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# APPLICATION OF THE BUCHERER REACTION TO CARBOHYDRATE DERIVATIVES*†

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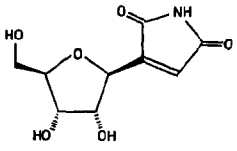
ABSTRACT

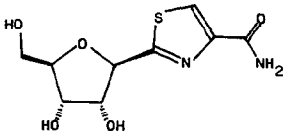
The Bucherer reaction of carbohydrate derivatives having a free carbonyl group proceeds normally, giving mainly the expected spiro-hydantoin derivatives. With derivatives having a free aldehydo group attached to an acetal ring in an α-position, the acetal ring is opened *via* an elimination reaction yielding unsaturated hydantoin derivatives. These reactions were studied using 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose, 2,3:4,5-di-*O*-isopropylidene-D-arabinose, -D-ribose, and -D-xylose, 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose, 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdo-1,4-mannofuranose, 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose, and 2,3:4,5-di-*O*-isopropylidene-β-D-*arabino*-hexosulo-2,6-pyranose.

## INTRODUCTION

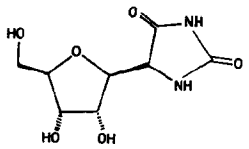
For several years, we have been engaged in the synthesis of nucleoside analogs, looking for compounds with cytostatic activity. Some *C*-nucleosides, *e.g.*, the natural product showdomycin[1] (**1**) and the synthetic compound tiazofurin[2] (**2**), have cytostatic activity. Hence, the corresponding hydantoin *C*-glycoside **3** was chosen for synthesis since the aglycon is similar to that of the aforementioned *C*-nucleosides.




1 (showdomycin)




2 (tiazofurin)

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*Dedicated to Professor Rezső Bognár in the year of his 75th birthday.
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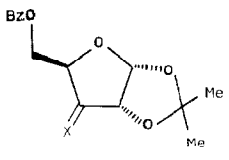
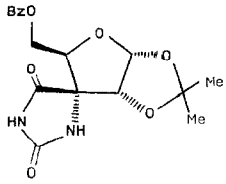
RESULTS AND DISCUSSION

*The Bucherer reaction of keto derivatives.* — Hydantoins can be synthesised conveniently by the Bucherer reaction[3,4], which has been applied only once to a carbohydrate derivative[5], namely, the 3-pentosulose derivative (**4**) for the introduction of an amino acid function. When the normal conditions of the Bucherer reaction were applied [KCN, $(NH_4)_2CO_3$ in $H_2O$–EtOH (1:1) at 50°], only the corresponding imine **5** was formed. In order to obtain the hydantoin **6**, the reaction had to be carried out in the presence of carbon dioxide using a pressure of 50 kg/cm$^2$. The product had the 3-amino-3-deoxy-D-*ribo* configuration as proved by its conversion into the 3,5-lactone **7**. Thus, **6** must have been formed *via* the *ribo*-cyanohydrin, which is formed under kinetic control, and not from the thermodynamically stable, *arabino* diastereomer[6].

1,2:5,6-Di-*O*-isopropylidene-α-D-hexofuranos-3-ulose (**8**) reacted smoothly under the normal Bucherer conditions, affording, besides traces of the cyanohydrin **10**, the corresponding 3-*C*-carbamoyl derivative **11** and the spiro-hydantoin **14** in



**4** X = O
**5** X = NH



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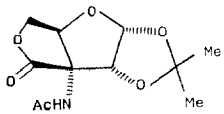

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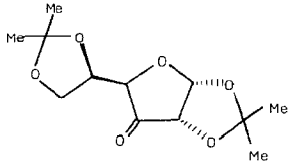

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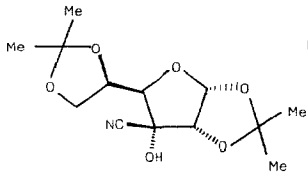

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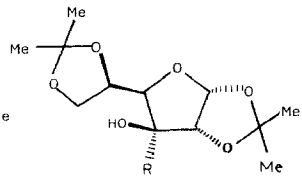
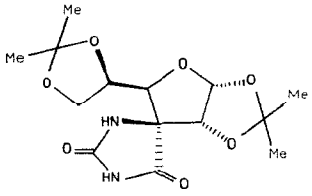
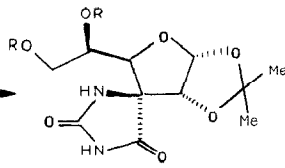


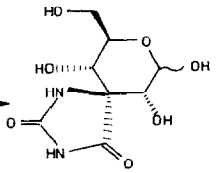
**10** R = CN
**11** R = $CONH_2$
**12** R = $CH_2NH_2$
**13** R = $CH_2NHAc$



**14**



**15** R = H
**16** R = Ac

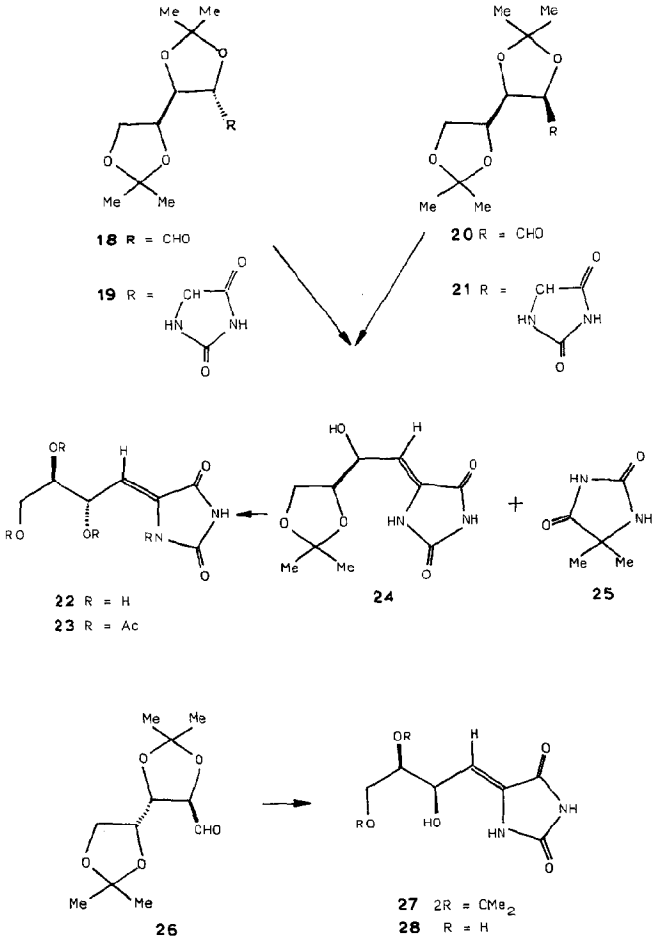


**17**

the ratio 1:3. The $^1$H-n.m.r. data showed each of these derivatives to possess the *gluco* configuration; consequently, **11** and **14** must have been formed from **10**, which is the thermodynamically stable intermediate[6]. In order to check this hypothesis, the known[6,7] diastereomeric cyanohydrins **9** and **10** were submitted to the Bucherer reaction. The proportions of products from each compound were as mentioned above, which means that the interconversion **9** → **10** is much faster than the formation of the further products. The carboxamide **11** is not an intermediate in the conversion **8** → **14**, since it was unchanged under the reaction conditions.

Because of the discrepancies in the data given in the literature[6,8] for the stereochemistry of **11**, it was proved unambiguously. Thus, reduction of **11** with lithium aluminium hydride gave the amine **12** which, on partial *N*-acetylation, afforded **13**, identical with the known[7] D-*gluco* derivative.

