Vycor-Filtered Irradiation of 9c. Preparation of the Tricyclic Enaminone 10a. A solution of **9c** (1.00 g, 3 mmol) in 500 mL of *p*-dioxane containing 5.0 mL of triethylamine was irridiated for 2 h under a nitrogen atmosphere in the apparatus described above. The crude photolysate was filtered and concentrated in vacuo, giving a residue. A methylene chloride solution of the residue was washed with 5% $NaHCO_3$, dried, and concentrated in vacuo, giving a brown oil which crystallized when treated with $CHCl_3$–hexane solution. Recrystallization gave 0.815 g (85%) of pure tricyclic β-enaminone: mp 222 °C; IR (KBr) 3400, 3300, 3100, 2950, 15500 m^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.12 (br s, 1 H), 6.79 (s, 1 H), 6.62 (s, 1 H), 5.92 (s, 2 H), 3.44 (m, 2 H), 2.76 (m, 2 H), 2.48 (m, 2 H), 2.25 (m, 2 H), 1.76 (m, 2 H); UV (MeOH) λ_{max} 301 nm (ε 13400), 203 (18100); mass spectrum, *m/e* 257.1043 ($C_{15}H_{15}NO_3$ requires 257.1052).

Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.04; H, 5.84; N, 5.46. Found: C, 69.63; H, 5.81; N, 5.37.

Vycor-Filtered Irradiation of 9f. Preparation of the Tricyclic β- and α-Enaminones 10b and 11. A solution of **9f** (0.1 g, 0.3 mmol) in 250 mL of *p*-dioxane containing 0.5 mL of triethylamine was irradiated as described above for 1 h. A workup in a fashion described above yielded 31 mg (43%) of the β-enaminone **10b** as a tan crystalline solid: mp 250 °C dec; IR (KBr) 3250, 3080, 2950, 1550 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 8.15 (br s, 1 H), 7.79 (s, 1 H), 6.66 (s, 1 H), 5.91 (s, 2 H), 3.40 (m, 2 H), 2.84 (m, 2 H), 2.50 (m, 2 H), 2.31 (m, 2 H); UV (MeOH) λ_{max} 302 nm (ε 13900); mass spectrum, *m/e* 243.0892 ($C_{14}H_{13}NO_3$ requires 243.0893).

Alternate purification of the crude photolysate by preparative layer chromatography on silica gel (10% MeOH–$CHCl_3$) led to the isolation of **10b** (35 mg, 47%) from a band with an R_f of ca. 0.6 and 32 mg (43%, R_f ca. 0.7) of the α-enaminone **11** as a crystalline solid: mp 250 °C dec; IR (KBr) 3400, 3040, 2900, 1650, 1540 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 6.94 (s, 1 H), 6.85 (s, 1 H), 5.97 (s, 2 H), 5.20 (br s, H), 3.96 (m, 2 H), 3.02 (m, 4 H), 2.23 (m, 2 H); UV (MeOH) λ_{max} 345 nm (ε 29700); mass spectrum *m/e* 243.0905 ($C_{14}H_{13}NO_3$ requires 243.0893).

Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.13; H, 5.35; N, 5.76. Found: C, 68.95; H, 5.41; N, 5.69.

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Nucleosides. 121. Improved and General Synthesis of 2′-Deoxy *C*-Nucleosides. Synthesis of 5-(2-Deoxy-β-D-*erythro*-pentofuranosyl)uracil, -1-methyluracil, -1,3-dimethyluracil, and -isocytosine[1]

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5-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-1,3-dimethyluracil (**6a**), -1-methyluracil (**6b**), -uracil (**6c**), and -isocytosine (**6d**) were synthesized. Compounds **6b–d** are *C*-nucleoside isosteres of thymidine, 2′-deoxyuridine, and 2′-deoxycytidine, respectively. 1,3-Dimethylpseudouridine (**1a**), 1-methylpseudouridine (**1b**), pseudouridine (**1c**), and pseudoisocytidine (**1d**) were treated with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane in pyridine to afford the corresponding 3′,5′-tetraisopropyldisiloxanyl derivatives **2** which were converted into the respective 2′-*O*-[(imidazol-1-yl)thiocarbonyl] *C*-nucleosides **3**. Compounds **3a,b** were converted directly into the corresponding 2′-deoxy β-*C*-nucleosides **5a,b** exclusively by reduction with *n*-Bu_3SnH. For the synthesis of 2′-deoxy β-*C*-nucleosides **5c,d**, the intermediates **3c,d** were trimethylsilylated prior to *n*-Bu_3SnH treatment. Deprotection of **5a–d** was effected by treatment with *n*-Bu_4NF, and the corresponding free 2′-deoxy β-*C*-nucleosides **6a–d** were obtained in good yields.

