C(5a)H), 3.89–3.54 (m, 2 H, C(3)H_2), 3.82 (s, 3 H, OCH_3), 2.53–1.71 (m, 6 H, C(1')H_2, C(4)–C(5)H_2), 2.00 (br s, 1 H, OH), 1.42 and 1.18 (2×s, 6 H, 2×CH_3).

Compound 30: R_f 0.43 (EtOAc); UV (MeOH) λ_{max} 217, 236, 272, 285 (sh), 304 (sh), 317 (sh), 335, 354 nm; EIMS (70 eV) m/z (relative intensity) 393 (M^+, 18), 252 (100), 222 (86); ^1H NMR δ 8.38 (s, 1 H, C(14)H), 7.93 (d, 1 H, C(13)H), 6.96 (s, 1 H, C(10)H), 6.90 (d, 1 H, C(12)H), 4.13 (m, 1 H, C(5a)H), 3.98–3.71 (m, 2 H, C(3)H_2), 3.86 (s, 3 H, OCH_3), 3.57 and 3.18 (AB spectrum, 2 H, ^2J = 14.5 Hz, C(15)H_2), 2.23–1.75 (m, 4 H, C(4)H_2–C(5)H_2), 1.61 and 1.24 (2×s, 6 H, 2×CH_3).

(-)-Verrucculogen TR-2 (2). To a stirred and cooled (0 °C) solution of the dehydro compound **6** (5 mg, 0.0127 mmol) in dry pyridine (0.5 mL) was added a solution of osmium tetroxide (100 μL, 0.0195 M in pyridine, 0.0195 mmol). The resulting orange-colored solution was stirred at 0 °C for 2 h and was then treated with saturated aqueous $NaHSO_3$ (0.5 mL). This reaction mixture was stirred at room temperature for 30 min, after which the aqueous layer was separated. The mixture was extracted with chloroform. The organic layer was washed with brine and subsequently dried (Na_2SO_4) and concentrated to dryness. The residue was subjected to column chromatography ($CHCl_3$/MeOH (97/3), v/v) to give 1.2 mg (22%) of **2**: oil; R_f 0.39 ($CHCl_3$/MeOH (93/7), v/v); $[\alpha]_D$ -45° (c = 0.55, CH_2Cl_2); EIMS (70 eV) 429, (M^+, 4), 411 (8), 335 (45), 278 (47), 219 (100); exact mass for $C_{22}H_{27}N_3O_6$ calcd 429.1912, found 429.1910; UV (methanol) λ_{max} 224, 267, 295 nm; ^1H NMR (200 MHz, $CDCl_3$) δ 9.04 (br s, 1 H, NH), 7.82 (d, 1 H, C(13)H), 6.86–6.77 (m, 2 H, C(10)H and C(12)H), 5.72 (d, 1 H, J = 2.9 Hz, C(14)H), 5.46 (dd, 1 H, J_{AX} + J_{BX} = 11.2 Hz, C(8)H, 4.60 (d, 1 H, J = 2.9 Hz, C(14)OH, 4.45 (m, 1 H, C(5a)H), 4.02 (s, 1 H, C(14a)OH), 3.85 (s, 3 H, OCH_3), 3.70–3.61 (m, 2 H, C(3)H_2), 2.51 and 2.12–1.65 (m, 7 H, C(1')H_2, C(4)–C(5)H_2), 1.25 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3); (90 MHz, DMSO-d_6) δ 10.55 (br s, 1 H, NH), 7.60 (d, 1 H, J = 9 Hz, C(13)H), 6.83 (s, 1 H, C(10)H), 6.58 (d, 1 H, J = 9 Hz, C(12)H), 6.13 (br s, 1 H, OH), 5.48 (d, 1 H, C(14)H), 5.32 (m, 1 H, C(8)H, 5.16 (d, 1 H, C(14)OH), 4.33 (m, 1 H, C(5a)H), 4.17 (br s, 1 H, OH), 3.70 (s, 3 H, OCH_3), 3.55 (m, 2 H, C(3)H_2), 2.36–1.60 (m, 6 H, C(1')H_2, C(4)–C(5)H_2), 1.09 and 0.94 (2×s, 6 H, 2× CH_3).

Supplementary Material Available: Spectroscopic data (^1H NMR, MS) for compounds **2**, **6**, and **26–30** (14 pages). This material is contained in many 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.

A Highly Stereoselective Synthesis of Anti-HIV 2',3'-Dideoxy- and 2',3'-Didehydro-2',3'-dideoxynucleosides[1]

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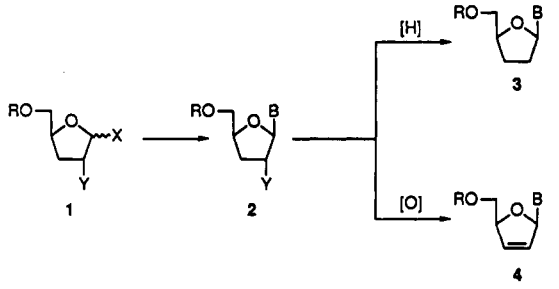
A general total synthetic method for the stereocontrolled synthesis of 2',3'-dideoxy- as well as 2',3'-didehydro-2',3'-dideoxynucleosides is presented. Introduction of an α-phenylselenenyl group at the 2-position of 2,3-dideoxyribosyl acetate directs the glycosyl bond formation to give ≥95% β-isomer. This 2'-phenylselenenyl nucleoside may be converted to either the 2',3'-dideoxynucleoside by treatment with n-Bu_3SnH and Et_3B at room temperature or to the unsaturated derivative by treatment with H_2O_2/cat. pyridine. The application of this method to the syntheses of pyrimidines (ddU, ddT, ddC), 6-substituted purines (ddA, ddI, 6-chloro-ddP, N^6-Me-ddA), and 2,6-disubstituted purines (2-F-ddA, 6-chloro-2-amino-ddP) as well as selected 2',3'-didehydro-2',3'-dideoxy derivatives is reported.

Since the discovery of 2',3'-dideoxy- and 2',3'-didehydro-2',3'-dideoxynucleosides such as 2',3'-dideoxycytidine (ddC),[2] 2',3'-dideoxyadenosine (ddA),[2] 2',3'-dideoxyinosine (ddI),[3] and 3'-deoxy-2',3'-didehydrothymidine (d4T)[4-6] as anti-HIV agents, a number of laboratories, including ours, have been interested in developing efficient syntheses of these nucleosides. The simplest synthetic method for these nucleosides is the deoxygenation of the 3'-hydroxyl group of 5'-protected 2'-deoxynucleosides.[7] However, this method may not be economically feasible due to the limited availability as well as expense of the starting material, 2'-deoxynucleosides. As part of our effort to develop practical methods for anti-HIV nucleosides, we have reported a general synthetic method for the 2',3'-dideoxy- and 2',3'-didehydro-2',3'-dideoxynucleosides from

Scheme I



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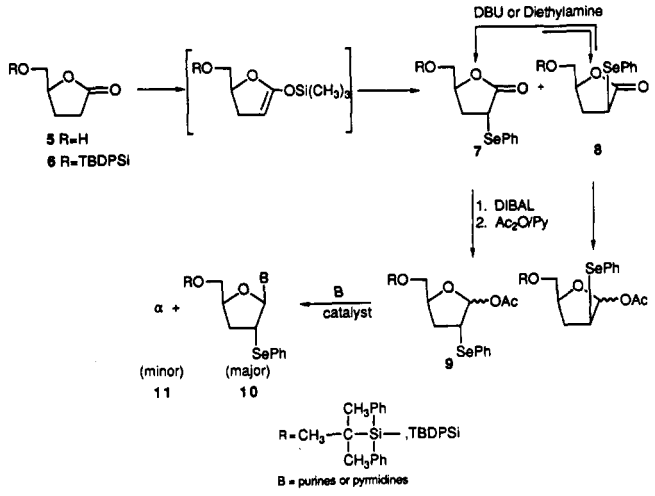
Scheme II



the corresponding ribonucleosides.[8] Although several total synthetic methods for these nucleosides have been reported in the literature, they have drawbacks, primary of which is the production of varying ratios of an α,β-mixture[9-11] requiring tedious and expensive chromatographic separation. Furthermore, these methods may not be applicable to large commercial-scale production to meet the demands for clinical trials and beyond, due to the need for column separation. Thus, we have been interested in developing an efficient and practical synthesis of the aforementioned anti-HIV nucleosides by a total synthetic approach. As indicated, the major drawback of previous total synthetic approaches is the formation of anomeric mixtures due to the lack of stereoselectivity during the condensation between the 2,3-dideoxysugar and heterocycles. In order to improve the condensation ratio in favor of the β-isomer we initially envisioned a bulky substituent at the $C_3\alpha$ position.[10] It was hoped that the bulky group would tend to block the α-face and thus improve the formation of the β-isomer. However, the condensation of $C_3\alpha$ phenylsulfenyl 1-acetate derivative gave a disappointing α/β (1:1) ratio.[10] In order to overcome the poor stereoselectivity, our attention turned to introducing a group "Y" at the 2-position,[12] which could result in the desired β stereoselectivity during the condensation of the carbohydrate 1 and heterocycle by providing bulkiness as well as a neighboring group effect, which prevents approach from the α-face (Scheme I).

Furthermore, the "Y" moiety should be readily removable by mild chemical reactions to obtain the desired nucleosides 3 and 4. For this purpose a phenylselenenyl group seemed to be an ideal choice due to its facile oxidative elimination (H_2O_2/cat. pyridine)[13] as well as reductive removal (n-Bu_3SnH/Et_3B)[14] under mild conditions.

In our previous paper we reported the syntheses of 3'-deoxythymidine and 3'-deoxy-2',3'-didehydrothymidine (d4T) using this methodology.[1] We now wish to report the details of the synthesis as well as the use of the method to demonstrate its general utility for the synthesis of other anti-HIV nucleosides such as ddC, ddI, ddA, and N^6-Me-ddA.

Our initial attempts to introduce the phenylselenenyl group at the C2-position of lithium enolate of lactone 6 (Scheme II) gave a poor α/β ratio as well as a low overall yield of the phenylselenenyl lactones 7 and 8. In order to overcome this difficulty we turned to the use of a silyl enol ether to react with the phenylselenenyl bromide. The enol ether was prepared in situ by first treating the lactone at −78 °C with lithium hexamethyldisilazide (LiHMDS) followed by addition of chlorotrimethylsilane[15] and allowing the reaction mixture to reach room temperature. The reaction mixture was again cooled to −78 °C, and phenylselenenyl bromide was rapidly added. Chromatographic separation of the reaction mixture gave the $C_2\alpha$-isomer 7 in 65% yield and the $C_2\beta$-isomer 8 in 30% yield (overall yield 95%). It is interesting to note that the $C_2\beta$-isomer 8 could be equilibrated by treatment with bases such as DBU or diethylamine to a mixture of the α- and β-isomer ($\alpha:\beta$ = 61:39) which could be readily separated to give the $C_2\alpha$ isomer 7 in 83% overall yield after one equilibration. Reduction of the desired lactone 7 with DIBAL-H at −78 °C followed by acetylation with Ac_2O/pyridine/DMAP in CH_2Cl_2 at 0 °C gave the key intermediate 9. The acetate 9 was found to be unstable to silica gel chromatography, which caused deacetylation. The lactol from the DIBAL-H reduction of 7 was found to partially undergo isomerization to the lactol of 8 on silica gel. Due to these problems the lactol of 7 and acetate 9 could not be purified. However, this step was found to be unnecessary for the condensation reaction of 9 with heterocycles.

