

Azido-(Amino-)furanosyl Nucleosides and their Phosphoramidates

Darinka Katalenić and Vinko Škarić*

Laboratory of Stereochemistry and Natural Products, 'Ruder Bošković' Institute, 41001 Zagreb, Croatia

The ring-opening of 2,2'-anhydro-1-[5-azido- **5** and 5-benzamido- **3** 5-deoxy-3-*O*-methylsulfonyl- β -D-arabinofuranosyl]uracil by the ion exchanger Dowex 50 (H^+) afforded the corresponding 1-[5-azido- **8** and 5-benzamido- **12** 5-deoxy-3-*O*-methylsulfonyl- β -D-arabinofuranosyl]uracil. Hydrogenolysis of the azido nucleosides over Pd-black in the presence of benzoic acid anhydride led to the corresponding benzamido nucleosides in high yields. The 5'-azido-2',3'-oxirane **10** on reaction with ethanolic ammonia generated 1-(3-amino-5-azido-3,5-dideoxy- β -D-arabinofuranosyl)uracil **15** and 1-(2-amino-5-azido-2,5-dideoxy- β -D-xylofuranosyl)uracil **16** in a ratio 2:1. The 5'-*O*-mesyl-2',3'-oxirane **25**, on being treated with NaN_3 in DMF at 100 °C, afforded 2',5'-anhydro-1-(3-azido-3-deoxy- β -D-arabinofuranosyl)uracil **26** (54.5%), 3',5'-diazido- β -D-arabinofuranosyl **27** (20.6%) and 2',5'-diazido- β -D-xylofuranosyl **28** (5.4%). The hydrogenolysis of **5** over Pd-black proceeded into 2,5'-imino-1-(3-*O*-methylsulfonyl- β -D-arabinofuranosyl)uracil **32** which, as the 5'-benzamido derivative **36**, was transformed into **3**. The 5'-azido compound **5** and **10** on reaction with triphenyl phosphite in aqueous dioxane gave the respective 5'-diphenylphosphoramidate **38** and **39**. Similarly, the 3'-azido compound **22** was converted into 3'-diphenylphosphoramidate **40**.

Appropriately activated uridine may undergo intramolecular transformation to give arabino-, lyxo- and xylo-furanosyl stereoisomers.¹⁻³ Recently, we described synthesis of 5'-azido-(5'-amino-)-5'-deoxyuridine and its furanosyl stereoisomers as well as 5'-*N*-aminoacyl- and 5'-*N*-peptidyl-5'-amino-5'-deoxy-5,6-dihydrouridine.⁴ Here, we extend our work on stereoisomeric azido-, amino-, phosphoramido pyrimidine nucleosides, and their intramolecular cyclisations.

Current interest in azido nucleoside chemistry stems from the antiviral activity^{5,6} of 3'-azido-3'-deoxythymidine (AZT).⁷ However, the increasing resistance of human immunodeficiency virus (HIV) to AZT stimulated syntheses of a number of novel azido nucleosides. For this purpose the silyl (Hilbert-Johnson)^{8,9} coupling of azido furanose with nucleic acid bases, the ring-opening of 1-(3,5-anhydro- β -D-xylofuranosyl)uracil by LiN_3 ¹⁰ and the nucleophilic substitution of 5'-*O*-sulfonyluridine by NaN_3 ,^{11,12} have most frequently been exploited.

Recently, we showed that the intramolecular transformations of 5'-benzamido-5'-deoxy-2',3'-di-*O*-methylsulfonyluridine **1** when heated under reflux in water gave 1-(5-benzamido-5-deoxy- β -D-lyxofuranosyl)uracil **4** (Scheme 1). We also reported that transformations of **1** on treatment with potassium phthalimide in dioxane stopped at 2,2'-anhydro-1-(5-benzamido-5-deoxy-3-*O*-methylsulfonyl- β -D-arabinofuranosyl)uracil **3**. We report here transformations of 2',3',5'-tri-*O*-methylsulfonyluridine¹ **4** on reaction with NaN_3 -DMF to yield 2,2'-anhydro-1-(5-azido-5-deoxy-3-*O*-methylsulfonyl- β -D-arabinofuranosyl)uracil **5**.

The arabinofuranosyl configuration of **5** was confirmed by the characteristic ¹H NMR spectral data, particularly by the coupling constant, $J_{1,2}$ 5.9†^{4,13} (Table 1). The UV absorbancy of **5** at λ_{max}/nm 245 indicated also its quinone-like structure.

The 2,2'-anhydro compound **5** when heated under reflux in water or dilute hydrochloric acid gave 1-(5-azido-5-deoxy- β -D-lyxofuranosyl)uracil **6**, characterized as its 2',3'-*O*-isopropylidene derivative **7**. In contrast to the specific rotation of the 2,2'-anhydro compound **5**, $[\alpha]_D^{27} -37$ † (*c* 1, DMF), the lyxofuranosyl stereoisomer **6**, $[\alpha]_D^{24} +163$ (*c* 0.86, MeOH), and **7**, $[\alpha]_D^{22} +158$ (*c* 1.15, MeOH), were significantly dextrorotatory.

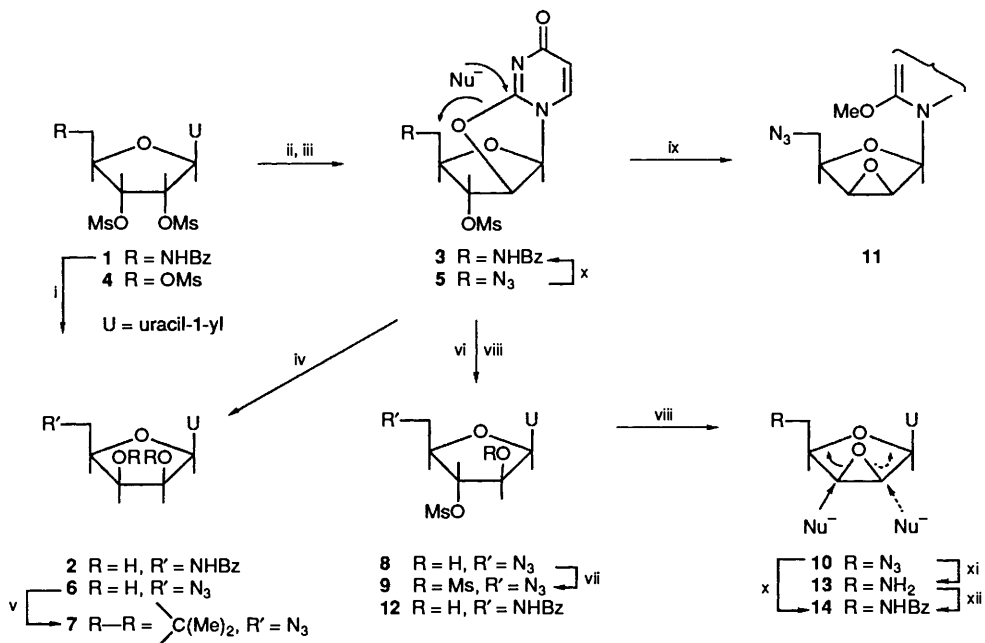
The ring-opening of **5**, on treatment with the ion exchanger Dowex 50 (H^+),² afforded 1-(5-azido-5-deoxy-3-*O*-methylsulfonyl- β -D-arabinofuranosyl)uracil **8**. The latter, on mesylation, gave the respective 2'-*O*-mesyl derivative **9**. Furthermore, treatment of **5** with aqueous NaOH gave 1-(5-azido-5-deoxy-2,3-epoxy- β -D-lyxofuranosyl)uracil **10**. Similarly, treatment of **5** with NaOMe-MeOH afforded 1-(5-azido-5-deoxy-2,3-epoxy- β -D-lyxofuranosyl)-2-*O*-methyluracil **11** through an ⁻OMe attack at the C-2 position of **5**, followed by the C(2)-O-C(2') ring-opening and ⁻O-C(2'), C(3') cyclisation.¹⁴ As expected, the anomeric H-C(1') in the ¹H NMR spectra of the 2',3'-oxiranes **10** and **11** exhibited the singlet-like signals at δ_H 6.1.

In analogy to the stereochemically controlled ring-opening of the azido compound **5** to give **8** (Scheme 1, pathway vi), the benzamido derivative **3** afforded 1-(5-benzamido-5-deoxy-3-*O*-methylsulfonyl- β -D-arabinofuranosyl)uracil **12**. The combined hydrogenolysis-benzoylation of the azido compounds **5** and **10** over Pd-black in the presence of benzoic acid anhydride smoothly proceeded to give the 5'-benzamido 2,2'-anhydro compound **3** (84.3%) and 1-(5-benzamido-5-deoxy-2,3-epoxy- β -D-lyxofuranosyl)uracil **14** (97%), respectively. It should be pointed out that hydrogenolysis of the 5'-azido compound **10**, followed by the benzoylation of the resulting 1-(5-amino-5-deoxy-2,3-epoxy- β -D-lyxofuranosyl)uracil **13** afforded the 5'-benzamido compound **14** in lower yield than that obtained from the above described hydrogenolysis-benzoylation of the 5'-azido compound **10**.