The assignment of the configuration of **14** was based on the $^1$H-n.m.r. data. Thus, the pattern of resonances for the $CMe_2$ groups was similar to that of **11**, *i.e.*,



three had similar shifts (1.40, 1.35, and 1.26 p.p.m.), whereas the fourth was shifted downfield significantly (1.56 p.p.m.). This situation can be explained by the influence of the 4-oxo group of the hydantoin ring on the *endo*-methyl group of the 1,2-*O*-isopropylidene moiety; a similar effect would be expected for the *allo* isomer, but on the *endo*-methyl group of the 5,6-*O*-isopropylidene moiety. However, partial acid hydrolysis of **14** afforded the 1,2-*O*-isopropylidene derivative **15**, which was converted into its 5,6-diacetate **16**. In the $^1$H-n.m.r. spectra of **15** and **16**, the $\Delta\delta$ values (~0.2 p.p.m.) for the resonances of the $CMe_2$ groups were large and identical, thereby proving the close proximity of the carbonyl *endo*-methyl groups and hence the D-*gluco* configuration.

Hydrolysis of **15** with acid gave the free sugar derivative **17**, the $^{13}$C-n.m.r. spectrum of which indicated a 3:2 $\alpha\beta$-mixture of the pyranose forms.

*The Bucherer reaction of aldehydo derivatives.* — When the Bucherer reaction was applied to 2,3:4,5-di-*O*-isopropylidene-D-arabinose (**18**), the expected hydantoin **19** was not formed, but a mixture of the unsaturated mono-*O*-isopropylidene derivative **24** (with the *Z* configuration) and 5,5-dimethylhydantoin (**25**) was obtained. As separation of these two compounds was difficult, the mixture was hydrolysed, when **24** was converted into the triol **22** which could be separated easily from the unchanged **25** and, on acetylation, gave the expected tetra-acetate **23**.

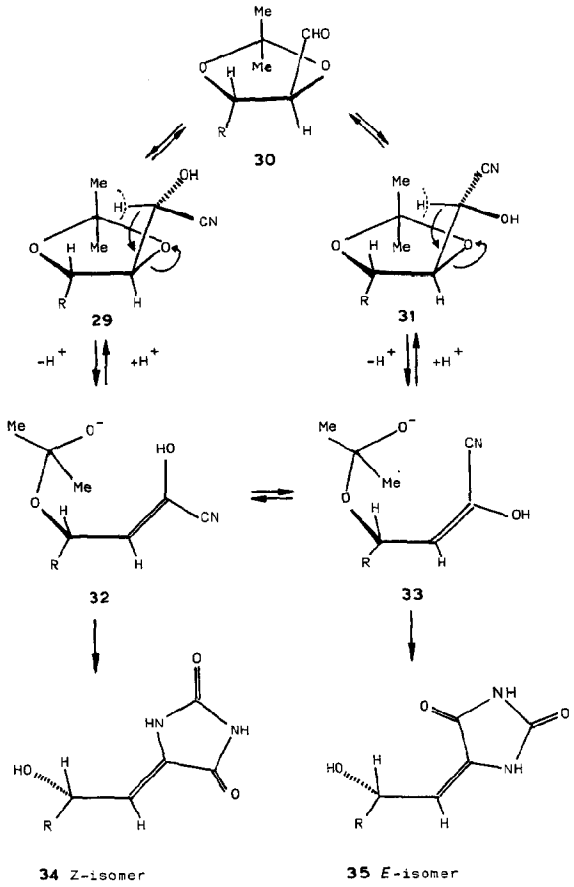
The formation of **24** and **25** indicates that the acetal group vicinal to the aldehyde group is eliminated *via* formation of a double bond, and that the liberated acetone undergoes a Bucherer reaction to afford **25**. Accordingly, the proportions of **25** and the unsaturated derivatives formed are similar but, as isolation of the latter compounds is difficult, their yields are always much lower.

During the elimination reaction, the chirality of C-2 is destroyed and therefore the D-*ribo* isomer **20** should yield the same products. When known[9] **20** was submitted to the Bucherer reaction, **24** and **25** were formed exclusively.

When the Bucherer reaction was applied to 2,3:4,5-di-*O*-isopropylidene-D-xylose (**26**), which differs from **18** in the chirality of both C-2 and C-3, in addition to **25**, only **27**, the diastereomer of **24**, was obtained. Hydrolysis of the mixture converted **27** into **28**, which was separated easily from **25**.

*The mechanism of the elimination reaction.* — The anomalous Bucherer reaction described above can be explained by the following mechanism.

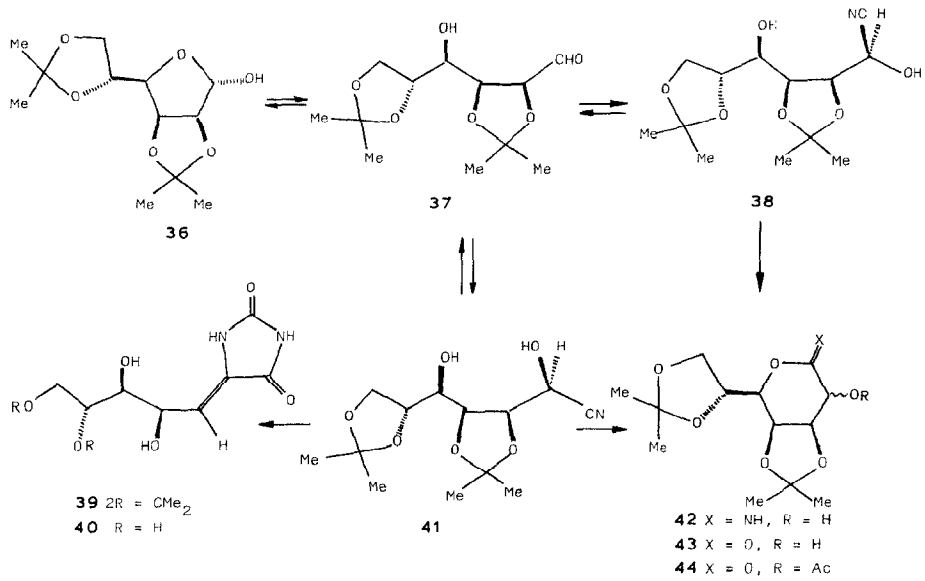
Aldehydes (**30**) substituted in the $\alpha$-position by an oxygen atom incorporated into an acetal ring can react with cyanide to give an equilibrium mixture of the diastereomeric cyanohydrins **29** and **31**. Because of the strong electron-withdrawing properties of the geminal hydroxyl and cyano groups, H-1 can be removed even under the very weakly basic conditions of the Bucherer reaction, leading simultaneously to *trans* elimination of O-2 and yielding the unsaturated derivatives **32** and **33**, respectively, from which the *O*-isopropylidene group is lost and the corresponding unsaturated hydantoins with the *Z* (**34**) and *E* configuration (**35**) are formed. The preference for the formation of the *Z* isomer **34** can be explained by the different stability of the intermediates **32** and **33**, since, only in the former, can




the OH group form a hydrogen bond with the charged oxygen atom of the *O*-isopropylidene group. In the proton-coupled $^{13}$C-n.m.r. spectrum of each of the unsaturated hydantoins, the resonance of C-5 appeared as a doublet with $J$ ~5 Hz, proving the *Z* configuration of the double bond.