In the condensation of the acetate 9 with various heterocyclic bases it was found that, in general, for pyrimidine bases the anomeric selectivity was high (99%) without paying special attention to temperature or time of reaction. In contrast, for purine bases, especially 6-chloropurine, both temperature and time of reaction played a critical role in the anomeric selectivity and gave slightly lower selectivity (95%) (Schemes III and IV). The condensation was usually carried out in 1,2-dichloroethane, initially cooling to 0 °C for pyrimidines and −20 °C for purines in the presence of trimethylsilyl triflate (TMSOTf). The small amounts of α-anomer produced were not fully characterized. Assignment of the anomeric configuration was based on the chemical shift of the β-anomeric protons in the NMR spectra, which were upfield relative to the α-anomeric signals. Furthermore, the 4'-proton of the β-anomers appeared upfield from that observed for the α-anomer and the 5'-protons of the β-anomer appeared downfield from those observed for the α anomers.[9a,16] The ultimate proof of these assignments was the agreement of the physical data for the final compounds with the published data or comparison with authentic samples.

Reaction of the acetate 9 with silylated thymine, uracil, or N^4-acetylcytosine (Scheme III) in 1,2-dichloroethane or CH_2Cl_2 in the presence of TMSOTf gave 70–80% yield of the respective 2'-phenylselenenyl-substituted nucleosides in high stereoselectivity. The phenylselenenyl group at the 2' position could be removed under mild conditions (n-Bu_3SnH/Et_3B, rt) followed by deprotection to give the

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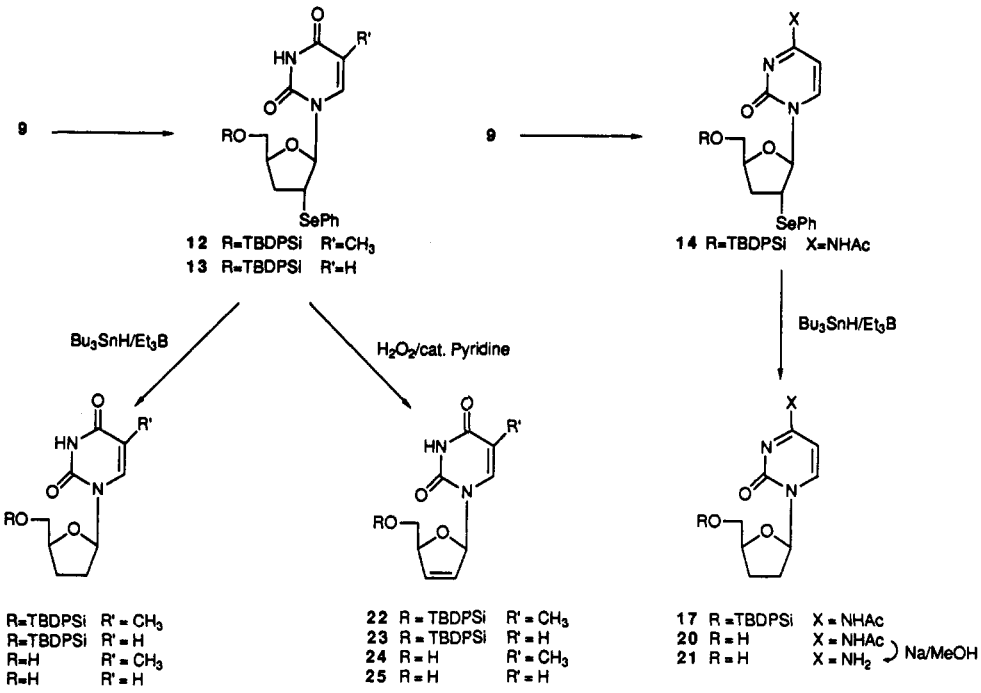
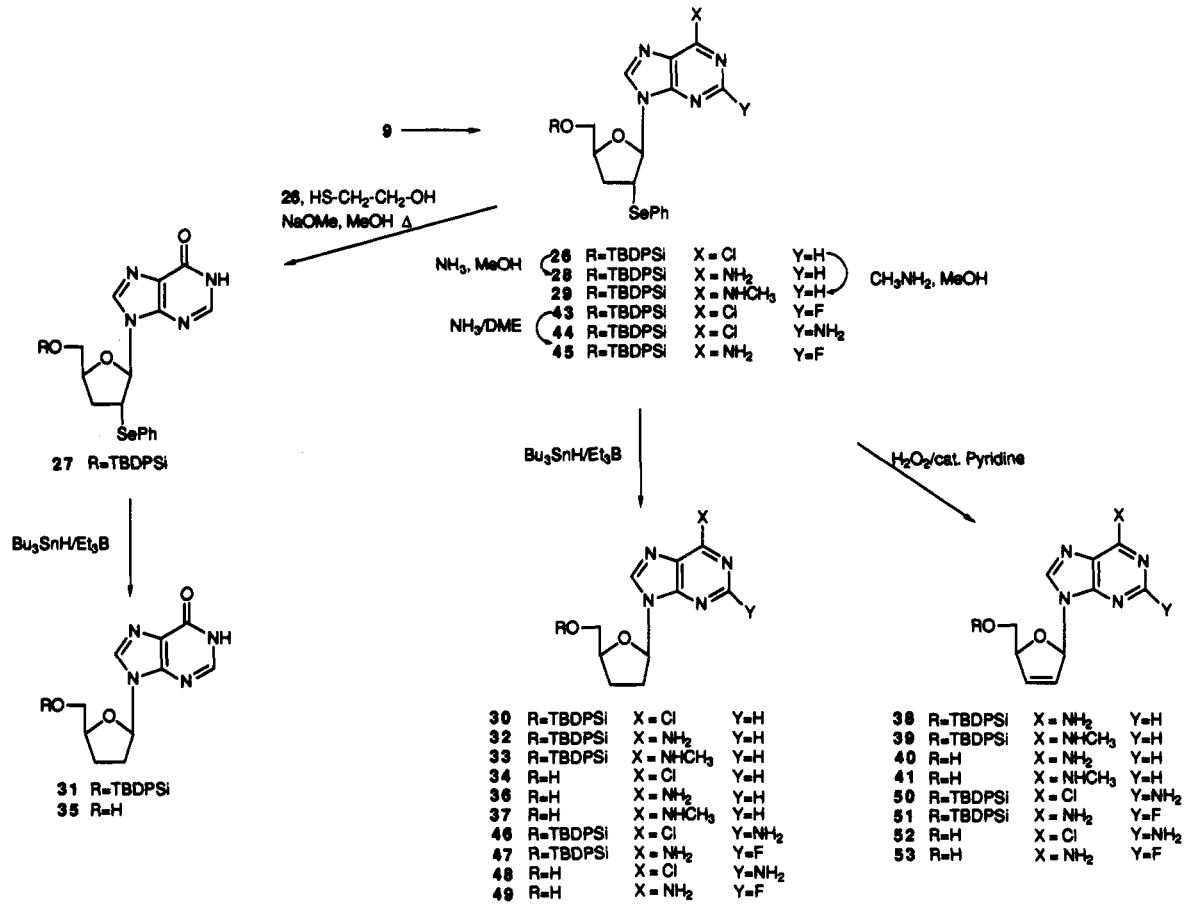
Scheme III



Scheme IV



2′,3′-dideoxynucleoside in good yield. Furthermore, 2′,3′-didehydro-2′,3′-dideoxynucleosides could also be prepared under mild oxidation conditions (H_2O_2, cat. pyridine, rt).

As mentioned previously condensation of the acetate **9** with silylated 6-chloropurine in 1,2-dichloroethane in the presence of TMSOTf gave the desired β-6-chloropurine selenenyl nucleoside **26** (Scheme IV) as a crystalline solid after chromatography in 90% yield. This material was used as the common precursor of ddI **35**, ddA **36**, and N^6-Me-ddA **37** as well as 6-chloropurine nucleoside **34**.

Treatment of the β-6-chloropurine selenenyl nucleoside **26** with 2-mercaptoethanol and sodium methoxide under reflux in MeOH cleanly converted the 6-chloropurine to inosine derivative **27**. In a similar manner, ddA **28** and N^6-Me-ddA **29** derivatives were prepared by treatment of

the 6-chloro derivative **26** with NH_3 or CH_3NH_2, respectively, in MeOH in a bomb at 80–100 °C. The phenylselenenyl group could be readily removed from all of the above compounds by treatment with Bu_3SnH/Et_3B in benzene at room temperature followed by silyl deprotection to give 6-Cl-ddP **34**, ddI **35**, ddA **36**, and N^6-Me-ddA **37**. The ddA **28** and N^6-Me ddA **29** derivatives on treatment with H_2C_2/cat. pyridine followed by silyl deprotection gave d4A **40** and d4N^6-Me-A **41**.

In a similar fashion silylated 6-chloro-2-fluoropurine was condensed with acetate **9** to give the silylated 6-chloro-2-fluoropurine nucleoside **43** in ~75% yield (Scheme IV). This compound on treatment with NH_3 in DME gave the 2-amino-6-chloro derivative **44** and the 6-amino-2-fluoro derivative **45** in 52% and 28% yields,[17] respectively. Both compounds could be converted to the dideoxynucleoside by the treatment with n-Bu_3SnH/Et_3B in benzene at room temperature followed by deprotection to give **48** and **49**. Compounds **44** and **45** were converted to their unsaturated derivatives by treatment with H_2O_2/pyridine followed by deprotection to give compounds **52** and **53**.

In summary, we have developed a highly stereocontrolled glycosylation reaction for the synthesis of 2′,3′-dideoxy- and 2′,3′-didehydro-2′,3′-dideoxynucleosides by a total synthetic method and demonstrated its general utility by synthesizing various anti-HIV nucleosides.

Experimental Section

Melting points were determined on a Mel-temp II and are uncorrected. ^1H NMR spectra were recorded on a JEOL FX 90Q fourier transform spectrometer for 90-MHz ^1H NMR spectra or a Bruker 250AM for 250-MHz with Me_4Si as internal standard: chemical shifts are reported in parts per million (δ), and signals are quoted as s (singlet), d (doublet), t (triplet), q (quartet) or m (multiplet). Spectra were acquired on the 90-MHz instrument unless otherwise indicated. UV spectra were obtained on a Beckman DU-7 spectrophotometer. Optical rotations were measured on a Jasco DIP-370 Digital Polarimeter. TLC was performed on Uniplates (silica gel) purchased from Analtech Co. Column chromatography was performed using either silica gel 60 (220–440 mesh) for flash chromatography or silica gel G (TLC grade >440 mesh) for vacuum flash chromatography. Elemental analyses were performed by Atlantic Microlab Inc., Norcross, GA, or Galbraith Laboratories, Inc., Knoxville, TN. Dry 1,2-dichloroethane and methylene chloride were distilled from CaH_2. Dry tetrahydrofuran was distilled from Na/benzophenone.

