Syntheses of Two Pyridine C-Nucleosides as "Deletion-Modified" Analogues of dT and dC

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Received March 15, 1995 (Revised Manuscript Received June 6, 1995)

Modified nucleosides can exhibit important anticancer[1] or antiviral[1] activities and, when incorporated into nucleic acids by normal enzymatic processes, can further alter the structure and/or function of these biopolymers. Nucleoside analogues that are only minimally altered with respect to the corresponding native nucleosides can be valuable tools for probing enzymatic binding and catalysis or, when present in DNA or RNA, can be used to probe related recognition or catalytic events[2] involving sequence-specific ligands,[3] proteins,[4] or enzymes.[5] In many cases, the simplest modifications are those which result in the deletion of a functional group, potentially involved in a critical interaction, without otherwise altering the functional group character of the nucleoside. In this respect, the nucleoside analogues containing the base residues, 2-aminopurine, purine, 2-pyrimidinone, uracil, and the 1-, 3-, or 7-deazapurines can all be considered "deletion-modified" in that, in each analogue, a single functional group has been excised from an otherwise common nucleoside.

Many ligands bind in the minor groove of double-stranded DNA, and some proteins, most notably the TATA sequence binding protein (TBP), a eukaryotic transcription factor,[6] interact primarily, if not solely, with DNA through contacts in the minor groove. Minor groove base analogues such as the 3-deazapurines and hypoxanthene can be used to probe, in part, such interactions, but the corresponding pyrimidine analogues (those lacking the O^2-carbonyl, a potential hydrogen-bonding site) are not presently available. We have previously described[7] the synthesis of a 5-methylpyrimidin-4-one nucleoside as one possible analogue of dT for probing minor groove interactions, but elimination of the O^2-carbonyl from the pyrimidine heterocycle results in a tautomeric change in the N^3-nitrogen with attendant changes in hydrogen-bonding character. The presence of this analogue in DNA results in significant duplex destabilization.[8] We have additionally prepared the corresponding dC analogue,[8] but the resulting 4-imino functionality is difficult to adequately protect and permit effective DNA synthesis.

Both the undesirable tautomeric change and the protection problems for these types of derivatives can best be eliminated by preparing the corresponding C-nucleosides containing pyridine bases (see Figure 1). Related pyrimidine C-nucleosides, such as 1-deazauridine and 1-deaza-2′-deoxyuridine,[9] represent some of the first pyridine C-nucleosides synthesized. The dT analogue is a 2-pyridone derivative, and this ring system generally prefers the carbonyl tautomer,[10] while the dC analogue is a 2-aminopyridine derivative, which prefers the amino (rather than imino) tautomeric form.[10] Both analogues should maintain the same tautomeric character and hydrogen-bonding functionality at O^4/N^4 and N^3 as do the native dT and dC nucleosides. In both derivatives, the O^2-carbonyl is absent, and this alteration could impact binding or recognition events involving either the simple monomeric nucleoside or those DNA sequences containing one or both analogues. Additionally, a number of pyridine C-nucleosides exhibit cytostatic activity, although such properties appear generally to result from the ability to mimic the activity of nicotinamide,[11] and not the common pyrimidine nucleosides.

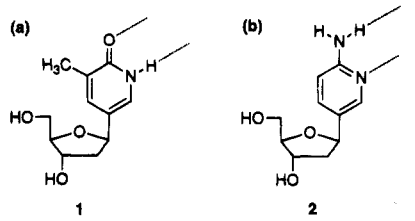

Figure 1. (a) C-nucleoside corresponding to dT but lacking the O^2-carbonyl and (b) C-nucleoside corresponding to dC but lacking the O^2-carbonyl. Dotted lines indicate hydrogen-bonding functional groups corresponding to those of the dT and dC nucleosides when present in double-stranded DNA.

A number of approaches have been employed to generate C-nucleosides. The simplest and most direct approach, in which the metalated form of the aglycon is reacted with a suitable sugar derivative, has not typically been very successful.[12] More commonly, the synthesis of C-nucleosides begins with an appropriately functionalized sugar.[13] However, we were attracted to recent work described by Daves et al.[14] in which a Heck-type coupling is employed with reasonable yields to form the C–C bond between a suitably protected glycal[14] (**7**, see for example Scheme 1) and an iodo-substituted heterocycle to generate solely the β-isomer of the C-nucleoside.

