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Carbohydrate Research 321 (1999) 190–196

CARBOHYDRATE RESEARCH

# Novel reversed cyclonucleoside analogues with a D-ribofuranose glycone

David F. Ewing [a,*], Gérard Goethals [b], Grahame Mackenzie [a], Patrick Martin [b], Gino Ronco [b], Laurence Vanbaelinghem [b], Pierre Villa [b]

[a] *Department of Chemistry, Faculty of Science and the Environment, University of Hull, Hull HU6 7RX, UK*
[b] *Laboratoire de Chimie Organique et Cinétique, Université de Picardie Jules Verne, F-80039 Amiens, France*

Received 26 April 1999; accepted 24 July 1999

**Abstract**

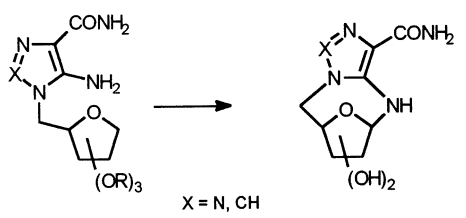
Two novel ribofuranose cyclonucleoside analogues have been synthesised by a route using 5-azido-5-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose as the starting material. This derivative was converted into two azole-reversed nucleosides, which were cyclised regiospecifically and stereospecifically by formation of a pentofuranosylamine. An alternative route, starting from a methyl β-D-ribofuranoside, was much less efficient, reflecting the need for the correct anomeric configuration in the cyclisation step. © 1999 Elsevier Science Ltd. All rights reserved.

*Keywords:* Reversed cyclonucleoside; 2,5-Epoxyimidazo[1,5-*a*][1,3]diazocine; 5,8-Epoxy[1,2,3]triazolo-[1,5-*a*][1,3]diazocine

## 1. Introduction

Cyclonucleosides are an interesting class of compounds because they have more than one structural characteristic that could contribute to raising their therapeutic index. Not only are such compounds of potential interest as antiviral nucleosides, but they are also macroheterocycles analogous to non-nucleoside antivirals such as TIBO [1]. We have recently reported a new method [2] for the formation of cyclonucleosides that generates a pentofuranose system bridged between the 1 and 5 positions by an azole ring (Scheme 1). The heteroaromatic ring is either imidazole or 1,2,3-triazole and is connected to the pentofuranose ring by one-atom bridges, i.e., the pentose C-5 carbon and an exocyclic nitrogen atom (amino group) in the heterocyclic moiety. The final ring-closure step involves attack by the heterocyclic amino group on the anomeric centre with displacement of the glycosidic OR group. This novel formation of a pentofuranosylamine give access to the hitherto inaccessible ring systems, 2,5-epoxyimidazo[1,5-*a*][1,3]diazocine (e.g., **2**, X = CH) and 5,8-epoxy[1,2,3]triazolo-[1,5-*a*][1,3]diazocine (e.g., **2**, X = N).

For the initial studies xylose was a convenient starting material for several reasons. It




**1** **2**

Scheme 1.

* Corresponding author. Tel.: +44-1482-465-687; fax: +44-1482-466-410.
*E-mail address:* d.f.ewing@chem.hull.ac.uk (D.F. Ewing)