5-*O*-(*tert*-Butyldiphenylsilyl)-2,3-dideoxy-D-*glycero*-pentonic Acid γ-Lactone (6). To a stirred solution of the lactone 5[18] (10.51 g, 90.6 mmol) in dry DMF (100 mL) under argon was added imidazole (13.87 g, 203.7 mmol) followed by slow addition of *tert*-butyldiphenylsilyl chloride (27.39 g, 99.6 mmol). The reaction mixture was stirred for 1 h at room temperature, and then the DMF was removed under reduced pressure. The residue was dissolved in $CHCl_3$ (150 mL), washed with water and brine, dried (Na_2SO_4), filtered, and concentrated to give the crude silyl derivative (31 g) as an oil. Crystallization from hot n-hexane gave **6** as a white solid (29.97 g, 98%).

5-*O*-(*tert*-Butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-D-*erythro*-pentonic Acid γ-Lactone (7) and 5-*O*-(*tert*-Butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-D-*threo*-pentonic Acid γ-Lactone (8). To a solution of **6** (20.0 g, 56.5 mmol) in dry THF (200 mL) stirred at −78 °C under argon was added lithium hexamethyldisilazide (LiHMDS, 1 M in THF) (63.2 mL, 63.2 mmol) over a period of 10 min. After the reaction mixture had stirred for 1 h at −78 °C, chlorotrimethylsilane (7.67 g, 70.6 mmol) was added dropwise, and the reaction mixture was allowed to reach room temperature and stirred for 30 min at this temperature. The reaction mixture was against cooled to −78 °C, and a solution of phenylselenenyl bromide (19.99 g, 84.7 mmol) in dry THF (100 mL) was rapidly added. The dark brown color of the phenylselenenyl bromide disappeared as it was added and finally persisted at the end. The reaction mixture was diluted with diethyl ether (200 mL), washed with water until the ether layer was light yellow in color, dried (Na_2SO_4), filtered, and concentrated. The resulting oily residue was purified by chromatography over silica gel. Elution with EtOAc (0–7%) in hexanes gave the desired $C_2\alpha$ isomer **7** (18.70 g, 65%): ^1H NMR ($CDCl_3$, 250 MHz) δ 1.02 (s, 9 H, *t*-Bu), 2.23–2.34 (m, 1 H, 3-H_a), 2.64–2.75 (m, 1 H, 3-Hb), 3.75 (dd, $J_{4,5a}$ = 3.2 Hz, $J_{5a,5b}$ = 11.6 Hz, 1 H, 5-Ha), 3.83 (dd, $J_{4,5b}$ = 3.2 Hz, $J_{5a,5b}$ = 11.6 Hz, 1 H, 5-Hb), 4.09 (dd, J = 9.2 and 4.4 Hz, 1 H, 2-H), 4.31–4.39 (m, 1 H, 4-H), 7.20–7.70 (m, 15 H, 3 × C_6H_5); IR (film) 1765 cm^{-1}. Anal. Calcd for $C_{27}H_{30}O_3SeSi$: C, 63.64; H, 5.93. Found: C, 63.75; H, 5.95. Elution with 10% EtOAc in hexanes gave the $C_2\beta$ isomer **8** (8.60 g, 30%): ^1H NMR ($CDCl_3$, 250 MHz) δ 1.04 (s, 9 H, *t*-Bu), 2.17–2.19 (m, 1 H, 3-Ha), 2.58–2.70 (m, 1 H, 3-Hb), 3.65 (m, 2 H, 5-H), 4.03 (t, J = 9.5 Hz, 1 H, 2-H), 4.45–4.57 (m, 1 H, 4-H), 7.20–7.50 (m, 10 H, 2 × C_6H_5), 7.60–7.70 (m, 5 H, C_6H_5): IR (film) 1770 cm^{-1}. Anal. Calcd for $C_{27}H_{30}O_3SeSi$: C, 63.64; H, 5.93. Found: C, 63.45; H, 5.96.

1-*O*-Acetyl-5-*O*-(*tert*-butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-α- and -β-D-*erythro*-pentofuranose (9). To a stirred solution of **7** (14.92 g, 29.31 mmol) in dry toluene (150 mL) at −78 °C under argon was added a 1 M solution of DIBAL-H in toluene (46.75 mL, 46.75 mmol, 1.6 equiv) over a 15-min period. After being stirred for 2 h at −78 °C the reaction mixture was quenched with MeOH (10 mL), allowed to warm to −20 °C, and stirred at this temperature for 30 min. The reaction mixture was then diluted with EtOAc (100 mL), washed with saturated sodium tartrate solution, water, and brine, dried (Na_2SO_4), filtered, and concentrated. The resulting crude lactol (14.34 g, 95.79%) without further purification was acetylated by treatment with acetic anhydride (7.17 g, 70.29 mmol), pyridine (13.89 g, 175.84 mmol), and DMAP (5 mg, cat. amount) in CH_2Cl_2 (75 mL) at 0 °C for 2 h. After removal of the solvent under reduced pressure, compound **9** (14.35 g, 96%) was obtained as a clear yellow liquid (mixture of α- and β-anomers): ^1H NMR ($CDCl_3$) δ 0.97 and 1.05 (s, 9 H, *t*-Bu), 2.10 (s, 3 H, Ac), 1.90–2.70 (m, 2 H, 3-H), 3.50–4.00 (m, 3 H, 2- and 5-H), 4.40 (m, 1 H, 4-H), 6.28 (s, 0.33 H, 1-H), 6.46 (d, 0.66 H, 1-H), 7.20–7.80 (m, 15 H, 3 × C_6H_5).

1-[5-*O*-(*tert*-Butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-β-D-*erythro*-pentofuranosyl]thymine (12). A suspension of thymine (0.454 g, 3.6 mmol) and ammonium sulfate (0.01 g) in hexamethyldisilazane (HMDS, 20 mL) was heated at reflux until a clear solution was obtained (2 h). The reaction mixture was cooled to room temperature, and the HMDS was removed under reduced pressure and anhydrous conditions. To the residue under nitrogen was added the acetate **9** (0.99 g, 1.8 mmol) in dry 1,2-dichloroethane. The reaction mixture was cooled to 5 °C, treated with TMSOTf (0.3 mL, 1.55 mmol), and allowed to stir at 5 °C for 10 min and then 10 min at room temperature at which time it was complete by TLC. The reaction mixture was poured into EtOAc and saturated $NaHCO_3$ with stirring. The layers were separated, and the organic layer washed once with saturated $NaHCO_3$ solution, water, and brine, dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed over silica gel eluting with hexanes and hexanes/EtOAc (6:1 to 4:1) to give **12** (0.86 g, 78%) as a foam: UV (MeOH) λ_{max} 266.0 nm; ^1H NMR ($CDCl_3$) δ 1.11 (s, 9 H, *t*-Bu), 1.45 (s, 3 H, 5-CH_3), 1.95–2.70 (m, 2 H, 3′-H), 3.60–4.30 (m, 4 H, 2′-, 4′-, and 5′-H), 6.16 (d, $J_{1'-2'}$ = 8.1 Hz, 1 H, 1′-H), 7.15–7.70 (m, 16 H, 3 × C_6H_5 and 6-H), 8.31 (br s, 1 H, NH). Anal. Calcd for $C_{32}H_{36}N_2O_4SeSi$: C, 62.02; H, 5.86; N, 4.52. Found: C, 61.94; H, 5.89; N, 4.49.

1-[5-*O*-(*tert*-Butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-β-D-*erythro*-pentofuranosyl]uracil (13). A suspension of uracil (0.41 g, 3.62 mmol) and ammonium sulfate (0.01 g) in hexamethyldisilazane (HMDS, 20 mL) was heated at reflux until a clear solution was obtained (2 h). The reaction mixture was cooled to room temperature, and the HMDS was removed under reduced pressure under anhydrous conditions. To the residue under nitrogen was added the acetate **9** (1.0 g, 1.81 mmol) in dry

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1,2-dichloroethane. The reaction mixture was cooled to 5 °C, treated with TMSOTf (0.3 mL, 1.55 mmol), and allowed to stir at 5 °C for 10 min and then 10 min at room temperature at which time it was complete by TLC. The reaction mixture was poured into CH_2Cl_2 and saturated $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed over silica using hexanes/EtOAc (1:1) as eluant to give **13** (0.730 g, 67%) as a hygroscopic foam: UV (MeOH) λ_{max} 264 nm; ^1H NMR ($CDCl_3$) δ 1.08 (s, 9 H, *t*-Bu), 2.15 (d, pseudo t, J = 7.7 and 12.9 Hz, 1 H, 3'-Ha), 2.5 (ddd, J = 5.2, 7.7 and 12.9 Hz, 1 H, 3'-Hb), 3.7 (m, 2 H, 5'-H), 4.1 (dd, J = 2.57 and 11.57 Hz, 1 H, 4'-H), 4.25 (m, 1 H, 2'H), 5.28 (d, J = 7.7 Hz, 1 H, 5-H), 6.15 (d, J = 5.2 Hz, 1 H, 1'-H), 7.20–7.90 (complex multiplet, 16 H, 3 × C_6H_5 and 6-H), 8.55 (br s, 1 H, NH). Anal. Calcd for $C_{31}H_{34}N_2O_4SeSi$: C, 61.02; H, 5.70; N, 4.59. Found: C, 60.91; H, 5.73; N, 4.47.

N^4-Acetyl-1-[5-*O*-(*tert*-butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-β-D-*erythro*-pentofuranosyl]cytosine (14). For the silylation of N^4-acetylcytosine, a mixture of N^4-acetylcytosine (0.294 g, 1.93 mmol), hexamethyldisilazane (20 mL), and ammonium sulfate (0.01 g, cat. amount) was refluxed for 3 h under nitrogen. After evaporation of HMDS with exclusion of moisture, the residue was dissolved in dry 1,2-dichloroethane (8 mL) and the acetate **9** (0.535 g, 0.97 mmol) was added in dry 1,2-dichloroethane (10 mL) to this solution under nitrogen. TMSOTf (0.37 mL, 1.93 mmol) was added, and the reaction mixture was stirred for 35 min at room temperature. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ (1 mL) and stirred for 30 min, and the solid was removed by filtration through Celite. The Celite pad was washed with $CHCl_3$ (50 mL), and the filtrate was dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by silica gel column chromatography (hexanes/EtOAc (1:1)) to yield **14** (0.453 g, 72.48%) as a white foam: UV (MeOH) λ_{max} 299.0 nm; ^1H NMR ($CDCl_3$) δ 1.09 (s, 9 H, *t*-Bu), 2.23 (s, 3 H, $COCH_3$), 1.99–2.52 (m, 2 H, 3'-H), 3.70 (dd, $J_{4',5'a}$ = 2.6 Hz, $J_{5'a,5'b}$ = 12.0 Hz, 1 H, 5'-H_a), 3.85 (dd, $J_{4',5'b}$ = 6.4 Hz, $J_{5'a,5'b}$ = 12.0 Hz, 1 H, 5'H_b), 4.15 (m, 1 H, 4'-H), 4.43 (m, 1 H, 2'-H), 6.16 (d, J = 3.3 Hz, 1 H, 1'-H), 7.12 (d, J = 7.6 Hz, 1 H, 5-H), 7.19–7.76 (m, 15 H, 3 × C_6H_5), 8.27 (d, J = 7.6 Hz, 1 H, 6-H), 9.44 (br s, 1 H, NH). Anal. Calcd for $C_{33}H_{37}N_3O_4SeSi$: C, 61.29; H, 5.77; N, 6.50. Found: C, 61.19; H, 5.77; N, 6.41.

