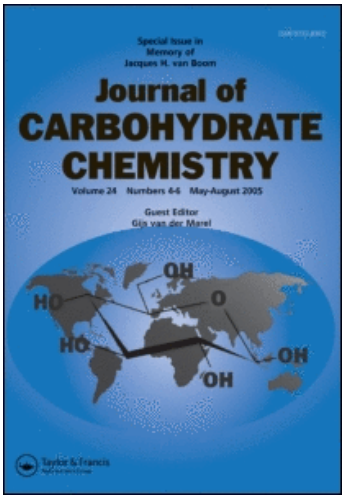

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Stereoselective Synthesis of *N*-(α- and β-Ribofuranosyl)-Formamtdes and Related Glycosyl Formamtdes - Precursors for Sugar Isocyantdes

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STEREOSELECTIVE SYNTHESIS OF *N*-(α- AND β-RIBOFURANOSYL)-FORMAMIDES AND RELATED GLYCOSYL FORMAMIDES — PRECURSORS FOR SUGAR ISOCYANIDES

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ABSTRACT

Efficient stereospecific *N*-formylation of ribosylamine has been achieved, affording the α-anomer directly (by reaction with formic-acetic anhydride) and the β-anomer *via* the corresponding formamidine derivative (by reaction with dimethylformamide dimethyl acetal). Dehydration of the α-anomer gave the corresponding isocyanide without compromising the anomeric purity. The amidine route was extended to give the *N*-formyl derivatives of α-xylosylamine and α-arabinosylamine.

INTRODUCTION

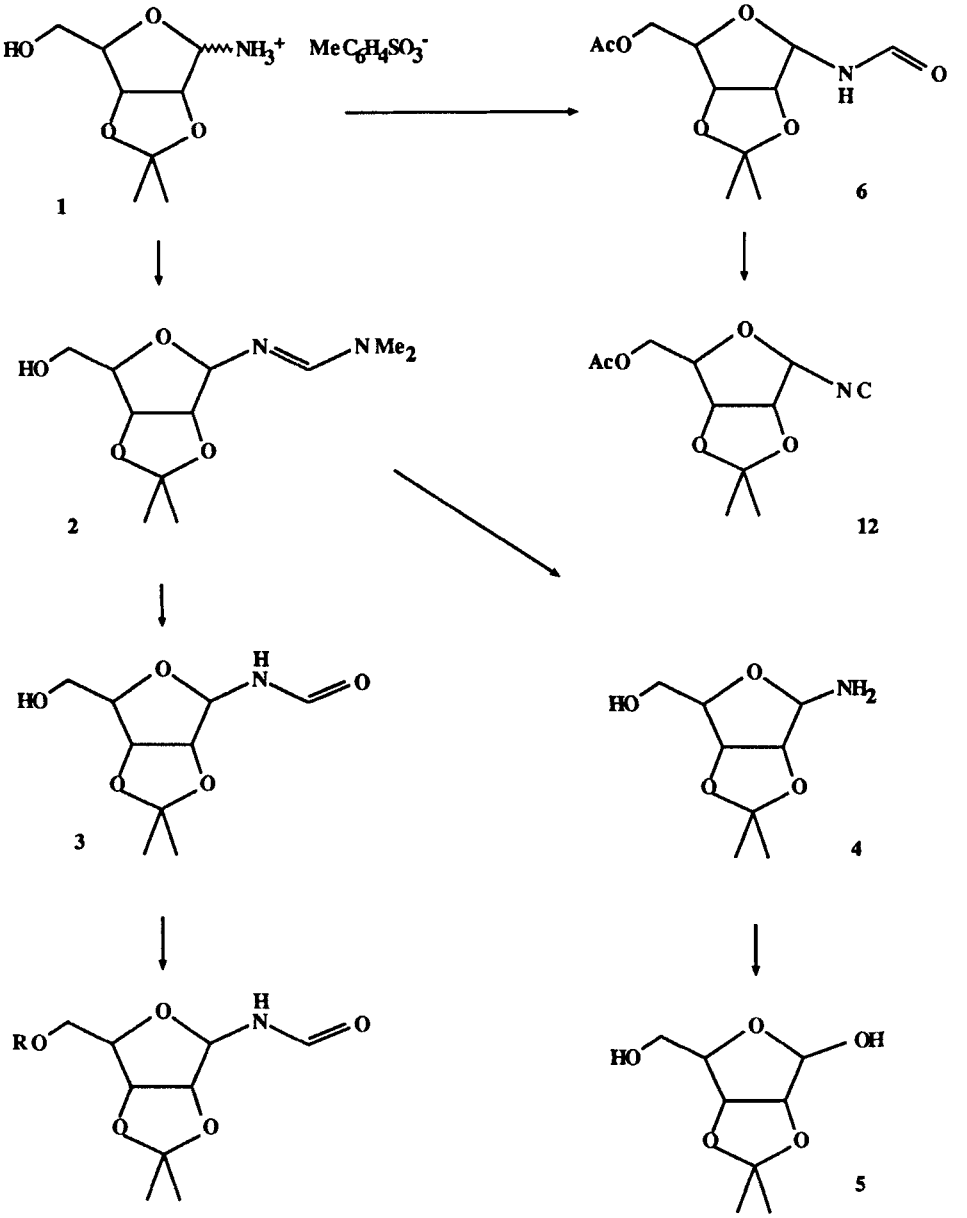
The chemistry of the isocyanide group has been extensively investigated and the synthetic potential of this group is well established.[1] Although glycofuranosyl and glycopyranosyl isocyanides have been made by most of the standard methods[2] there has been little application of these derivatives to the development of useful routes to

