Stereochemical Transformations of 5'-Amino-5'-deoxyuridine and Its 5,6-Dihydro-analogue. 5'-*N*-Aminoacyl Derivatives of 5'-Amino-5'-deoxy-5,6-dihydrouridine

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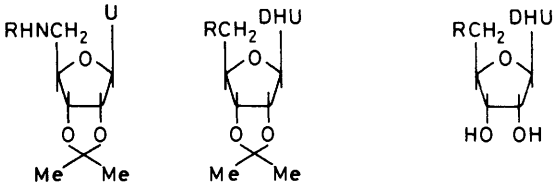
The synthesis of 5'-*N*-(*N*-t-butoxycarbonyl-glycyl)-(6), 5'-*N*-(*N*-t-butoxycarbonyl-L-phenylalanyl)- (7), and 5'-*N*-(*N*-benzyloxycarbonyl-L-phenylalanyl)- (8) derivatives of 5'-amino-5'-deoxy-2',3'-*O*-isopropylidene-5,6-dihydrouridine by the active ester method is described. The 5'-*N*-(*N*-benzyloxycarbonyl-L-phenylalanyl-L-phenylalanyl) derivative (10) was built by elongation of the 5'-*N*-(L-phenylalanyl)-5,6-dihydrouridine unit (9).

The transformations of 5'-benzamido-5'-deoxy-2',5'-dimethylsulphonyloxy-derivatives of uridine (20) and 5,6-dihydrouridine (21) in refluxing water afforded 2,2'-anhydro-1-(5-benzamido-5-deoxy-3-*O*-methylsulphonyl-β-D-arabinofuranosyl)uracil (22), 1-(5-benzamido-5-deoxy-β-D-lyxofuranosyl)uracil (24), and 1-(5-benzamido-5-deoxy-3-*O*-methylsulphonyl-β-D-arabinofuranosyl)-5,6-dihydrouracil (25), respectively. On the other hand treatment of the 2',3'-dimesyloxy-compounds (20) and (21) with potassium phthalimide in dioxan yielded selectively the corresponding 2,2'-anhydro-1-(5-benzamido-5-deoxy-3-*O*-methylsulphonyl-β-D-arabinofuranosyl)-uracil (22) and 5,6-dihydrouracil (23). 1-(5-Benzamido-5-deoxy-2,3-epoxy-β-D-lyxofuranosyl)uracil (27) was generated when 2',3'-dimesyloxyuridine (20) was treated with aqueous sodium hydroxide.

THE structure–activity relationships for 3'-amino-,[1] 2'-amino-,[2,3] and 5'-amino-[4] purine nucleosides, and their pyrimidine analogues[5,6] indicate that many of them have significant biochemical and chemotherapeutical properties. Thus, on the basis of the antibiotic properties of puromycin[7] and the fungicidal activities of polyoxynes[8,9] extensive studies directed towards the synthesis and properties of the amino-nucleosides and their *N*-aminoacyl derivatives have been reported.[10-14] This paper is concerned with the synthesis of 2',3'-*O*-isopropylidene derivatives of 5-amino-5-deoxyuridine (1) and its 5,6-dihydro-analogue (2), and their transformations into arabinofuranosyl, lyxofuranosyl, and *N*-aminoacyl derivatives.

In view of the reported synthesis of 5'-amino-5'-deoxy-2',3'-*O*-isopropylideneuridine[15,16] (1) the introduction of the azide group into 2',3'-*O*-isopropylidene-5'-*O*-methylsulphonyl-5,6-dihydrouridine (2), followed by reductive cleavage of the resulting 5'-azido-derivative (3) seemed the most appropriate one for the preparation of the hitherto unknown 5'-amino-5'-deoxy-2',3'-*O*-isopropylidene-5,6-dihydrouridine (4). It is worth noting that together with the mesylation of 2',3'-*O*-isopropylidene-5,6-dihydrouridine[17] to afford the 5'-*O*-mesyl compound (2) concomitant hydrolysis of the latter gave rise to 5'-*O*-methylsulphonyl-5,6-dihydrouridine (5), most probably due to the presence of water.

The coupling of 5'-amino-5'-deoxy-2',3'-*O*-isopropylidene-5,6-dihydrouridine (4) with the *p*-nitrophenyl esters of *N*-t-butoxycarbonyl-glycine and *N*-t-butoxycarbonyl-L-phenyalanine was a particularly satisfactory approach to the corresponding 5'-*N*-glycyl-(6) and 5'-*N*-L-phenylalanyl-(7) 5'-amino-5,6-dihydrouridine derivatives. The same active ester method[18] facilitated the synthesis of 5'-*N*-(*N*-benzyloxycarbonyl-L-phenylalanyl)-5'-amino-deoxy-5,6-dihydrouridine (8), and then its *N*-deprotection by hydrogenolysis over Pd black to give 5'-*N*-(L-phenylalanyl)-5'-amino-5'-deoxy-2',3'-*O*-isopropylidene-5,6-dihydrouridine (9). The latter was conveniently condensed with *N*-benzyloxycarbonyl-L-phenylalanine *p*-nitrophenyl ester to give crystalline 5'-*N*-(*N*-benzyloxycarbonyl-L-phenylalanyl-L-phenylalanyl) 5'-amino-5'-deoxy-2',3'-*O*-isopropylidene-5,6-dihydrouridine (10).



(1) R = H
(15) R = Ac
(16) R = Bz

(2) R = OMs
(3) R = N_3
(4) R = NH_2
(6) R = NHGly-Boc
(7) R = NHPhe-Boc
(8) R = NHPhe-Z
(9) R = NHPheH
(10) R = NHPhePhe-Z
(17) R = NHBz

(5) R = OMs
(11) R = NHPhe-Z
(12) R = NHPheH

Boc-Gly = t-butoxycarbonyl-glycyl; Boc-Phe = t-butoxycarbonyl-L-phenylalanyl; Z-Phe = benzyloxycarbonyl-L-phenylalanyl

To prepare 5'-*N*-(L-phenylalanyl)-5'-amino-5'-deoxy-5,6-dihydrouridine (12) compound (8) was first 2',3'-*O*-deblocked by 50% formic acid to give 5'-*N*-(*N*-benzyloxycarbonyl-L-phenylalanyl)-5'-amino-5'-deoxy-5,6-dihydrouridine (11) and then *N*-deprotected by hydrogenolysis over Pd black.