2′-Deoxypseudoisocytidine,[3] a *C*-nucleoside isostere of deoxycytidine, was first synthesized in small amounts by exploitation of several new reactions developed in our laboratory in the following manner: pseudouridine (**1c**) was converted into the 2′-chloro derivative[4] which was reductively dechlorinated to 2′-deoxypseudouridine (**6c**). Conversion of the latter into 1,3-dimethylpseudouridine (**1a**), followed by guanidine treatment,[5] afforded the 2′-deoxypseudoisocytidine (**6d**). This original procedure, however, requires careful chromatographic separation of the products in almost every step, resulting in a low yield of **6d**.

Recently, we developed an improved procedure[6] in which the proton at N-1 of **1c** was replaced by a methyl group to prevent undesirable α,β-isomerization. Thus, the 2′,3′-O-cyclic thiocarbonate of 1-methyl-5′-*O*-trityl-

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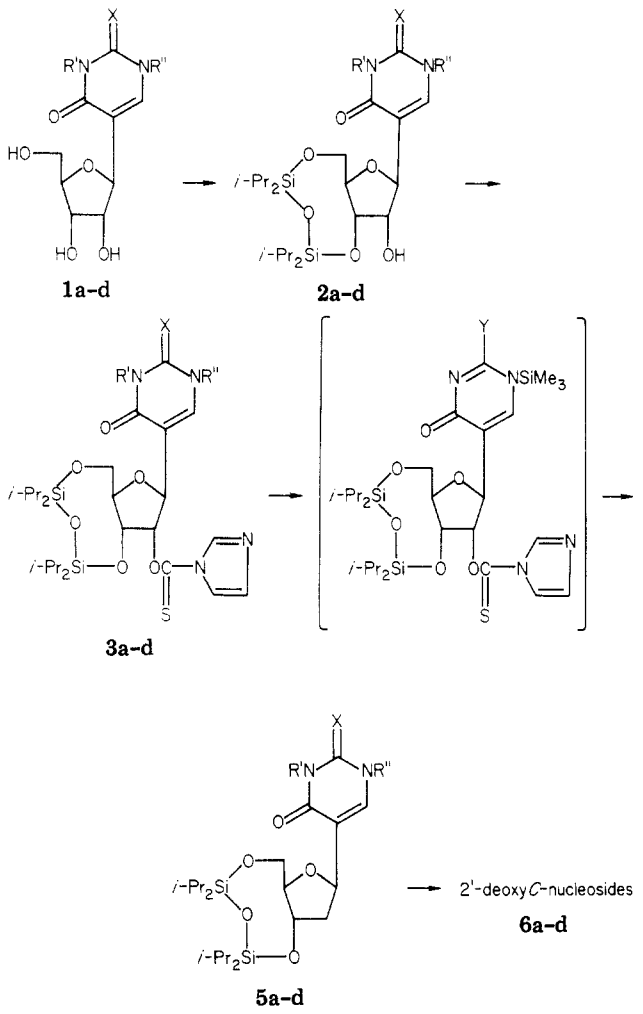
Scheme I[a]



[a] a, X = O, R' = R'' = Me; b, X = O, R' = H; R'' = Me; c, X = O, R' = R'' = H; d, X = NH, R' = R'' = H.

pseudouridine was prepared and then treated with tri-*n*-butyltin hydride (*n*-Bu_3SnH). 2'-Deoxy-1-methyl-5'-*O*-tritylpseudouridine was obtained as the major product (45% yield). This major product was methylated to the 1,3-dimethyl derivative which was subsequently treated with guanidine. From the reaction mixture, the desired β isomer (**6d**) was isolated in 38% yield. This improved method of preparation of **6d** is much superior to the original method in its simplicity and higher yields. However, during the Barton reduction, two undesirable byproducts, 2',3'-didehydro-2',3'-dideoxy-1-methyl-5'-*O*-tritylpseudouridine and 3'-deoxy-5'-*O*-tritylpseudouridine, were formed in sizable amounts (18% and 25% yields, respectively). Also, in the final step, an isomerization took place to give an approximately 1:1 mixture of the α and β isomers.