PII: S0008-6215(99)00189-5

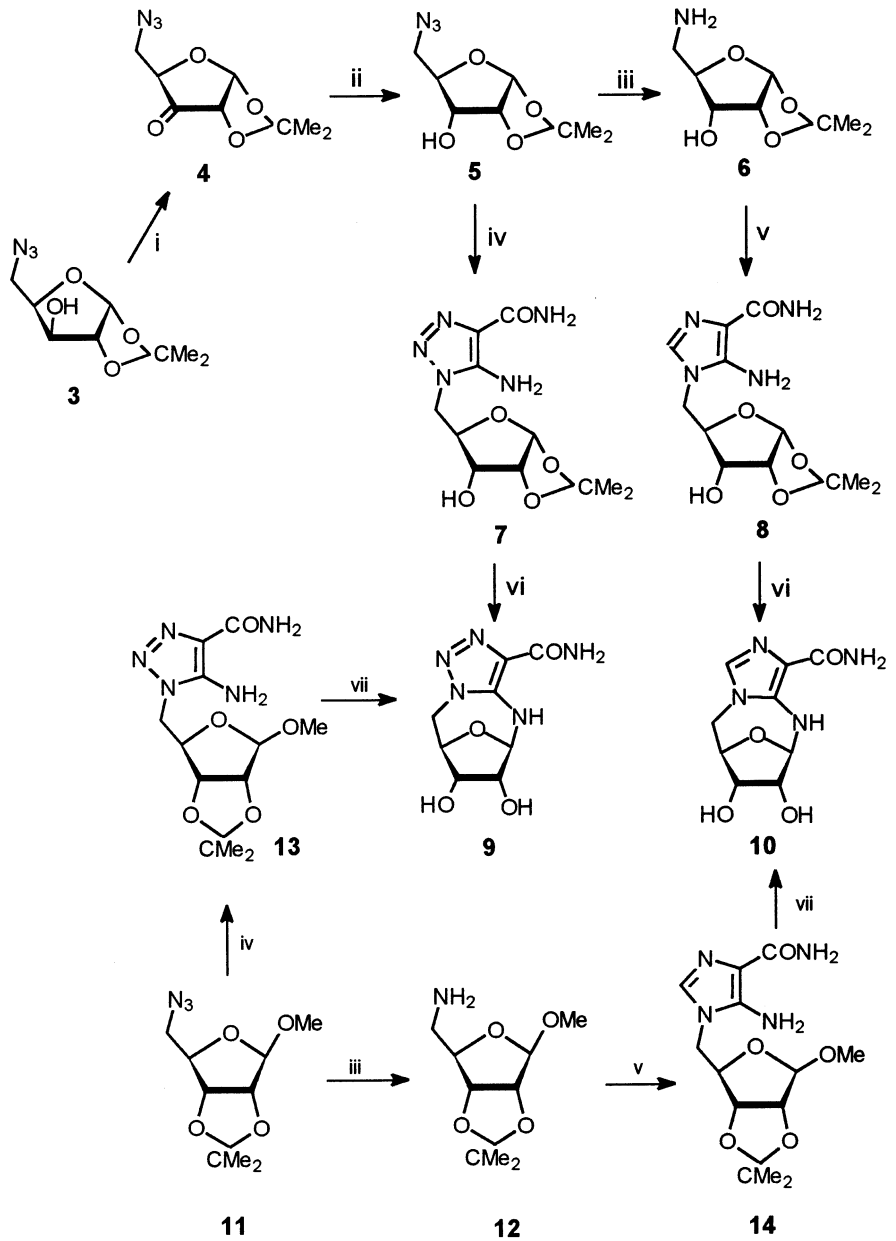
can easily be converted to a 5-azido derivative, which in turn provides access to the 5-triazolo and 5-imidazolo compounds (e.g., **1**, X = N or CH, respectively) that are required for the cyclisation shown in Scheme 1. It was anticipated that a measure of both stereo- and regiocontrol would be possible with the pentofuranose ring in the xylo configuration, since the disposition of the three secondary hydroxy groups is such that the sugar can be maintained in the α configuration by acetonation across the 1,2 positions. This strategy promotes facile attack on the β face of the ring by the amino group and provides a good leaving group. Furthermore, attack at the C-2 position may be sterically hindered by the 3-OH group, thereby enhancing the regioselectivity of the cyclisation. In the event, complete regio- and stereocontrol was observed in the formation of the xylo versions of compound **2** (X = CH or N).

## 2. Results and discussion

In order to further explore the regiochemistry of this new cyclisation reaction, we have now applied our methodology to the formation of compounds **1** and **2** with a ribo configuration in the pentofuranose ring. A convenient starting point is the protected 5-azido-5-deoxy-α-D-xylofuranose derivative **3** (Scheme 2) used previously [2] to obtain compounds **1** and **2** in a xylo configuration. Compound **3** was converted to the ribo analogue **5** by a modification of the method of Kefurt et al. [3] (using pyridinium chlorochromate [4] as the oxidising agent). Using the methodology described previously [2], compound **5** was converted to the azole derivatives **7** and **8**, which were then cyclised to afford the novel cyclonucleoside analogues[1] 1,5′-*cyclo*-5-(5′-deoxy-β-D-ribofuranosylamino)-1,2,3-triazol-4-carboxamide (**9**) and 1,5′-*cyclo*-5-(5′-deoxy-β-D-ribofuranosylamino)imidazol-4-carboxamide (**10**). The structures were confirmed by NMR spectroscopy, in particular the coupling between the NH group and the pentose H-1 proton and the upfield shift of 10–11 ppm for C-1 relative to the uncyclised precursor.

