A Facile Route to Pyrimidine-Based Nucleoside Olefins: Application to the Synthesis of d4T (Stavudine)[1]

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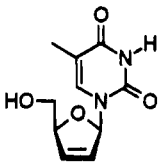
An efficient synthetic route to nucleoside olefins in the uridine, cytidine, and thymidine series is described which utilizes the Garegg–Samuelsson iodine/triphenylphosphine/imidazole-promoted deoxygenation of the 2′,3′-hydroxyl groups as the key step. Cyclopentylidene ketal protection was employed for all the nucleoside 2′,3′-hydroxyls to facilitate blocking of the 5′-hydroxyl and the pyrimidine nitrogens with the benzyl or 4-methoxybenzyl (PMB) groups. Deblocking of the cyclopentylidene group followed by olefination of the resulting diols provided protected nucleoside olefins **18**–**20**. Starting with 5-methyluridine **4** and utilizing the 4-methoxybenzyl group for 5′,N^3 protection, the overall scheme provided the anti-HIV compound d4T (**1**) after deprotection of the PMB groups. The dibenzylhypoxanthine nucleoside diol **17** derived from inosine gave either unreacted starting material or decomposition products under several sets of conditions.

The quest for new compounds which are active in the inhibition of the human immunodeficiency virus (HIV) has fostered a flurry of research in the area of 2′,3′-dideoxynucleoside synthesis.[2] Such compounds have been successful since they target HIV reverse transcriptase and inhibit the biosynthesis of viral DNA by providing no anchorage for the 5′,3′-phosphodiester linkage thus resulting in chain termination.[3] The preparation and utilization of nucleoside olefins have been significant in the development of synthetic routes to dideoxynucleosides and unsaturated HIV-active compounds such as d4T (**1**).[4] In the ribonucleoside series



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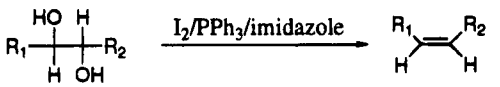
several methods will effect the deoxygenation of the 2′,3′ vicinal diol function to the corresponding olefin.[5] In general these require derivatization of the vicinal diol in a separate step prior to the actual deoxygenation reaction. The cited methods include the Corey–Winter reaction,[6a] bromoacetylation–debromoacetylation,[6b] elimination of 2-methoxy-1,3-dioxolane derivatives,[6c] the Barton reduction of bis-*O*,*O*′-dithiocarbonates,[6d] and the Hanessian elimination of 1-(dimethylamino)methylene acetals.[6e] In comparison, the Garegg–Samuelsson[7] procedure (eq 1) will accomplish the conversion directly in



(1)

one step under mild conditions with the desired product being easily separated from the unwanted organic and inorganic byproducts. Furthermore, the procedure is not restricted to deoxygenation of *cis*-1,2-cyclic diols and has been reported to deoxygenate a variety of *trans*-1,2 diols in the carbohydrate series.[8] We have developed a mild and efficient scheme to uracil-, thymine-, and cytosine-based nucleoside olefins which demonstrates the application of the iodine/triphenylphosphine/imidazole-promoted conversion of vicinal *cis*-diols in the ribonucleoside series to the corresponding olefins. In exploring the scope and limitations of the deoxygenation reaction we evaluated nucleoside diols which might have utility as intermediates to biologically active compounds as well as those

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(8) See, for example: Garegg, P. J.; Johansson, R.; Samuelsson, B. *J. Carbohyd. Chem.* **1984**, *3*, 189–195. Schulte, G.; Meyer, W.; Starkloff, A.; Dyong, I. *Chem. Ber.* **1981**, *114*, 1809–1821. Garegg, P. J.; Johansson, R.; Ortega, C.; Samuelsson, B. *J. Chem. Soc., Perkins Trans. 1* **1982**, 681–683. Nagel, A. A.; Vincent, L. A. *J. Org. Chem.* **1982**, *47*, 4796–4799. Chen, S. Y.; Joullié, M. M. *J. Org. Chem.* **1984**, *49*, 1769–1772. Valverde, S.; Bernabé, M.; Garcia-Ochoa, S.; Gomez, A. M. *J. Org. Chem.* **1990**, *55*, 2294–2298. Pakulski, Z.; Zamojski, A. *Carbohydr. Res.* **1990**, *205*, 410–414. Garegg, P. J. *Pure Appl. Chem.* **1984**, *56*, 845–858. Baer, H. H. *Pure Appl. Chem.* **1989**, *61*, 1217–1234.

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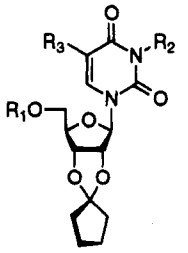
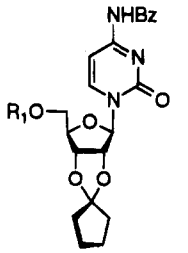
which would demonstrate generality in the pyrimidine series. To this end diols **14**–**17** were selected as substrates, and the details of their preparation and deoxygenation are discussed herein.