corresponding heterocyclic derivatives.[3] In particular the use of isocyanides as precursors to nucleosides has not been reported. This lack of application of these synthons in nucleoside chemistry can be understood when the available routes to anomeric glycosyl isocyanides are examined. Acetylated glycosyl bromides react with silver cyanide[4] to give the isocyanide derivatives as expected but the yields are variable, being strongly dependent on the nature of the group at the C-2 site. Furthermore, the intrinsic stereoselectivity of this reaction is compromised by anomerisation of the product in the reaction mixture and pure anomers are only accessible by chromatographic separation.

Recently Et_2AlCN has been used as a source of the NC group but with glucosyl fluorides this reagent shows poor regioselectivity and only moderate stereoselectivity.[5] Thus a four component mixture of α,β-cyanides and α,β-isocyanides is obtained by this method, for both pyranosyl and furanosyl sugars. Reduction of glycosyl isothiocyanates[6] with Bu_3SnH gives the corresponding isocyanides in 58-76% yield without anomerisation but the isocyanates themselves are only available as anomeric mixtures in most cases. A classical route to compounds of the type R-NC is dehydration of the corresponding formamide, R-NHCHO, with phosphorus oxychloride in presence of a suitable amine and this conversion is fairly stereoselective in the case of glycofuranosyl derivatives[7] (95% retention of anomeric configuration), and of glucopyranosyl isocyanide[8] (90% retention). However, the fact that the formamides are accessible only by a multi-step sequence involving an azide[7] diminishes the usefulness of this method. In our view this dehydration reaction is the most promising method for the stereospecific formation of sugar isocyanide anomers. Hence we have sought alternative, more convenient routes to α- and β-glycosylformamides, routes which exhibit better stereoselectivity than any of those described above. We report here short stereoselective routes to *O*-protected derivatives of both α- and β-ribofuranosyl formamides starting from the same compound, 2,3-*O*-isopropylidene-α,β-D-ribofuranosyl-ammonium *p*-toluenesulphonate (**1**).