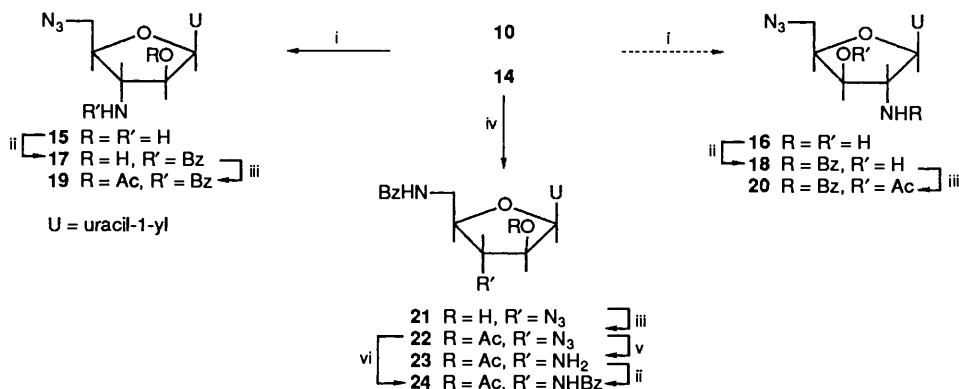
For the reason we shall deal with below, treatment of the 2',3'-oxirane **10** with ammonia in ethanol¹⁵ generated 1-(3-amino-5-azido-3,5-dideoxy- β -D-arabinofuranosyl)uracil **15** and 1-(2-amino-5-azido-2,5-dideoxy- β -D-xylofuranosyl)uracil **16** in a 2:1 ratio (established by their ¹H NMR spectra). These stereoisomers were separated as 1-(5-azido-3-benzamido-3,5-dideoxy- β -D-arabinofuranosyl)uracil **17**, R_f 0.19 (47%), and 1-(5-azido-2-benzamido-2,5-dideoxy- β -D-xylofuranosyl)uracil **18**, R_f 0.15 (36%), characterized also as the 2'-*O*-acetyl **19** and 3'-*O*-acetyl derivative **20**, respectively (Scheme 2).

The 5'-benzamido-2',3'-oxirane **14** on reaction with NaN_3 -DMF gave 1-(3-azido-5-benzamido-3,5-dideoxy- β -D-arabinofuranosyl)uracil **21** (78%), characterized as its 2'-*O*-acetyl derivative **22**. Comparing the ¹H NMR spectra of the 2'-hydroxy compound **21** with that of the 2'-acetoxy derivative **22**,

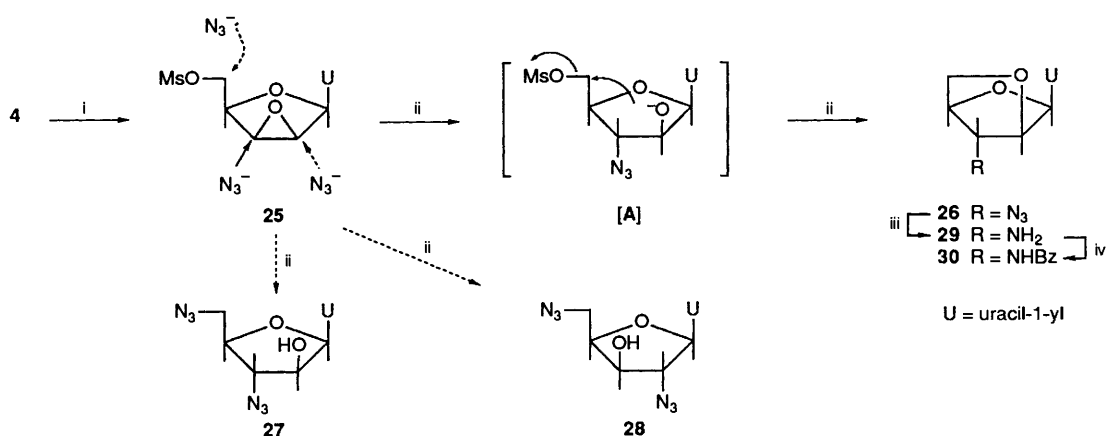
† J Values in Hz and $[\alpha]_D$ values in units of 10^{-1} deg cm^2 g^{-1} throughout.



Scheme 1 Reagents and conditions: i, H₂O, heat; ii, Pht-K-dioxane; iii, NaN₃-DMF; iv, H₂O or HCl-H₂O; v, Me₂CO-CuSO₄-H₂SO₄; vi, Dowex 50(H⁺)-Me₂CO-H₂O; vii, MsCl-py; viii, NaOH-H₂O; ix, NaOMe-MeOH; x, [H₂]-Pd black-Bz₂O-MeOH; xi, [H₂]-Pd black-EtOH; xii, Bz₂O-py



Scheme 2 Reagents and conditions: i, NH₃-EtOH; ii, Bz₂O-py; iii, Ac₂O-py; iv, NaN₃-DMF; v, [H₂]-Pd black-EtOH; vi, [H₂]-Pd black-Bz₂O-MeOH



Scheme 3 Reagents and conditions: i, NaOH-H₂O; ii, NaN₃-DMF; iii, [H₂]-Pd black-EtOH; iv, Bz₂O-py

the latter showed the expected downfield resonances for the 2'-H (0.86 ppm) and 3'-H (0.43 ppm) (Table 1). Moreover, the ¹³C NMR spectrum of **22** (Table 2) confirmed the so-called β-acetyl effect¹⁶ by exhibiting a downfield C-2' shift (1.2 ppm) and an upfield C-3' shift (2.3 ppm).

Hydrogenolysis of the 3'-azido isomer **22** over Pd-black in

ethanol yielded 1-(2-O-acetyl-3-amino-5-benzamido-3,5-dideoxy-β-D-arabinofuranosyl)uracil **23** which, on benzylation, yielded the 3',5'-dibenzamido compound **24** (81%). The latter was prepared by hydrogenolysis-benzylation of the azido compound **22** in 92% yield.

Treatment of 1-(5-O-methylsulfonyl-2,3-epoxy-β-D-lyxo-

Table 1 ^1H NMR chemical shifts (δ_{H}), and coupling constants, given in parentheses, for the 1-(furanos-1'-yl)uracil isomers^{a,b,c,d,e,f,g,h}

| Compound | Solvent* | 6-H d | 1'-H d | 5-H d | 2'-H | 3'-H | 4'-H | 5'-H _A dd | 5'-H ₂ 5'-H _B dd |
|---|----------|---------------|---------------|---------------|----------------------|------------------------|------------------------|-------------------------|--|
| Data for arabino-, lyxo- and xylo-isomers | | | | | | | | | |
| 6 | A | 7.83 (8.2) | 6.07 (6.5) | 5.55 (8.2) | 4.40dd (6.5, 4.7) | 4.08 — | 3.91 | | 3.57d (6.2) |
| 7 ⁱ | B | 7.49 (8.2) | 5.85 (3.2) | 5.73 (8.2) | 4.93 — | 4.72 | 3.93sext (3.2, 6.2) | | 3.65d (6.2) |
| 8 | A | 7.52 (8.2) | 6.06 (4.1) | 5.60 (8.2) | 4.88dd (4.1, 3.2) | 4.43dd (3.2, 4.7) | 4.29–4.07 | | 3.68d (5.6) |
| 9 | C | 7.55 (8.2) | 6.25 (5.0) | 5.76 (8.2) | 5.48dd (5.0, 3.2) | 5.31dd (3.2, 5.3) | 4.34sext (5.3, 4.1) | | 3.84–3.76 |
| 12 | A | 7.70 (8.2) | 6.48 (3.8) | 5.53 (8.2) | 5.02t (2.1) | 4.44 — | 4.18 | | 3.82–3.64 |
| 19 | D | 7.88 (8.2) | 6.27 (5.6) | 5.75 (8.2) | 5.67dd (5.6, 4.1) | 4.82 — | 4.60 | | 3.78–3.66 |
| 20 ^j | D | 7.76 (8.2) | 6.46 (5.3) | 5.71 (8.2) | 5.73–5.62 | 5.80sext (4.1, 7.3) | 4.38–4.21 | | 3.85–3.74 |
| 21 | D | 7.77 (8.2) | 6.11 (4.7) | 5.55 (8.2) | 4.49 br s | 4.29 | — | | 3.81 |
| 22 | D | 7.77 (8.2) | 6.21 (4.9) | 5.63 (8.2) | 5.35dd (4.9, 3.5) | 4.48dd (3.5, 5.6) | 4.14dd (5.6, 10.4) | | 3.97–3.84 |
| 24 | A | 7.74 (8.2) | 6.32 (4.9) | 5.61 (8.2) | 5.46dd (4.9, 3.5) | 4.52sext (3.5, 6.7) | 4.33–4.14 | | 3.80–3.68 |
| 40 ^k | D | 7.73 (8.2) | 6.29 (4.7) | 5.59 (8.2) | 5.41t | 4.38 | 4.02 | | 3.86–3.65 |
| Data for imino nucleosides | | | | | | | | | |
| 32 | A | 7.41 (7.6) | 5.83 (6.7) | 5.60 (7.6) | 4.91d (2.3) | 4.56 — | 4.49 | 3.47 (14.2, 3.1) | 3.21 (14.2, 1.8) |
| 33 | A | 7.39 (7.6) | 6.16 (6.7) | 5.61 (7.6) | 5.36dd (6.7, 1.8) | 5.19d (1.8) | 4.73–4.58 | 3.52 (16.2, 2.9) | 3.26 (16.2, 1.8) |
| 34 | A | 7.95 (7.6) | 6.39 (7.3) | 6.08 (7.6) | 5.49d (7.3) | 4.85 s br | 4.77d (2.6) | 4.99 (14.6, 2.6) | 3.22 (14.6, 1.8) |
| 35 | C | 7.28 (7.6) | 6.15 (6.8) | 5.68 (7.6) | 5.84dd (6.8, 1.5) | 5.44d (1.5) | 4.81 s br | 4.06 (14.5, 2.9) | 3.47 (14.5, 1.8) |
| 37 ^l | A | 7.94 (7.6) | 6.64 (6.5) | 5.89 (7.5) | 5.71 — | 5.68 | 4.97 s br | 4.79 (14.5, 2.9) | 3.50 (14.5, 1.8) |