Results and Discussion

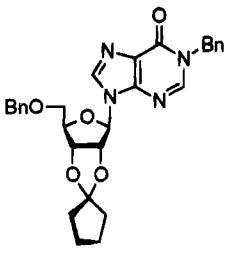
The preparation of diol substrates **14**–**17** required the development of a general protection/deprotection sequence in order to avoid anhydronucleoside formation during the olefination reaction. The sequence involved protection of the 2′,3′ hydroxyls by ketalization followed by protection of both the 5′ hydroxyl and the nitrogens of the heterocycle bearing acidic hydrogens. Deprotection of the ketal will then release the 2′,3′ diol for the olefination reaction. While the cyclohexylidene and isopropylidene groups have been used to protect the 1,2-diol function of ribonucleosides[9] we elected to evaluate the utility of the cyclopentylidene group for this application.[10] Treatment of commercially available uridine **2**, N^4-benzoylcytidine **3**, or inosine **5** with 1,1-dimethoxycyclopentane/*p*-toluenesulfonic acid under several sets of conditions provided the crystalline cyclopentylidene ketals **6**, **7**, and **9**, respectively, in good to excellent yields (Table 1). 5-Methyluridine **4**,[11] which served as the starting material for the preparation of d4T, responded well to the ketalization reaction thus providing the cyclopentylidene derivative **8** in 95% yield (Table 1). Protection of cyclopentylidene uridine **6** as the N^3,5′-*O*-dibenzyl derivative **10** was accomplished in 93% yield by treatment with sodium hydride/benzyl bromide in 1,2-dimethoxyethane (DME). Under similar conditions dibenzylation of cyclopentylidene inosine **9** gave the N^1,5′-*O*-dibenzyl derivative **13** (89%). In order to facilitate mild removal, the 4-methoxybenzyl (PMB)[12] group was selected to protect the N^3,5′-*O*-positions of cyclopentylidene-5-methyluridine and the 5′-hydroxyl of N^4-benzoylcytidine. N^4-Benzoyl-5′-*O*-PMB-cyclopentylidene cytidine **11** and its 5′-*O*-benzyl analog **11a** were prepared by deprotonation of **7** with sodium hydride in 1,2-dimethoxyethane followed by alkylation with freshly prepared 4-methoxybenzyl bromide (88%) and benzyl bromide (89%), respectively. Similarly, thymidine precursor **8** was treated with sodium hydride/DME followed by addition of 4-methoxybenzyl bromide (2 equiv) which provided the 5′-*O*,N^3-diPMB-cyclopentylidene derivative **12** (75%). Several sets of conditions were explored for the mild cleavage of the cyclopentylidene group from the benzylated nucleosides **10**–**13**. Removal of the cyclopentylidene group from the dibenzyluridine derivative **10** was facilitated by treatment with 30% aqueous trifluoroacetic acid (TFA), thereby providing the dibenzyl diol **14** in 85% yield after column chromatography. The cleavage of the dibenzyl cyclopentylidine inosine derivative **13** to the corresponding diol **17** was also effected (98%) by treatment with 30% aqueous TFA at 0 °C. The hydrolysis of the cytidine and 5-methyluridine-derived cyclopentylidene compounds **11** and **12** to **15** and **16**, respectively, required aqueous dichloroacetic acid (66%/0 °C).[13] Exposure of **12** to aqueous TFA, under the same conditions as **10**, resulted in clean removal of the 5′-O-PMB group. Furthermore, the cyclopentylidene group of **12** was very slowly hydrolyzed after treatment with aqueous acetic acid after 7 days at room temperature. During the initial examination of the cyclopentylidene hydrolysis, diacetate derivatives of diols **14**–**17** were prepared[14] in order to ascertain



10 R_1=R_2=Bn; R_3=H
12 R_1=R_2=PMB; R_3=CH_3



11 R_1=PMB
11a R_1=Bn



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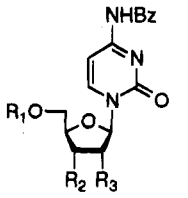
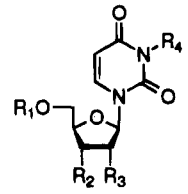


21 R_1=PMB; R_2=OH; R_3=I-β
21a R_1=Bn; R_2=OH; R_3=I-β
22 R_1=TBDMS; R_2=R_3=OH



23 R_1=R_4=Bn; R_2=R_3=H
24 R_1=R_2=R_3=R_4=H

the extent of hydrolysis as well as confirm structure by ^{1}H NMR spectroscopy. Treatment of diols **14** and **16** with iodine/triphenylphosphine/imidazole in toluene/acetonitrile (2:1,**14**; 1:2,**16**) provided the corresponding olefins **18** and **20** in 87% and 82% yield, respectively, after purification by silica gel column chromatography (Table 2). Given the structural similarity of diols **14** and **16**,

(9) Greene, T. W.; Wuts, P. G. M. *Protecting Groups in Organic Synthesis*; John Wiley & Sons: New York, 1991.

(10) Soll, R. M.; Seitz, S. P. *Tetrahedron Lett.* **1987**, *28*, 5457–5461. Reese, C. B.; Ward, J. G. *Tetrahedron Lett.* **1987**, *28*, 2309–2312. In separate experiments comparing the hydrolysis rate of 2′,3′-*O*-cyclopentylideneuridine, isopropylideneuridine and cyclohexylideneuridine in 70% aqueous trifluoroacetic acid at 0 °C, we find the relative ease of hydrolysis follows the order cyclopentylidene > isopropylidene > cyclohexylidene.

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(12) Takaku, H.; Kamaike, K.; Tsuchiya, J. *J. Org. Chem.* **1984**, *49*, 51–56. Marco, J. L.; Hueso-Rodriquez, J. A. *Tetrahedron Lett.* **1988**, *29*, 2459–2463.

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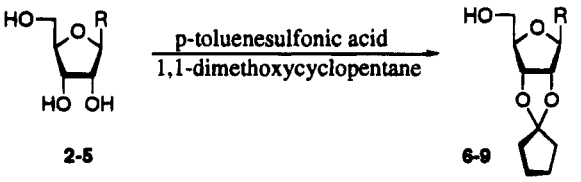
(14) 2′,3′-Diacetates of **14**–**17** were prepared by treatment of the diols with acetic anhydride (100 equiv) and pyridine (200 equiv) at room temperature (16 h) followed by removal of the volatile reaction components under high vacuum and silica gel chromatography of the syrupy residue. The spectral details are included in the supplementary material.

