; H, 3.50; N, 14.38. Found: C, 49.56; H, 3.28; N, 14.32.

Similar treatment of **8** afforded the bis(*p*-nitrobenzoate) **9** (74%), m.p. 196–198° (from methanol), $[\alpha]_D$ −46° (*c* 0.8, chloroform).

Anal. Found: C, 49.41; H, 3.70; N, 14.47.

Reduction of azide **6**. — Azide **6** (400 mg) in ethanol (9 ml) was hydrogenated at atmospheric pressure over 5% palladium–charcoal (160 mg). After removal of the catalyst by filtration, the solution was evaporated to a colourless syrup (316 mg, 96%). P.c. (solvent *A*) showed one ninhydrin-positive compound having the same R_{GLCN} value as **3**. The amine was dissolved in water (7 ml), and acetic anhydride (7 ml) was added with stirring. After 20 min, the solvents were evaporated and the residue was crystallised from ethyl acetate. Recrystallised from ethanol–ethyl acetate, the amide **4** (205 mg, 52%) had m.p. 106–108° and was indistinguishable from the sample prepared by ammonolysis.

*Ammonolysis of methyl 2,3-anhydro-5-*O*-p-nitrobenzoyl-α-*D*-ribofuranoside* (**11**). — The epoxide **11** (5.50 g) was heated with conc. aqueous ammonia (55 ml) in a Carius tube at 100° for 18 h. The solution was evaporated to dryness, the residue extracted with water, and the extract evaporated to give a syrup (3.01 g, 99%) which contained (p.c., solvent *A*) two components reactive to ninhydrin (R_{GLCN} 1.40 and 1.55).

The syrup (1.50 g) was dissolved in water (3 ml) and chromatographed[17] on Dowex 1 (HO^-) resin (430 ml) with water (3 ml/min); the elution was monitored by using a flow-through cell in the automatic polarimeter. Fractions (50 ml) were collected; fractions 8–11 (*A*) contained the amine of lower R_F value, and fractions 13–18 (*B*) contained the second amine. The fractionation was repeated on the remaining syrupy mixture, and the appropriate fractions were combined.

Evaporation of fraction *A* yielded a colourless syrup (880 mg, 29%) which gave crystalline **13**, m.p. 122–123° (from ethanol–heptane), $[\alpha]_D$ +229° (*c* 1.0 methanol), ν_{max}^{KBr} 3320 cm^{-1} (OH, NH); lit.[5] m.p. 122–123°, $[\alpha]_D$ +236° (chloroform); lit.[9] m.p. 117–119°, $[\alpha]_D$ +194° (chloroform). Montgomery *et al.*[9] misquote the m.p. from Ref. 5. N.m.r. (90 MHz, D_2O) data: τ 5.07 (d, 1 H, $J_{1,2}$ 4.5 Hz, H-1), 5.80 (m, 1 H, H-4), 6.04 (dd, 1 H, $J_{1,2}$ 4.5, $J_{2,3}$ 8.0 Hz, H-2), 6.30 (m, 2 H, H-5,5′), 6.57 (s, 3 H, OMe), and 6.60 (t, 1 H, $J_{2,3} = J_{3,4} = 8$ Hz, H-3).

Evaporation of fraction *B* gave 1.86 g (62%) of a colourless syrup from which pure **12** crystallised, m.p. 80–81° (from ethanol–heptane), $[\alpha]_D$ +128° (*c* 1.0 methanol), ν_{max}^{KBr} 3310 cm^{-1} (OH, NH); lit.[9] m.p. 75–77°, $[\alpha]_D$ +100.8° (chloroform). N.m.r. (90 MHz, D_2O) data: τ 5.19 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 5.98 (m, 1 H, H-4), 6.17 (dd, 1 H, $J_{2,3}$ 3.8, $J_{3,4}$ 2.0 Hz, H-3), 6.26 (m, 2 H, H-5,5′), 6.59 (s, 3 H, OMe), 6.81 (dd, 1 H, $J_{1,2}$ 2.0, $J_{2,3}$ 3.8 Hz, H-2).

