

5'-SUBSTITUTED-5'-DEOXY NUCLEOSIDES

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Abstract—The methyl esters of the uronic acids derived from uridine, 5-fluorodeoxyuridine, 6-aza-2'-deoxyuridine and 2',3'-*o*-isopropylideneadenosine were converted to the amides with aqueous *d*0.88 ammonia. After protection of the sugar hydroxyls each 5'-carboxamide was dehydrated with phosphoryl chloride at -5° to yield, after deprotection, the respective novel 5'-nitrile nucleosides. Treatment of the protected 5'-nitrile nucleosides with ammonium azide in DMF gave, after deprotection, the novel 5'-C-tetrazole nucleosides.

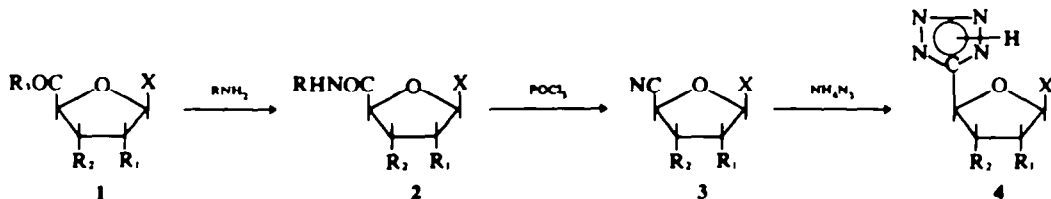
A variety of nucleosides has been prepared with modifications at the 5'-position. Esterification of the primary alcoholic function in thymidine, for example, has led to an interesting series of thymidine kinase inhibitors.¹ Other types of analogues include 5'-cyclopropyl-5'-deoxythymidine,² 5'-C-monomethyl- and 5'-C-dimethyl-5'-deoxythymidine,³ and 5'-fluoro-5'-deoxythymidine, which is a potent inhibitor of thymidylate kinase.⁴ Some esters have been prepared from the uronic acids of thymidine,⁵ uridine,⁶ 5-fluorodeoxyuridine (FUDR),⁷ and 2',3'-*o*-isopropylideneadenosine.⁸ In this paper, the esters of the uronic acids of uridine, FUDR, 2',3'-*o*-isopropylideneadenosine and 6-aza-2'-deoxyuridine have been converted *via* the amides to the novel 5'-nitriles and 5'-tetrazoles.

The readily available 1'-uracil-1-yl- β -D-ribofuranuronic acid, **1a** ($R_1 = R_2 = R_3 = OH$) was converted by treatment with the appropriate alcohol and mineral acid to a series of esters (Table I). The methyl ester, **1a** ($R_1 = R_2 = OH$; $R_3 = OMe$) was treated with *d*0.88 ammonia, ethylamine or isopropylamine to give the amides, **2a** ($R = H$, Et or Pr; $R_1 = R_2 = OH$). 1'-Uracil-1-yl- β -D-ribofuranuronamide, protected by acetylation with acetic anhydride, was dehydrated with phosphoryl

chloride⁹ at -5° to give the protected nitrile, **3a** ($R_1 = R_2 = OAc$). Brief treatment with 50% (v/v) aqueous ammonia, followed by fractionation on a silicic acid column gave the nitrile, **3a** ($R_1 = R_2 = OH$) in 20% overall yield from the amide. The protected nitrile was converted to the protected tetrazole nucleoside with ammonium azide at 90° for 4 h. Deacetylation gave the tetrazole, **4a** ($R_1 = R_2 = OH$) a non-phosphorus-containing analogue of uridine-5'-monophosphate.

FUDR, prepared unambiguously from deoxyuridine by the method of Robins *et al.*¹⁰ was oxidized with platinum/oxygen to the uronic acid and converted *via* the methyl ester⁷ to the amide, **2b** ($R = R_1 = H$; $R_2 = OH$). The corresponding nitrile and tetrazole nucleosides were obtained by the method described above.

