Synthesis and Antiretrovirus Properties of 5'-Isocyano-5'-deoxythymidine, 5'-Isocyano-2',5'-dideoxyuridine, 3'-Azido-5'-isocyano-3',5'-dideoxythymidine, and 3'-Azido-5'-isocyano-2',3',5'-trideoxyuridine[1]

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The 5'-azidonucleosides **3** and **4** were obtained by treating thymidine and 2'-deoxyuridine with TPP/DEAD/HN_3. The 3'-*O*-silylated 5'-azido-5'-deoxythymidine **5** and the corresponding 2'-deoxyuridine derivative **6** were transformed to the formamides (**7** and **8**, respectively) and dehydrated to the protected 5'-isocyano derivatives **9** and **10**; deblocking gave 5'-isocyano-5'-deoxythymidine (**11**) and 5'-isocyano-2',5'-dideoxyuridine (**12**). 2,3'-Anhydro-5'-formamido derivatives of thymidine and 2'-deoxyuridine (**19** and **20**, respectively) were prepared by three different ways. In the most direct synthesis **3** and **4** were transformed to the 2,3'-anhydro-5'-azidonucleosides **17** and **18** by using TPP/DEAD; following the reaction with TPP/HCO_2COCH_3 gave **19** and **20**. Nucleophilic opening reaction with LiN_3 yielded the 3'-azido-5'-formylamino derivatives **21** and **22**. Dehydration to 3'-azido-5'-isocyano-3',5'-dideoxythymidine (**23**) and 3'-azido-5'-isocyano-2',3',5'-trideoxyuridine (**24**) was achieved with tosyl chloride/pyridine. In contrast with 3'-azido-3'-deoxythymidine, compounds **11**, **12**, **23**, and **24** were devoid of any marked inhibitory effect against DNA and RNA viruses including human immunodeficiency virus type I (HIV).

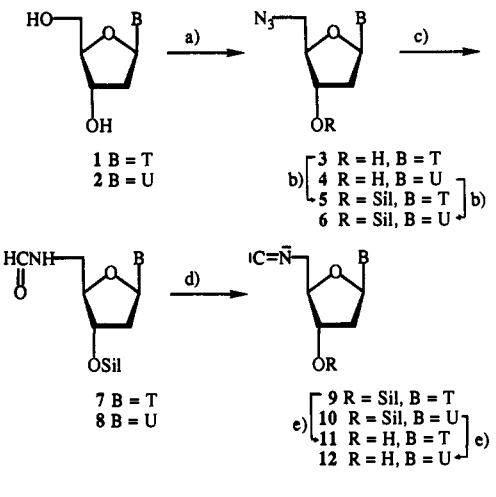
The discovery of 3'-azido-3'-deoxythymidine (AZT, AzddThd) as a retrovirus inhibitor[2] provided the impetus for the synthesis of a series of other structurally related nucleoside analogues and their investigation as potential antiretroviral agents (for a review see refs 3–5). Electronically comparable compounds containing cyano,[6-9] ethynyl,[10] thiocyano,[6,11] isothiocyano,[6] allyl,[12] 2-propynyl,[13,14] or 3-cyanomethyl[13,14] instead of the azido group have been synthesized. Recently, the synthesis and the antiretrovirus properties of the corresponding 3'-isocyano-3'-deoxythymidine and 3'-isocyano-2',3'-dideoxyuridine were described by our group[15] and others.[16,17] The major difference between the chemical properties of the azido and the isocyano group is that the first is electrophilic whereas the second is nucleophilic.

Nucleoside analogues with azido group in the 5' position, especially 5'-azido-5'-deoxythymidine and 5'-azido-2',5'-dideoxy-5-iodouridine, show antivirial activity against herpes simplex virus (HSV).[18] In continuation of our work we have now prepared the title compounds with an isocyano group in the 5' position.

Chemistry

The individual steps leading to the title compounds are summarized in Schemes I–III. The starting materials for the synthesis of 5'-isocyano-5'-deoxythymidine (**11**) and 5'-isocyano-2',5'-dideoxyuridine (**12**) were 5'-azido-5'-deoxythymidine (**3**) and 5'-azido-2',5'-dideoxyuridine (**4**). They were prepared by using HN_3/triphenylphosphine (TPP)/diethyl azodicarboxylate (DEAD).[19] An alternative way is reported by Yamamoto et al. using the system TPP/CBr_4/LiN_3.[20] The disadvantage of TPP/CBr_4/LiN_3 is the sensitivity against traces of moisture. After protection of the 3'-hydroxyl group with *tert*-butyldimethylchlorosilane to give the silyl ether derivatives **5** and **6** the azido function was transformed to the corresponding formamides **7** and **8** by using TPP/acetic formic anhydride HCO_2COCH_3.[21] Dehydration to 5'-isocyano-5'-deoxythymidine (**9**) and 5'-isocyano-2',5'-dideoxyuridine (**10**) was achieved in good yields with tosyl chloride/pyridine.[22] The usual method with $POCl_3$/diisopropylamine[23] gave rather low yields. Finally, the 3'-*tert*-butyldimethylsilyl group was removed by tetrabutylammonium fluoride[24] (**11**, **12**, Scheme I).

Scheme I[a]



Sil = *t*-butyldimethylsilyl

[a] (a) TPP/DEAD/HN_3, toluene/DMF (1:1), <40 °C, 1 h; (b) TBDMSi-Cl, imidazole, DMF, 12 h, 20 °C; (c) TPP/HCO_2COCH_3, toluene, 60 °C, 4 h; (d) TosCl, pyridine, 16 h, 20 °C; (e) TBAF, THF, 2 h, 20 °C.

The key compounds for the synthesis of 3'-azido-5'-isocyano-3',5'-dideoxythymidine (**23**) and 3'-azido-5'-iso-

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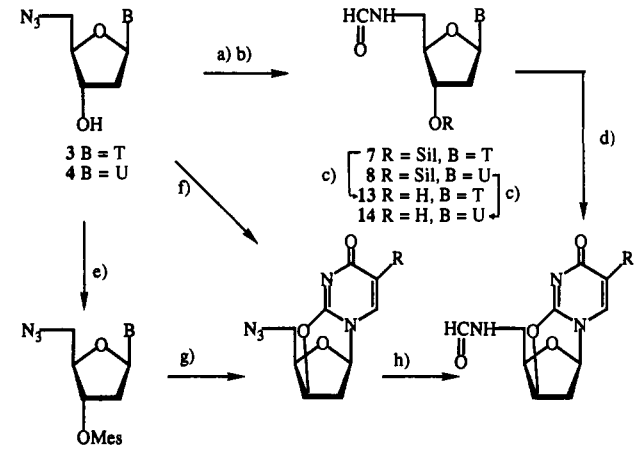
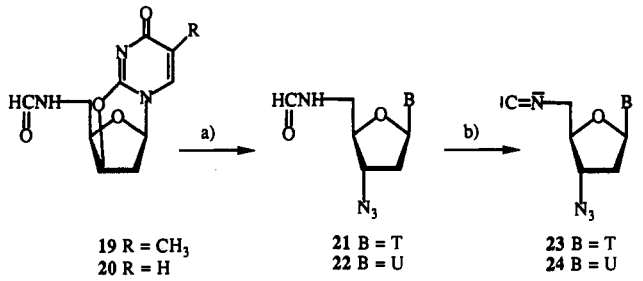
Scheme II[a]