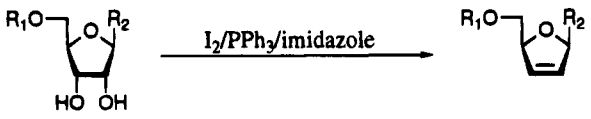
Table 1. Formation of Cyclopentylidene Ketals



2-5 6-9

entry	substrate	R	condns/solvent	product/ yield (%)
1	**2**	uracil	25 m (90 °C)/DMF	**6**/70
2	**3**	N^4-Benzoyl-cytosine	20 m (65 °C)/1,2-DCE	**7**/88
3	**4**	5-methyluracil	60 m (70 °C)/1,2-DCE	**8**/95
4	**5**	hypoxanthine	60 m (90 °C)/DMF	**9**/87

Table 2. Deoxygenation of 2′,3′-Hydroxyl Groups



14-17 18-20

entry	substrate	R_1	R_2	product	yield (%)
1	**14**	Bn	N^3-benzyluracil	**18**	87
2	**15**	PMB	N^4-benzoylcytosine	**19**	71
3	**15a**	Bn	N^4-benzoylcytosine	**19a**	24
4	**16**	PMB	N^3-(*p*-methoxybenzyl)-5-methyluracil	**20**	82
5	**17**	Bn	N^1-benzylhypoxanthine		0

an optimal rate of conversion of **16** to **20** was gained by reversing the solvent ratio, thus increasing the polarity of the reaction solvent mixture. Treatment of the 5′-*O*-PMB cytidine-based diol **15** or its 5′-*O*-benzyl-derived analog **15a** under the same conditions as the conversion of **16** to **20** gave the iodo alcohols **21** and **21a** in addition to the expected olefins **19** and **19a**. The yield of olefin **19** was increased at the expense of **21** to 71% by using the more polar solvent ratio and adding a second portion of iodination reagent. The dibenzylated inosine derivative **17** did not respond to olefination over a range of conditions. Increasing the amount of iodination reagent from that required for the conversion of **14** or **16** to that required for **19** over a temperature range of 70-90 °C resulted in recovery of **17**. As expected, higher temperature ranges of 90-100 °C together with the increased amounts of reagents led only to decomposition of starting material. Using tributylphosphine, triphenyl phosphite, or triethyl phosphite in place of triphenylphosphine over a range of conditions led to recovery of unreacted starting material. In light of previous studies by Manchand[15] and co-workers our attempts to olefinate N^4-benzoyl-5′-*O*-(*tert*-butyldimethylsilyl)cytidine (**22**), the preparation of which avoided the cyclopentylidene ketal intermediate **7** by virtue of selective 5′-O-silylation, were not successful under standard conditions. In the uridine series treatment of dibenzylated olefin **18** with hydrogen gas at atmospheric pressure with platinum or palladium under a range of conditions failed to simultaneously reduce the double bond and remove the benzyl groups. Only 5′-*O*,N^3-dibenzyldideoxyuridine **23** was obtained (96%) when **18** was hydrogenated over platinum on carbon (8 h/760 mm/tetrahydrofuran). The structure of **23** was confirmed after comparison of spectral data with a sample prepared by dibenzylation of commercially available ddU (**24**) (NaH/DME/benzyl bromide). Failure of mild catalytic hydrogenation to cleave the benzyl groups of **18** was the deciding factor in the choice of the PMB blocking group for the d4T synthesis. Cleavage of both the PMB groups of **20** with ceric ammonium nitrate (3 h, rt, CH_3CN/H_2O) provided crystalline d4T (**1**) in 68% yield.

While uridine and cytidine have served as starting points for several syntheses of the corresponding dideoxy derivatives[16] and thymidine-derived olefins in the 2′-deoxy series have been available through β-elimination-type reactions,[17] we find the above scheme a servicable alternative to existing methods. The smooth response of the pyrimidine-derived 1,2-diol function to the Garegg–Samuelsson deoxygenation together with the viability of the cyclopentylidene protecting group combine to provide an effective synthetic route. The failure of the inosine-derived diol **17** to respond to the olefination as well as the requirement for a high excess of reagent for the conversion of cytidine diol **15** indicates that the nitrogen heterocycle function may inhibit the reaction. Studies of the manner in which the heterocyclic base affects the olefination are in progress and will be the topic of a future communication.

Experimental Section

General. NMR spectra were recorded with Varian XL-300 and Bruker AMX-500 instruments using $CDCl_3$, DMSO, and pyridine as solvent and internal standard. Infrared spectra were recorded with a Mattson Galaxy Series 5000 FT instrument. Melting points (uncorrected) were obtained using a Thomas Hoover apparatus. 1,2-Dimethoxyethane was distilled from sodium metal immediately prior to use as a reaction solvent. Tetrahydrofuran was distilled from sodium/benzophenone. All other reaction solvents were used as commercially supplied. Chromatography solvents were ACS reagent grade and were used as commercially supplied. Thin layer chromatography (TLC) analyses utilized glass-backed silica gel plates (E. Merck, 5715) and were visualized with sulfuric acid/ethanol stain, anisaldehyde stain, and UV lamp. Standard gravity column chromatographic separations employed Kieselgel 60 (E. Merck, 7734, 70–230 mesh). Standard flash column chromatographic separations employed Kieselgel 60 (E. Merck, 9835). Celite filtrations were done with Johns-Manville Celite 521. Filtrates and chromatographic fractions were concentrated under vacuum at room temperature using a standard rotary evaporator. Mass spectral analyses were done by the Midwest Center for Mass Spectrometry, Lincoln, NE. Combustion analyses were performed by Galbraith Laboratories, Knoxville, TN.

1-(2′-*O*,3′-*O*-Cyclopentyl-5′-hydroxy-β-D-*erythro*-pentofuranosyl)uracil (6). A mixture of **2** (5.0 g, 20.48 mmol), 1,1-dimethoxycyclopentane (7.15 g, 59 mmol), and *p*-toluenesulfonic acid monohydrate (100 mg, 0.52 mmol) in DMF (50 mL) was heated (90 °C, oil bath) for 25 min. The reaction mixture was added to water (100 mL) and extracted with dichloromethane (5 × 10 mL). The combined dichloromethane extracts were then washed with brine (100 mL) followed by drying over

(15) See ref 5a.

(16) (a) Huang, H.; Chu, C. K. *Synthetic Comm.* **1990**, *20*, 1039–1046. (b) Marumoto, R.; Honjo, M. *Chem. Pharm. Bull.* **1974**, *50*, 2197–2198. (c) Ozaki, S.; Katakami, T.; Saneyoshi, M. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2197–2198. (d) Robins, M. J.; Wilson, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 932–933. (e) Wu, J. C.; Patak, T.; Vial, J. M.; Remaud, G.; Chattopadhyaya, J. *Tetrahedron* **1988**, *44*, 6705–6722. (f) Wu, J. C.; Chattopadhyaya, J. *Tetrahedron* **1989**, *45*, 4507–4522. (g) Tong, W.; Wu, J. C.; Sandstrom, A.; Chattopadhyaya, J. *Tetrahedron* **1990**, *46*, 3037–3060.