The cyclisation was totally regiospecific in both cases. When compared with the similar regiospecificity shown for the formation of the xylo analogues [2], it appears that the hydroxyl group in the 3 position of the pentofuranose probably exerts little steric influence on the reaction shown in Scheme 1. This route to the ribose cyclonucleoside analogues controls the stereochemistry of the cyclisation step by fixing the furanose ring in its α configuration (as was the case for the formation of the xylo compounds [2]). In order to further examine the importance of this factor, cyclonucleosides **9** and **10** were synthesised by an alternative route in which the anomeric configuration is not constrained and the ribose derivatives adopt the (mainly) β configuration (Scheme 2). Starting from D-ribose, the protected 5-azido-5-deoxy-α-D-ribofuranoside **11** was obtained in four steps by standard procedures. This compound was then converted to the corresponding 5-imidazo and 5-triazolo derivatives **13** and **14** by the methodology described above. This series of ribose derivatives are all methyl glycosides and, on the basis of NMR spectroscopy, all compounds were in the β configuration. The final cyclisation step proved to be difficult. Under the conditions used to cyclise compounds **7** and **8** (90% trifluoroacetic acid at room temperature), the glycosidic bond (C–OMe) in compounds **13** and **14** is more resistant to hydrolysis than in the acetonated derivatives. Norris et al. [5] have successfully hydrolysed the analogue of **13** without the 5-amino group using an aqueous hydrochloric acid–acetonitrile mixture. Application of that method to compounds **13** and **14** resulted in the formation of the desired cyclic products **9** and **10** in low yield (ca. 16%), together with several degradation products. It appears that the configuration at the anomeric centre is crucial and the β configuration of **13** and **14** hinders an attack by the amino group.

[1] The systematic names of these compounds are (5*R*,6*R*,7*S*,8*R*)-6,7-dihydroxy-4,5,6,7,8,9-hexahydro-5,8-epoxy-[1,2,3]triazolo[1,5-*a*][1,3]diazocin-3-carboxamide (**9**) and (2*R*,3*R*,4*S*,5*R*)-3,4-dihydroxy-1,2,3,4,5,6-hexahydro-2,5-epoxy-imidazo[1,5-*a*][1,3]diazocin-10-carboxamide (**10**). The normal nucleoside nomenclature is more useful in the present context.




Scheme 2. Reagents and conditions: (i) pyridinium chlorochromate, 3 days at rt; (ii) $NaBH_4$, 4 h, rt; (iii) $PPh_3$, aq THF, 1 h at rt; (iv) $CNCH_2CONH_2$, KOH in aq DMF, 24 h at rt; (v) $CH(OEt)_3$, and aminocyanoacetamide in MeCN, reflux 45 min; (vi) aq TFA, 6 h at rt; (vii) aq HCl in MeCN, 8 h at 80 °C.

Simple molecular mechanics calculations have been used to examine the conformation of the ribose cyclonucleoside analogue **10** for comparison with the corresponding xylose analogue [2]. The minimum-energy molecular conformation was obtained for all combinations of the normal staggered conformations of the hydroxyl groups. Most forms were too high in energy to be significantly populated and only data for the two lowest-energy forms are given in Table 1, together with data for the xylo analogue [2]. The two ribo forms have the two hydroxyl groups mutually weakly hydrogen bonded. The overall molecular shape is very similar to that observed for the corresponding xylose derivative, i.e., a distorted boat shape with the imidazole ring coplanar with one end face of the boat. In all conformations, including the high energy forms, the ribose ring has a conformation that lies on the pseudorotation cycle in the range $E_O{-}_OT^1$.

The xylose analogue has greater conformational freedom for the hydroxyl groups since these cannot interact with each other. This is reflected in the number of contributing forms (Table 1). The conformation of the sugar ring shows a small shift round the pseudorotation cycle to the other side of the $E_O$ position when compared with the ribo configuration, but there is very little variation across the set and all populated forms lie in the comformation range $^4T_O$ and $E_O$ (Table 1). This is slightly closer to the southern conformation common in DNA duplexes than it is to the northern conformation preferred by RNA. The two different configurations of the imidazole cyclonucleoside analogues are compared in Fig. 1. The distance between the centre of the imidazole ring and the opposite face of the boat is 3.44 Å in the xylo configuration and 3.40 Å in the ribo configuration. The angle between the pentose end face of the boat and the bottom face is ca. 116° in both systems and the corresponding angle at the other end of the boat is 145° in the ribo form and 142° in the xylo form. These data confirm that the geometry of the tricyclic system is essentially independent of the pentose configuration.

Both the ribo and xylo configurations of the cyclonucleosides **2** are severely conformationally restricted and the normal N ⇌ S equilibrium does not occur. Since conformational inflexibility is expected to be an important way of increasing the binding affinity in duplex formation [6], we intend to explore further applications of the novel cyclisations reported here and elsewhere [2] in order to obtain nucleoside analogues capable of incorporation into an oligonucleotide.