[a] (a) TBDMSi–Cl, imidazole, DMF; (b) TPP/HCO_2COCH_3, DMF/toluene (1:1), 60 °C, 1 h; (c) TBAF, THF; (d) TPP/DEAD, DMF/toluene (1:1), 80 °C, 2 h; (e) MesCl, pyridine, 12 h, 4 °C; (f) TPP/DEAD, DMF/toluene (1:1), 80 °C, 1 h; (g) DBU, THF, 60 °C, 4 h; (h) TPP/HCO_2COCH_3, DMF/toluene (1:1), 60 °C, 1 h.

Scheme III[a]



[a] (a) LiN_3, BzOH, DMF, 130 °C, 4 h; (b) TosCl, pyridine, 12 h, 20 °C.

cyano-2′,3′,5′-trideoxyuridine (**24**) are the 2,3′-anhydro-5′-formamido nucleoside derivatives **19** and **20**. These compounds were prepared by three different ways (Scheme II).

In the first route (49%, 4 steps from **3** and **4**), the 5′-formamido-3′-*O*-(*tert*-butyldimethylsilyl)-5′-deoxythymidine (**7**) and 5′-formamido-3′-*O*-(*tert*-butyldimethylsilyl)-2′,5′-dideoxyuridine (**8**) were cleaved with tetrabutylammonium fluoride to give the derivatives **13** and **14**, respectively. These compounds were transformed to the 2,3′-anhydro nucleosides **19** and **20** by using TPP/DEAD.[25]

The second procedure (57%, 3 steps from **3** and **4**) consists of mesylation of 3′-OH to give **15** and **16** followed by the formation of **17** and **18** in the known neighboring group reaction.[16] Subsequent reaction with TPP/HCO_2COCH_3 gave the 5′-formamido compounds **19** and **20**.

The 5′-formamido derivatives **19** and **20** could be prepared also in two steps from **3** and **4** (65%/45%). In the most direct synthesis **3** and **4** were transformed to **17** and **18** by a combination of the Mitsunobu[25] (formation of the 2,3′-anhydro-bridge) and Staudinger [$R—N_3 \rightarrow R—N{=}P(C_6H_5)_3$] reactions, followed by the addition of HCO_2C-OCH_3 to afford **19** and **20**.

These compounds were transformed (Scheme III) by a nucleophilic opening reaction with lithium azide/benzoic acid in DMF[26] to 3′-azido-5′-(formylamino)-3′,5′-dideoxythymidine (**21**) and 3′-azido-5′-(formylamino)-2′,3′,5′-trideoxyuridine (**22**). Dehydration to 3′-azido-5′-isocyano-3′,5′-dideoxythymidine (**23**) and 3′-azido-5′-isocyano-2′,3′,5′-trideoxyuridine (**24**) was achieved with tosyl chloride/pyridine.[22] Surprisingly, $POCl_3$/diisopropylamine[23] or TPP/CCl_4/triethylamine (Appel procedure)[27] gave no isocyano compounds.

Table I. Inhibitory Effects of 5′-Isocyano-5′-deoxythymidine and 5′-Isocyano-2′,5′-dideoxyuridine Derivatives on HIV-1 Replication in MT-4 Cells and MSV-Induced Transformation of C3H/3T3 Cells

	HIV-1		MSV	
compd	EC_{50},[a] μM	CC_{50},[b] μM	EC_{50},[a] μM	MIC,[c] μM
11	>200	144	>3.2	3.2
12	>200	125	>3.2	3.2
23	>40	122		
24	>40	104		
AZT[d]	0.004	20	0.02	>400

[a] 50% effective concentration, or compound concentration required to inhibit HIV-1-induced cytopathogenicity of MSV-induced transformation of C3H/3T3 cells by 50%. [b] 50% cytotoxic concentration, or compound concentration required to reduce MT-4 cell viability by 50%. [c] Minimal inhibitory concentration or compound concentration that causes a microscopically visible alteration of C3H cell morphology. [d] Data taken from ref 33.

Antiviral Activity of 5′-Isocyano-5′-deoxythymidine (11), 5′-Isocyano-2′,5′-dideoxyuridine (12), 3′-Azido-5′-isocyano-3′,5′-dideoxythymidine (23), and 3′-Azido-5′-isocyano-2′,3′,5′-trideoxyuridine (24)

The antiretroviral activity and cytotoxicity data of compounds 11, 12, 23, and 24 are shown in Table I. None of the compounds were inhibitory to human immunode-

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ficiency virus type 1 (HIV-1) induced cytopathogenicity in MT-4 cells and Moloney murine sarcoma virus (MSV) induced transformation of C3H/3T3 cells at subtoxic concentrations. Compounds 11 and 12 were more toxic to C3H/3T3 cells than MT-4 cells. In contrast, 3'-azido-3'-deoxythymidine was effective against HIV-1 and MSV at a concentration of 0.004 and 0.04 μM, respectively, and cytotoxic to MT-4 cells at a concentration of 6.3 μM (Table I). The lack of significant antiretroviral activity of the test compounds is most likely due to the presence of the isocyano group at the 5'- position which prevents phosphorylation (activation) of the test compounds by cellular kinases. When evaluated against a series of DNA viruses [i.e. herpes simplex virus type 1 (KOS) and type 2 (G), vaccinia virus], and RNA viruses [vesicular stomatitis virus (VSV), polio-1, Sindbis, parainfluenza-3, Semliki forest, Coxsackie B4, and reovirus-1], none of the test compounds proved effective at 200 μg/mL (data not shown).

Experimental Section

Melting points were determined on a Kofler apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker WM 250 spectrometer operating at 250 MHz for ^{1}H NMR and 62.9 MHz for ^{13}C NMR. Chemical shifts are expressed in parts per million downfield from tetramethylsilane. If not indicated otherwise, $CDCl_3$ was used as solvent. Precoated Merck silica gel F 254 plates were used for TLC, and the spots were examined with UV light and by spraying with a solution of 2% $Ce(NO_3)_4$ in 2N H_2SO_4 followed by heating at 200 °C. Flash chromatography[28] was performed with 230–400 mesh silica gel from E. Merck. Infrared spectra were recorded with a Perkin-Elmer 377 spectrophotometer. Mass spectra were recorded on a Varian CH-7 apparatus (70 eV). The source of the anhydrous solvents was as follows: tetrahydrofuran was obtained by distillation after reflux with potassium/benzophenone; toluene was dried by distillation after it had been refluxed in the presence of sodium; DMF was refluxed on CaH_2 and distilled; dichloromethane was refluxed over phosphorus pentoxide and distilled. Thymidine (1) and 2'-deoxyuridine (2) were purchased from Fluka. Abbreviations used are EA (ethyl acetate), PE (petroleum ether), TPP (triphenylphosphine), TPPO (triphenylphosphine oxide), and DEAD (diethyl azodicarboxylate).