RESULTS AND DISCUSSION

The usefulness of **1**, a stable crystalline derivative of ribosylamine, readily available in 70% yield from ribose in two steps as an anomeric mixture (α,β ratio = 1:1), was first demonstrated by Shaw and coworkers[9] in their synthesis of anomeric mixtures of imidazole and pyrimidine nucleosides and we have recently prepared a variety of *N*-acyl derivatives of 2,3-*O*-isopropylidene-D-ribofuranosylamine from **1**, obtaining an anomeric mixture in most cases.[10] The reaction of compound **1** with dimethylformamide dimethyl acetal gives a sugar amidine (**Scheme**). In our hands the stereospecificity of this acylation reaction is excellent[11] giving only *N*-(dimethylaminomethylene)-2,3-*O*-isopropylidene-β-D-ribo-



Scheme

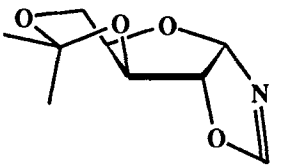
furanosylamine (2). The high stereospecificity can probably be attributed to the large steric requirement of the reagent $HC(NMe_2)(OMe)_2$.

Hydrolysis of the amidino sugar can formally occur in two ways to afford either the *N*-formylribosylamine derivative (3), or the corresponding ribosylamine (4). Under hydrolytic conditions 4 is labile and is rapidly converted to 2,3-*O*-isopropylidene-β-D-ribofuranose (5). In aqueous ethanol the hydrolysis of 2 is regiospecific *and* stereospecific giving a product (75% yield) which is *N*-formyl-2,3-*O*-isopropylidene-β-D-ribofuranosylamine (3) containing about 5% of the α-anomer and only a trace of 5. However, in the presence of only a catalytic amount of acetic acid the rate of the alternative hydrolysis is greatly enhanced, to the extent that the product is a mixture of 3 and 5 (ratio *ca.* 3:2) and the anomeric purity of 3 is seriously reduced (α,β ratio = 1:4). Prolonged heating in presence of acid yields 5 as the only product.

The anomeric configuration of 3 and related compounds was determined by the criteria established previously,[10] in particular by the value of the coupling $J_{1,2}$ which is *ca.* 1 Hz in the β-anomer and *ca.* 4 Hz in the α-anomer. Also the C-1 resonance is characteristically at about 5 ppm higher frequency than the β-anomer. In both anomers the spectra reveal the presence of two conformational isomers arising from the restricted rotation of the amide bond. These are labelled in the obvious way as s-*cis* and s-*trans*. This results in the reversal of the conventional use of these labels for conformers of disubstituted amides. Typically, in the (generally) predominant *trans* conformer the formyl proton is an obvious doublet, $J_{CHO,NH}$ 11.5 Hz, the NH proton a broadened triplet, and H-1 is shifted to low frequency. The minor *cis* conformer has only a small coupling between CHO and NH protons (< 2 Hz) and H-1 is shifted to high frequency. Most other protons and carbons show small shift differences between conformers..

The *N*-formylribosylamine derivative (3) was further characterised by protection of the 5-OH group. Thus the 5-*O*-acetyl derivative (7) and the 5-*O*-*t*-butyldimethylsilyl derivative (8) were obtained by standard methods. Compound 8 was identical to that obtained previously by a much longer route.[7]

Direct formylation of 1 with formic-acetic anhydride is completely stereospecific giving only the α-anomer. Concomitant acetylation of the 5-hydroxy group occurs and the only product is the fully protected *N*-formyl-α-D-ribofuranosylamine derivative (6). Acetylation at *O*-5 is expected to predominate since *O*-formyl derivatives are much less stable. The high stereospecificity of this reaction is notable and has been observed by us in similar acylation reactions where both the anomeric site and *O*-5 are involved. Selectivity for the α-anomer probably results from a combination of the steric effect of the 5-*O*-acetyl group across the *endo* face and a preferential stabilisation of the intermediate (formed by reaction at *N*-1) by hydrogen bonding on the *exo* face to *O*-2 or *O*-4.



