A new construct for the *anti* conformational locking of nucleosides: the dioxomethine transglycosidic tether†

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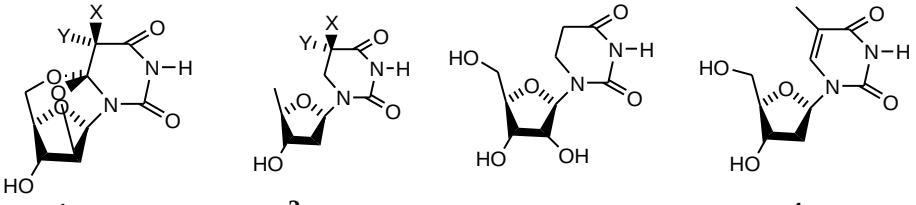
Abstract
Two members of a new class of *anti* conformationally locked 2'-deoxynucleoside mimics were synthesized starting from uridine through key 1-(β-D-arabinofuranosyl)uracil-6-carboxaldehyde intermediates. O5'-Mesylation of 1-(β-D-arabinofuranosyl)uracil-6-carboxaldehyde (5c) followed by pyridine-mediated transglycosidic displacement by the dominant 7,O2'-cyclic hemiacetal gave the locked 2',5'-dideoxyuridine mimic (7). Transglycosidic transacetalation in the 7,O2'-cyclic hemiacetal of 1-(5-deoxy-5,5-dimethoxy-β-D-arabinofuranosyl)uracil-6-carboxaldehyde (18) gave the locked O5'-methyl-2'-deoxyuridine mimic (6b). These transglycosidic dioxomethine tether constructions involve proximity-assisted displacement reactions and provide an entry into new, highly biomimetic, *anti* conformationally locked 2'-deoxynucleoside mimics for use as probes of conformation-activity relationships.

Keywords: Transglycosidic displacement, dioxomethine tether, 2'-deoxynucleoside mimics

Introduction

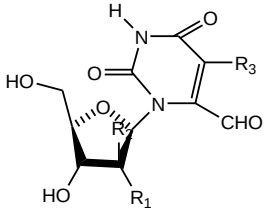
Conformational restriction is a very useful tool for studying the relationship between molecular topography and biochemical or medicinal activity of nucleosides.[1] Transglycosidically tethered analogs are particularly useful when the focus of attention is the glycosidic bond, but in most cases the rotation of this bond is incompletely restricted—some residual rotational flexibility remains. The C6-spiro-fused 5,6-dihydrouridines 1 (X, Y = F, Cl, Br, NO_2) reported by Honjo are a rare exception.[2] They are 5,6-dihydrouridine arabinofuranosides in which both the 2' and 5' hydroxyl group oxygens have been attached to the pyrimidine C6 position. They are, in essence, completely rigidified mimics of the corresponding 2',5'-dideoxy-5,6-dihydrouridines (2). The cage-like carbohydrate moiety in 1 is related in a near-enantiomeric sense to 1,2,5-*O*-benzylidyne-β-L-arabinofuranose orthoesters reported by Kochetkov[3] and to 1,2,5-*O*-ethylidyne-α-D-galactofuranose orthoesters reported by Bertolini and Glaudemans.[4]
The structural differences between 1 and its closest natural counterparts in RNA and DNA (dihydrouridine 3 and thymidine 4, respectively) limit their utility as probes of conformation/activity relationships.[5] Nevertheless, the idea of transforming arabinofuranosides

into conformationally locked 2'-deoxyribonucleoside mimics by constructing a tether over the βface of the furanose ring has merit and would be particularly valuable if a high degree of biomimicry could be maintained by minimizing structural disturbances.

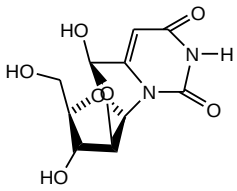


1 **2** **3** **4**

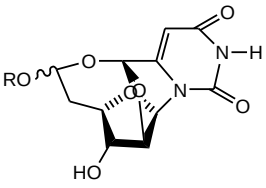
Some of the findings from our previous investigations[6] into the chemistry of 6-formyluridine, 6-formyl-2'-deoxyuridine, 6-formyl-1-(β-D-arabinofuranosyl)uracil, and 6-formylthymidine (5a-d, respectively) convinced us that this could be accomplished. The structures displayed by these compounds are dictated by their highly electrophilic carboxaldehyde group. While the ribonucleosides 5a,b and d exist as a solvent-sensitive collection of open (hydroxy-aldehyde) and 7,O5'-cyclic hemiacetal solution structures, the arabinofuranoside 5c exists exclusively as the 7,O2'-cyclic hemiacetal in all solvents examined. When taken together with the fact that 5'-carboxaldehyde nucleoside derivatives are known to be susceptible to hydrate and hemiacetal formation,[7] this raised the intriguing possibility that the 5'-carboxaldehyde derivative of 5c might exist at least partly in transglycosidically tethered form (6a). This form would be a highly biomimetic, *anti* conformationally locked and yet fully *O*-functionalizable 2'-deoxyribonucleoside mimic. As the nucleoside or even the nucleotide (*i.e.*, 6, R = PO_3H_2), it would be a valuable bioprobe of conformation-activity relationships by virtue of an exceptionally close structural resemblance to naturally occurring counterparts. The anticipation of access not only to separate C5' epimeric versions but also to purine-based versions (from 8-formyl purine nucleosides[8]) only enhanced our interest in this attractive design construct, and so we began working on the construction of dioxomethine-tethered nucleosides.



5a, R_1 = OH, R_2 = R_3 = H
b, R_1 = R_2 = R_3 = H
c, R_1 = R_3 = H, R_2 = OH
d, R_1 = R_2 = H, R_3 = Me



5c: 7,O2'-cyclic hemiacetal form

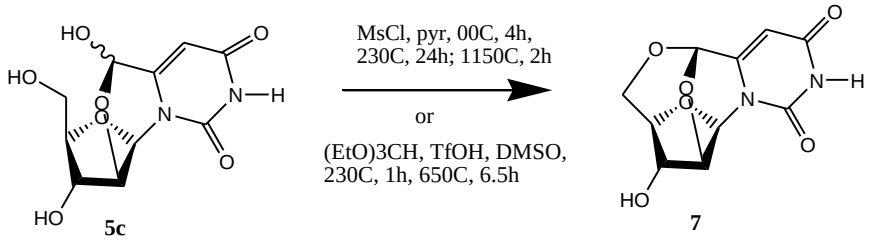


6a, R = H
b, R = Me

Results and Discussion

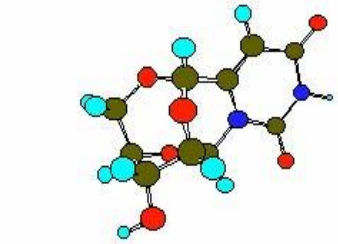
We searched for conditions that would assemble the desired dioxomethine tether, and first examined the ease of intramolecular dehydration in 5c to give a cyclic acetal. Even when heated at 65 °C, 5c was inert to exposure to TsOH or TfOH in $(CH_3)_2SO$ solution. The fact that the expected dioxomethine-tethered 2',5'-dideoxyuridine mimic 7 did not form under these conditions reflects the known difficulty of acetal formation in electron-deficient carbonyl

groups,[9] seen before for 5.[6b,c] Conversion of the 5'- or hemiacetal hydroxyl group in 5c to a good leaving group for intramolecular displacement was explored next. Treatment of 5c with an equivalent of MsCl in pyridine at increasingly elevated temperatures eventually produced 7, which was isolated in a 43% yield. Under different conditions, exposure of 5c to $(EtO)_3CH$ in the presence of TfOH gave 7 in a 57% yield.