*Scope of the anomalous Bucherer reaction.* — The Bucherer reaction of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**36**), in which the free aldehyde group is present only under equilibrium conditions (**37**), afforded, in addition to 5,5-dimethylhydantoin (**25**) and the unsaturated hydantoin derivative **39** (separated as the tetraol **40**), a mixture of the corresponding D-*glycero*-D-*galacto*- and -D-*talo*-heptonic acid δ-lactone derivatives **43**, which was isolated after acetylation (→ **44**) as the main component (51%). The formation of the lactones **43** can be explained on the basis of the diastereomeric cyanohydrins **38** and **41** in which attack of HO-4 on the cyano group affords **43** *via* the imine **42**.

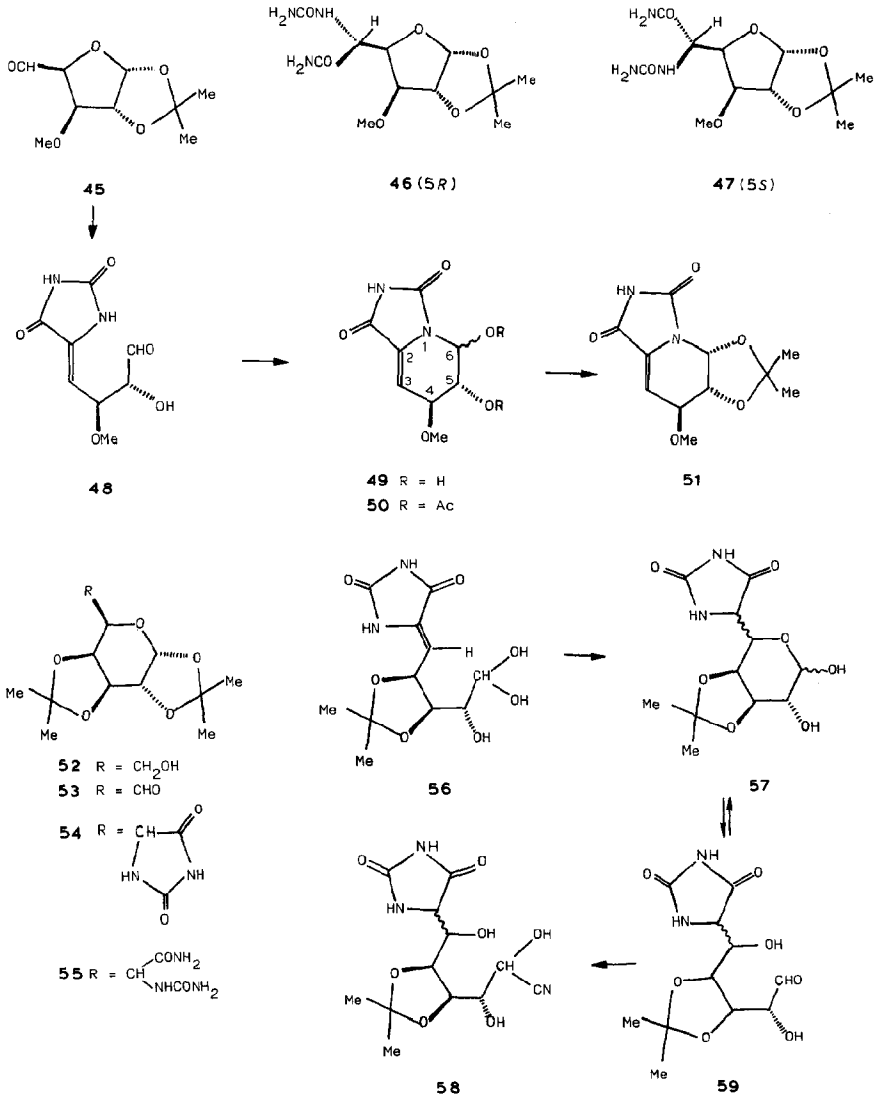
1,2-*O*-Isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdo-1,4-furanose (**45**) contains an aldehyde group α to an acetal-linked oxygen of an oxolane and not a dioxolane ring. From the multicomponent mixture of products obtained on applica-




tion of the Bucherer reaction to **45**, in addition to the diastereomeric 5-deoxy-5-ureidohexuronamide derivatives **46*** (2.8%) and **47** (0.2%), corresponding to the side-products of the normal reaction[3,4], and 5,5-dimethylhydantoin (**25**), the pyrido-imidazole derivative **49** was obtained and isolated as the diacetate **50** (7%). Formation of the fused ring system in **49** from the acyclic intermediate **48** is not surprising since similar intramolecular cyclisation occurs spontaneously[11]. The $^1$H-n.m.r. spectra indicated **49** and **50** to be mixtures of two isomers, differing mainly in the shift of the resonances of the vinyl protons ($\Delta\delta_{H\text{-}3}$ 0.18 and 0.14 p.p.m., respectively) and the methoxyl groups ($\Delta\delta_{OMe}$ 0.15 and 0.10 p.p.m., respectively). Since the $J_{5,6}$ value was the same (3 Hz) for the anomeric proton (H-6) of each isomer, they cannot differ in their anomeric configuration (each is an $\alpha$ anomer) but only in the steric arrangement of the lone pair of electrons of the bridgehead nitrogen (N-1). The crystalline *O*-isopropylidene derivative **51** could be obtained from **49** as a single isomer.

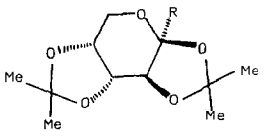
The Bucherer reaction of 1,2:3,4-di-*O*-isopropylidene-$\alpha$-D-*galacto*-hexodialdo-1,5-pyranose (**53**), prepared by oxidation[12] of **52**, yielded, in addition to the hydantoin derivative **54** (15.7%), which is the product of the normal reaction, the diastereomeric 6-ureidohepturonamides **55** (23%), which are usually only by-products, 5,5-dimethylhydantoin (**25**, 45%), and, instead of the expected unsaturated hydantoin derivative, only a saturated compound (**58**) which could be isolated in low yield (2%). Nevertheless, **58** must have been formed *via* the unsaturated compound **56** which can undergo further reactions **56**→**57**→**59**, affording finally **58** which according to n.m.r. represents one single isomer.

*The 5*R* configuration of **46** was established by X-ray crystallography[10].

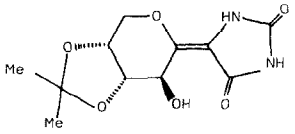



Application of the Bucherer reaction to 2,3:4,5-di-*O*-isopropylidene-β-D-*arabino*-hexosulo-2,6-pyranose (**61**), obtained from 2,3:4,5-di-*O*-isopropylidene-D-fructose (**60**) by oxidation[12], gave mixtures of diastereomers of the cyanohydrins **62** (2%) and the hydroxyamides **64** (7.3%), together with **25** (78%). The ratio of the diastereomers in **62** was the same (15:85) as in the equilibrium mixture obtained on treating **61** with potassium cyanide. After acetylation, the major component could be isolated as a single isomer **63**. The high yield of **25** makes it likely that **61** is converted, *via* the anomalous Bucherer reaction, mainly into **65** which, however, is not stable and decomposes.

Thus, aldehydes having an acetal ring in the α-position can undergo an



**60** R = $CH_2OH$
**61** R = CHO
**62** R = $CH(OH)CN$
**63** R = $CH(OAc)CN$
**64** R = $CH(OH)CONH_2$



**65**

anomalous Bucherer reaction *via* elimination of acetone, but the yields of the unsaturated hydantoin derivatives formed depend very much on the structure of the starting material.