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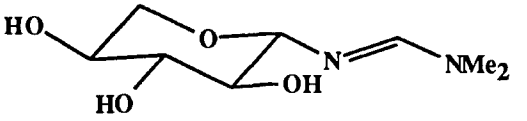

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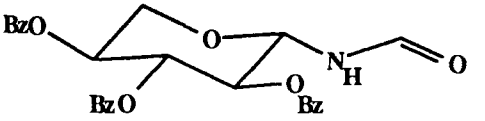

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To further illustrate the usefulness of the sugar amidine route to *N*-formyl derivatives we have examined the reaction of xylofuranosylamine and arabinopyranosyl-amine with dimethylformamide dimethyl acetal. In the case of 3,5-*O*-isopropyl-idene-α,β-D-xylo-furanosylamine, the corresponding amidine cannot be isolated, since it undergoes intramolecular elimination and cyclisation[11] to afford the oxazoline derivative (**9**). Formation of an oxazoline is clearly stereoselective and hydrolysis to the *N*-formyl-xylo-furanosylamine derivative can only give the α-anomer. Conversion of D-arabino-pyranosyl-amine to the corresponding amidine derivative (**10**) has been reported previously[14] but the anomeric configuration was not established. Hydrolysis of **10** to the *N*-formyl derivative appeared to be stereospecific and this has been confirmed in the present work since the only product is the α-anomer, characterised as its tribenzoyl derivative (**11**).

The dehydration of *N*-formylglycosylamines with $POCl_3/(Me_2CH)_2NH$ has been achieved routinely in high yield,[7] although usually only with anomeric mixtures which were predominantly beta. Anomerically pure materials were only obtained by chromatographic separation. Using this dehydration procedure the anomerically pure *N*-formyl-α-ribosylamine derivative (**6**) was converted to the corresponding α-ribosylisocyanide derivative (**12**) in 70% yield and with complete retention of anomeric configuration. The configuration was established by the value of $J_{1,2}$ 6.0 Hz and δ(C-1) 84.0. Corresponding values[7] for the analogous compounds 5-*O*-TBDMS-2,3-*O*-isopropylidene-α- and β-D-ribofuranosylisocyanide are $J_{1,2}$ 5.0 Hz, δ(C-1) 84.9 and $J_{1,2}$ <1 Hz, δ(C-1) 88.5, respectively.

The stereoselective routes described above for anomeric isomers of *N*-formyl derivatives of sugar amines are convenient and inexpensive and greatly enhance the usefulness of the sequence of steps R–NH_2 → R–NHCHO → R–NC. This is a

convenient strategy for the synthesis of novel heterocyclic derivatives of sugars and will find application in nucleoside chemistry and related areas of chemotherapeutic potential.

EXPERIMENTAL

NMR spectra were recorded with a JEOL GX270 spectrometer at 21 °C using standard conditions with a data point resolution of *ca.* 0.1 Hz. ^1H chemical shifts were measured relative to Me_4Si and ^{13}C chemical shifts relative to $CDCl_3$ (77.05 ppm) or Me_2SO (39.5 ppm). Optical rotations were obtained using an ETL-NPL automatic polarimeter at 21-23 °C. In the case of some compounds obtained as a syrup, satisfactory elemental analysis data were not obtained but these compounds were fully characterised by spectroscopic data.

***N*-(Dimethylaminomethylene)-2,3-*O*-isopropylidene-β-D-ribofuranosylamine (2).** This compound was obtained by the method of Shaw and coworkers.[11,12] Using a reaction time of 1.25 h only the β-anomer was obtained.