^a Me(Ms) of (8, 9, 12, 32–37) at 3.43–3.13 (s). ^b *N*- and *O*-Benzoyl of (12, 19–22, 24, 35, 37, 40) at 8.01–7.71 and 7.64–7.28. ^c H–N(3) of (6, 8, 9, 12, 19–22, 24, 40) at 11.21–9.41 (br s), D₂O-exchangeable. ^d 5'-NH of (19, 21, 22, 24, 32, 33, 35, 40) at 8.56–6.62, D₂O-exchangeable. ^e 3'-NH of (19, 24, 40) at 8.85–5.82, D₂O-exchangeable. ^f 2'-OH and 3'-OH of (6, 8, 12, 21, 32) at 6.62–4.07, D₂O-exchangeable. ^g Me(C) of (19, 20, 22, 24, 33, 34, 40) at 2.29–1.83 (s). ^h Two dimensional spectra of (34, 35, 37) on JEOL Varian Gemini-300 instrument. ⁱ (Me)₂ at 1.47 and 1.32. 2'-NH at 8.41–8.34, D₂O-exchangeable. ^k NPO(OPh)₂ at 7.46–7.06. ^l NCOPh at 7.52–6.70.

* A = [2H₆]-DMSO, B = C²HCl₃, C = C²H₃CN, D = [2H₆]acetone.

furanosyl)uracil¹⁷ **25** with NaN₃ at 100 °C afforded 2',5'-anhydro-1-(3-azido-3-deoxy-β-D-arabinofuranosyl)uracil **26** (54.5%), most probably *via* the intermediacy of [A] (Scheme 3). This reaction (depicted by dotted lines) led also to 1-(3,5-diazido-3,5-dideoxy-β-D-arabinofuranosyl)uracil **27** (20.6%), *R_f* 0.43, and in lesser extent to 1-(2,5-diazido-2,5-dideoxy-β-D-xylofuranosyl)uracil **28**, *R_f* 0.42. The hydrogenolysis of **26** over Pd-black–EtOH gave the corresponding 3'-amino compound **29**, characterized as its 3'-benzamido derivative **30**. The ¹³C NMR spectra of the 2',5'-oxolanes **26**, **29** and **30** exhibited C-5' downfield shifts (11 ppm) as recorded in the 2,5'-anhydro series.¹⁸

The hydrogenolysis of the 5'-azido-2,2'-anhydro compound **5** over Pd-black in ethanol afforded 2,2'-anhydro-1-(5-amino-5-deoxy-3-*O*-methylsulfonyl-β-D-arabinofuranosyl)uracil **31** which spontaneously rearranged into the hitherto unknown 2,5'-imino-1-(3-*O*-methylsulfonyl-β-D-arabinofuranosyl)uracil **32** (94%) (Scheme 4).

While the imino compound **32** on reaction with acetic anhydride yielded 2,5'-imino-1-(2-*O*-acetyl-3-*O*-methylsulfonyl-β-D-arabinofuranosyl)uracil **33** (79.6%), on reaction with acetyl chloride it gave 5'-*N*-acetyl-2,5'-imino-1-(2-*O*-acetyl-3-*O*-methylsulfonyl-β-D-arabinofuranosyl)uracil **34** (85%). The benzoylation of **32** with benzoic acid anhydride afforded 2,5'-imino-1-(2-*O*-benzoyl-3-*O*-methylsulfonyl-β-D-arabinofuranosyl)uracil **35** (53.7%) and 5'-benzamido-2,2'-anhydro com-

pound **3** (33.7%) (Scheme 1). The latter was unexpectedly formed by an intramolecular ⁻O-C(2') attack at the C-2 position of the 5'-benzamido-2,5'-imino intermediate **36**. The structure of the 2'-*O*-benzoyl derivative **35** was supported by its facile hydrolysis into the hydroxy compound **32**.

It is worth noting that compound **32** on reaction with benzoyl chloride afforded the 2,2'-anhydro compound **3** (74%) which then partly cleaved to give up 5'-benzamido-3'-*O*-mesyl compound **12** (Scheme 1). Such a rearrangement was prevented when the β-oriented 2'-hydroxy group was blocked as in 5'-*N*-benzoyl-2,5'-imino-1-(2-*O*-benzoyl-3-*O*-methylsulfonyl-β-D-arabino-furanosyl)uracil **37**. The latter was easily prepared from the 2'-*O*-benzoyl derivative **35** on reaction with benzoyl chloride. The aromatic protons of the *N,O*-dibenzoyl derivative **37**, were clearly assigned by two-dimensional (COSY) ¹H NMR spectrum showing the *O*-benzoyl signals at δ_{H} 7.96–7.93, 7.81–7.63, 7.61–7.56 and *N*-benzoyl signals at δ_{H} 7.52–7.50, 7.25–7.21, 6.74–6.70 for *meta*-(2H), *para*-(1H) and *ortho*-(2H), respectively.

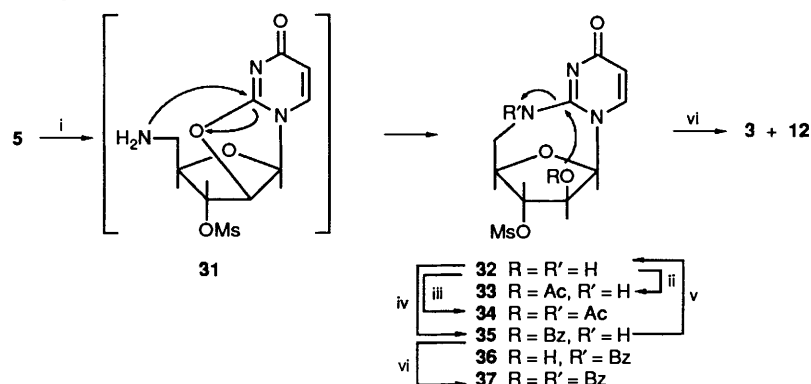
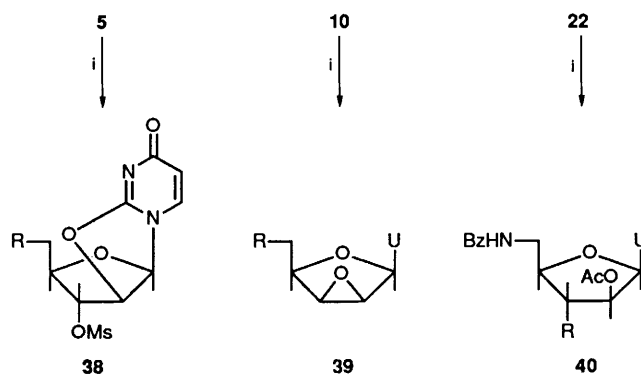
Phosphorylation of the azido nucleosides facilitated the regioselective phosphorodiamido bond formation. Thus, the 5'-azido compounds **5** and **10** on reaction with triphenyl phosphite in dioxane–water^{19,20} afforded 2,2'-anhydro-1-(5-deoxy-5-diphenylphosphoramido-β-D-arabinofuranosyl)uracil **38** (89.3%) and 1-(5-deoxy-5-diphenylphosphoramido-2,3-epoxy-β-D-lyxofuranosyl)uracil **39** (78%); respectively