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(5) See for example: Aiken, C. R.; McLaughlin, L. W.; Gumport, R. I. *J. Biol. Chem.* **1991**, *266*, 19070–19078.
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(10) See: Newkome, G. R.; Paudler, W. W. *Contemporary Heterocyclic Chemistry, Syntheses, Reactions and Applications*; John Wiley & Sons: New York, 1982; pp 232–238 and references therein.
(11) For the initial discovery, see: Kabat, M. M.; Pankiewicz, K. W.; Watanabe, K. A. *J. Med. Chem.* **1987**, *30*, 924–931.
(12) For reviews, see: (a) Knutsen, L. J. S. *Nucleosides Nucleotides* **1992**, *11*, 961–983. (b) Watanabe, K. A. In *Chemistry of Nucleosides and Nucleotides*; Townsend, L., Ed.; Plenum Press: New York, 1993; Vol. 3, pp 421–535. For recent developments, see: (c) Schweitzer, B. A.; Kool, E. T. *J. Org. Chem.* **1994**, *59*, 7238–7242.
(13) Reviewed in: (a) Hacksell, U.; Daves, G. D. In *Progress in Medicinal Chemistry*; Ellis, G. P., West, G. B., Eds.; Elsevier Science: 1985; Vol. 22, pp 2–65. For a recent example, see: (b) Patil, S. A.; Otter, B. A.; Klein, R. S. *Tetrahedron Lett.* **1994**, *35*, 5339–5342.
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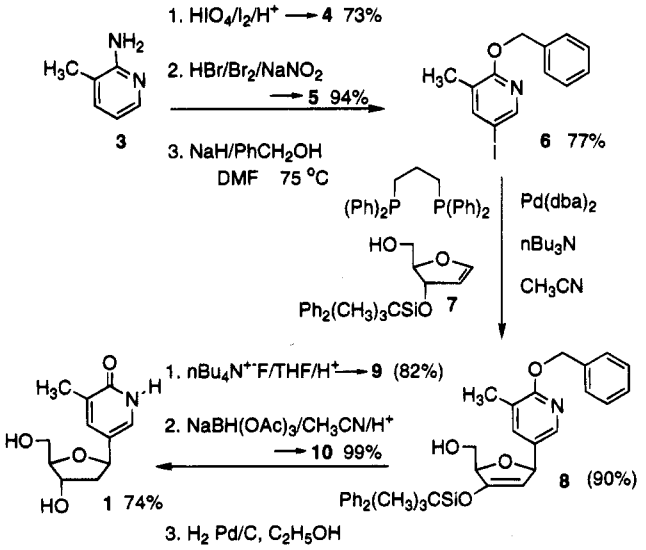
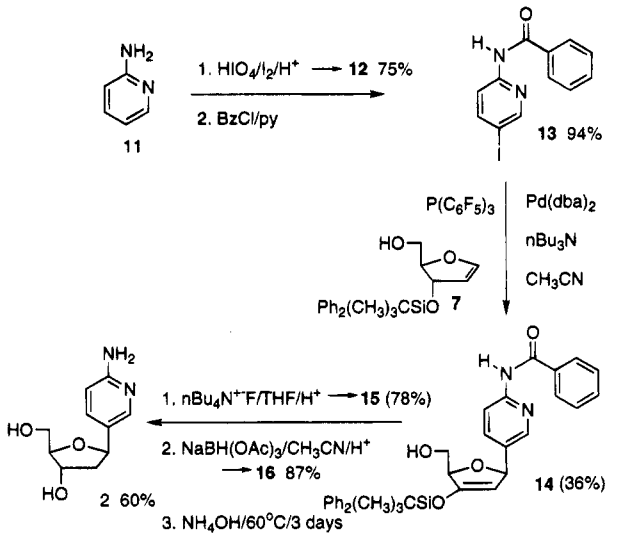
Scheme 1