## 3. Experimental

*General methods.*—Melting points were determined on an electrothermal automatic apparatus, and are uncorrected. Optical rotations, for solns in $CHCl_3$ or MeOH, were measured with a Jasco model DIP-370 digital polarimeter at 25 °C. NMR spectra were recorded with a Jeol Lambda 400 or a Bruker WB-300 spectrometer for solns in $CDCl_3$ or $(CD_3)_2SO$ ($Me_2SO$). All couplings are given in Hz. Assignments were confirmed by standard 2D correlation methods (COSY and HMQC). Elemental analyses were performed on a Fisons EA 1108 instrument. Reactions were monitored by TLC on aluminium plates of silica gel (Kieselgel 60 $F_{254}$) and spots were detected by spraying with an ethanolic soln of phosphomolybdic acid–$H_2SO_4$. Column chromatography was performed on silica gel (60 mesh, Matrex). Molecular modelling calculations were carried out with the Nemesis package [8] mounted on a PC (166 MHz). The standard parameterisation of the Cosmic force field was used throughout.

*5-Azido-5-deoxy-1,2-*O*-isopropylidene-α-*D*-ribofuranose* (**5**).—5-Azido-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose [2] (9.0 g, 42 mmol) in $CH_2Cl_2$ (90 mL) was added dropwise to a soln of pyridinium chlorochromate (27.4 g, 127 mmol) in $CH_2Cl_2$ (90 mL) standing over 3 Å molecular sieves (27.5 g). This mixture was stirred for 3 days at room temperature (rt), filtered on Celite and the filtrate evaporated to dryness in vacuo. The residue was chromatographed (acetone–hexane) to give 5-azido-5-deoxy-1,2-*O*-isopropylidene-α-

Table 1
Conformation of the pentose ring in ribo and xylo forms of compound **2** (X = CH)

| Pentose configuration | Hydroxyl conformation [a] | Pentose ring conformation [b] | Relative energy [c] | Population (%) |
|---|---|---|---|---|
| Ribose | $tg^-$ | $_OT^1$ | 0 | 49 |
| Ribose | $g^-g^+$ | $E_O$ | 0.05 | 45 |
| Xylose | $g^+g^-$ | $^4T_O$ | 0 | 51 |
| Xylose | $g^-g^-$ | $^4T_O$ | 0.53 | 21 |
| Xylose | $tg^+$ | $E_O$ | 0.77 | 14 |
| Xylose | $g^-g^+$ | $E_O$ | 1.10 | 8 |
| Xylose | $tg^-$ | $^4T_O$ | 1.19 | 7 |

[a] Defined by the two torsion angles H–O-2–C-2–C-1, H–O-3–C-3–C-2.
[b] Defined using the standard symbols for the twist and envelope forms.
[c] Relative to the lowest-energy form of each type of ring configuration (in kcal $mol^{-1}$). The lowest-energy ribo form is ca. 0.4 kcal $mol^{-1}$ more stable than the corresponding xylo species.

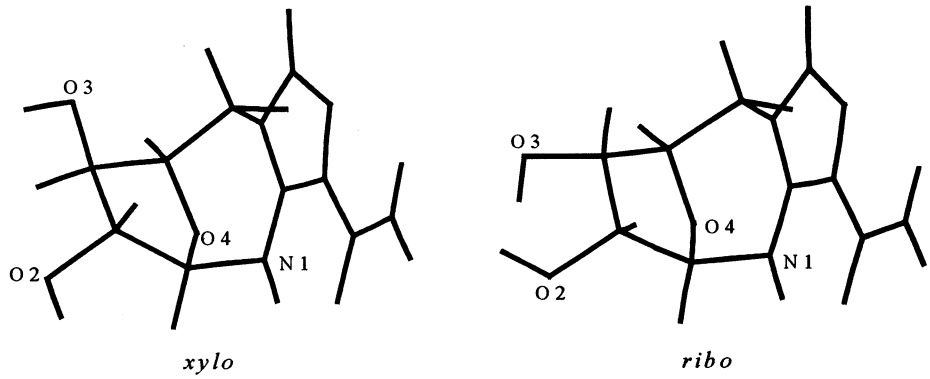



Fig. 1. Comparison of the xylo and ribo configurations of the cyclonucleoside analogue **2**. The pentofuranose heteroatoms are labelled (sugar numbering).