6-Aza-2'-deoxyuridine, prepared *via* the silylation method,¹¹ was shown by NMR spectroscopy to contain about 10% of the α -anomer. The mixture was converted to the amide **2c** ($R = R_1 = H$; $R_2 = OH$) isolated as the pure β -anomer in 78% yield, after a single recrystallisation of the anomeric mixture. The amide was acetylated and dehydrated to the protected nitrile, which after deacetylation gave **3c** ($R_1 = H$; $R_2 = OH$) in 36% overall yield. The tet-



- a: X = uracil-1-yl
 b: X = 5-fluorouracil-1-yl
 c: X = 6-azauracil-1-yl
 d: X = adenin-9-yl

razole 4c ($R_1 = H$; $R_2 = OH$) was obtained by the usual sequence in 59% yield.

Methyl - 1' - adenin - 9 - yl - 2',3' - o - isopropylidene - β - D - ribofuranuronate¹ was converted via the amide to the protected nitrile 3d ($R_1 + R_2 = -OCMe_2O-$) in 46% overall yield. Treatment of the protected nitrile with ammonium azide, followed by deacetonation, gave the tetrazole, 4d ($R_1 = R_2 = OH$), isolated as its hygroscopic sodium salt by preparative TLC on silicic acid.

The chemical shift of the H-4' proton in each series of analogues varied in a consistent manner according to the nature of the group on the 5'-position. For example, when the 5'-variant was a nitrile, the H-4' signal was found in the region δ 4.7-4.9, whereas for the ester variants the signal was in the region δ 4.2-4.5, and for the amide variants in the region δ 4.0-4.2. The C-tetrazole variants gave the furthest downfield shift of the H-4' proton, which occurred between δ 4.9-5.3. These results indicate that the chemical shift values of the H-4' proton in each case can be correlated with the electron-withdrawing capacity of the substituent on the 5'-position of the carbohydrate moiety.

All of the analogues were tested against a wide variety of bacterial and viral strains and also as inhibitors of mitosis in cultured mouse fibroblasts. In all cases no significant *in vitro* or *in vivo* biological activity was observed.

EXPERIMENTAL

General. M.p.s were determined by use of a Büchi M.P. apparatus and were uncorrected.

Evaporations under reduced pressure were carried out with the aid of a Rotavapor R (Büchi, Switzerland) at 30°, 24 mm Hg unless otherwise stated.

Column chromatography was carried out on silicic acid (Kieselguhr 7734, mesh 70-200, Merck). Preparative TLC was effected by use of silicic acid (GF254, Merck) on 20 x 20 cm plates.

Solvents used in the chromatographic procedures are designated as follows:

Solvent 1: chloroform:ethanol (19:1 v/v)

Solvent 2: acetonitrile:water (22:3 v/v)

NMR spectra were recorded in DMSO d_6 by use of a Varian HA100 spectrometer.

UV spectra were recorded in a spectroscopic EtOH by use of a Varian Cary 17 = 16 UV spectrometer.

Methyl 1' - uracil - 1 - yl - β - D - ribofuranuronate. A soln of 1a ($R_1 = R_2 = R_3 = OH$)¹ (1.05 g) in dry MeOH (50 ml) and 98% H_2SO_4 (0.1 ml) was heated under reflux for 12 h and left to cool. The mixture was evaporated to a small volume (5 ml) and water (10 ml) added. The white crystals that deposited were filtered off, washed with water and re-crystallised from EtOH to give 0.74 g (66%) of white needles of 1a ($R_1 = R_2 = OH$; $R_3 = OMe$). The same procedure was used for the following esters 1a ($R_1 = R_2 = OH$; R_3 : see Table 1).