(17) (a) Horwitz, J. P.; Chua, J.; Da Rooge, M. A.; Noel, M.; Klundt, I. *J. Org. Chem.* **1966**, *31*, 205–211. (b) Prisbe, E. J.; Martin, J. C. *Synth. Commun.* **1985**, *15*, 401–409. (c) Chattopadhyaya, J.; Wu, J. C. *Tetrahedron* **1989**, *45*, 855–862. (d) Wilson, D.; Liotta, D. *Tetrahedron Lett.* **1990**, *31*, 1815–1818.

anhydrous sodium sulfate. Removal of the drying agent by filtration followed by concentration of the filtrate afforded a crude yellow syrup which was purified by gravity column silica gel chromatography ($CHCl_3$/MeOH, 9:1) to give a white solid. Recrystallization from diethyl ether gave **6** (4.43 g, 70%) as white needles (mp 167–169 °C): TLC R_f = 0.46 ($CHCl_3$/MeOH, 9:1); IR 1654 (C=O), 1702 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.54 (1H, d, 3.1 Hz), 4.97 (1H, dd, 3.1, 3.2 Hz), 4.86 (1H, dd, 3.2, 3.3 Hz), 4.27 (1 H dd, 3.3 Hz), 3.77–3.91 (2H, *gem*, m); ^{13}C NMR (CDCl3, 125 MHz) δ 23.1, 36.5, 62.6, 80.3, 83.3, 86.4, 95.7, 102.6, 1423.8, 143.0, 150.3, 163.1. Anal. Calcd for $C_{14}H_{18}N_2O_6$: C, 54.19; H, 5.85; N, 9.03. Found: C, 54.08; H, 5.86; N, 9.02.

1-(2′-*O*,3′-*O*-Cyclopentyl-5′-hydroxy-β-D-*erythro*-pentofuranosyl)-N^4-benzoylcytosine (7). A mixture of **3** (1.50 g, 4.32 mmol), 1,1-dimethoxycylopentane (1.41 g, 10.8 mmol), and *p*-toluenesulfonic acid monohydrate (164 mg, 0.86 mmol) in 1,2-dichloroethane (6 mL) was heated (70 °C, oil bath) for 30 min. The reaction mixture was concentrated *in vacuo*, and the residual oil was chromatographed ($CHCl_3$/MeOH, 40:1). The ketalized nucleoside **7** (1.51 g, 88%) was isolated as a white solid: mp 132–133 °C; TLC R_f = 0.51 ($CHCl_3$/MeOH, 9:1); IR 1659 (C=O), 1693 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.58 (1H, d, 2.5 Hz), 5.10 (1H, dd, 2.5, 6.4 Hz), 4.93 (1H, dd, 6.4, 3.1 Hz), 4.38 (1H, dd, 3.1, 8.8 Hz), 3.82–3.93 (2H, *gem*, m, 8.8 Hz); ^{13}C NMR (CDCl3, 125 MHz) δ 23.5, 36.4, 62.7, 80.6, 83.8, 87.9, 98.0, 123.4, 127.7, 129.0, 133.3, 147.8, 163.0.

1-(2′-*O*,3′-*O*-Cyclopentyl-5-hydroxy-β-D-*erythro*-pentofuranosyl)-5-*methyluracil* (8). A mixture of **4** (450 mg, 1.74 mmol), 1,1-dimethoxycyclopentane (568 mg, 4.36 mmol), and *p*-toluenesulfonic acid monohydrate (33.2 mg, 0.17 mmol) in 1,2-dichloroethane (9 mL) was heated (65 °C, oil bath) for 80 min. The reaction mixture was treated with triethylamine (882 mg, 8.72 mmol) and directly gravity column chromatographed ($CHCl_3$/MeOH, 9:1). Impure target material fractions were collected and concentrated *in vacuo* to give a yellow oil which was purified by gravity column silica gel chromatography ($CHCl_3$/MeOH, 20:1). The ketalized nucleoside **8** (539 mg, 95%) was isolated as a white solid: mp 82–85 °C; TLC R_f = 0.51 ($CHCl_3$/MeOH, 9:1); IR 1707 (C=O), 1692 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.45 (1H, d, 3.4 Hz), 5.02 (1H, dd, 3.4, 6.6 Hz), 4.89 (1H, dd, 6.6, 3.1 Hz), 4.26 (1H, ddd, 3.1, 3.1, 2.7 Hz), 3.79–3.91 (2H, *gem*, 3.1, 2.7 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 23.5, 36.5, 62.7, 80.4, 83.3, 86.4, 96.0, 111.2, 123.8, 139.1, 150.5, 163.3.

1-(2′-*O*,3′-*O*-Cyclopentyl-5′-hydroxy-β-D-*erythro*-pentofuranosyl)inosine (9). A mixture of inosine (1.0 g, 3.73 mmol), 1,1-dimethoxycyclopentane (1.46 g, 11.18 mmol), and *p*-toluenesulfonic acid monohydrate (71 mg, 0.37 mmol) in DMF (6 mL) was heated (75 °C, oil bath) for 3 h. The mixture was concentrated *in vacuo*, and the resulting syrup was chromatographed ($CHCl_3$/MeOH, 9:1) to give **9** (1.09 g, 87%) as a white solid: mp 232 °C, dec; TLC R_f = 0.32 (EtOAc/MeOH/H_2O, 85:10:5); IR 1707 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 500 MHz) δ 6.10 (1H, d, 2.5 Hz), 5.22 (1H, dd, 2.5, 6.3 Hz), 4.86 (1H, dd, 2.3, 6.3 Hz), 4.22 (1H, dd, 2.3, 4.6 Hz), 3.52 (1H, d, 4.6 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.7, 23.0, 36.0, 61.5, 91.4, 83.6, 86.4, 89.3, 122.4, 124.5, 147.8, 156.5.