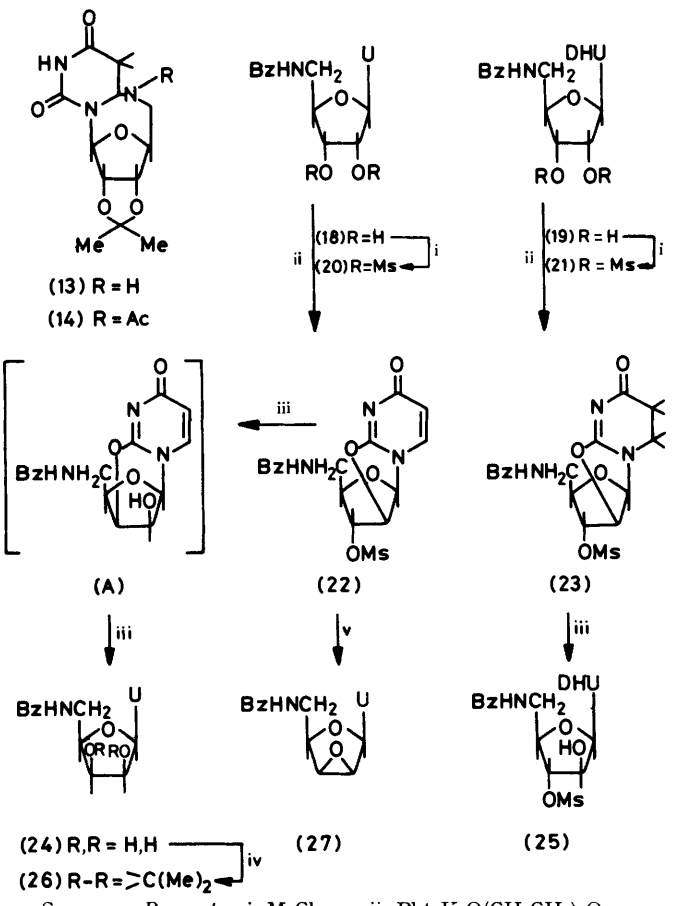
The main difference between the ^1H n.m.r. spectra of the glycyl-(6) and the L-phenylalanyl-(7) and (8) 5,6-dihydrouridine derivatives was the downfield shift (*ca.* 0.41 p.p.m.) in the resonances of the C-6 protons of compound (6). Several factors could account for this downfield shift. It may be noted, however, that the resonances of the C-6 protons of 5'-*O*-acetyl-2',3'-*O*-isopropylidene-5,6-dihydrouridine[19] (at τ 6.48) and the 5'-*N*-L-phenylalanyl derivatives (7) and (8) (at τ 6.55 and

6.52, respectively) were consistent with the view that the conformation of the furanose ring of the 5′-aminouridine analogues could be related to the parent oxygen compounds, and showing in solution a strong preference for the *anti*-arrangement.[20]

The attempted 5′-*N*-aminoacylations of 2′,3′-*O*-isopropylidene-5′-amino-5′-deoxyuridine (1) gave rise to the unwanted 5′-deoxy-5′,6-epimino-2′,3′-*O*-isopropylidene-5,6-dihydrouridine (13).[10,21,22] It should be noted that this 5′,6-epimino-system could, on treatment with sodium methoxide in methanol or potassium hydroxide in ethanol, be reopened to give 2′,3′-*O*-isopropylidene-5′-amino-5′-deoxyuridine (1) although similar experiments [21] indicated the formation of an unidentified unsaturated product which gave rise to a rapid increase in u.v. absorbancy at $\lambda_{max.}$ 258 nm. We found also that acetylation of compound (13) conserved its 5′,6-epimino-structure and yielded 5′-*N*-acetyl-5′-amino-5′-deoxy-5′,6-epimino-2′,3′-*O*-isopropylidene-5,6-dihydrouridine (14); this on treatment with sodium methoxide in methanol gave 5′-acetamido-5′-deoxy-2′,3′-*O*-isopropylideneuridine (15).[10,18] In order to prepare arabino- and lyxofuranosyl, stereoisomers from 5′-amino-5-deoxyuridine and 5′-amino-5′-deoxy-5,6-dihydrouridine 5′-benzamido-5′-deoxy-2′,3′-dimesyloxy-derivatives of uridine (20) and 5,6-dihydrouridine (21) were conveniently used as the chemical precursors. The synthetic sequence leading to these activated precursors involved the *O*-deprotection of the 5′-benzamido-5′-deoxy-2′,3′-*O*-isopropylidene derivatives (16) and (17) by acid hydrolysis, and the mesylation of the resulting 5′-benzamido-5′-deoxyuridine (18) and 5′-benzamido-5′-deoxy-5,6-dihydrouridine (19), respectively. The ^{1}H n.m.r. spectra of compounds (18) and (19) revealed signals for the secondary hydroxy-groups in the τ region 4.60—5.02, exchanging in D_2O, and for the 2′- and 3′-H at τ 5.80—6.29, the latter being shifted downfield to τ 4.49—4.84 in the spectra of the corresponding 2′,3′-dimesyloxy derivatives (20) and (21).

The intramolecular reaction of the 2′,3′-dimesyloxy-compounds (20) and (21) by means of potassium phthalimide in dioxan seemed the most appropriate one for the synthesis of the hitherto unknown 2,2′-anhydro-1-(5-benzamido-5-deoxy-3-*O*-methylsulphonyl-β-D-arabino-furanosyl) derivatives of uracil (22) and 5,6-dihydrouracil (23), respectively. The ^{1}H n.m.r. spectra of thus formed cyclic products (22) and (23) revealed the coupling constants between the 1′-H and 2′-H (*J* 5.9 Hz) in good accordance with the assigned arabino-configuration.[23,24]

Whereas the 2′-3′-dimesyloxyuridine derivative (20) on being heated under reflux in water was converted into 1-(5-benzamido-5-deoxy-β-D-lyxofuranosyl)uracil (24), under the same conditions the corresponding 2′,3′-dimesyloxy-derivative (21) in the 5,6-dihydrouridine series was transformed only into 1-(5-benzamido-5-deoxy-3-*O*-methylsulphonyl-β-D-arabinofuranosyl)-5,6-dihydrouracil (25). The intramolecular transformation necessary to give the lyxofuranosyl isomer (24), involving 2,3′-anhydro-1-(5-benzamido-5-deoxy-β-D-lyxofuranosyl)uracil (A) as one of the intermediates, was accomplished by the procedure used for the analogous epimerization of 2′,3′-dimesyloxy-5-fluorouridine into 1-β-D-lyxofuranosyl-5-fluorouracil.[25] The intermediate 2,3′-anhydro-structure (A) formation in the uridine series indicated that the aromatic uracil ring may bring this about.



SCHEME *Reagents*: i, MsCl-py; ii, Pht-K-O$(CH_2CH_2)_3$O; iii, H_2O; iv, Me_2CO–$CuSO_4$–H_2SO_4; v, NaOH–H_2O

The *cis*-2′,3′-dihydroxy-geometry of the lyxo-nucleoside (24), which was independently obtained from the 2,2′-anhydro-arabino-compound (22), was characterized as the corresponding 2′,3′-*O*-isopropylidene derivative (26), $[\alpha]_D^{18}$ +210.7° (*c* 0.65). The configuration of the arabinofuranosyl compound (25) was confirmed by the characteristic coupling constant (*J* 5.9 Hz) between 1′-H and 2′-H.[23,24] It is worth noting that the specific rotations of the lyxofuranosyl compounds (24), (26), and (27) reported here were dextrorotatory and in significant contrast to those of the arabinofuranosyl derivatives (22), (23), and (25) which exhibited negative signs of rotations.

In evaluating the conditions inducing the above described intramolecular reactions we found that the conversion of the 2′,3′-dimesyloxyuridine (20) into 1-(5-benzamido-5-deoxy-2,3-epoxy-β-D-lyxofuranosyl)uracil

(27) could be accomplished by the method for the preparation of 2',3'-epoxides from sulphonyloxyuridines, using aqueous sodium hydroxide as agent.[26] We also found that the 2,2'-anhydro-compound (22), as a possible intermediate, could be transformed into the 2',3'-epoxide (27) under these reaction conditions. The 2',3'-epoxide (27) showed in the ^{1}H n.m.r. spectrum the characteristic singlet at τ 3.94 due to very small coupling between 1'-H and 2'-H.[27]

It is worth noting that the mesyl derivatives (21) and (23) in the 5,6-dihydrouridine series, under the above described basic conditions gave rise to unidentified products, possibly due to the 5,6-dihydrouracil ring opening.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were obtained for potassium bromide pellets on a Perkin-Elmer 137 spectrophotometer, u.v. spectra for solutions in 95% ethanol on a Perkin-Elmer 124 spectrophotometer, and ^{1}H n.m.r. spectra for solutions in dimethyl sulphoxide unless otherwise stated, on a JEOL JNM-FX 100 spectrometer with tetramethylsilane as internal standard. Optical rotations were measured in methanol, unless otherwise stated, on a 179707 Zeiss-Winhel apparatus. Column chromatography was performed on silica gel (Merck; 0.05—0.2 mm). The silica gel (Merck HF_{254}, type 60) for t.l.c. was activated at 110 °C for 60 min; the products developed in methylene chloride–methanol (9 : 1) and recovered with acetone unless otherwise stated, were rendered visible by u.v. illumination and anisaldehyde, or a Ninhydrin spray.