5'-Azido-5'-deoxythymidine (3). A total of 2.0 g (8.26 mmol) of thymidine and 2.596 g (9.91 mmol) of triphenylphosphine (TPP) were dissolved in 20 mL of DMF and 20 mL of toluene. To this solution were added 12 mL of 0.1 M toluenic HN_3 solution[29] and 1.560 mL (9.91 mmol) of diethyl azodicarboxylate (DEAD); temperature was kept below 40 °C. After 2 h (TLC: $CHCl_3$/MeOH, 5:1) the solvents were removed, and the residue was dissolved in chloroform and applied on to a silica gel column. First, TPP and triphenylphosphine oxide (TPPO) were separated with chloroform as solvent; then, 3 and unreacted thymidine were eluted with $CHCl_3$/MeOH, (20:1): yield 2.004 g (91%); mp 163–165 °C, lit.[20] mp 164–166.5 °C (MeOH); R_f = 0.70 ($CHCl_3$/MeOH, 5:1); ^{1}H NMR ($CDCl_3$/DMSO-d_6, 1:1) δ 1.81 (s, 3, 5-CH_3), 2.16 (m, 2, 2'-Ha, 2'-Hb), 3.54 (ABX system, 2, $J_{5'a,5'b}$ = 13.0 Hz, $J_{5'a,4'}$ = 5.0 Hz, $J_{5'b,4'}$ = 4.0 Hz, 5'-Ha, 5'-Hb), 3.86 (m, 1,4'-H), 4.22 (m, 1,3'-H), 5.32 (br s, 1,3'-OH), 6.19 (t, 1, $J_{1',2'}$ = 6.5 Hz, 1'-H), 7.33 (s, 1,6-H), 11.20 (br s, 1,3-H). Anal. ($C_{10}H_{13}N_5O_4$) C, H, N.

5'-Azido-2',5'-dideoxyuridine (4). Compound 4 was prepared in the same manner as described for 3, with 2'-deoxyuridine as starting material: yield 80%, mp 139–140 °C (MeOH); R_f = 0.62 ($CHCl_3$/MeOH, 5:1); ^{1}H NMR ($CDCl_3$/DMSO-d_6, 1:1), δ 2.21 (dd, 2, $J_{2',1'}$ = 6.0 Hz, $J_{2',3'}$ = 7.0 Hz, 2'-Ha, 2'-Hb), 3.56 (m, 2,5'-Ha, 5'-Hb), 3.89 (m, 1,4'-H), 4.22 (m, 1,3'-H), 5.35 (d, 1, $J_{3',OH}$ = 4.0 Hz, 3'-OH), 5.60 (d, 1, $J_{5,6}$ = 8.0 Hz, 5-H), 6.17 (t, 1, $J_{1',2'}$ = 6.0 Hz, 1'-H), 7.56 (d, 1,6-H), 11.48 (br s, 1,3-H). Anal. ($C_9H_{11}N_5O_4$) C, H, N.

5'-Azido-3'-*O*-(*tert*-butyldimethylsilyl)-5'-deoxythymidine (5). Compound 3 (2.7 g, 10.1 mmol) and imidazole (1.72 g, 25.30 mmol) were dissolved in 20 mL of DMF and then *tert*-butyldimethylchlorosilane (2.0 g, 13.27 mmol) was added dropwise. The mixture was kept at room temperature overnight. Then DMF was removed and the residue was partitioned between ethyl acetate (EA) (50 mL) and water (10 mL). The water phase was extracted three times with 50 mL of EA. The organic phase was dried with Na_2SO_4 and evaporated. The remaining solid crude material (99% yield) could be used directly for the next step. For analyses a small sample was purified by crystallization from petroleum ether (PE): yield after crystallization 3.7 g (96%); mp 94–96 °C; R_f = 0.46 (PE/EA, 1:1); ^{1}H NMR δ 0.07 (s, 6, $Si(CH_3)_2$), 0.87 (s, 9, $SiC(CH_3)_3$), 1.94 (d, 3, $J_{CH3,6}$ = 1.0 Hz, 5-CH_3), 2.14 (ddd, 1, $J_{2'a,2'b}$ = 13.5 Hz, $J_{2'a,1'}$ = $J_{2'a,3'}$ = 7.0 Hz, 2'-Ha), 2.27 (ddd, 1, $J_{2'b,1'}$ = 7.0 Hz, $J_{2'b,3'}$ = 3.5 Hz, 2'-Hb), 3.56 (ABX system, 2, $J_{5'a,5'b}$ = 13.0 Hz, $J_{5'a,4'}$ = $J_{5'b,4'}$ = 3.5 Hz, 5'-Ha, 5'-Hb), 3.90 (q, 1, $J_{3',4'}$ = 3.5 Hz, 4'-H), 4.33 (dt, 1,3'-H), 6.24 (t, 1,1'-H), 7.30 (d, 1,6-H), 8.70 (br s, 1,3-H); ^{13}C NMR δ -5.13, -4.90, 12.33, 17.67, 25.46, 40.36, 51.56, 71.55, 84.61, 84.83, 111.06, 135.30, 150.40, 163.95; MS (150 °C) *m/e* (%) 324 (38) (M^+ - $C(CH_3)_3$); IR (CH_2Cl_2) 2110 cm^{-1} (N_3). Anal. ($C_{16}H_{27}N_5O_4Si$) C, H, N.