## EXPERIMENTAL

*General methods.* — Organic solutions were dried ($Na_2SO_4$) and concentrated under diminished pressure. T.l.c. was performed on Kieselgel G with carbon tetrachloride–ethyl acetate (*A*, 3:1 and *B*, 1:1); *C*, ethyl acetate; ethyl acetate–ethanol (*D*, 9:1 and *E*, 3:1); *F*, ethyl acetate–methanol (8:2); and *G*, methanol. For detection, 0.1M potassium permanganate–M sulfuric acid (1:1) at 105° was used and, for hydantoin derivatives, chlorine–*o*-tolidine. Column chromatography was performed on Kieselgel 40 (63–200 $\mu$m). Melting points are uncorrected. Optical rotations were determined on 1% solutions, if not stated otherwise. I.r. spectra were recorded for KBr pellets with a Bruker IFS-85 spectrometer. The following characteristic $\nu_{max}$ data were recorded: hydantoins, 1800–1690; amides, 1660–1680; esters, 1740–1750; and lactones, 1770 $cm^{-1}$. $^1H$- (90 MHz) and $^{13}C$-n.m.r. spectra (25.2 MHz) were recorded at room temperature with Varian EM 390 and XL-100 FT spectrometers, respectively, for solutions in $CDCl_3$ (internal $Me_4Si$), $D_2O$, or $(CD_3)_2SO$ (internal sodium 4,4-dimethyl-4-silapentane-1-sulfonate).

Two general methods were used for the Bucherer reaction. Method *A*. To a solution of the carbohydrate derivative (10 mmol) in ethanol–water (1:1, 40 mL) were added ammonium carbonate (3.85 g, 40 mmol) and potassium cyanide (1.31 g, 20 mmol), the mixture was stirred in a closed vessel at 50° until all the starting material was consumed (t.l.c.) and then concentrated, and methanol was evaporated from the residue which was filtered with ethanol to remove the bulk of the inorganic salts and then processed as indicated. Method *B*. The reaction was carried out as described in method *A*, but 120 mL of the solvent, 80 mmol of ammonium carbonate, and 40 mmol of potassium cyanide were used.

*Bucherer reaction of 1,2:5,6-di-*O*-isopropylidene-α-*D*-ribo-hexofuranos-3-*

*ulose* (**8**). — Application of method *A*, for 48 h, to **8**[12] (25.8 g) and concentration of the ethanolic filtrate gave a semi-solid which was filtered with ether to yield crude **14** (17 g). Recrystallisation from ethanol–water (1:3, 80 mL) yielded 3-amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-*C*-spiro-5′-hydantoin (**14**; 12.25 g, 37.3%), m.p. 220–222°, $[\alpha]_D^{20}$ +48° (chloroform), $R_F$ 0.4 (solvent *B*). $^1$H-N.m.r. data ($CDCl_3$): δ 10.5 (bs, 1 H, NH), 7.3 (bs, 1 H, NH), 5.9 (d, *J* 4 Hz, H-1), 4.5 (d, *J* 4 Hz, H-2), 4.0 (m, 4 H, H-4,5,6,6), and 1.56, 1.40, 1.35, and 1.26 (4 s, each 3 H, 2 $CMe_2$).

*Anal.* Calc. for $C_{14}H_{20}N_2O_7$: C, 51.20; H, 6.14; N, 8.53. Found: C, 51.02; H, 6.12; N, 8.26.

Column chromatography (solvent *B*) of the material in the mother liquor gave 3-*C*-cyano-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**10**; 0.8 g, 2.8%), m.p. 98–99°, $[\alpha]_D^{20}$ +49° (chloroform), $R_F$ 0.8; lit.[7] m.p. 99–100°, $[\alpha]_D^{20}$ +51.6° (chloroform).

The fractions having $R_F$ 0.3 gave, after concentration and recrystallisation of the residue from acetone–light petroleum, 3-*C*-carbamoyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**11**; 4 g, 13.4%), m.p. 172–174°, $[\alpha]_D^{20}$ +35° (chloroform); lit.[6] m.p. 172.7–173.4°, $[\alpha]_D^{20}$ +40° (chloroform). $^1$H-N.m.r. data ($CDCl_3$): δ 6.65 and 6.23 (2 bs, 2 H, $NH_2$), 5.9 (d, *J* 4 Hz, H-1), 4.6 (s, 1 H, OH), 4.35 (d, *J* 4 Hz, H-2), 4.1 (m, 4 H, H-4,5,6,6), 1.6, 1.37, 1.35, and 1.3 (4 s, each 3 H, 2 $CMe_2$).

Similar results were obtained when, instead of **8**, the cyanohydrins **9**[7] or **10**[7] (28.5 g) were used.

*3-C-Acetamidomethyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose* (**13**). — To a stirred solution of amide **11** (3 g) in 1,4-dioxane (40 mL) was added lithium aluminium hydride (1.5 g), and the slurry was boiled for 4 h under reflux to give, after the usual processing, a semi-solid residue that was recrystallised from ether–light petroleum to afford **12** (2.4 g, 82.5%), m.p. 112–113°, $[\alpha]_D^{20}$ +39° (ethanol); lit.[7] m.p. 112–113.5°.

Treatment of **10** (1.9 g) with acetic anhydride (20 mL) in methanol (100 mL) and column chromatography of the product (solvent *C*) gave **13** (1.3 g, 60%), m.p. 117–118°, $[\alpha]_D^{20}$ +67° (ethanol), $R_F$ 0.35; lit.[7] m.p. 126–127°, $[\alpha]_D^{20}$ +67° (ethanol); lit.[13] m.p. 120–121°, $[\alpha]_D^{20}$ +63.8° (ethanol).

*3-Amino-3-deoxy-1,2-O-isopropylidene-α-D-glucofuranose-3-C-spiro-5′-hydantoin* (**15**). — A solution of **14** (1.6 g) in ethanol (20 mL), water (5 mL), and M hydrochloric acid (0.5 mL) was boiled for 45 min under reflux, then cooled, neutralised with sodium hydrogencarbonate, filtered, and concentrated, and the solid residue was filtered with ether. The dried crude **15** was boiled with ethanol (10 mL), the extract was cooled, filtered, and concentrated to 5 mL, and acetone was added to turbidity. Thereafter, the solution was filtered with charcoal and concentrated, and the residue was filtered with ether to give **15** (0.8 g, 57%), m.p. 98–102°, $[\alpha]_D^{20}$ +71° (water), $R_F$ 0.3 (solvent *C*). $^1$H-N.m.r. data [$(CD_3)_2SO$]: δ 7.75 (bs, 1 H, NH), 5.73 (d, *J* 4 Hz, H-1), 5.0 (bs, 2 H, HO-6, NH), 4.43 (d, *J* 4 Hz, H-2), 4.0 (d, *J* 7.5 Hz, HO-5), 3.4 (m, 4 H, H-4,5,6,6) and 1.48 and 1.25 (2 s, each 3 H, $CMe_2$).

*Anal.* Calc. for $C_{11}H_{16}N_2O_7$: C, 45.8; H, 5.6; N, 9.7. Found: C, 45.6; H, 5.7; N, 9.5.

Acetylation of **15** (0.7 g) with acetic anhydride (1 mL) in pyridine (2 mL) gave, after the usual processing, **16** (0.52 g, 58%), m.p. 114–116°, $[\alpha]_D^{20}$ +11° (chloroform), $R_F$ 0.65 (solvent *B*). $^1$H-N.m.r. data [$(CD_3)_2SO$]: $\delta$ 10.1 and 9.55 (2 bs, 2 H, NH), 5.88 (d, *J* 4 Hz, H-1), 4.72 (d, *J* 1 Hz, H-2), 4.44 (m, 4 H, H-4,5,6,6), 2.08 (bs, 6 H, 2 OAc), and 1.6 and 1.43 (2 s, each 3 H, $CMe_2$).