1-[5-*O*-(*tert*-Butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pentofuranosyl]thymine (15). To a solution of **12** (0.282 g, 0.45 mmol) in dry benzene was added Et_3B 1 M in hexane (0.5 mL, 0.5 mmol) and *n*-Bu_3SnH (0.18 mL, 0.67 mmol) and the reaction mixture stirred for 4 h at room temperature. The solvent was evaporated and the residue dissolved in acetonitrile and washed with hexanes (3×). The acetonitrile layer was evaporated and the residue chromatographed over silica using CH_2Cl_2 followed by CH_2Cl_2/MeOH (97:3) as eluant to give **15** (0.186 g, 89%) as a foam: UV (MeOH) λ_{max} 266.0 nm; ^1H NMR ($CDCl_3$) δ 1.10 (s, 9 H, *t*-Bu), 1.65 (d, J = 1.1 Hz, 3 H, 5-CH_3), 1.90–2.40 (m, 4 H, 2'- and 3'-H), 3.70–4.30 (m, 3 H, 4'- and 5'-H), 6.11 (pseudo t, J = 4.0 Hz, 1 H, 1'-H), 7.26 (s, 1 H, 6-H), 7.40–7.90 (m, 10 H, 2 × C_6H_5), 8.32 (br s, 1 H, NH). Anal. Calcd for $C_{28}H_{32}N_2O_4Si$: C, 67.21; H, 6.94; N, 6.03. Found: C, 67.09; H, 6.96; N, 6.01.

1-[5-*O*-(*tert*-Butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pentofuranosyl]uracil (16). Using a procedure similar to that used for **15**, **13** (0.24 g, 0.4 mmol)) was converted to **16** (0.146 g, 81.1%) crystallized from CH_2Cl_2/hexanes: mp 144–146 °C; UV (MeOH) λ_{max} 262 nm; ^1H NMR ($CDCl_3$) δ 1.09 (s, 9 H, *t*-Bu), 2.00–2.50 (complex multiplet, 4 H, 2'- and 3'-H), 3.73 (dd, $J_{4',5'a}$ = 3.2, $J_{5'a,5'b}$ = 12.0 Hz, 1 H, 5'H_a), 4.08 (dd, $J_{4',5'b}$ = 2.3, $J_{5'a,5'b}$ = 12.0 Hz, 1 H, 5'-H_b), 4.10 (m, 1 H, 4'-H), 5.42 (d, J = 8.2 Hz, 1 H, 5-H), 6.2 (dd, J = 3.4 and 6.2 Hz, 1 H, 1'-H), 7.30–7.80 (complex multiplet, 10 H, 2 × C_6H_5), 7.94 (d, J = 8.2 Hz, 6-H), 9.4 (br s, 1 H, NH). Anal. Calcd for $C_{25}H_{30}N_2O_4Si$: C, 66.64; H, 6.71; N, 6.22. Found: C, 66.58; H, 6.76; N, 6.23.

N^4-Acetyl-1-[5-*O*-(*tert*-butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pentofuranosyl]cytosine (17). Conversion of **14** (0.4 g, 0.62 mmol) to **17** (0.288 g, 94.74%) was accomplished using a procedure similar to that described for **15**. Crude **17** was purified by silica gel column chromatography (hexanes:EtOAc = 1:3) to give **17** as a white foam: UV (MeOH) λ_{max} 299 nm; ^1H NMR ($CDCl_3$) δ 1.11 (s, 9 H, *t*-Bu), 2.24 (s, 3 H, $COCH_3$), 1.78–2.55 (m, 4 H, 2'- and 3'-H), 3.74 (dd, $J_{4',5'a}$ = 3.5 Hz, $J_{5'a,5'b}$ = 12.0 Hz, 1 H, 5'-H_a), 4.27–4.00 (m, 2 H, 4'- and 5'-H), 6.09 (dd, J = 2.1 and 6.3 Hz, 1 H, 1'-H), 7.21 (d, J = 8.2 Hz, 1 H, 5-H), 7.32–7.73 (m, 10 H, 2 × C_6H_5), 8.39 (d, J = 8.2 Hz, 1 H, 6-H), 9.33 (br s, 1 H, NH). Anal. Calcd for $C_{27}H_{33}N_3O_4Si$·0.4 $CH_3CO_2C_2H_5$: C, 65.20; H, 6.93; N, 7.98. Found: C, 65.17; H, 6.86; N, 8.28.

1-(2,3-Dideoxy-β-D-*glycero*-pentofuranosyl)thymine (18). To a solution of **15** (0.162 g, 0.35 mmol) in THF (3 mL) was added a 1 M solution of TBAF in THF (0.35 mL, 0.35 mmol), and the reaction mixture was stirred at room temperature for 3 h. When the TLC showed complete disappearance of the starting material, the solvent was removed under reduced pressure. Silica gel column chromatography eluted with MeOH in $CHCl_3$ (0–6%) gave **18** (0.063 g, 80%) as a white crystalline solid from EtOAc: mp 151–152 °C (lit.[19] mp 149–159 °C); ^1H NMR (DMSO-d_6), δ 1.77 (s, 3 H, 5-CH_3), 1.70–2.30 (m, 4 H, 2'- and 3'-H), 3.60 (m, 2 H, 5'-H), 4.00 (m, 1 H, 4'-H), 5.01 (t, J = 5.4 Hz, 1 H, 5'-OH), 5.95 (dd, J = 5.5 and 6.5 Hz, 1 H, 1'-H), 7.79 (s, 1 H, 6-H), 11.20 (br s, 1 H, NH); $[\alpha]^{25}_D$ 18.3° (*c* 0.999, MeOH).

1-(2,3-Dideoxy-β-D-*glycero*-pentofuranosyl)uracil (19). Reaction of **16** (0.09 g, 0.2 mmol) using conditions as described for **18** gave **19** (0.036 g, 84.8%): mp 121–122 °C (lit.[19] mp 117.5–118.5 °C); UV (MeOH) λ_{max} 263.5 nm (ϵ 9503), (pH 11) 262 nm (ϵ 7057); ^1H NMR (DMSO-d_6) δ 1.70–2.40 (complex multiplet, 4 H, 2'- and 3'-H), 3.60 (dd, J = 6.3 and 8.8 Hz, 2H, 5'-H), 4.00 (m, 1 H, 4'-H), 5.00 (t, J = 5.3 Hz, 1 H, 5'-OH), 5.50 (d, J = 7.9 Hz, 1 H, 5-H), 5.95 (dd, J = 3.5 and 6.9 Hz, 1 H, 1'-H), 7.95 (d, J = 7.9 Hz, 1 H, 6-H), 11.22 (br s, 1 H, NH); $[\alpha]^{25}_D$ +32.4° (*c* 1.03, H_2O) [lit.[19] $[\alpha]^{25}_D$ +31° (*c* 0.43, H_2O)]. Anal. Calcd for $C_9H_{12}N_2O_4$: C, 50.94; H, 5.70; N, 13.23. Found: C, 51.04; H, 5.72; N, 13.14.

N^4-Acetyl-1-(2,3-dideoxy-β-D-*glycero*-pentofuranosyl)cytosine (20). Using a procedure similar to that used for **18**, **17** (0.238 g, 0.48 mmol) was converted to **20** (0.122 g, 99.5%) obtained as a white solid after purification by silica gel column chromatography ($CHCl_3$–MeOH (20:1)): mp 138–139 °C (lit.[8] mp 143–145 °C); UV (MeOH) λ_{max} 299 nm; ^1H NMR ($CDCl_3$) δ 1.74–2.80 (m, 2 H, 2'- and 3'-H), 2.25 (s, 3 H, $COCH_3$), 3.39 (t, J = 6.7 Hz, 1 H, 5'-OH), 3.75 (dd, J = 3.5 and 8.1 Hz, 1 H, 4'-H), 4.00–4.34 (m, 2 H, 5'-H), 6.07 (dd, J = 2.9 and 6.7 Hz, 1 H, 1'-H), 7.41 (d, J = 7.3 Hz, 1 H, 5-H), 8.42 (d, J = 7.3 Hz, 1 H, 6-H), 9.28 (br s, 1 H, NH). Anal. Calcd for $C_{11}H_{15}N_3O_4$·0.7 H_2O: C, 49.69; H, 5.95; N, 15.80. Found: C, 49.72; H, 6.19; N, 15.98.

1-(2,3-Dideoxy-β-D-*glycero*-pentofuranosyl)cytosine, ddC (21). A mixture of **20** (0.1 g, 0.39 mmol) and sodium methoxide (1 mg of Na in 0.5 mL MeOH, 0.039 mmol) in MeOH (10 mL) was stirred for 1 h at room temperature. After evaporation of solvent, the residue was purified by silica gel column chromatography ($CHCl_3$:MeOH = 10:1) to yield **21** (0.074 g, 88.73%) as a white solid which was crystallized from EtOH–benzene: mp 212–214 °C (lit.[19] mp 209–210 °C, lit.[8] mp 207–209 °C, lit.[9a] mp 214–217 °C); UV (MeOH) λ_{max} 271 nm; ^1H NMR (DMSO-d_6) δ 1.76 (m, 1 H, 2'-H_a), 1.84 (m, 1 H, 2'-H_b), 2.22 (m, 2 H, 3'-H), 3.55 (m, 1 H, 5'-H_a) 3.66 (m, 1 H, 5'-H_b), 4.01 (m, 1 H, 4'-H), 4.97 (t, J = 5.4 Hz, 1 H, 5'-OH), 5.71 (d, J = 7.3 Hz, 1 H, 5-H), 5.92 (dd, J = 3.1 and 6.5 Hz, 1 H, 1'-H), 7.01 (br s, 1 H, NH), 7.90 (d, J = 7.3 Hz, 1 H, 6-H).