D-*erythro*-pentofuranos-3-ulose (**4**) as a colourless liquid (7.1 g, 80%): $[\alpha]_D^{25}$ +185.2° (*c* 1.1, $CHCl_3$); IR ($cm^{-1}$): 2108 (N=N=N), 1775 (C=O); $^1H$ NMR ($CDCl_3$): 6.08 (1 H, d, $J_{1,2}$ 4.4, H-1), 4.44 (1 H, dd, $J_{4,5a}$ 3.2, H-4), 4.32 (1 H, d, H-2), 3.62 (1 H, dd, $J_{4,5b}$ 3.3, H-5a), 3.47 (1 H, dd, $J_{5a,5b}$ 13.2, H-5b), 1.42, 1.36 (6 H, 2 s, Me); $^{13}C$ NMR ($CDCl_3$): 114.3, 27.3, 26.9 (isopropylidene), 103.0 (C-1), 78.3 (C-4), 76.0 (C-2), 51.2 (C-5), 208.0 (C-3). Compound **4** (4.0 g, 19 mmol) was reduced by the method of Kefurt et al. [3] to afford the ribose derivative **5**; $^1H$ NMR ($CDCl_3$): 5.76 (1 H, d, $J_{1,2}$ 3.7, H-1), 4.51 (1 H, t, $J_{2,3}$ 4.5, H-2), 3.84 (2 H, m, H-3, H-4), 3.62 (1 H, dd, H-5b), 3.31 (1 H, dd, $J_{5a,5b}$ 13.4, H-5a), 2.57 (1 H, d, $J_{3,OH}$ 5.3, OH), 1.50, 1.30 (6 H, 2 s, Me); $^{13}C$ NMR ($CDCl_3$): 112.8, 26.4 (isopropylidene), 103.9 (C-1), 79.2 (C-4), 78.3 (C-2), 72.0 (C-3), 50.6 (C-5). Anal. Calcd. for $C_8H_{13}N_3O_4$ (215.21): C, 44.65; H, 6.09; N, 19.52. Found: C, 44.74; H, 6.32; N, 19.47.

*5-Amino-5-deoxy-1,2*-O-*isopropylidene*-α-D-*ribofuranose* (**6**).—Triphenylphosphine (4.9 g, 19 mmol) was added to a soln of compound **5** (3.7 g, 18 mmol) in a 4:1 mixture of THF–water (40 mL) and the mixture stirred for 1 h. The THF was removed by evaporation and the residue extracted twice with $Et_2O$. The aq phase was concd under reduced pressure to give the 5-amino-5-deoxy-α-D-ribofuranose derivative **6** (3.0 g, 92%): mp 107–108 °C (from EtOH–EtAc); $[\alpha]_D^{25}$ +41.1° (*c* 1.0, $CHCl_3$); $^1H$ NMR ($CDCl_3$): 5.71 (1 H, d, $J_{1,2}$ 3.8, H-1), 4.49 (1 H, t, $J_{2,3}$ 4.5, H-2), 3.76 (2 H, m, $J_{3,4}$ 0, H-3, H-4), 3.01 (1 H, dd, H-5b), 2.83 (1 H, dd, $J_{5a,5b}$ 13.9, H-5a), 1.51, 1.30 (6 H, 2 s, Me); $^{13}C$ NMR ($CDCl_3$): 112.4, 26.4(isopropylidene), 103.7 (C-1), 80.5 (C-4), 78.9 (C-2), 72.7 (C-3), 42.4 (C-5). Anal. Calcd. for $C_8H_{15}NO_4$ (189.21): C, 50.78; H, 7.99; N, 7.40. Found: C, 50.70; H, 8.16; N, 7.25.