Table 2 ^{13}C NMR spectroscopic data [δ_{C} (ppm)] for the 1-(furanos-1'-yl)uracil isomers^{a,b,c,d,e}

| Compound | Solvent* | C-4 (s) | C-2 (s) | C-6 (d) | C-5 (d) | C-1' (d) | C-4' (d) | C-2' (d) | C-3' (d) | C-5' (t) |
|----------------------------------|----------|------------|------------|------------|------------|-------------|-------------|-------------|-------------|-------------|
| Arabino-, lyxo- and xylo-isomers | | | | | | | | | | |
| 6 | A | 162.9 | 150.5 | 142.2 | 99.8 | 83.2 | 77.3 | 70.3 | 69.2 | 49.9 |
| 7 ^f | D | 163.1 | 150.3 | 142.0 | 100.3 | 84.8 | 80.1 | 78.9 | 77.7 | 49.7 |
| 8 | C | 164.7 | 151.6 | 143.2 | 101.9 | 86.1 | 84.4 | 74.6 | 80.4 | 51.8 |
| 9 | C | 164.1 | 151.2 | 142.3 | 102.9 | 84.5 | 81.3 | 80.0 | 80.6 | 51.2 |
| 12 | A | 163.3 | 150.5 | 142.6 | 100.3 | 85.7 | 84.7 | 72.9 | 80.8 | 40.9 |
| 19 | D | 163.5 | 151.5 | 140.9 | 103.4 | 87.7 | 79.1 | 76.4 | 61.0 | 50.9 |
| 20 | D | 163.3 | 150.9 | 141.9 | 102.1 | 84.1 | 80.4 | 57.4 | 76.9 | 52.7 |
| 21 | D | 163.4 | 150.8 | 142.7 | 100.7 | 85.7 | 79.9 | 74.9 | 68.1 | 41.6 |
| 22 | D | 163.0 | 150.3 | 141.8 | 101.2 | 84.2 | 80.2 | 76.1 | 65.8 | 41.0 |
| 24 | A | 162.9 | 150.0 | 141.7 | 100.9 | 83.5 | 79.7 | 75.9 | 56.7 | 41.2 |
| 40 | D | 163.6 | 150.3 | 142.2 | 101.1 | 83.8 | 80.7 | 77.3 | 58.1 | 41.0 |
| 2,2'-Anhydro compounds | | | | | | | | | | |
| 3 | A | 172.1 | 159.8 | 137.4 | 109.7 | 90.5 | 84.1 | 86.7 | 82.1 | 40.9 |
| 5 | A | 171.1 | 159.7 | 136.8 | 109.2 | 90.1 | 83.9 | 86.3 | 81.9 | 51.2 |
| 38 | A | 170.8 | 159.3 | 136.8 | 109.0 | 89.7 | 84.6 | 86.1 | 81.0 | 42.2 |
| Oxiranes | | | | | | | | | | |
| 10 | A | 162.6 | 149.9 | 140.7 | 101.8 | 80.6 | 75.4 | 55.4 | 55.1 | 49.7 |
| 11 ^g | D | 169.5 | 155.8 | 138.7 | 108.4 | 83.4 | 76.8 | 56.1 | 55.9 | 50.5 |
| 14 | A | 163.3 | 150.6 | 141.3 | 101.9 | 81.2 | 75.6 | 56.1 | 55.9 | 39.2 |
| 39 | A | 163.0 | 150.7 | 141.3 | 101.9 | 81.0 | 76.7 | 56.3 | 55.5 | 40.7 |
| Oxolanes | | | | | | | | | | |
| 26 | A | 163.2 | 150.5 | 140.6 | 100.6 | 89.1 | 79.6 | 75.6 | 65.2 | 72.6 |
| 29 | A | 163.4 | 150.6 | 141.1 | 100.3 | 89.8 | 81.8 | 77.6 | 59.6 | 72.8 |
| 30 | A | 163.4 | 150.6 | 140.9 | 100.5 | 89.4 | 79.5 | 75.9 | 58.2 | 72.2 |
| Imino nucleosides | | | | | | | | | | |
| 32 | A | 169.9 | 158.7 | 143.7 | 107.2 | 93.8 | 87.8 | 77.7 | 81.4 | 47.7 |
| 33 | A | 169.2 | 158.1 | 143.1 | 107.4 | 91.7 | 83.7 | 78.1 | 81.1 | 47.3 |
| 34 | B | 169.4 | 152.1 | 143.9 | 111.2 | 93.9 | 82.4 | 79.2 | 82.1 | 45.7 |
| 35 | D | 170.1 | 160.3 | 143.9 | 108.7 | 93.9 | 85.4 | 79.2 | 83.4 | 48.4 |
| 37 | A | 171.9 | 153.6 | 145.3 | 108.9 | 92.9 | 83.2 | 79.7 | 82.2 | 47.5 |

^a CO(amide) and CO(ester) of (3,12,14,19-22, 24, 30, 33, 35, 37, 40) at 171.1-166.2. ^b Aromatic C-atoms of (3, 12, 14, 19-22, 24, 30, 35, 37, 40) at 135.1-127.3. ^c Me(Ms) of (3,5,8,9,12,32-35,37, 38) at 38.9-37.6 (q). ^d Me(OAc) of (19, 20, 22, 24, 33, 34, 40) at 20.8-19.5 (q) and Me(NAc) of 34 at 23.9 (q). ^e PO(OPh)₂ of (38-40) at 150.6 and 129.9-120.2. ^f O-C-O at 113.2 (s), Me₂ at 25.0 (q) and 23.6 (q). ^g Me-O-C(2) at 55.1 (q).

* A = [²H₆]-DMSO, B = C²HCl₃, C = C²H₃CN, D = [²H₆]acetone.

**Scheme 4** Reagents and conditions: i, [H_2]-Pd black-EtOH; ii, Ac_2O -py; iii, AcCl -py; iv, Bz_2O -py; v, NaOH - H_2O ; vi, BzCl -py**Scheme 5** Reagents and conditions: i, $(\text{PhO})_3\text{P}$ -dioxane- H_2O

(Scheme 5); both exhibited characteristic ^{13}C NMR spectra²¹ (Table 2).

The 2-*O*-acetyl-3-azido-5'-benzamido-arabinofuranosyl compound **22** was analogously converted into 1-(2-*O*-acetyl-3-benzamido-3,5-dideoxy-3-diphenylphosphoramido- β -D-arabinofuranosyl)uracil **40** in 83% yield.

The ^1H and ^{13}C NMR spectral characteristics of all the reported compounds (Tables 1 and 2), together with their optical rotations (see Experimental section), IR (in particular, for the azido compounds with characteristic $\nu_{\text{max}}/\text{cm}^{-1}$ \sim 2100), UV (in particular for the 2,5'- and 2,2'-anhydro as well as 2-OMe compound with $\lambda_{\text{max}}/\text{nm}$ \sim 245) and elemental analyses agreed with the proposed structures presented in this paper.

Experimental

M.p.s, uncorrected, were determined on a Kofler hot-stage apparatus. IR spectra were obtained for KBr pellets on a Perkin-Elmer 782 spectrophotometer. UV spectra were taken for solutions in ethanol on a Perkin-Elmer double-beam spectrophotometer model 124. ^1H and ^{13}C NMR spectra were recorded on a JEOL FX90Q and JEOL FX 100Q spectrometers with tetramethylsilane as the internal standard. Multiplicities s, d, t and q refer to off-resonances decoupled spectra. Optical rotations were measured in methanol, unless otherwise stated, on a Zeiss-Winkel 179707 apparatus. The silica gel (Merck HF₂₅₄, type 60) for TLC was activated at 110 °C for 60 min. *R_f* Values of the products were determined by developments in CH_2Cl_2 -MeOH, 10:1 and located by UV illumination and a ninhydrin spray. Removal of the solvents under reduced pressure. DMF (dimethylformamide) and pyridine were dried and distilled over CaH_2 and stored over molecular sieves (4 Å). Mass spectra were recorded on a SHIMADZU GC-MS QP-1000 spectrometer; electron impact, ionizing voltage 70 eV.

General Procedure for the Hydrogenolysis-Benzylation of the Azides 5, 10 and 22.—To a solution of the azide (0.34–1.31 mmol) in methanol (7–35 cm³) Pd-black (7–28 mg) and benzoic acid anhydride (0.43–1.71 mmol) were added. The suspension was stirred in a H_2 atmosphere at 0.35 MPa at room temperature for 24 h. The catalyst was filtered off and the filtrate evaporated to dryness. The residue was triturated with diethyl ether and recrystallized from methanol to give compounds **3**, **14** and **24**.

2,2'-Anhydro-1-(5-benzamido-5-deoxy-3-*O*-methylsulfonyl- β -D-arabinofuranosyl)uracil 3. From **5**, 84.3%; *R_f* 0.17; m.p. 194–200 °C; identical (mixed m.p., NMR and IR spectra) with an authentic specimen (ref. 4).

1-(5-Benzamido-5-deoxy-2,3-epoxy- β -D-lyxofuranosyl)uracil 14. From **10**: 97%; *R_f* 0.36; m.p. 186–188 °C; identical (mixed m.p., NMR and IR spectra) with an authentic specimen (ref. 4).

1-(2-*O*-Acetyl-3,5-dibenzamido-3,5-dideoxy- β -D-arabinofuranosyl)uracil 24. From **22**: 92%; *R_f* 0.39; m.p. 264–265 °C (Found: C, 60.8; H, 4.75; N, 11.25. $\text{C}_{25}\text{H}_{24}\text{N}_4\text{O}_7$ requires C, 60.95; H, 4.9; N, 11.4%); $[\alpha]_{\text{D}}^{22} + 46$ (*c* 1 in DMF); $\lambda_{\text{max}}/\text{nm}$ 227 (log ϵ 4.22); $\lambda_{\text{inf}}/\text{nm}$ 262 (log ϵ 3.98); $\lambda_{\text{min}}/\text{nm}$ 246 (log ϵ 4.06); $\nu_{\text{max}}/\text{cm}^{-1}$ 3271, 3063, 1750, 1717, 1706, 1690, 1639, 1534, 1268, 1226, 1218, 1210, 1114, 822, 803, 715 and 694.