1-[5-*O*-(*tert*-Butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl]thymine (22). Compound **12** (0.496 g, 0.8 mmol) was dissolved in CH_2Cl_2 (5 mL) containing a catalytic amount of pyridine (1 drop), and the solution was cooled in an ice–water bath. A 30% solution of hydrogen peroxide (0.5 mL, 4.4 mmol) was diluted with water (1 mL) and was added dropwise to the above solution over a period of 20 min with stirring. The reaction was monitored by TLC (CH_2Cl_2/MeOH (9.5:0.5)). Meanwhile, the temperature of the reaction mixture was allowed to come to 20 °C slowly, and the mixture was stirred at room temperature further for 0.5 h. The reaction mixture was diluted with CH_2Cl_2, washed with water, saturated $NaHCO_3$ solution, and finally with water. After the reaction mixture was dried over anhydrous Na_2SO_4, the solvent was removed and the residue was chromatographed over a column of silica gel (230–400 mesh) eluting first with CH_2Cl_2 and then with 2–3% MeOH/CH_2Cl_2 to give **22** (0.283 g, 76%) as a thick syrup: ^1H NMR ($CDCl_3$) δ 1.08 (s, 9 H, *t*-Bu), 1.49 (d, J = 1.3 Hz, 3 H, 5-CH_3),

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3.90 (d, J = 4.2 Hz, 2 H, 5'-H), 4.92 (m, 1 H, 4'-H), 5.89 (m, 1 H, 2'-H), 6.35 (m, 1 H, 3'-H), 7.00 (m, 1 H, 1'-H), 7.14 (d, J = 1.3 Hz, 1 H, 6-H), 7.25–7.17 (m, 10 H, 2 × C_6H_5), 9.00 (br s, 1 H, NH). Anal. Calcd for $C_{28}H_{30}N_2O_4Si$: C, 67.50; H, 6.54; N, 6.06. Found: C, 67.03; H, 6.98; N, 5.35.

1-[5-*O*-(*tert*-Butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl]uracil (23). Conversion of **13** (0.180 g, 0.3 mmol) to **23** (0.096 g, 71%) was accomplished using a procedure similar to that described for **22**. Crude **23** was chromatographed over silica using hexanes/EtOAc (1:1) to give **23** as a white foam: UV (MeOH) λ_{max} 260 nm; ^{1}H NMR ($CDCl_3$) δ 1.07 (s, 9 H, t-Bu), 3.80 (dd, $J_{4',5'a}$ = 3.3 Hz, $J_{5'a,5'b}$ = 11.6 Hz, 1 H, 5'-H_a), 4.05 (dd, $J_{4',5'b}$ = 3.0 Hz, $J_{5'a,5'b}$ = 11.6 Hz, 1 H, 5'-H_b), 4.9 (br m, 1 H, 4'-H), 5.20 (d, J = 8.1 Hz, 1 H, 5-H), 5.85 (br d, J = 5.9 Hz, 1 H, 2'-H), 6.29 (br d, J = 5.9 Hz, 1 H, 3'-H), 7.00 (m, 1 H, 1'-H), 7.20–7.80 (complex multiplet, 11 H, 2 × C_6H_5 and 6-H), 8.70 (br s, 1 H, NH). Anal. Calcd for $C_{25}H_{28}N_2O_4Si$: C, 66.92; H, 6.3; N, 6.25. Found: C, 66.74; H, 6.23; N, 6.19.

1-(2,3-Dideoxy-β-D-*glycero*-pent-2-enofuranosyl)thymine, d4T (24). Using a procedure similar to that used for **18**, **22** (0.18 g, 0.39 mmol) was converted to **24** (0.068 g, 78%) crystallized from a mixture of ethanol–ether: mp 174 °C (lit.[19] mp 165–165 °C); UV (H_2O) λ_{max} 266.0 nm (ε 10149); ^{1}H NMR (DMSO-d_6) δ 1.73 (s, 3 H, 5-CH_3), 3.61 (m, 2 H, 5'-H), 4.99 (t, 1 H, 5'-OH), 5.91 (m, 1 H, 2'-H), 6.38 (m, 1 H, 3'-H), 6.82 (m, 1 H, 1'-H), 7.64 (s, 1 H, 6-H); $[\alpha]^{25}_D$ −39.4° (c 0.701, H_2O) [lit.[19] $[\alpha]^{25}_D$ −42° (c 0.69, H_2O)].

1-(2,3-Dideoxy-β-D-*glycero*-pent-2-enofuranosyl)uracil, d4U (25). Reaction of **23** (0.200 g, 0.45 mmol) using conditions as described for **18** gave **25** (0.084 g, 90%) after chromatography over silica gel using $CHCl_3$/MeOH (10:1) as eluant and crystallization from MeOH: mp 150.5 °C (MeOH), (lit.[18] mp 153–154 °C, lit.[20] mp 154.5–155.5 °C); UV (MeOH) λ_{max} 259.4 nm (ε 9322), (pH 11) 259.5 nm (ε 7090); ^{1}H NMR (DMSO-d_6) δ 3.57 (d, J = 3.2 Hz, 2 H, 5'-H), 4.75 (m, 1 H, 4'-H), 4.95 (br, 1 H, 5'-OH), 5.56 (d, J = 8.2 Hz, 1 H, 5-H), 5.98 (dt, J = 1.7 and 6.2 Hz, 1 H, 2'-H), 6.39 (dt, J = 1.7 and 6.2 Hz, 1 H, 3'-H), 6.80 (m, 1 H, 1'-H), 7.84 (d, J = 8.2 Hz, 1 H, 6-H), 12.70 (br s, 1 H, NH); $[\alpha]^{25}_D$ −15.6° (c 0.22, MeOH) [lit.[21] $[\alpha]^{25}_D$ −15.4° (c 0.2, MeOH)].

6-Chloro-9-[5-*O*-(*tert*-butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-β-D-*erythro*-pentofuranosyl]-9*H*-purine (26). A suspension of 6-chloropurine (0.40 g, 2.59 mmol) and $(NH_4)_2SO_4$ (0.01 g) in hexamethyldisilazane (HMDS, 25 mL) was refluxed under argon until a complete solution was obtained (1 h). The reaction mixture was allowed to cool and the HMDS removed under vacuum and anhydrous conditions. To the solid obtained under argon was added 1,2-dichloroethane (10 mL) followed by the acetate **9** (1 g, 1.8 mmol) in 1,2-dichloroethane (10 mL), the reaction mixture was cooled to −22 °C, and TMSOTf (0.52 mL, 2.7 mmol) was added slowly over several minutes. When addition was complete the reaction mixture was allowed to stir at −22 °C for 15 min and then warm to room temperature. After 0.5 h TLC indicated completion of reaction. The reaction mixture was poured into ice-cold EtOAc (100 mL) and saturated $NaHCO_3$ (20 mL) and stirred for 30 min, the layers were separated, and the organic layer was washed twice with saturated $NaHCO_3$, dried, filtered, and concentrated. The residue was separated by chromatography over silica using 15% EtOAc in hexanes as eluant to give **26** (1.05 g, 89%) as a crystalline solid from hexanes/CH_2Cl_2: mp 113–114 °C; UV (MeOH) λ_{max} 265.5 nm; ^{1}H NMR ($CDCl_3$, 250 mHz) δ 1.08 (s, 9 H, t-Bu), 2.20 (ddd, J = 7.6, 7.6, and 13.3 Hz, 1 H, 3'-H_a), 2.69 (ddd, J = 5.9, 7.5, and 13.3 Hz, 1 H, 3'-H_b), 3.77 (dd, $J_{4'5'a}$ = 3.7 Hz, $J_{5'a,5'b}$ = 11.3 Hz, 1 H, 5'-H_a), 3.99 (dd, $J_{4'5'b}$ = 3.6 Hz, $J_{5'a,5'b}$ = 11.3 Hz, 1 H, 5'-H_b), 4.35 (d, pseudo t, $J_{1',2'}$ = 5.8 Hz, $J_{2',3'ab}$ = 7.5, 1 H, 2'-H), 4.43 (m, 1 H, 4'-H), 6.24 (d, $J_{1'2'}$ = 5.8 Hz, 1 H, 1'-H), 7.00–7.52 (m, 15 H, 3 × C_6H_5), 8.19 (s, 1 H, 8-H), 8.61 (s, 1 H, 2-H). Anal. Calcd for $C_{32}H_{33}N_4O_2SiClSe$: C, 59.31; H, 5.10; N, 8.65. Found: C, 59.37; H, 5.11; N, 8.64.

9-[5-*O*-(*tert*-Butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-β-D-*erythro*-pentofuranosyl]hypoxanthine (27). To a solution of **26** (0.310 g, 0.48 mmol) in MeOH (25 mL) was added mercaptoethanol (0.12 mL, 1.9 mmol) and 1 N NaOMe (1.8 mL, 1.8 mmol) and the reaction heated at reflux for 4 h. The reaction mixture was cooled, acidified with acetic acid, diluted with water (100 mL), and extracted with EtOAc (100 mL). The organic layer was washed with water (50 mL) and saturated $NaHCO_3$ solution (50 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed over silica using EtOAc/hexanes (7:3) as eluant to give **27** (0.271 g, 90%) as a solid from hexanes: mp 95 °C softens 145 °C dec; UV (MeOH) λ_{max} 245 nm, 264 (sh) nm, 270 (sh) nm, (pH 11) 257.5 nm; ^{1}H NMR ($CDCl_3$) δ 1.08 (s, 9 H, t-Bu), 2.20 (m, 1 H, 3'-H_a), 2.65 (m, 1 H, 3'-H_b), 3.75 (dd, $J_{4',5'a}$ = 4.0 Hz, $J_{5'a,5'b}$ = 11.2 Hz, 1 H, 5'-H_a), 4.00 (dd, $J_{4',5'b}$ = 3.7 Hz, $J_{5'a,5'b}$ = 11.2 Hz, 1 H, 5'-H_b), 4.40 (m, 2 H, 2'- and 4'-H), 6.16 (d, $J_{1',2'}$ = 5.3 Hz, 1 H, 1'-H), 7.00–7.80 (complex multiplet, 15 H, 3 × C_6H_5), 7.93 (s, 1 H, 8-H), 7.99 (s, 1 H, 2-H). Anal. Calcd for $C_{32}H_{34}N_4O_3SiSe$: C, 61.05; H, 5.41; N, 8.90. Found: C, 61.22; H, 5.49; N, 8.88.

9-[5-*O*-(*tert*-Butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-β-D-*erythro*-pentofuranosyl]adenine (28). To a solution of **26** (1.3 g, 2.01 mmol) in MeOH (5 mL) was added saturated MeOH/NH_3 (40 mL), and the reaction mixture was heated at 80 °C in a steel bomb for 16 h. After the reaction mixture was cooled, the solvent was removed by distillation under vacuum. The residue was purified by silica gel column chromatography (hexanes: EtOAc = 1:1) to give **28** (0.75 g, 59%) as a syrup which was crystallized from diethyl ether: mp 122–123 °C; UV (MeOH) λ_{max} 260 nm; ^{1}H NMR ($CDCl_3$) δ 1.07 (s, 9 H, t-Bu), 2.24 (m, 1 H, 3'-H_a), 2.64 (m, 1 H, 3'-H_b), 3.78 (dd, $J_{4',5'a}$ = 4.0 Hz, $J_{5'a,5'b}$ = 11.3 Hz, 1 H, 5'-H_a), 3.97 (dd, $J_{4',5'a}$ = 4.0 Hz, $J_{5'a,5'b}$ = 11.3 Hz, 1 H, 5'-H_b), 4.16–4.47 (m, 2 H, 2'- and 4'-H), 5.17 (br s, 2 H, NH_2), 6.19 (d, J = 5.49 Hz, 1 H, 1'-H), 7.11–7.71 (m, 15 H, 3 × C_6H_5), 7.85 (s, 1 H, 8-H), 8.26 (s, 1 H, 2-H). Anal. Calcd for $C_{32}H_{35}N_5O_2SiSe$: C, 61.13; H, 5.61; N, 11.14. Found: C, 61.21; H, 5.65; N, 11.19.

