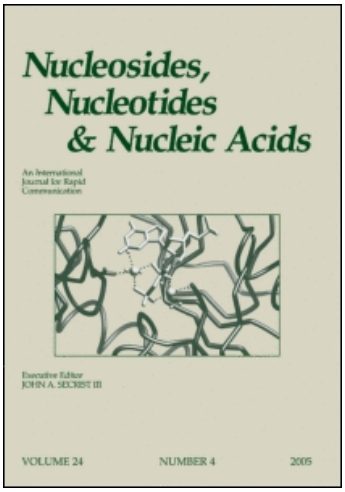

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Synthesis of 2'-Methylene-Substituted 5-Azapyrimidine, 6-Azapyrimidine, and 3-Deazaguanine Nucleoside Analogues as Potential Antitumor/Antiviral Agents

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SYNTHESIS OF 2'-METHYLENE-SUBSTITUTED 5-AZAPYRIMIDINE, 6-AZAPYRIMIDINE, AND 3-DEAZAGUANINE NUCLEOSIDE ANALOGUES AS POTENTIAL ANTITUMOR/ANTIVIRAL AGENTS

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Abstract: 2'-Deoxy-2'-methylene-6-azauridine (**5**) and 2'-deoxy-2'-methylene-6-azacytidine (**8**) have been synthesized via a multi-step procedure from 6-azauridine. 2'-Deoxy-2'-methylene-5-azacytidine (**14a**) and 2'-deoxy-2'-methylene-3-deazaguanosine (**19a**) and their corresponding α-anomers (**14b** and **19b**) have been synthesized by the transglycosylation of 3',5'-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2'-deoxy-2'-methyleneuridine (**12**) with silylated 5-azacytosine and silylated *N*2-palmitoyl-3-deazaguanine, respectively, in the presence of trimethylsilyl trifluoromethanesulfonate as the catalyst in anhydrous dichloroethane, followed by separation of the isomers and deprotection of the blocking groups. These compounds were tested for cytotoxicity against $B_{16}F_{10}$, L1210, and CCRF-CEM tumor cell lines and for antiviral activity against HIV-1, HSV-1, and HSV-2.

Various aza/deaza nucleoside analogs, in which the carbon or nitrogen atoms in the natural base were replaced by the bioisosteric nitrogen or carbon, have shown significant anticancer and/or antiviral activities. For example, 5-azacytidine (AZC),[1,2] 5-aza-2'-deoxycytidine (dAZC),[3] and 6-azauridine[4] have exhibited antitumor activity both experimentally and clinically. 3-Deazaguanosine has been reported to possess broad spectrum antiviral activity against a variety of DNA and RNA viruses, as well as potent antitumor activity against the L1210 leukemia and several mammary adenocarcinomas in mice.[5-7] Considerable progress has been made in the search for novel nucleoside structures with anticancer and/or antiviral activity by modification of the carbohydrate portion of the molecule. Thus, 2'-deoxy-2'-methylenecytidine[8-11] and 2'-deoxy-2'-fluoromethylenecytidine[12,13] have been reported to exhibit potent antitumor activity and to

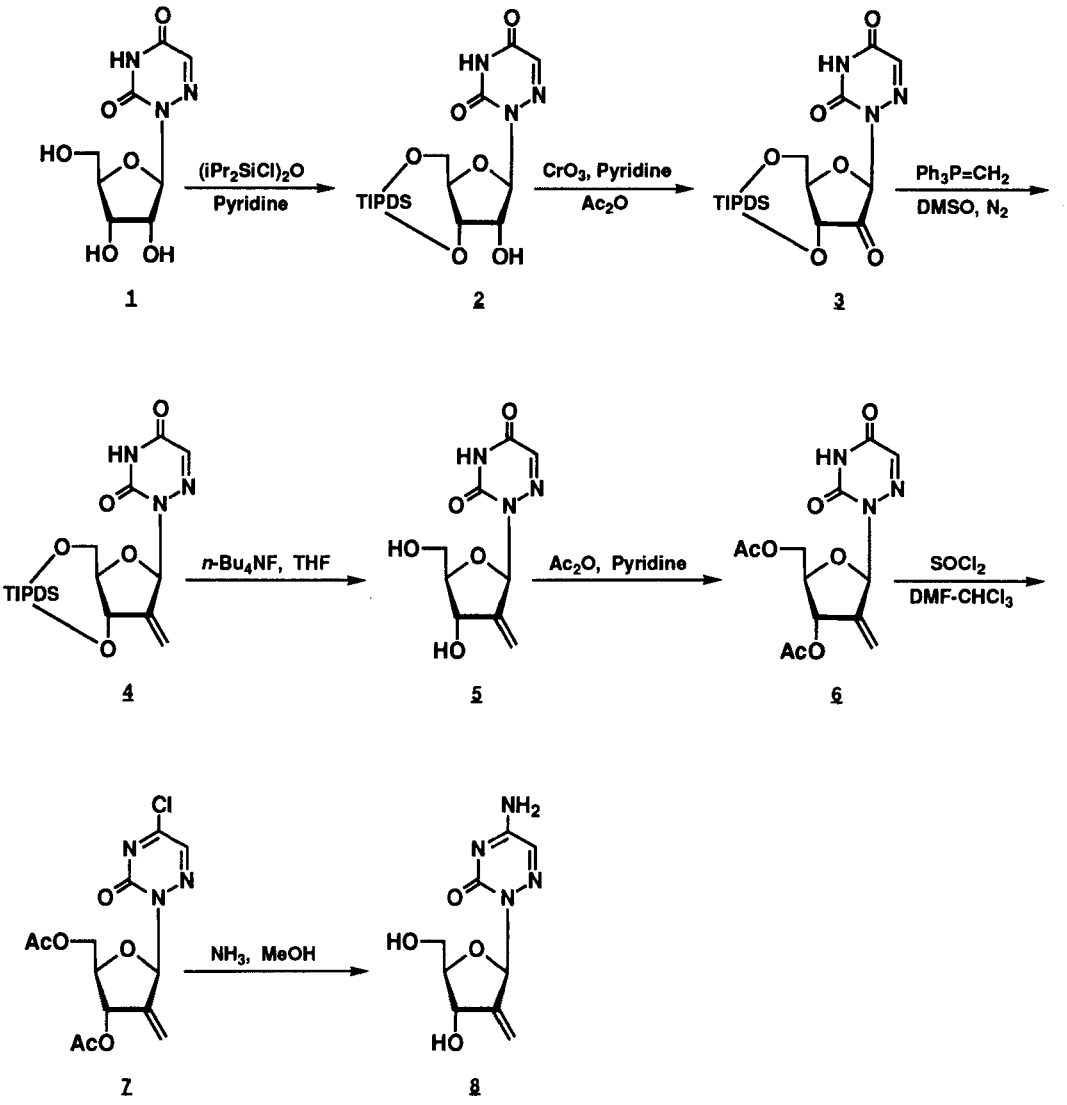
† *Deceased*

be resistant to cytidine deaminase,[10] an enzyme responsible for the short biological life of 1-β-D-arabinofuranosylcytosine (ara-C), a useful chemotherapeutic agent in the treatment of acute myelogenous leukemia.[14] In this paper, we report the synthesis and biological activity of 2'-deoxy-2'-methylene derivatives of 3-deazaguanosine, 5- and 6-azacytidine, and 6-azauridine.