1' - Uracil - 1 - yl - β - D - ribofuranuronamide. A soln of 1a ($R_1 = R_2 = OH$; $R_3 = OMe$) (0.74 g) in *d* 0.88 ammonia (20 ml) was left to stand for 30 min at room temp

Table 1

| R ₃ | Yield, % | M.p., °C | NMR H-4' (S) | ϵ_{max} at 261 nm |
|----------------|----------|----------|--------------|----------------------------|
| OMe | 66 | 247 | 4.35(d) | 10100 |
| OEt | 57 | 252-253 | 4.37(d) | 10100 |
| OPr-n | 62 | 224-225 | 4.38(d) | 10050 |
| OPr-i | 82 | 219-220 | 4.33(d) | 10150 |
| OBu-n | 59 | 199-200 | 4.39(d) | 10100 |
| OOct-n | 45 | 182 | ca 4.41 | 10150 |
| ODodec-n | 43 | 178 | 4.36(d) | 9900 |
| OBz | 84 | 190-191 | 4.48(d) | 9750 |

Table 1. Elemental analysis

| R ₃ | Found % | | | Required % | | |
|----------------|---------|-----|------|------------|-----|------|
| | C | H | N | C | H | N |
| OMe | 44.4 | 4.3 | 10.5 | 44.2 | 4.4 | 10.2 |
| OEt | 46.3 | 5.2 | 10.1 | 46.1 | 4.9 | 9.8 |
| OPr-n | 48.0 | 5.4 | 9.3 | 48.0 | 5.4 | 9.4 |
| OPr-i | 47.7 | 5.4 | 9.6 | 48.0 | 5.4 | 9.4 |
| OBu-n | 49.8 | 5.8 | 8.9 | 49.8 | 5.8 | 8.9 |
| OOct-n | 55.3 | 7.2 | 7.4 | 55.2 | 7.1 | 7.6 |
| ODodec-n | 59.1 | 8.2 | 6.4 | 59.1 | 8.1 | 6.6 |
| OBz | 55.2 | 4.7 | 7.6 | 55.2 | 4.6 | 8.1 |

and then evaporated to dryness. The solid obtained was crystallised from EtOH to give 0.67 g (93%) of white needles of 2a ($R = H$; $R_1 = R_2 = OH$): m.p. 256° dec; λ_{max} 259 nm (ϵ 10,100); NMR δ 4.23 (d, H-4', $J_{H-3, H-4} = 2$ Hz). (Found: C, 41.6; H, 4.3; N, 16.0. Calcd for $C_{10}H_{11}N_2O_6$: C, 42.0; H, 4.3; N, 16.4%).

N - Ethyl 1' - uracil - 1 - yl - β - D - ribofuranuronamide. 2a ($R = Et$; $R_1 = R_2 = OH$) was similarly obtained from the action of ethylamine on the methyl ester as white needles (81%): m.p. 252-253°; λ_{max} 260 nm (ϵ 9,700); NMR δ 4.21 (d, H-4', $J_{H-3, H-4} = 2$ Hz). (Found: C, 46.4; H, 5.3; N, 14.6. Calcd for $C_{10}H_{12}N_2O_6$: C, 46.3; H, 5.3; N, 14.7%).

N - n - Propyl 1' - uracil - 1 - yl - β - D - ribofuranuronamide. 2a ($R = Pr-n$; $R_1 = R_2 = OH$) was similarly obtained in 89% yield: m.p. 255° dec; λ_{max} 260 nm (ϵ 10,200); NMR δ 4.24 (d, H-4', $J_{H-3, H-4} = 2$ Hz). (Found: C, 48.0; H, 5.5; N, 14.0. Calcd for $C_{11}H_{13}N_2O_6$: C, 48.1; H, 5.7; N, 14.0%).

1' - Uracil - 1 - yl - 2',3' - di - O - acetyl - β - D - ribofuranuronamide. 2a ($R = Pr-n$; $R_1 = R_2 = OH$) was OH (1.35 g) in dry pyridine (50 ml) was added Ac_2O (2 ml) and the mixture set aside at room temp overnight. Water (5 ml) was added and the solvent evaporated to dryness under reduced pressure. The residue was repeatedly dissolved in water and the solvent evaporated to dryness until no trace of pyridine remained. The solid thus obtained was crystallised from EtOH to give 1.74 g (70%) of 2a ($R = H$; $R_1 = R_2 = OAc$): m.p. 150° (sinter 110°); λ_{max} 260 nm (ϵ 10,150); NMR δ 4.49 (s, H-4'). (Found: C, 43.5; H, 4.8; N, 11.6. Calcd for $C_{11}H_{11}N_2O_8$. 1H₂O: C, 43.5; H, 4.7; N, 11.7%).