5'-Azido-3'-*O*-(*tert*-butyldimethylsilyl)-2',5'-dideoxyuridine (6). Compound 6 was prepared in the same manner as 5, with 4 as starting material: yield 82%; mp 106–107 °C (PE); R_f = 0.54 (PE/EA, 1:1); ^{1}H NMR δ 0.08 (s, 6, $Si(CH_3)_2$), 0.88 (s, 9, $SiC(CH_3)_3$), 2.15 (ddd, 1, $J_{2'a,2'b}$ = 14.0 Hz, $J_{2'a,1'}$ = $J_{2'a,3'}$ = 7.0 Hz, 2'-Ha), 2.31 (ddd, 1, $J_{2'b,1'}$ = 7.0 Hz, $J_{2'b,3'}$ = 4.8 Hz, 2'-Hb), 3.50 (dd, 1, $J_{5'a,5'b}$ = 14.0 Hz, $J_{5'a,4'}$ = 4.0 Hz, 5'-Ha), 3.69 (dd, 1, $J_{5'b,4'}$ = 4.0 Hz, 5'-Hb), 3.92 (m, 1,4'-H), 4.33 (dt, 1, $J_{3',4'}$ = 4.8 Hz, 3'-H), 5.77 (dd, 1, $J_{5,6}$ = 8.0 Hz, J = 0.8 Hz, 5-H), 6.22 (t, 1,1'-H), 7.51 (d, 1,6-H), 9.02 (br s, 1,3-H); ^{13}C NMR δ -5.03, -4.79, 17.79, 25.56, 40.64, 51.58, 71.51, 84.71, 85.13, 102.76, 139.61, 150.27, 163.40; MS (150 °C) *m/e* (%) 310 (46) (M^+ - $C(CH_3)_3$); IR (CH_2Cl_2) 2100 cm^{-1} (N_3). Anal. ($C_{15}H_{25}N_5O_4Si$) C, H, N.

3'-*O*-(*tert*-Butyldimethylsilyl)-5'-deoxy-5'-formamidothymidine (7). Compound 5 (0.419 g, 0.84 mmol) and TPP (0.262 g, 1.0 mmol) were dissolved in 10 mL of toluene. Then acetic formic anhydride[30] (0.176 mL) was added, and the reaction mixture was heated to 60 °C. After 4 h TLC showed complete reaction. Toluene was removed, and the residue was applied on to silica gel (PE/EA, 1:2) and purified from TPP and TPPO: yield 0.323 g (77%); mp 110–113 °C; R_f = 0.74 ($CHCl_3$/MeOH, 5:1); ^{1}H NMR (acetone-d_6) δ 0.11 (s, 6, $Si(CH_3)_2$), 0.89 (s, 9, $SiC(CH_3)_3$), 1.83 (d, 3, $J_{CH3,6}$ = 1.0 Hz, 5-CH_3), 2.19 (ddd, 1, $J_{2'a,2'b}$ = 13.5 Hz, $J_{2'a,1'}$ = 6.1 Hz, $J_{2'a,3'}$ = 3.0 Hz, 2'-Ha), 2.33 (ddd, 1, $J_{2'b,1'}$ = 8.0 Hz, $J_{2'b,3'}$ = 6.0 Hz, 2'-Hb), 3.51 (m, 2, $J_{5'a,5'b}$ = 7.0 Hz, $J_{5'a,NH}$ = 2.0 Hz, 5'-Ha, 5'-Hb), 3.90 (m, 1, $J_{3',4'}$ = 3.0 Hz, $J_{4',5'a}$ = $J_{4',5'b}$ = 6.0 Hz, 4'-H), 4.48 (m, 1, 3'-H), 6.25 (dd, 1, 1'-H), 7.46 (br s, 1, N*H*CHO), 7.54 (d, 1, 6-H), 8.19 (s, 1, CHO), 10.05 (br s, 1, 3-H); ^{13}C NMR δ -4.99, 12.12, 17.70, 25.45, 25.53, 39.29, 39.52, 72.52, 85.20, 87.39, 110.91, 111.00, 137.14, 150.53, 161.87, 164.14; MS (150 °C) *m/e* (%) 383 (<1) (M^+), 368 (<1) (M^+ - CH_3), 326 (5) (M^+ - $C(CH_3)_3$). Anal. ($C_{17}H_{29}N_3O_5Si$) C, H, N.

3'-*O*-(*tert*-Butyldimethylsilyl)-2',5'-dideoxy-5'-formamidouridine (8). Compound 8 was prepared in the same manner as described for 7, with 6 as starting material: yield 76%; mp 156–158 °C (EA); R_f = 0.11 (ether/acetone, 9:1); ^{1}H NMR δ 0.12 (s, 6, $Si(CH_3)_2$), 0.87 (s, 9, $SiC(CH_3)_3$), 2.13 (ddd, 1, $J_{2'a,2'b}$ = 13.5 Hz, $J_{2'a,1'}$ = 7.0 Hz, $J_{2'a,3'}$ = 4.0 Hz, 2'-Ha), 2.38 (ddd, 1, $J_{2'b,1'}$ = $J_{2'b,3'}$ = 7.0 Hz, 2'-Hb), 3.55 (m, 2, $J_{5'a,5'b}$ = 15.0 Hz, $J_{5'a,4'}$ = 5.0 Hz, $J_{5'b,4'}$ = 6.0 Hz, 5'-Ha, 5'-Hb), 3.92 (m, 1, 4'-H), 4.30 (dt, 1, $J_{3',4'}$ = 4.0 Hz, 3'-H), 5.73 (dd, 1, $J_{5,6}$ = 8.0 Hz, J = 1.0 Hz, 5-H), 5.93 (t, 1, 1'-H), 6.54 (br s, 1, N*H*CHO), 7.29 (d, 1, 6-H), 8.22 (s, 1, CHO), 9.41 (s, 1, 3-H); ^{13}C NMR δ -5.06, -4.95, 17.63, 25.48, 39.18, 39.81, 72.34, 85.25, 86.70, 102.37, 141.13, 150.38, 162.03, 163.79; MS (150 °C) *m/e* (%) 354 (1) (M^+ - CH_3), 312 (60) (M^+ - $C(CH_3)_3$). Anal. ($C_{16}H_{27}N_3O_5Si$) C, H, N.

3'-*O*-(*tert*-Butyldimethylsilyl)-5'-deoxy-5'-isocyanothymidine (9). Compound 9 was prepared in the same manner as 23, with 7 as starting material: yield 73%; white foam; R_f = 0.80 (ether/acetone, 9:1); ^{1}H NMR δ 0.08 (s, 6, $Si(CH_3)_2$), 0.87 (s, 9, $SiC(CH_3)_3$), 1.90 (s, 3, 5-CH_3), 2.28 (t, 2, 2'-Ha, 2'-Hb), 3.71 (ABX system, 2, $J_{5'a,5'b}$ = 16.0 Hz, $J_{5'a,4'}$ = 3.0 Hz, $J_{5'b,4'}$ = 4.0 Hz, 5'-Ha, 5'-Hb), 3.88 (m, 1, 4'-H), 4.41 (m, 1, $J_{3',4'}$ = 6.0 Hz, 3'-H), 6.24 (t, 1, $J_{1',2'}$ = 6.5 Hz, 1'-H), 7.32 (s, 1, 6-H), 9.38 (br s, 1, 3-H);

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(29) *Org. React.* **1946**, *3*, 327.
(30) Krimen, L. I. *Org. Synth.* **1970**, *50*, 1.