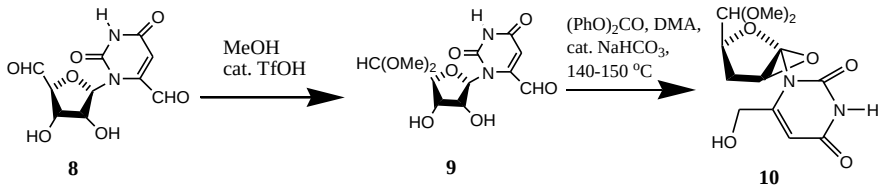
5c **7**

The dioxomethine-tethered 7 featuring a five-, a six-, a seven, and an eight-membered carbohydrate-associated ring was characterized by ^1H, ^{13}C, COSY, and short-range ^1H-^{13}C HETCOR NMR, and both low- and high-resolution FAB mass spectral analyses. The ^1H NMR spectrum was especially diagnostic. Both the large (14.2 Hz) geminal coupling of the diastereotopic 5'-CH_2 hydrogens and the moderate (6.6 Hz) vicinal one between H1' and H2' are consistent with the severe conformational restriction caused by the tether. A similar coupling constant pattern was found in the ^1H NMR spectrum of 2',3'-*O*-(isopropylidene)orotidine 5'-lactone, a reference compound we prepared from 2',3'-*O*-isopropylidenated 5a. In addition, only one of the H5' resonances (the downfield *pro-R*) is coupled (5.2 Hz) to the H4' one in 7. This same pattern is displayed not only by 2',3'-*O*-(isopropylidene)orotidine 5'-lactone, but also by certain 6,O5'-methanouridines reported by others.[1k] By an MM calculation (Figure 1), 7 has a χvalue (O4'-C1'-N1-C2 dihedral) of 276º, placing the glycosidic torsion in the "high" *anti* range.



Molecular mechanics energy miminized structure of 7.

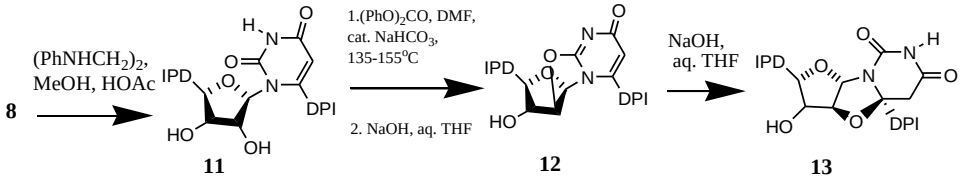
The task of preparing a nucleoside like 7 but with an additional oxygen functionality at C5' was addressed next. Deprotection of 2',3'-*O*-isopropylidene-6-formyluridine 5'-carboxaldehyde[13] gave dialdehyde 8 (Scheme 1), but we were unable to generate its 2,2'-anhydride with $(PhO)_2CO$, and thus could not access the arabinofuranoside. As shown in Scheme 1, only the 5'-carboxaldehyde of 8 could be acetalated under standard conditions (60%), and unfortunately a dehydration with $(PhO)_2CO$ intended to give the 2,2'-anhydride gave instead a complex mixture from which the epoxy acetal 10 was isolated as the major product.[10] The multistep pathway from 9 to 10 apparently involves a hydride transfer from C1' to the carboxaldehyde at some point.



8 **9** **10**

Scheme 1

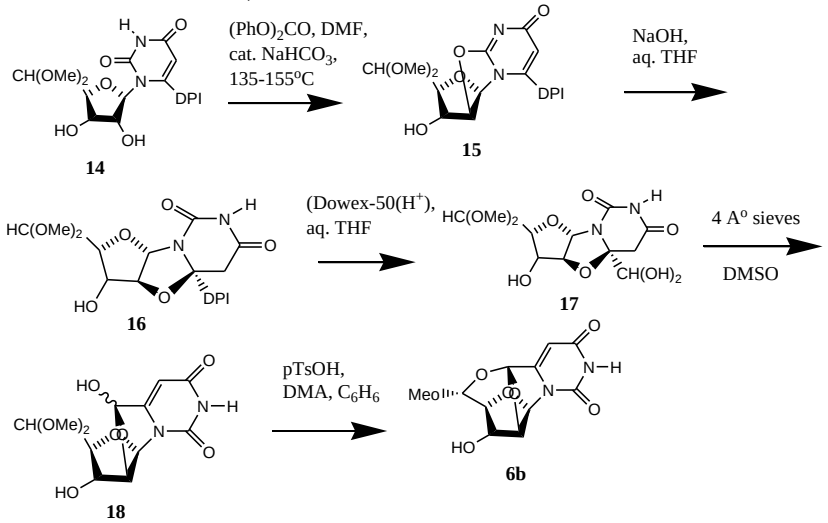
As shown in Scheme 2, the simultaneous masking of both carboxaldehyde groups in 8 as 1,3-diphenylimidazolidin-2-yls (DPIs) gave 11 (40%), but the reaction was sluggish and actually produced the 6-DPI 5'-dimethyl acetal (14, Scheme 3) to a greater extent (47%).



Scheme 2

Our first attempt to convert 11 to its 2,2'-anhydride employed 1.3 equivalents of $(PhO)_2CO$. This did give some of the desired 12, but the yield was very low (7%) and the O3'-phenoxycarbonylated derivative and a substantial amount of starting material were isolated. In the second attempt, 3.5 equivalents of $(PhO)_2CO$ and a slightly higher temperature were used to give the O3'-phenoxycarbonyl derivative of 12 in a satisfactory yield (66%). Rapid saponification (NaOH, THF, H_2O, 23 °C, 1 h) of this gave the desired 12 (77%). Longer reaction times produced inseparable mixtures of 12 and the 6,O2'-cyclonucleoside 13, a compound generated by proximity-assisted intramolecular conjugate addition reaction in the open arabinofuranoside. Nucleoside 12 was treated with pTsOH in Me_2CO/CH_2Cl_2 in an attempt to remove both DPI groups prior to opening the 2,2'-anhydro linkage, but this failed.