Scheme 2



Direct coupling of 5-iodo-3-methyl-2-pyridone and the aglycon **7** (see Scheme 1) did not produce any observable C-nucleoside, although this approach works well in the preparation of pseudouridine from 5-iodouracil.[14e] Use of the 2-methoxy-3-methylpyridine derivative analogous to **6** (see Scheme 1) masked the 2-pyridone functionality during the Pd-mediated formation of the C–C bond. Unfortunately, while the Heck-type coupling proceeded with reasonable yields (35%), we were unable to cleave the 2-methoxy-3-methylpyridine derivative analogous to **10** with either BBr_3 or TMSI to unmask the 2-pyridone ring system.[15] The 2-(trimethylacetoxy)-3-methylpyridine derivative derived from 2-methoxy-3-methylpyridine should be easily converted to the desired 3-methyl-2-pyridone C-nucleoside under Na/CH_3OH conditions.[14d] However, the Heck-type coupling of this heterocycle under a variety of conditions failed to yield significant amounts of product. The successful sequence of reactions involved the preparation of the 2-(benzyloxy)-3-methyl-5-iodopyridine (**6**) and the coupling of this derivative to the glycal (**7**) to generate **8** (Scheme 1). A critical factor in all of the Pd-mediated coupling reactions was the choice of the ancillary ligand.[16] In our hands, use of tris(pentafluorophenyl)phosphine ($P(C_6F_5)_3$),[17] triphenylarsine ($As(C_6H_5)_3$),[13e] or 1,1′-bis(diphenylphosphino)ferrocene (DPPF)[18] resulted in only moderate yields of coupled product in this system, while use of the bidentate ligand 1,3-bis(diphenylphosphino)propane[18] resulted in an estimated[19] 90% yield of C-nucleoside in the conversion of **6** to **8**. After deprotection of the silyl enol ether, reduction of the ketone with $NaBH(OAc)_3$[14,20] generated the 2′-deoxyribose sugar. The benzyloxy-protecting group was removed by catalytic hydrogenation. Extensive hydrogenation caused some cleavage of the $C_{1'}–O_{4'}$, but by careful monitoring of the reaction time, it was possible to selectively remove the benzyl-protecting group without significant cleavage of the "benzylic" $C_{1'}–O_{4'}$ bond.

The final product **1** exhibited an infrared band at 1661 cm^{-1}. The corresponding benzyl ether (**10**) exhibited no such band in the IR. This observation suggests that the C-nucleoside **1** is present as the desired 2-pyridone tautomer rather than as the corresponding hydroxypyridine, and this observation is consistent with other studies on this heterocyclic system.[21]

In a similar fashion, the C-nucleoside analogue of dC, in which the O^2-carbonyl has been deleted, was prepared from 2-aminopyridine (**11**, Scheme 2). Direct coupling of the iodo derivative of **11** (containing an unprotected amino group) failed. Iodonation of **11** followed by protection of the amino group generated **13**, which could be coupled to the glycal **7** in the presence of palladium and an ancillary ligand. In this case, the use of 1,3-bis(diphenylphosphino)propane resulted in multiple products that could not be satisfactorily identified. Of several different ancillary ligands examined, only the reaction employing $P(C_6F_5)_3$ resulted in moderate yields of product (36%). The remaining steps to generate **2** were strictly analogous to those described in Scheme 1.

Both of the described C-nucleosides should function as valuable mimics of the two common pyrimidine nucleosides dT and dC. In addition to potential antiviral or anticancer properties, these analogues should provide important information about the role of the O^2-carbonyl in a variety of recognition and catalytic processes.

Experimental Section

Materials. Thin-layer chromatography (TLC) was performed on 5 × 10 cm silica gel 60 F_{254} glass-backed plates (E. Merck, Darmstadt, Germany). The compounds were visualized by UV light or by spraying with 10% sulfuric acid followed by heating. Silica gel 60 (particle size 0.040–0.063 mm; E. Merck, Darmstadt, Germany) was used for flash chromatography. Mass spectral analysis was performed by the Mass Spectrometry Laboratory at the University of Illinois at Urbana-Champaign.

Methods. 2-Amino-5-iodo-3-methylpyridine (4). A mixture of 2-amino-3-picoline (**3**) (5.5 g, 50 mmol), periodic acid

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(19) The product (**8**) comigrated with unreacted **7**. We obtained **8** in better than 90% purity, and on the basis of this analysis, removal of the silyl-protecting group occurred with 82% yield. The yield of **9** from **7** (two steps) occurred with 74% yield.