***N*^{6}-Methyl-9-[5-*O*-(*tert*-butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-β-D-*erythro*-pentofuranosyl]adenine (29).** A mixture of **26** (0.800 g, 1.24 mmol), MeOH (50 mL), and 40% methylamine in water (6.24 mL, 80.5 mmol) was heated at 85 °C in a steel bomb for 18 h. After the solvent was evaporated, the residue was dissolved in $CHCl_3$ (200 mL) and the organic layer was washed with water and brine, dried over $MgSO_4$, and evaporated to dryness. The residue was purified by silica gel column chromatography (hexanes/EtOAc (2:1)) to give **29** (0.678 g, 85.5%): UV (MeOH) λ_{max} 266 nm, (pH 2) 259 nm; FTIR (KBr) 3400 cm^{-1} (–NH); ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 9 H, t-Bu), 2.40 (m, 2 H, 3'-H), 3.17 (d, J = 5.0 Hz, 3 H, NHCH_3), 3.73 (dd, $J_{4',5'a}$ = 4.0 Hz, $J_{5'a,5'b}$ = 11.2 Hz, 1 H, 5'-H_a), 3.97 (dd, $J_{4',5'b}$ = 4.2 Hz, $J_{5'a,5'b}$ = 11.2 Hz, 1 H, 5'-H_b), 4.35 (m, 2 H, 2'- and 4'-H), 5.79 (br d, 1 H, NH), 6.17 (d, J = 5.5 Hz, 1 H, 1'-H), 7.40 (m, 5 H, SePh), 7.30–7.60 (m, 10 H, 2 × C_6H_5), 7.79 (s, 1 H, 8-H), 8.32 (s, 1 H, 2-H). Anal. Calcd for $C_{33}H_{37}N_5O_2SiSe$: C, 61.67; H, 5.80; N, 10.90. Found: C, 61.63; H, 5.84; N, 10.96.

6-Chloro-9-[5-*O*-(*tert*-butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pentofuranosyl]-9*H*-purine (30). Using a procedure similar to that used for **15**, **26** (2.76 g, 4.25 mmol) was converted to **30** (1.871 g, 93%): UV (MeOH) λ_{max} 264 nm, (pH 2) 263 nm; ^{1}H NMR ($CDCl_3$) δ 1.06 (s, 9 H, t-Bu), 2.09 (m, 2 H, 3'-H), 2.52 (m, 2 H, 2'-H), 3.71 (dd, $J_{4',5'a}$ = 3.4 Hz, $J_{5'a,5'b}$ = 11.6 Hz, 1 H, 5'-H_a), 3.93 (dd, $J_{4',5'b}$ = 2.9 Hz, $J_{5'a,5'b}$ = 11.3 Hz, 1 H, 5'-H_b), 4.28 (m, 1 H, 4'-H), 6.36 (t, 1 H, J = 4.7 Hz, 1'-H), 7.25–7.70 (m, 10 H, 2 × C_6H_5) 8.44 (s, 1 H, 8-H), 8.69 (s 1 H, 2-H). Anal. Calcd for $C_{26}H_{29}N_4SiCl$: C, 63.33; H, 5.92; N, 11.36. Found: C, 63.09; H, 5.94; N, 11.33.

9-[5-*O*-(*tert*-Butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pentofuranosyl]hypoxanthine (31). Conversion of **27** (0.25 g, 0.397 mmol) to **31** (0.170 g, 90%) was accomplished using a procedure similar to that described for **15**. Crude **31** was chromatographed over silica using 5% MeOH in EtOAc to give **31**: mp 159–161 °C (hexane/CH_2Cl_2); UV (MeOH) λ_{max} 250 nm, (pH 11), 256 nm; ^{1}H NMR ($CDCl_3$) δ 1.08 (s, 9 H, t-Bu), 2.15 (m, 2 H, 3'-H), 2.48 (m, 2 H, 2'-H), 3.72 (dd, $J_{4',5'a}$ = 4.5 Hz, $J_{5'a,5'b}$ = 11.3 Hz, 1 H, 5'-H_a), 4.08 (dd, $J_{4',5'b}$ = 3.8 Hz, $J_{5'a,5'b}$ = 11.3 Hz, 1 H, 5'-H_b), 4.28 (m, 1 H, 4'-H), 6.29 (pseudo t, $J_{1',2'}$ = 5.1 and 5.5 Hz, 1 H, 1'-H), 7.2–7.8 (complex multiplet, 10 H, 2 × C_6H_5), 8.13 (s, 1 H, 8-H), 8.16 (s, 1 H, 2-H). Anal. Calcd for $C_{26}H_{30}$-

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$N_4O_3Si·0.5\ H_2O$: C, 64.59; H, 6.41; N, 11.59. Found: C, 64.53; H, 6.44; N, 11.55.

9-[5-*O*-(*tert*-Butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pentofuranosyl]adenine (32). Reaction of **28** (0.6 g, 0.954 mmol) using conditions as described for **15** gave crude **32** which was purified by silica gel column chromatography (hexanes/EtOAc (1:1)) to yield **32** (0.41 g, 90.9%) as a white foam: UV (MeOH) λ_{max} 260 nm; ^{1}H NMR ($CDCl_3$) δ 1.08 (s, 9 H, *t*-Bu), 2.00–2.55 (m, 2 H, 2'- and 3'-H), 3.76 (dd, $J_{4',5'a}$ = 4.18 Hz, $J_{5'a,5'b}$ = 11.5 Hz, 1 H, 5'-H_a), 3.87 (dd, $J_{4',5'b}$ = 4.18 Hz, $J_{5'a,5'b}$ = 11.5 Hz, 1 H, 5'-H_b), 4.27 (m, 1 H, 4'-H), 5.89 (br s, 2 H, NH_2), 6.32 (t, *J* = 4.4 Hz, 1 H, 1'-H), 7.28–7.73 (m, 10 H, 2 × C_6H_5), 8.14 (s, 1 H, 8-H), 8.33 (s, 1 H, 2-H). Anal. Calcd for $C_{26}H_{31}N_5O_2Si·0.2H_2O$: C, 65.43; H, 6.63; N, 14.67. Found: C, 65.15; H, 6.69; N, 14.42.

***N*^{6}-Methyl-9-[5-*O*-(*tert*-butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pentofuranosyl]adenine (33).** Using a procedure similar to that used for **15**, **29** (0.25 g, 0.39 mmol) was converted to **33** (0.18 g, 95%): UV (MeOH) λ_{max} 265.3 nm; ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 9 H, *t*-Bu), 2.10 (m, 2 H, 3'-H), 2.50 (m, 2 H, 2'-H), 3.17 (d, *J* = 5.1 Hz, 3 H, NHCH_3), 3.75 (dd, $J_{4',5'a}$ = 4.0 Hz, $J_{5'a,5'b}$ = 11.1 Hz, 1 H, 5'-H_a), 3.95 (dd, $J_{4',5'b}$ = 4.4 Hz, $J_{5'a,5'b}$ = 11.1 Hz, 1 H, 5'-H_b), 4.25 (m, 1 H, 4'-H), 6.08 (br d, 1 H, NH), 6.31 (t, *J* = 4.7 Hz, 1 H, 1'-H), 7.40–7.65 (m, 10 H, 2 × C_6H_5), 8.06 (s, 1 H, 8-H), 8.38 (s, 1 H, 2-H). Anal. Calcd for $C_{27}H_{33}N_5O_2Si·CH_3OH$: C, 64.75; H, 7.12; N, 13.48. Found: C, 64.37; H, 6.80; N, 13.40.

6-Chloro-9-(2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-9*H*-purine (34). Conversion of **30** (1.85 g, 3.91 mmol) to **34** (0.826 g, 83%) was accomplished using a procedure similar to that described for **18**: mp 96–99 °C (lit.[16] mp 97–99 °C); UV (MeOH) λ_{max} 265 nm, (pH 2 and 11) 264 nm; ^{1}H NMR (DMSO-d_6) δ 2.10 (m, 2 H, 3'-H), 2.51 (m, 2 H, 2'-H), 3.54 (m, 2 H, 5'-H); 4.21 (m, 1 H, 4'-H), 6.32 (t, *J* = 5.8 Hz, 1 H, 1'-H), 8.78 (s, 1 H, 8-H), 8.84 (s, 1 H, 2-H); $[\alpha]^{25}_D$ −8.30° (*c* 1, MeOH) [lit.[16] $[\alpha]^{25}_D$ −8.35° (*c* 1.172, MeOH)]. Anal. Calcd for $C_{10}H_{11}N_4O_2Cl$: C, 47.15; H, 4.35; N, 22.00. Found: C, 47.09; H, 4.35; N, 21.91.

9-(2,3-Dideoxy-β-D-*glycero*-pentofuranosyl)hypoxanthine, ddI (35). Reaction of **31** (0.105 g, 0.22 mmol) using conditions as described for **18** gave **35** (0.039 g, 79%) as a solid from CH_2Cl_2/acetone: mp[23] 145 °C softens, >200 °C dec; UV (MeOH) λ_{max} 249.5 nm, (pH 11) 254.5 nm; ^{1}H NMR (DMSO-d_6) δ 2.08 (m, 2 H, 3'-H), 2.39 (m, 2 H, 2'-H), 3.57 (m, 2 H, 5'-H), 4.05 (m, 1 H, 4'-H), 6.2 (dd, $J_{1',2'}$ = 4.1 and 5.7 Hz, 1 H, 1'-H), 8.03 (s, 1 H, 8-H), 8.3 (s, 1 H, 2-H); $[\alpha]^{25}_D$ −25.2° (*c* 0.34, H_2O) [ddI[24] $[\alpha]^{25}_D$ −25.5° (*c* 0.82, H_2O)].

9-(2,3-Dideoxy-β-D-*glycero*-pentofuranosyl)adenine, ddA (36). Using a procedure similar to that used for **18**, **32** (0.35 g, 0.74 mmol) was converted to **36** (0.136 g, 82.4%). Crude **36** was purified by silica gel column chromatography ($CHCl_3$:MeOH = 10:1) to give **36** as a white solid: mp 185–186 °C (lit.[8] mp 184–186 °C, lit.[21] mp 185–187 °C); UV (MeOH) λ_{max} 260 nm; ^{1}H NMR (DMSO-d_6) δ 2.17 (m, 1 H, 2'-H), 2.38 (m, 1 H, 3'-H), 3.57 (m, 2 H, 5'-H), 4.15 (m, 1 H, 4'-H), 5.04 (t, *J* = 5.05 Hz, 1 H, 5'-OH), 6.22 (t, *J* = 5.05 Hz, 1 H, 1'-H), 7.22 (br s, 2 H, NH_2), 8.14 (s, 1 H, 8-H), 8.34 (s, 1 H, 2-H).