2',3'-O-Isopropylidene-5'-O-methylsulphonyl-5,6-dihydrouridine (2).—To a solution of 2',3'-*O*-isopropylidene-5,6-dihydrouridine [17] (3.78 g, 10.37 mmol) in anhydrous pyridine, cooled at −40 °C, methanesulphonyl chloride (1.84 ml, 24.24 mmol) was added; the mixture was then left at 8 °C for 24 h protected from moisture. The solvent was removed under reduced pressure and the residue partitioned between water and chloroform. The product (4.77 g, 99.2%) separated from the organic layer, m.p. 166—169 °C (from methanol), R_F *ca.* 0.55, $[\alpha]_D^{23}$ −22.5° (*c* 1, CH_2Cl_2) (Found: C, 42.6; H, 5.6; N, 7.95. $C_{13}H_{20}N_2O_8S$ requires C, 42.85; H, 5.55; N, 7.7%), $\nu_{max.}$ 3 228, 2 948br, and 1 696br cm^{-1}; τ −0.40 (1 H, s, 3-NH), 4.30 (1 H, d, $J_{1',2'}$ 2.8 Hz, 1'-H), 5.10 (1 H, dd, $J_{2',1'}$ 2.8 Hz and $J_{2',3'}$ 6.5 Hz, 2'-H), 5.34 (1 H, dd, $J_{3',2'}$ 6.5 Hz and $J_{3',4'}$ 3.6 Hz, 3'-H), 5.57—5.97 (3 H, m, 4'-H and 5'-H_2), 6.60 (2 H, t, $J_{6,5}$ 6.5 Hz, 6-H_2), 6.77 (3 H, s, Ms–Me), 7.44 (2 H, t, $J_{5,6}$ 6.5 Hz, 5-H_2), and 8.49 and 8.67 (each 3 H, 2 × s, CMe_2).

5'-Azido-5'-deoxy-2',3'-O-isopropylidene-5,6-dihydrouridine (3).—To a solution of the mesyl derivative (2) (595 mg, 1.64 mmol) in dimethylformamide (7 m) sodium azide (225 mg, 3.46 mmol) was added and heated at 85 °C for 7 h. The mixture was then cooled at room temperature. The precipitate was filtered off and the filtrate evaporated to dryness under reduced pressure. The residue was chromatographed on a silica gel (15 g) column. Methylene chloride (100 ml) and methylene chloride–methanol (97 : 3; 200 ml) eluted a foamy product (371 mg, 73%), R_F *ca.* 0.78, precipitated from ether–n-hexane, $[\alpha]_D^{24}$ +17.5° (*c* 0.94, EtOH) (Found: C, 46.4; H, 5.85; N, 22.55. $C_{12}H_{17}N_5O_5$ requires C, 46.3; H, 5.5; N, 22.5 %), $\nu_{max.}$ 3 410, 3 218br, 2 990, 2 938, 2 100, 1 728sh, and 1 710br cm^{-1}; τ($CDCl_3$) 1.43 (1 H, s, 3-NH), 4.40 (1 H, d, $J_{1',2'}$ 2.7 Hz, 1'-H), 5.05 (1 H, dd, $J_{2',1'}$ 2.7 Hz and $J_{2',3'}$ 6.5 Hz, 2'-H), 5.27 (1 H, dd, $J_{3',2'}$ 6.5 Hz and $J_{3',4'}$ 4 Hz, 3'-H), 5.83 (1 H, dt, $J_{4',3'}$ 4 Hz and $J_{4',5'}$ 5 Hz, 4'-H), 6.43 (2 H, t, $J_{6,5}$ 6.5 Hz, 6-H_2), 6.46 (2 H, d, $J_{5',4'}$ 5 Hz, 5'-H), 7.30 (2 H, t, $J_{5,6}$ 6.5 Hz, 5-H_2), and 8.45 and 8.65 (3 H, 2 × s, CMe_2).

5'-Amino-5-deoxy-2',3'-O-isopropylidene-5,6-dihydrouridine (4).—To a solution of the azido-derivative (3) (500 mg, 1.60 mmol) in ethanol (23 ml) Pd-black (23 mg) was added. This suspension was stirred and hydrogenated at 0.35 MPa for 5 h. The catalyst was filtered off and the filtrate evaporated to dryness. It afforded the chromatographically pure product (455 mg), used for further experiments.

5'-O-Methylsulphonyl-5,6-dihydrouridine (5).—To a solution of 2',3'-*O*-isopropylidene-5,6-dihydrouridine [17] (500 mg, 1.75 mmol) in pyridine (12 ml) containing traces of water methanesulphonyl chloride (0.24 ml, 3.16 mmol) was added and worked up as described for compound (2). It yielded the product (395 mg, 62%), R_F *ca.* 0.13, m.p. 148—150 °C (from methanol), $[\alpha]_D^{23}$ −26° (*c* 1, H_2O) (Found: C, 37.15; H, 5.1; N, 8.4. $C_{10}H_{16}N_2O_8S$ requires C, 37.05; H, 4.95; N, 8.65%), $\nu_{max.}$ 3 400 sh, 3 300br, 2 905br, 1 717, and 1 671 cm^{-1}; τ − 0.30 (1 H, s, 3-NH), 4.32 (1 H, d, $J_{1',2'}$ 5.0 Hz, 1'-H), 4.65—4.75 (2 H, m, 2' and 3'-H), 5.65—5.82 [2 H, m, 4'-H and 2'(3')-OH], 5.95—6.25 [3 H, m, 5'-H_2 and 3'(2')-OH], 6.68 (2 H, t, 6-H_2, $J_{6,5}$ 6.5 Hz), 6.77 (3 H, s, Ms–Me), and 7.45 (2 H, t, $J_{5,6}$ 6.5 Hz, 5-H_2).

5'-N-(N-t-Butoxycarbonylglycyl)-5'-amino-5'-deoxy-2',3'-O-isopropylidene-5,6-dihydrouridine (6).—A solution of the crude 5'-amino-5,6-dihydrouridine (4) (139 mg, 0.487 mmol) and *N*-t-butoxycarbonylglycine *p*-nitrophenyl ester (158.6 mg, 0.531 mmol) in tetrahydrofuran (10 ml) was stirred at room temperature for 26 h. The solution was then evaporated to dryness. The residue was dissolved in methylene chloride and applied to a silica gel (21 g) column. Elution with methylene chloride–methanol (8 : 2) gave a foamy product (111 mg, 52%), R_F *ca.* 0.54, m.p. 105—107 °C (from ether–n-hexane), $[\alpha]_D^{21}$ −29° (*c* 1) (Found: C, 51.45; H, 7.05; N, 12.4. $C_{19}H_{30}N_4O_8$ requires C, 51.55; H, 6.85; N, 12.65%), $\lambda_{max.}$ 207 nm (log ε 3.30); $\nu_{max.}$ 3 530sh, 3 350br, 2 950, 2 940, 1 700br, 1 549sh, 1 530br, and 760 cm^{-1}; τ($CDCl_3$) 1.78—2.10 (1 H, m, 3-NH), 2.76—3.18 (1 H, m, 5'-NH), 4.34—4.60 (1 H, m, Boc-NH), 4.80—4.99 (2 H, m, 1'-H and 2'-H), 5.12—5.37 (1 H, m, 3'-H), 5.77—5.97 (1 H, m, 4'-H), 6.13 (2 H, t, $J_{6,5}$ 6.8 Hz, 6-H_2), 7.27 (2 H, t, $J_{5,6}$ 6.8 Hz, 5'-H_2), 8.46 and 8.67 (each 3 H, 2 × s, CMe_2), and 8.54 (9 H, s, CMe_3).