SYNTHESIS

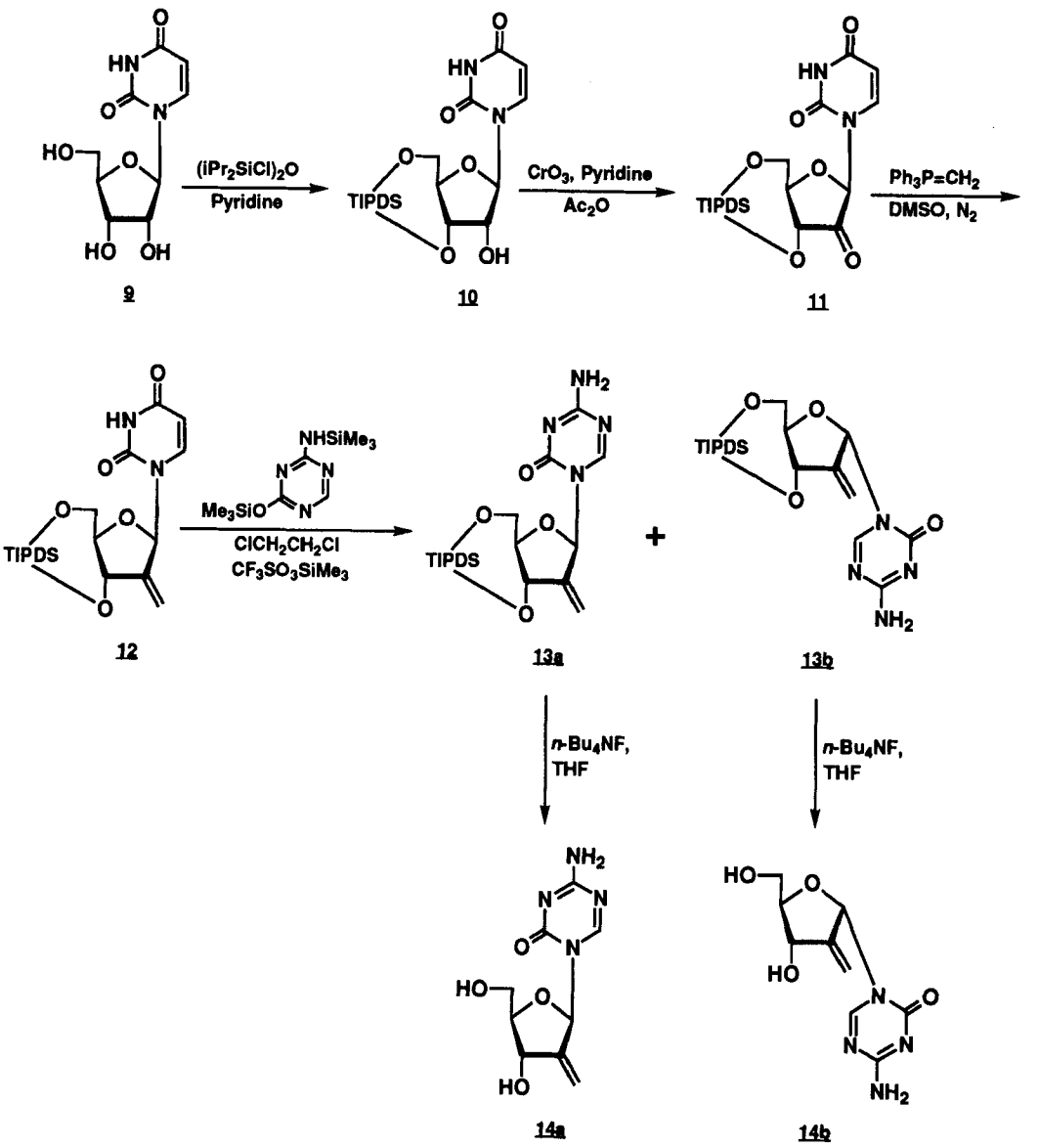
The syntheses of 2'-deoxy-2'-methylene-6-azauridine (**5**) and 2'-deoxy-2'-methylene-6-azacytidine (**8**) are described in **SCHEME 1**. Treatment of 6-azauridine (**1**) with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane in pyridine at room temperature[15] gave the cyclic 3',5'-protected derivative **2**. Oxidation of compound **2** with a chromium (VI) oxide/pyridine/acetic anhydride complex (1:2:1, molar ratio) in methylene chloride[16] yielded the corresponding 2'-ketonucleoside **3**, which was then converted to the 2'-methylene analogue **4** by reaction with methyltriphenylphosphonium bromide and sodium hydride in anhydrous methyl sulfoxide at 50 °C under nitrogen.[17] Deprotection of **4** with tetra-*n*-butylammonium fluoride in tetrahydrofuran (THF) under nitrogen afforded 2'-deoxy-2'-methylene-6-azauridine (**5**). Acetylation of **5** with acetic anhydride in pyridine gave the diacetate **6**. An attempt to convert **6** to **8** via the 4-(1,2,4-triazolyl)pyrimidinone intermediate by treatment of **6** with 4-chlorophenyl phosphorodichloridate and 1,2,4-triazole in pyridine[18] was unsuccessful. However, reaction of compound **6** with thionyl chloride and *N,N*-dimethylformamide in absolute chloroform at reflux temperature for 6 h[19] afforded the corresponding 4-chloro derivative **7**, which was converted to 2'-deoxy-2'-methylene-6-azacytidine (**8**) by treatment with saturated methanolic ammonia.

2'-Deoxy-2'-methylene-5-azacytidine (**14a**) was synthesized by a transglycosylation reaction which was a modification of the methodology described by Spadari et al.[20] (**SCHEME 2**). The transglycosylation reaction of 3',5'-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2'-deoxy-2'-methyleneuridine (**12**), which was readily prepared from uridine (**9**) by a previously described procedure,[10] with silylated 5-azacytosine, using trimethylsilyl trifluoromethanesulfonate as a catalyst in anhydrous dichloroethane, afforded a mixture of β- and α-anomers of 3',5'-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2'-deoxy-2'-methylene-5-azacytidine (**13a** and **13b**), which were separable on a silica gel column. Deprotection of compounds **13a** and **13b** with tetra-*n*-butylammonium fluoride in THF produced the target compound **14a** and its α-anomer **14b**, respectively.