*Anal.* Calc. for $C_{15}H_{20}N_2O_9$: C, 48.4; H, 5.4; N, 7.5. Found: C, 48.4; H, 5.5; N, 7.4.

*3-Amino-3-deoxy-*D*-glucopyranose-3-*C*-spiro-5'-hydantoin* (**17**). — A solution of **14** (3.3 g) in trifluoroacetic acid (20 mL) and water (10 mL) was boiled for 30 min under reflux and then concentrated. Water and then ethanol were evaporated from the residue which was filtered with ethanol–acetone to give **17** (2.1 g, 84%), m.p. 236–238°, $[\alpha]_D^{20}$ +41° (water), $R_F$ 0.5 (solvent *D*). N.m.r. data ($D_2O$): $^1$H, $\delta$ 5.21 (d, *J* 3.5 Hz, H-1*e*), 4.73 (d, *J* 8 Hz, H-1*a*), 3.9 (d, *J* 3.5 Hz, H-2), 3.72 (d, *J* 8 Hz, H-2), 3.7 (m, 4 H, H-4,5,6,6); $^{13}$C, $\delta$ 179.5 and 162.0 (2 CO, 15-$\alpha$), 178.8 and 162.4 (2 CO, 15-$\beta$), 96.8 (C-1, 15-$\beta$), 94.0 (C-1, 15-$\alpha$), 74.2, 70.6, 70.0, 66.8, and 63.0 (C-2/6, 15-$\alpha$), and 77.7, 74.9, 73.2, 69.4, and 63.3 (C-2/6, 15-$\beta$) (ref. 26).

*Anal.* Calc. for $C_8H_{12}N_2O_7$: C, 38.7; H, 4.9; N, 11.3. Found: C, 38.6; H, 5.0; N, 11.3.

*The Bucherer reaction of 2,3:4,5-di-*O*-isopropylidene-*D*-arabinose* (**18**). — Compound **18**[14] (7.2 g) was treated according to method *A* for 24 h. The ethanolic filtrate was concentrated and the residue was subjected to column chromatography (solvent *C*).

The fractions containing material with $R_F$ 0.7 gave, on concentration, an oily mixture (7 g) of **24** and **25**. Part (2 g) of this mixture was recrystallised thrice from ethanol to give 5-(D-*erythro*-2-hydroxy-3,4-isopropylidenedioxybutylidene)imidazole-2,4-dione (**24**, 0.3 g), m.p. 208–210°. N.m.r. data [$(CD_3)_2SO$]: $^1$H, $\delta$ 11.06 and 10.06 (2 bs, 2 NH), 5.45 (d, *J* 9 Hz, H-1'), 5.33 (d, $J_{H,OH}$ 6 Hz, OH), 4.3 (m, H-2'), 3.9 (m, 3 H, H-3',4'), and 1.35 and 1.27 (2 s, each 3 H, $CMe_2$); $^{13}$C, $\delta$ 164.2 and 154.25 (2 CO), 130.5 (C-5), 110.8 (C-1'), 109.4 (acetal C), 78.6 (C-2'), 68.3 (C-3'), 66.7 (C-4'), and 27.3 and 26.3 (acetal Me).

*Anal.* Calc. for $C_{10}H_{14}N_2O_5$: C, 49.6; H, 5.8; N, 11.6. Found: C, 49.3; H, 5.9; N, 11.9.

Concentration of the mother liquors gave 5,5-dimethylhydantoin (**25**; 0.5 g), m.p. 170–174° (subl.); lit.[15] m.p. 174–175°. $^{13}$C-N.m.r. data [$(CD_3)_2SO$]: $\delta$ 185.1 (4 CO), 157.1 (2 CO), 61.0 (C-5), and 26.2 (2 Me).

*Hydrolysis of the mixture of* **24** *and* **25**. — A solution of the foregoing mixture (3.5 g) in acetic acid (35 mL) and water (140 mL) was concentrated at room temperature and the residue was subjected to column chromatography (solvent *C*). Concentration of the fraction containing material with $R_F$ 0.7 gave **25** (1.6 g, 84%).

Concentration of the fractions containing material with $R_F$ 0.15 and filtration of the residue with ethanol gave 5-(D-*erythro*-2,3,4-trihydroxybutylidene)imid-

azole-2,4-dione (**22**; 1.05 g, 32%), m.p. 155–156°, $[\alpha]_D^{20}$ −38° (water). N.m.r. data [$(CD_3)_2SO$]: $^1H$, δ 10.5 (bs, 2 H, 2 NH), 4.52 (d, *J* 7.5 Hz, H-1′), 4.2 (dd, *J* 7.5 and 6 Hz, H-2′), and 3.45 (m, 3 H, H-3′,4′,4′); $^{13}C$, δ 167 and 157 (2 CO), 132.6 (C-5), 113.95 (C-1′), 76.85 (C-2′), 69.7 (C-3′), and 64.9 (C-4′).

*Anal.* Calc. for $C_7H_{10}N_2O_5$: C, 41.6; H, 5.0; N, 13.8. Found: C, 41.5; H, 5.3; N, 13.7.

Acetylation of **22** (0.5 g) with pyridine (5 mL) and acetic anhydride (5 mL) and column chromatography (solvent *C*) of the product gave **23** (0.9 g, 84%), isolated as a colourless syrup, $[\alpha]_D^{20}$ +7°, $R_F$ 0.85. $^1H$-N.m.r. data ($CDCl_3$): δ 8.7 (bs, NH), 6.15 (bs, H-1′), 5.35 (m, H-2′), 4.2 (m, 3 H, H-3′,4′,4′), 2.65 (NAc), and 2.1 (bs, 9 H, 3 OAc). Mass spectrum: *m/z* 268 ([$M^+ - CH_2CO - CH_3COOH$], 18%), 226 (49), 184 (78), 165 (11), 144 ([AcO–CH=CH–OAc]$^+$, 29), 141 (50), 102 (18), and 43 (100).

*Anal.* Calc. for $C_{15}H_{18}N_2O_9$: C, 48.6; H, 4.9; N, 7.6. Found: C, 48.4; H, 5.0; N, 7.3.

*Bucherer reactions.* — *(a) 2,3:4,5-Di-*O*-isopropylidene-*D*-ribose* (**20**). The reaction of **20**[9] (0.8 g), as described for **18**, gave a product having $R_F$ 0.7, which was hydrolysed as for the mixture of **24** and **25**, to give, after similar processing, **25** (0.4 g, 93%) and **22** (0.1 g, 14.4%).

*(b) 2,3:4,5-Di-*O*-isopropylidene-*D*-xylose* (**26**). Reaction of **26**[16] (2.3 g), as described for **20**, gave **25** (0.8 g, 62.5%) and 5-(D-*threo*-2,3,4-trihydroxybutylidene)imidazole-2,4-dione (**28**; 0.3 g, 15%), m.p. 158–160°, $R_F$ 0.1 (solvent *C*), 0.7 (solvent *F*). N.m.r. data [$(CD_3)_2SO$]: $^1H$, δ 11.0 and 9.8 (bs, 2 H, 2 NH), 5.55 (d, *J* 7.5 Hz, H-1′), 4.5 (dd, *J* 7.5 and 3 Hz, H-2′), and 3.45 (m, 3 H, H-3′,4′,4′); $^{13}C$, δ 164.9 and 154.9 (2 CO), 130.2 (C-5), 112 (C-1′), 74.5 (C-2′), 67.6 (C-3′), and 62.6 (C-4′).