In searching for an even better procedure for the synthesis of **6d**, we have found a simpler and general method for preparing 2'-deoxy β-*C*-nucleosides. The 3',5'-hydroxyl groups of *C*-nucleosides **1a–d** were protected by treatment with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane[7] in pyridine (Scheme I) to give the corresponding protected nucleosides (**2a–d**) in which only the 2'-hydroxyl group is available for modification. Compounds **2a–d** were converted quantitatively into the crystalline 2'-*O*-(thiocarbonyl)imidazole derivatives (**3a–d**) by treatment with (thiocarbonyl)diimidazole in dimethylformamide (DMF). It is interesting to note that under the conditions employed for the synthesis of **3a–d**, no formation of 2,4'-anhydro *C*-nucleosides or bis[3',5'-*O*-(tetraisopropyldisiloxanyl) *C*-nucleosidyl]-2',2'-thiocarbonates occurred. Such formation of anhydro nucleosides or dinucleosidyl thiocarbonates are rather common when regular nucleosides are treated with (thiocarbonyl)diimidazole.[9-11] Removal of the silyl protecting group of **3c** with tetra-*n*-butylammonium fluoride (*n*-Bu_4NF) in tetrahydrofuran (THF)[8] caused formation of the 2',3'-cyclic thiocarbonate. Thus, deprotection of compounds **3** has to be performed after reduction. Upon treatment of compounds **3a** and **3b** with *n*-Bu_3SnH in the presence of 2,2'-azobis(2-methylpropionitrile),[12] the corresponding β-*C*-nucleosides **5a** and **5b** were obtained in good yields as the only isolable products, whereas **3c** and **3d** (in which a dissociable proton is present at the N-1 position) yielded a mixture of the corresponding α and β isomers of 2'-deoxy *C*-nucleosides as evidenced by ^1H NMR. Thus, the crude product from **3c** showed in the ^1H NMR spectrum (Me_2SO-d_6) two H-6 signals at δ 7.35 for the α isomer and at δ 7.24 for the β isomer with relative intensities of 1:4, indicating that epimerization had occurred to about 20%. After removal of the disiloxanyl group, the ^1H NMR spectrum (Me_2SO-d_6) showed the product also to be a 1:4 mixture of the α and β isomers (H-6 signals at δ 7.38 for β and δ 7.29 for α with relative intensities of 4:1). This result indicates that epimerization did not occur during deprotection. Isomerization seemed to occur more readily with **3d** which gave a crude mixture of the α and β isomers in almost a 1:1 proportion, as two signals for H-6 appeared in the ^1H NMR spectrum at δ 7.58 and 7.54 in about equal intensities. It is apparent, therefore, that substitution on N-1 is necessary to prevent isomerization. For preparation of the β isomer of 2'-deoxy *C*-nucleosides of pseudouridine and pseudoisocytidine (**6c** and **6d**), protection of **3c** and **3d** at N-1 is required. The N-1 protecting group has to be removed readily under very mild conditions since 2'-deoxy *C*-nucleosides isomerize more easily than the corresponding ribo *C*-nucleosides.[13,14] Consequently, compounds **3c** and **3d** were trimethylsilylated to **4c** and **4d**, respectively, prior to reduction. The corresponding 2'-deoxy *C*-nucleosides **5c** and **5d** were obtained in good yields after treatment of **4c** and **4d** with *n*-Bu_3SnH. The formation of an α,β mixture during reduction of **3c** and **3d** is difficult to explain, since the mechanism of α,β-isomerization is considered to be an ionic process,[15] whereas the *n*-Bu_3SnH reduction is a free-radical reaction.[16] Desilylation of **5a–d** was effected by treatment with *n*-Bu_4NF. The three *C*-nucleosides of biological interest, namely, isosteres of deoxyuridine, thymidine, and deoxycytidine, were thus synthesized in good overall yields from pseudouridine. 2'-Deoxypseudouridine-5'-monophosphate was reported to be a potent inhibitor of thymidylate synthetase.[17] The isosteres of thymidine and deoxycytidine, i.e., **6b** and **6d**, showed inhibitory activity against mouse mastcytoma P815 cells in tissue culture.[3]

The procedure for the synthesis of 2'-deoxy *C*-nucleosides described herein should have wide applicability in the *C*-nucleoside area. Thus far, the overall yields of py-

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rimidine 2′-deoxy C-nucleosides synthesized herein are somewhat lower than those reported[7,18] for the synthesis of certain 2′-deoxy N-nucleosides.