***N*^{6}-Methyl-9-(2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-adenine (37).** Conversion of **33** (0.170 g, 0.35 mmol) to **37** (0.082 g, 94%) was accomplished using a procedure similar to that described for **18**: UV (MeOH) λ_{max} 265.3 nm; ^{1}H NMR ($CDCl_3$) δ 2.4 (m, 4 H, 2'-H and 3'-H), 3.17 (d, *J* = 5.0 Hz, 3 H, NHCH_3), 3.85 (m, 2 H, 5'-H), 4.35 (m, 1 H, 4'-H), 6.2 (pseudo t, *J* = 5.4 and 4.0 Hz, 1 H, 1'-H), 6.4 (br d, 1 H, NH), 8.02 (s, 1 H, 8-H), 8.35 (s, 1 H, 2-H); $[\alpha]^{25}_D$ −11.98° (*c* 1, MeOH) [lit.[16] $[\alpha]^{25}_D$ −11.5° (*c* 1, MeOH)].

9-[5-*O*-(*tert*-butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl]adenine (38). Using a procedure similar to that used for **22**, **28** (0.3 g, 0.913 mmol) was converted to **38** (0.15 g, 66.8%). Crude **38** was purified by silica gel column chromatography ($CHCl_3$/MeOH (20:1)) to give **38** as a white solid: mp 155–157 °C; UV (MeOH) λ_{max} 260 nm; ^{1}H NMR ($CDCl_3$) δ 1.06 (s, 9 H, *t*-Bu), 3.81 (d, *J* = 4.84 Hz, 2 H, 5'-H), 5.02 (m, 1 H, 4'-H), 5.91 (br s, 2 H, NH_2), 6.09 (dt, *J* = 1.6 and 6.3 Hz, 1 H, 2'-H), 6.46 (dt, *J* = 1.6 and 6.3 Hz, 1 H, 3'-H), 7.10 (m, 1 H, 1'-H), 7.23–7.66 (m, 10 H, 2 × C_6H_5), 7.87 (s, 1 H, 8-H), 8.36 (s, 1 H, 2-H). Anal. Calcd for $C_{26}H_{29}N_5O_2$: C, 66.21; H, 6.20; N, 14.85. Found: C, 66.31; H, 6.24; N, 14.41.

***N*^{6}-Methyl-9-[5-*O*-(*tert*-butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl]adenine (39).** Reaction of **29** (0.100 g, 0.15 mmol) using conditions as described for **22** gave **39** (0.073 g, 96.5%) after purification by silica gel column chromatography (hexanes/EtOAc (1:10)): UV (MeOH) λ_{max} 262.3 nm; ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 9 H, *t*-Bu), 3.17 (d, *J* = 5.1 Hz, 3 H, NHCH_3), 3.80 (m, 2 H, 5'-H), 5.00 (m, 1 H, 4'-H), 6.08 (m, 1 H, 2'-H), 6.43 (dt, *J* = 1.6 and 6.0 Hz, 1 H, 3'-H), 7.07 (quintet, *J* = 1.6 Hz, 1 H, 1'-H), 7.35–7.60 (m, 10 H, 2 × C_6H_5), 7.80 (s, 1 H, 8-H), 8.42 (s, 1 H, 2-H). Anal. Calcd for $C_{27}H_{31}O_2N_5Si·0.6H_2O$: C, 65.32; H, 6.54; N, 14.10. Found: C, 65.26; H, 6.42; N, 13.77.

9-(2,3-Dideoxy-β-D-*glycero*-pent-2-enofuranosyl)adenine, d4A (40). Conversion of **38** (0.12 g, 0.255 mmol) to **40** was accomplished using a procedure similar to that described for **18**. Crude **40** was purified by silica gel column chromatography ($CHCl_3$:MeOH = 10:1) to give **40** (0.058 g, 97.8%) as a white solid: mp 188–190 °C (lit.[22] mp 185–187 °C); UV (MeOH) λ_{max} 260 nm; ^{1}H NMR (DMSO-d_6) δ 3.58 (t, *J* = 4.61 Hz, 2 H, 5'-H), 4.94 (m, 1 H, 4'-H), 5.03 (t, *J* = 5.5 Hz, 1 H, 5'-OH), 6.14 (ddd, *J* = 1.5, 1.8, and 5.9 Hz, 1 H, 2'-H), 6.47 (ddd, *J* = 1.5, 1.8 and 5.9 Hz, 1 H, 3'-H), 6.94 (m, 1 H, 1'-H), 7.24 (br s, 2 H, NH_2), 8.15 (s, 1 H, 8-H), 8.16 (s, 1 H, 2-H).

***N*^{6}-Methyl-9-(2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)adenine (41).** Reaction of **39** (0.060 g, 0.12 mmol) using conditions as described for **18** gave **41** (0.027 g, 90%): mp 136–140 °C (lit.[16] mp 139–145 °C); ^{1}H NMR ($CDCl_3$) δ 3.14 (d, *J* = 4.5 Hz, 3 H, NHCH_3), 3.9 (m, 3 H, 4'- and 5'-H), 5.07 (br s, 1 H, 5'-OH), 6.0 (m, 1 H, 2'-H), 6.50 (dt, *J* = 1.6 and 5.9 Hz, 1 H, 3'-H), 7.00 (quintet, *J* = 1.6 Hz, 1 H, 1'-H), 7.95 (s, 1 H, 8-H), 8.30 (s, 1 H, 2-H); $[\alpha]^{25}_D$ 27.14° (*c* 1, MeOH).

6-Chloro-2-fluoropurine[17] (42). To a stirred suspension of 2-amino-6-chloropurine (10.0 g, 58.96 mmol) in fluoroboric acid (48%, 160 mL) maintained at −15 °C was added a saturated aqueous solution of sodium nitrite (6.51 g, 94.36 mmol) over a period of 20 min. After complete addition, the reaction mixture was stirred for 30 min at −10 to 0 °C and then neutralized (<0 °C) to pH 7 with 50% NaOH solution. The neutral slurry obtained was evaporated to dryness under reduced pressure, and the powdered residue was extracted with ether in a Soxhlet extractor to give **38** (9.0 g, 89%).

6-Chloro-2-fluoro-9-[5-*O*-(*tert*-butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-β-D-*erythro*-pentofuranosyl]-9*H*-purine (43). A suspension of 6-chloro-2-fluoropurine **42** (8.43 g, 48.90 mmol) and ammonium sulfate (10 mg, cat. amount) in hexamethyldisilazane (120 mL) was refluxed until a clear solution was obtained (3 h). The reaction mixture was concentrated under reduced pressure to give a pale yellow solid to which a solution of the acetate **9** (12 g, 21.69 mmol) in anhydrous 1,2-dichloroethane (120 mL) was added. The reaction mixture was cooled to −25 °C, treated dropwise with TMSOTf (6.95 mL, 34.78 mmol), and stirred for 30 min. The reaction mixture was poured into an ice-cold mixture of CH_2Cl_2 and saturated $NaHCO_3$ solution (2:1, 450 mL) and stirred for 15 min, and the layers were separated. The organic layer was washed with water (2 × 150 mL) and brine (200 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was chromatographed over silica gel using EtOAc (10–30%) in hexanes to give a β/α mixture (24:1) (10.83 g, 75%). Crystallization from MeOH gave the pure β isomer **43**: mp 60 °C; UV (MeOH) λ_{max} 269 nm; ^{1}H NMR ($CDCl_3$) δ 1.08 (s, 9 H, *t*-Bu), 2.25 (m, 1 H, 3'-H_a), 2.66 (m, 1 H, 3'-H_b), 3.75 (dd, $J_{4',5'a}$ = 3.8 Hz, $J_{5'a,5'b}$ = 11.5 Hz, 1 H, 5'-H_a), 3.95 (dd, $J_{4',5'b}$ = 3.8 Hz, $J_{5'a,5'b}$ = 11.5 Hz, 1 H, 5'-H_b),

(23) DDI has been reported to have widely differing melting points; see ref 8 (mp softens at 184–186 °C but does not melt up to 300 °C (EtOH-H_2O)) in: Webb, R. R., II; Wos, J. A.; Martin, J. C.; Brodfuehrer, P. R. *Nucleoside Nucleotides* **1988**, *7*, 147 (mp 160–160 °C). Comparison of the material obtained in this paper with that obtained from NCI showed no great difference in melting point characteristics. When the melting point determination was carried out in a capillary tube, both materials soften at approximately 145 °C and then slowly decompose at >200 °C. When a hot stage microscope apparatus was employed, both compounds were observed to melt and then resolidify at 140 °C and slowly decompose as the temperature was increased.

(24) Dideoxyinosine (NSC 612049) was obtained from the National Cancer Institute.

(25) Murakami, K.; Shirasaka, T.; Yoshioka, H.; Kojima, E.; Aoki, S.; Ford, H. Jr.; Driscoll, J. S.; Kelley, J. A.; Mitsuya, H. *J. Med. Chem.* **1991**, *34*, 778.

4.30 (m, 2 H, 2'- and 4'-H), 6.13 (d, J = 5.7 Hz, 1 H, 1'-H), 7.04–7.70 (complex multiplet, 15 H, 3 × C_6H_5), 8.17 (s, 1 H, 8-H). Anal. Calcd for $C_{32}H_{32}N_4O_2FClSiSe$: C, 57.69; H, 4.84; N, 8.41; F, 2.85; Cl, 5.32. Found: C, 57.79; H, 4.82; N, 8.25; F, 2.68; Cl, 5.62.