Anal. Calc. for $C_6H_{13}NO_4$: C, 44.10; H, 7.98; N, 8.59. Found: C, 44.08; H, 8.12; N, 8.46.

Deamination of aminodeoxyglycosides with nitrous acid. — (*a*) *Methyl 3-amino-3-deoxy-β-*D*-xylofuranoside* (**3**). To a cooled (0°) solution of **3** (222 mg) in aqueous acetic acid (25% v/v, 6.5 ml) was added sodium nitrite (100 mg), and the mixture was kept at 4° overnight. Evaporation of the solution afforded a pale-yellow syrup, which was examined by p.c. (solvent *B*); the epoxide spray showed the presence of **1** (R_F 0.75) and the glycol spray detected pentosides at R_F 0.58. A preparative chromatogram was performed (solvent *B*), the band of R_F 0.58 was eluted with water, and the com-

ponents were subjected to acid hydrolysis (0.25M sulphuric acid, 1 h, 100°). Paper chromatography of the hydrolysate (solvent *B*, aniline hydrogen phthalate spray) showed the presence of ribose (R_F 0.30) and xylose (R_F 0.25) in the ratio ~1:2.

The aqueous solution of deamination products was continuously extracted with ether for 5 h, giving a syrup (147 mg, 74%) consisting mainly of **1**. The syrup (140 mg) was treated with *p*-nitrobenzoyl chloride (300 mg) in pyridine (4 ml) overnight. Isolation of the product gave the *p*-nitrobenzoate **2** (246 mg, 85%), m.p. 98–99°, indistinguishable from an authentic sample.

(*b*) *Methyl 3-amino-3-deoxy-α-*D*-xylofuranoside* (**13**). The xyloside **13** (30 mg) in aqueous acetic acid (25% v/v, 1 ml) was treated with sodium nitrite (13 mg) and kept at 4° for 16 h. Solvents were evaporated, the residue was dissolved in water, and sodium ions were removed with a short column of Amberlite IRC-50 (H^+) resin. P.c. (solvent *B*) showed the presence of an unidentified compound (R_F 0.76) reactive to aniline hydrogen phthalate, epoxide **10** (R_F 0.69), and pentosides (R_F 0.53). The pentosides were isolated from a preparative chromatogram (solvent *B*), and hydrolysed with aqueous sulphuric acid (0.25M, 1 h, 100°). P.c. (solvent *B*) showed the presence of ribose (R_F 0.30) and xylose (R_F 0.25) in the ratio ~3:1.

(*c*) *Methyl 2-amino-2-deoxy-α-*D*-arabinofuranoside* (**12**). The glycoside (1.0 g) was dissolved in aqueous acetic acid (25% v/v, 30 ml) and treated with sodium nitrite (430 mg) at 4° overnight. After evaporation of solvent, the residue was dissolved in water (20 ml) and the solution passed through a column of Amberlite IRC-50 (H^+) resin (10 ml). The aqueous eluate, after evaporation, was examined by p.c. (solvent *B*). 2-*O*-Methyl-D-ribose (**14**, R_F 0.51) was the major product, detected by aniline hydrogen phthalate and by the characteristic colour (yellow becoming green)[40] with the periodate–Schiff's reagent spray. Methyl 2,3-anhydro-α-D-ribofuranoside (**10**) was detected with the epoxide spray, as a minor component.