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dihydrate (2.28 g, 10 mmol), and iodine (5.1 g, 20 mmol) was heated in a mixed solution of acetic acid (30 mL), water (6 mL), and sulfuric acid (0.9 mL) at 80 °C for 4 h.[22] It was then poured into a solution of 10% aqueous $Na_2S_2O_3$ to remove any unreacted iodine, and the resulting mixture was extracted with ether. The organic extract was washed with aqueous 10% NaOH, dried (K_2CO_3), and concentrated *in vacuo*. The residue was isolated by column chromatography on silica gel, eluting with ether and methylene chloride (1:1) to give colorless solids of **4** (73%, 8.5 g). This material was sufficiently pure to be used directly in the following step: R_f 0.4 (Et_2O/CH_2Cl_2, 1:1); UV−vis λ_{max} 237, 296 nm; ^1H NMR ($CDCl_3$) δ 8.08 (1H, d), 7.52 (1H, m), 4.54 (2H, br), 2.06 (3H, s).

2-Bromo-5-iodo-3-methylpyridine (5). In a 250 mL three-necked flask fitted with a mechanical stirrer, a dropping funnel, and a thermometer was placed 15.8 mL (140.8 mmol) of 48% hydrobromic acid.[23] The flask and contents were cooled to 10−20 °C in an ice/salt bath, and 7.5 g (32 mmol) of compound **4** was added over a period of about 10 min. While the temperature was kept at or below 0 °C, 5.0 mL (96 mmol) of bromine was added dropwise, during which a solid orange perbromide separated. A solution of 5.5 g (200 mmol) of sodium nitrite in 8 mL of water was then added dropwise over a period of 2 h so that the temperature did not rise above 0 °C. After an additional 30 min of stirring, a solution of 12.1 g (743.8 mmol) of sodium hydroxide in 12.1 mL of water was added at such a rate that the temperature remained below 25 °C. The nearly colorless reaction mixture was extracted with ether (4 × 25 mL). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel, eluting with petroleum ether and methylene chloride (1:2) to give white solids of **5** (94%, 9.0 g): R_f 0.5 (petroleum ether/CH_2Cl_2, 1:1); UV−vis λ_{max} 234, 275 nm; ^1H NMR ($CDCl_3$) δ 8.38 (1H, d), 7.80 (1H, m), 2.32 (3H, s); MS calcd for C_6H_5NBrI 296.864 90, found 296.865 0.

2-(Benzyloxy)-5-iodo-3-methylpyridine (6). To a suspension of NaH (1.0 g, 60% in mineral oil, 25.17 mmol, washed three times with hexane) in dry DMF (15 mL) at 0 °C was added dropwise compound **5** (5.0 g, 16.78 mmol) dissolved in 3 mL of DMF.[24] Benzyl alcohol (2.08 mL, 20.14 mmol) was then added to this mixture dropwise over 10 min. The reaction mixture was allowed to warm to ambient temperature over a period of 3 h and was then heated to 75 °C for 16 h. The resulting mixture was poured into aqueous 1 M HCl (70 mL) and extracted with ether (4 × 50 mL). The ethereal layers were combined, dried, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel, eluting with petroleum ether and methylene chloride (1:3) to give solids of **6** (77%, 4.29 g): R_f 0.43 (petroleum ether/CH_2Cl_2, 1:2); UV−vis λ_{max} 234, 281 nm; ^1H NMR ($CDCl_3$) δ 8.18 (1H, d, J = 1.2 Hz), 7.66 (1H, d, J = 1.2 Hz), 7.45−7.32 (5H, m), 5.37 (2H, s), 2.20 (3H, s); MS calcd for $C_{13}H_{12}ONI$ 324.995 80, found 324.996 36.