*5-(5-Amino-4-carbamoyl-1,2,3-triazol-1-yl)-5-deoxy-1,2*-O-*isopropylidene*-α-D-*ribofuranose* (**7**).—5-Azido-5-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**9**) (2.0 g, 9.3 mmol) was added to a soln of KOH (0.86 g, 14 mmol) and cyanoacetamide (1.3 g, 14 mmol) in water (2 mL) and DMF (20 mL). After 24 h, the mixture was filtered through Celite and the filtrate evaporated to dryness in vacuo. A soln of the residue in MeOH (40 mL) was neutralised with Dowex 50 ($H^+$), filtered and taken to dryness in vacuo. The resulting syrup was chromatographed (acetone–hexane) to give compound **7** as white crystals (2.36 g, 85%): mp 169 °C (from a 9:1 mixture of acetone–EtOH); $[\alpha]_D^{25}$ +17.7° (*c* 0.5, MeOH); $^1H$ NMR ($Me_2SO$): 7.43, 7.08 (2 H, two br s, $CONH_2$), 6.08 (2 H, br s, $NH_2$), 5.64 (1 H, d, $J_{1,2}$ 3.4, H-1), 4.48 (1 H, dd, $J_{2,3}$ 4.3, H-2), 4.42 (1 H, dd, $J_{4,5a}$ 2.2, H-5a), 4.27 (1 H, dd, $J_{5a,5b}$ 15.0, H-5b), 4.09 (1 H, m, $J_{4,5'}$ 6.6, H-4), 3.70 (1 H, m, $J_{3,4}$ 8.8, $J_{3,OH}$ 6.4, H-3), 1.41, 1.25 (6 H, 2 s, Me); $^{13}C$ NMR ($Me_2SO$): 111.6, 26.2, 26.4 (isopropylidene), 103.3 (C-1), 78.8 (C-2), 77.3 (C-4), 72.3 (C-3), 46.3 (C-5), 121.6 (triazole C-4), 145.3 (triazole C-5), 164.2 ($CONH_2$). Anal. Calcd for $C_{11}H_{17}N_5O_5$ (299.29): C, 44.14; H, 5.72; N, 23.40. Found: C, 44.48; H, 5.72; N, 23.10.

*5-(5-Amino-4-carbamoylimidazol-1-yl)-5-deoxy-1,2-O-isopropylidene-α-D-ribofuranose* (**8**).—A mixture of triethyl orthoformate (2.7 g, 18.5 mmol) and aminocyanoacetamide (1.8 g, 18.5 mmol) in anhyd MeCN (20 mL) was heated under reflux for 45 min, then cooled and a soln of amine **6** (2.0 g, 10.6 mmol) in MeCN (20 mL) was added. After 15 h at rt, the soln was filtered, concd under reduced pressure and the residue chromatographed (3:1 mixture of acetone–hexane) to give compound **12** (2.3 g, 58%): mp 216 °C (from a 9:1 mixture of acetone–EtOH); $[\alpha]_D^{25}$ +16.9° (*c* 0.5, MeOH); $^1$H NMR ($Me_2SO$): 7.06 (1 H, s, imidazole H-2), 6.78, 6.65 (2 H, 2 br s, $CONH_2$), 5.67 (1 H, d, $J_{1,2}$ 3.5, H-1), 5.57 (2 H, br s, $NH_2$), 4.48 (1 H, t, $J_{2,3}$ 3.9, H-2), 4.12 (1 H, d, H-5a), 3.96 (1 H, m, $J_{4,5b}$ 6.5, H-4), 3.88 (1 H, m, $J_{5a,5b}$ 14.1, H-5b), 3.52 (1 H, m, H-3), 1.42, 1.25 (6 H, 2 s, Me); $^{13}$C NMR ($Me_2SO$): 111.6, 26.2, 26.4 (isopropylidene), 103.2 (C-1), 78.7 (C-2), 77.3 (C-4), 72.0 (C-3), 43.4 (C-5), 130.5 (imidazole C-2), 111.6 (imidazole C-4), 143.1 (imidazole C-5), 166.5 ($CONH_2$). Anal. Calcd for $C_{12}H_{18}N_4O_5$ (298.30): C, 48.32; H, 6.08; N, 18.78. Found: C, 48.43; H, 6.10; N, 18.38.

*1,5′-cyclo-5-(5′-Deoxy-β-D-ribofuranosyl-amino)-1,2,3-triazole-4-carboxamide* (**9**).—The triazole derivative **7** (500 mg, 1.7 mmol) was dissolved in a 9:1 mixture of $CF_3COOH$–water (5 mL) and the soln was stirred for 5 min at rt. Trifluoroacetic acid was removed by evaporation and the residue was chromatographed (acetone–hexane) to give compound **9** as a hygroscopic white powder (225 mg, 56%): mp 250 °C (from EtOH); $[\alpha]_D^{25}$ +79.1° (*c* 0.5, water); $^1$H NMR ($Me_2SO$): 7.56, 7.18 (2 H, two br s, $CONH_2$), 7.56 (1 H, d, $J_{1',NH}$ 3.8, NH), 5.22 (1 H, d, OH-3′), 5.21 (1 H, d, H-1′), 5.18 (1 H, d, $J_{2',OH}$ 4.9, OH-2′), 4.83 (1 H, dd, $J_{4',5a'}$ 1.3, H-5a′), 4.40 (1 H, m, $J_{4',5b'}$ 2.7, H-4′), 4.23 (1 H, dd, $J_{5a',5b'}$ 14.3, H-5b′), 3.89 (1 H, dt, $J_{3',4'}$ 2.1, H-3′), 3.72 (1 H, t, $J_{2',3'}$ 5.9, H-2′); $^{13}$C NMR ($Me_2SO$): 92.4 (C-1′), 81.9 (C-4′), 76.1 (C-2′), 71.6 (C-3′), 54.8 (C-5′), 122.7 (C-4), 144.7 (C-5), 163.8 ($CONH_2$). Anal. Calcd for $C_8H_{11}N_5O_4$ (241.21): C, 39.83; H, 4.60; N, 29.04. Found: C, 39.90; H, 4.68; N, 28.58.

