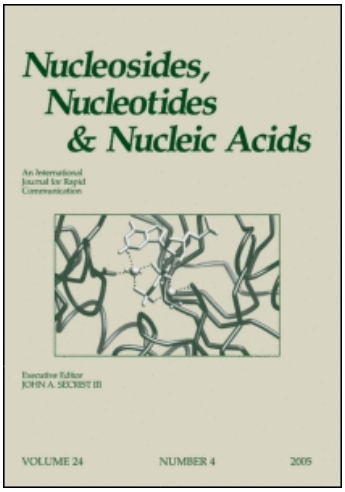

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NUCLEOSIDES AND NUCLEOTIDES. 104. RADICAL AND PALLADIUM-CATALYZED DEOXYGENATION OF THE ALLYLIC ALCOHOL SYSTEMS IN THE SUGAR MOIETY OF PYRIMIDINE NUCLEOSIDES§, 1

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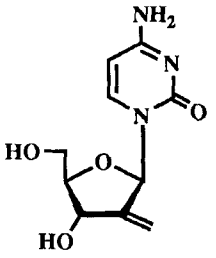
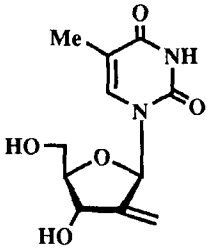
ABSTRACT: New methods for the synthesis of 2',3'-didehydro-2',3'-dideoxy-2' (and 3')-methyl-5-methyluridines and 2',3'-dideoxy-2' (and 3')-methylidene pyrimidine nucleosides have been developed from the corresponding 2' (and 3')-deoxy-2' (and 3')-methylidene pyrimidine nucleosides. Treatment of a 3'-deoxy-3'-methylidene-5-methyluridine derivative **8** with 1,1'-thiocarbonyldiimidazole gave the allylic rearranged 2',3'-didehydro-2',3'-dideoxy-3'-[(imidazol-1-yl)carbonylthiomethyl] derivative **24**. On the other hand, reaction of **8** with methyloxalyl chloride afforded 2'-*O*-methyloxalyl ester **25**. Radical deoxygenation of both **24** and **25** gave **26** exclusively. Palladium-catalyzed reduction of 2',5'-di-*O*-acetyl-3'-deoxy-3'-methylidene-5-methyluridine (**32**) with triethylammonium formate as a hydride donor regioselectively afforded the 2',3'-dideoxy-3'-methylidene derivative **35** and 2',3'-didehydro-2',3'-dideoxy-3'-methyl derivative **34** in a ratio of 95 : 5 in 78% yield. These reactions were used on the corresponding 2'-deoxy-2'-methylidene derivatives. An alternative synthesis of 2',3'-dideoxy-2'-methylidene pyrimidine nucleosides (**43**, **52**, and **54**) was achieved from the corresponding 1-(3-deoxy-β-D-*threo*-pentofuranosyl)pyrimidines (**44** and **45**). The cytotoxicity against L1210 and KB cells and inhibitory activity of the pathogenicity of HIV-1 are also described.

A new type of antineoplastic nucleoside, 2'-deoxy-2'-methylidenecytidine (DMDC) has been synthesized and its activity evaluated.[2-5] DMDC showed, unlike the activity of 1-β-D-arabinofuranosylcytosine, highly potent cytotoxicity against not only mouse and human leukemia cells but also human adenocarcinoma and carcinoma cells *in vitro*.[2,3] DMDC also had therapeutic activity against some human tumor xenografts.[5] Moreover,

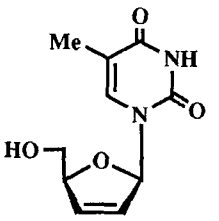
§This paper is dedicated to the memory of the late Professor Tohru Ueda, the former editor of this journal.