***N*-Formyl-2,3-*O*-isopropylidene-β-D-ribofuranosylamine (3).** The amidine (2) (1.0 g, 4.1 mmol) in ethanol (8 mL) and water (2 mL) was refluxed for about 1 h, until the starting material was no longer detected (TLC). The solution was concentrated to dryness *in vacuo* and the residual gum azeotroped with ethanol (3 x 5 mL) and purified by flash chromatography on silica gel (ethyl acetate). This procedure gave (3), α,β ratio = 1:19, as a gum (0.68 g, 75%), $[\alpha]_D$ −70° (*c* 1.6, $CHCl_3$); ^1H NMR ($CDCl_3$), *cis/trans* ratio 1.0:1.2, *trans*-conformer, δ 5.27 (dd, 1 H, $J_{1,2}$ = 1.4 Hz, $J_{1,NH}$ = 10.8 Hz, H-1), 4.63 (m, 1 H, H-2), 4.87 (m, 1 H, H-3), 4.35 (m, 1 H, H-4), 3.6-3.7 (m, 2 H, H-5, H-5'), 1.34, 1.53 (two s, 6 H, Me), 7.84 (br t, 1 H, NH), 8.12 (d, $J_{NH,CHO}$ = 11 Hz, CHO); *cis*-conformer, δ 5.80 (dd, 1 H, $J_{1,2}$ = 1.7 Hz, $J_{1,NH}$ = 9.1 Hz, H-1), 4.62 (m, 1 H, H-2), 4.84 (m, 1 H, H-3), 4.31 (m, 1 H, H-4), 3.6-3.7 (m, 2 H, H-5, H-5'), 1.335, 1.53 (two s, 6 H, Me), 7.69 (br d, 1 H, NH), 8.13 (s, CHO); ^{13}C NMR ($CDCl_3$), *trans*-conformer, δ 91.3 (C-1), 86.7, 85.5 (C-2, C-4), 82.5 (C-3), 63.2 (C-5), 112.7, 25.2, 26.7 (CMe_2), 164.4 (CHO); *cis*-conformer, δ 85.8, 86.2, 86.4 (C-1, C-2, C-4), 82.0 (C-3), 63.2 (C-5), 112.9, 24.9, 26.8 (CMe_2), 161.4 (CHO).

5-*O*-Acetyl-*N*-formyl-2,3-*O*-isopropylidene-β-D-ribofuranosylamine (7). To a solution of 3 (0.5 g, 2.3 mmol) in pyridine (10 mL) at 0 °C, acetic anhydride (0.66 mL, 6.9 mmol) was added dropwise. The reaction mixture was maintained at 0 °C for about 3 h until completion (TLC), poured on to ice, extracted with chloroform and worked up to give a gum. This material was purified by chromatography on silica gel (chloroform) to give the β-anomer of 7 as a colourless gum, (354 mg, 60%), $[\alpha]_D$ −37° (*c* 5.4, $CHCl_3$); ^1H NMR ($CDCl_3$), *cis/trans* ratio 1.5:1.0, *trans*-conformer, δ 5.28 (dd, 1 H, $J_{1,2}$ = 2.5 Hz, $J_{1,NH}$ = 10.4 Hz, H-1), 4.61 (m, 1 H, H-2), 4.68 (m, 1 H, H-3), 4.1-4.35 (m, 3 H, H-4, H-5, H-5'), 2.14 (s, 3

H, MeCO), 1.35, 1.55 (two s, 6 H, Me), 7.42 (br t, 1 H, NH), 8.19 (d, $J_{NH,CHO}$ = 11.2 Hz, CHO); *cis*-conformer, δ 5.62 (dd, 1 H, $J_{1,2}$ = 1.9 Hz, $J_{1,NH}$ = 7.0 Hz, H-1), 4.67 (m, 1 H, H-2), 4.75 (m, 1 H, H-3), 4.1-4.35 (H-4, H-5, H-5'), 2.12 (s, 3 H, MeCO), 1.34, 1.54 (two s, 6 H, Me), 7.00 (br d, 1 H, NH), 8.19 (d, $J_{NH,CHO}$ = 1.2 Hz, CHO); ^{13}C NMR ($CDCl_3$), *trans*-conformer, δ 89.9 (C-1), 82.6 (C-2), 81.5 (C-3), 85.1 (C-4), 64.6 (C-5), 114.2, 25.2, 26.9 (CMe_2), 164.4 (CHO), 20.85, 170.3 (MeCO); *cis*-conformer, δ 86.8 (C-1), 83.7 (C-2), 81.4 (C-3), 85.3 (C-4), 64.5 (C-5), 113.9, 25.2, 26.8 (CMe_2), 161.1 (CHO), 20.9, 171.0 (MeCO).