*1,5′-cyclo-5-(5′-Deoxy-β-D-ribofuranosyl-amino)imidazol-4-carboxamide* (**10**).—The imidazole derivative **8** (1.0 g, 3.4 mmol) was dissolved in a 9:1 mixture of $CF_3COOH$–water (10 mL) and the soln was stirred for 5 min at rt. Trifluoroacetic acid was removed by evaporation and the residue was chromatographed (hexane–acetone) to give compound **6** as a white powder (480 mg, 60%): mp 214 °C (from EtOH); $[\alpha]_D^{25}$ +183.2° (*c* 0.5, water); $^1$H NMR ($Me_2SO$): 7.22 (1 H, d, $J_{1',NH}$ 4.4, NH), 7.22 (1 H, s, H-2), 6.93, 6.80 (2 H, 2 br s, $CONH_2$), 5.13 (1 H, d, $J_{2',OH}$ 5.6, OH-2′), 5.08 (1 H, d, H-1′), 5.05 (1 H, d, $J_{3',OH}$ 5.6 Hz, OH-3′), 4.47 (1 H, dd, $J_{4',5a'}$ 2.2, H-5a′), 4.32 (1 H, m, H-4′), 3.87–3.78 (2 H, m, $J_{5a',5b'}$ 14.1 Hz, H-3′, H-5b′), 3.67 (1 H, dd, H-2′); $^{13}$C NMR ($Me_2SO$): 92.9 (C-1′), 83.0 (C-4′), 76.1 (C-2′), 71.4 (C-3′), 51.7 (C-5′), 131.9 (C-2), 114.8 (C-4), 142.9 (C-5), 166.1 ($CONH_2$). Anal. Calcd for $C_9H_{12}N_4O_4$ (240.22): C, 45.00; H, 5.04; N, 23.32. Found: C, 45.20; H, 5.02; N, 22.92.

*Methyl 5-azido-5-deoxy-2,3-O-isopropylidene-β-D-ribofuranoside* (**11**).—This compound was obtained in 89% yield by the method of Brimacombe et al. [7]: $[\alpha]_D^{25}$ −60.1° (*c* 1.0, $CHCl_3$) {Lit. [7] $[\alpha]_D^{25}$ −58° ($CHCl_3$)}; $^1$H NMR ($CDCl_3$): 4.93 (1 H, s, H-1), 4.54 (2 H, s, H-2, H-3), 4.23 (1 H, t, $J_{4,5a}$ 7.1, H-4), 3.39 (1 H, dd, $J_{5a,5b}$ 12.5, H-5a), 3.20 (1 H, dd, $J_{4,5b}$ 6.8, H-5b), 3.31 (1 H, s, OMe), 1.42, 1.26 (6 H, 2 s, Me); $^{13}$C NMR ($CDCl_3$): 112.3, 26.3, 24.8 (isopropylidene), 109.7 (C-1), 85.3 (C-4), 85.0 (C-3), 82.0 (C-2), 55.1 (OMe), 53.7 (C-5).

*Methyl 5-amino-5-deoxy-2,3-O-isopropylidene-β-D-ribofuranoside* (**12**).—Triphenylphosphine (4.7 g, 17.6 mmol) was added to a soln of the azido derivative **11** (3.7 g, 16 mmol) in a 4:1 mixture of THF–water (37 mL) and the mixture stirred for 1 h. The THF was removed by evaporation and the residue extracted twice with $Et_2O$. The aq phase was concd under reduced pressure to give the 5-amino-5-deoxy-α-D-ribofuranoside (**12**) as an oil (3.0 g, 92%): $[\alpha]_D^{25}$ −70.7° (*c* 0.5, $CHCl_3$) {Lit. [8] $[\alpha]_D^{25}$ −71° ($CHCl_3$)}; $^1$H NMR ($CDCl_3$): 4.83 (1 H, s, H-1), 4.48 (1 H, s, H-2), 4.44 (1 H, s, H-3), 4.02 (1 H, t, $J_{4,5}$ 7.0, H-4), 3.22 (1 H, s, OMe), 2.65 (2 H, d,

H-5a, H-5b), 1.35, 1.18 (6 H, 2 s, Me); $^{13}$C NMR ($CDCl_3$): 112.1, 26.2, 24.8 (isopropylidene), 109.4 (C-1), 88.8 (C-4), 85.3 (C-3), 82.0 (C-2), 54.9 (OMe), 45.4 (C-5).