Experimental Section

General Methods. Melting points were determined on a Thomas-Hoover capillary apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a JEOL J1M-PFT-100 spectrometer, and Me_2SO-d_6 was used as the solvent with Me_4Si as the internal standard. Chemical shifts are reported in parts per million (δ), and signals are described as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Values for coupling constants were first order. TLC was performed on Uniplates purchased from Analtech Co. and column chromatography on Woelm silica gel (70–230 mesh). The eluents described are volume to volume proportions of solvents. Elemental analyses were performed by Galbraith Laboratories, Inc., and Spang Microanalytical Laboratory.

1,3-Dimethyl-3′,5′-*O*-(tetraisopropyldisiloxanyl)pseudouridine (2a). 1,3-dimethylpseudouridine[5] (**1a**; 2.72 g, 10 mmol) was dissolved in pyridine (30 mL), and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (3.48 g, 11 mmol) was added. The mixture was stirred at room temperature for 4 h and then evaporated in vacuo. The residue was partitioned between $CHCl_3$ (100 mL) and water (50 mL). The organic layer was separated, washed with water (2 × 50 mL), dried (Na_2SO_4), and concentrated to dryness in vacuo. The residue was chromatographed over a column of silica gel (2 × 30 cm) with $CHCl_3$–Me_2CO (5:1) as the eluent to give **2a**: 5.0 g (97%); a foam; ^{1}H NMR δ 1.02 (m, 28 H, *i*-Pr), 3.16 (s, 3 H, NMe), 3.28 (s, 3 H, NMe), 3.34 (m, 2 H, H-5′,5″), 3.7–4.2 (m, 3 H, H-2′,3′,4′), 4.56 (s, 1 H, H-1′), 5.10 (d, 1 H, OH exchangeable), 7.47 (s, 1 H, H-6).

Anal. Calcd for $C_{23}H_{42}N_2O_7Si_2$: C, 53.70; H, 8.17; N, 5.45. Found: C, 53.59; H, 8.13; N, 5.36.

1,3-Dimethyl-3′,5′-*O*-(tetraisopropyldisiloxanyl)-2′-*O*-[(imidazol-1-yl)thiocarbonyl]pseudouridine (3a). A mixture of **2a** (5.0 g, 9.73 mmol) and (thiocarbonyl)diimidazole (4.3 g, 24.2 mmol) in DMF (20 mL) was stirred for 4 h at room temperature and then partitioned between EtOAc (350 mL) and water (100 mL). The organic layer was separated, washed with water (2 × 100 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography with EtOAc as the eluent. The product was crystallized from EtOH to give **3a**: 4.2 g (69%); mp 140 °C; ^{1}H NMR δ 1.02 (m, 28 H, *i*-Pr), 3.17 (s, 3 H, NMe), 3.31 (s, 3 H, NMe), 4.02 (m, 2 H, H-5′,5″), 4.72 (m, 2 H, H-3′,4′), 4.93 (s, 1 H, H-1′), 6.15 (d, 1 H, H-2′, $J_{2',3'}$ = 4.0 Hz), 7.11 (s, 1 H, imidazole), 7.70 (s, 1 H, H-6), 7.88 (s, 1 H, imidazole), 8.56 (s, 1 H, imidazole).

Anal. Calcd for $C_{27}H_{44}N_4O_7SSi_2$: C, 51.89; H, 7.10; N, 8.96; S, 5.13. Found: C, 52.05; H, 7.10; N, 8.93; S, 4.99.

2′-Deoxy-1,3-dimethyl-3′,5′-*O*-(tetraisopropyldisiloxanyl)pseudouridine (5a). A mixture of 2,2′-azobis(2-methylpropionitrile) (700 mg) and *n*-Bu_3SnH (4.5 g, 25.6 mmol) in dry toluene (30 mL) was added dropwise over 1 h to a refluxing solution of **3a** (4.0 g, 6.4 mmol) in dry toluene (40 mL). The solvent was removed in vacuo, and the residue was applied on a silica gel column. The column was eluted with $CHCl_3$–EtOAc (7:1) to give a product contaminated with a small amount of tri-*n*-butyltin derivative. After the second chromatography (C_6H_6–EtOAc–Et_2O, 20:1:1), pure **5a** was obtained as a colorless oil which solidified upon standing at room temperature: 2.1 g (65%); mp 70 °C; ^{1}H NMR δ 1.03 (m, 28 H, *i*-Pr), 2.16 (m, 2 H, H-2′,2″), 3.16 (s, 3 H, NMe), 3.30 (s, 3 H, NMe), 3.70 (m, 1 H, H-4′), 3.90 (m, 2 H, H-5′,5″), 4.41 (m, 1 H, H-3′),4.82 (t, 1 H, H-1′, $J_{1',2'} = J_{1',2''}$ = 7.1 Hz), 7.52 (s, 1 H, H-6).