5'-N-(N-t-Butoxycarbonyl-L-phenylalanyl)-5'-amino-5'-deoxy-2',3'-O-isopropylidene-5,6-dihydrouridine (7). A solution of the crude 5'-amino-5,6-dihydrouridine (4) (138 mg, 0.47 mmol) and *N*-t-butoxycarbonyl-L-phenylalanine *p*-nitrophenyl ester (199.6 mg, 0.516 mmol) in tetrahydrofuran (10 ml) was stirred at room temperature for 40 h. The solution was then evaporated to dryness and the residue triturated with ether (20 ml) to give the product (198.6 mg, 77%), R_F *ca.* 0.57, m.p. 195—196 °C (from ethyl acetate), $[\alpha]_D^{22}$ −25° (*c* 1) (Found: C, 58.75; H, 7.05; N, 10.75. $C_{26}H_{36}N_4O_8$ requires C, 58.65; H, 6.85; N, 10.5%), $\lambda_{max.}$ (MeOH) 215 nm (log ε 3.82); $\nu_{max.}$ 3 495br, 3 350, 3 213sh, 2 973, 2 923, 1 721, 1 699sh, 1 695sh, 1 684, 1 676, 1 639, 1 602, 1 540br, 1 510, 770, 752, and 695 cm^{-1}; τ($CDCl_3$) 1.87—2.15 (1 H, m, 3-NH), 2.75 (5 H, s, ArH), 2.95—3.23 (1 H, m, 5'-NH), 4.78—4.93 (2 H, m, 1'-H and Boc-NH), 5.06—5.21 (1 H, m, 2'-H), 5.49—5.74 (2 H, m, 3'-H and CH-Ph), 5.86—6.0 (1 H, m, 4'-H), 6.55 (2 H, t, $J_{6,5}$ 6.8 Hz, 6-H_2), 6.86—7.07 (2 H, m, CH_2Ph), 7.32 (2 H, t, $J_{5,6}$ 6.8 Hz,

5-H_2), 8.49 and 8.68 (each 3 H, 2 × s, CMe_2), and 8.62 (9 H, s, CMe_3).

5′-N-(N-*Benzyloxycarbonyl*-L-*phenylalanyl*)-5′-*amino*-5′-*deoxy*-2′,3′-O-*isopropylidene*-5,6-*dihydrouridine* (8).—A solution of the crude 5′-amino-5,6-dihydrouridine (4) (254 mg, 0.89 mmol) and *N*-benzyloxycarbonyl-L-phenylalanine *p*-nitrophenyl ester (411.7 mg, 0.98 mmol) in tetrahydrofuran (20 ml) was stirred at room temperature for 48 h and then evaporated to dryness. The residue was dissolved in methylene chloride and applied to a silica gel (50 g) column. Elution with methylene chloride–methanol (9 : 1) gave the product (285 mg, 56.7%), R_F *ca.* 0.64, m.p. 100—102 °C (from ethyl acetate–ether–n-hexane), $[\alpha]_D^{22}$ −11.5° (*c* 1) (Found: C, 61.3; H, 6.35; N, 9.85. $C_{29}H_{34}N_4O_8$ requires C, 61.45; N, 6.05; N, 9.9%), $\lambda_{max.}$ 211 nm (log ε 3.25); $\nu_{max.}$ 3 530sh, 3 310br, 3 090, 3 045, 2 990, 2 937, 1 700br, 1 665sh, 1 530sh, 745br, and 698 cm^{-1}; τ($CDCl_3$) 2.10—2.24 (1 H, m, 3-NH), 2.68 and 2.74 (each 5 H, 2 × s, 2 × Ph), 2.94—3.06 (1 H, m, 5′-NH), 4.84—5.05 (2 H, m, 1′-H and Z-NH), 5.09—5.19 (1 H, m, 2′-H), 5.40—5.80 (2 H, m, 2′- and 3′-H), 5.82—6.0 (1 H, m, 4′-H), 6.52 (2 H, t, $J_{6,5}$ 6.4 Hz, 6-H_2), 6.88—7.01 (2 H, m, CH_2Ph), 7.33 (2 H, t, $J_{5,6}$ 6.4 Hz, 5-H_2), and 8.49 and 8.68 (each 3 H, 2 × s, CMe_2).

5′-N-(L-*Phenylalanyl*)-5′-*amino*-5′-*deoxy*-2′,3′-O-*isopropylidene*-5,6-*dihydrouridine* (9).—A solution of 5′-*N*-(*N*-benzyloxycarbonyl-L-phenylalanyl)-5′-amino-5,6-dihydrouridine (8) (228 mg, 0.409 mmol) in methanol (20 ml) was hydrogenated over Pd-black (150 mg) until evolution of carbon dioxide was complete. The catalyst was filtered off and the filtrate evaporated to dryness to give a foamy, chromatographically pure product (161 mg, 91.5%), R_F *ca.* 0.15, used for further experiments.

5′-N-(N-*Benzyloxycarbonyl*-L-*phenylalanyl*-L-*phenylalanyl*)-5′-*amino*-5′-*deoxy*-2′,3′-O-*isopropylidene*-5,6-*dihydrouridine* (10).—The mixture of 5′-*N*-(L-phenylalanyl)-5′-amino-5,6-dihydrouridine (9) (161 mg, 0.372 mmol) and *N*-benzyloxycarbonyl-L-phenylalanine *p*-nitrophenyl ester (172 mg, 0.409 mmol) in anhydrous tetrahydrofuran (10 ml) was stirred at room temperature for 48 h. The solution was evaporated to give the product (208 mg, 78.2%), R_F *ca.* 0.76, m.p. 117—119 °C (from methylene chloride–ether), $[\alpha]_D^{24}$ −20° (*c* 1) (Found: C, 63.75; H, 6.05; N, 10.0. $C_{38}H_{43}N_5O_9$ requires C, 63.95; H, 6.05; N, 9.8%), $\lambda_{max.}$ 218.5 nm (log ε 3.54); $\nu_{max.}$ 3 407sh, 3 320sh, 3 290, 3 060, 3 030, 2 987, 2 935, 1 722sh, 1 705br, 1 650, 1 540sh, 1 526br, 744, and 696 cm^{-1}.

5′-N-(N-*Benzyloxycarbonyl*-L-*phenylalanyl*)-5′-*amino*-5′-*deoxy*-5,6-*dihydrouridine* (11).—A solution of 2′,3′-*O*-isopropylidene-5,6-dihydrouridine (8) (75 mg, 0.125 mmol) in 50% formic acid was stirred for 24 h at room temperature and then azeotropically evaporated to dryness by means of ethanol. The resulting foamy product (59 mg, 89.7%) was crystallized from methanol–n-hexane, m.p. 180—182 °C, R_F *ca.* 0.57, $[\alpha]_D^{23}$ −23.8° (*c* 0.88, 50% HOAc) (Found: C, 59.6; H, 5.8; N, 10.55. $C_{26}H_{30}N_4O_8$ requires C, 59.3; H, 5.75; N, 10.65%), $\lambda_{max.}$ 215 nm (log ε 3.05); $\nu_{max.}$ 3 350, 3 280sh, 2 955br, 1 720, 1 696, 1 677, 1 663, 1 656sh, 1 550sh, 1 537sh, 1 528, 760sh, 740br, and 700 cm^{-1}.