1 - Uracil - 1 - yl - β - D - ribofuranuronitrile. To a soln of 2a ($R = H$, $R_1 = R_2 = OAc$) (0.93 g), in dry pyridine

(50 ml) at -5° , was added POCl_3 (0.5 ml) and the mixture stirred at -5° for 2 h. Crushed ice (10 ml) was added to destroy the excess of POCl_3 , and the solvent removed under reduced pressure. The residual gum was applied in a soln of chloroform to a silicic acid column, which was eluted with solvent 1. The fractions containing the major product were pooled and evaporated to a white solid, which was crystallised from EtOH to give 0.59 g (68%) of $3a(\text{R}_1 = \text{R}_2 = \text{OAc})$: m.p. 202–203 $^{\circ}$; λ_{max} 259 nm (ϵ 10,000); NMR δ 5.05 (d, H-4', $J_{\text{H-3',H-4'}} = 6$ Hz). (Found: C, 48.2; H, 4.3; N, 13.3. Calcd for $\text{C}_{11}\text{H}_{11}\text{N}_3\text{O}_7$: C, 48.3; H, 4.0; N, 13.0%.)

A soln of the above diacetate (0.2 g) in aqueous ammonia (10 ml, 50% v/v) was left to stand for 1 h at room temp and the solvent removed by evaporation under reduced pressure. The residue was crystallised from EtOH to give 0.11 g (74%) of $3a(\text{R}_1 = \text{R}_2 = \text{OH})$: m.p. 215–216 $^{\circ}$ dec; λ_{max} 260 nm (ϵ 10,000); NMR δ 4.73 (d, H-4', $J_{\text{H-3',H-4'}} = 4$ Hz). (Found: C, 45.1; H, 3.9; N, 17.4. Calcd for $\text{C}_8\text{H}_8\text{N}_3\text{O}_7$: C, 45.1; H, 3.8; N, 17.6%.)

1' - Uracil - 1 - yl - 4' - (R) - C - tetrazolo - β - D - erythrofuranosyl. To a soln of $3a(\text{R}_1 = \text{R}_2 = \text{OAc})$ (0.1 g) in dry DMF was added sodium azide (0.022 g) and ammonium chloride (0.018 g), the mixture maintained at 90° for 4 h and then left to cool. The inorganic ppt was filtered off and the filtrate evaporated to dryness under reduced pressure (30 $^{\circ}$, 0.1 mm Hg). The oily residue was fractionated by preparative TLC in solvent 2. The major bands were excised and eluted with EtOH. Evaporation of the solvent yielded a hygroscopic gum which resisted crystallisation and gave a non-reproducible chemical analysis (C, H, N). The gum was dissolved in water (pH 4.5) and passed through a short column of Dowex 50-WX (Na^+ form). The pH of the eluate and water washings was found to be 7.0. Given that the pK_a of 5-methyltetrazole is 5.56,¹² it was predicted that the tetrazole nucleoside was present in the form of its sodium salt. Evaporation of the water yielded 0.062 g (55%) of a white powder of $4a(\text{R}_1 = \text{R}_2 = \text{OAc})$: m.p. 250 $^{\circ}$ dec; λ_{max} 260 nm (ϵ 10,050); NMR δ 5.47 (s, H-4'). (Found: C, 37.6; H, 4.2; N, 20.1. Calcd for $\text{C}_{11}\text{H}_{10}\text{N}_6\text{O}_7\text{Na} \cdot 1.5\text{H}_2\text{O}$: C, 37.5; H, 3.9; N, 20.2%.)