The same 6-DPI 5'-dimethyl acetal 14 obtained previously from 8 was also obtained from 9, but in a better yield (86%). As shown in Scheme 3, 2,2'-anhydro formation in 14 gave 15 (31%) together with its O3'-phenoxycarbonylated derivative (58%). Saponification of either of these gave the same 6,O2'-cyclonucleoside 16. Selective deprotection of 16 gave the hydrate 17 in a quantitative yield. Facile hydration in the corresponding aldehyde can be attributed to its two electronegative α-heteroatoms. In a transformation critically important to the construction of the dioxomethine tether, hydrate 17 afforded hemiacetal 18 (quantitative) simply upon desiccation. Just as had been found for 5c,[6b,c] 18 exists as a 3:1 mixture of 7,O2'-cyclic hemiacetal diastereomers. Acid-catalyzed hydrolysis of the 5'-dimethyl acetal in 18 was sluggish, but eventually proceeded to give not the desired 6a, but its open 7, O2'-cyclic hemiacetal instead (60%, 2:1 mixture of diastereomers).



Scheme 3

Attempts to close this to 6a by heating $(CH_3)_2SO$ containing 4Å molecular sieves, in C_6H_6/DMA containing PPTS, in HMDS containing $(NH_4)_2SO_4$, or in pyridine containing Ac_2O were unsuccessful. Similar attempts to access 6b by heating 18 in $(CH_3)_2SO$ containing TfOH or TsOH also failed, but intramolecular acetal formation in 18 was promoted by the action of TsOH in C_6H_6/DMA, and 6b was isolated in a 25% yield. This dioxomethine-tethered O5'-methylated 2'-deoxynucleoside mimic was characterized by ^1H and ^{13}C NMR and low- and high-resolution mass spectral analyses. Interestingly, it was isolated as a single diastereomer tentatively assigned the 5'-*R* configuration because the ^3J4'-5' value (3.8 Hz) is close to the non-zero (5.2 Hz) ^3J4'-5'-*pro*-*R* one observed in 7. The fate of the absent 5'-*S* diastereomer will be investigated, as will other, milder methods for generating 6a and methods for generating the nucleotide (6, R = PO_3H_2) analogs.

Conclusions

Our synthesis of 7 and 6b demonstrates how a β-facial dioxomethine tether can be constructed onto a natural β-ribonucleoside framework by the careful and deliberate management of proximity-assisted addition and displacement reactions in arabinofuranoside intermediates. The new *anti* conformationally locked nucleosides now accessible are highly biomimetic and should prove to be valuable bioprobes for the study of conformation-activity relationships involving 2'-deoxynucleosides, 2'-deoxynucleotides, and related species.

Experimental Section

General Procedures. Melting points were determined on a Thomas-Hoover UniMelt capillary apparatus and are uncorrected. Radial preparative-layer chromatography was performed on a Chromatotron instrument (Harrison Research, Inc., Palo Alto, CA) using Merck silica gel60 PF_{254} as the adsorbent, flash column chromatography was performed using 230-400 mesh ASTM Merck silica gel-60, and TLC analyses were performed on Analtech 250 μm silica gel GF Uniplates. Lyophilizations were conducted on a Labconco Lypho-Lock 4.5 liter bench-top freeze-dryer. ^1H and ^{13}C NMR spectra were recorded on a Varian VXR-300 (300 and 75 MHz) or VXR-500 (500 and 125 MHz) instrument using (CH3)4Si or 2,2-dimethyl-2-silapentane-5-sulfonic acid, sodium salt (DSS) (δ= 0.0 for ^1H), and $CDCl_3$ (δ = 77.0 for ^{13}C), $(CD_3)2SO$ (δ = 39.5 for ^{13}C), or 1,4-dioxane (δ= 66.5 for ^{13}C in D_2O) as internal reference. Short-range ^1H-^{13}C heteronuclear shift correlation (HETCOR) 2D NMR spectra were obtained on the VXR-300 instrument. Except where noted, the purity of compounds was shown to be >95% by TLC and high-field ^1H NMR. BuLi, iPr2NH, HCO_2Et, $(PhNHCH_2)2$, 2-iodobenzoic acid, $KBrO_3$, TsOH, $NaBH_4$, 2,2'-biquinoline, anhydrous iBuOH, and 1 M TBAF in THF solution were purchased from the Aldrich Chemical Co. TBDMS-Cl and TBDPS-Cl were obtained from Hüls America, Inc. The BuLi was titrated by the modified Watson-Eastham procedure.[11] THF and Et_2O were dried by distillation from Na-benzophenone ketyl under argon. Pyridine and iPr_2NH were dried by distillation from CaH_2 under argon. The HCO_2Et was dried by distillation from P_2O_5 under argon. Dowex-50(H^+) was obtained from the Sigma Chemical Co., and before use was washed with 1N HCl and then rinsed with distilled water until pH neutral. The Dess-Martin periodinane

reagent was prepared according to the literature procedure.[12] Elemental microanalyses and mass spectral analyses were obtained from the University of Illinois. MM calculations were performed using Chem3D Pro v.5.0 from Cambridge Scientific Computing, Inc.

(*7S*)-1-(β-D-Arabinofuranosyl)-6-(dihydroxymethyl)-7,O2':7,O5'-dianhydrouracil (7). **Method A.** A solution of 5c[6b,c] (30.0 mg, 0.110 mmol) in 0.5 mL of anhydrous pyridine was treated with one equivalent of MsCl (0.2 mL) and the solution was stirred at 0 ºC for 4 h, 23 ºC for 24 h, and then was heated at reflux for 2 h. The mixture was evaporated to dryness in vacuo and the residue was separated by ascending preparative chromatography on silica gel (15% MeOH/CH_2Cl_2 as eluent) to give 12.0 mg (43%) of 7: ^{1}H NMR ($(CD_3)_2SO$) δ 11.6 (1H, bs, NH, exchanges with D_2O), 6.34 (1H, d, H1'), 5.92 (1H, s, H7), 5.79 (1H, s, H5), 5.67 (1H, d, 3'-OH, exchanges with D_2O), 4.67 (1H, d, H2'), 4.41 (1H, d, H3'), 4.25 (1H, d, H4'), 4.08 (1H, d of d, H5'-*pro-R*), 3.49 (1H, d, H5'-*pro-S*); ^3J1'-2' = 6.6, ^3J3'-3'-OH = 4.8, ^3J4'-5'-*pro-R* = 5.2, ^3J4'-5'*pro-S* = 0, ^2J5'-*pro-R*-5'-*pro-S* = 14.2 Hz. ^{13}C NMR ($(CD_3)_2SO$) δ 163.0 (C4), 150.8 (C2), 146.4 (C6), 102.1 (C5), 91.3 (C7), 82.9 (C4'), 79.8 (C2'), 77.3 (C3'), 76.2 (C1'), 68.4 (C5'). Low-resolution FAB-mass spectrum, *m/e* 255.0 (MH^+). High-resolution FAB-mass spectrum for $C_{10}H_{11}N_2O_6(MH^+)$: calcd 255.0617, found 255.0618.

Method B. A solution of 5c[6b,c] (15.0 mg, 0.055 mmol) in 0.5 mL of $(CH_3)_2SO$ was treated with 50 µL of TfOH and 0.2 mL (excess) of $(EtO)_3CH$. The reaction mixture was stirred first at 23 ºC for 1 h and then at 65 ºC for 6.5 h, and then it was evaporated to dryness in vacuo. The residue was separated by the same procedure used in Method A to give 8.0 mg (57%) of 7.