General Procedure for the Azidolysis of the Mesylate 4¹ and Oxiranes 14,⁴ 25.¹⁷—To a solution of mesylate or oxirane (1 mmol) in DMF (40 cm³) sodium azide (2 mmol) was added. The mixture was stirred at 100 °C for 1 h for **4**, 2 h for **25** or for 1 day for **14** and then cooled. A precipitate was filtered off and the filtrate evaporated to dryness. The residue was crystallized from water as in the case of the azide **5** and purified by TLC

$[\text{CH}_2\text{Cl}_2$ -MeOH (10:0.5), two developments] as in the case of the azido compounds **21** and **26**.

2,2'-Anhydro-1-(5-azido-5-deoxy-3-*O*-methylsulfonyl- β -D-arabinofuranosyl)uracil 5. From **4**: 93%; *R_f* 0.20; m.p. 155–156 °C (from MeOH) (Found: C, 36.2; H, 3.6; N, 21.25. $\text{C}_{10}\text{H}_{11}\text{N}_6\text{O}_5\text{S}$ requires C, 36.45; H, 3.35; N, 21.25%); $[\alpha]_{\text{D}}^{27} - 37.5$ (*c* 1 in DMF); $\lambda_{\text{max}}/\text{nm}$ 245 (log ϵ 3.99); $\nu_{\text{max}}/\text{cm}^{-1}$ 2154, 2113, 1664, 1637, 1613, 1528, 1495, 1362, 1284, 1179, 1094, 961 and 829; $\delta_{\text{H}}([\text{H}_6\text{DMSO}] 7.85$ (1 H, d, *J* 7.6, 6-H), 6.44 (1 H, d, *J* 5.9, 1'-H), 5.89 (1 H, d, *J* 7.6, 5-H), 5.64 (1 H, d, *J* 5.9, 2'-H), 5.38 (1 H, m, 3'-H), 4.64–4.49 (1 H, m, 4'-H), 3.60 (1 H, dd, *J* 13.5 and 4.4, 5'-H_A), 3.37 (3 H, s, MsMe), 3.36 (1 H, dd, *J* 13.5 and 6.7, 5'-H_B).

1-(3-Azido-5-benzamido-3,5-dideoxy- β -D-arabinofuranosyl)uracil 21. From **14**: 78%; *R_f* 0.31; m.p. 115–117 °C (from acetone-hexane) (Found: C, 51.35; H, 4.7; N, 22.35. $\text{C}_{16}\text{H}_{16}\text{N}_6\text{O}_5$ requires C, 51.6; H, 4.45; N, 22.55%); $[\alpha]_{\text{D}}^{24} - 117$ (*c* 1.02 in MeOH); $\lambda_{\text{max}}/\text{nm}$ 218.5 and 260 (log ϵ 4.13 and 4.03), $\lambda_{\text{min}}/\text{nm}$ 246 (log ϵ 3.99); $\nu_{\text{max}}/\text{cm}^{-1}$ 3314br, 3104, 3054, 2924, 2109, 1719, 1684br, 1634infl, 1534, 1459, 1270, 1069, 797, 707 and 688.

1-(2,5-Anhydro-3-azido-3-deoxy- β -D-arabinofuranosyl)uracil 26. From **25**: 54.5%; *R_f* 0.45; m.p. 227–229 °C (from MeOH) (Found: C, 43.2; H, 3.85; N, 27.65. $\text{C}_9\text{H}_9\text{N}_5\text{O}_4$ requires C, 43.05; H, 3.6; N, 27.9%); $[\alpha]_{\text{D}}^{28} + 238$ (*c* 0.5 in MeOH); $\lambda_{\text{max}}/\text{nm}$ 264.5 (log ϵ 3.89); $\nu_{\text{max}}/\text{cm}^{-1}$ 3126, 3011, 2892, 2110, 1714, 1689, 1674, 1468, 1397, 1267, 1058 and 1016; $\delta_{\text{H}}([\text{H}_6\text{DMSO}] 11.27$ (1 H, br s, 3-NH), 7.78 (1 H, d, *J* 8.2, 6-H), 5.92 (1 H, s, 1'-H), 5.59 (1 H, d, *J* 8.2, 5-H), 4.82 (1 H, s, 2'-H), 4.65 (1 H, d, *J* 2.6, 3'-H), 4.52 (1 H, q, *J* 2.6 and 0.9, 4'-H), 4.07 (1 H, d, *J* 12.9, 5'-H_A) and 3.97 (1 H, d, *J* 12.9, 5'-H_B).

1-(5-Azido-5-deoxy- β -D-lyxofuranosyl)uracil 6.—(a) A solution of the 2,2'-anhydro compound **5** (100 mg, 0.3 mmol) in water (4 cm³) was heated under reflux for 3 h and then evaporated to dryness. The residue crystallized from ethyl acetate to give the lyxofuranosyl isomer **6** (76 mg, 94%); *R_f* 0.18; m.p. 139–141 °C (Found: C, 40.25; H, 4.4; N, 26.0. $\text{C}_9\text{H}_{11}\text{N}_5\text{O}_5$ requires C, 40.15; H, 4.1; N, 26.0%); $[\alpha]_{\text{D}}^{24} + 163$ (*c* 0.86 in MeOH); $\lambda_{\text{max}}/\text{nm}$ 259 (log ϵ 3.93); $\nu_{\text{max}}/\text{cm}^{-1}$ 3423, 3232, 3110, 2110, 1702, 1677, 1475, 1276, 1110, 1064 and 813.

(b) A solution of compound **5** (200 mg, 0.61 mmol) in 0.1 mol dm⁻³ aq. HCl (5 cm³) was heated under reflux for 1 h and then evaporated to dryness. The residue was purified by preparative TLC [CH_2Cl_2 -MeOH (10:0.6), two developments] to give **6** (145 mg, 90%), m.p. 138–140 °C (from ethyl acetate); identical (mixed m.p., NMR and IR spectra) with those obtained under (a).

1-(5-Azido-5-deoxy-2,3-*O*-isopropylidene- β -D-lyxofuranosyl)uracil 7.—A suspension of the lyxofuranosyl compound **6** (70 mg, 0.26 mmol) and dry cuprous sulfate (126 mg, 0.77 mmol) in acetone (4 cm³) and sulfuric acid (2.4×10^{-3} cm³) was heated at 37 °C for 45 h. The resulting precipitate was filtered off (Celite column) and the filtrate treated with dry calcium hydroxide (62 mg, 0.84 mmol). This mixture was stirred at room temperature for 1 h after which the resulting precipitate was filtered off and the filtrate evaporated to dryness. The residue was subjected to preparative TLC [CH_2Cl_2 -MeOH (10:0.6), two developments] to give the acetonide **7** (74 mg, 92.5%); *R_f* 0.39; m.p. 112–115 °C (from MeOH) (Found: C, 46.5; H, 5.15; N, 22.6. $\text{C}_{12}\text{H}_{15}\text{N}_5\text{O}_5$ requires C, 46.6; H, 4.9; N, 22.65%); $[\alpha]_{\text{D}}^{22} + 158$ (*c* 1.15 in MeOH); $\lambda_{\text{max}}/\text{nm}$ 260 (log ϵ 3.99); $\nu_{\text{max}}/\text{cm}^{-1}$ 3549, 3474, 3429, 2103, 1714infl, 1694br, 1625, 1458, 1386, 1285, 1210, 1112 and 880.

1-(5-Azido-5-deoxy-3-*O*-methylsulfonyl- β -D-arabinofuranosyl)uracil 8.—To a solution of compound **5** (200 mg, 0.61

mmol) in acetone–water (1:1; 50 cm³) the ion exchanger Dowex 50 (H⁺) (640 mg) was added. The mixture was stirred at room temperature for 72 h and then filtered. The filtrate was evaporated to dryness and the residue crystallized from dichloromethane–diethyl ether–hexane to give the ring-opened product **8** (174 mg, 82.5%); *R*_f 0.3; m.p. 83–84 °C (Found: C, 34.4; H, 3.95; N, 19.9. C₁₀H₁₃N₅O₇S requires C, 34.6; H, 3.75; N, 20.15%); [α]_D²³ + 215 (*c* 0.91 in MeOH); λ_{max}/nm 258 (log ε 4.08); ν_{max}/cm⁻¹ 3480infl, 3247br, 3032, 2111, 1694br, 1630infl, 1469, 1360, 1281, 1177, 966, 843 and 812.