^{13}C NMR δ -5.19, -4.95, 12.10, 17.52, 25.33, 39.87, 42.76, 71.60, 82.52, 84.83, 111.30, 135.31, 150.22, 159.37, 163.67; MS (130 °C) *m/e* (%) 308 (17) (M^+ - $C(CH_3)_3$), 281 (5) (M^+ - $C(CH_3)_3$ - HCN); IR (CH_2Cl_2) 2150 cm^{-1} (N=C). Anal. ($C_{17}H_{27}N_3O_4Si$) C, H, N.

3'-*O*-(*tert*-Butyldimethylsilyl)-2',5'-dideoxy-5'-isocyanouridine (10). This compound was prepared from **8** as described for **23**: yield 77%; colorless oil; R_f = 0.62 (ether/acetone, 9:1); ^{1}H NMR δ 0.10 (s, 6, $Si(CH_3)_2$), 0.87 (s, 9, $SiC(CH_3)_3$), 2.26 (ddd, 1, $J_{2'a,2'b}$ = 14.0 Hz, $J_{2'a,1'}$ = $J_{2'a,3'}$ = 7.0 Hz, 2'-Ha), 2.41 (ddd, 1, $J_{2'b,1'}$ = 7.0 Hz, $J_{2'b,3'}$ = 5.0 Hz, 2'-Hb), 3.62 (dd, 1, $J_{5'a,5'b}$ = 15.0 Hz, $J_{5'a,4'}$ = 4.0 Hz, 5'-Ha), 3.79 (dd, 1, $J_{5'b,4'}$ = 4.0 Hz, 5'-Hb), 3.90 (m, 1, 4'-H), 4.42 (dt, 1, $J_{3',4'}$ = 5.0 Hz, 3'-H), 5.79 (d, 1, $J_{5,6}$ = 8.0 Hz, 5-H), 6.24 (t, 1, 1'-H), 7.49 (d, 1, 6-H), 9.03 (br s, 1, 3-H); ^{13}C NMR δ -5.08, -4.84, 17.63, 25.45, 40.04, 42.86, 71.73, 82.77, 85.30, 102.86, 139.82, 150.23, 159.21, 163.35; MS (170 °C) *m/e* (%) 336 (1) (M^+ - CH_3), 3.09 (1) (M^+ - CH_3 - HCN), 294 (53) (M^+ - $C(CH_3)_3$), 267 (15) (M^+ - $C(CH_3)_3$ - HCN); IR (CH_2Cl_2) 2145 cm^{-1} (N=C). Anal. ($C_{16}H_{25}N_3O_4Si$) C, H, N.

5'-Isocyano-5'-deoxythymidine (11). TBAF (0.7 mL, 0.5 M) solution in dry THF were added to a solution of 127 mg (1.45 mmol) of **9** in dry THF (10 mL). After 30 min TLC ($CHCl_3$/MeOH, 5:1) indicated complete reaction. THF was removed in vacuo and the residue was chromatographed with $CHCl_3$/MeOH (30:1) as solvent system: yield 74 mg (85%); mp. 175–183 °C dec; R_f = 0.60 ($CHCl_3$/MeOH, 5:1); ^{1}H NMR (acetone-d_6) δ 1.93 (d, 3, $J_{CH3,6}$ = 1.0 Hz, 5-CH_3), 2.29–2.49 (m, 2, $J_{2'a,2'b}$ = 14.0 Hz, $J_{2'a,1'}$ = 7.0 Hz, $J_{2'a,3'}$ = 4.0 Hz, $J_{2'b,1'}$ = $J_{2'b,3'}$ = 7.0 Hz, 2'-Ha, 2'-Hb), 3.89 (m, 2, 5'-Ha, 5'-Hb), 4.03 (m, 1, 4'-H), 4.49 (m, 1, 3'-H), 4.79 (d, 1, $J_{3',OH}$ = 4.0 Hz, 3'-OH), 6.35 (t, 1, 1'-H), 7.54 (d, 1, 6-H), 10.06 (br s, 1, 3-H); IR (KBr) 2153 cm^{-1} (N=C). Anal. ($C_{11}H_{13}N_3O_4$) C, H, N.

5'-Isocyano-2',5'-dideoxyuridine (12). Deblocking was accomplished with TBAF as described above for compound 11: yield 78%; mp 170–173 (acetone); R_f = 0.56 ($CHCl_3$/MeOH, 5:1); ^{1}H NMR (acetone-d_6) δ 2.38 (m, 2, $J_{2'a,1'}$ = 7.0 Hz, $J_{2'b,3'}$ = 2.5 Hz, 2'-Ha, 2'-Hb), 3.87 (ABX system, 2, $J_{5'a,5'b}$ = 15.0 Hz, $J_{5'a,4'}$ = $J_{5'b,4'}$ = 5.0 Hz, 5'-Ha, 5'-Hb), 4.04 (m, 1, 4'-H), 4.46 (m, 1,3'-H), 4.77 (d, 1, $J_{OH,3'}$ = 4.5 Hz, 3'-OH), 5.65 (d, 1, $J_{5,6}$ = 8.0 Hz, 5-H), 6.30 (t, 1, 1'-H), 7.65 (d, 1, 6-H), 10.08 (br s, 1, 3-H); IR (KBr) 2162 cm^{-1} (N=C). Anal. ($C_{10}H_{11}N_3O_4$) C, H, N.

5'-Formamido-5'-deoxythymidine (13). The silyl group of compound **7** was removed with TBAF as described for 11: yield 0.945 (78%); mp 207–209 °C; R_f = 0.15 ($CHCl_3$/MeOH, 9:1); ^{1}H NMR (acetone-d_6) δ 1.86 (d, 3, $J_{5\text{-}CH_3,6}$ = 1.5 Hz, 5-CH_3), 2.21–2.33 (m, 2,2'-Ha, 2'-Hb), 3.51 (m, 2, 5'-Ha, 5'-Hb), 3.92 (m, 1, 4'-H), 4.37 (m, 1, 3'-H), 4.59 (d, 1, $J_{3',OH}$ = 4.0 Hz, 3'-OH), 6.27 (t, $J_{1',2'}$ = 7.0 Hz, 1'-H), 7.49 (br s, 1, N*H*CHO), 7.56 (d, 1, 6-H), 8.19 (s, 1, CHO), 9.98 (br s, 1, 3-H). Anal. ($C_{11}H_{15}N_3O_5$) C, H, N.

2',5'-Dideoxy-5'-formamidouridine (14). The protecting group of compound **8** was removed with TBAF as described for compound 11: yield 81%, colorless oil; R_f = 0.19 ($CHCl_3$/MeOH, 5:1); ^{1}H NMR (acetone-d_6) δ 2.29 (d, 1, $J_{2'a,1'}$ = 7.0 Hz, 2'-Ha), 2.32 (d, 1, $J_{2'b,1'}$ = 7.0 Hz, 2'-Hb), 3.21 (m, 2, $J_{5'a,5'b}$ = 14.0 Hz, $J_{5'a,4'}$ = 8.0 Hz, $J_{5'b,4'}$ = 6.0 Hz, 5'-Ha, 5'-Hb), 3.95 (m, 1, 4'-H), 4.37 (dd, 1, $J_{3',4'}$ = 9.0 Hz, $J_{3',OH}$ = 4.0 Hz, 3'-H), 4.62 (d, 1, 3'-OH), 5.63 (d, 1, $J_{5,6}$ = 8.0 Hz, 5-H), 6.26 (t, 1, 1'-H), 7.48 (br s, 1, N*H*CHO), 7.73 (d, 1, 6-H), 8.20 (s, 1, CHO), 10.07 (br s, 1, 3-H). Anal. ($C_{10}H_{13}N_3O_5$) C, H, N.