1-(2′-*O*,3′-*O*-Cyclopentyl-5′-benzyl-β-D-*erythro*-pentofuranosyl)-N^3-benzyluracil (10). Sodium hydride (17.6 mg, 0.64 mmol, from 50% mineral oil dispersion) was added to a stirred solution of **6** (100 mg, 0.32 mmol) in freshly distilled DME (4 mL) at rt. After the bubbling which accompanied the addition of the base ceased, benzyl bromide (86.7 μL, 0.7 mmol) was added by syringe. Stirring was continued with heating (90 °C, oil bath) for 10 h. The mixture was concentrated *in vacuo*, and the residual oil was column chromatographed on silica gel (Tol/EtOAc, 1:1). The pure dibenzylated nucleoside **10** (147.4 mg, 93%) was obtained as a light yellow syrup: TLC R_f = 0.62 (toluene/EtOAc, 1:1); IR 1668 (C=O), 1710 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.98 (1H, d, 2.5 Hz), 5.59 (1H, dd, 2.5, 13.6 Hz), 5.0 (1H, dd, 6.3, 13.6 Hz), 4.70 (1H, ddd, 2.6, 3.6, 6.3 Hz), 3.79 (1H, *gem* d, 2.6 Hz), 3.69 (1H, *gem* d, 3.6 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 23.2, 36.5, 44.1, 70.2, 73.7, 80.9, 85.2, 101.4, 123.5, 125.3, 129.0, 138.7, 150.9, 162.6; HRMS calcd for $C_{28}H_{30}N_2O_6$ *m/z* 490.5548 (M^+), found *m/z* 490.209 07 (M + 1).

1-[2′-*O*,3′-*O*-Cyclopentyl-5′-*O*-(4-methoxybenzyl)-β-D-*erythro*-pentofuranosyl]-N^4-benzoylcytosine (11). Sodium hydride (15.5 mg, 0.57 mmol from 50% mineral oil dispersion) was added to a stirred solution of **7** (150 mg, 0.38 mmol) in DMF (4 mL) at rt. Vigorous bubbling accompanied the addition of the base. After the mixture was stirred at rt (20 min), *p*-methoxybenzyl bromide (62.3 mg, 0.57 mmol) was added by syringe. Stirring was continued with heating (90 °C, oil bath) for 1 h. The reaction mixture was concentrated *in vacuo*, and the remaining syrup was chromatographed (toluene/EtOAc, 4:1) to give the 5′-O-benzylated nucleoside **11** as a white foam (176 mg, 88%): TLC R_f = 0.36 (toluene/EtOAc, 1:1); IR 1665 (C=O), 1705 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.55 (1H, d, 3.0 Hz), 4.95 (1H, dd, 3.0, 6.5 Hz), 4.89 (1H, dd, 6.5, 3.2 Hz), 4.29 (1H, ddd, 3.2, 2.7 Hz, *gem*), 3.78–3.92 (2H, *gem*, 2.7 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 23.1, 23.6, 36.5, 45.5, 55.3, 62.8, 80.3, 83.5, 86.5, 96.8, 98.6, 113.8, 123.7, 128.3, 129.8, 130.6, 132.5, 135.7, 138.6, 150.5, 154.8, 159.2, 177.3.

1-(2′-*O*,3′-*O*-Cyclopentyl-5′-*O*-benzyl-β-D-*erythro*-pentofuranosyl)-N^4-benzoylcytosine (11a). Sodium hydride (7.3 mg, 0.27 mmol from 50% mineral oil dispersion) was added to a stirred solution of **7** (100 mg, 0.24 mmol) in DMF (2 mL) at rt. Vigorous bubbling accompanied the addition of the base. After the mixture was stirred at rt (20 min), benzyl bromide (62 mg, 0.36 mmol) was added by syringe. Stirring was continued with heating (90 °C, oil bath) for 2 h. The reaction mixture was concentrated *in vacuo*, and the remaining oil was chromatographed (toluene/EtOAc, 4:1). The fully protected nucleoside **11a** (108.7 mg, 89%) was isolated as a colorless syrup: TLC R_f = 0.43 (Tol/EtOAc, 1:1); IR 1651 (C=O), 1701 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.46 (1H, d, 3.3 Hz), 4.85 (1H, dd, 3.3, 6.0 Hz), 4.80 (1H, dd, 2.0, 6.0 Hz), 4.20 (1H, dd, 2.0, 4.5, 4.5 Hz), 3.70 (2H, *gem*, 4.5, 4.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 23.4, 36.5, 44.2, 62.5, 77.4, 80.4, 83.9, 86.5, 95.6, 101.9, 123.7, 125.3, 127.7, 128.3, 129.0, 136.3, 140.5, 151.0, 162.7.

1-[2′-*O*,3′-*O*-Cyclopentyl-5′-*O*-(4-methoxybenzyl)-β-D-*erythro*-pentofuranosyl]-N^3-(4-methoxybenzyl)-5-methyluracil (12). Sodium hydride (16.8 mg, 0.62 mmol, 50% mineral oil dispersion) was added to a stirred solution of **8** (100 mg, 0.31 mmol) in freshly distilled DME (4 mL) at rt. Vigorous bubbling accompanied the addition of the base. After the mixture was stirred at rt (20 min), *p*-methoxybenzyl bromide (74.7 mg, 0.68 mmol) was added by syringe, and stirring was continued with heating (65 °C, oil bath) for 18 h. The reaction mixture was treated with saturated aqueous $NaHCO_3$ (15 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The combined extracts were concentrated and chromatographed (toluene/EtOAc, 8:1). The pure dibenzylated nucleoside **12** (131 mg, 75%) was obtained as a yellow syrup: TLC R_f = 0.76 (toluene/EtOAc, 1:1); IR 1705 (C=O), 1670 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.95 (1H, d, 2.8 Hz), 4.67 (1H, dd, 2.8, 6.3 Hz), 4.73 (1H, dd, 6.3, 3.2 Hz), 4.34 (1H, ddd, 3.2 Hz, m), 3.58–3.71 (2H, *gem*, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.0, 23.2, 36.6, 44.8, 55.2, 69.9, 73.3, 80.9, 92.5, 110.0, 113.6, 123.5, 129.1, 130.8, 134.7, 151.3, 159.8, 159.5, 163.5.