2-Benzyloxy-5-([3′-[[(1,1-dimethylethyl)diphenylsilyl]-oxy]-β-D-*glycero*-pentofuran-3′-ulos-1′-yl]-3-methylpyridine (8). A mixture of bis(dibenzylideneacetone)palladium(0) (62 mg, 0.107 mmol) and 1,3-bis(diphenylphosphino)propane (44 mg, 0.107 mmol) in dry acetonitrile (9 mL) was stirred under nitrogen at room temperature for 20 min. This mixture was then transferred by syringe to a solution of compound **6** (700 mg, 2.14 mmol), Daves' sugar[25] (1,4-anhydro-2-deoxy-3-O-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-1-enitol) (**7**) (380 mg, 1.07 mmol), and tri-*n*-butylamine (0.764 mL, 3.21 mmol) in dry acetonitrile (18 mL). The resulting yellow-orange solution was stirred under argon at 80 °C for 8 h. The reaction mixture was then filtered through Celite, and the volatiles were removed by rotary evaporation. The residue was separated by column chromatography (petroleum ether/ether, 2:1) to give 530 mg of 2-(benzyloxy)-5-[(2′*R*)-*cis*-3′-2′,5′-dihydro-4′-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-5′-(hydroxymethyl)-2′-furanyl]-3-methylpyridine (**8**) as a colorless oil (530 mg, ~90%). This material could not be completely purified since it coeluted during chromatographic procedures with small quantities of the unreacted glycal **7**. TLC and ^1H NMR characteristics of this crude material are as follows: R_f 0.40 (petroleum ether/ether, 1:1); ^1H NMR ($CDCl_3$) δ 7.84−7.68 (5H, m), 7.48−7.30 (12H, m), 5.52 (1H, q), 5.37 (2H, s), 4.75 (1H, br), 4.28 (1H, br), 3.87 (2H, m), 2.15 (3H, s), 1.10 (9H, s).

To a solution of compound **8** (530 mg, 0.96 mmol) in THF (13 mL) at 0 °C was added acetic acid (0.24 mL, 3.92 mmol), followed by 1.99 mL of a 1 M solution of tetra-*n*-butylammonium fluoride in THF (1.99 mmol). The desilylation reaction was complete in 10 min on the basis of TLC analysis. The volatiles were removed by rotary evaporation, and the residue was separated by column chromatography (ether/methylene chloride, 1:4) to afford 247 mg (~82%) of compound **9**. The yield for the conversion of **7** to **9** (two steps) was 74%: R_f 0.28 (ether/CH_2Cl_2, 1:4); UV−vis λ_{max} 232, 269 nm; ^1H NMR ($CDCl_3$) δ 8.04 (1H, d, H_6 of pyridine ring), 7.53 (1H, d), 7.47−7.28 (5H, m), 5.42 (2H, s), 5.13 (1H, q), 4.01 (1H, t), 3.93 (2H, d), 2.84−2.78 (1H, dd), 2.57−2.50 (1H, dd), 2.25 (3H, s); MS calcd for $C_{18}H_{19}NO_4$ 313.130 80, found 313.131 40.

2-(Benzyloxy)-5-(2′-deoxy-β-D-ribofuranosyl)-3-methylpyridine (10). To a solution of compound **9** (240 mg, 0.77 mmol) in acetonitrile (25 mL) and acetic acid (25 mL) at 0 °C was added sodium triacetoxyborohydride (0.4 g, 1.78 mmol). The reaction was complete within 10 min on the basis of TLC analysis. Volatiles were then removed, and the resulting residue was separated by column chromatography (eluting with methanol/methylene chloride, 1:12) to afford compound **10** (240 mg, 99%): R_f 0.31 (CH_3OH/CH_2Cl_2, 1:12); UV−vis λ_{max} 232, 267 nm; IR ($CHCl_3$) 3378, 2926, 2885, 1613, 1480, 1426, 1357, 1256 cm^{-1}; ^1H NMR (CD_3OD) δ 8.14 (1H, d), 7.75 (1H, d), 7.60−7.44 (5H, m), 5.52 (2H, s), 5.25 (1H, q), 4.53 (1H, m), 4.13 (1H, m), 3.86 (2H, d), 2.38 (3H, s), 2.37−2.31 (1H, dd), 2.19−2.11 (1H, dd); MS calcd for $C_{18}H_{21}NO_4$ 315.147 40, found 315.147 06.