5'-Azido-5'-deoxy-3'-*O*-mesylthymidine (15). 5-Azido-5'-deoxythymidine (**3**) (0.219 g, 0.84 mmol) was dissolved in pyridine (5 mL). Mesyl chloride (0.075 mL, 0.82 mmol) was added dropwise at 0 °C. After 14 h at 4 °C the reaction mixture was concentrated in vacuo. Then water (5 mL) and EA (50 mL) were added; the water phase was extracted with EA (3 × 50 mL); the organic phase was dried with Na_2SO_4, evaporated, and chromatographed (silica gel, EA): yield 0.2 g (71%); mp 131–132.5 °C (acetone/PE); R_f = 0.53 (EA); ^{1}H NMR δ 1.94 (d, 3, $J_{5\text{-}CH_3,6}$ = 1.0 Hz, 5-CH_3), 2.38 (ddd, 1, $J_{2'a,2'b}$ = 14.0 Hz, $J_{2'a,1'}$ = 8.5 Hz, $J_{2'a,3'}$ = 7.0 Hz, 2'-Ha), 2.59 (ddd, 1, $J_{2'b,1'}$ = 6.0 Hz, $J_{2'b,3'}$ = 2.8 Hz, 2'-Hb), 3.10 (s, 3, CH_3), 3.73 (ABX system, 2, $J_{5'a,5'b}$ = 14.0 Hz, $J_{5'a,4'}$ = 3.5 Hz, $J_{5'b,4'}$ = 3.0 Hz, 5'-Ha, 5'-Hb), 4.33 (m, 1, 4'-H), 5.24 (dt, 1, $J_{3',4'}$ = 3.0 Hz, 3'-H), 6.28 (dd, 1, 1'-H), 7.29 (d, 1, 6-H), 9.02 (br s, 1, 3-H); MS (180 °C), *m/e* (%) = 345 (2) (M^+), 249 (16) (M^+ - MesOH); IR (CH_2Cl_2) 2110 cm^{-1} (N_3). Anal. ($C_{11}H_{15}N_5O_6S$) C, H, N.

5'-Azido-2',5'-dideoxy-3'-*O*-mesyluridine (16). Compound **16** was prepared in the same manner as **15**, with 5'-azido-2',5'-dideoxyuridine (**4**) as starting material: yield 84%; colorless oil; R_f = 0.46 (EA); ^{1}H NMR δ 2.35 (ddd, 1, $J_{2'a,2'b}$ = 14.5 Hz, $J_{2'a,1'}$ = 9.0 Hz, $J_{2'a,3'}$ = 7.0 Hz, 2'-Ha), 2.62 (ddd, 1, $J_{2'b,1'}$ = 6.0 Hz, $J_{2'b,3'}$ = 2.8 Hz, 2'-Hb), 3.10 (s, 3, CH_3), 3.73 (ABX system, 2, $J_{5'a,5'b}$ = 13.5 Hz, $J_{5'a,4'}$ = 3.0 Hz, $J_{5'b,4'}$ = 3.0 Hz, 5'-Ha, 5'-Hb), 4.33 (m, 1, 4'-H), 5.22 (dt, 1, $J_{3',4'}$ = 2.8 Hz, 3'-H), 5.79 (d, 1, $J_{5,6}$ = 8.0 Hz), 6.24 (dd, 1, 1'-H), 7.49 (d, 1, 6-H), 9.33 (br s, 1, 3-H); MS (160 °C) *m/e* (%) = 331 (<1) (M^+), 235 (5) (M^+ - MesOH); IR (CH_2Cl_2) 2115 cm^{-1} (N_3). Anal. ($C_{10}H_{13}N_5O_3S$) C, H, N.

2,3'-Anhydro-5'-azido-5'-deoxythymidine (17). Method A. DBU (0.06 mL, 0.4 mmol) was added to a solution of 118 mg (0.34 mmol) of **15** in dry THF. The mixture was heated at 80 °C for 6 h. After complete reaction the solvent was evaporated and the product was purified on silica gel ($CHCl_3$/MeOH, 5:1): yield 93%, mp 184–185 °C (acetone/PE); R_f = 0.58 ($CHCl_3$/MeOH, 1:1).

Method B. To a homogenous solution of 1.39 g (5.20 mmol) of 5'-azido-5'-deoxythymidine (**3**) in toluene (10 mL) and dioxane (10 mL) were added 1.2 equiv of TPP/DEAD complex in toluene, prepared externally. The mixture became turbid and was heated to 60 °C for 4 h. The workup procedure was the same as described above: yield 75%; ^{1}H NMR (acetone-d_6) δ 1.81 (d, 3, $J_{5\text{-}CH_3,6}$ = 1.3 Hz, 5-CH_3), 2.65 (ddd, 1, $J_{2'a,2'b}$ = 13.0 Hz, $J_{2'a,1'}$ = 4.0 Hz, $J_{2'a,3'}$ = 3.0 Hz, 2'-Ha), 2.71 (dd, 1, $J_{2'b,1'}$ < 1.0 Hz, $J_{2'b,3'}$ = 1.5 Hz, 2'-Hb), 3.59 (ABX system, 2, $J_{5'a,5'b}$ = 13.0 Hz, $J_{5'a,4'}$ = 7.0 Hz, $J_{5'b,4'}$ = 6.0 Hz, 5'-Ha, 5'-Hb), 4.48 (ddd, 1, $J_{3',4'}$ = 2.5 Hz, 4'-H), 5.30 (m, 1, 3'-H), 5.86 (d, 1, 1'-H), 7.43 (d, 1, 6-H); MS (300 °C) *m/e* (%) = 249 (5) (M^+), 221 (2) (M^+ - N_2); IR (Nujol) 2101 cm^{-1} (N_3). Anal. ($C_{10}H_{11}N_5O_3$) C, H, N.

2,3'-Anhydro-5'-azido-2',5'-dideoxyuridine (18). Compound **18** was prepared by two different ways as described for **17**.

Method A: Starting material **16**: yield 95%; mp 230–233 °C (acetone): R_f = 0.21 ($CHCl_3$/MeOH, 5:1).