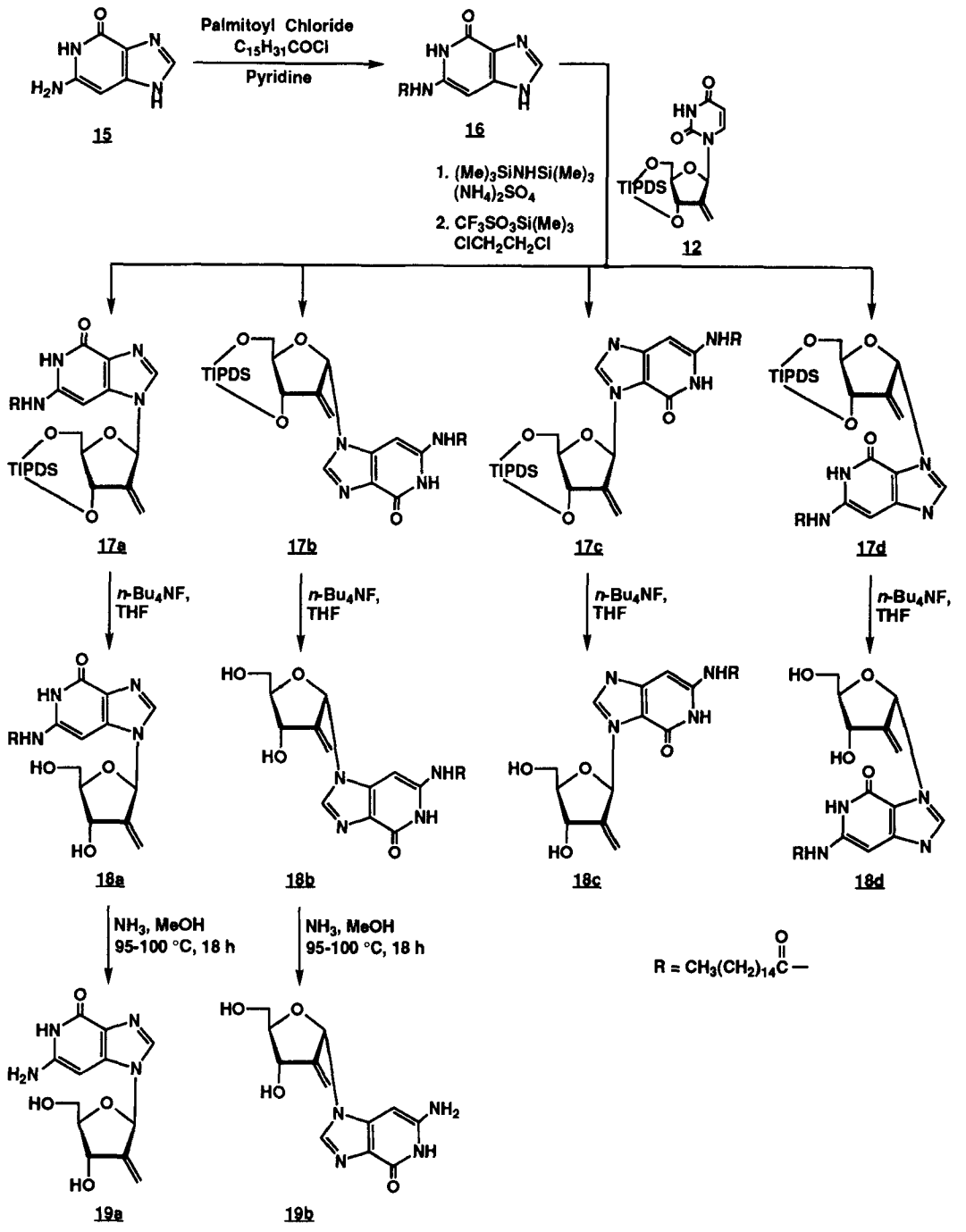


SCHEME 1

The synthesis of 2'-deoxy-2'-methylene-3-deazaguanosine (**19a**) is described in **SCHEME 3**. Replacement of silylated 5-azacytosine by silylated *N*2-palmitoyl-3-deazaguanine (**16**), which was obtained by treatment of 3-deazaguanine (**15**) with palmitoyl chloride, in the transglycosylation reaction yielded a complex mixture of crude products which was chromatographed over a silica gel column twice to afford β- and α-



SCHEME 2



SCHEME 3

anomers of the 2'-deoxy-2'-methylene-3-deazaguanosine derivatives **17a** and **17b**, and the corresponding N^7-isomers **17c** and **17d**. Our attempt to use N^2-acetyl-3-deazaguanine in the transglycosylation reaction was unsuccessful due to a low yield and difficulty in separating the isomers. This was attributed to the low solubility of 6-acetyl-3-deazaguanine and its derivatives. Deprotection of **17a-d** with tetra-*n*-butylammonium fluoride in THF gave the corresponding N^2-palmitoyl-2'-deoxy-2'-methylene-3-deazaguanosine derivatives (**18a-d**). Treatment of **18a** and **18b** with saturated methanolic ammonia in a steel bomb at 95-100 °C with stirring for 18 h produced the desired compound **19a** and its α-anomer **19b**, respectively. However, we were unable to deblock the corresponding N^2-palmitoyl protecting group of the N^7-isomers, **18c** and **18d**. Treatment of **18c** and **18d** with saturated methanolic ammonia under conditions similar to those used for the N^9-isomers only gave 3-deazaguanine, indicating cleavage of the glycosylic bond, and no reaction occurred under milder conditions. These findings are consistent with the observation of Seela et al.[21] that 3-deaza-2'-deoxyguanosine and its N^7-regioisomer exhibit different stabilities, with the N^7-isomer being significantly less stable than the N^9-isomer. This difference is attributed to the destabilization of the *N*-glycosylic bond due to a steric repulsion between the C(6)=O group of the nucleobase and the sugar moiety in the N^7-isomers.

The assignment of the anomeric configuration of these nucleosides was made on the basis of the characteristics of the proton NMR spectra. The 4'-H protons of the α-anomers appear at a lower field than those of the β-anomers. Conversely, the 5'-H protons of the α-anomers appear at a higher field than those of the β-anomers (**TABLE 1**). These shifts are attributed to the fact that protons at the syn-position relative to the base are more deshielded than those in anti-position to the base. The 4'-H protons of the α-anomers and the bases are on the same side of the sugar ring and those of β-anomers are on the opposite side. In contrast, the 5'-H protons of the α-anomers and the bases are on the opposite side of the sugar ring and those of β-anomers are on the same side. The findings are consistent with reports by others with both pyrimidine and purine nucleosides.[22-24]

The assignment of the *N*-glycosidic linkage of the N^7- and N^9-isomers of the 3-deazaguanine nucleosides (**17a-d**) was based upon the UV spectra of these derivatives. The UV spectra of the N^9-3-deazaguanine nucleoside isomers showed a maximum peak at 212, 270, and 300 nm, while the N^7-isomers showed a maximum peak at 224, 279, and 310 nm. Furthermore, the NMR spectra of the 2-H protons of the N^7-isomers were downfield from those of the corresponding N^9-isomers. For example, the chemical shifts

TABLE 1. Proton NMR chemical shifts δ (ppm).

Compd	4'-H[a]	Δ δ	5'-H[a]	Δ δ
13a (β)[b]	4.05 (anti)		3.70 (syn)	
13b (α)[b]	4.20 (syn)	0.15	3.35 (anti)	0.35
14a (β)[c]	3.70 (anti)		3.62 (syn)	
14b (α)[c]	4.07 (syn)	0.37	3.40 (anti)	0.22
17a (β)[c]	4.05 (anti)		3.85 (syn)	
17b (α)[c]	4.45 (syn)	0.40	3.70 (anti)	0.15
17c (β)[c]	4.15 (anti)		3.90 (syn)	
17d (α)[c]	4.50 (syn)	0.35	3.80 (anti)	0.10
18a (β)[c]	3.88(anti)		3.60 (syn)	
18b (α)[c]	4.10 (syn)	0.22	3.35 (anti)	0.25
18c (β)[c]	4.05 (anti)		3.68 (syn)	
18d (α)[c]	4.20 (syn)	0.15	3.32 (anti)	0.36
19a (β)[c]	3.79 (anti)		3.56 (syn)	
19b (α)[c]	4.00 (syn)	0.21	3.27 (anti)	0.29

[a]Stereochemistry relative to the base. [b]Spectra were recorded in $CDCl_3$; [c]in DMSO-d_6.

of the 2-H protons of the N^7-β- and α-isomers (**17c** and **17d**) appeared at 8.00 and 7.82 ppm, and of the N^9-β- and α-isomers (**17a** and **17b**) at 7.80 and 7.70 ppm, respectively. Those results are similar to those obtained with other 3-deazaguanine nucleosides.[7,25]

BIOLOGICAL EVALUATION

The synthesized compounds **5**, **8**, **14a**, **14b**, **19a**, and **19b** were evaluated *in vitro* for their cytotoxicity against the $B_{16}F_{10}$ melanoma, L1210 leukemia, and CCRF-CEM lymphoblastic leukemia cell lines by previously reported methodology[26]. 1-(2-Deoxy-2-methylene-β-D-*erythro*-pentofuranosyl)-4-amino-1,3,5-triazine-2(1*H*)-one (**14a**) produced ED_{50} values of 50, 50, and 10 μM against $B_{16}F_{10}$, L1210, and CCRF-CEM cells, respectively, and 6-amino-1[2-deoxy-2-methylene-β-D-*erythro*-pentofuranosyl]-1,5-dihydro-4*H*-imidazo[4,5-c]pyridin-4(5*H*)-one (**19a**) produced an ED_{50} value of 75 μM against L1210 cells. The remaining compounds had no activity up to 100 μM against these

three tumor cell lines. Evaluation of the compounds for antiviral activity[26,27] against HIV-1, HSV-1, and HSV-2 demonstrated a lack of activity up to a concentration of 100 μM.