A soln of the above diacetate (0.2 g) in aqueous ammonia (10 ml, 50% v/v) was left to stand for 30 min at room temp and the solvent removed by evaporation under reduced pressure. The residue was fractionated by preparative TLC in solvent 2. The major product was isolated similarly to the above diacetate to give 0.135 g (93%) of $4a(\text{R}_1 = \text{R}_2 = \text{OH})$: m.p. > 300 $^{\circ}$; λ_{max} 261 nm (ϵ 9900); NMR δ 4.35 (s, H-4'). (Found: C, 36.3; H, 3.8; N, 25.6. Calcd for $\text{C}_8\text{H}_8\text{N}_6\text{O}_7\text{Na} \cdot 0.5\text{C}_2\text{H}_5\text{OH}$: C, 36.7; H, 3.8; N, 25.6%.)

1' - (5 - Fluorouracil) - 1 - yl - 2' - deoxy - β - D - ribofuranuronamide. The ester $1b(\text{R}_1 = \text{H}; \text{R}_2 = \text{OH}; \text{R}_3 = \text{OMe})$ (0.55 g) was treated with d 0.88 ammonia in the usual way to give, after crystallisation from EtOH, 0.42 g (82%) of $2b(\text{R} = \text{R}_1 = \text{H}; \text{R}_2 = \text{OH})$: m.p. 265–266 $^{\circ}$; λ_{max} 269 nm (ϵ 8600); NMR δ 4.2 (s, H-4'). (Found: C, 41.8; H, 4.0; N, 16.0; F, 7.5. Calcd for $\text{C}_8\text{H}_{10}\text{N}_4\text{O}_7\text{F}$: C, 41.7; H, 3.9; N, 16.2; F, 7.3%.)

1' - (5 - Fluorouracil) - 1 - yl - 3' - O - acetyl - 2' - deoxy - β - D - ribofuranuronamide. The above amide (0.35 g) was acetylated in the usual way to give, after crystallisation from EtOH, 0.42 g (89%) of $2b(\text{R} = \text{R}_1 = \text{H}; \text{R}_2 = \text{OAc})$: m.p. 137–138 $^{\circ}$; λ_{max} 269 nm (ϵ 9250); δ 4.39 (d, H-4', $J_{\text{H-3',H-4'}} = 2$ Hz). (Found: C, 45.3; H, 5.3; N, 11.7; F, 5.6. Calcd for $\text{C}_{11}\text{H}_{11}\text{N}_4\text{O}_7\text{F} \cdot \text{C}_2\text{H}_5\text{OH}$: C, 45.0; H, 5.2; N, 12.0; F, 5.5%.)

1' - (5 - Fluorouracil) - 1 - yl - 3' - O - acetyl - 2' - deoxy - β - D - ribofuranuronitrile. The above protected amide (0.57 g) was dehydrated with POCl_3 in the usual way to give, after crystallisation from EtOH, 0.32 g (68%) of $3b(\text{R}_1 = \text{H}; \text{R}_2 = \text{OAc})$: m.p. 149–150 $^{\circ}$; λ_{max} 269 nm (ϵ 8500); NMR δ 5.08 (d, H-4', $J_{\text{H-3',H-4'}} = 2$ Hz). (Found: C, 47.0; H, 3.7; N, 15.0. Calcd for $\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}_7\text{F}$: C, 46.7; 3.5; N, 14.8%.)

1' - (5 - Fluorouracil) - 1 - yl - 2' - deoxy - β - D - ribofuranuronitrile. The above nitrile (80 mg) was deprotected in the usual way to give 0.054 g (80%) of $3b(\text{R}_1 = \text{H}; \text{R}_2 = \text{OH})$: m.p. 190 $^{\circ}$; λ_{max} 269 nm (ϵ 8500); NMR δ 4.70 (d, H-4', $J_{\text{H-3',H-4'}} = 2$ Hz). (Found: C, 44.7; H, 3.4; N, 17.3. Calcd for $\text{C}_8\text{H}_8\text{N}_4\text{O}_7\text{F}$: C, 44.8; H, 3.3; N, 17.4%.)