*Methyl 5-(5-amino-4-carbamoyl-1,2,3-triazol-1-yl)-5-deoxy-2,3-*O*-isopropylidene-β-*D*-ribofuranoside* (**13**).—Azidosugar **11** was converted to the analogous triazolo derivative **13** by the procedure described above. After chromatography (3:2 acetone–hexane), compound **13** was obtained as a white solid (80%): mp 178–180 °C (from acetone); $[\alpha]_D^{25}$ −40.1° (*c* 0.5, MeOH); $^1$H NMR ($Me_2SO$): 7.43, 7.10 (2 H, two br s, $CONH_2$), 6.40 (2 H, br s, $NH_2$), 4.97 (1 H, s, H-1), 4.76 (1 H, d, $J_{2,3}$ 6.0, H-2), 4.67 (1 H, d, H-3), 4.41 (1 H, t, $J_{4,5}$ 7.4, H-4), 4.27 (2 H, d, H-5), 3.32 (3 H, s, OMe), 1.36, 1.24 (6 H, 2 s, Me); $^{13}$C NMR ($Me_2SO$): 111.5, 24.5, 26.1 (isopropylidene), 109.0 (C-1), 84.3 (C-3), 82.9 (C-4), 81.1 (C-2), 54.6 (OMe), 48.2 (C-5), 121.6 (triazole C-4), 144.7 (triazole C-5), 164.1 ($CONH_2$). Anal. Calcd for $C_{12}H_{19}N_5O_5 \cdot 0.25\ H_2O$ (317.82): C, 45.35; H, 6.18; N, 22.04. Found: C, 45.65; H, 6.22; N, 21.72.

*Methyl 5-(5-amino-4-carbamoylimidazol-1-yl)-5-deoxy-2,3-*O*-isopropylidene-β-*D*-ribofuranoside* (**14**).—Azidosugar **11** was reduced and then converted to the analogous imidazolo derivative **14** by the procedure described above. After chromatography (7:3 acetone–hexane), compound **14** was obtained as a hygroscopic white solid (59%): mp 191–193 °C (from acetone); $[\alpha]_D^{25}$ −7.6° (*c* 0.9, MeOH); $^1$H NMR ($Me_2SO$): 7.14 (1 H, s, H-2), 6.75, 6.66 (2 H, two br s, $CONH_2$), 5.83 (2 H, br s, $NH_2$), 4.96 (1 H, s, H-1), 4.72 (1 H, d, $J_{2,3}$ 5.8, H-2), 4.66 (1 H, d, H-3), 4.38 (1 H, t, $J_{4,5a}$ 7.6, $J_{4,5b}$ 7.2, H-4), 3.97 (1 H, dd, $J_{5a,5b}$ 14.4, H-5a), 3.85 (1 H, dd, H-5b), 3.31 (3 H, s, OMe), 1.30, 1.25 (6 H, 2 s, Me); $^{13}$C NMR ($Me_2SO$): 112.7, 26.2, 26.4 (isopropylidene), 109.2 (C-1), 84.4 (C-3), 83.3 (C-4), 81.1 (C-2), 54.7 (OMe), 45.7 (C-5), 130.1 (C-2), 111.5 (C-4), 142.7 (C-5), 166.6 ($CONH_2$). Anal. Calcd for $C_{13}H_{20}N_4O_5 \cdot 0.1\ H_2O$ (314.12): C, 49.70; H, 6.43; N, 17.84. Found: C, 49.43; H, 6.54; N, 17.95.

*Cyclisation of compounds* **13** *and* **14**.—Compounds **13** and **14** were each treated with $CF_3COOH$ as described above for compound **7**. In both cases, the crude product was shown by NMR to be the uncyclised methyl riboside without the isopropylidene protecting group. This material was not purified further. Treatment of compound **13** with dilute HCl in MeCN for 8 h at 80 °C gave a complex mixture of products. The crude mixture was chromatographed (1:4 hexane–acetone) to give compound **9** in 16% yield. Similar treatment of compound **14** followed by chromatography (1:9 hexane–acetone) gave the cyclic compound **10** in 17% yield.

## Acknowledgements

We thank the Conseil Regional de Picardie and the Ministère de la Recherche for financial support.

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