EXPERIMENTAL SECTION

Melting points were determined with a Thomas-Hoover Unimelt apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian EM-390 (90 MHz) or on a Gemini-300 (300 MHz) NMR spectrometer with Me_4Si as the internal reference. The UV spectra were recorded on a Beckman-25 spectrophotometer. Mass spectra were recorded on a VG-ZAB-SE mass spectrometer in the fast bombardment (FAB) mode (glycerol matrix). Column chromatography was conducted with Merck silica gel 60, 230-400 mesh. TLC was performed on EM precoated silica gel sheets containing a fluorescent indicator. Elemental analyses were carried out by the Baron Consulting Co., Orange, CT, USA.

2-[3,5-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-β-D-*erythro*-pentofuranosyl]-1,2,4-triazine-3,5(2*H*,4*H*)-dione (2). A mixture of 6-azauridine (Aldrich, 2.4 g, 10 mmol) and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (3.1 g, 10 mmol) in 90 mL of dry pyridine was stirred at room temperature for 3 days. The reaction mixture was evaporated *in vacuo* to dryness, and co-evaporated twice with CH_2Cl_2. The residue was dissolved in CH_2Cl_2 (100 mL), washed with water, and dried ($MgSO_4$). The filtrate was evaporated to dryness *in vacuo*, and the residue was chromatographed on a silica gel column (CH_2Cl_2/EtOAc, 2:1, v/v) to afford 2.8 g (59%) of product as a foam: (lit.[28] mp 125-126 °C) TLC, R_f 0.64 (CH_2Cl_2/EtOAc, 2:1, v/v); ^{1}H NMR ($CDCl_3$) δ 1.00-1.15 (m, 28 H, $CHMe_2$), 3.90-4.05 (m, 4 H, 3'-H, 4'-H and 5'-H), 4.25-4.35 (m, 1 H, 2'-H), 4.60-4.75 (m, 1 H, 2'-OH, D_2O exchangeable), 6.10 (d, 1 H, 1'-H), 7.30 (s, 1 H, 6-H), 9.80 (br s, 1 H, 4-NH, D_2O exchangeable). Anal. Calcd. for $C_{20}H_{37}N_3O_7Si_2$: C, 49.25; H, 7.65; N, 8.62. Found: C, 49.53; H, 7.61; N, 8.47.

2-[3,5-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-2-keto-β-D-*erythro*-pentofuranosyl]-1,2,4-triazine-3,5(2*H*,4*H*)-dione (3). A mixture of CH_2Cl_2 (10 mL), CrO_3 (0.6 g, 6 mmol), pyridine (1 mL, 12 mmol), and acetic anhydride (0.6 mL, 6 mmol) was stirred for 3 min, after which compound **2** (1.0 g, 2 mmol) in 2 mL of CH_2Cl_2 was added to the mixture, then stirred at room temperature for 30 min. The dark brown solution was poured into 100 mL of EtOAc with stirring, and the resulting mixture was filtered through a 2-cm layer of silica gel in a 4-cm diameter sinter-glass filter. The precipitated solid and silica gel were washed with EtOAc (100 mL), and the combined

filtrate was evaporated. The residue was co-evaporated with toluene, then CH_2Cl_2, to give 1.0 g of product as a foam, which was immediately used for the next reaction without further purification.

2-[3,5-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-2-deoxy-2-methylene-β-D-*erythro*-pentofuranosyl]-1,2,4-triazine-3,5(2*H*,4*H*)-dione (4). A suspension of NaH (0.29 g, 60% dispersion in mineral oil, 7.2 mmol) in 6.6 mL of anhydrous DMSO was heated at 65 °C under nitrogen until all of the sodium hydride had dissolved. The reaction mixture was cooled to room temperature and methyltriphenylphosphonium bromide (2.6 g, 7.2 mmol) was added. After stirring for 45 min, compound **3** (1.0 g, 2 mmol) was added to the reaction mixture and stirred at room temperature for 20 min, then at 50 °C for 1 hour. The resulting solution was poured into ice-water (50 mL), and the pH of the solution was adjusted to 7 with acetic acid. The solution was extracted with CH_2Cl_2 (4 x 20 mL), and the combined extracts were washed with water, dried ($MgSO_4$), and filtered. The filtrate was evaporated *in vacuo* to a small volume and purified by chromatography on a silica gel column (CH_2Cl_2/EtOAc, 2:1, v/v) to give 0.7 g (69%) of product as a white foam: TLC, R_f 0.69 (CH_2Cl_2/EtOAc, 1:1, v/v); ^1H NMR ($CDCl_3$) δ 1.00-1.10 (m, 28 H, $CHMe_2$), 3.60-3.80 (m, 1 H, 4'-H), 3.90-4.05 (m, 2 H, 5'-H), 4.95-5.10 (m, 1 H, 3'-H), 5.25-5.40 (m, 2 H, methylene), 6.60 (s, 1 H, 1'-H), 7.30 (s, 1 H, 6-H), 9.70 (br s, 1 H, 4-NH, D_2O exchangeable). Anal. Calcd. for $C_{21}H_{37}N_3O_6Si_2$: C, 52.14; H, 7.71; N, 8.69. Found: C, 52.39; H, 7.91; N, 8.42.

2-(2-Deoxy-2-methylene-β-D-*erythro*-pentofuranosyl)-1,2,4-triazine-3,5(2*H*,4*H*)-dione (5). To a stirred solution of compound **4** (0.60 g, 1.2 mmol) in THF (50 mL) was added dropwise 4 mL of tetra-*n*-butylammonium fluoride (1 M solution in THF, 4 mmol) at ambient temperature. The reaction was completed within 45 min, and the solvent was removed *in vacuo*. The residue was dissolved in 17 mL of water and extracted with CH_2Cl_2 (2 x 10 mL). The water layer was evaporated with 3.5 g of silica gel to dryness and the residue was chromatographed on a silica gel column (EtOAc/EtOH, 6:1, v/v) to afford 0.24 g (80%) of product as a white solid: mp 143-145 °C; TLC, R_f 0.60 (EtOAc/EtOH, 4:1, v/v); UV (MeOH) λ_{max} 266 nm (ε 10,671), λ_{min} 230 nm; UV (0.01 N HCl) λ_{max} 260 nm (ε 8,016), λ_{min} 226 nm; UV (0.01 N NaOH) λ_{max} 250 nm (ε 8,670), λ_{min} 218 nm; MS m/z 242 (MH^+); ^1H NMR (DMSO-d_6) δ 3.40-3.55 (m, 2 H, 5'-H), 4.40 (m, 1 H, 4'-H), 4.60 (br s, 1 H, 3'-OH, D_2O exchangeable), 5.05 [t (overlap dd), 1 H, methylene-A, J = 2.0 Hz], 5.18 [t (overlap dd), 1 H, methylene-B, J = 1.9 Hz], 5.50 (t, 1 H, 5'-OH, D_2O exchangeable), 6.48 (s, 1 H, 1'-H), 7.40 (s, 1 H, 6-H), 12.10

(br s, 1 H, 4-NH, D_2O exchangeable). Anal. Calcd. for $C_9H_{11}N_3O_5 \cdot 0.5C_2H_5OH$: C, 45.45; H, 5.33; N, 15.90. Found: C, 45.12; H, 5.44; N, 15.69.