5-*O*-(*t*-Butyldimethylsilyl)-*N*-formyl-2,3-*O*-isopropylidene-β-D-ribo-furanosyl-amine (8). To a solution of **3** (0.5 g, 2.3 mmol) and imidazole (0.32 g) in dichloromethane (30 mL) a solution of *t*-butyldimethylsilyl chloride (0.7 g, 4.6 mmol) in dichloromethane was added dropwise at 20 °C. After 15 h the solution was washed (water, 2 x 15 mL), dried and concentrated to a gum. Chromatography on silica gel (chloroform) gave the β-anomer **8** as a white amorphous solid (525 mg, 69%), mp 87-88 °C (lit.[6] 86-88 °C), $[\alpha]_D$ −74° (*c* 2.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$), *cis/trans* ratio 1.3:1.0, *trans*-conformer, δ 5.30 (dd, 1 H, $J_{1,2}$ < 1 Hz, $J_{1,NH}$ = 11.2 Hz, H-1), 4.55 (m, 1 H, H-2), 4.76 (m, 1 H, H-3), 4.32 (m, 1 H, H-4), 3.7-3.85 (m, H-5, H-5'), 1.34, 1.525 (two s, 6 H, Me), 0.96 (s, 9 H, CMe_3), 0.16, 0.185 (two s, 6 H, $SiMe_2$), 6.98 (br t, 1 H, NH), 8.18 (d, $J_{NH,CHO}$ = 11.5 Hz, CHO); *cis*-conformer, δ 5.97 (dd, 1 H, $J_{1,2}$ = 1.0 Hz, $J_{1,NH}$ = 8.4 Hz, H-1), 4.52 (m, 1 H, H-2), 4.74 (m, 1 H, H-3), 4.32 (m, 1 H, H-4), 3.7-3.85 (H-5, H-5'), 1.33, 1.52 (two s, 6 H, Me), 0.94 (s, 9 H, CMe_3), 0.145, 0.15 (two s, 6 H, $SiMe_2$), 7.15 (br d, 1 H, NH), 8.12 (d, $J_{NH,CHO}$ 1.8 Hz, CHO); ^{13}C NMR ($CDCl_3$), *trans*-conformer, δ 91.1 (C-1), 87.1 (C-2), 82.1 (C-3), 86.6 (C-4), 65.2 (C-5), 112.8, 25.3, 26.8 (CMe_2), 159.7 (CHO), 18.4, 26.0 (CMe_3), 25.0, 26.7 ($SiMe_2$); *cis*-conformer, δ 86.6 (C-1), 85.4 (C-2), 82.5 (C-3), 86.6 (C-4), 65.3 (C-5), 112.8, 25.0, 26.7 (CMe_2), 163.4 (CHO), 18.45, 26.2 (CMe_3), 25.3, 26.9 ($SiMe_2$).

5-*O*-Acetyl-*N*-formyl-2,3-*O*-isopropylidene-α-D-ribofuranosylamine (6). Acetic-formic anhydride[13] (25 mL) was added to **1** (5.0 g, 13.9 mmol) in dry dichloromethane (250 mL) and the mixture stirred for 48 h. Pyridine (13.9 mmol) was added and stirring continued for a further 16 h. The solvent was removed in vacuo and the residue taken up in $CHCl_3$, and washed with aqueous NaOH until acid free. After workup the residue was purified by flash chromatography on silica gel (ethyl acetate) to give a colourless oil (60%), $[\alpha]_D$ −34.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR, *cis/trans* ratio 2:1, *trans*-conformer, δ 5.37 (dd, 1 H, $J_{1,2}$ = 3.5 Hz, $J_{1,NH}$ = 10.0 Hz, H-1), 4.64 (m, 2 H, H-2, H-3), 4.23 (m, 1 H, H-4), 4.00 (dd, 1 H, $J_{4,5}$ = 3.1 Hz, $J_{5,5'}$ = 11.2 Hz, H-5), 4.18 (m, 1 H, H-5'), 2.05 (s, 3 H, MeCO), 1.30, 1.47 (two s, 6 H, Me), 6.5 (br t, 1 H, NH), 8.20 (d, $J_{NH,CHO}$ = 11.5 Hz, CHO); *cis*-conformer, δ 5.83 (dd, 1 H, $J_{1,2}$ = 3.8 Hz, $J_{1,NH}$ = 9.6 Hz, H-1), 4.64 (m, 2 H, H-2, H-3), 4.23 (m, 1 H, H-4), 4.12 (dd, 1 H, $J_{4,5}$ = 4.0 Hz, $J_{5,5'}$ = 11.8 Hz, H-5), 4.07 (dd, 1 H, $J_{4,5'}$ = 4.0 Hz, H-5'), 2.04 (s, 3 H, MeCO), 1.31, 1.49 (two s, 6 H, Me), 6.60 (br d, 1 H, NH), 8.22 (s, CHO); ^{13}C NMR