Anal. Calcd for $C_{23}H_{42}N_2O_6Si_2$: C, 55.38; H, 8.49; N, 5.62. Found: C, 55.50; H, 8.60; N, 5.69.

2′-Deoxy-1,3-dimethylpseudouridine (6a). To a solution of **5a** (1.8 g, 3.6 mmol) in THF (50 mL) was added dropwise a 1 M solution of *n*-Bu_4NF in THF, and the reaction was followed by TLC (Me_2CO–$CHCl_3$ 6:4). After the reaction was completed, the mixture was concentrated to dryness and the residue chromatographed with Me_2CO–$CHCl_3$ (6:4) as the eluent. The product was rechromatographed ($CHCl_3$–MeOH, 9:1) to give crystalline **6a**: 700 mg (75%); mp 137–138 °C (recrystallized from EtOH) (lit.[3] mp 136–137 °C); ^{1}H NMR δ 1.97 (m, 2 H, H-2′,2″, $J_{2',2''}$ = 12.6, $J_{1',2'}$ = 5.8, $J_{2',3'}$ = 2.1, $J_{1',2''}$ = 9.6, $J_{2'',3'}$ = 5.5 Hz), 3.18 (s, 3 H, NMe), 3.33 (s, 3 H, NMe) 3.45 (m, 2 H, H-5′,5″), 3.70 (m, 1 H, H-4′), 4.15 (m, 1 H, H-3′), 4.86 (dd, 1 H, H-1′, $J_{1',2'}$ = 5.8, $J_{1',2''}$ = 9.6 Hz), 7.68 (s, 1 H, H-6). The ^{1}H NMR spectrum parameters obtained in D_2O were identical with those reported for **6a**.[3]

1-Methyl-3′,5′-*O*-(tetraisopropyldisiloxanyl)pseudouridine (2b). The same procedure as that described for the preparation of **2a** from **1a** was utilized in the synthesis of **2b** from 1-methylpseudouridine[19] (**1b**; 4.8 g, 18.6 mmol). The crude product was chromatographed ($CHCl_3$–EtOAc, 1:1) to give **2b**: 6.3 g (68%); colorless foam; ^{1}H NMR δ 1.02 (m, 28 H, *i*-Pr), 3.21 (s, 3 H, NMe), 3.33 (m, 2 H, H-5′,5″), 3.7–4.2 (m, 3 H, H-2′,3′,4′), 4.50 (s, 1 H, H-1′), 5.08 (d, 1 H, OH exchangeable), 7.44 (s, 1 H, H-6), 11.37 (s, 1 H, NH exchangeable).

Anal. Calcd for $C_{22}H_{40}N_2O_7Si_2$: C, 52.77; H, 8.05; N, 5.59. Found: C, 52.62; H, 8.13; N, 5.41.

1-Methyl-3′,5′-*O*-(tetraisopropyldisiloxanyl)-2′-*O*-[(imidazol-1-yl)thiocarbonyl]pseudouridine (3b). The preparation of **3b** from **2b** (6.0 g, 12 mmol) followed the same procedure as described for **3a**. After chromatographic purification (EtOAc–CCl_4, 3:2), **3b** was obtained: 6.8 g (93%); foam; ^{1}H NMR δ 1.03 (m, 28 H, *i*-Pr), 3.24 (s, 3 H, NMe), 3.33 (m, 2 H, H-5′,5″), 4.00 (m, 2 H, H-3′,4′), 4.86 (s, 1 H, H-1′), 6.15 (d, 1 H, H-2′, $J_{2',3'}$ = 5.5 Hz), 7.10 (s, 1 H, imidazole), 7.69 (s, 1 H, H-6), 7.87 (s, 1 H, imidazole), 8.55 (s, 1 H, imidazole), 14.49 (s, 1 H, NH exchangeable).

Anal. Calcd for $C_{26}H_{42}N_4O_7SSi_2$: C, 51.12; H, 6.93; N, 9.15; S, 5.25. Found: C, 51.30; H, 7.06; N, 9.10; S, 5.12.

2′-Deoxy-1-methyl-3′,5′-*O*-(tetraisopropyldisiloxanyl)pseudouridine (5b). Compound **3b** (5.6 g, 9.2 mmol) was reduced according to the procedure described for the preparation of **5a**. Pure **5b** (3.3 g, 74.3%) was obtained as a foam after chromatography (CCl_4–EtOAc, 5:3): ^{1}H NMR δ 1.03 (m, 28 H, *i*-Pr), 2.11 (m, 2 H, H-2′,2″), 3.22 (s, 3 H, NMe), 3.70 (m, 1 H, H-4′), 3.88 (m, 2 H, H-5′,5″), 4.43 (m, 1 H, H-3′), 4.77 (t, 1 H, H-1′, $J_{1',2'} = J_{1',2''}$ = 7.0 Hz), 7.48 (s, 1 H, H-6), 11.36 (s, 1 H, NH exchangeable).