2-(3,5-Di-*O*-acetyl-2-deoxy-2-methylene-β-D-*erythro*-pentofuranosyl)-1,2,4-triazine-3,5(2*H*,4*H*)-dione (6). Acetic anhydride (1.5 g, 14.7 mmol) was added dropwise to a solution of **5** (0.60 g, 2.5 mmol) in 6 mL of dry pyridine at 0 °C. After stirring at 4 °C overnight, the reaction mixture was quenched by slowly adding 1.5 mL of water (ice bath). The solvent was removed *in vacuo* to give a thick syrup. This residue was dissolved in 50 mL of $CHCl_3$ and washed with water, saturated $NaHCO_3$ solution, and water again, then dried with anhydrous $MgSO_4$. After filtration, the solution was concentrated to a small volume and purified by passing through a silica gel column (CH_2Cl_2/EtOH, 10:1, v/v). The fractions containing **6** were collected (R_f 0.66), combined, and evaporated to dryness *in vacuo* to give a white foam (0.64 g, 79%). ^1H NMR ($CDCl_3$) δ 2.00-2.10 (2 s, 6 H, $OCOCH_3$), 4.10-4.30 (m, 3 H, 4'-H and 5'-H), 5.30-5.50 (m, 2 H, methylene), 5.70 (m, 1 H, 3'-H), 6.70 (s, 1 H, 1'-H), 7.40 (s, 1 H, 6-H), 8.60 (br s, 1 H, 4-NH, D_2O exchangeable).

2-(2-Deoxy-2-methylene-β-D-*erythro*-pentofuranosyl)-5-amino-1,2,4-triazine-3(2*H*)-one (8). Thionyl chloride (20 mL) and dry DMF (0.1 mL) were added to a stirred solution of **6** (0.64 g, 2 mmol) in 20 mL of anhydrous $CHCl_3$. The reaction mixture was stirred under reflux for 6 h, after which it was evaporated *in vacuo* to dryness. The residue was co-evaporated twice with benzene (2 x 20 mL), then treated with 120 mL of saturated methanolic ammonia overnight. The solution was evaporated *in vacuo* to give a syrup, which was absorbed on 16 g of silica gel and chromatographed on a silica gel column (EtOAc/EtOH, 4:1, v/v) to yield 0.35 g (74%) of product as a white solid: mp 170-172 °C; TLC, R_f 0.34 (EtOAc/EtOH, 3:1, v/v); UV (MeOH) λ_{max} 266 nm (ε 10,738), λ_{min} 232 nm; UV (0.01 N HCl) λ_{max} 260 nm (ε 9,963), λ_{min} 226 nm; UV (0.01 N NaOH) λ_{max} 260 nm (ε 9,520), λ_{min} 226 nm; MS m/z 241 (MH^+); ^1H NMR (DMSO-d_6) δ 3.45-3.55 (m, 2 H, 5'-H), 3.62 (m, 1 H, 4'-H), 4.42 (m, 1 H, 3'-H), 4.70 (t, 1 H, 5'-OH, D_2O exchangeable), 5.15 [t (overlap dd), 1 H, methylene-A, J = 2.0 Hz], 5.28 [t (overlap dd), 1 H, methylene-B, J = 1.9 Hz], 5.45 (d, 1 H, 3'-OH, D_2O exchangeable), 6.60 (s, 1 H, 1'-H), 7.50 (s, 1 H, 6-H), 7.90 (br s, 1 H, 5-NH_2, D_2O exchangeable). Anal. Calcd. for $C_9H_{12}N_4O_4$: C, 45.00; H, 5.04; N, 23.32. Found: C, 44.73; H, 5.28; N, 22.97.

1-[3,5-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-2-deoxy-2-methylene-β-D-*erythro*-pentofuranosyl]-4-amino-1,3,5-triazine-2(1*H*)-one (13a) and 1-[3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2-deoxy-2-

methylene-α-D-*erythro*-pentofuranosyl]-4-amino-1,3,5-triazine-2(1*H*)-one (13b). A suspension of 5-azacytosine (1.6 g, 14 mmol) and ammonium sulfate (100 mg) in 50 mL of hexamethyldisilazane was heated to reflux temperature. After all of the solid material had dissolved (~2 h), the reaction mixture was refluxed for an additional hour. The solution was evaporated *in vacuo*, with traces of hexamethyldisilazane being removed by co-evaporation of toluene. To the remaining gum of silylated 5-azacytosine was added 3',5'-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2'-deoxy-2'-methyleneuridine[10] (**12**, 2.8 g, 5.8 mmol) in 40 mL of dichloroethane, followed by trimethylsilyl trifluoromethanesulfonate (1.4 mL, 8.0 mmol) with stirring. The mixture was stirred at room temperature overnight, then diluted with 150 mL of CH_2Cl_2 and washed with 5% sodium bicarbonate solution (50 mL), brine, and water. The organic layer was dried with anhydrous $MgSO_4$ and filtered. The filtrate was then reduced to a small volume *in vacuo* and chromatographed on a silica gel column (CH_2Cl_2/EtOAc, 4:1, v/v) to give compounds **13a** (0.55 g, 20%) and **13b** (0.90 g, 32%), respectively.

Compound **13a** was isolated as a foam: TLC, R_f 0.78 (EtOAc/EtOH, 4:1, v/v); ^1H NMR ($CDCl_3$) δ 1.02-1.12 (m, 28 H, $CHMe_2$), 3.70 (m, 2 H, 5'-H), 4.05 (m, 1 H, 4'-H), 4.85 (m, 1 H, 3'-H), 5.40-5.60 (m, 2 H, methylene), 6.10 (br s, 1 H, NH_A, D_2O exchangeable), 6.40 (s, 1 H, 1'-H), 7.50 (br s, 1 H, NH_B, D_2O exchangeable), 8.20 (s, 1 H, 6-H). Anal. Calcd. for $C_{21}H_{38}N_4O_5Si_2$: C, 52.25; H, 7.94; N, 11.61. Found: C, 52.49; H, 7.85; N, 11.34.

Compound **13b** was isolated as a foam: TLC, R_f 0.64 (EtOAc/EtOH, 4:1, v/v); ^1H NMR ($CDCl_3$) δ 1.05-1.15 (m, 28 H, $CHMe_2$), 3.35 (m, 2 H, 5'-H), 4.20 (m, 1 H, 4'-H), 4.40-4.50 (m, 2 H, methylene), 4.90 (m, 1 H, 3'-H), 5.80 (br s, 1 H, NH_A, D_2O exchangeable), 6.50 (s, 1 H, 1'-H), 7.10 (br s, 1 H, NH_B, D_2O exchangeable), 8.05 (s, 1 H, 6-H). Anal. Calcd. for $C_{21}H_{38}N_4O_5Si_2$: C, 52.25; H, 7.94; N, 11.61. Found: C, 51.92; H, 8.21; N, 11.33.

1-(2-Deoxy-2-methylene-β-D-*erythro*-pentofuranosyl)-4-amino-1,3,5-triazine-2(1*H*)-one (14a). To a stirred solution of compound **13a** (0.45 g, 0.93 mmol) in 30 mL of THF was added dropwise 3 mL of 1 M tetra-*n*-butylammonium fluoride (1 M solution in THF, 3.0 mmol) at ambient temperature. The resultant mixture was stirred for about 45 min. When TLC showed the reaction was complete, the solution was evaporated *in vacuo* to dryness and the oily residue was partitioned between CH_2Cl_2 and H_2O. The aqueous phase was co-evaporated with 3.5 g of silica gel *in vacuo* to dryness and the residue was chromatographed on a silica gel column (EtOAc/EtOH, 3:1, v/v). The product was obtained as white needles (0.18 g, 78%): mp 180-182 °C; TLC,

R_f 0.32 (EtOAc/EtOH, 4:1, v/v); UV (MeOH) λ_{max} 238 nm shoulder (ε 7,378); UV (0.01 N HCl) λ_{max} 240 nm (ε 6,118), λ_{min} 220 nm; UV (0.01 N NaOH) λ_{max} 242 nm shoulder (ε 7,378); MS m/z 241 (MH^+); ^1H NMR (DMSO-d_6) δ 3.62 (m, 2 H, 5'-H), 3.70 (m, 1 H, 4'-H), 4.55 (m, 1 H, 3'-H), 4.98 (s, 1 H, 5'-OH, D_2O exchangeable), 5.30 [t (overlap dd), 1 H, methylene-A, J = 1.5 Hz], 5.35 [t (overlap dd), 1 H, methylene-B, J = 1.3 Hz], 5.18 (br s, 1 H, 3'-OH, D_2O exchangeable), 6.35 (s, 1 H, 1'-H), 7.60 (br s, 2 H, 4-NH_2, D_2O exchangeable), 8.32 (s, 1 H, 6-H). Anal. Calcd. for $C_9H_{12}N_4O_4 \cdot 0.25H_2O$: C, 44.16; H, 5.14; N, 22.89. Found: C, 44.47; H, 4.83; N, 22.51.