2',3'-*O*-Isopropylideneorotidine 5'-lactone. A solution of 2',3'-*O*-isopropylidenated 5a[6c] (312 mg, 1.0 mmol) and DCC (0.8 g, 3.9 mmol) in 10 mL of anhydrous $(CH_3)_2SO$ was treated with anhydrous pyridine (0.1 mL) and TFA (0.05 mL), and the mixture was stirred at 23 ºC for 50 h. Water (1 mL) was added and the mixture was stirred for additional 0.5 h. The dicyclohexylurea precipitate was removed by suction filtration, and the filtrate was evaporated to dryness at 50 ºC in vacuo. Radial chromatography (5% CH_3OH/CH_2Cl_2 as eluent) gave 161 mg (52%) of the lactone as a white solid: mp 270-275 ºC (dec.). ^{1}H NMR ($CDCl_3$) δ 8.32 (1H, bs, NH), 6.08 (1H, s, H5), 5.98 (1H, d, H1'), 5.02 (1H, m, H5'), 4.97 (1H, d of d, H2'), 4.78 (1H, d, H3'), 4.72 (1H, m, H4'), 4.25 (1H, m, H5'), 1.58 (3H, s, CH_3), 1.37 (3H, s, CH_3). ^{1}H NMR ($(CD_3)_2SO$) δ 11.74 (1H, bs, NH), 5.76 (1H, s, H5), 5.73 (1H, d, H1'), 5.11 (1H, d, H5'), 4.68 (1H, t, H3'), 4.63 (1H, t, H2'), 4.55 (d of d, 1H, H4'), 4.17 (1H, t, H5''), 1.45 (3H, s, CH_3), 1.28 (3H, s, CH_3). ^{13}C NMR ($(CD_3)_2SO$) δ 165.5 (C7), 162.8 (C4), 148.7 (C2), 143.1 (C6), 112.0 (C5 or $C(CH_3)_2$), 103.0 (C5 or $C(CH_3)_2$), 95.0, 86.4, 85.4, and 79.7 (each C1', C2', C3', or C4'), 66.2 (C5'), 26.3 and 24.7 ($C(CH_3)_2$). Low-resolution ACE-mass spectrum, *m/e* 310.2 (M^+), 311.2 (MH^+).

6-Formyluridine 5'-carboxaldehyde (8). A solution of 2',3'-*O*-isopropylidene-6-formyluridine 5'-carboxaldehyde[13] (51.4 mg, 0.17 mmol) in 50% aqueous TFA (1 mL) was stirred at 23 ºC for 2 h. The reaction mixture was evaporated to dryness, and residual TFA was removed from the residue by repetitive azeotropic coevaporation with water. Lyophilization afforded NMR-pure 8 in a quantitative yield: 210-220 ºC (dec.). The NMR spectral features of 8 in D_2O solution were consistent with dihydrate structure: ^{1}H NMR (D_2O) δ 6.14 (s, 1H, H5), 5.98 (m, 2H, H1' and H7), 5.12 (d, 1H, H5'), 4.84 (s, H2' under HOD), 4.50 (pseudo-t, 1H, H3'), 3.80 (pseudo-t, 1H, H4'); ^3J1'-2' not well resolved, ^3J2'-3' = 6.2, ^3J3'-4' = 5.9, ^3J4'-5' = 5.7 Hz. ^{13}C NMR (D_2O) δ 165.7 (C4), 156.0 (C2), 151.6 (C6), 100.2 (C5), 92.1 (C1'), 89.9 (C5'), 85.8 (C7), 85.5 (C4'), 71.6 (C2'), 70.3 (C3'). UV λmax, nm (ε× 10^{-3}): (H_2O) 261 (8.9), 204 (9.2); (pH 1) 262 (7.8), 209 (7.2).

Low-resolution CIMS, *m/e* 271.1 (MH^+); High-resolution CIMS calcd for $C_{10}H_{11}N_2O_7$ (MH^+): calcd 271.0566, found 271.0564.

6-Formyluridine 5'-carboxaldehyde, 5'-dimethyl acetal (9). A suspension of 8 (2.00 g, 7.40 mmol) in 20 mL of absolute MeOH containing TfOH (100 µL) was heated at reflux under argon. After 20 min, the mixture became homogeneous and 8 had been consumed, by TLC analysis. The solution was concentrated in vacuo and the residue was purified by radial chromatography (10% MeOH/CH_2Cl_2 as eluent) to give, after Abderhalden (P_2O_5) drying, 1.40 g (60%) of 9 as a yellow foam: ^{1}H NMR (D_2O) δ 6.12 (1H, s, H5), 5.96 (1H, d, H1'), 5.95 (1H, s, hemiacetal CH), 4.81 (1H, m, H2'), 4.62 (1H, d, H5'), 4.54 (1H, pseudo-t, H3'), 3.89 (1H, pseudo-t, H4'), 3.51 and 3.44 (each 3H, each s, each OCH_3); ^3J1'-2' = 3.3, ^3J3'-4' = 6.6, ^3J4'-5' = 6.9 Hz. ^{13}C NMR (D_2O) δ165.7 (C4), 155.9 and 151.4 (C_2/C6), 104.2 (C5'), 100.2 (C5), 92.4 (C7), 85.8 (C1'), 82.2 (C4'), 72.0 (C2'), 70.3 (C3'), 55.3 and 54.2 (two CH_3O).

1-(1-Dehydro-1-hydroxy-5-deoxy-5,5-dimethoxy-1,2-anhydro-α-lD-arabinofuranosyl)-6-hydroxymethyluracil (10). A solution of monoacetal 9 (100.0 mg, 0.316 mmol) and $(PhO)_2CO$ (101.5 mg, 0.474 mmol) in 0.3 mL of anhydrous DMA was treated with $NaHCO_3$ (2.0 mg) and then was heated at 140-150 °C for 15 min. The solution was concentrated in vacuo, and the oily residue treated with 5 mL of anhydrous Et_2O. The resulting solid was collected, rinsed with additional anhydrous Et_2O (3 × 3 mL), and then purified by ascending preparative chromatography (10% MeOH/CH_2Cl_2 as eluent) to give 26.6 mg (27%) of 10: ^{1}H NMR (D_2O) δ 5.74 (1H, s, H5), 5.49 (1H, s, H2'), 4.94 and 4.74 (each 1H, each d, each H7), 4.55 (1H, d, H5'), 3.99 (1H, d, H3'), 3.95 (1H, d of d, H4'), 3.48 and 3.42 (each 3H, each s, each OCH_3); ^3J2'-3' = 0, ^3J3'-4' = 2.8, ^3J4'-5' = 7.3, ^2J7a-7b = 16.8 Hz. ^{1}H NMR ($(CD_3)_2SO$) δ11.5 (1H, bs, NH, exchanges with D_2O), 7.3 (1H, bs, 7-OH, exchanges with D_2O), 5.7 (1H, d, 3'-OH, exchanges with D_2O), 5.53 (1H, s, H5), 5.30 (1H, s, H2'), 4.65 (2H, q, CH2), 4.28 (1H, d, H5'), 4.71 (1H, d of d, H4'), 3.62 (1H, d of d, H3'), 3.26 and 3.22 (each 3H, each s, each OCH_3); ^3J2'-3' = 0, ^3J3'-4' = 2.2, ^3J3'-3'-OH = 6.0, ^3J4'-5' = 7.7 Hz. ^{13}C NMR ($(CD_3)_2SO$)δ 162.0 (C4), 151.0 and 148.0 (C2/C6), 103.1 (C5'), 99.0 (C1'), 96.7 (C5), 82.8 (C4'), 78.2 (C2'), 74.4 (C3'), 57.6 (CH_2), 54.0 and 52.7 (two CH_3O). Low-resolution FAB-mass spectrum, *m/e* 317.1 (MH^+). High-resolution FAB-mass spectrum for $C_{12}H_{17}N_2O_8(MH^+)$: calcd 317.0985, found 317.0986.