1-(5-Azido-5-deoxy-2,3-di-O-methylsulfonyl-β-D-arabinofuranosyl)uracil 9.—A solution of the arabinofuranosyluracil **8** (160 mg, 0.46 mmol) in pyridine (5 cm³) was treated with methanesulfonyl chloride (75.5 mg, 0.66 mmol) at room temperature for 24 h. The solvent was coevaporated with toluene and the residue washed with ice–water. It was then subjected to preparative TLC [CH₂Cl₂–MeOH (10:0.6), two developments] to give the 2'-*O*-mesyl compound **9** (147 mg, 75%); *R*_f 0.42; m.p. 80–82 °C (from dichloromethane–diethyl ether–hexane) (Found: C, 31.25; H, 3.7; N, 16.6. C₁₁H₁₅N₅O₉S₂ requires C, 31.05; H, 3.55; N, 16.45%); [α]_D²⁶ + 103 (*c* 0.75 in MeOH); λ_{max}/nm 253.5 (log ε 3.98); ν_{max}/cm⁻¹ 3440br, 3214, 3032, 2113, 1695br, 1632, 1463, 1365, 1288, 1179, 968, 879 and 821.

1-(5-Azido-5-deoxy-2,3-epoxy-β-D-lyxofuranosyl)uracil 10.—A solution of compound **5** (300 mg, 0.91 mmol) in 0.48 mol dm⁻³ NaOH (3.79 cm³, 1.82 mmol) was kept at room temperature for 30 min. The mixture was neutralized with 0.65 mol dm⁻³ aq. HCl. The crystalline precipitate was filtered off and washed with methanol. It afforded the oxirane **10** (210 mg, 92%); *R*_f 0.42; m.p. 186–188 °C (from MeOH) (Found: C, 43.1; H, 3.75; N, 28.15. C₉H₉N₅O₄ requires C, 43.05; H, 3.6; N, 27.9%); [α]_D²⁴ + 116 (*c* 0.56 in MeOH); λ_{max}/nm 259 (log ε 3.93); ν_{max}/cm⁻¹ 3125, 3003, 2807, 2131, 2092, 1695, 1682, 1469, 1388, 1260, 1120, 1083, 851, 828 and 800; δ_H([²H₆]-DMSO) 11.12 (1 H, br s, 3-NH), 7.64 (1 H, d, *J* 8.2, 6-H), 6.08 (1 H, s, 1'-H), 5.64 (1 H, d, *J* 8.2, 5-H), 4.29–3.99 (3 H, m, 2', 3'- and 4'-H) and 3.60 (2 H, d, *J* 5.9, 5'-H₂).

1-(5-Azido-5-deoxy-2,3-epoxy-β-D-lyxofuranosyl)-2-*O*-methyluracil 11.—A solution of compound **5** (200 mg, 0.61 mmol) in methanolic 0.35 mol dm⁻³ sodium methoxide (3.5 cm³, 1.22 mmol) was set aside at room temperature for 30 min. The solution was neutralized with 0.65 dm⁻³ aq. HCl to give a crystalline product, identified as the oxirane **10** (49 mg, 32%), m.p. 185–188 °C; identical (mixed m.p., NMR and IR spectra) with an authentic specimen. The mother liquor was evaporated to dryness and the oily residue purified by preparation TLC [CH₂Cl₂–MeOH (10:0.6), two developments] to give the 2-*O*-methyluracil **11** (108 mg, 66.7%); *R*_f 0.40 (Found: C, 45.4; H, 4.45; N, 26.3. C₁₀H₁₁N₅O₄ requires C, 45.25; H, 4.2; N, 26.4%); [α]_D²⁴ + 51 (*c* 0.36 in MeOH); λ_{max}/nm 242.5 (log ε 4.14); ν_{max}/cm⁻¹ 2103, 1650, 1524, 1454, 1384, 1240, 1101 and 828; δ_H([²H₆]-DMSO) 7.77 (1 H, d, *J* 7.9, 6-H), 6.18 (1 H, s, 1'-H), 5.84 (1 H, d, *J* 7.9, 5-H), 4.43–4.07 (3 H, m, 2', 3'- and 4'-H), 3.96 (3 H, s, 2-Me), 3.70 (2 H, d, *J* 5.9, 5'-H₂).

1-(5-Benzamido-5-deoxy-3-*O*-methylsulfonyl-β-D-arabinofuranosyl)uracil 12.—To a solution of the 2,2'-anhydro-5'-benzamido compound **3** (100 mg, 0.25 mmol) in acetone–water 1:1 (20 cm³) the ion exchanger Dowex 50 (H⁺) (260 mg) was added. This suspension was stirred at room temperature for 72 h and filtered. The filtrate was evaporated to dryness and the residue crystallized from methanol–diethyl ether to give the ring-opened product **12** (89 mg, 84%); *R*_f 0.27; m.p. 174–176 °C (Found: C, 48.05; H, 4.6; N, 10.0. C₁₇H₁₉N₃O₈S requires C, 48.0; H, 4.5; N, 9.9%); [α]_D²⁸ + 161 (*c* 1.09 in MeOH);

λ_{max}/nm 219 and 260 (log ε 4.10 and 4.00); λ_{min}/nm 244 (log ε 3.96); ν_{max}/cm⁻¹ 3394, 3313, 3107, 3019, 1722, 1695, 1630, 1542, 1454, 1354, 1280, 1180, 965 and 847.

1-(3-Amino-5-azido-3,5-dideoxy-β-D-arabinofuranosyl)uracil 15 and **1-(2-Amino-5-azido-2,5-dideoxy-β-D-xylofuranosyl)uracil 16**.—A solution of the oxirane **10** (200 mg, 0.79 mmol) in 15% ethanolic ammonia (7 cm³) was heated in a pressure vessel at 130 °C for 5 h and then evaporated to dryness. It afforded the arabinofuranosyl **15**, *R*_f 0.05, and xylofuranosyl isomer **16**, *R*_f 0.04, in a ratio 2:1 (established by ¹H NMR spectra), used for further experiments.

General Procedure for the Hydrogenolysis of Azides 10, 22, 26 and 5.—To a solution of the azides (0.4 mmol) in ethanol (30 cm³) Pd-black (9 mg) was added and stirred in a H₂ atmosphere at 0.35 MPa at room temperature for 18 h. The catalyst was filtered off and the filtrate evaporated to dryness as in the case of the amino compounds **13** and **23** (used for further experiment). The residue was recrystallized from methanol as in the case of the amino compound **29** and rearranged imine **32**.

1-(5-Amino-5-deoxy-2,3-epoxy-β-D-lyxofuranosyl)uracil 13. From **10**: 99%; *R*_f 0.03.

1-(2-*O*-Acetyl-3-amino-5-benzamido-3,5-dideoxy-β-D-arabinofuranosyl)uracil 23. From **22**: 98%; *R*_f 0.13.

1-(3-Amino-2,5-anhydro-3-deoxy-β-D-arabinofuranosyl)uracil 29. From **26**: 82%; *R*_f 0.09; m.p. 244–246 °C (Found: C, 47.75; H, 5.15; N, 18.4. C₉H₁₁N₃O₄ requires C, 48.0; H, 4.9; N, 18.65%); [α]_D²⁵ + 337 (*c* 0.23 in MeOH); λ_{max}/nm 264 (log ε 3.93); ν_{max}/cm⁻¹ 3388, 3318, 3103, 3023, 2993, 1772, 1708, 1683infl, 1665, 1650infl, 1601, 1463, 1414, 1382, 1272, 1262, 1095 and 963; δ_H([²H₆]-DMSO) 7.91 (1 H, d, *J* 8.2, 6-H), 6.25 (1 H, s, 1'-H), 5.69 (1 H, d, *J* 8.2, 5-H), 4.51 (1 H, s, 2'-H), 4.29 (1 H, q, *J* 2.4 and 1.2, 4'-H), 4.04 (2 H, br s, 5'-H₂), 3.77 (1 H, d, *J* 2.4, 3'-H).

2,5'-Imino-1-(2-*O*-methylsulfonyl-β-D-arabinofuranosyl)uracil 32. From **5**, 94%; *R*_f 0.05; m.p. 201–203 °C (Found: C, 39.4; H, 4.4; N, 13.65. C₁₀H₁₃N₃O₆S requires C, 39.6; H, 4.3; N, 13.85%); [α]_D²³ – 73 (*c* 0.85 in DMF); λ_{max}/nm 215.5 (log ε 4.38); ν_{max}/cm⁻¹ 3550infl, 3480, 3429, 3240infl, 2899, 1649, 1611, 1532, 1496, 1453, 1342, 1178, 997 and 972.

General Procedure for the Benzoylation of Amines 13, 15 + 16, 23, 29 and the Imine 32.—To a solution of amine (0.4 mmol) or imine (0.16 mmol) in pyridine (5 cm³) benzoic acid anhydride (0.44 mmol) was added and the mixture kept at room temperature (45 min in the case of the amino compounds and 6 h in the case of the imino compound). The solvent was coevaporated with toluene. The residue was washed with diethyl ether and subjected to preparative TLC [CH₂Cl₂–MeOH (10:0.5), three developments].

1-(5-Benzamido-3-deoxy-2,3-epoxy-β-D-lyxofuranosyl)uracil 14. From **13**: 92%; m.p. 186–188 °C; identical (mixed m.p., NMR and IR spectra) with a specimen obtained by the hydrogenolysis–benzoylation of the azido compound **10**.

1-(5-Azido-3-benzamido-3,5-dideoxy-β-D-arabinofuranosyl)uracil 17 and **1-(5-Azido-2-benzamido-2,5-dideoxy-β-D-xylofuranosyl)uracil 18**. From a mixture of the amino compound **15** and **16**: 47% of **17**; *R*_f 0.19, and 36% of **18**; *R*_f 0.15; both used for further experiments.