5′-N-(L-*Phenylalanyl*)-5′-*amino*-5′-*deoxy*-5,6-*dihydrouridine Monohydrate* (12).—A solution of 5′-*N*-(*N*-benzyloxycarbonyl-L-phenylalanyl)-5′-amino-5,6-dihydrouridine (11) (105.4 mg, 0.2 mmol) in methanol (20 ml) was hydrogenated in the presence of Pd-black (100 mg) until evolution of carbon dioxide was complete. The catalyst was filtered off and the filtrate evaporated to dryness. The residue was dissolved in water (2 ml) and the solution was lyophilized to yield the product (62 mg, 78.9%), R_F *ca.* 0.1 (CH_2Cl_2–MeOH, 8.5 : 1.5), m.p. 105—107 °C, $[\alpha]_D^{24}$ −23° (*c* 0.5, H_2O) (Found: C, 52.5; H, 6.75. $C_{18}H_{24}N_4O_6 \cdot H_2O$ requires C, 52.65; H, 6.4%), $\nu_{max.}$ 3 359br, 3 079br, 2 939br, 1 708sh, 1 689, 1 667sh, and 1 574br cm^{-1}.

5′-N-*Acetyl*-5′-*amino*-5′-*deoxy*-5′,6-*epimino*-2′,3′-O-*isopropylidene*-5,6-*dihydrouridine* (14).—A solution of 5′,6-epiminouridine (13) [10] (400 mg, 1.41 mmol) in anhydrous pyridine (15 ml) was treated with acetic anhydride (14.2 ml, 0.15 mmol) at 60—70 °C for 4 h. Preparative t.l.c. separated the product (242 mg, 52.7%), R_F *ca.* 0.44, m.p. 187—188 °C (from methanol), $[\alpha]_D^{24}$ −104.5° (*c* 1) (Found: C, 51.55; H, 6.0; N, 12.65. $C_{14}H_{19}N_3O_6$ requires C, 51.7; H, 5.9; N, 12.9%), $\nu_{max.}$ 3 362, 3 342, 3 227br, 2992, 2947, 2 847br, 1 718sh, 1 710, 1 692, 1 681, 1 607, and 1 507 cm^{-1}; τ − 0.12br (1 H, s, 3-NH), 4.08 (1 H, s, 1′-H), 5.36 (1 H, d, $J_{2',3'}$ 6.9 Hz, 2′-H), 5.50 (1 H, d, $J_{3',2'}$ 6.0 Hz, 3′-H), 5.60 (1 H, t, $J_{6,5}$ 9.0 Hz, 6-H), 5.78 (1 H, q, $J_{4',3'}$ 3.6 Hz and $J_{4',5'}$ 1.6 Hz, 4′-H), 7.13 (2 H, d, $J_{5,6}$ 9.0 Hz, 5-H_2), 7.89 (3 H, s, Ac), and 8.58 and 8.73 (each 3 H, 2 × s, CMe_2).

5′-*Acetamido*-5′-*deoxy*-2′,3′-O-*isopropylideneuridine* (15).—(*a*) A solution of 5′-aminouridine (1) [15] (110 mg, 0.39 mmol) in anhydrous pyridine (5 ml) was treated with acetic anhydride (0.08 ml, 0.79 mmol) at room temperature for 16 h and then evaporated to dryness. Preparative t.l.c. separated the product (79 mg, 63%), R_F *ca.* 0.33, m.p. 143—145 °C (from methanol–ether), $[\alpha]_D^{27}$ −10.9° (*c* 0.82) (Found: C, 51.5; H, 6.25; N, 12.55. $C_{14}H_{19}N_3O_6$ requires C, 51.7; H, 5.9; N, 12.9%), $\lambda_{max.}$ 260 nm (log ε 3.80), $\lambda_{min.}$ 232 nm (log ε 3.34); $\nu_{max.}$ 3 301, 2 990, 2 940, 1 721, 1 682, 1 654, 1 651, and 1 550br, cm^{-1}; τ($CDCl_3$) 0.74 (1 H, s, 3-NH), 2.78 (1 H, d, $J_{6,5}$ 8.20 Hz, 6-H), 3.30—3.55 (1 H, m, 5′-NH), 4.21 (1 H, d, with secondary splitting, $J_{5,6}$ 8.20 Hz, 5-H), 4.65 (1 H, d, $J_{1',2'}$ 2.3 Hz, 1′-H), 4.84 (1 H, dd, $J_{2',1'}$ 2.3 Hz and $J_{2',3'}$ 6.5 Hz, 2′-H), 5.21 (1 H, dd, $J_{3',2'}$ 6.5 Hz and $J_{3',4'}$ 4.1 Hz, 3′-H), 5.67—5.90 (1 H, t, $J_{4',3'}$ 4.1 Hz, 4′-H), 6.17—6.61 (2 H, m, 5′-H_2), 7.99 (3 H, s, Ac), and 8.45 and 8.66 (each 3 H, 2 s, 2Me).

(*b*) To a solution of 5′-acetyl-5′,6-epiminouridine (14) (20 mg, 0.06 mmol) in anhydrous methanol (2.9 ml) methanolic 0.1 mol dm^{-3} sodium methoxide (0.12 ml) was added and set aside at room temperature for 3 h. The solvent was removed under reduced pressure and the residue crystallized by trituration with ether in 78.5% yield (15.7 mg), identical (mixed m.p., i.r., and n.m.r. spectra) with the product described under (*a*).

5′-*Benzamido*-5′-*deoxy*-2′,3′-O-*isopropylideneuridine* (16).—To a solution of 5′-aminouridine (1) [15] (500 mg, 1.76 mmol) in anhydrous and freshly distilled pyridine (14 ml) benzoic acid anhydride (423 mg, 1.87 mmol) was added; the mixture was then stirred at room temperature for 30 min. The solvent was azeotropically removed under reduced pressure by means of benzene and methanol and the residue was washed with ether and then subjected to preparative t.l.c. (methylene chloride–methanol, 10 : 0.6, 2 developments). It afforded the product (520 mg, 77%), R_F *ca.* 0.36, m.p. 108—111 °C (from methanol–ether), $[\alpha]_D^{25}$ +4.9° (*c* 0.72) (Found: C, 58.9; H, 6.0; N, 10.95. $C_{19}H_{21}N_3O_6$ requires C, 58.9; H, 5.45; N, 10.85%), $\lambda_{max.}$ 220 and 253 nm (log ε 4.10 and 4.02); $\lambda_{min.}$ 245 nm (log ε 4.02); $\nu_{max.}$ 3 349br, 3 059, 2 989, 1 710sh, 1 690, 1 650, 1 604, 1 579, 1 538, 717, and 698 cm^{-1}; τ($CDCl_3$) 0.39 (1 H, s, exchanging in D_2O, 3-NH), 2.06—2.21 and 2.48—2.64 (2 + 3 H, 2 × m, ArH), 2.77 (1 H, d, $J_{6,5}$ 8.1 Hz, 6-H), 2.76—2.92 (1 H, m,

exchanging in D_2O, 5'-NH), 4.26 (1 H, d, $J_{5,6}$ 8.1 Hz, 5-H), 4.60 (1 H, d, $J_{1',2'}$ 2.0 Hz, 1'-H), 4.86 (1 H, dd, $J_{2',1'}$ 2.0 Hz and $J_{2',3'}$ 6.6 Hz, 2'-H), 5.09 (1 H, dd, $J_{3',2'}$ 6.6 Hz and $J_{3',4'}$ 4.6 Hz, 3'-H), 5.60—5.79 (1 H, m, 4'-H), 6.01 (1 H, dd, $J_{a,4'}$ 5.6 Hz and $J_{a,b}$ 14.5 Hz, 5'-H_a), 6.28 (1 H, dd, $J_{b,4'}$ 4.6 Hz and $J_{b,a}$ 14.5 Hz, 5'-H_b), and 8.45 and 8.67 (each 3 H, 2 × s, CMe_2).