1-(2′,3′-*O*-Cyclopentyl-5′-benzyl-β-D-*erythro*-pentofuranosyl)-N^1-benzylinosine (13). Sodium hydride (300 mg, 0.58 mmol, 50% mineral oil dispersion) was added to a stirred solution of **9** (300 mg, 0.58 mmol) in DMF (4 mL) at rt. Vigorous bubbling accompanied the addition of the base, and stirring was continued (1 h). Benzyl bromide (218 mg, 1.28 mmol) was then added by syringe and stirring was continued while heating (90 °C, oil bath) for 16 h. The volatile solvents were removed and the crude product was chromatographed (toluene/EtOAc, 1:1) to yield **13** (410 mg, 89%) as a white foam: TLC R_f = 0.25 ($CHCl_3$/MeOH, 9:1); IR 1701 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 500 MHz) δ 6.07 (1H, d, 2.6 Hz), 5.07 (1H, dd, 2.6, 6.0 Hz), 4.81 (1H, dd, 2.5, 6.0 Hz), 4.48 (1H, ddd, 2.5 m), 3.57–3.63 (24, *gem*, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 23.2, 23.6, 36.4, 36.5, 49.1, 70.1, 73.6, 81.8, 84.9, 85.5, 123.6, 124.9, 127.9, 128.2, 128.3, 128.5, 129.0, 136.0, 137.1, 138.6, 147.1, 156.5.

1-(2′,3′-Dihydroxy-5′-*O*-benzyl-β-D-*erythro*-pentofuranosyl)-N^3-benzyluracil (14). Aqueous trifluoroacetic acid (30%, 10 mL) was added to **10** (2.0 g, 4.22 mmol) while stirring at 0 °C (20 min). After concentration of the mixture *in vacuo* the residual clear syrup was column chromatographed on silica gel (toluene/EtOAc, 1:1) to give the pure diol **14** (1.52 g, 85%) as a colorless syrup: TLC R_f = 0.22 (toluene/EtOAc, 1:1); IR 1706 (C=O), 1677 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.76 (1H, d, 3.9 Hz), 4.28 (1H, dd, 3.9, 4.3 Hz), 4.25 (1H, dd, 4.3, 4.9 Hz), 4.18 (1H, ddd, 2.3, 2.4, 4.3 Hz), 3.78 (1H, *gem* d, 2.4, 10.7 Hz), 3.63 (1H, *gem* d, 2.3, 10.7 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 44.1, 53.5, 69.1, 71.0, 73.8, 76.0, 84.5, 91.5, 101.5, 127.9, 129.0, 151.8, 162.6; HRMS calcd for $C_{23}H_{24}N_2O_6$ *m/z* 425.4603 (M + 1), found *m/z* 425.1662 (M + 1).

1-[2′,3′-Dihydroxy-5′-*O*-(4-methoxybenzyl)-β-D-*erythro*-pentofuranosyl]-N^4-benzoylcytosine (15). Aqueous dichloroacetic acid (66%, 1.5 mL) was added to **11** (50 mg, 0.096 mmol) with stirring at 0 °C (1 h). The reaction mixture was then warmed to room temperature over 2 h. Solid sodium bicarbonate was added until bubbling ceased and the resulting suspension was filtered through silica gel while washing with $CHCl_3$/MeOH, (20:1) which removed insoluble salts. Concentration of the filtrate and column chromatography of the residue (toluene/EtOAc, 1:1 then eluting with 1:2) gave **15** as a white foam (28.1 mg, 62.7%): TLC R_f = 0.14 ($CHCl_3$/MeOH, 9:1); IR 1655 (C=O), 1703 cm^{-1} (C=O); ^{1}H NMR (DMSO, 500 MHz) δ 5.26 (1H, d, 5.4 Hz), 4.06 (1H, dd, 5.0, 5.4 Hz), 3.97 (1H, dd, 3.1, 5.0 Hz), 3.73 (1H, 3.1, 3.9, 4.0 Hz), 3.56, 3.66 (2H, *gem*, 4.0, 3.9); ^{13}C NMR (pyridine, 125 MHz) δ 45.1, 54.5, 60.6, 70.0, 75.6, 85.5, 90.8, 97.6, 113.6, 123.8, 128.1, 129.8, 132.0, 137.2, 150.4, 161.4.

1-(2′,3′-Hydroxy-5′-*O*-benzyl-β-D-*erythro*-pentofuranosyl)-N^4-benzoylcytosine (15a). Aqueous TFA (70%, 7 mL) was added to **11a** (432.6 mg, 0.86 mmol) with stirring (−10 °C). Stirring was continued (2 h) while warming to 5 °C. The reaction mixture was concentrated *in vacuo*. The residual syrup was chromatographed ($CHCl_3$/MeOH, 9:1) to give **15a** (368 mg, 98%) as a white foam: TLC R_f = 0.18 ($CHCl_3$/MeOH, 9:1); IR 1661 (C=O), 1707 cm^{-1} (C=O); ^{1}H NMR (DMSO, 500 MHz) δ 5.44 (1H, d, 5.5 Hz), 4.05 (1H, dd, 4.9, 5.5 Hz), 3.99 (1H, dd, 3.0, 4.9 Hz), 3.87 (1H, ddd, 3.0, 3.9, 3.9 Hz); ^{13}C NMR (DMSO, 125 MHz) δ 43.6, 60.8, 69.8, 73.9, 85.0, 89.1, 127.3, 128.5, 137.2, 151.1, 162.1.

1-[2′,3′-Dihydroxy-5′-*O*-(4-methoxybenzyl)-β-D-*erythro*-pentofuranosyl]-N^3-(4-methoxybenzyl)-5-methyluracil (16). Aqueous dichloroacetic acid (66%, 0.6 mL) was added to **12** (148 mg, 0.26 mmol) with stirring at 9 °C (3 h). Saturated aqueous $NaHCO_3$ (7 mL) was added, and stirring was continued (20 min). H_2O (10 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined extracts were dried with Na_2SO_4 and concentrated. Purification of the residual gum by column chromatography ($CHCl_3$/MeOH, 20:1) gave **16** (126 mg, 96%) as a white solid: TLC R_f = 0.17 (toluene/EtOAc, 1:1); IR 1669 (C=O), 1698 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.85 (1H, d, 2.5 Hz), 4.31 (1H, dd 2.5, 6.2 Hz), 4.29 (1H, dd, 6.2, 3.2 Hz), 4.13 (1H, ddd, 3.2, m), 3.62−3.65 (2H, *gem*, m); ^{13}C NRM ($CDCl_3$, 125 MHz) δ 13.1, 44.0, 50.26, 55.3, 61.4, 67.7, 70.5, 74.5, 85.0, 90.9, 110.8, 113.6, 128.5, 129.8, 130.0, 134.8, 151.7, 159.0, 163.4, 170.2.