1-(2-Deoxy-2-methylene-α-D-*erythro*-pentofuranosyl)-4-amino-1,3,5-triazine-2(1*H*)-one (14b). Compound **14b** was synthesized by the same procedure described for **14a** and was isolated as a white solid (0.12 g, 66%): mp 118-120 °C; TLC, R_f 0.10 (EtOAc/EtOH, 4:1, v/v); UV (MeOH) λ_{max} 240 nm shoulder (ε 7,860); UV (0.01 N HCl) λ_{max} 246 nm (ε 7,449), λ_{min} 226 nm; UV (0.01 N NaOH) λ_{max} 240 nm shoulder (ε 7,860); MS m/z 241 (MH^+); ^1H NMR (DMSO-d_6) δ 3.40 (m, 2 H, 5'-H), 4.07 (m, 1 H, 4'-H), 4.10 (s, 1 H, methylene-A), 4.35 (s, 1 H, methylene-B), 4.45 (m, 1 H, 3'-H), 4.85 (s, 1 H, 5'-OH, D_2O exchangeable), 5.12 (br s, 1 H, 3'-OH, D_2O exchangeable), 6.60 (s, 1 H, 1'-H), 7.25 (br s, 2 H, 3-NH_2, D_2O exchangeable), 8.15 (s, 1 H, 6-H). Anal. Calcd. for $C_9H_{12}N_4O_2 \cdot 0.25H_2O$: C, 44.16; H, 5.14; N, 22.89. Found: C, 44.16; H, 4.83; N, 22.51.

***N*2-Palmitoyl-3-deazaguanine (16).** Palmitoyl chloride (4.5 g, 16.4 mmol) was added dropwise to a suspension of 3-deazaguanine[7] (0.8 g, 5.3 mmol) in pyridine (30 mL) at 0-5 °C (ice bath) with stirring. The mixture was stirred at room temperature for 1 h, then evaporated to dryness. The residue was refluxed with 25 mL of ethanol for 1 h, filtered while hot, and washed with hot ethanol (3 x 10 mL) to give 1.2 g (57%) of product: mp 273-275 °C; MS m/z 389 (MH^+); UV (MeOH) λ_{max} 214 nm (ε 19,070), 270 nm (ε 18,600), 298 nm (ε 15,800); UV (0.01 N HCl) λ_{max} 212 nm (ε 23,600), 266 nm (ε 9,400), 306 nm (ε 12,100); UV (0.01 N NaOH) λ_{max} 230 nm (ε 29,000), 272 nm (ε 29,300); ^1H NMR (DMSO-d_6) δ 1.10-1.25 [m, 29 H, $(CH_2)_{13}Me$], 2.35 (m, 2 H, CH_2CO), 6.50 (s, 1 H, 7-H), 8.50 (s, 1 H, 2-H), 10.80 (br s, 1 H, NH, D_2O exchangeable), 11.70 (br s, 1 H, NH, D_2O, exchangeable), 12.75 (br s, 1 H, NH, D_2O exchangeable). Anal. Calcd. for $C_{22}H_{36}N_4O_2$: C, 68.00; H, 9.34; N, 14.42. Found: C, 68.10; H, 9.56; N, 14.30.

6-Palmitoylamino-1-[2-deoxy-2-methylene-3,5-*O*-(1,1,3,3,-tetraisopropyldisiloxane-1,3-diyl)-β-D-*erythro*-pentofuranosyl]-1,5-

dihydro-4*H*-imidazo[4,5-c]pyridin-4(5*H*)-one (17a) and 6-palmitoylamino-1-[2-deoxy-2-methylene-3,5-*O*-(1,1,3,3,-tetraisopropyldisiloxane-1,3-diyl)-α-D-*erythro*-pentofuranosyl]-1,5-dihydro-4*H*-imidazo[4,5-c]pyridin-4(5*H*)-one (17b). A suspension of N^2-palmitoyl-3-deazaguanine (**16**, 0.88 g, 2.3 mmol), compound **12** (1.0 g, 2.1 mmol), and ammonium sulfate (50 mg) in hexamethyldisilazane (40 mL) was refluxed overnight with careful exclusion of moisture to give a clear solution. After the cooled solution was evaporated *in vacuo*, trace amounts of hexamethyldisilazane were removed by co-evaporation with toluene. The residue was dissolved in 20 mL of anhydrous dichloroethane, followed by 0.5 mL (2.9 mmol) of trimethylsilyl trifluoromethanesulfonate. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2 (80 mL), then stirred with 5% sodium bicarbonate (20 mL). The mixture was filtered, and the organic layer was separated, washed with water, dried with anhydrous $MgSO_4$, and evaporated *in vacuo*. The residue (1.8 g) was dissolved in a small amount of CH_2Cl_2 and applied to a silica gel column, eluted first with 1000 mL of CH_2Cl_2/EtOAc (4:1, v/v), then 1000 mL each of 2, 3, 4, and 5% EtOH in CH_2Cl_2/EtOAc (4:1, v/v). Five UV active fractions were collected, and each of these fractions was evaporated to dryness. The fastest running spot was identified as the starting material **12**; the second was the α-anomer of (**12**); the third was a mixture of **17c** and **17d**; the fourth was **17a**; and the fifth was **17b**.

Compound **17a** was isolated as a white solid (0.25 g, 15%): mp 135-137 °C; TLC, R_f 0.71 (EtOAc/EtOH, 10:1, v/v); UV (MeOH) λ_{max} 212 nm (ε 36,700), 270 nm (ε 25,500), 300 nm (ε 24,700); UV (0.01 N HCl) λ_{max} 212 nm (ε 32,800), 290 nm (ε 21,800); UV (0.01 N NaOH) λ_{max} 215 nm (ε 30,700), 286 nm (ε 18,500); MS m/z 759(M); ^{1}H NMR (DMSO-d_6) δ 1.05-1.15 (m, 28 H, $CHMe_2$), 1.20-1.30 [m, 29 H, $(CH_2)_{13}Me$], 2.40 (m, 2 H, CH_2CO), 3.85 (m, 2 H, 5'-H), 4.05 (m, 1 H, 4'-H), 4.90 (m, 1 H, 3'-H), 5.50 and 5.62 (m, 2 H, methylene), 6.45 (s, 1 H, 7-H), 7.30 (s, 1 H, 1'-H), 7.80 (s, 1 H, 2-H), 10.70 and 11.90 (br s, 2 H, 5- and 6-NH, D_2O exchangeable). Anal. Calcd. for $C_{40}H_{70}N_4O_6Si_2$: C, 63.28; H, 9.29; N, 7.38. Found: C, 62.96; H, 9.20; N, 7.14.

Compound **17b** was isolated as a white solid (0.12 g, 7%): mp 150-152 °C; TLC, R_f 0.60 (EtOAc/EtOH, 10:1, v/v); UV (MeOH) λ_{max} 213 nm (ε 32,330), 271 nm (ε 24,600), 300 nm (ε 23,200); UV (0.01 N HCl) λ_{max} 212 nm (ε 31,000), 288 nm (ε 21,000); UV (0.01 N NaOH) λ_{max} 215 nm (ε 30,000), 286 nm (ε 18,400); MS m/z 759(M); ^{1}H NMR (DMSO-d_6) δ 1.00-1.15 (m, 28 H, $CHMe_2$), 1.20-1.30 [m, 29 H, $(CH_2)_{13}Me$], 2.42 (m, 2 H, CH_2CO), 3.70 (m, 2 H, 5'-H), 4.45 (m, 1 H, 4'-H), 4.90

(m, 2 H, methylene), 5.10 (m, 1 H, 3'-H), 6.50 (s, 1 H, 7-H), 7.15 (s, 1 H, 1'-H), 7.70 (s, 1 H, 2-H), 10.70 and 11.80 (br s, 2 H, 5- and 6-NH, D_2O exchangeable). Anal. Calcd. for $C_{40}H_{70}N_4O_6Si_2$: C, 63.28; H, 9.29; N, 7.38. Found: C, 63.10; H, 9.06; N, 7.10.