Anal. Calcd for $C_{22}H_{40}N_2O_6Si_2$: C, 54.51; H, 8.32; N, 5.78. Found: C, 54.62; H, 8.43; N, 5.71.

2′-Deoxy-1-methylpseudouridine (6b). Deblocking of **5b** (3.3 g, 6.8 mmol) was performed according to the procedure described for the preparation of **6a**. The reaction was monitored by TLC ($CHCl_3$–MeOH, 3:1). After completion of the reaction, the mixture was concentrated to a syrup which was chromatographed with Me_2CO–$CHCl_3$ (3:1) as the eluent. The product was rechromatographed (Me_2CO) and crystallized from EtOH–Et_2O to give **6b**: 1.0 g (61%); mp 163–164 °C (lit.[3] mp 158–160 °C). The ^{1}H NMR spectrum taken in D_2O was identical with that of an authentic sample.[3]

3′,5′-*O*-(Tetraisopropyldisiloxanyl)pseudouridine (2c). Pseudouridine (**1c**; 7.5 g, 30.7 mmol) was allowed to react with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (10 g, 31.7 mmol) in pyridine (100 mL) for 4 h at room temperature. The mixture was diluted with water (10 mL), and the solvent was removed in vacuo to a syrup which was dissolved in $CHCl_3$ (300 mL), washed with water (2 × 100 mL), dried (Na_2SO_4), and evaporated to a foam (15 g). Direct crystallization of this foam from EtOAc–*n*-C_6H_{14} afforded 12.7 g of **2c**, mp 146–150 °C. From the mother liquor an additional crop of **2c** (1.2 g) was obtained after chromatography ($CHCl_3$–EtOH, 95:5): total yield 93%; ^{1}H NMR δ 1.02 (m, 28 H, *i*-Pr), 3.7–4.2 (m, 4 H, H-3′,4′,5′,5″), 4.51 (s, 1 H, H-1′), 5.10 (d, 1 H, OH dissociable), 7.30 (s, 1 H, H-6), 10.91 (s, 1 H, NH dissociable), 11.16 (s, 1 H, NH dissociable).

Anal. Calcd for $C_{21}H_{38}N_2O_7Si_2$: C, 51.82; H, 7.87; N, 5.75. Found: C, 51.83; H, 7.98; N, 5.68.

3′,5′-*O*-(Tetraisopropyldisiloxany)-2′-*O*-[(imidazol-1-yl)-thiocarbonyl]pseudouridine (3c). Compound **2c** (13.0 g, 26.7 mmol) was treated with (thiocarbonyl)diimidazole (11.8 g, 66.3 mmol) in DMF (50 mL) for 4 h. The reaction mixture was diluted

(18) Robins and Wilson[7] used phenoxythiocarbonyl instead of the (thiocarbonyl)imidazole group for reductive deoxygenation.

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with EtOAc (700 mL) and extracted with water (7 × 100 mL). The organic layer was dried (Na_2SO_4) and concentrated in vacuo, and the residue was crystallized from EtOH to afford 12.7 g of **3c**. From the mother liquor was obtained an additional crop (1.35 g) of crystalline **3c** after chromatography ($CHCl_3$–EtOH, 95:5): total yield 87.7%; mp 177–179 °C; ^1H NMR δ 1.02 (m, 28 H, *i*-Pr), 3.99 (m, 3 H, H-4′,5′,5″), 4.7–4.9 (m, 2 H, H-1′,3′), 6.14 (d, 1 H, H-2′, $J_{2',3'}$ = 3.6 Hz), 7.12 (s, 1 H, imidazole), 7.47 (d, 1 H, H-6), 7.85 (s, 1 H, imidazole), 8.53 (s, 1 H, imidazole), 11.05 (d, 1 H, NH dissociable), 11.23 (s, 1 H, NH dissociable).

Anal. Calcd for $C_{25}H_{40}N_4O_7SSi_2$: C, 50.31; H, 6.75; N, 9.39; S, 5.36. Found: C, 50.39; H, 6.72; N, 9.40; S, 5.30.