($CDCl_3$), *trans*-conformer, δ 84.2 (C-1), 81.7, 79.5 (C-2, C-4), 64.5 (C-5), 113.8, 24.7, 26.3 (CMe_2), 163.6 (CHO), 21.0, 170.3 (CH_3CO); *cis*-conformer, δ 82.0 (C-1), 79.1, 79.3, 79.7 (C-2, C-3, C-4), 65.0 (C-5), 113.5, 24.7, 26.3 (CMe_2), 160.7 (CHO), 21.0, 170.4 (CH_3CO).

***N*-Formyl-3,5-*O*-isopropylidene-α-D-xylofuranosylamine (9).** Treatment of 3,5-*O*-isopropylidene-α-D-xylofuranosylamine with dimethylformamide dimethyl acetal gave the corresponding xylose oxazoline.[11] The oxazoline (1.0 g, 5 mmol) in ethanol (8 mL) and water (2 mL) was refluxed for 2 h until the starting material was absent (TLC). The solvent was removed in vacuo, the residue azeotroped with ethanol (3 x 5 mL) and purified by flash chromatography (chloroform: methanol 97:3) to give **9** as a gum (688 mg, 63%); $[\alpha]_D$ +6.5° (*c* 5.1, $CHCl_3$); ^1H NMR ($CDCl_3$), *cis/trans* ratio 1.0:1.3, *trans*-conformer, δ 5.595 (dd, 1 H, $J_{1,2}$ = 3.5 Hz, $J_{1,NH}$ = 10.6 Hz, H-1), 4.3 (m, 1 H, H-2), 4.1-4.15 (m, H-3, H-4), 3.9-4.05 (m, H-5, H-5'), 1.39, 1.45 (two s, 6 H, Me), 7.12 (br t, 1 H, NH), 8.26 (d, $J_{NH,CHO}$ = 11.6 Hz, CHO); *cis*-conformer, δ 6.025 (dd, 1 H, $J_{1,2}$ = 3.5 Hz, $J_{1,NH}$ = 9.4 Hz, H-1), 4.3 (m, 1 H, H-2), 4.1-4.15 (m, H-3), 4.32 (m, 1 H, H-4), 3.9-4.05 (m, H-5, H-5'), 1.37, 1.43 (two s, 6 H, Me), 7.25 (br d, 1 H, NH), 8.24 (s, CHO); ^{13}C NMR ($CDCl_3$), *trans*-conformer, δ 85.2 (C-1), 71.5, 74.8, 75.3 (C-2, C-3, C-4), 60.9 (C-5), 97.4, 19.0, 28.9 (CMe_2), 165.2 (CHO); *cis*-conformer, δ 80.2 (C-1), 71.5, 75.0, 75.2 (C-2, C-3, C-4), 60.7 (C-5), 97.5, 19.3, 28.6 (CMe_2), 162.4 (CHO).

***N*-Formyl-α-D-arabinopyranosylamine (10).** Dimethylformamide dimethyl acetal (3.0 g, 25 mmol) and α,β-D-arabinopyranosylamine (3.0 g, 20 mmol) in MeOH (150 mL) were refluxed for 1 h. The solvent was removed *in vacuo* and the residue triturated with 95% aqueous ethanol to give a colourless solid. Recrystallisation (EtOH) gave **10** (1.9 g, 75%), mp 156-157 °C (Lit.[14] 156-157 °C); $[\alpha]_D$ −76° (*c* 2.3, H_2O).

Anal. Calcd for $C_6H_{11}NO_5$: C, 40.65; H, 6.2; N, 7.90. Found: C, 41.0; H, 6.15; N, 7.95.