6-Palmitoylamino-3-[2-deoxy-2-methylene-3,5-*O*-(1,1,3,3,-tetraisopropyldisiloxane-1,3-diyl)-β-D-*erythro*-pentofuranosyl]-3,5-dihydro-4*H*-imidazo[4,5-c]pyridin-4(5*H*)-one (17c) and 6-palmitoylamino-3-[2-deoxy-2-methylene-3,5-*O*-(1,1,3,3,-tetraisopropyldisiloxane-1,3-diyl)-α-D-*erythro*-pentofuranosyl]-3,5-dihydro-4*H*-imidazo[4,5-c]pyridin-4(5*H*)-one (17d). The mixture of **17c** and **17d** from the third fractions of the preceding reaction was isolated by chromatography on a silica gel column (CH_2Cl_2/EtOAc, 1:1, v/v). Compound **17c** was isolated as a foam (0.18 g, 11%): TLC, R_f 0.70 (CH_2Cl_2/EtOAc, 1:1, v/v); UV (MeOH) λ_{max} 224 nm (ε 34,500), 279 nm (ε 23,000), 310 nm (ε 20,200); UV (0.01 N HCl) λ_{max} 224 nm (ε 32,200), 280 nm (ε 21,000), 312 nm (ε 18,200); UV (0.01 N NaOH) λ_{max} 226 nm (ε 31,200), 281 nm (ε 21,000), 313 nm (ε 14,200); MS m/z 759 (M); ^{1}H NMR (DMSO-d_6) δ 1.00-1.15 (m, 28 H, $CHMe_2$), 1.20-1.30 [m, 29 H, $(CH_2)_{13}Me$], 2.42 (m, 2 H, CH_2CO), 3.90 (m, 2 H, 5'-H), 4.15 (m, 1 H, 4'-H), 4.85 (m, 1 H, 3'-H), 5.44 and 5.65 (m, 2 H, methylene), 6.50 (s, 1 H, 7-H), 7.25 (s, 1 H, 1'-H), 8.00 (s, 1 H, 2-H), 10.20 and 12.20 (br s, 2 H, 5- and 6-NH, D_2O exchangeable). Anal. Calcd. for $C_{40}H_{70}N_4O_6Si_2$: C, 63.28; H, 9.29; N, 7.38. Found: C, 63.05; H, 9.40; N, 7.08.

Compound **17d** was isolated as a foam (0.15 g, 9%): TLC, R_f 0.50 (CH_2Cl_2/EtOAc, 1:1, v/v); UV (MeOH) λ_{max} 224 nm (ε 35,000), 280 nm (ε 27,700), 310 nm (ε 23,100); UV (0.01 N HCl) λ_{max} 224 nm (ε 33,000), 280 nm (ε 22,000), 312 nm (ε 17,800); UV (0.01 N NaOH) λ_{max} 227 nm (ε 31,000), 281 nm (ε 20,500), 313 nm (ε 12,200); MS m/z 759 (M); ^{1}H NMR (DMSO-d_6) δ 1.00-1.20 (m, 28 H, $CHMe_2$), 1.24-1.30 [m, 29 H, $(CH_2)_{13}Me$], 2.40 (m, 2 H, CH_2CO), 3.80 (m, 2 H, 5'-H), 4.50 (m, 1 H, 4'-H), 5.10-5.25 (m, 3 H, 3'-H and methylene), 6.18 (s, 1 H, 7-H), 6.70 (s, 1 H, 1'-H), 7.82 (s, 1 H, 2-H), 10.42 and 12.20 (br s, 2 H, 5- and 6-NH, D_2O exchangeable). Anal. Calcd. for $C_{40}H_{70}N_4O_6Si_2$: C, 63.28; H, 9.29; N, 7.38. Found: C, 62.90; H, 9.08; N, 7.10.

6-Palmitoylamino-1-[2-deoxy-2-methylene-β-D-*erythro*-pentofuranosyl]-1,5-dihydro-4*H*-imidazo[4,5-c]pyridin-4(5*H*)-one (18a). To a stirred solution of compound **17a** (0.24 g, 0.41 mmol) in THF was added dropwise 1 mL of tetra-*n*-butylammonium fluoride (1 M solution in THF, 1 mmol) at ambient

temperature. The reaction was completed after 1 h, and the solvent was evaporated *in vacuo* to dryness. The residue was dissolved in a small amount of CH_2Cl_2 and purified on a silica gel column (EtOAc/EtOH, 2:1, v/v) to yield 0.12 g (74%) of product as a white solid: mp 187-189 °C; TLC, R_f 0.80 (CH_2Cl_2/EtOH, 2:1, v/v); UV (MeOH) λ_{max} 210 nm (ε 35,500), 270 nm (ε 24,500), 300 nm (ε 24,200); UV (0.01 N HCl) λ_{max} 212 nm (ε 30,200), 290 nm (ε 21,000); UV (0.01 N NaOH) λ_{max} 214 nm (ε 30,100), 286 nm (ε 18,300); MS m/z 517 (MH^+); ^1H NMR (DMSO-d_6) δ 1.15-1.30 [m, 29 H, $(CH_2)_{13}Me$], 2.40 (m, 2 H, CH_2CO), 3.60 (m, 2 H, 5'-H), 3.88 (m, 1 H, 4'-H), 4.50 (m, 1 H, 3'-H), 4.85 (t, 1 H, 5'-OH, D_2O exchangeable), 5.15 (m, 1 H, methylene-A) 5.50 (m, 1 H, methylene-B), 5.82 (d, 1 H, 3'-OH, D_2O exchangeable), 6.54 (s, 1 H, 7-H), 6.55 (s, 1 H, 1'-H), 8.00 (s, 1 H, 2-H), 10.40 and 11.10 (br s, 2 H, 5- and 6-NH, D_2O exchangeable). Anal. Calcd. for $C_{28}H_{44}N_4O_5$: C, 65.09; H, 8.58; N, 10.84. Found: C, 64.81; H, 8.30; N, 10.45.

Compounds **18b-18d** were synthesized by methodology similar to that described for the preparation of compound **18a**.

6-Palmitoylamino-1-[2-deoxy-2-methylene-α-D-*erythro*-pentofuranosyl]-1,5-dihydro-4*H*-imidazo[4,5-c]pyridin-4(5*H*)-one (18b). Compound **18b** was isolated as a white solid (0.057 g, 83%): mp 194-196 °C; TLC, R_f 0.72 (CH_2Cl_2/EtOH, 2:1, v/v); UV (MeOH) λ_{max} 212 nm (ε 31,230), 271 nm (ε 22,200), 300 nm (ε 21,800); UV (0.01 N HCl) λ_{max} 212 nm (ε 30,600), 289 nm (ε 20,900); UV (0.01 N NaOH) λ_{max} 214 nm (ε 30,000), 286 nm (ε 18,200); MS m/z 517 (MH^+); ^1H NMR (DMSO-d_6) δ 1.20-1.31 [m, 29 H, $(CH_2)_{13}Me$], 2.35 (m, 2 H, CH_2CO), 3.35 (m, 2 H, 5'-H), 4.10 (m, 1 H, 4'-H), 4.30 (m, 1 H, 3'-H), 4.70 (t, 1 H, 5'-OH, D_2O exchangeable), 4.80 (m, 2 H, methylene), 5.20 (d, 1 H, 3'-OH, D_2O exchangeable), 6.55 (s, 1 H, 7-H), 7.02 (s, 1 H, 1'-H), 7.80 (s, 1 H, 2-H), 10.30 and 11.00 (br s, 2 H, 5- and 6-NH, D_2O exchangeable). Anal. Calcd. for $C_{28}H_{44}N_4O_5$: C, 65.09; H, 8.58; N, 10.84. Found: C, 64.80; H, 8.35; N, 10.56.