5'-Benzamido-5'-deoxy-2',3'-O-isopropylidene-5,6-dihydrouridine (17). A solution of the crude 5'-amino-5,6-dihydrouridine (4) (1.17 g, 4.10 mmol) in anhydrous and freshly distilled pyridine (22 ml) was treated with benzoic acid anhydride (1.01 g, 4.44 mol) for 30 min and then worked up as for compound (16). The product was obtained in 95% yield (1.17 g), R_F *ca.* 0.43, m.p. 112—114 °C (from methanol), $[\alpha]_D^{28}$ −14.5° (*c* 1) (Found: C, 56.95; H, 6.45; N, 10.15. $C_{19}H_{23}N_3O_6{\cdot}CH_3OH$ requires C, 57.0; H, 6.45; N, 9.95%), $\lambda_{max.}$ 222 nm (log ε 4.11); $\nu_{max.}$ 3 536, 3 456, 3 410, 3 070br, 2 986, 1 721sh, 1 712sh, 1 704, 1 698, 1 694, 1 691, 1 650, 1 603, 1 577, 727, and 696 cm^{-1}; τ −0.35 (1 H, s, exchanging in D_2O, 3-NH), 1.30—1.49 (1 H, m, 5'-NH, exchanging in D_2O, 5'-NH), 2.09—2.20 and 2.49—2.56 (2 and 3 H, 2 × m, ArH), 4.30 (1 H, d, $J_{1',2'}$ 2.7 Hz, 1'-H), 5.07 (1 H, dd, $J_{2',1'}$ 2.7 Hz and $J_{2',3'}$ 6.5 Hz, 2'-H), 5.34 (1 H, dd, $J_{3',2'}$ 6.5 Hz $J_{3',4'}$ 4.4 Hz, 3'-H), 5.86—6.08 (1 H, m, 4'-H), and 8.54 and 8.73 (each 3 H, 2 × s, CMe_2).

5'-Benzamido-5'-deoxyuridine (18).—To a solution of 2',3'-*O*-isopropylidene-5'-amino-5'-deoxyuridine (16) (230 mg, 0.59 mmol) in ethanol (11.3 ml), concentrated hydrochloric acid (0.21 ml) was added; the mixture was then heated under reflux for 1.5 h. The mixture was azeotropically evaporated to dryness by means of benzene and methanol. The product was obtained in 89% yield (184 mg), R_F *ca.* 0.12, m.p. 216—217 °C (from methanol), $[\alpha]_D^{28}$ +17.8° (*c* 0.98) (Found: C, 55.5; H, 5.0; N, 12.25. $C_{16}H_{17}N_3O_6$ requires C, 55.35; H, 4.95; N, 12.1%), $\lambda_{max.}$ 221 and 258 nm (log ε 4.12 and 4.02); $\lambda_{min.}$ 247.5 nm (log ε 4.0); $\nu_{max.}$ 3 396br, 3 336, 3 286br, 3 066, 2 956, 2 924, 1 704, 1 687, 1 684, 1 676, 1 631, 1 618sh, 1 605, 1 577, 1 544, 776, and 692 cm^{-1}; τ − 1.33 (1 H, s, exchanging in D_2O, 3-NH), 1.28—1.49 (1 H, m, exchanging in D_2O, 5'-NH), 2.11—2.18 and 2.48—2.60 (2 + 3 H, 2 × m, ArH), 2.23 (1 H, d, $J_{6,5}$ 8.2 Hz, 6-H), 4.26 (1 H, d, $J_{1',2'}$ 5.6 Hz, 1'-H), 4.39 (1 H, d, $J_{5,6}$ 8.2 Hz, 5-H), 4.60 [1 H, d, $J_{OH,H}$ 5.3 Hz, in D_2O, 2'-(3'-)OH], 4.81 [1 H, d, $J_{OH,H}$ 4.4 Hz, exchanging in D_2O, 3'-(2'-)OH], 5.80—6.13 (3 H, m, 2'-,3'-, and 4'-H), and 6.38—6.57 (2 H, m, 5'-H_2).

5'-Benzamido-5'-deoxy-5,6-dihydrouridine (19). A solution of 2',3'-*O*-isopropylidene-5'-amino-5'-deoxy-5,6-dihydrouridine (17) (660 mg, 1.89 mmol) in 80% acetic acid (155 ml) was heated at 60 °C for 4 h. The solvent was then removed azeotropically under reduced pressure by means of benzene and ethanol. The residue was purified by preparative t.l.c. (CH_2Cl_2–MeOH, 10 : 0.8; two developments recovery with acetone) and then by recrystallization from methanol; yield 493 mg (84%), R_F *ca.* 0.12, m.p. 193—195 °C, $[\alpha]_D^{25}$ −15.5° (*c* 1) (Found: C, 54.95; H, 5.15; N, 11.9. $C_{16}H_{19}N_3O_6$ requires C, 55.0; H, 5.5; N, 12.05%), $\lambda_{max.}$ 223 nm (log ε 4.12); $\nu_{max.}$ 3 400sh, 3 349, 3 285, 3 069br, 2 949br, 1 718, 1 700, 1 687, 1 679, 1 631, 1 601, 1 579, 1 540br, 775, and 689 cm^{-1}; τ −0.26 (1 H, s, exchanging in D_2O, 3-NH), 1.33—1.53 (1 H, m, exchanging in D_2O, 5'-NH), 2.09—2.19 and 2.41—2.55 (2 and 3 H, 2 × m, ArH), 4.32 (1 H, d, $J_{1',2'}$ 5.9 Hz, 1'-H), 4.79—5.02 (2 H, m, exchanging in D_2O, 2'- and 3'-OH), and 5.94—6.29 (3 H, m, 2'-, 3', and 4'-H).

5'-Benzamido-5'-deoxy-2',3'-dimethylsulphonyloxyuridine (20).—A solution of 5'-benzamidouridine (18) (220 mg, 0.63 mmol) in anhydrous and freshly distilled pyridine (11 ml) was treated with methanesulphonyl chloride (0.29 ml, 3.82 mmol) over a period of 24 h; it was then worked up by a standard method. The preparative t.l.c. (CH_2Cl_2–MeOH, 10 : 0.7; three developments) separated the product which crystallized from methylene chloride–ether–n-hexane (250 mg, 78.6%), R_F *ca.* 0.38, m.p. 128—130 °C, $[\alpha]_D^{26}$ +8.5° (*c* 1. EtOH) (Found: C, 43.1; H, 4.6; N, 8.25. $C_{18}H_{21}N_3O_{10}S_2$ requires C, 42.95; H, 4.2; N, 8.35%); $\lambda_{max.}$ 225 nm (log ε 4.07); $\lambda_{infl.}$ 254 nm (log ε 3.94); $\nu_{max.}$ 3 400br, 3 020br, 2 940, 1 710sh, 1 690, 1 650br, 1 600, 1 580, 1 538br, 715, and 691 cm^{-1}; τ($CDCl_3$) 0.78 (1 H, s, 3-NH), 2.11—2.21 and 2.51—2.58 (2 and 3 H, m, ArH), 2.76 (1 H, d, $J_{6,5}$ 8.2 Hz, 6-H), 3.05—3.30 (1 H, m, 5'-NH), 4.28 (1 H, d, $J_{5,6}$ 8.2 Hz, 5-H), 4.49—4.84 (3 H, m, 1'-, 2'-, and 3'-H), 5.59—5.68 (1 H, m, 4'-H), 6.23—6.55 (2 H, m, 5'-H_2), and 6.79 and 6.84 (each 3 H, 2 × s, 2 × MsMe).