1' - (5 - Fluorouracil) - 1 - yl - 4' (R) - C - tetrazolo - 2' - deoxy - β - D - erythrofuranosyl. $3b(\text{R}_1 = \text{H}; \text{R}_2 = \text{OAc})$ (0.12 g) was treated with sodium azide/ammonium chloride in the usual way. The product $4b(\text{R}_1 = \text{H}; \text{R}_2 = \text{OAc})$ 0.146 g (84%) was isolated by preparative TLC in solvent 2, as the sodium salt, monoethanol solvate, monohydrate: m.p. 211 $^{\circ}$ dec; λ_{max} 269 nm (ϵ 8400); NMR δ 5.19 (s, H-4'). (Found: C, 38.1; H, 4.4; N, 20.3. Calcd for $\text{C}_{11}\text{H}_{10}\text{N}_6\text{O}_7\text{FNa} \cdot \text{C}_2\text{H}_5\text{OH} \cdot \text{H}_2\text{O}$: C, 38.4; H, 4.4; N, 20.3%.)

The acylated tetrazole (0.081 g) was deprotected in the usual way to give 0.033 g (47%) of $4b(\text{R}_1 = \text{H}; \text{R}_2 = \text{OH})$ as the sodium salt hemi-hydrate: m.p. 192–193 $^{\circ}$; λ_{max} 269 nm (ϵ 8350); NMR δ 5.10 (s, H-4'). (Found: C, 34.8; H, 3.3; N, 26.6. Calcd for $\text{C}_8\text{H}_8\text{N}_6\text{O}_7\text{FNa} \cdot 0.5\text{H}_2\text{O}$: C, 34.4; H, 2.9; N, 26.6%.)

2' - Deoxy - D - ribofuranosyl - 6 - azauracil. To a soln of 3,5 - bis(trimethylsiloxy) - as - triazine¹¹ (14.5 g) in dichloromethane (200 ml) was added 2 - deoxy - 3,5 - di - O - p - toluyl - D - ribofuranosyl chloride (20.1 g). The mixture was stirred for 6 days at room temp and MeOH (3 ml) added and the solvent removed under reduced pressure. The residue was dissolved in CHCl_3 and filtered through Celite to remove unchanged 6-azauracil. The soln was evaporated to dryness to yield 14 g (61%) of an anomeric mixture of 3',5' - bis - O - p - toluyl - 2' - deoxy - D - ribofuranosyl - 6 - azauracil.

The anomeric mixture (12 g) was stirred with anhydrous MeOH (200 ml) containing 0.5M OMe soln (96 ml) at room temp overnight. The excess of base was neutralised by addition of Dowex 50-X8 (H^+ form) and the soln filtered. The filtrate was evaporated to a residual gum, which was crystallised from EtOH to give the nucleoside, 4.06 g (88%) as a mixture shown by NMR spectroscopy to contain the α - and β -anomers in the ratio 1:9 respectively. (Found: C, 41.7; H, 4.9; N, 18.4. Calcd for $\text{C}_8\text{H}_{11}\text{N}_4\text{O}_7$: C, 41.8; H, 4.9; N, 18.4%.)

1' - 6 - Azauracil - 1 - yl - 2' - deoxy - β - D - ribofuranuronamide. 2' - Deoxy - D - ribofuranosyl - 6 - azauracil (4 g) was oxidised with reduced Adam's catalyst/oxygen for 24 h at 80° in the usual way.⁶ The product, 1' - 6 - azauracil - 1 - yl - 2' - deoxy - D - ribofuranuronic acid (1.88 g) was converted without further purification into its methyl ester by the procedure described above. The ester was shown by NMR spectroscopy to contain both α - and β -anomers in the ratio 1:9 respectively. The syrupy ester was treated with d 0.88 ammonia in the usual way. The product was crystallised from EtOH to give $2c(\text{R} = \text{R}_1 = \text{H}; \text{R}_2 = \text{OH})$ 1.48 g (78.5% based on 5'-carboxylic acid) as its pure β -anomer: m.p. 211–212 $^{\circ}$; λ_{max} 262 nm (ϵ 4800); NMR δ 4.02 (d, H-4', $J_{\text{H-3',H-4'}} = 3$ Hz). (Found: C, 40.0; H, 4.1; N, 23.1. Calcd for $\text{C}_8\text{H}_{10}\text{N}_4\text{O}_7$: C, 39.7; H, 4.1; N, 23.0%.)