Method B: Starting material **4**: yield 63%; ^{1}H NMR (acetone-d_6) δ 2.66 (ddd, 1, $J_{2'a,2'b}$ = 13.0 Hz, $J_{2'a,1'}$ = 4.0 Hz, $J_{2'a,3'}$ = 2.5 Hz, 2'-Ha), 2.77 (dd, 1, $J_{2'b,1'}$ < 1.0 Hz, $J_{2'b,3'}$ = 2.0 Hz, 2'-Hb), 3.61 (ABX system, 2, $J_{5'a,5'b}$ = 13.0 Hz, $J_{5'a,4'}$ = 7.0 Hz, $J_{5'b,4'}$ = 6.0 Hz, 5'-Ha, 5'-Hb), 4.50 (ddd, 1, $J_{3',4'}$ = 2.5 Hz, 4'-H), 5.34 (m, 1, 3'-H), 5.80 (d, 1, $J_{5,6}$ = 7.5 Hz, 5-H), 5.93 (d, 1, 1'-H), 7.58 (d, 1, 6-H); MS (300 °C) *m/e* (%) = 235 (6) (M^+); IR (Nujol) 2109 cm^{-1} (N_3). Anal. ($C_{10}H_{11}N_5O_3$) C, H, N.

2,3'-Anhydro-5'-deoxy-5'-formamidothymidine (19). Method A. DEAD (0.425 mL, 2.7 mmol) was added at 80 °C to a homogenous solution of 0.606 g (2.25 mmol) of **13** and 0.708 g (2.7 mmol) of TPP in dry DMF (10 mL) and toluene (10 mL). After 15 min the solution became turbid and showed red color. Heating was stopped after 4 h and the reaction mixture was cooled (ice bath). Crystalline **19** (0.234 g) could be obtained by filtration. The filtrate was concentrated in vacuo, and the residue was chromatographed on silica gel; TPP and TPPO were eluted with chloroform; unreacted starting material (20%) and 0.151 g of **19** were separated with $CHCl_3$/MeOH (5:1): yield 0.480 g (85%) of crude product (light red colored), which could be used directly for the next step.

Method B. Acetic formic anhydride (0.610 mL) was added to a homogenous solution (dry DMF, toluene) of 0.865 g (3.47 mmol) of **17** and 1.091 g (4.2 mmol) of TPP, and the mixture was heated at 60 °C for 4 h. When the mixture was allowed to cool down, 0.580 g (66.5%) of crystalline **19** precipitated. The filtrate was concentrated in vacuo. After chromatography (silica gel, $CHCl_3$/MeOH, 5:1), 0.188 g (22%) of pure **19** were obtained: yield 0.768 g (86.5%); mp 221–223 °C dec (acetone); R_f = 0.11 ($CHCl_3$/MeOH, 5:1); ^{1}H NMR (MeOH-d_4) δ 1.93 (s, 3, 5-CH_3), 2.59 (ddd, 1, $J_{2'a,2'b}$ = 13.5 Hz, $J_{2'a,1'}$ = 3.5 Hz, $J_{2'a,3'}$ = 3.0 Hz, 2'-Ha), 2.67 (d, 1, $J_{2'b,1'}$ < 1.0 Hz, $J_{2'b,3'}$ < 1.0 Hz, 2'-Hb), 3.46 (ABX system, 2, $J_{5'a,5'b}$ = 15.0 Hz, $J_{5'a,4'}$ = 6.5 Hz, $J_{5'b,4'}$ = 7.5 Hz, 5'-Ha, 5'-Hb), 4.41 (ddd, 1, $J_{3',4'}$ = 2.0 Hz, 4'-H), 5.32 (d, 1, 3'-H), 5.83 (d, 1, $J_{1',2'a}$ = 3.5 Hz, 1'-H), 7.60 (s, 1, 6-H), 8.06 (s, 1, CHO). Anal. ($C_{11}H_{13}N_3O_4$) C, H, N.

2,3'-Anhydro-5'-formamido-2',5'-dideoxyuridine (20). Compound **20** was prepared by two ways, as described for **19**.

Method A. Starting material **14**: yield 80%.

Method B. Starting material **18**: yield 72%; mp 171–174 °C (acetone): R_f = 0.04 ($CHCl_3$/MeOH, 5:1); ^{1}H NMR (MeOH-d_4) δ 2.50 (ddd, 1, $J_{2'a,2'b}$ = 13.0 Hz, $J_{2'a,1'}$ = 3.0 Hz, $J_{2'a,3'}$ = 2.0 Hz, 2'-Ha), 2.58 (d, 1, $J_{2'b,1'}$ < 1.0 Hz, $J_{2'b,3'}$ < 1.0 Hz, 2'-Hb), 3.38 (ABX system, 2, $J_{5'a,5'b}$ = 14.0 Hz, $J_{5'a,4'}$ = 6.0 Hz, $J_{5'b,4'}$ = 7.5 Hz, 5'-Ha,

5'-Hb), 4.32 (ddd, 1, $J_{3',4'}$ = 2.0 Hz, 4'-H), 5.25 (br s, 1, 3'-H), 5.77 (d, 1, 1'-H), 5.90 (d, 1, $J_{5,6}$ = 7.5 Hz, 5-H), 7.56 (d, 1, 6-H), 7.96 (s, 1, CHO). Anal. ($C_{10}H_{11}N_3O_4$) C, H, N.

3'-Azido-5'-formamido-3',5'-dideoxythymidine (21). Lithium azide (0.117 g, 2.40 mmol) and 97.6 mg (0.80 mmol) of benzoic acid were added to a solution of 0.20 g (0.80 mmol) of **19** in 20 mL of DMF. The mixture was heated to 130 °C for 4 h. Then DMF was removed in vacuo, and the residue was dissolved in water and EA. The water phase was extracted three times with EA, and the organic phase was dried with Na_2SO_4, concentrated, and chromatographed (silica gel, $CHCl_3$/MeOH, 50:1): yield 0.152 g (65%); white foam; R_f = 0.61 ($CHCl_3$/MeOH, 5:1); ^{1}H NMR δ 1.91 (s, 3, 5-CH_3), 2.36 (ddd, 1, $J_{2'a,2'b}$ = 14.0 Hz, $J_{2'a,1'}$ = 6.5 Hz, $J_{2'a,3'}$ = 5.5 Hz, 2'-Ha), 2.67 (ddd, 1, $J_{2'b,1'}$ = 6.5 Hz, $J_{2'b,3'}$ = 8.0 Hz, 2'-Hb), 3.52 (ddd, 1, $J_{5'a,5'b}$ = 15.0 Hz, $J_{5'a,4'}$ = $J_{5'a,NH}$ = 4.0 Hz, 5'-Ha), 3.75 (ddd, 1, $J_{5'b,4'}$ = 5.0 Hz, $J_{5'b,NH}$ = 7.5 Hz, 5'-Hb), 3.90 (m, 1, $J_{4',3'}$ = 5.5 Hz, 4'-H), 4.23 (dt, 1, 3'-H), 5.76 (t, 1, 1'-H), 6.43 (br s, 1, N*H*CHO), 7.02 (s, 1, 6-H), 8.25 (s, 1, CHO), 8.78 (br s, 1, 3-H); ^{13}C NMR δ 12.30, 36.43, 39.31, 61.05, 82.56, 88.14, 111.56, 137.50, 150.46, 161.98, 163.76; MS (220 °C) *m/e* (%) 294 (2) (M^+); IR (CH_2Cl_2) 2105 cm^{-1} (N_3). Anal. ($C_{11}H_{14}N_6O_4$) C, H, N.