5-(2′-Deoxy-β-D-ribofuranosyl)-3-methyl-2-pyridone (1). Compound **10** (133 mg, 0.42 mmol) was dissolved in absolute ethanol (20 mL), and 13 mg of 10% palladium on carbon was added to the solution. After hydrogenolysis for 8 h at 45 psi, the catalyst was removed by filtration and washed several times with methanol. After rotary evaporation of the solvent *in vacuo*, the residue was chromatographed on silica gel (methanol/methylene chloride, 1:4) to obtain the desired product (**1**) (70 mg, 74%): R_f 0.38 (CH_3OH/CH_2Cl_2, 1:4); UV−vis λ_{max} 234, 291 nm; IR (CH_3OH) 3300, 2926, 2885, 1661, 1622 cm^{-1}; ^1H NMR (CD_3OD) δ 7.66 (1H, s, H_6 of pyridone ring), 7.45 (1H, s), δ 5.09 (1H, q), 4.50 (1H, d), 4.09 (1H, q), 3.84 (2H, m), 2.29−2.26 (4H, m), 2.17−2.14 (1H, m); MS calcd for $C_{11}H_{15}NO_4$ 225.100 00, found 225.100 10.

2-Amino-5-iodopyridine (12). The iodo compound **12** was prepared by Ogura's method.[1] A mixture of 2-aminopyridine (**11**) (3.8 g, 40 mmol), periodic acid dihydrate (1.83 g, 8 mmol), and iodine (4.08 g, 4 mmol) was heated in a mixed solution of acetic acid (24 mL), water (4.8 mL), and sulfuric acid (0.79 mL) at 80 °C for 4 h. It was then poured into 10% aqueous $Na_2S_2O_3$ solution to remove unreacted iodine and extracted with ether. The extract was washed with 10% aqueous NaOH, dried (K_2CO_3), and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel, eluting with ethyl acetate, and then recrystallization from ethanol gave colorless prisms of compound **12** (75%, 6.6 g): UV−vis λ_{max} 237, 297 nm; ^1H NMR (CD_3OD) δ 8.03 (1H, s), 7.57 (1H, d), 6.34 (1H, d).

2-(*N*-Benzoylamino)-5-iodopyridine (13). **13** was Prepared by a procedure similar to that described.[1] To a solution of 1.2 g of **12** (5.45 mmol) and 0.43 g (5.45 mmol) of pyridine in an ice bath was added slowly 0.70 mL (6 mmol) of benzoyl chloride while the solution was stirred. After stirring for 18 h, the resulting mixture was extracted with chloroform and the chloroform solution washed with water, 5% HCl, 5% NaOH, and water and dried (Na_2SO_4). After the solvents were removed *in vacuo*, the residue was purified by column chromatography on silica gel, eluting with chloroform, and the product was then recrystallized from chloroform/methanol (1:1) to yield colorless solids of compound **13** (90%, 1.59 g): UV−vis λ_{max} 234, 249, 285 nm; ^1H NMR ($CDCl_3$) δ 8.39 (1H, br), 8.25 (1H, d), 8.02−7.48 (6H, m).

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2-(Benzoylamino)-5-(β-D-*glycero*-pentofuran-3′-ulos-1′-yl)pyridine (14). A mixture of bis(dibenzylideneacetone)-palladium(0) (29 mg, 0.05 mmol) and tris(pentafluorophenyl)-phosphine (53 mg, 0.10 mmol) in dry acetonitrile (4 mL) was stirred under nitrogen at room temperature for 20 min. This mixture was then transferred by syringe to a solution of compound **13** (163 mg, 0.5 mmol), Daves' sugar[4] (1,4-anhydro-2-deoxy-3-O-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-1-enitol) (**7**) (212 mg, 0.6 mmol), and tri-*n*-butylamine (0.36 mL, 1.5 mmol) in dry acetonitrile (8 mL). The resulting yellow-orange solution was stirred under argon at 80 °C for 8 h. The reaction mixture was then filtered through Celite, and the volatiles were removed. The residue was purified by column chromatography (petroleum ether/ether, 2:3) to yield 100 mg (36%) of 2-(benzoylamino)-5-[(2′*R*)-*cis*-3′-2′,5′-dihydro-4′-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-5′-(hydroxymethyl)-2′-furanyl])pyridine (**14**) as a colorless solid slightly contaminated by trace amounts of the unreacted glycal **7**. The characteristics of the crude material are as follows: R_f 0.80 (diethyl ether); ^{1}H NMR ($CDCl_3$) δ 8.00–7.78 (8H, m), 7.58–7.41 (9H, m), 7.29–7.26 (1H, m), 5.49 (1H, q), 4.82 (1H, t), 3.98 (2H, d), 1.13 (9H, s).