2-Amino-6-chloro-9-[5-*O*-(*tert*-butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-β-D-*erythro*-pentofuranosyl]-9*H*-purine (44) and 2-Fluoro-9-[5-*O*-(*tert*-butyldiphenylsilyl)-3-deoxy-2-*Se*-phenyl-2-seleno-β-D-*erythro*-pentofuranosyl]-9*H*-adenine (45). Dry ammonia gas was bubbled into a stirred solution of **43** (2.0 g, 3.0 mmol) in DME for 18 h. The solvent was removed under reduced pressure, and the residue was chromatographed over silica gel. Elution with 30% EtOAc in hexanes gave **44** (1.04 g, 52%) as a crystalline solid: mp 65 °C (MeOH); UV (MeOH) λ_{max} 311 nm; ^{1}H NMR ($CDCl_3$) δ 1.07 (s, 9 H, *t*-Bu), 2.17 (m, 1 H, 3'-H_a), 2.60 (m, 1 H, 3'-H_b), 3.75 (dd, $J_{4',5'a}$ = 3.8 Hz, $J_{5'a,5'b}$ = 11.5 Hz, 1 H, 5'-H_a), 3.97 (dd, $J_{4',5'b}$ = 3.8 Hz, $J_{5'a,5'b}$ = 11.5 Hz, 1 H, 5'-H_b), 6.03 (d, $J_{1',2'}$ = 5.5 Hz, 1 H, 1'-H), 7.08–7.70 (complex multiplet, 15 H, 3 × C_6H_5), 7.79 (s, 1 H, 8-H). Anal. Calcd for $C_{32}H_{34}N_5O_2ClSiSe$: C, 57.95; H, 5.16; N, 10.56. Found: C, 57.86; H, 5.21; N, 10.48. Elution with 50% EtOAc in hexanes gave **45** (0.54 g, 28%) as white needles: mp 178–179 °C; UV (MeOH) λ_{max} 262 nm, 270 (sh) nm; ^{1}H NMR ($CDCl_3$) δ 1.07 (s, 9 H, *t*-Bu), 2.15 (m, 1 H, 3'-H_a), 2.65 (m, 1 H, 3'-H_b), 3.73 (dd, $J_{4',5'a}$ = 3.8 Hz, $J_{5'a,5'b}$ = 11.5 Hz, 1 H, 5'-H_a), 3.98 (dd, $J_{4',5'b}$ = 3.7 Hz, $J_{5'a,5'b}$ = 11.5 Hz, 1 H, 5'-H_b), 4.30 (m, 2 H, 2'- and 4'-H), 5.93 (br s, 2 H, NH_2), 6.05 (d, J = 5.49 Hz, 1 H, 1'-H), 7.12–7.70 (complex multiplet, 15 H, 3 × C_6H_5), 7.82 (s, 1 H, 8-H). Anal. Calcd for $C_{32}H_{34}N_5O_2FSiSe$: C, 59.43; H, 5.29; N, 10.83; F, 2.93. Found: C, 59.28; H, 5.29; N, 10.85; F, 2.74.

2-Amino-5-chloro-9-[5-*O*-(*tert*-butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pentofuranosyl]-9*H*-purine (46). Using a procedure similar to that used for **15**, **44** (0.70 g, 1.06 mmol) was converted to **46** (0.508 g, 94.7%): mp 150–152 °C; UV (MeOH) λ_{max} 310 nm; ^{1}H NMR ($CDCl_3$) δ 1.06 (s, 9 H, *t*-Bu), 2.06–2.50 (complex multiplet, 4 H, 2'- and 3'-H), 3.87 (t, J = 4.6 Hz, 2 H, 5'-H), 4.24 (m, 1 H, 4'-H), 5.09 (br s, 2 H, NH_2), 6.15 (pseudo, t, J = 4.8 and 5.1 Hz, 1 H, 1'-H), 7.25–7.70 (complex multiplet, 10 H, 2 × C_6H_5), 8.02 (s, 1 H, 8-H).

2-Fluoro-9-[5-*O*-(*tert*-butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pentofuranosyl]adenine (47). Reaction of **45** (0.537 g, 0.83 mmol) using conditions as described for **15** gave **47** (0.37 g, 91%) as a crystalline solid: mp 170–172 °C; UV (MeOH) λ_{max} 262 nm; ^{1}H NMR ($CDCl_3$) δ 1.09 (s, 9 H, *t*-Bu), 1.98–2.56 (complex multiplet, 4 H, 2'- and 3'-H), 3.76 (dd, $J_{4',5'a}$ = 3.8 Hz, $J_{5'a,5'b}$ = 11.5 Hz, 1 H, 5'-H_a), 3.99 (dd, $J_{4',5'b}$ = 3.8 Hz, $J_{5'a,5'b}$ = 11.5 Hz, 1 H, 5'-H_b), 4.25 (m, 1 H, 4'-H), 6.17 (br s, 2 H, NH_2), 6.21 (pseudo t, J = 3.8 and 5.1 Hz, 1 H, 1'-H), 7.31–7.76 (m, 10 H, 2 × C_6H_5), 8.10 (s, 1 H, 8-H).

2-Amino-6-chloro-9-(2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-9*H*-purine (48). Conversion of **46** (0.30 g, 0.59 mmol) to **48** was accomplished using a procedure similar to that described for **18**. Crude **48** was chromatographed over silica gel (5% MeOH/$CHCl_3$) to yield **48** (0.135 g, 85%) as a crystalline solid: mp 129–133 °C (MeOH) [lit.[25] mp 138–140 °C (H_2O)]; UV (MeOH) λ_{max} 310 nm; ^{1}H NMR (DMSO-d_6) δ 1.88–2.52 (complex multiplet, 4 H, 2'- and 3'-H), 3.55 (m, 2 H, 5'-H), 4.10 (m, 1 H, 4'-H), 4.92 (pseudo t, J = 5.3 and 5.5 Hz, 1 H, 5'-OH), 6.11 (pseudo t, J = 3.4 and 5.3 Hz, 1 H, 1'-H), 6.90 (br s, 2 H, NH_2), 8.36 (s, 1 H, 8-H); $[\alpha]^{25}_D$ 13.50° (*c* 1.06, MeOH). Anal. Calcd for $C_{10}H_{12}N_5O_2Cl$: C, 44.53; H, 4.49; N, 25.97; Cl, 13.14. Found: C, 44.61; H, 4.47; N, 25.93; Cl, 13.11.

2-Fluoro-9-(2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-adenine (49). Using a procedure similar to that used for **18**, **47** (0.37 g, 0.75 mmol) was converted to **49** (0.15 g, 79%) obtained after silica gel chromatography (15% MeOH/$CHCl_3$) as a crystalline solid: mp 200–202 °C (MeOH); UV (MeOH) λ_{max} 261 nm (ε 23 700), 269 (sh) nm, (pH 2) 262 nm (ε 22 900), (pH 11) 261 nm (ε 23 900); ^{1}H NMR (DMSO-d_6) δ 1.98–2.41 (complex multiplet, 4 H, 2'- and 3'-H), 3.55 (m, 2 H, 5'-H), 4.12 (m, 1 H, 4'-H), 4.91 (pseudo t, J = 3.8 and 5.1 Hz, 1 H, 5'-OH), 6.12 (pseudo t, J = 3.8 and 5.1 Hz, 1 H, 1'-H), 7.76 (br s, 2 H, NH_2), 8.32 (s, 1 H, 8-H); $[\alpha]^{25}_D$ −13.24° (*c* 1.02, MeOH). Anal. Calcd for $C_{10}H_{12}N_5O_2F$: C, 47.42; H, 4.78; N, 27.66; F, 7.50. Found: C, 47.62; H, 4.84; N, 28.09; F, 7.34.

2-Amino-6-chloro-9-[5-*O*-(*tert*-butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl]-9*H*-purine (50). Conversion of **44** (0.400 g, 0.60 mmol) to **50** was accomplished using a procedure similar to that described for **22**. Crude **50** was purified by silica gel column chromatography (EtOAc/hexanes (1:1)) to give compound **50** (0.255 g, 83%) as a white solid: mp 66–68 °C; UV (MeOH) λ_{max} 308 nm; ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 9 H, *t*-Bu), 3.78 (dd, J = 1.5 and 5.1 Hz, 2 H, 5'-H), 5.03 (m, 1 H, 4'-H), 5.13 (br s, 2 H, NH_2), 6.01 (m, 1 H, 2'-H), 6.46 (m, 1 H, 3'-H), 6.93 (m, 1 H, 1'-H), 7.30–7.65 (complex multiplet, 10 H, 2 × C_6H_5), 7.77 (s, 1 H, 8-H).

2-Fluoro-9-[5-*O*-(*tert*-butyldiphenylsilyl)-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl]adenine (51). Reaction of **45** (0.760 g, 1.18 mmol) using conditions as described for **22** gave **51** (0.329 g, 57%) as a white solid after purification by silica gel chromatography (EtOAc/hexanes (60:40)): UV (MeOH) λ_{max} 265 nm 270 (sh) nm; ^{1}H NMR ($CDCl_3$) δ 1.06 (s, 9 H, *t*-Bu), 3.81 (d, J = 4.6 Hz, 2 H, 5'-H), 5.00 (m, 1 H, 4'-H), 5.85 (br s, 2 H, NH_2) 6.00 (d, J = 6.9 Hz, 1 H, 2'-H), 6.41 (d, J = 6.2 Hz, 1 H, 3'-H), 6.98 (br s, 1 H, 1'-H), 7.29–7.64 (complex multiplet, 10 H, 2 × C_6H_5) 7.86 (s, 1 H, 8 H).

2-Amino-6-chloro-9-(2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)-9*H*-purine (52). Conversion of **50** (0.235 g, 0.46 mmol) to **52** was accomplished using a procedure similar to that described for **18**. Crude **52** was purified by preparative TLC ($CHCl_3$/MeOH (95:5)) to yield compound **52** (0.120 g, 96%) as a white solid: mp 167 °C; UV (MeOH) λ_{max} (pH 7) 308 nm (ε 5432), (pH 2) 311 nm (ε 5000), (pH 11 308 nm (ε 5494); ^{1}H NMR (DMSO-d_6) δ 3.15 (m, 1 H, 4'-H), 3.56 (br s, 2 H, 5'-H), 4.90 (br s, 1 H, OH), 6.12 (d, J = 5.9 Hz, 1 H, 2'-H), 6.47 (d, J = 5.9 Hz, 1 H, 3'-H), 6.81 (s, 1 H, 1'-H), 6.94 (br s, 2 H, NH_2), 8.12 (s 1 H, 8-H); $[\alpha]^{25}_D$ 89.05° (*c* 2.0, MeOH). Anal. Calcd for $C_{10}H_{10}N_5O_2Cl$: C, 44.86; H, 3.76; N, 26.16; Cl, 13.24. Found: C, 44.82; H, 3.80; N, 25.92; Cl, 13.35.

2-Fluoro-9-(2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)adenine (53). Using a procedure similar to that used for **18**, **51** (0.325 g, 0.66 mmol) was converted to **53** (0.142 g, 85%) obtained as a white solid after purification by silica gel column chromatography ($CHCl_3$:MeOH = 9:1): mp >350 °C; UV (MeOH) λ_{max} (pH 7) 261 nm (ε 14 040), 268 (sh) nm (ε 11 217), (pH 2) 264 nm (ε 11 515), (pH 11) 260 nm (ε 14 343), 268 (sh) nm (ε 11 616); ^{1}H NMR (DMSO-d_6) δ 3.15 (m, 1 H, 4'-H), 3.48–3.59 (m, 2 H, 5'-H), 4.90 (br t, 1 H, 5'-OH), 6.12 (d, J = 6.12 Hz, 1 H, 2'-H), 6.48 (d, J = 6.15 Hz, 1 H, 3'-H), 6.83 (br s, 1 H, 1'-H), 7.75 (br s, 2 H, NH_2), 8.15 (s, 1 H, 8-H); $[\alpha]_D$ 18.30 (*c* 1.26, MeOH). Anal. Calcd for $C_{10}H_{10}N_5O_2F$: C, 47.80; H, 4.01; N, 27.87; F, 7.56. Found: C, 47.86; H, 4.20; N, 27.77; F, 7.27.

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