5'-Deoxy-5',6-*bis*-(1,3-diphenylimidazolidin-2-yl)uridine (11) and 6-(1,3-diphenylimidazolidin-2-yl) uridine-5'-carbox- aldehyde, dimethyl acetal (14). A solution of crude 8 prepared from 200 mg of its 2',3'-*O*-isopropylidene derivative,[11] $(PhNHCH_2)_2$ (303 mg, 1.42 mmol), and 0.12 mL of glacial AcOH in 10 mL of absolute CH_3OH was stirred for 3 d at 23 °C. The reaction mixture was partitioned between saturated aqueous $NaHCO_3$ and CH_2Cl_2, and the layers were separated and the aqueous phase was extracted with fresh CH2Cl2. The organic solutions were combined, dried ($MgSO_4$), and then rotary evaporated to dryness. Column chromatography (5% CH_3OH/CH_2Cl_2 as eluent) gave 168 mg (40%) of 11 as a pink powder and 155 mg (47%) of the 6-DPI, 5'-dimethyl acetal derivative (14) as a yellowish foam. For 11: ^{1}H NMR ($CDCl_3$) δ 9.6 (1H, bs, NH), 7.35-6.58 (20H, m, four C_6H_5); 5.90 (1H, s, H1'), 5.78 (1H, s, H5), 5.68 (1H, d, H5'), 5.46 (1H, s, H7), 4.64-4.61 (2H, m, H2' and H3'), 3.90 (1H, d of d, H4'), 3.72-3.25 (10H, m, 2'-OH, 3'-OH, and two NCH_2CH_2N); ^3J1'-2' = 0, ^3J3'-4' = 7.2, ^3J4'-5' = 1.9 Hz. ^{13}C NMR ($CDCl_3$) δ 163.0 (C4), 153.4, 150.8, 147.6, 146.4, 146.3, and 145.2 (C2, C6, and four C_6H_5), 129.5, 129.4, 129.1, 128.9, 122.5, 119.6, 118.3, 117.6, 117.4, 114.3, 113.5 and 113.0 (four C_6H_5), 102.7 (C5), 91.7 (C7), 83.3 (C4'), 75.6 (C1'), 73.3 (C5'), 72.1 and 69.7 (C2'/C3'), 50.8, 47.0, 46.8 and 46.1 (two NCH_2CH_2N). Low-resolution CI-mass spectrum, *m/e* 335.2 (80%, B+1), 306.2 (30%, M^+-B-H_2O), 223.1 (100%). Low-resolution EI-mass spectrum, *m/e* 334.1

(15%, B^+), 306.1 (10%, M^+-B-H_2O), 223.1 (100%). Low-resolution FAB-mass spectrum, *m/e* 659.2 (80%, MH^+). 14: ^{1}H NMR ($CDCl_3$) δ 10.2 (1H, bs, NH), 7.28-6.69 (10H, m, two C_6H_5), 5.90 (1H, s, H5), 5.82 (1H, s, H7), 5.62 (1H, d, H1'), 4.75 (1H, d of d, H2'), 4.53-4.49 (2H, m, H3' and H5'), 3.64 (1H, pseudo-t, H4'), 3.61-3.40 (6H, m, NCH_2CH_2N, 2'-OH, and 3'-OH), 3.39 and 3.37 (each 3H, each s, each CH_3O); ^3J1'-2' = 2.4, ^3J2'-3' = 6.3, ^3J4'-5' = 7.2 Hz. ^{13}C NMR ($CDCl_3$) δ 63.2 (C4), 153.4, 151.4, 147.3, 145.7 (C2, C6, and two C_6H_5), 129.5, 129.4, 122.2, 120.3, 118.1 and 115.3 (two C_6H_5), 104.0 (C5'), 102.5 (C5), 92.3 (C7), 82.1 (C4'), 75.9 (C1'), 72.5 and 70.5 (C2'/C3'), 54.7 and 53.4 (two CH_3O), 50.5 and 47.5 (NCH_2CH_2N). Low-resolution CI-mass spectrum, *m/e* 511.3 (25%, MH^+), 479.3 (40%, MH^+-CH_3OH), 447.3 (40%, MH^+-$2CH_3OH$), 223.2 (100%). Low-resolution EI-mass spectrum, *m/e* 510.4 (15%, M^+), 446.3 (30%, M^+-$2CH_3OH$), 223.2 (100%). High-resolution CI-mass spectrum for $C_{26}H_{31}N_4O_7$ (MH^+): calcd 511.2192, found 511.2170.