To a solution of crude compound **14** (180 mg, 0.33 mmol) in THF (5 mL) at 0 °C was added acetic acid (0.075 mL, 1.31 mmol), followed by 0.66 mL of a 1 M solution of tetra-*n*-butylammonium fluoride in THF (0.66 mmol). The desilylation reaction was complete in 10 min on the basis of TLC analysis. The volatiles were removed, and the residue was separated by column chromatography (eluting with diethyl ether) to afford 80 mg (78%) of compound **15**. The yield for the conversion of **13** to **15** (two steps) was 28%: R_f 0.30 (diethyl ether); UV–vis λ_{max} 232, 249, 267 nm; ^{1}H NMR ($CDCl_3$) δ 8.30 (2H, d), 7.86 (3H, m), 7.53–7.37 (3H, m), 5.13 (1H, q), 3.95 (1H, t), 3.83 (2H, d), 2.83–2.76 (1H, dd), 2.48–2.40 (1H, dd); MS calcd for $C_{17}H_{16}N_2O_4$ 312.110 60, found 312.111 01.

2-(Benzoylamino)-5-(2′-deoxy-β-D-ribofuranosyl)pyridine (16). To a solution of compound **15** (80 mg, 0.26 mmol) in acetonitrile (8.5 mL) and acetic acid (8.5 mL) at 0 °C was added sodium triacetoxyborohydride (0.142 g, 0.64 mmol). The reaction was complete within 10 min on the basis of TLC analysis. Volatiles were then removed, and the resulting residue was separated by column chromatography (eluting with methanol/methylene chloride, 1:12) to afford compound **16** (70 mg, 87%): R_f 0.27 (CH_3OH/CH_2Cl_2, 1:15); UV–vis λ_{max} 236, 250, 279 nm; ^{1}H NMR (DMSO-d_6) δ 10.80 (1H, s), 8.38 (1H, s), 8.15 (1H, m), 8.05 (2H, m), 7.82 (1H, m), 7.60 (1H, m), 7.50 (2H, m), 5.12 (1H, d), 5.05 (1H, m), 4.82 (1H, m), 4.23 (1H, m), 3.79 (1H, m), 3.48 (2H, m), 3.35 (s), 2.47 (m), 2.10 (1H, m), 1.85 (1H, m); MS calcd for $C_{17}H_{18}N_2O_4$ 314.126 20, found 314.126 66.

2-Amino-5-(2′-deoxy-β-D-ribofuranosyl)pyridine (2). The benzoxylamino compound **16** (50 mg, 0.16 mmol) was dissolved in 28% NH_4OH/H_2O (10 mL) and heated for 3 days at 55 °C. After the volatile solvents were removed, the resulting residue was purified by preparative TLC (CH_2Cl_2/CH_3OH, 2:1) to obtain the desired free amino compound **2** (20 mg, 60%): R_f 0.42 (CH_3OH/CH_2Cl_2, 1:2); UV–vis λ_{max} 232, 290 nm; ^{1}H NMR (CD_3OD) δ 8.07 (1H, br), 7.74 (1H, d), 6.78 (1H, d), 5.17 (1H, q), 4.51 (1H, m), 4.08 (1H, m), 3.83 (2H, d), 2.33–2.26 (1H, m), 2.20–2.13 (1H, m); MS calcd for $C_{10}H_{14}N_2O_3$ 210.100 03, found 210.100 04.

Acknowledgment. This work was supported by a grant from the NSF (MCB-9507040). L.W.M. is the recipient of an American Cancer Society Faculty Research Award (FRA-384).

Supporting Information Available: NMR spectra of compounds **1**, **2**, **4–6**, **7** and **8**, **9**, **10**, and **14–16** (11 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.

JO950506D