1-(2-*O*-Acetyl-3,5-dibenzamido-3,5-dideoxy-β-D-arabinofuranosyl)uracil 24. From **23**: 81%; *R*_f 0.39; m.p. 264–265 °C (from MeOH); identical (mixed m.p., NMR and IR spectra) with a specimen obtained by the hydrogenolysis–benzoylation of the azido compound **22**.

1-(2,5-Anhydro-3-benzamido-3-deoxy-β-D-arabinofuranosyl)uracil 30. From **29**: 76%; *R*_f 0.26; m.p. 263–265 °C (from MeOH) (Found: C, 58.5; H, 4.45; N, 12.95. C₁₆H₁₅N₃O₅ requires C, 58.35; H, 4.6; N, 12.75%); [α]_D²⁵ + 92 (*c* 0.45 in MeOH);

λ_{\max}/nm 220 and 261.5 (log ϵ 4.16 and 4.12); λ_{\min}/nm 245 (log ϵ 4.06); $\nu_{\max}/\text{cm}^{-1}$ 3312, 3262, 3012, 2957, 1707, 1689, 1685, 1632, 1527, 1456, 1280, 1262, 1039, 921 and 859; $\delta_{\text{H}}-([\text{}^2\text{H}_6\text{]}-\text{DMSO})$ 11.37 (1 H, br s, 3-NH), 9.07–9.03 (1 H, m, 3'-NH), 7.98–7.87 and 7.58–7.41 (2 + 3 H, 2 \times m, ArH), 7.86 (1 H, d, J 7.9, 6-H), 5.99 (1 H, s, 1'-H), 5.61 (1 H, d, J 7.9, 5-H), 4.91 (1 H, s, 2'-H), 4.70 (1 H, d, J 2.6, 3'-H), 4.34 (1 H, t, J 2.6, 4'-H) and 4.04 (2 H, br s, 5'-H₂).

2,5'-Imino-1-(2-O-benzoyl-3-O-methylsulfonyl- β -D-arabinofuranosyl)uracil 35. From **32**: 53.7%; R_f 0.30; m.p. 148–150 °C (from dichloromethane–diethyl ether–hexane) (Found: C, 49.85; H, 4.35; N, 10.4. $\text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_7\text{S}$ requires C, 50.1; H, 4.2; N, 10.3%); $[\alpha]_{\text{D}}^{25} + 32$ (c 0.55 in MeOH); λ_{\max}/nm 222.5 (log ϵ 4.43); $\nu_{\max}/\text{cm}^{-1}$ 3393, 3156, 3022, 2935, 1735, 1661, 1497, 1409, 1354, 1262, 1176, 1114, 965, 870 and 826. The by-product **3** was isolated in 33.7% yield; identical (NMR and IR spectra) with an authentic specimen.

General Procedure for the Acetylation of Secondary Alcohols 17, 18, 21 and Imine 32.—To a solution of alcohol or imine (0.19 mmol) in pyridine (7 cm³) acetic anhydride (0.39 mmol) was added and the mixture kept at room temperature for 24 h as in the case of alcohols or 2 h as in the case of the imino compound. The solvent was coevaporated with toluene. The residue was purified by preparative TLC [CH_2Cl_2 –MeOH (10:0.6)].

1-(2-O-Acetyl-5-azido-3-benzamido-3,5-dideoxy- β -D-arabinofuranosyl)uracil 19. From **17**: 62%; R_f 0.24; m.p. 184–186 °C (from MeOH) (Found: C, 52.1; H, 4.65; N, 20.1. $\text{C}_{18}\text{H}_{18}\text{N}_6\text{O}_8$ requires C, 52.15; H, 4.4; N, 20.3%); $[\alpha]_{\text{D}}^{22} - 67$ (c 0.93 in DMF); λ_{\max}/nm 224 and 255 (log ϵ 3.78 and 3.74); λ_{\min}/nm 244 (log ϵ 3.72); $\nu_{\max}/\text{cm}^{-1}$ 3317, 3178, 3053, 2089, 1746, 1696, 1674, 1622, 1537, 1468, 1420, 1258, 1223, 1212, 1043, 859, 802 and 714.

1-(3-O-Acetyl-5-azido-2-benzamido-2,5-dideoxy- β -D-xylofuranosyl)uracil 20. From **18**: 67%; R_f 0.24; m.p. 125–127 °C (from acetone) (Found: C, 52.25; H, 4.3; N, 20.15. $\text{C}_{18}\text{H}_{18}\text{N}_6\text{O}_8$ requires C, 52.15; H, 4.4; N, 20.3%); $[\alpha]_{\text{D}}^{21} + 272$ (c 1.19 in MeOH); λ_{\max}/nm 219.9 and 256.8 (log ϵ 4.03 and 3.95); λ_{\min}/nm 247.5 (log ϵ 3.94); $\nu_{\max}/\text{cm}^{-1}$ 3460infl, 3295, 3062, 2109, 1756, 1689, 1645, 1537, 1533, 1462, 1273, 1225, 1217, 1064, 816, 717 and 692.

1-(2-O-Acetyl-3-azido-5-benzamido-3,5-dideoxy- β -D-arabinofuranosyl)uracil 22. From **21**: 71%; R_f 0.44; m.p. 86–88 °C (from dichloromethane–diethyl ether–hexane) (Found: C, 52.4; H, 4.55; N, 20.25. $\text{C}_{18}\text{H}_{18}\text{N}_6\text{O}_8$ requires C, 52.15; H, 4.4; N, 20.3%); $[\alpha]_{\text{D}}^{22} + 87.5$ (c 0.8 in MeOH); λ_{\max}/nm 220 and 256 (log ϵ 4.01 and 3.89); λ_{\min}/nm 246 (log ϵ 3.88); $\nu_{\max}/\text{cm}^{-1}$ 3344, 3203, 3061, 2932, 2111, 1753, 1713infl, 1693br, 1647infl, 1536, 1459, 1377, 1280, 1218, 1104, 810, 714 and 693.

2,5'-Imino-1-(2-O-acetyl-3-O-methylsulfonyl- β -D-arabinofuranosyl)uracil 33. From **32**: 79.6%; R_f 0.22; m.p. 217–219 °C (from MeOH) (Found: C, 41.9; H, 4.65; N, 12.3. $\text{C}_{12}\text{H}_{15}\text{N}_3\text{O}_7\text{S}$ requires C, 41.75; H, 4.4; N, 12.15%); $[\alpha]_{\text{D}}^{23} - 46$ (c 0.75 in MeOH); λ_{\max}/nm 218.5 (log ϵ 4.35); $\nu_{\max}/\text{cm}^{-1}$ 3414, 3225, 3084, 2934, 1750, 1663, 1624, 1576, 1502, 1410, 1223, 1177, 1000 and 970. From methanolic mother liquor an additional amount of **33** was isolated by preparative TLC; overall yield 92%.

Intramolecular Rearrangements of the 2,5'-Imino Compound 32.—To a solution of **32** (50 mg, 0.16 mmol) in pyridine (6 cm³) benzoyl chloride (50 mg, 0.36 mmol) was added and the mixture stirred at room temperature for 1.5 h; it was then treated with methanol (8 cm³). The solvent was coevaporated with toluene. The residue was recrystallized from methanol to give the crystalline 2,2'-anhydro compound **3** (48 mg, 74%), m.p. 186–188 °C; identical (mixed m.p., NMR and IR spectra) with an

authentic specimen. From the mother liquor **12** was also isolated by preparative TLC [CH_2Cl_2 –MeOH (10:0.6)] (16 mg, 23.5%), m.p. 173–176 °C; identical (mixed m.p., NMR and IR spectra) with that obtained from the 2,2'-anhydro compound **3**.

5'-N-Acetyl-2,5'-imino-1-(2-O-acetyl-3-O-methylsulfonyl- β -D-arabinofuranosyl)uracil 34.—To a solution of the 2,5'-imino compound **32** (80 mg, 0.26 mmol) in pyridine (5 cm³) acetyl chloride (98 mg, 1.25 mmol) was added and the mixture stirred at room temperature for 1 h. The solvent was coevaporated with toluene and the residue purified by preparative TLC [CH_2Cl_2 –MeOH (10:0.6), two developments] and recrystallized from methanol–diethyl ether. It afforded the 5'-N-acetyl compound **34** (86 mg, 85%); R_f 0.42; m.p. 126–129 °C (Found: C, 43.2; H, 4.75; N, 10.75. $\text{C}_{14}\text{H}_{17}\text{N}_3\text{O}_8\text{S}$ requires C, 43.4; H, 4.4; N, 10.85%); $[\alpha]_{\text{D}}^{22} - 131$ (c 0.54 in MeOH); λ_{\max}/nm 230 (log ϵ 4.33); $\nu_{\max}/\text{cm}^{-1}$ 1750, 1689, 1668, 1657, 1651, 1645, 1520, 1361, 1220, 1175, 1069 and 968.