5'-Deoxy-5',6-bis-(1,3-diphenylimidazolidin-2-yl)-2,2'-anhydrouridine (12). A solution of 11 (110.0 mg, 0.167 mmol) and $(PhO)_2CO$ (46 mg, 0.215 mmol) in 0.3 mL of anhydrous DMF was treated with 1 mg of $NaHCO_3$ and was heated at 110-130 ºC for 0.5 h and then concentrated to dryness in vacuo. The mixture was then separated by ascending preparative chromatography using 5% MeOH/CH_2Cl_2 as eluent to give 12 (8.0 mg, 7%) and its 3'-phenyl carbonate (25.2 mg, 20%). Treatment of 11 (80 mg, 0.121 mmol) with excess $(PhO)_2CO$ (92 mg, 0.429 mmol), additional $NaHCO_3$ (2.0 mg), and at 135-155 ºC in this procedure gave the O3'-phenoxycarbonylated derivative of 12 in a 66% yield. 12: ^{1}H NMR ($CDCl_3$) δ 7.35-6.55 (20H, m, four C6H5), 6.10 (1H, d, H1'), 6.06 (1H, s, H5), 6.03 (1H, s, H7), 5.84 (1H, s, 3'-OH), 5.53 (1H, s, H5'), 4.89 (1H, d of d, H2'), 4.52 (1H, m, H3'), 4.25 (1H, d, H4'), 3.80-3.32 (8H, m, two NCH_2CH_2N); ^3J1'-2' = 5.7, ^3J2'-3' = 2.1 Hz, ^3J3'-4' = 6.6. ^{13}C NMR ($CDCl_3$) δ 172.4 (C4), 160.7 (C2), 148.0, 147.2, 146.5, 145.8, 144.8 (C6 and four C_6H_5), 129.7, 129.6, 129.4, 129.2, 122.5, 118.8, 118.2, 118.1, 117.8, 113.4, 113.3, and 112.8 (two C_6H_5), 108.1 (C5), 89.4 (C2'), 86.7 (C1'), 85.7 (C4'), 74.9 (C3'), 73.8 (C7), 73.5 (C5'), 50.8, 47.0, 46.9 and 45.6 (two NCH_2CH_2N). Low-resolution FAB-mass spectrum, *m/e* 641.3 (70%, MH^+), 223.2 (100%). High-resolution FAB-mass spectrum for $C_{38}H_{37}N_6O_4(MH^+)$: calcd 641.2876, found 641.2887. O3'-Phenoxycarbonylated 12: ^{1}H NMR ($CDCl_3$) δ 7.45-6.62 (25H, m, five C_6H_5), 6.47 (1H, d, H1'), 6.14 (1H, s, H5), 5.96 (1H, s, H7), 5.79 (1H, d, H5'), 5.60 (1H, d, H3'), 5.27 (1H, d, H2'), 4.82 (1H, d of d, H4'), 3.80-3.35 (8H, m, two NCH_2CH_2N); ^3J1'-2' = 5.4, ^3J3'-4' = 2.7, ^3J4'-5' = 1.2 Hz. ^{13}C NMR ($CDCl_3$) δ171.6 (C4), 160.4 (C2), 152.6, 150.5, 147.8, 147.3, 146.2, 145.8, 144.9 (C6, $C_6H_5OCO_2$, and five C_6H_5), 129.8, 129.7, 129.6, 129.5, 129.4, 126.7, 122.5, 120.6, 119.6, 119.3, 118.7, 117.8, 114.8, 113.6 and 113.2 (three C_6H_5), 109.6 (C5), 88.5 (C4'), 88.3 (C1'), 85.8 (C2'), 78.0 (C3'), 74.5 (C7), 73.4 (C5'), 50.7, 49.3, 47.6 and 46.0 (two NCH_2CH_2N). Low-resolution FAB-mass spectrum, *m/e* 761.3 (60%, MH^+).

(*6R*)-6,O2'- Anhydro-1-[5-deoxy-5-(1,3-diphenylimidazolidin-2-yl)-β]-D-arabinofuranosyl]-6-(1,3-diphenylimidazo-lidin-2-yl)-5,6-dihydrouracil (13). Saponification of 60 mg (0.079 mmol) of the O3'-phenoxycarbonylated 12 in a mixture of 0.123 mL of 1 M NaOH, 0.9 mL of H_2O, and 1.4 mL of THF at 23 ºC for 0.5 h gave, after chromatographic separation, 39.1 mg (77%) of 12. Saponification of 12 in THF/MeOH/H_2O at 23 ºC for 2.5 h afforded an inseparable mixture of 12 and the dihydrouracil 13 by ^{1}H NMR analysis. 13: ^{1}H NMR ($CDCl_3$) δ 2.94 and 2.29 (each 1H, each d, H5a and H5b), 2.8 (1H, bs, 3'-OH); ^2J5a-5b = 15.9 Hz).

5'-Deoxy-5',5'-dimethoxy-6-(1,3-diphenylimidazolidin-2-yl)-2,2'-anhydrouridine (15). A solution of 14 (120 mg, 0.235 mmol), $(PhO)_2CO$ (100.7 mg, 0.47 mmol) and $NaHCO_3$ (2.0 mg) in 0.5 mL of DMF was heated at 135-155 ºC for 1 h. The solution was rotary evaporated to

dryness in vacuo, and the residue purified by chromatography to afford 15 (35.8 mg, 31%) and 3'-phenoxycarbonylated 15 (83.7 mg, 58%). 15: ^{1}H NMR ($CDCl_3$) δ 7.32-6.66 (10H, m, two C_6H_5), 6.53 (1H, d, H1'), 6.23 and 6.03 (each 1H, each s, H5 and H7), 6.20 (1H, bs, 3'-OH, exchanges with D_2O), 5.43 (1H, d, H2'), 4.75 (1H, s, H3'), 4.42 and 4.24 (each 1H, each d, H4'/H5'), 3.75-3.45 (4H, m, NCH_2CH_2N), 3.30 (6H, s, two CH_3O); ^3J1'-2' = 6.3, ^3J4'-5' = 3.3 Hz. ^{13}C NMR ($CDCl_3$) δ 173.4 (C4), 161.4 (C2), 148.7, 148.2, and 144.5 (C6 and two C_6H_5), 129.5, 129.4, 122.8, 118.8, 118.1, and 112.4 (two C_6H_5), 107.3 and 103.3 (C5/C5'), 90.1, 88.9, 88.8, 76.5, and 73.1 (C1', C4', C2', C3', and C7), 56.2 and 55.9 (each CH_3O), 51.7 and 45.0 (NCH_2CH_2N). Low-resolution FAB-mass spectrum, *m/e* 493.1 (35%, MH^+). High-resolution FAB-mass spectrum for $C_{26}H_{29}N_4O_6(MH^+)$: calcd 493.2087, found 493.2090.

O3'-Phenoxycarbonylated 15: ^{1}H NMR ($CDCl_3$.) δ 7.42-6.65 (15H, m, three C_6H_5), 6.66 (1H, d, H1'), 6.27 and 6.12 (each 1H, each s, H5 and H7), 5.42 (1H, s, H3'), 5.33 (1H, d, H2'), 4.45 (1H, d, H4'), 4.25 (1H, d, H5'), 3.75-3.35 (8H, m, two NCH_2CH_2N), 3.32 (6H, s, two CH_3O); ^3J1'-2' = 6.0, ^3J4'-5' = 3.0 Hz. ^{13}C NMR ($CDCl_3$) δ 173.2 (C4), 161.1 (C2), 152.4, 150.5, 148.9, 147.8, 144.6 (C6, $C_6H_5OCO_2$, and three C_6H_5), 129.6, 129.5, 129.3, 126.5, 123.0, 120.5, 118.2, 115.4, and 112.5 (three C_6H_5), 107.7 (C5), 102.9 (C5'), 89.9 (C1'), 86.0 (C4'), 85.1 (C3'), 81.4 (C2'), 73.1 (C7), 56.8 and 56.6 (each CH_3O), 52.2 and 44.9 (NCH_2CH_2N). Low-resolution FAB-mass spectrum, *m/e* 613.3 (40%, MH^+). High-resolution FAB-mass spectrum for $C_{33}H_{33}N_4O_8(MH^+)$: calcd 613.2298, found 613.2288.

(*6R*)-6,O2'-Anhydro-1-(5-deoxy-5,5-dimethoxy-β-D-arabinofuranosyl)-6-(1,3-diphenylimidazolidin-2-yl)-5,6-dihy-drouracil (16). Saponification of the O3'-phenoxycarbonylated 15 from above (83.7 mg, 0.136 mmol) in a mixture of 0.2 mL of 1M NaOH and 2.0 mL of 50% aqueous THF at 23 ºC overnight gave, after ascending chromatographic purification (silica gel, 5% MeOH/CH_2Cl_2 as eluent), the dihydrouridine 16 (62.7 mg, 90%). The intermediacy of 15 in this transformation was verified by TLC. A similar saponification of 15 (25.0 mg, 0.136 mmol) for 24 h also gave 16 (23.8 mg, 92%) in a reaction which when halted after only 12 h was found to afford 1-(5-deoxy-5,5-dimethoxy-β-D-arabinofuranosyl)-6-(1,3-diphenylimidazolidin-2-yl)uracil (19%) in addition to 16 (66%).