1'-6-Azauracil-1-yl-3'-O-acetyl-2'-deoxy- β -D-ribofuranuronamide. The amide (0.5 g) was acetylated in the usual way to give 2c(R = R₁ = H; R₂ = OAc) 0.54 g (92%): m.p. 216°; λ_{max} 262 nm (ϵ 4850); NMR δ 4.27 (d, H-4', $J_{\text{H-3'-H-4'}} = 3$ Hz). (Found: C, 42.5; H, 4.4; N, 19.9. Calcd for C₁₀H₁₁N₅O₆: C, 42.3; H, 4.3; N, 19.7%.)

1'-6-Azauracil-1-yl-2'-deoxy- β -D-ribofuranurononitrile. The protected amide (0.2 g) was dehydrated to the nitrile in the usual way and the product deacetylated as before to give 3c(R₁ = H; R₂ = OH) 0.11 g (67%): m.p. 165°; λ_{max} 262 nm (ϵ 4800); NMR δ 4.65 (s, H-4'). (Found: C, 41.4; H, 3.6; N, 23.6. Calcd for C₉H₉N₅O₅.0.5H₂O: C, 41.3; H, 3.9; N, 24.0%.)

1'-6-Azauracil-1-yl-4'(R)-C-tetrazolo-2'-deoxy- β -D-erythrofuranoose. The protected nitrile, 3c (R₁ = H; R₂ = OAc) (0.2 g) was treated with sodium azide and ammonium chloride as previously described. The protected tetrazole 4c(R₁ = H; R₂ = OAc) (0.1 g) was isolated by preparative TLC in solvent 2. It was treated with 50% (v/v) aqueous ammonia in the usual way and the product isolated by preparative TLC in solvent 2 to give the tetrazole 4c(R₁ = H; R₂ = OH) 0.08 g (33% from protected nitrile) as its sodium salt dihydrate: m.p. 210° dec; λ_{max} 262 nm (ϵ 4850); NMR δ 4.8 (s, H-4'). (Found: C, 29.6; H, 3.6. Calcd for C₉H₉N₅O₅.Na.2H₂O: C, 29.5; H, 3.7%.)

1-Adenin-9-yl-2',3'-O-isopropylidene- β -D-ribofuranurononitrile. Methyl-1'-adenin-9-yl-2',3'-O-isopropylidene- β -D-ribofuranuronate⁸ (3 g) was converted to the protected nitrile via the amide as previously described. The product was isolated after silicic acid chromatography in solvent 1 as an amorphous powder, which crystallised as needles from EtOH to give 1.25 g (46% from the ester) of 3d(R₁ + R₂ = -OC(Me)₂O-): m.p. 161-162°; λ_{max} 259 nm (ϵ 15350); NMR δ 5.35 (d, H-4', $J_{\text{H-3'-H-4'}} = 2$ Hz). (Found: C, 51.6; H, 4.6; N, 28.0. Calcd for C₁₁H₁₄N₆O₅: C, 51.5; H, 4.8; N, 27.8%.)

1'-Adenin-9-yl-4'(R)-C-tetrazolo- β -D-erythrofuranoose. The protected nitrile 3d(R₁ + R₂ = -OC(Me)₂O-) (0.58 g) was converted to the protected tet-

razole as previously described. This was deacetonated without purification by treatment with 50% (v/v) formic acid (10 ml) at room temp overnight. The solvent was evaporated off under reduced pressure (30°; 1 mm Hg) to leave a brown oil, fractionated by preparative TLC in solvent 2. The major product was isolated as an amorphous powder 0.26 g (45%) of 4d(R₁ = R₂ = OH): m.p. 222°; λ_{max} 259 nm (ϵ 15000); NMR δ 5.26 (m, H-4'). (Found: C, 28.6; H, 4.7; N, 30.0. Calcd for C₁₀H₁₀N₆O₅.Na.0.5H₂O: C, 28.8; H, 4.7; N, 30.2%.)

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