*Anal.* Calc. for $C_7H_{10}N_2O_5$: C, 41.6; H, 5.0; N, 13.8. Found: C, 41.4; H, 5.3; N, 13.7.

*(c) 2,3:5,6-Di-*O*-isopropylidene-α-*D*-mannofuranose* (**36**). Compound **36**[17] (5.3 g) was treated according to method *A* for 16 h. Column chromatography (solvent *C* then solvent *G*) of the product gave, first, a fraction (1 g), $R_F$ 0.7 (**25** + **39**), which was hydrolysed with aqueous acetic acid as described for the mixture of **24** and **25**, to give, after similar processing and column chromatography (solvent *F*), **25** (0.35 g, 11%) and 5-(D-*arabino*-2,3,4,5-tetrahydroxypentylidene)imidazole-2,4-dione (**40**; 0.1 g, 1.7%), m.p. 125–127°, $[\alpha]_D^{20}$ +19° (c 0.16, water), $R_F$ 0.35. $^1H$-N.m.r. data [$(CD_3)_2SO$]: δ 10 (bs, 1 H, NH), 5.63 (d, *J* 7.5 Hz, H-1′), 4.6 (m, 5 H, NH,OH), 4.5 (dd, *J* 7.5 and 3 Hz, H-2′), and 3.45 (m, 4 H, H-3′,4′,5′,5′).

*Anal.* Calc. for $C_8H_{12}N_2O_6$: C, 41.1; H, 5.2; N, 12.0. Found: C, 41.2; H, 5.2; N, 11.7.

The material eluted with solvent *G* (6.1 g) was acetylated conventionally with pyridine (30 mL) and acetic anhydride (30 mL). Column chromatography (solvent *B*) of the product gave 2-*O*-acetyl-3,4:6,7-di-*O*-isopropylidene-D-*glycero*-D-*galacto*- and -D-*talo*-heptono-1,5-lactone (**44**; 4.2 g, 51%), as a 1:2 mixture of two di-

astereomers which, after recrystallisation from ethanol, gave the minor component (1.8 g, 21.9%), m.p. 149–150°, $R_F$ 0.6, $[\alpha]_D^{20}$ +78° (methyl sulfoxide). N.m.r. data ($CDCl_3$): $^1H$, $\delta$ 5.4 (s, $J$ 2.5 Hz, H-2), 4.8 (m, 2 H, H-3,4), 4.4 (m, 1 H, H-5), 4.1 (m, 3 H, H-6,7,7), 2.26 (s, 3 H, OAc), and 1.40, 1.43, 1.50, and 1.53 (4 s, each 3 H, 2 $CMe_2$); $^{13}C$, $\delta$ 169.7 and 165.5 (2 CO), 110.9 and 109.6 (2 acetal C), 76.3, 73.4, 72.6, 72.3, 68.8, and 66.2 (C-2/7), 26.5, 25.5, 24.8, and 24.0 (4 acetal Me), and 20.0 (acetyl Me). Mass spectrum: $m/z$ 330 ([M+], 315 ([M$^+$ − Me] 100), 197 (12), 187 (11), 155 (12), 101 (47), and 43 (46).

*(d) 1,2-O-Isopropylidene-3-O-methyl-α-*D*-*xylo*-pentodialdo-1,4-furanose* (**45**). Reaction of **45**[18] (30.6 g) by method *A* for 6 h and column chromatography (solvent *C* then solvent *F*) gave, first, a syrup (19 g) which was acetylated in pyridine (100 mL) with acetic anhydride (100 mL). Column chromatography (solvent *B*) of the product gave 1-acetyl-5,5-dimethylhydantoin (2.9 g, 11.4%), m.p. 190–192°, $R_F$ 0.75; lit.[19] m.p. 192°.

Eluted second was (4*S*,5*R*,6*R*)-5,6-diacetoxy-5,6-dihydro-4-methoxy-4-*H*-pyrido[2,1-*e*]imidazole-2,4-dione (**50**; 3.2 g, 7.1%), isolated as a syrup, $[\alpha]_D^{20}$ +80° (methyl sulfoxide), $R_F$ 0.65, containing (n.m.r. data) two isomers in the ratio ~1:5. N.m.r. data[25] ($CDCl_3$): $^1H$, major isomer, $\delta$ 11.65 (bs, NH), 6.65 (d, $J$ 3 Hz, H-6), 6.06 (d, $J$ 2 Hz, H-3), 5.04 (dd, $J$ 9 and 3 Hz, H-5), 4.30 (dd, $J$ 9 and 2 Hz, H-4), 3.40 (s, OMe), 2.10 and 2.03 (2 s, OAc); $^{13}C$, $\delta$ 169.6 and 169.1 (2 acetyl C), 161.0 and 151.2 (2 hydantoin CO), 128.8 (C-2), 106.3 (C-3), 72.4, 70.0, and 68.9 (C-4/6), 56.6 (OMe), and 20.3 (2 acetyl Me); minor isomer, $\delta$ 6.2 (d, $J$ 5 Hz, H-3) and 3.17 (s, OMe); $^{13}C$, $\delta$ 104.4 (C-3) and 48.5 (OMe).

*Anal.* Calc. for $C_{12}H_{14}N_2O_7$: C, 48.3; H, 4.7; N, 9.4. Found: C, 48.0; H, 4.5; N, 9.2.

Eluted last was **25** (3.3 g, 17.2%), $R_F$ 0.3.

The product eluted with solvent *F* was subjected to further repeated column chromatography (solvent *F*). Concentration of the fraction containing material of $R_F$ 0.3 and recrystallisation of the residue from ethanol gave 5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-ureido-β-L-idofuranuronamide (**46**; 1.25 g, 3.8%), m.p. 188–190°, $[\alpha]_D^{20}$ −29° (methanol), −6° (methyl sulfoxide). N.m.r. data [$(CD_3)_2SO$]: $^1H$, $\delta$ 7.05 and 7.00 (2 s, 2 H, $NH_2$), 6.27 (d, $J$ 8 Hz, NH), 5.77 (d, $J$ 3.8 Hz, H-1), 5.57 (s, 2 H, $NH_2$), 4.59 (d, $J$ 3.8 Hz, H-2), 4.24 (t, $J$ 8 Hz, H-5), 4.10 (dd, $J$ 8 and 3 Hz, H-4), 3.57 (d, $J$ 3 Hz, H-3), 3.29 (s, 3 H, MeO), and 1.21 and 1.35 (2 s, 6 H, $CMe_2$); ($CD_3OD$): $\delta$ 7.43 and 7.13 (2 $NH_2$); $^{13}C$, $\delta$ 175.7 (C-6), 161.6 (ureido C), 113.0 (acetal C), 106.2 (C-1), 85.9, 83.0, and 80.7 (C-2,3,4), 58.1 (OMe), 54.1 (C-5), and 27.1 and 26.5 (acetal Me). Mass spectrum: $m/z$ 289 [M+], 2%), 274 (6), 245 ([M$^+$ − $CONH_2$], 76), 228 (12), 202 (17), 173 (100), 155 (32), 129 (40), 85 (39), 73 (25), 59 (26), 58 (30), and 43 (63).