16: ^{1}H NMR ($CDCl_3$) δ7.5 (1H, bs, NH), 7.25-6.70 (10H, m, two C_6H_5), 5.92 (1H, d, H1'), 5.71 (1H, s, H7), 4.49 (1H, d, H5'), 4.43 (1H, d of d, H2'), 4.29 (1H, d, H3'), 3.85-3.30 (5H, m, H4' and NCH_2CH_2N), 3.47 and 3.46 (each 3H, each s, each CH_3O), 2.97 and 2.43 (each 1H, each d, H5a and H5b), 2.5 (1H, bs, 3'-OH); ^3J5a-5b = 15.9, ^3J1'-2' = 4.2, ^3J3'-4' = 6.6, ^3J4'-5' = 4.5 Hz. ^{13}C NMR ($CDCl_3$) δ 165.7 (C4), 150.1, 147.8 and 146.3 (C2 and two C_6H_5), 129.1, 128.9, 119.8, 119.0 116.3 and 114.1 (two C_6H_5), 104.1 (C5'), 100.2 (C6), 89.2 (C2'), 88.8 (C1'), 84.6 (C4'), 77.7 (C7), 74.4 (C3'), 56.7 and 55.1 (each CH_3O), 49.8 and 48.4 (NCH_2CH_2N), 38.5 (C5). Low-resolution CI-mass spectrum, *m/e* 511.3 (30%, MH^+), 479.2 (30%, MH^+-MeOH). High-resolution CI-mass spectrum for $C_{26}H_{31}N_4O_7(MH^+)$: calcd 511.2193, found 511.2183.

1-(5-Deoxy-5,5-dimethoxy-β-D-arabinofuranosyl)-6-(1,3-diphenylimidazolidin-2-yl)uracil. ^{1}H NMR ($CDCl_3$) δ 9.0 (1H, br, NH, exchanges with D_2O), 7.32-6.50 (10H, m, two C_6H_5), 6.22 (1H, d, H1'), 6.00 and 5.81 (each 1H, each s, H7/H5), 4.56 (2H, pseudo-t, H5'/H2'), 4.48 (1H, d, H2'), 4.29 (1H, d, H3'), 3.75 (1H, d of d, H4'), 3.58 and 3.27 (each 3H, each m, NCH_2CH_2N), 3.44 and 3.40 (each 3H, each s, each CH_3O), 2.6 and 1.8 (each 1H, each br, 2'-OH/3'-OH, exchanges with D_2O); ^3J5a-5b = 15.9, ^3J1'-2' = 4.2, ^3J3'-4' = 6.6, ^3J4'-5' = 4.5 Hz. ^{13}C NMR ($CDCl_3$) δ162.4 (C4), 150.9, 150.8, 147.8 and 146.0 (C2, C6, and two C_6H_5), 129.3, 129.2, 122.2, 119.3, 117.4 and 112.8 (two C_6H_5), 103.6 and 100.7 (C5/C5'), 82.5, 81.2, 80.8, 76.8 and 76.0 (C7/C1'/C4'/C2'/C3'), 56.6 and 55.4 (each CH_3O), 47.5 and 41.7 (NCH_2CH_2N). Low-

resolution FAB-mass spectrum, *m/e* 511.3 (40%, MH^+), 479.2 (20%, MH^+-MeOH). High-resolution FAB-mass spectrum for $C_{26}H_{31}N_4O_7(MH^+)$: calcd 511.2193, found 511.2199.

(*6R*)-6,O2'-Anhydro-1-(5-deoxy-5,5-dimethoxy-β-D-arabinofuranosyl)-6-(dihydroxymethyl)-5,6-dihydro-uracil (17). When an attempt at hydrolyzing the DPI group in 16 using TsOH in Me_2CO/CH_2Cl_2 gave a chromatographically inseparable mixture, this deprotection was instead effected by stirring a mixture of 16 (32.9 mg, 0.064 mmol) and Dowex50 (500 mg, H^+-form) in 2.0 mL of 67% aqueous THF at 23 °C for 3 d. Upon a removal of the resin and solvents, hydrate 17 was isolated (21.5 mg, quantitative). ^{1}H NMR ($(CD_3)_2SO$) δ 10.3 (1H, bs, NH, exchanges with D_2O), 6.45 (1H, d, hydrate OH, exchanges with D_2O), 6.15 (1H, d, exchanges upon addition of D_2O, hydrate OH), 5.89 (1H, d, H1'), 5.54 (1H, d, exchanges, 3'-OH), 4.75 (1H, pseudo-t, hydrate CH), 4.44 (1H, d, H2'), 4.41 (1H, d, H5'), 4.01 (1H, pseudo-t, H3'), 3.73 (1H, d of d, H4'), 3.32 and 3.27 (each 3H, each s, each CH_3O), 2.87 (1H, d, H5a), 2.54 (1H, d, H5b); ^2J5a-5b = 15.8, ^3J7-7-OH = 4.4 and 5.8, ^3J1'-2' = 4.0, ^3J3'-3'-OH = 5.4, ^3J4'-5' = 7.2 Hz. ^{13}C NMR ($(CD_3)_2SO$) δ 168.7 (C4), 151.1 (C2), 102.9 (C5'), 95.2 (C6), 91.8 (C7), 89.4 (C1'), 87.8 (C2'), 84.8 (C4'), 74.9 (C3'), 54.1 and 52.2 (two CH_3O), 34.2 (C5). Low-resolution FAB-mass spectrum, *m/e* 317.0 (20%, MH^+-H_2O), 309.0 (100%, MH^+-$2H_2O$).

1-(5-Deoxy-5,5-dimethoxy-β-D-arabinofuranosyl)uracil-6-carboxaldehyde 7,O2'-cyclichemiacetal (18). Compou-nd 17 in $(CD_3)_2SO$ solution was observed by ^{1}H NMR to slowly equilibrate to a quaternary mixture of hydrate 17, its corresponding aldehyde, and the diastereomers of 18. This process was inhibited by the presence of water and promoted by heating or desiccation with 4Å molecular sieves. Aldehyde: ^{1}H NMR ($(CD_3)_2SO$) δ 10.8 (1H, br, NH, exchanges with D_2O), 9.35 (1H, s, CHO), 5.99 (1H, d, H1'), 5.71 (1H, d, 3'-OH, exchanges with D_2O), 4.65 (1H, d, H2'), 4.42 (1H, d, H5'), 4.13 (1H, pseudo-t, H3'), 3.79 (1H, pseudo-t, H4'), 3.30 and 3.29 (each 3H, each s, each CH_3O), 3.04 (1H, d, H5a), 2.85 (1H, d, H5b); ^2J5a-5b = 15.6, ^3J1'-2' = 3.8, ^3J3'-3'-OH = 5.5, ^3J4'-5' = 5.2 Hz.