2′-Deoxy-3′,5′-*O*-(tetraisopropyldisiloxanyl)pseudouridine (5c). Method 1. Compound **3c** (13.0 g, 22.0 mmol) was reduced with *n*-Bu_3SnH according to the procedure described for the preparation of **5a**. After reduction, the solvent was removed in vacuo and the residue chromatographed (C_6H_6–EtOAc 5:3) to give an approximately 1:1 mixture of the α and β isomers of **5c**, 7.68 g (75%). Several recrystallizations of this product from Et_2O–*n*-C_6H_{14} gave the pure β isomer: 1.0 g (9.8%); mp 202–204 °C; ^1H NMR δ 1.02 (m, 28 H, *i*-Pr), 2.12 (m, 2 H, H-2′,2″), 3.55 (m, 1 H, H-4′), 3.85 (m, 2 H, H-5′,5″), 4.41 (m, 1 H, H-3′), 4.77 (dd, 1 H, H-1′, $J_{1',2'}$ = 6.4, $J_{1',2''}$ = 6.7 Hz), 7.24 (s, 1 H, H-6), 10.83 (s, 1 H, NH exchangeable), 11.12 (s, 1 H, exchangeable).

Anal. Calcd for $C_{21}H_{38}N_2O_6Si_2$: C, 53.58; H, 8.14; N, 5.96. Found: C, 53.42; H, 8.20; N, 5.90.

Method 2. A suspension of **3c** (1.2 g, 2 mmol) and $(NH_4)_2SO_4$ (10 mg) in hexamethyldisilazane (30 mL) was heated under reflux until a clear solution was obtained. The solvent was removed in vacuo and the residue dissolved in toluene (20 mL). This solution was treated with a mixture of 2,2′-azobis(2-methylpropionitrile) (250 mg) and *n*-Bu_3SnH (1.4 g) in toluene (20 mL) for 30 min at reflux. The mixture was concentrated in vacuo, and the residue was treated with a few drops of water and reevaporated. The residue was chromatographed by using C_6H_6–EtOAc (5:3) as the eluent. Compound **5c** (0.67 g, 71%) was obtained with a melting point of 203–204 °C which did not alter on admixture with a sample from method 1. The ^1H NMR spectrum of this sample was identical with that of the β isomer obtained by method 1.

2′-Deoxypseudouridine (6c). A solution of **5c** (3.5 g, 7.4 mmol) in THF (30 mL) was treated with 1 M *n*-Bu_4NF as described for the preparation of **6a**. After deblocking, the solvent was removed in vacuo, the residue dissolved in a mixture of pyridine–MeOH–water (3:1:1 60 mL), and the solution filtered through a pad of Dowex 50 (pyridinium form, 20 mL). The column was washed with pyridine–MeOH–water (3:1:1). The combined filtrate and washings were evaporated to dryness, and the residue was crystallized from EtOH to give **6c**: 1.51 g (89%); mp 220–221 °C (lit.[3] mp 221–223 °C, lit.[20] mp 216–217.5 °C). The ^1H NMR measured in deuterium oxide was identical with that of an authentic sample.[3]

2′,3′-*O*-(Thiocarbonyl)pseudouridine from 2c. A solution of **2c** (1.2 g, 2 mmol) in THF (20 mL) was treated with 1 M *n*-Bu_4NF in THF (4 mL) for 10 min at room temperature with stirring. The solvent was removed in vacuo, and the residue chromatographed ($CHCl_3$–EtOH, 9:1). The product was crystallized from EtOH to give 2′,3′-*O*-(thiocarbonyl)pseudouridine: 0.3 g (42%); mp 202–205 °C; ^1H NMR δ 3.56 (m, 2 H, H-5′,5″), 4.06 (m, 1 H, H-4′), 4.88 (d, 1 H, H-1′, $J_{1',2'}$ = 3.3 Hz), 5.08 (t, 1 H, OH exchangeable), 5.42 (dd, 1 H, H-3′, $J_{2',3'}$ = 7.5, $J_{3',4'}$ = 4.1 Hz), 5.61 (dd, 1 H, H-2′, $J_{1',2'}$ = 3.3, $J_{2',3'}$ = 7.5 Hz), 7.6 (d, 1 H, H-6), 11.08 (d, 1 H, NH exchangeable), 11.26 (s, 1 H, exchangeable).

Anal. Calcd for $C_{10}H_{10}N_2O_6S$: C, 41.96; H, 3.52; N, 9.78; S, 11.20. Found: C, 41.91; H, 3.70; N, 9.69; S, 11.12.