6-Palmitoylamino-3-[2-deoxy-2-methylene-β-D-*erythro*-pentofuranosyl]-3,5-dihydro-4*H*-imidazol[4,5-c]pyridin-4(5*H*)-one (18c). Compound **18c** was isolated as a white solid (0.12 g, 74%): mp 175-177 °C; TLC, R_f 0.50 (CH_2Cl_2/EtOH, 6:1, v/v); UV (MeOH) λ_{max} 223 nm (ε 33,000), 278 nm (ε 20,300), 310 nm (ε 18,000); UV (0.01 N HCl) λ_{max} 220 nm (ε 19,000), 285 nm (ε 12,000); UV (0.01 N NaOH) λ_{max} 224 nm (ε 29,000), 285 nm (ε 15,600); MS m/z 517 (MH^+); ^1H NMR (DMSO-d_6) δ 1.18-1.35 [m, 29 H, $(CH_2)_{13}Me$], 2.37 (m, 2 H, CH_2CO), 3.68 (m, 2 H, 5'-H), 4.05 (m, 1 H, 4'-H), 5.52 (m, 1 H, 3'-H), 4.90 (t, 1 H, 5'-OH, D_2O

exchangeable), 5.30-5.55 (m, 2 H, methylene), 5.70 (d, 1 H, 3'-OH, D_2O exchangeable), 6.42 (s, 1 H, 7-H), 7.23 (s, 1 H, 1'-H), 8.30 (s, 1 H, 2-H), 10.45 and 11.00 (br s, 2 H, 5- and 6-NH, D_2O exchangeable). Anal. Calcd. for $C_{28}H_{44}N_4O_5$: C, 65.09; H, 8.58; N, 10.84. Found: C, 64.88; H, 8.37; N, 10.70.

6-Palmitoylamino-3-[2-deoxy-2-methylene-α-D-*erythro*-pentofuranosyl)]-3,5-dihydro-4*H*-imidazol[4,5-c]pyridin-4(5*H*)-one (18d). Compound **18d** was isolated as a white solid (0.08 g, 84%): mp 180-182 °C; TLC, R_f 0.17 (CH_2Cl_2/EtOH, 10:1, v/v); UV (MeOH) λ_{max} 224 nm (ε 34,700), 277 nm (ε 22,300), 310 nm (ε 18,900); UV (0.01 N HCl) λ_{max} 220 nm (ε 20,000), 286 nm (ε 13,000); UV (0.01 N NaOH) λ_{max} 224 nm (ε 30,000), 285 nm (ε 16,000); MS m/z 517 (MH^+); ^1H NMR (DMSO-d_6) δ 1.12-1.32 [m, 29 H, $(CH_2)_{13}Me$], 2.37 (m, 2 H, CH_2CO), 3.32 (m, 2 H, 5'-H), 4.20 (m, 1 H, 4'-H), 4.46 (m, 1 H, 3'-H), 4.85 (t, 1 H, 5'-OH, D_2O exchangeable), 5.08 (m, 2 H, methylene), 5.22 (d, 1 H, 3'-OH, D_2O exchangeable), 6.32 (s, 1 H, 7-H), 6.70 (s, 1 H, 1'-H), 8.02 (s, 1 H, 2-H), 10.40 and 11.80 (br s, 2 H, 5- and 6-NH, D_2O exchangeable). Anal. Calcd. for $C_{28}H_{44}N_4O_5$: C, 65.09; H, 8.58; N, 10.84. Found: C, 65.20; H, 8.69; N, 10.70.

6-Amino-1-[2-deoxy-2-methylene-β-D-*erythro*-pentofuranosyl]-1,5-dihydro-4*H*-imidazol[4,5-c]pyridin-4(5*H*)-one (19a). Compound **18a** (0.098 g, 0.19 mmol) in 60 mL of saturated methanolic ammonia solution was heated at 95-100 °C in a steel bomb for 18 h. The cooled reaction mixture was evaporated to dryness, and the residue was purified on a silica gel column (EtOH/EtOAc, 2:1, v/v) to yield 0.035 g (66%) of product as a white solid: mp 220-222 °C; TLC, R_f 0.20 (EtOH/EtOAc, 2:1, v/v); UV (MeOH) λ_{max} 210 nm (ε 15,580), 270 nm (ε 18,800), 305 nm (ε 14,200); UV (0.01 N HCl) λ_{max} 215 nm (ε 17,500), 285 nm (ε 16,700); UV (0.01 N NaOH) λ_{max} 218 nm (ε 14,300), 274 nm (ε 15,300), 305 nm (ε 11,700); MS m/z 279 (MH^+); ^1H NMR (DMSO-d_6) δ 3.56 (m, 2 H, 5'-H), 3.79 (m, 1 H, 4'-H), 4.42 (m, 1 H, 3'-H), 4.89 (t, 1 H, 5'-OH, D_2O exchangeable), 5.12 [t (overlap dd), 1 H, methylene-A, J = 1.4 Hz], 5.47 [t, (overlap dd, 1 H, methylene-B, J = 1.3 Hz), 5.49 (s, 1 H, 7-H), 5.65 (br s, 2 H, 6-NH_2, D_2O exchangeable), 5.82 (d, 1 H, 3'-OH, D_2O exchangeable), 6.39 (s, 1 H, 1'-H), 7.71 (s, 1 H, 2-H), 10.38 (br s, 1 H, 5-NH, D_2O exchangeable). Anal. Calcd. for $C_{12}H_{14}N_4O_4$: C, 51.79; H, 5.07; N, 20.14. Found: C, 51.43; H, 5.44; N, 20.09.

6-Amino-1-[2-deoxy-2-methylene-α-D-*erythro*-pentofuranosyl]-1,5-dihydro-4*H*-imidazol[4,5-c]pyridin-4(5*H*)-one (19b). Compound **19b** was synthesized from compound **18b** (0.052 g, 0.1 mmol) by the methodology described for the synthesis of compound **19a**. Compound **19b** was isolated as a white solid (0.028 g,

64%): mp 225-227 °C; TLC, R_f 0.32 (EtOH/EtOAc, 2:1, v/v); UV (MeOH) λ_{max} 212 nm (ε 16,080), 271 nm (ε 18,000), 306 nm (ε 14,000); UV (0.01 N HCl) λ_{max} 215 nm (ε 17,000), 284 nm (ε 16,200); UV (0.01 N NaOH) λ_{max} 216 nm (ε 13,900), 273 nm (ε 15,000), 304 nm (ε 11,400); MS m/z 279 (MH^+); ^1H NMR (DMSO-d_6) δ 3.27 (m, 2 H, 5'-H), 4.00 (m, 1 H, 4'-H), 4.34 (m, 1 H, 3'-H), 4.85 (t, 1 H, 5'-OH, D_2O exchangeable), 5.05 (m, 2 H, methylene H), 5.43 (s, 1 H, 7-H), 5.60 (br s, 2 H, 6-NH_2, D_2O exchangeable), 5.75 (d, 1 H, 3'-OH, D_2O exchangeable), 6.67 (s, 1 H, 1'-H), 7.50 (s, 1 H, 2-H), 10.28 (br s, 1 H, 5-NH, D_2O exchangeable). Anal. Calcd. for $C_{12}H_{14}N_4O_4$: C, 51.79; H, 5.07; N, 20.14. Found: C, 51.49; H, 5.20; N, 19.88.

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