2,3,5-Tri-*O*-benzoyl-*N*-formyl-α-D-arabinopyranosylamine (11). The *N*-formyl derivative (**10**) was benzoylated at 0 °C with benzoyl chloride in pyridine. The crude material was purified by flash chromatography (ethyl acetate) to give an amorphous solid (2.0 g, 73%); $[\alpha]_D$ −268° (*c* 0.2, $CHCl_3$); ^1H NMR ($CDCl_3$), *cis/trans* ratio 4:1, *trans*-conformer, δ 4.90 (t, 1 H, $J_{1,2}$ = 9.0 Hz, $J_{1,NH}$ = 9.0 Hz, H-1), 5.69-5.77 (m, H-2, H-3, H-4), 4.31 (dd, 1 H, $J_{4,5}$ = 1.5 Hz, $J_{5,5'}$ = 13.6 Hz, H-5), 4.00 (dd, 1 H, $J_{4,5'}$ < 1 Hz, H-5'), 6.66 (br t, 1 H, NH), 8.26 (d, $J_{NH,CHO}$ = 11.5 Hz, CHO); *cis*-conformer, δ 5.54 (t, 1 H, $J_{1,2}$ = 9.0 Hz, $J_{1,NH}$ = 9.0 Hz, H-1), 5.69-5.77 (m, H-2, H-3, H-4), 4.30 (dd, 1 H, $J_{4,5}$ = 1.5 Hz, $J_{5,5'}$ = 13.6 Hz, H-5), 4.06 (dd, 1 H, $J_{4,5'}$ < 1 Hz, H-5'), 6.85 (br d, 1 H, NH), 8.23 (d, $J_{NH,CHO}$ = 1.8 Hz, CHO); ^{13}C NMR ($CDCl_3$), *trans*-conformer, δ 83.0 (C-1), 69.1 (C-2), 71.2 (C-3), 69.0 (C-4), 66.1 (C-5), 161.3 (CHO); *cis*-conformer, δ 77.7 (C-1), 69.5 (C-2), 71.3 (C-3), 69.3 (C-4), 66.5 (C-5), 161.3 (CHO).

Anal. Calcd for $C_{24}H_{23}NO_3$ (373.4): C, 63.6; H, 5.1; N, 3.1. Found: C, 63.9; H, 4.7; N, 3.3.

5-*O*-Acetyl-2,3-*O*-isopropylidene-α-D-ribofuranosylisocyanide (12). To a solution of the α-amide (**6**) (350 mg, 1.49 mmol) in dry $CHCl_3$ (10 mL) diisopropylamine (0.56 mL) and phosphorus oxychloride (0.21 mL) were added at 0 °C and the mixture stirred at this temperature for 30 min. After a further 16 h at 25 °C the mixture was poured into a solution of Na_2CO_3 (0.5 g) in water (50 mL) and stirred for 15 min. After workup the oily product was purified by chromatography on silica gel (petroleum ether: ethyl acetate: triethylamine = 50:50:3) to give a colourless oil (244 mg, 70%); IR ν 2140 cm^{-1} (NC); $[\alpha]_D$ −10.1° (*c* 2.4, $CHCl_3$); ^1H NMR, δ 5.35 (d, 1 H, $J_{1,2}$ = 6.0 Hz, H-1), 4.75 (dd, 1 H, $J_{2,3}$ = 7.0 Hz, H-2), 4.67 (dd, 1 H, $J_{3,4}$ = 3.0 Hz, H-3), 4.49 (m, 1 H, H-4), 4.23 (dd, 1 H, $J_{4,5}$ = 5.0 Hz, $J_{5,5'}$ = 12.0 Hz, H-5), 4.27 (dd, 1 H, $J_{4,5'}$ = 4.0 Hz, H-5'), 2.10 (s, 3 H, MeCO), 1.40, 1.69 (two s, 6 H, Me); ^{13}C NMR ($CDCl_3$), δ 84.0 (C-1), 80.2, 80.7, 81.3 (C-2, C-3, C-4), 63.4 (C-5), 117.0 (OCO), 25.4, 26.0 (Me), 20.7, 170.2 (CH_3CO), 163.8 (NC).

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