3′,5′-*O*-(Tetraisopropyldisiloxanyl)pseudoisocytidine (2d). Pseudoisocytidine hydrochloride[5] (**1d**; 2.8 g, 10 mmol) was treated with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane in pyridine as described for the preparation of **2a**. The crude product was purified by chromatography ($CHCl_3$–EtOH, 12:1) to give 3.7 g (76%) of **2d** as a foam: ^1H NMR δ 1.02 (m, 28 H, *i*-Pr), 3.89 (m, 3 H, H-4′,5′,5″), 4.11 (m, 1 H, H-3′), 4.58 (s, 1 H, H-1′), 4.96 (d, 1 H, OH exchangeable), 6.68 (s, 2 H, NH_2 exchangeable), 7.64 (s, 1 H, H-6), 11.20 (s, 1 H, NH exchangeable).

Anal. Calcd for $C_{21}H_{39}N_3O_6Si_2$: C, 51.93; H, 8.09; N, 8.65. Found: C, 51.82; H, 8.16; N, 8.51.

3′,5′-*O*-(Tetraisopropyldisiloxanyl)-2′-*O*-[(imidazol-1-yl)thiocarbonyl]pseudoisocytidine (3d). A solution of **2d** (7.4 g, 15.2 mmol) and (thiocarbonyl)diimidazole (6.8 g) in DMF (30 mL) was stirred at room temperature for 5 h. The product which precipitated was collected by filtration and washed with EtOAc to give 4.8 g of **3d**, mp 202–203 °C. The mother liquor was partitioned between EtOAc (500 mL) and water (100 mL). The organic layer was separated, washed with water, dried (Na_2SO_4), and concentrated to a small volume. An additional crop of crystalline **3d** was obtained: 1.1 g (total yield 5.9 g, 65%); mp 202–203 °C; ^1H NMR δ 1.04 (m, 28 H, *i*-Pr), 3.97 (m, 3 H, H-4′,5′,5″), 4.86 (m, 2 H, H-1′,3′), 6.14 (dd, 1 H, H-2′, $J_{1',2'}$ = 0.2, $J_{2',3'}$ = 5.5 Hz), 6.69 (s, 2 H, NH_2 exchangeable), 7.10 (s, 1 H, imidazole), 7.65 (s, 1 H, H-6), 7.85 (s, 1 H, imidazole), 8.53 (s, 1 H, imidazole), 11.09 (s, 1 H, NH exchangeable).

Anal. Calcd for $C_{25}H_{41}N_5O_6SSi_2$: C, 50.39; H, 6.93; N, 11.75; S, 5.38. Found: C, 50.37; H, 6.94; N, 11.82; S, 5.27.

2′-Deoxy-3′,5′-*O*-(tetraisopropyldisiloxanyl)pseudoisocytidine (5d). Compound **3d** (1.2 g, 2 mmol) was converted into the 2′-deoxy nucleoside **5d** via the trimethylsilylated intermediate **4d** by method 2 as described for the preparation of **5c**. The product was purified by chromatography ($CHCl_3$–EtOH, 95:5), and **5d** was obtained: 0.74 g (78%); ^1H NMR δ 1.02 (m, 28 H, *i*-Pr), 2.10 (m, 2 H, H-2′,2″), 3.63 (m, 1 H, H-4′), 3.85 (m, 2 H, H-5′,5″), 4.45 (m, 1 H, H-3′), 4.82 (t, 1 H, H-1′, $J_{1',2'}$ = $J_{1',2''}$ = 6.4 Hz), 6.61 (s, 2 H, NH_2), 7.55 (s, 1 H, H-6), 11.02 (s, 1 H, NH).

Anal. Calcd for $C_{21}H_{39}N_3O_5Si_2$: C, 53.70; H, 8.37; N, 8.95. Found: C, 53.52; H, 8.43; N, 8.89.

2′-Deoxypseudoisocytidine (6d). A solution of **5d** (2.8 g, 5.97 mmol) in THF (20 mL) was treated with 1 M *n*-Bu_4NF in THF solution (12 mL). The precipitated product, after being collected by filtration, was dissolved in a mixture of pyridine–MeOH–water (3:1:1) and the solution passed through a bed of Dowex 50 (pyridinium form, 20 mL). The resin was washed with the same mixture of solvents. The combined filtrate and washings were concentrated in vacuo, and the residue was chromatographed over a column of silica gel (*i*-PrOH–EtOAc–water, 2:2:1) to give 0.54 g (40%) of 2′-deoxypseudoisocytidine (**6d**). The ^1H NMR spectrum (D_2O) of this sample was identical with that of an authentic sample.[3]

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