5'-N-Benzoyl-2,5'-imino-1-(2-O-benzoyl-3-O-methylsulfonyl- β -D-arabinofuranosyl)uracil 37.—To a solution of the 2,5'-imino compound **35** (36 mg, 0.09 mmol) in pyridine (5 cm³) benzoyl chloride (24.4 mg, 0.17 mmol) was added. The mixture was then stirred at room temperature for 15 min and treated with methanol (4 cm³). The solvent was coevaporated with toluene and the residue purified by preparative TLC (CH_2Cl_2 –MeOH 10:0.6). It afforded the 5'-N-benzoyl compound **37** (38 mg, 82.6%); R_f 0.42; m.p. 151–153 °C (from acetone) (Found: C, 56.15; H, 4.05; N, 8.35. $\text{C}_{24}\text{H}_{21}\text{N}_3\text{O}_8\text{S}$ requires C, 56.35; H, 4.15; N, 8.2%); $[\alpha]_{\text{D}}^{22} - 171$ (c 0.42 in MeOH); λ_{\max}/nm 228.5 (log ϵ 4.34); $\nu_{\max}/\text{cm}^{-1}$ 1736, 1652, 1512, 1451, 1358, 1269, 1175, 1119, 1071, 971, 878 and 830.

General Procedure for the Preparation of Diphenylphosphoramidates 38–40.—To a suspension of the azide **5**, **10** or **22** (0.45 mmol) in dioxane (9 cm³) triphenyl phosphite (3.05 mmol) was added and the mixture heated under reflux in the presence of equimolar amount of water (1.5 h in the case of **5** and 3 h in the case of **10** and **22**). The reaction mixture was evaporated to dryness and the residue subjected to preparative TLC [CH_2Cl_2 –MeOH (10:0.7), two developments].

2,2'-Anhydro-1-(5-deoxy-5-diphenylphosphoramido-3-O-methylsulfonyl- β -D-arabinofuranosyl)uracil 38. From **5**: 89.3%; R_f 0.18; m.p. 228–230 °C (from MeOH) (Found: C, 49.15; H, 4.4; N, 8.1. $\text{C}_{22}\text{H}_{22}\text{N}_3\text{O}_9\text{PS}$ requires C, 49.35; H, 4.15; N, 7.85%); $[\alpha]_{\text{D}}^{24} - 40$ (c 0.2 in DMF); λ_{\max}/nm 221 and 245 (log ϵ 3.79 and 3.72); λ_{\min}/nm 234 (log ϵ 3.70); $\nu_{\max}/\text{cm}^{-1}$ 3152, 3092, 2932, 1660, 1634infl, 1638infl, 1622, 1534, 1477, 1337, 1254, 1196, 1173, 1023, 951, 940, 915, 902, 841 and 823; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]}-\text{DMSO})$ 7.75 (1 H, d, J 7.6, 6-H), 7.45–7.11 (10 H, m, ArH), 6.40 (1 H, d, J 5.6, 1'-H), 6.05 (1 H, m, 5'-NH), 5.85 (1 H, d, J 7.6, 5-H), 5.62 (1 H, d, J 5.6, 2'-H), 5.46 (1 H, d, J 2.4, 3'-H), 4.33 (1 H, sext, J 2.4 and 7.1, 4'-H), 3.28 (3 H, s, MsMe) and 3.02–2.91 (2 H, m, 5'-H₂); m/z 535 (M^+).

1-(5-Deoxy-5-diphenylphosphoramido-2,3-epoxy- β -D-lyxofuranosyl)uracil 39. From **10**: 78%; R_f 0.36; m.p. 128–130 °C (from dichloromethane–diethyl ether–hexane) (Found: C, 54.95; H, 4.65; N, 9.05. $\text{C}_{21}\text{H}_{20}\text{N}_3\text{O}_7\text{PS}$ requires C, 55.15; H, 4.4; N, 9.2%); $[\alpha]_{\text{D}}^{22} + 21$ (c 1 in MeOH); λ_{\max}/nm 256 (log ϵ 3.94); $\nu_{\max}/\text{cm}^{-1}$ 3419, 3168, 3067, 2922, 1758, 1717, 1696, 1673, 1648, 1634, 1519, 1488, 1459, 1385, 1255, 1218, 1196, 1103, 957, 907, 888 and 811; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]}-\text{DMSO})$ 11.06 (1 H, br s, 3-NH), 7.59 (1 H, d, J 8.2, 6-H), 7.46–7.06 (10 H, m, ArH), 5.99 (1 H, s, 1'-H), 5.91–5.72 (1 H, m, 5'-NH), 5.57 (1 H, d, J 8.2, 5-H), 4.07–3.87 (3 H, m, 2', 3'- and 4'-H), 3.30 (1 H, dd, J 12.6 and 1.8, 5'-H_A), 3.22 (1 H, dd, J 12.6 and 2.1, 5'-H_B); m/z 457 (M^+).

1-(2-O-Acetyl-5-benzamido-3,5-dideoxy-3-diphenylphosphoramido- β -D-arabinofuranosyl)uracil 40. From **22**: 83%; R_f 0.42;

m.p. 197–200 °C (from MeOH) (Found: C, 57.9; H, 4.95; N, 9.0. $C_{30}H_{29}N_4O_9P$ requires C, 58.05; H, 4.7; N, 9.05%); $[\alpha]_D^{23} + 66$ (*c* 0.7 in MeOH); λ_{max}/nm 253 (log ϵ 4.07); λ_{infr}/nm 228 (log ϵ 4.09); λ_{min}/nm 240 (log ϵ 4.05); ν_{max}/cm^{-1} 3369, 3168, 3067, 2922, 1758, 1717, 1696, 1673, 1648, 1634, 1519, 1488, 1459, 1385, 1255, 1218, 1196, 1103, 957, 907 and 811; *m/z* 621 (M^+).

Acknowledgements

We thank the Croatian Scientific Research Foundation and the European Communities Commission—International Scientific Cooperation (Contract No. CI1/0523) for their support of this work.

References

- 1 J. F. Codington, R. Fecher and J. J. Fox, *J. Am. Chem. Soc.*, 1960, **82**, 2794.
- 2 R. Fecher, J. F. Codington and J. J. Fox, *J. Am. Chem. Soc.*, 1961, **83**, 1889.
- 3 N. C. Yung, J. H. Burchenal, R. Fecher, R. Duschinsky and J. J. Fox, *J. Am. Chem. Soc.*, 1961, **83**, 4060.
- 4 V. Škarić, D. Katalenić, D. Škarić and I. Salaj, *J. Chem. Soc. Perkin Trans. 1*, 1982, 2091.
- 5 T.-S. Lin, J.-Y. Guo, R. F. Schinazi, C. K. Chu, J.-N. Xiang and W. H. Prusoff, *J. Med. Chem.*, 1988, **31**, 336.
- 6 M. Millard, A. Faraj, F. Frappier, J.-C. Florent, D. S. Grierson and C. Monneret, *Tetrahedron Lett.*, 1989, **30**, 197.
- 7 H. Mitsuya, K. J. Weinhold, P. A. Furman, M. H. St. Clair and S. Nusinoff, *Proc. Nat. Acad. Sci. USA*, 1985, **82**, 7096.
- 8 F. M. Unger, R. Christian and P. Waldstätten, *Tetrahedron Lett.*, 1979, 605.
- 9 A. M. Ozols, A. V. Azhayev, A. A. Krayevsky, A. S. Ushakov, N. V. Gnuchev and B. P. Gottikh, *Synthesis*, 1980, 559.
- 10 K. Kikugawa, M. Ichino, T. Kusama and T. Ukita, *Chem. Pharm. Bull.*, 1969, **17**, 798.
- 11 J. P. Horwitz, A. J. Thompson and J. A. Urbanski, *J. Org. Chem.*, 1962, **27**, 3045.
- 12 T.-S. Lin and W. H. Prusoff, *J. Carbohydr. Nucleosides Nucleotides*, 1975, **2**, 185.
- 13 M. Hirata, *Chem. Pharm. Bull.*, 1968, **16**, 291.
- 14 T. Naito, M. Hirata, Y. Nakai, T. Kobayashi and M. Kano, *Chem. Pharm. Bull.*, 1965, **13**, 1258.
- 15 J. Brokeš and J. Beránek, *Collect. Czech. Chem. Commun.*, 1975, **40**, 3061.
- 16 M. Christl, H. J. Reich and J. D. Roberts, *J. Am. Chem. Soc.*, 1971, **93**, 3463.
- 17 J. F. Codington, R. Fecher and J. J. Fox, *J. Org. Chem.*, 1962, **27**, 163.
- 18 A. J. Jones, D. M. Grant, M. W. Winkley and R. K. Robins, *J. Am. Chem. Soc.*, 1970, **92**, 4079.
- 19 W. Freist, K. Schattka, F. Cramer and B. Jastroff, *Chem. Ber.*, 1972, **105**, 991.
- 20 V. Kvitá and G. Baschang, *Helv. Chim. Acta*, 1972, **55**, 2683.
- 21 H. H. Mantsch and J. C. P. Smith, *Biochem. Biophys. Res. Commun.*, 1972, **46**, 808.

Paper 1/051051

Received 8th October 1991

Accepted 8th January 1992