The crude, deionised deamination product (0.98 g) was stirred, at 0°, with conc. hydrochloric acid (1 ml) and ethanethiol (3.4 ml) for 30 min. Water (3.5 ml) was added and stirring continued for 30 min. After neutralisation with conc. aqueous ammonia, the mixture was evaporated to dryness, the residue dissolved in water (3 ml), and the solution subjected to continuous extraction with ethyl acetate for 3 h. The crude diethyl dithioacetal (700 mg) was chromatographed on silica gel (20 g). Benzene–ether (7:3) eluted the chromatographically homogeneous dithioacetal (400 mg) [n.m.r. (60 MHz, $CDCl_3$) data: τ 6.43 (s, 3 H, OMe)]. Treatment of the dithioacetal (160 mg) with *p*-nitrobenzoyl chloride (580 mg) in pyridine (7 ml) gave a yellow syrup (400 mg, 83%) which, on treatment with methanol, afforded a yellow, amorphous solid. "Recrystallisation" from methanol gave pure 2-*O*-methyl-3,4,5-tri-*O*-(*p*-nitrobenzoyl)-D-ribose diethyl dithioacetal (**15**), m.p. 54–58° (preliminary softening), $[\alpha]_D$ +73° (*c* 1.3, chloroform). The physical and spectral properties were identical, apart from the sign of optical rotation, with those of an authentic sample of the L isomer (**22**) whose synthesis is described below.

*Methyl 3,4-O-isopropylidene-α-*L*-arabinopyranoside* (**16**). — Methyl α-L-arabinopyranoside[31], prepared from L-arabinose by the benzoate route[32], was

stirred with acetone (60 ml) and 2,2-dimethoxypropane (4.0 g) in the presence of toluene-*p*-sulphonic acid (80 mg) for 30 min. The solution was neutralised with solid carbonate, filtered, and evaporated, and the syrupy residue was partitioned between chloroform and aqueous sodium hydrogen carbonate. The dried chloroform layer, on evaporation and treatment of the resulting syrup with light petroleum, gave the crystalline acetal **16** (6.12 g, 80%). Recrystallisation from 2-propanol gave pure **16**, m.p. 72–73°; lit.[41], m.p. 73–74° for the D isomer.

Oxidation of **16** *with methyl sulphoxide–acetic anhydride.* — The acetal **16** (4.40 g) was dissolved in methyl sulphoxide (50 ml), acetic anhydride (35 ml) was added, and the mixture kept at room temperature for 24 h. The products were isolated by using chloroform and water, care being taken that the final chloroform solution was neutral. The resulting yellow syrup (5.5 g) contained two products (t.l.c.), which were separated by chromatography on silica gel (150 g). Benzene–ether (9:1) eluted methyl 3,4-*O*-isopropylidene-2-*O*-methylthiomethyl-α-L-arabinopyranoside (**17**; 4.10 g, 70%), which crystallised from ether–light petroleum; m.p. 56–57°, $[\alpha]_D$ +46.5° (*c* 1.0 chloroform). N.m.r. (60 MHz, $CDCl_3$) data: τ 5.22 (s, 2 H, SCH_2O), 6.60 (s, 3 H, OMe), 7.89 (s, 3 H, SMe), 8.50, 8.69 (2 s, 6 H, CMe_2), 5.78 (d, 1 H, $J_{1,2}$ ~8 Hz, H-1), 6.07, 6.18 (m, 2 H, H-5,5'). Mass spectrum: *m/e* 264 (M) and 249 (M − CH_3).

Anal. Calc. for $C_{11}H_{20}O_5S$: C, 49.79; H, 7.63. Found: C, 50.04; H, 7.64.

Benzene–ether (1:1) then eluted methyl 3,4-*O*-isopropylidene-α-L-*erythro*-pentopyranosid-2-ulose (**18**; 800 mg, 18%), which crystallised from ether–light petroleum; m.p. 89–90°, $[\alpha]_D$ +9.4° (*c* 0.5, chloroform); ν_{max}^{KBr} 1760 cm^{-1} (C=O). N.m.r. (60 MHz, $CDCl_3$) data: τ 5.19 (s, 1 H, H-1), 5.23 (m, 2 H, H-3,4), 5.93, 6.01 (m, 2 H, H-5,5'), 6.48 (s, 3 H, OMe), 8.55, 8.63 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_9H_{14}O_5$: C, 53.50; H, 6.93. Found: C, 53.34; H, 6.92.