Concentration of the fraction containing material with $R_F$ 0.25 gave, after recrystallisation of the residue from ethanol, 5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-ureido-α-D-glucofuranuronamide (**47**; 0.05 g, 0.2%), m.p. 227–230°, $[\alpha]_D^{20}$ +12° (methanol), −8° (methyl sulfoxide). N.m.r. data [$(CD_3)_2SO$]: $^1H$, $\delta$ 7.26 and

6.94 (2 s, 2 H, $NH_2$), 6.14 (d, *J* 9 Hz, NH), 5.77 (d, *J* 4 Hz, H-1), 5.55 (s, 2 H, $NH_2$), 4.56 (d, *J* 4 Hz, H-2), 4.32 (t, *J* 9 Hz, H-5), 4.09 (dd, *J* 9 and 3 Hz, H-4), 3.57 (d, *J* 3 Hz, H-3), 3.28 (s, 3 H, MeO, and 1.34 and 1.21 (2 s, 5 H, $CMe_2$); ($CD_3OD$): $\delta$ 7.48 and 7.12 (2 $NH_2$); $^{13}C$, $\delta$ 175.8 (C-6), 161.4 (ureido C), 113.1 (acetal C), 106.6 (C-1), 85.9, 82.8, and 80.4 (C-2,3,4), 58.3 (OMe), 53.7 (C-5), and 27.1 and 26.5 (acetal Me). Mass spectrum: *m/z* 289 ([$M^+$], 0.8%), 274 (3), 245 ([$M^+ - CONH_2$], 15), 228 (3), 202 (10), 173 (46), 155 (12), 129 (29), 85 (35), 73 (38), 59 (30), 58 (24), and 43 (100).

*Anal.* Calc. for $C_{11}H_{19}N_3O_6$: C, 45.6; H, 6.6; N, 14.5; O, 33.2. Found: **46**, C, 45.5; H, 6.6; N, 14.8; O, 33.6; **47**, C, 45.5; H, 6.7; N, 14.7; O, 33.7.

*(4*S*,5*R*,6*RS*)-5,6-Dihydro-5,6-dihydroxy-4-methoxy-4*H*-pyrido[2,1-*e*]imidazole-2,4-dione* (**49**). — A solution of **50** (4 g) in dry methanol (60 mL) and methanolic 4M sodium methoxide (5 mL) was kept overnight at room temperature, then neutralised with solid carbon dioxide, and concentrated. Column chromatography (solvent *C*) of the residue gave **49** (1.7 g, 60.7%), isolated as a syrup, $[\alpha]_D^{20}$ +143° (water), $R_F$ 0.5, containing (n.m.r. data) two isomers in the ratio ~1:3. $^1$H-N.m.r. data [$(CD_3)_2SO$]: major isomer, $\delta$ 11.3 (bs, NH), 6.7 (bs, OH), 5.9 (d, *J* 2 Hz, H-3), 5.45 (bs, OH), 5.25 (d, *J* 3 Hz, H-6), 4.05 (dd, *J* 9 and 2 Hz, H-4), 3.6 (dd, *J* 9 and 3 Hz, H-5), and 3.45 (s, OMe); minor isomer, $\delta$ 11.35 (bs, NH), 6.7 (bs, OH), 6.08 (d, *J* 5 Hz, H-3), 5.45 (bs, OH), 5.25 (d, *J* 3 Hz, H-6), 4.05 (dd, *J* 9 and 5 Hz, H-4), 3.6 (dd, *J* 9 and 3 Hz, H-5), and 3.3 (s, OMe).

*Anal.* Calc. for $C_8H_{10}N_2O_5$: C, 44.9; H, 4.7; N, 13.1. Found: C, 44.5; H, 4.8; N, 12.7.

*(4*S*,5*R*,6*R*)-5,6-Dihydro-5,6-isopropylidenedioxy-4-methoxy-4*H*-pyrido[2,1-*e*]imidazole-2,4-dione* (**51**). — To a solution of **49** (0.5 g) in dry *N,N*-dimethylformamide (7 mL) were added 2-methoxypropene (0.7 mL) and a trace of toluene-*p*-sulfonic acid. The mixture was kept overnight at room temperature, then neutralised with solid sodium hydrogencarbonate, and concentrated. Column chromatography (solvent *B*) of the residue gave **51** (0.2 g, 46%), m.p. 155–156° (from carbon tetrachloride), $[\alpha]_D^{20}$ −2° (methyl sulfoxide), $R_F$ 0.6. N.m.r. data ($CDCl_3$): $^1$H, $\delta$ 9.2 (bs, 1 H, NH), 6.16 (d, *J* 5 Hz, H-3), 5.75 (d, *J* 4.5 Hz, H-6), 4.45 (dd, *J* 4.5 and 3 Hz, H-5), 4.2 (dd, *J* 5 and 3 Hz, H-4), 3.47 (s, 3 H, OMe), and 1.47 and 1.40 (2 s, each 3 H, $CMe_2$); $^{13}C$, $\delta$ 161.5 and 152.5 (2 CO), 130.4 (C-2), 110.6 (acetal C), 104.6 (C-3), 77.3 (C-4), 75.0 (C-6), 71.8 (C-5), 57.3 (OMe), and 27.8 and 26.1 (2 acetal Me).

*Anal.* Calc. for $C_{11}H_{14}N_2O_5$: C, 52.0; H, 5.4; N, 11.0. Found: C, 52.1; H, 5.5; N, 10.8.

*1,2:3,4-Di-*O*-isopropylidene-α-*D*-galacto-hexodialdo-1,5-pyranose* (**53**). — Distilled **52**[20] (17 g) was oxidised with pyridinium dichromate–acetic anhydride[12]. The crude product was distilled to give **53** (11.4 g, 67.6%), b.p. 95–97°/0.1 mmHg, $[\alpha]_D^{20}$ −104° (5 min), −88° (15 min), −74° (24 h) (chloroform); lit.[21] b.p. 104–105°/0.5 mmHg, $[\alpha]_D^{20}$ −131° (*c* 0.9, chloroform); lit.[22] b.p. 105°/0.5 mmHg, $[\alpha]_D^{20}$ −111° (*c* 2.3, chloroform); lit.[23] $[\alpha]_D^{20}$ −109° (chloroform).

The Bucherer reaction of **53** (14 g) by method *B* for 24 h and column chromatography of the product on Kieselgel 40 gave, on elution with solvent *B* (1 L), a product (2.5 g), column chromatography (solvent *B*) of which gave 5-[1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-pentopyranos-5(*R*)-yl]hydantoin (**54**; 2.8 g, 15.7%), m.p. sinters at 80°, $[\alpha]_D^{20}$ −8° (chloroform), $R_F$ 0.2 $^1$H-N.m.r. data ($CDCl_3$): δ 9.33 and 6.18 (2 bs, 2 H, NH), 5.45 (d, *J* 5 Hz, H-1), 4.45 (m, 5 H, H-2/6), and 1.53, 1.48, 1.34, and 1.31 (4 s, each 3 H, 2 $CMe_2$).

*Anal.* Calc. for $C_{14}H_{20}N_2O_7$: C, 51.2; H, 6.1; N, 8.6. Found: C, 51.0; H, 6.4; N, 8.5.

Elution with solvent *C* (1 L) gave a product (5.3 g) that was filtered with ether to give **25** (3.4 g, 45%), m.p. 174–176°. Recrystallisation of the material in the mother liquor from ethanol (15 mL) gave 5-(4,5-*O*-isopropylidene-L-glucono- or -L-mannono-nitrile-6-yl)hydantoin (**58**; 0.35 g, 2%), m.p. 224° (dec.), $[\alpha]_D^{20}$ +49° (pyridine), $R_F$ 0.45 (solvent *C*). N.m.r. data ($CDCl_3$, 250-MHz Bruker AC-250 spectrometer): $^1$H–$^1$H COSY (45°), δ 10.7 and 7.3 (2 bs, 2 H, NH), 5.9 (d, *J* 5 Hz, HO-2), 4.36 (dd, *J* 5.5 and 2.5 Hz, H-4), 4.32 (d, *J* 3.7 Hz, H-6), 4.20 (dd, *J* 5.5 Hz, H-1), 4.0 (dd, *J* 5.5 Hz, H-3), 3.67 (ddd, *J* 5.5 and 5 Hz, H-2), 3.48 (m, 1 H, H-5), 2.98 (d, *J* 5 Hz, HO-5), 2.93 (d, *J* 5.5 Hz, HO-1), 1.45 and 1.30 (2 s, 6 H, $CMe_2$); $^{13}$C (62.8 MHz), δ 174.3 and 157.8 (2 CO), 118.7 (CN), 109.0 (acetal C), 77.1, 73.7, 67.3, 59.3, 51.7, and 49.9 (C-1/6), and 27.8 and 26.2 (acetal Me).