1-(2′,3′-Dihydroxy-5′-*O*-benzyl-β-D-*erythro*-pentofuranosyl)-N^1-benzylinosine (17). Aqueous TFA (70%, 1 mL) was added to **13** (50 mg, 0.01 mmol) with stirring at 0 °C (1 h). The reaction mixture was concentrated *in vacuo*, and the residual yellow syrup was chromatographed ($CHCl_3$/MeOH, 9:1) to yield **17** (43 mg, 98%) as a white solid: TLC R_f = 0.20 ($CHCl_3$/MeOH, 9:1); IR 1682 cm−1 (C=O); ^{1}H NMR (DMSO, 500 MHz) δ 6.01 (1H, d, 5.1 Hz) 4.62 (1H, dd, 5.1, 6.3 Hz), 4.41 (1H, dd, 4.3, 6.3 Hz), 4.29 (1H, complex m), 3.60−3.71 (2H, *gem*, m); ^{13}C NMR (DMSO, 125 MHz) δ 13.9, 21.7, 33.5, 48.5, 70.5, 72.4, 75.8, 83.5, 87.6, 123.8, 127.5, 127.6, 127.7, 127.9, 128.3, 128.6, 137.6, 147.6, 155.8, 157.9, 158.2.

5′-*O*-Benzyl-2′,3′-didehydro-2′,3′-dideoxy-N^3-benzyluridine (18). Triphenylphosphine (179 mg, 0.68 mmol) was added in one portion to a stirred solution of iodine (174 mg, 0.68 mmol) and imidazole (93.4 mg, 1.37 mmol) in dry toluene/acetonitrile (2:1, 2.0 mL). To the resulting yellow-white suspension was added **14** (70 mg, 0.17 mmol) dissolved in toluene/acetonitrile (2:1, 1.0 mL) with stirring. The reaction mixture was then heated (90 °C, oil bath) under nitrogen (10 h) whereupon the color changed from a yellow-white to a red-brown. The reaction mixture was concentrated *in vacuo*, and the residual gum was flash-chromatographed on silica gel (toluene/EtOAc, 4:1). The olefinic nucleoside derivative **18** (55.9 mg, 87%) was obtained as a colorless syrup: TLC R_f = 0.34 (toluene/EtOAc, 4:1); IR 1668 (C=O), 1709 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.03 (1H, d, 2.8 Hz), 6.26, (1H, dd, 2.8, 6.0 Hz), 5.74 (1H, dd, 1.4, 2.8 Hz), 4.94 (1H, ddd, 1.4, 2.5, 2.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 44.2, 70.7, 73.6, 85.8, 90.4, 101.7, 126.3, 127.6, 128.1, 129.1, 134.3, 136.9, 139.3, 151.5, 162.8; HRMS calcd for $C_{23}H_{22}N_2O_4$ *m/z* 391.1658 (M + H), found *m/z* 391.1651.

5′-*O*-(4-Methoxybenzyl)-2′,3′-didehydro-2′,3′-dideoxy-N^4-benzoylcytidine (19). Triphenylphosphine (97.9 mg, 0.37 mmol) was added in one portion to a stirred solution of iodine (94.7 mg, 0.37 mmol) and imidazole (50.2 mg, 0.74 mmol) in dry toluene/acetonitrile (1:2, 2.0 mL). To the resulting yellow/white suspension was added **15** (41.5 mg, 0.09 mmol) with stirring. The reaction mixture was then heated (90 °C, oil bath) under nitrogen (1 h). To the reaction mixture was added a second portion of reagent; triphenylphosphine (97.9 mg, 0.37 mmol), iodine (94.7 mg, 0.37 mmol), and imidazole (50.2 mg, 0.74 mmol) in dry toluene/acetonitrile (1:2, 1.0 mL). Stirring was continued for an additional 1.5 h, whereupon the color changed from yellow-white to a red-brown. The reaction mixture was concentrated *in vacuo*, and the residual gummy solid was flash chromatographed (toluene/EtOAc, 10:1). The olefinic nucleoside derivative **19** (27.3 mg, 71%) was obtained as a colorless syrup: TLC R_f = 0.35 (toluene/EtOAc, 4:1); IR 1651 (C=O), 1699 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.97 (1H, d, 3.25 Hz), 6.43 (1H, dd, 3.25, 6.0 Hz), 5.97 (1H, dd, 3.5, 6.0 Hz), 4.97 (1H, ddd, 3.5, 4.4, 6.7 Hz), 3.23, 3.42 (2H, *gem*, 4.4, 6.7 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 45.7, 55.3, 84.7, 91.3, 98.6, 113.7, 126.7, 128.2, 128.6, 129.8, 130.5, 132.4, 135.8, 136.1, 136.5, 150.8, 155.0, 159.1, 177.3. Continued elution during chromatography resulted in the isolation of product **21** (4 mg, 8%): TLC R_f = 0.27 (toluene/EtOAc, 4:1); IR 1668 (C=O), 1710 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.83 (1H, d, 5.0 Hz), 4.49 (1H, dd, 3.7, 5.0 Hz), 4.04 (1H, dd, 2.3, 3.7 Hz), 3.87 (1H, ddd, 2.3, 3.9, 4.0 Hz), 3.43−3.47 (2H, *gem* dd, 3.9, 4.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.9, 22.4, 31.7, 34.0, 45.9, 55.2, 64.5, 74.9, 81.9, 91.5, 99.6, 113.9, 128.2, 130.5, 132.4, 151.1, 154.5, 159.5.