Thus, 18 was obtained (quantitative by ^{1}H NMR) by heating 17 in $(CD_3)_2SO$ solution at 45 °C for 6 h over 4Å molecular sieves. As had been found for 5c,[6b,c] the ^{1}H NMR spectrum of 18 in $(CD_3)_2SO$ solution revealed the presence of a 3:1 mixture of the two 7,O2'-cyclic hemiacetal diastereomers. Major diastereomer: ^{1}H NMR ($(CD_3)_2SO$) δ 11.5 (1H, bs, NH, exchanges with D_2O), 7.63 (1H, d, hemiacetal OH, exchanges with D_2O), 5.77 (1H, d, 3'-OH, exchanges with D_2O), 5.67 (1H, d, hemiacetal CH), 5.63 (1H, d, H1'), 5.62 (1H, s, H5), 4.39 (1H, d, H2'), 4.26 (1H, d, H5'), 4.04 (1H, d, H3'), 3.73 (1H, d, H4'); ^3J7-7-OH = 6.4, ^3J1'-2' = 2.6, ^3J3'-3'-OH = 4.8, ^3J4'-5' = 7.6 Hz. ^{13}C NMR ($(CD_3)_2SO$) δ 162.5 (C4), 150.6 and 148.8 (C2/C6), 102.9 (C5'), 99.5 (C5), 87.1 (C7), 84.2 (C4'), 78.0 (C1'), 75.4 (C3'), 73.8 (C2'), 54.2 and 54.8 (two CH_3O). Minor: ^{1}H NMR ($(CD_3)_2SO$) δ 11.5 (1H, br, NH, exchanges with D_2O), 7.92 (1H, d, hemiacetal OH, exchanges with D_2O), 5.78 (1H, d, 3'-OH, exchanges with D_2O), 5.76 (1H, s, H5), 5.54 (1H, d, H1'), 5.46 (1H, d, hemiacetal CH), 4.32 (1H, d, H2'), 4.23 (1H, d, H5'), 4.04 (1H, d, H3'), 3.72 (1H, d, H4'); ^3J7-7-OH = 7.7, ^3J1'-2' = 2.4, ^3J3'-3'-OH = 4.9, ^3J4'-5' = 8.0 Hz. ^{13}C NMR ($(CD_3)_2SO$) δ162.4 (C4), 151.0 and 150.8 (C2/C6), 102.9 (C5'), 98.1 (C5), 89.3 (C7), 84.3 (C4'), 78.6 (C1'), 77.7 (C2'), 75.4 (C3'), 54.0 and 52.5 (two CH_3O). Low-resolution CI-mass spectrum, *m/e* 317.1 (50%, MH^+), 309.0 (100%, MH^+-CH_3OH). High-resolution CI-mass spectrum for $C_{12}H_{17}N_2O_8(MH^+)$: calcd 317.0985, found 317.0987.

Deprotection of 18. Hydrolysis of the 5'-(dimethyl) acetal in 18 (18.3 mg, 0.058 mmol) with 50% aqueous TFA (0.5 mL) was sluggish (23 °C, 4 d), but proceeded. The residue obtained upon rotary evaporation to dryness in vacuo was separated by ascending preparative chromatography (silica gel, 15% $MeOH/CH_2Cl_2$ as eluent), and the purified compound was dried (Abderhalden,

P_2O_5, 45-50 °C). Lyophilization of an aqueous solution followed by desiccation gave the deprotected material (8.4 mg, 54%) found to exist as a 2:1 mixture of 7,O2'-cyclic hemiacetal diastereomers in $(CD_3)_2SO$ solution, by ^1H NMR. Major diastereomer: ^1H NMR ($(CD_3)_2SO$) δ11.6 (1H, bs, NH), 9.41 (1H, s, 4'-CHO), 7.77 (1H, d, 7-OH), 6.20 (1H, d, 3'-OH), 5.84 (1H, d, H1'), 5.64 (1H, d, H7), 5.63 (1H, s, H5), 4.47 (1H, d, H2'), 4.30 (1H, s, H4'), 4.25 (1H, d, H3'). ^{13}C NMR ($(CD_3)_2SO$) δ201.4 (C5'), 158.1 (C4), 150.7 and 148.1 (C2/C6), 99.9 (C5), 89.2 (C7), 87.1 (C4'), 79.6 (C1'), 76.9 and 71.4 (C2'/C3'); 3J7-7-OH = 6.5 Hz. Minor: ^1H NMR ($(CD_3)_2SO$) δ 11.6 (1H, bs, NH), 9.42 (1H, s, 4'-CHO), 8.00 (1H, d, 7-OH), 6.20 (1H, d, 3'-OH), 5.79 (1H, d, H1'), 5.60 (1H, s, H5), 5.50 (1H, d, H7), 4.37 (1H, d, H2'), 4.26 (1H, s, H4'), 4.24 (1H, d, H3'); 3J7-7-OH = 7.7 Hz. ^{13}C NMR ($(CD_3)_2SO$) δ 201.6 (C5'), 157.7 (C4), 150.6 and 148.3 (C2/C6), 98.3 (C5), 89.1 (C7), 89.0 (C4'), 79.9 (C1'), 77.2 and 75.9 (C2'/C3').

(*5'-R*)-1-(5-Methoxy-β-D-arabinofuranosyl)-6-(dihydroxymethyl)-7,O2':7,O5'-dianhydrouracil (6b). A solution of 18 (20.0 mg) in a mixture of anhydrous DMA (0.2 mL) and anhydrous C6H6 (0.4 mL) was treated with pTsOH monohydrate (0.3 mg). The resultant mixture was heated at reflux for 24 h under argon and then was evaporated to dryness in vacuo. The residue was dissolved in a small amount of methanol and separated by ascending preparative chromatography twice (silica gel, 10% $MeOH/CH_2Cl_2$ as eluent) to give 6b as a gum (4.5 mg, 25%). ^1H NMR ($(CD_3)_2SO$) δ 11.5 (1H, br, NH), 6.37 (1H, d, H1'), 5.83 and 5.77 (each 1H, each s, H5 and H7), 5.71 (1H, d, 3'-OH), 4.93 (1H, d, H5'), 4.67 (1H, d, H2'), 4.38 (1H, d, H3'), 4.21 (1H, d, H4'), 3.23 (3H, s, CH3O); ^3J1'-2' = 6.4, ^3J3'-3'-OH = 4.3, ^3J4'-5' = 3.8 Hz. ^{13}C NMR ($(CD_3)_2SO$) δ 162.4 (C4), 150.8 and 149.1 (C2/C6), 99.4 and 99.2 (C5'/C5), 88.0 (C7), 83.1 (C4'), 79.7 (C1'), 76.7 and 76.4 (C2'/C3'), 55.3 (CH_3O). Low-resolution FAB-mass spectrum, *m/e* 285.1 (40%, MH^+). High-resolution FAB-mass spectrum for $C_{11}H_{13}N_2O_7(MH^+)$: calcd 285.0723, found 285.0722.

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