*Anal.* Calc. for $C_{12}H_{17}N_3O_7$: C, 45.7; H, 5.4; N, 13.3. Found: C, 45.6; H, 5.6; N, 13.2.

Elution with solvent *E* (2 L) gave a product (8 g), column chromatography (solvent *D*) of which gave 6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-ureido-DL-*glycero*-α-D-*galacto*-heptopyranuronamide (**55**; 4.3 g, 23%), as an amorphous yellow powder, m.p. 80–85°, $[\alpha]_D^{20}$ −70° (chloroform), $R_F$ 0.15. N.m.r. data ($CDCl_3$): $^1$H, δ 6.5 and 6.3 (2 bs, 2 H, $NH_2$), 5.5 (d, *J* 5 Hz, H-1), 5.35 (bs, 2 H, $NH_2$), 4.3 (m, 6 H, H-2/6 and NH) and 1.53, 1.46, and 1.3 (3 s, 3, 3, and 6 H, 2 $CMe_2$); $^{13}$C (not all signals of the two diastereomers had different chemical shifts), δ 174.4 and 160.3 (2 CO), 174.8 and 160.1 (2 CO), 109.8 and 109.5 (2 acetal C), 96.7 (C-1), 71.5, 71.0, 67.4, 67.2, 58.0, 54.7, and 54.3 (C-2/6), and 26.0, 25.1, and 24.5 (2:1:1, acetal Me).

*Anal.* Calc. for $C_{14}H_{23}N_3O_7$: C, 48.7; H, 6.7; N, 12.2. Found: C, 48.5; H, 6.9; N, 12.0.

*2,3:4,5-Di-O-isopropylidene-β-*D-arabino-*hexosulo-2,6-pyranose* (**61**). — 2,3:4,5-Di-*O*-isopropylidene-D-fructose[24] (**60**, 26 g) was oxidised with pyridinium dichromate–acetic anhydride[12]. The crude syrupy product was distilled to give **61** (15.2 g, 59%), b.p. 90–94°/0.02 mmHg, $[\alpha]_D^{20}$ −58° (chloroform), −82° (acetone), $R_F$ 0.6 (solvent *B*); lit.[22] $[\alpha]_D^{20}$ −72° (chloroform); lit.[25] $[\alpha]_D^{20}$ −46.5° (acetone). The $^1$H-n.m.r. spectrum was identical with that reported[22].

*Reaction of* **61** *with potassium cyanide.* — To a stirred solution of **61** (2.6 g) in ether (60 mL) and water (6.5 mL) were added sodium hydrogencarbonate (1.5 g) and potassium cyanide (1.3 g). The mixture was stored for 2 h at room tempera-

ture when all of **61** had been consumed (t.l.c.). The organic solution was separated, washed with water, dried, and concentrated to give 3,4:5,6-di-*O*-isopropylidene-β-D-*arabino*-DL-*glycero*-3-heptulopyranosononitrile (**62**) as an amorphous solid foam (2.6 g, 91%), $[\alpha]_D^{20}$ −22° (chloroform), $R_F$ 0.45 and 0.40 (solvent *A*). According to the $^{13}C$-n.m.r. data, the two diastereomers were present in the ratio 15:85. N.m.r. data ($CDCl_3$): $^1H$, δ 4.56 (s, H-2), 4.35 (m, 3 H, H-4,5,6), 3.87 (bs, 2 H, H-7,7), 3.75 (bs, 1 H, OH), and 1.59, 1.46, and 1.33 (3 s, 3, 6, and 3 H, 2 $CMe_2$); $^{13}C$, major component, δ 117.6 (CN), 110.4 and 109.5 (2 acetal C), 101.6 (C-3), 70.5, 69.8, 69.7, 63.9, and 62.0 (C-2,4/7), and 26.4, 25.6, 25.2, and 23.9 (acetal Me); minor component, δ 117.1 (CN), 110.0 and 109.5 (2 acetal C), 102 (C-3), 71.6, 70.1, 69.6, 66.5, and 61.7 (C-2,4/7), and 26.0, 25.2, 24.9, and 24.6 (acetal Me).

*Anal.* Calc. for $C_{13}H_{19}NO_6$: C, 54.7; H, 6.7; N, 4.9. Found: C, 54.3; H, 7.0; N, 4.6.

Acetylation of **62** with acetic anhydride (2 mL) in pyridine (5 mL) conventionally gave 2-*O*-acetyl-3,4:5,6-di-*O*-isopropylidene-β-D-*arabino*-D(or L)-*glycero*-3-heptulopyranosononitrile (**63**; 0.5 g, 66%), m.p. 119–121°, $[\alpha]_D^{20}$ −69° (chloroform), $R_F$ 0.6 (solvent *A*). $^1H$-N.m.r. data ($CDCl_3$): δ 5.35 (s, H-2), 4.6 (dd, *J* 10 and 2 Hz, H-5), 4.23 (d, *J* 10 Hz, H-4), 4.20 (d, *J* 2 Hz, H-6), 3.86 (m, 2 H, H-7), and 1.56, 1.50, and 1.33 (3 s, 3, 6, and 3 H, 2 $CMe_2$).

*Anal.* Calc. for $C_{15}H_{21}NO_7$: C, 55.0; H, 6.5; N, 4.3. Found: C, 54.8; H, 6.8; N, 4.1.

The Bucherer reaction of **61** (7 g) by method *B* for 72 h with column chromatography of the product, as described for the reaction of **53**, gave a fraction, $R_F$ 0.4 (solvent *A*), which was a mixture of the two distereomers of **62** (0.15 g, 2%).

The fraction having $R_F$ 0.5 (solvent *B*) gave 3,4:5,6-di-*O*-isopropylidene-β-D-*arabino*-DL-*glycero*-3-heptulopyranosonamide (**64**; 0.6 g, 7.3%), isolated as a syrup, $[\alpha]_D^{20}$ −14° (chloroform). $^1H$-N.m.r. data ($CDCl_3$): δ 6.75 and 6.35 (2 bs, 2 H, $NH_2$), 4.4 (m, 4 H, H-4,5,6 OH), 4.2 (d, *J* 6.5 Hz, H-2), 3.9 (m, 2 H, H-7,7), and 1.53, 1.50, 1.43, and 1.37 (4 s, each 3 H, 2 $CMe_2$). Mass spectrum: *m/z* 288 ($[M^+ - Me]$, 85%), 229 ($[M^+ - (CHOH\text{–}CONH_2)]$, 88), 171 (85), 127 (55), 117 (26), 113 (32), 85 (26), 59 (70), and 43 (100).

*Anal.* Calc. for $C_{13}H_{21}NO_7$: C, 51.5; H, 7.0; N, 4.6. Found: C, 51.2; H, 7.3; N, 4.4.

The fraction containing material with $R_F$ 0.5 (solvent *C*) as the main component gave **25** (2.7 g, 77.8%), m.p. 174–176°.

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