Methyl 3,4-O-isopropylidene-α-L-ribopyranoside (**19**). — To a solution of **18** in ethanol (10 ml) was added sodium borohydride (0.25 g), and the mixture was kept at room temperature overnight. After addition of acetone (20 ml), the solution was evaporated to dryness and the product isolated by using chloroform. The resulting syrup (516 mg, 99%) was chromatographically homogeneous, and crystallised from ether–light petroleum to give pure **19**, m.p. 92–93°, $[\alpha]_D$ −138° (*c* 0.4 chloroform). N.m.r. (60 MHz, $CDCl_3$) data: τ 5.40 (d, 1 H, $J_{1,2}$ 4.4 Hz, H-1), 6.59 (s, 3 H, OMe), 8.52 and 8.68 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_9H_{16}O_5$: C, 52.90; H, 7.84. Found: C, 52.78; H, 7.78.

Methyl 3,4-O-isopropylidene-2-O-methyl-α-L-ribopyranoside (**20**). — To a solution of **19** (350 mg) in *N*,*N*-dimethylformamide (8 ml) was added sodium hydride (300 mg), and the suspension was swirled for 15 min. The mixture was then cooled to 0°, methyl iodide (1.7 ml) was added slowly until the effervescence ceased, and the combined solvents were removed under reduced pressure. The residue was extracted with chloroform to give **20** as a chromatographically homogeneous syrup (369 mg, 99%) which did not crystallise. A pure sample of **20** was obtained by distillation (40°/0.14 mmHg); $[\alpha]_D$ −86° (*c* 0.75, chloroform). N.m.r. (60 MHz, $CDCl_3$) data:

τ 5.20 (d, 1 H, $J_{1,2}$ 4.5 Hz, H-1), 5.48 (dd, 1 H, $J_{1,2}$ 4.5, $J_{2,3}$ 4.7 Hz, H-2), 6.49 (s, 3 H, OMe, probably glycosidic), 6.56 (s, 3 H, OMe), 8.47 and 8.65 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_{10}H_{18}O_5$: C, 55.05; H, 8.27. Found: C, 54.84; H, 8.38.

*2-O-Methyl-*L*-ribose* (**21**). — The methyl ether **20** (320 mg) was heated at 100° for 4 h with 0.25M sulphuric acid (10 ml). The solution was cooled and neutralised ($BaCO_3$), and the filtrate was evaporated to give a colourless syrup which was chromatographically homogeneous (solvent *B*, R_F 0.50) and gave the same colours (red–brown with aniline hydrogen phthalate, and green with periodate–Schiff's reagent) as the major deamination product of **12**.

*2-O-Methyl-3,4,5-tri-*O-(p-*nitrobenzoyl*)-L-*ribose diethyl dithioacetal* (**22**). — 2-*O*-Methyl-L-ribose (**21**, 230 mg) was stirred with conc. hydrochloric acid (0.2 ml) and ethanethiol (1 ml) at 0° for 30 min. Water (1 ml) was added and stirring continued for a further 30 min. The solution was neutralised with aqueous ammonia and evaporated to dryness. The residue was dissolved in water (3 ml) and extracted continuously with ethyl acetate for 3 h, affording a chromatographically homogeneous syrup (t.l.c.) whose ^{1}H-n.m.r. spectrum showed a 1:2 ratio for MeO-2 (τ 6.42) and SEt methyl signals (τ 8.74).

The diethyl dithioacetal (100 mg) in pyridine (4 ml) was treated with *p*-nitrobenzoyl chloride (370 mg) at room temperature overnight. Isolation of the product with chloroform afforded a yellow syrup (234 mg, 78%), which was "crystallised" from methanol to give **22**, m.p. 55–59° (preliminary softening), $[\alpha]_D$ −71° (*c* 1.3, chloroform); N.m.r. (60 MHz, $CDCl_3$) data: τ 1.89 (m, 12 H, Ar), 6.24 (s, 3 H, OMe), 7.24 (2 q, 4 H, SCH_2), and 8.74 (2 t, 6 H, C–CH_3).

Anal. Calc. for $C_{31}H_{34}N_3S_2O_{13}$: C, 51.80; H, 4.32; N, 5.88. Found: C, 51.60; H, 4.33; N, 6.20.

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