5′-*O*-Benzyl-2′,3′-didehydro-2′,3′-dideoxy-N^4-benzoylcytidine (19a). Triphenylphosphine (175 mg, 0.67 mmol) was added in one portion to a stirred solution of iodine (169 mg, 0.67 mmol) and imidazole (91 mg, 1.33 mmol) in dry toluene/acetonitrile (1:2, 0.5 mL). To the resulting yellow/white suspension was added **15a** (66 mg, 0.17 mmol) suspended in dry toluene/acetonitrile (1:2, 2.5 mL) with stirring. The reaction mixture was then heated (90 °C, oil bath) under nitrogen (3 h) whereupon the color changed to a red-brown. The reaction mixture was concentrated *in vacuo*, and the residual gummy solid was flash chromatographed on silica gel (toluene/EtOAc, 10:1). The olefinic nucleoside derivative **19a** (15.7 mg, 24%) was obtained as a colorless syrup: TLC R_f = 0.26 (toluene/EtOAc, 10:1); IR 1653 (C=O), 1699 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.99 (1H, d, 3.3 Hz), 6.40 (1H, dd, 3.3, 6.0 Hz), 5.95 (1H, dd, 3.0, 6.0 Hz), 4.94 (1H, ddd, 3.0, 4.3, 6.6 Hz), 3.20, 3.38 (2H, *gem*, 4.3, 6.6 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 46.4, 60.4, 74.5, 81.9, 91.3, 99.3, 127.6, 128.2, 128.5, 129.8, 132.6, 135.4, 136.3, 150.4, 153.9, 173.2. The intermediate product **21a** (22 mg, 25%) was isolated upon further elution during flash chromatography: TLC R_f = 0.10 (toluene/EtOAc, 10:1); IR 1668 (C=O), 1708 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.36 (1H, d, 5.0 Hz), 4.49 (1H, dd, 3.5, 5.0 Hz), 4.05 (1H, dd, 2.3, 3.5 Hz), 3.87 (1H, ddd, 2.3, 4.0, 4.7 Hz), 3.43−3.50 (2H, gem dd, 3.9, 4.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.1, 21.2, 22.8, 45.9, 55.2, 75.7, 81.1, 91.1, 99.6, 114.0, 128.2, 127.8, 130.5, 132.8, 135.1, 159.5, 169.9, 177.6.

5′-*O*-(4-Methoxybenzyl)-2′,3′-didehydro-2′,3′-dideoxy-N^3-(4-methoxybenzyl)-5-methyluridine (20). Triphenylphosphine (96.0 mg, 0.37 mmol) was added in one portion to a

stirred solution of iodine (93 mg, 0.37 mmol) and imidazole (49 mg, 0.72 mmol) in dry toluene/acetonitrile (1:2, 1.0 mL). To the resulting yellow-white suspension was added **16** (43 mg, 0.09 mmol) dissolved in toluene/acetonitrile (1:2, 0.5 mL) with stirring. The reaction mixture was then heated to 65 °C (oil bath) under nitrogen (30 m) whereupon the color changed from yellow-white to a red-brown. The reaction mixture was concentrated *in vacuo*, and the residual gummy solid was flash chromatographed on silica gel (toluene/EtOAc (8:1)). The olefinic nucleoside derivative **20** (33.1 mg, 82%) was obtained as a colorless syrup: TLC R_f = 0.54 (toluene/EtOAc 1:1); IR 1674 (C=O), 1707 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 500 MHz) δ 7.06 (1H, d, 2.7 Hz), 6.25 (1H, dd, 2.7, 5.7 Hz), 5.75 (1H, dd, 5.7, 2.3 Hz), 4.91 (1H, dd, 2.3, 2.7 Hz), 3.58–3.71 (2H, *gem*, 2.7 Hz, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.8, 43.9, 55.2, 70.4, 73.1, 85.7, 90.2, 110.3, 113.6, 113.9, 126.4, 128.5, 129.3, 130.9, 132.0, 134.1, 134.8, 152.4, 159.4, 159.8, 163.8.

2′,3′-Dideoxy-2′,3′-didehydrothymidine (d4T, 1). Ammonium cerium(IV) nitrate (55 mg, 0.10 mmol) was added to a solution of **20** (11.0 mg, 0.025 mmol) in CH_3CN/H_2O (3:1, 0.40 mL). The reaction mixture was stirred (3 h) at rt and concentrated *in vacuo* to a syrup which was column chromatographed ($CHCl_3$/MeOH, 9:1) to give **1** (3.8 mg, 68%): TLC R_f = 0.24 ($CHCl_3$/MeOH, 9:1). The proton NMR spectrum (500 MHz) of **1** thus obtained was superimposable on a spectrum of d4T prepared according to ref 17a.

5′-*O*-Benzyl-2′,3′-dideoxy-N^3-benzyluridine (23). Platinum on carbon (10 mg, 10% wt/wt) was added to a solution of the olefinic nucleoside **18** (62.1 mg, 0.159 mmol) and dry tetrahydrofuran (5.0 mL) in a round-bottom flask fitted with a T-stopcock and a stir bar. Hydrogen gas was introduced using a rubber balloon, and vigorous stirring was continued (8 h). Removal of the catalyst by vacuum filtration through Celite and removal of the solvent afforded the crude product which was column chromatographed on silica gel (toluene/EtOAc, 4:1). The saturated dideoxy nucleoside **23** (59.8 mg, 96%) was obtained as a white solid: mp 141–142 °C; TLC R_f = 0.39 (toluene/EtOAc, 4:1); IR 1661 (C=O), 1703 cm^{-1} (C=O), ^1H NMR ($CDCl_3$, 500 MHz) δ 6.04 (1H, m), 3.87 (1H, dd, 2.9, 10.7 Hz), 3.59 (1H, 2.9, 10.7 Hz), 2.33 (1H, m), 2.01 (2H, m), 1.97 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 33.2, 37.6, 40.8, 72.3, 85.8, 122.4, 126.2, 129.4, 137.7, 141.8, 151.9, 161.5; HRMS calcd for $C_{23}H_{24}N_2O_4$ *m/z* 392.4536 (M + H), found *m/z* 392.1804 (M + H).

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Supplementary Material Available: Procedures for the preparation of **4** and copies of the ^1H or ^{13}C NMR spectra of compounds **7**, **8**, **9**, **10**, **11**, **11a**, **12**, **13**, **14**, **15**, **15a**, **16**, **17**, **18**, **19**, **19a**, **20**, **21**, **21a**, **24** and diacetates of **14**, **15**, **15a**, **16** and **17** (30 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.