3'-Azido-5'-formamido-2',3',5'-trideoxyuridine (22). Compound **22** was prepared in the same manner as **21**, with **20** as starting material: yield 48%; colorless oil; R_f = 0.49 ($CHCl_3$/MeOH, 5:1); ^{1}H NMR δ 2.42 (ddd, 1, $J_{2'a,2'b}$ = 14.5 Hz, $J_{2'a,1'}$ = 8.0 Hz, $J_{2'a,3'}$ = 6.0 Hz, 2'-Ha), 2.64 (ddd, 1, $J_{2'b,1'}$ = 6.0 Hz, $J_{2'b,3'}$ = 8.0 Hz, 2'-Hb), 3.56 (ddd, 1, $J_{5'a,5'b}$ = 15.0 Hz, $J_{5'a,4'}$ = 4.0 Hz, $J_{5'a,NH}$ = 4.0 Hz, 5'-Hz), 3.74 (ddd, 1, $J_{5'b,4'}$ = 5.0 Hz, $J_{5'b,NH}$ = 8.0 Hz, 5'-Hb), 3.94 (m, 1, 4'-H), 4, 23 (ddd, 1, $J_{3',4'}$ = 6.0 Hz, 3'-H), 5.74–5.85 (m, 2, $J_{5,6}$ = 8.5 Hz, 1'-H, 5-H), 6.37 (br s, 1, N*H*CHO), 7.26 (d, 1, 6-H), 8.28 (s, 1, CHO), 8.83 (br s, 1, 3-H); ^{13}C NMR (acetone-d_6) δ 37.15, 40.06, 62.26, 83.45, 86.10, 102.90, 141.69, 151.27, 162.46, 163.68; MS (200 °C) *m/e* (%) 280 (1) (M^+); IR (CH_2Cl_2) 2110 cm^{-1} (N_3). Anal. ($C_{10}H_{12}N_6O_4$) C, H, N.

3'-Azido-5'-isocyano-3',5'-dideoxythymidine (23). Compound **21** (40 mg, 0.136 mmol) was dissolved in 2 mL of pyridine and cooled to 0 °C. Then tosyl chloride (44 mg, 0.23 mmol) was added. After 16 h the reaction mixture was poured into a Na_2CO_3 solution and stirred for 15 min. Then it was extracted with EA, dried with Na_2SO_4, concentrated, and chromatographed (silica gel, EA): yield 24 mg (64%); colorless oil; R_f = 0.69 (EA); ^{1}H NMR δ 1.92 (d, 3, $J_{5\text{-}CH_3,6}$ = 1.0 Hz, 5-CH_3), 2.51 (m, 2, 2'-Ha, 2'-Hb), 3.79 (ABX system, 2, $J_{5'a,5'b}$ = 15.0 Hz, $J_{5'a,4'}$ = 4.0 Hz, $J_{5'b,4'}$ = 5.0 Hz, 5'-Ha, 5'-Hb), 3.92 (m, 1, 4'-H), 4.34 (dt, 1, $J_{3',4'}$ = 7.5 Hz, $J_{3',2'a}$ = $J_{3',2'b}$ = 5.5 Hz, 3'-H), 6.14 (t, 1, $J_{1',2'a}$ = $J_{1',2'b}$ = 6.5 Hz, 1'-H), 7.28 (d, 1, 6-H), 9.52 (br s, 1, 3-H); ^{13}C NMR δ 12.07, 36.59, 43.27, 60.58, 80.20, 85.38, 111.50, 135.77, 150.35, 159.66, 163.90; MS (180 °C) *m/e* (%) 276 (8) (M^+); IR (CH_2Cl_2) 2150 cm^{-1} (NC), 2115 (N_3). Anal. ($C_{11}H_{12}N_6O_3$) C, H, N.

3'-Azido-5'-isocyano-2',3',5'-trideoxyuridine (24). Compound **24** was prepared in the same manner as described for **23**, with **22** as starting material: yield 62%; colorless oil; R_f = 0.81 ($CHCl_3$/MeOH, 5:1); ^{1}H NMR (400 MHz) δ 2.55 (m, 2, 2'-Ha, 2'-Hb), 3.81 (ABX, 2, $J_{5'a,5'b}$ = 15.6 Hz, $J_{5'a,4'}$ = 3.5 Hz, $J_{5'b,4'}$ = 3.6 Hz, 5'-Ha, 5'-Hb), 3.96 (m, 1, 4'-H), 4.35 (dt, 1, $J_{3',4'}$ = 6.0 Hz, $J_{3',2'a}$ = $J_{3',2'b}$ = 6.0 Hz, 3'-H), 5.82 (d, 1, $J_{5,6}$ = 8.1 Hz, 6-H), 6.14 (t, 1, $J_{1',2'}$ = 6.6 Hz, 1'-H), 7.46 (d, 1, 5-H), 9.10 (s, 1, 3-H); ^{13}C NMR δ 37.20, 43.46, 60.82, 80.56, 85.91, 103.36, 139.56, 150.03, 160.60, 162.78; MS (160 °C) *m/z* (%) = 262 (3) (M^+); IR (CH_2Cl_2) 2150 cm^{-1} (NC), 2110 (N_3). Anal. ($C_{10}H_{10}N_6O_3$) C, H, N.

Antiviral Assay Procedures. The anti-HIV-1 assays were carried out with the HTLV-III$_B$ strain (kindly provided by Dr. R. C. Gallo, National Cancer Institute, Bethesda, MD). These assays were based on the inhibition of HIV-1-induced cytpathogenicity in human MT4 lymphocyte cells. The anti-MSV assays were based on the inhibition of Moloney murine sarcoma virus (MSV) induced transformation of murine embryo fibroblast C3H/3T3 cells. Both assay procedures have been previously described.[31]

The antiviral assays, other than the antiretrovirus assays, were based on an inhibition of virus-induced cytopathogenicity in either HeLa cells [for vesicular stomatitis virus (VSV), polio-1, and Coxsackie], Vero cells (for Sindbis, parainfluenza-3, Semliki forest, Coxsackie B4, and reovirus-1), or E$_6$SM cells [for herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2), vaccinia virus (VV), and VSV], following previously established procedures.[32]

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