5'-Benzamido-5'-deoxy-2',3'-dimethylsulphonyloxy-5,6-dihydrouridine (21).—A solution of 5'-benzamido-5,6-dihydrouridine (19) (140 mg, 0.40 mmol) in anhydrous and freshly distilled pyridine (15 ml) was treated with methanesulphonyl chloride (0.14 ml, 1.85 mmol) for 4 h and the mixture then worked up as described in compound (20). Preparative t.l.c. (CH_2Cl_2–MeOH, 10 : 0.6; two developments, recovery with acetone) afforded the product which crystallized from methylene chloride–ether–n-hexane (146 mg, 73%), R_F *ca.* 0.42, m.p. 123—125 °C, $[\alpha]_D^{26}$ −15.1° (*c* 1.4) (Found: C, 42.85; H, 4.75; N, 8.25. $C_{18}H_{23}N_3O_{10}S$ requires C, 42.75; H, 4.6; N, 8.3%); $\lambda_{max.}$ 225 nm (log ε 4.07); $\nu_{max.}$ 3 401br, 3 022, 2 935, 1 721sh, 1 701br, 1 643br, 1 602, 1 581, 1 537, 720, and 700 cm^{-1}; τ($CDCl_3$) 2.09—2.21 (3 H, m, 3-NH and ArH), 2.46—2.65 (3 H, m, ArH), 3.07—3.30 (1 H, m, 5'-NH), 4.64—4.84 (3 H, m, 1'-, 2'-, and 3'-H), 5.59—5.81 (1 H, m, 4'-H), 6.39 (2 H, t, $J_{6,5}$ 6.5 Hz, 6-H_2), 6.28—6.55 (2 H, m, 5'-H_2), 6.83 and 6.85 (each 3 H, 2 × s, 2 × MsMe), and 7.29 (2 H, t, $J_{5,6}$ 6.5 Hz, 5-H_2).

2,2'-Anhydro-1-(5-benzamido-5-deoxy-3-O-methylsulphonyl-β-D-arabinofuranosyl)uracil (22).—To a solution of 2',3'-dimesyloxyuridine (20) (47 mg, 0.09 mmol) in anhydrous dioxan (24 ml) potassium phthalimide (17.3 mg, 0.09 mmol) was added. This suspension was stirred and heated under reflux for 24 h and then filtered. The filtrate was evaporated to dryness under reduced pressure. The residue crystallized from methanol (21 mg, 55.2%), R_F *ca.* 0.17, m.p. 192—201 °C, $[\alpha]_D^{26}$ −34° (*c* 1) (Found: C, 49.75; H, 4.25; N, 10.6. $C_{17}H_{17}N_3O_7S$ requires C, 50.1; H, 4.2; N, 10.3%), $\lambda_{max.}$ 227 nm (log ε 4.28); $\lambda_{infl.}$ 250 nm (log ε 4.01); $\nu_{max.}$ 3 428br, 3 282, 3 082, 3 022, 3 002, 2 942, 2 925, 1 655, 1 635sh, 1 630, 1 602sh, 1 580, 1 532br, 720, and 700 cm^{-1}; τ 1.17—1.40 (1 H, m, 5'-NH), 2.08 (1 H, d, $J_{6,5}$ 7.3 Hz, 6-H), 2.16—2.26 and 2.49—2.56 (2 and 3 H, 2 × m, ArH), 3.55 (1 H, d, $J_{1',2'}$ 5.9 Hz, 1'-H), 4.08 (1 H, d, $J_{5,6}$ 7.3 Hz, 5-H), 4.35 (1 H, d, $J_{2',1'}$ 5.9 Hz, 2'-H), 4.39 (1 H, s, 3'-H), 5.35—5.57 (1 H, m, 4'-H), and 6.78 (3 H, s, MsMe).

2,2'Anhydro-1-(5-benzamido-5-deoxy-3-O-methylsulphonyl-β-D-arabinofuranosyl)-5,6-dihydrouracil (23).—A solution of 2',3'-dimesyloxydihydrouridine (21) (70 mg, 0.14 mmol) in anhydrous dioxan (35 ml) was treated with potassium phthalimide (26 mg, 0.14 mmol) and heated under reflux for 3 h. It was worked up as described for compound (22). Preparative t.l.c. (CH_2Cl_2–MeOH, 10 : 0.6; two developments, recovery with acetone) afforded the purified product, which crystallized from methylene chloride–ether–n-hexane (28 mg, 49.5%), R_F *ca.* 0.24, m.p.

116—119 °C, $[\alpha]_D^{18}$ −48° (*c* 0.97) (Found: C, 49.4; H, 5.1; N, 10.05. $C_{17}H_{19}N_3O_7S$ requires C, 49.85; H, 4.7; N, 10.25%), $\nu_{max.}$ 3 420br, 3 345, 3 260br, 3 030, 2 930, 2 875, 1 730, 1 693, 1 650, 1 601br, 1 536br, 713, and 692 cm^{-1}; τ($CDCl_3$) 2.07—2.20 (3 H, m, 5′-NH and ArH), 2.52—2.68 (3 H, m, ArH), 4.12 (1 H, d, $J_{1',2'}$ 5.9 Hz, 1′-H), 4.55 (1 H, s, 3′-H), 4.56 (1 H, d, $J_{2',1'}$ 5.9 Hz, 2′-H), 5.23—5.37 (1 H, m, 4′-H), 6.19 (2 H, t, $J_{6,5}$ 6.8 Hz, 6-H_2), 6.27—6.68 (2 H, m, 5′-H_2), 6.86 (3 H, s, MsMe), and 7.39 (2 H, t, $J_{5,6}$ 6.8 Hz, 5-H_2).

1-(5-*Benzamido*-5-*deoxy*-β-D-*lyxofuranosyl*)*uracil* (24).—(*a*) A solution of the 2,2′-anhydro-derivative (22) (110 mg, 0.27 mmol) in water (22 ml) was heated under reflux for 4 h, and then evaporated under reduced pressure to dryness. The residue was purified by preparative t.l.c. (CH_2Cl_2–MeOH, 10 : 0.6; two developments). It crystallized from methylene chloride–ether–n-hexane (61 mg, 67.8%), R_F *ca.* 0.16, m.p. 192—193 °C, $[\alpha]_D^{27}$ +87.6° (*c* 0.68) (Found: C, 55.35; H, 5.2; N, 11.9. $C_{16}H_{17}N_3O_6$ requires C, 55.35; H, 4.95; N, 12.1%), $\lambda_{max.}$ 221 and 260 nm (log ε 4.07 and 3.97); $\lambda_{min.}$ 246 nm (log ε 3.94); $\nu_{max.}$ 3 501, 3 451, 3 401, 3 319, 3 201, 3 123, 3 062, 2941, 1 696, 1 662, 1 657, 1 653, 1 651, 1 644sh, 1 623, 1 603, 1 573, 1 564, 739, and 716 cm^{-1}; τ — 1.23 (1 H, s, 3-NH), 1.24—1.46 (1 H, m, 5′-NH), 2.03 (1 H, d, $J_{6,5}$ 8.3 Hz, 6-H), 2.09—2.19 and 2.49—2.61 (2 and 3 H, 2 × m, ArH), 3.95 (1 H, d, $J_{1',2'}$ 6.7 Hz, 1′-H), 4.43 (1 H, d, $J_{5,6}$ 8.3 Hz, 5-H), 4.43—4.53 (2 H, m, 2′- and 3′-H), 5.53—5.69 (1 H, m, 4′-H), 5.85—5.99 (2 H, m, 5′-H_2), and 6.39—6.44 (2 H, m, 2′- and 3′-OH).

(*b*) A solution of dimesyloxyuridine (20) (35 mg, 0.07 mmol) in water (7 ml) was heated under reflux for 5 h and worked up as described under (*a*). It yielded 17 mg (59.4%) of the purified product, m.p. 192—194 °C, identical (mixed m.p., i.r., and n.m.r. spectra) with that obtained under (*a*).

1-(5-*Benzamido*-5-*deoxy*-2,3-O-*isopropylidene*-β-D-*lyxofuranosyl*)*uracil* (26).—A suspension of the lyxofuranosyl derivative (24) (35 mg, 0.1 mmol) in acetone (1 ml), sulphuric acid (6.10^{-4} ml), and anhydrous cuprous sulphate (49 mg, 0.3 mmol) was heated at 37 °C for 43 h. The precipitate was then filtered off. The filtrate was treated with anhydrous calcium chloride (24.5 mg, 0.33 mmol) and stirred at room temperature for 1 h. This mixture was filtered and the filtrate evaporated to dryness under reduced pressure. The preparative t.l.c. (CH_2Cl_2–MeOH, 10 : 0.6; two developments) separated the product (35 mg, 90.4%), R_F *ca.* 0.41, m.p. 141—143 °C (from methylene chloride–ether–n-hexane), $[\alpha]_D^{18}$ +210.7° (*c* 0.65) (Found: C, 58.9; H, 5.75; N, 10.65. $C_{19}H_{21}N_3O_6$ requires C, 58.9; H, 5.46; N, 10.85%); $\lambda_{max.}$ 220 nm and 260 nm (log ε 4.01 and 3.93), $\lambda_{min.}$ 245 nm (log ε 3.88); $\nu_{max.}$ 3 327br, 3 106, 3 032, 2 997, 2 920, 1 710, 1 704, 1 690, 1 603, 1 600, 1 578, 1 544, 1 535, 711, and 691 cm^{-1}; τ($CDCl_3$) 0.41 (1 H, s, 3-NH), 2.11—2.21 and 2.47—2.68 (2 and 3 H, 2 × m, ArH), 2.53 (1 H, d, $J_{6,5}$ 8.2 Hz, 6-H), 2.92—3.12 (1 H, m, 5′-NH), 4.23 (1 H, d, $J_{1',2'}$ 3.2 Hz, 1′-H), 4.36 (1 H, d, $J_{5,6}$ 8.2 Hz, 5-H), 5.19 (1 H, d, $J_{2',3'}$ 5.9 Hz, 2′-H), 5.34 (1 H, d, $J_{3',4'}$ 5.9 Hz, 3′-H), 5.81—5.98 (2 H, m, 5′-H_2), 6.20—6.49 (1 H, m, 4′-H), and 8.55 and 8.72 (each 3 H, 2 × s, CMe_2).

1-(5-*Benzamido*-5-*deoxy*-3-O-*methylsulphonyl*-β-D-*arabinofuranosyl*)-5,6-*dihydrouracil* (25).—A solution of dimesyloxy-5,6-dihydrouridine (21) (70 mg, 0.14 mmol) in water (14 ml) was heated under reflux for 2 h and then evaporated to dryness under reduced pressure. The preparative t.l.c. (CH_2Cl_2–MeOH, 10 : 0.7) separated the product, which crystallized from methylene chloride–ether–n-hexane (46 mg, 78%), R_F *ca.* 0.23, m.p. 80—82 °C, $[\alpha]_D^{17}$ −59.8° (*c* 0.9) (Found: C, 47.8; H, 4.6; N, 10.05. $C_{17}H_{21}N_3O_8$ requires C, 47.75; H, 4.95; N, 9.85%); $\nu_{max.}$ 3 430br, 3 341, 3 206, 3 016br, 2 931, 2 851, 1 766br, 1 666, 1 651, 1 645, 1 601, 1 576, 1 533br, 710, and 689 cm^{-1}; τ 1.07—1.30 (1 H, m, exchanging in D_2O, 5′-NH), 2.06—2.21 and 2.45—2.62 (2 and 3 H, 2 × m, ArH), 3.04 (1 H, s, exchanging in D_2O, 3-NH), 4.14 (1 H, d, $J_{1',2'}$ 5.9 Hz, 1′-H), 4.60 (1 H, s, 3′-H), 4.81 (1 H, d, $J_{2',1'}$ 5.9 Hz, 2′-H), 5.50—5.70 (1 H, m, 4′-H), and 6.70 (3 H, s, MsMe).

1-(5-*Benzamido*-5-*deoxy*-2,3-*epoxy*-β-D-*lyxofuranosyl*)-*uracil* (27).—(*a*) A solution of dimesyloxyuridine (20) (80 mg, 0.36 mmol) in 0.5 mol dm^{-3} NaOH (0.96 ml, 0.48 mmol) was stirred at room temperature for 1 h, and then evaporated to dryness under reduced pressure. The preparative t.l.c. (CH_2Cl_2–MeOH, 10 : 0.5; three developments) separated the product which crystallized from methanol (41 mg, 79%), R_F *ca.* 0.36, m.p. 188—191 °C, $[\alpha]_D^{25}$ +129.6° (*c* 0.73, EtOH) (Found: C, 58.15; H, 4.8; N, 12.9. $C_{16}H_{15}N_3O_3$ requires C, 58.35; H, 4.6; N, 12.75%), $\lambda_{max.}$ 223 and 254 nm (log ε 4.09 and 3.99); $\lambda_{min.}$ 247 nm (log ε 3.98); $\nu_{max.}$ 3 328, 3 198br, 3 123, 3 113, 3 063, 3 008, 2 948, 2 828, 1 762, 1 721br, 1 680br, 1 676, 1 668, 1 640, 1 625sh, 1 603, 1 580, 1 530br, 711, 696, and 688 cm^{-1}; τ — 1.41 (1 H, s, exchanging in D_2O, 3-NH), 1.18—1.38 (1 H, m, exchanging in D_2O, 5′-NH), 2.09—2.19 and 2.49—2.54 (2 and 3 H, 2 × m, ArH), 2.31 (1 H, d, $J_{6,5}$ 8.2 Hz, 6-H), 3.94 (1 H, s, 1′-H), 4.34 (1 H, d, $J_{5,6}$ 8.2 Hz, 5-H), 5.63 (1 H, d, $J_{2',3'}$ 7.3 Hz, 2′-H), 5.75 (1 H, d, $J_{3',2}$ 7.3 Hz, 3′-H), 5.87—5.99 (1 H, m, 4′-H), and 6.32—6.48 (2 H, m, 5′-H_2).

(*b*) A solution of 2,2′-anhydro-3′-*O*-mesylarabinofuranosyluracil (22) (30 mg, 0.07 mmol) in 0.5 mol dm^{-3} NaOH (0.3 ml, 0.15 mmol) was stirred at room temperature for 30 min and then worked up as described under (*a*). The product was isolated in 81% yield (19.7 mg), identical (mixed m.p., i.r., and n.m.r. spectra) with that obtained under (a).

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