DMDC

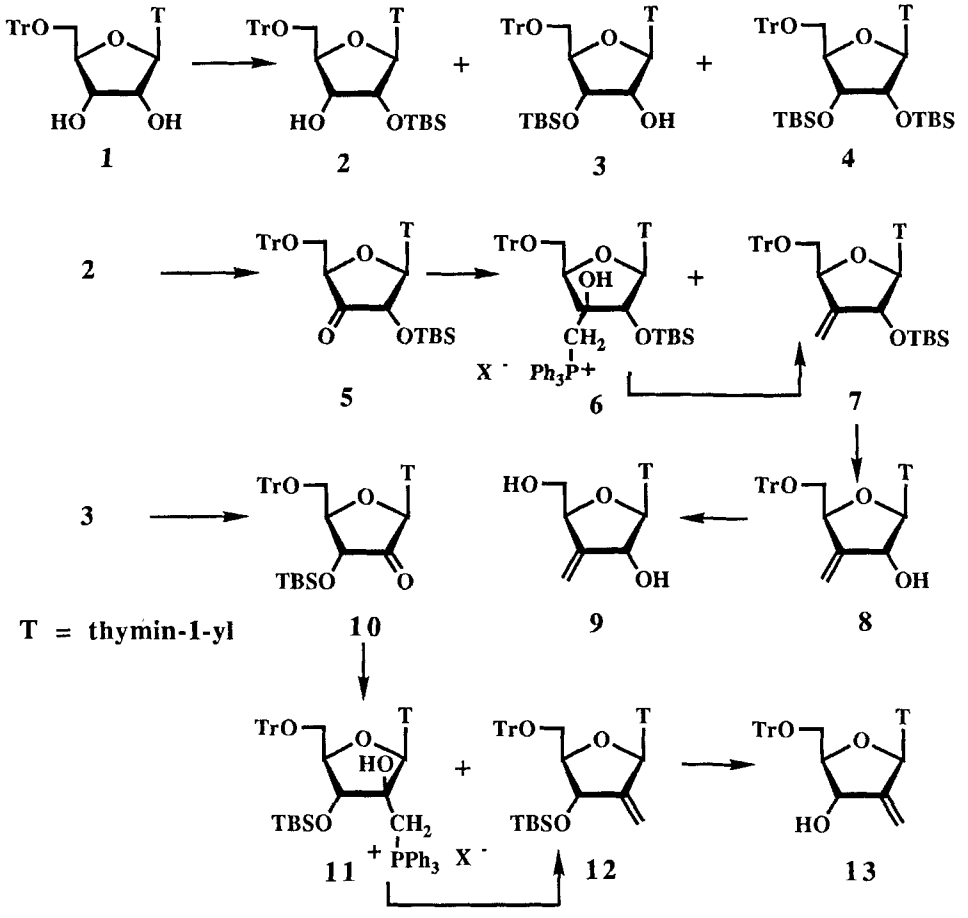


DMDT



D4T

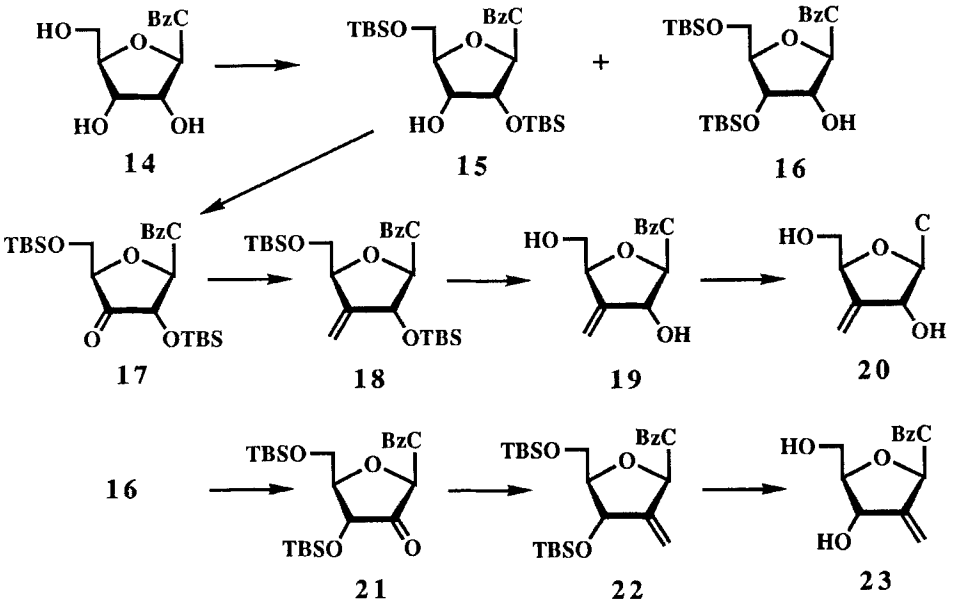
Chart 1



Scheme 1

the thymine derivative of DMDC (DMDT) had antiviral activity toward human cytomegalovirus.[6] Recently, 2',3'-didehydro-2',3'-dideoxythymidine (D4T) has been reported by us[7] and others[8,9] to be a potent inhibitor of the growth of human immunodeficiency virus (HIV) *in vitro*. Common structural feature of these nucleosides can be found in a double bond functionality in the sugar moiety, which may be important for such biological activities. In this paper, we describe the synthesis of new types of unsaturated-deoxysugar nucleosides such as 2',3'-dideoxy-3' (and 2')-methylidene nucleosides as well as 2',3'-didehydro-2',3'-dideoxy-3' (and 2')-methyl-5-methyluridines from corresponding 3' (and 2')-deoxy-3' (and 2')-methylidene pyrimidine nucleosides via radical and palladium-catalyzed deoxygenation reaction as part of our program in the design and syntheses of potential anticancer and antiviral agents.[10,11]

As starting materials of the deoxygenation reaction, we synthesized 3'-deoxy-3'-methylidene-5'-*O*-trityl-5-methyluridine (**8**) and 2'-deoxy-2'-methylidene-5'-*O*-trityl-5-methyluridine (**13**) as outlined in Scheme 1. Partial silylation of 5'-*O*-trityl-5-methyluridine (**1**)[12] with *tert*-butyldimethylsilyl chloride (TBSCl) in DMF in the presence of imidazole gave a mixture of 2'-*O*-TBS, 3'-*O*-TBS, and 2',3'-di-*O*-TBS derivatives **2**, **3**, and **4** as foams in 45, 33, and 8% yields, respectively. Each isomer can be separable by silica gel column chromatography and were assigned according to an empirical ^{1}H NMR rule developed by Reese *et al.*[13] Oxidation of the 3'-hydroxyl group in **2** by CrO_3-pyridine-acetic anhydride system[14] in CH_2Cl_2 gave the 3'-ketone **5** in 93% yield. Wittig methylenation of **5** with methylenetriphenylphosphorane (3 equiv. prepared by the reaction of 4 equiv. of methytriphenylphosphonium bromide and 3 equiv. of BuLi in THF) gave the desired 3'-methylidene derivative **7** in only 25% yield as a foam. During the course of the reaction, by careful checking with thin-layer chromatography (TLC), we found an additional nucleosidic spot near the origin on the TLC plate after complete consumption of **5**. This polar nucleoside **6** was obtained in 83% yield after partial purification by silica gel column chromatography, and its ^{31}P-NMR showed a peak at δ 21.84 ppm (triethyl phosphate as internal standard), which is assigned as a phosphonium salt.[3] Treatment of **6** with NaH in THF afforded the 3'-methylidene derivative **7** in 52% (total yield of **7** was 77%).[3] Therefore, it seems that the oxaphosphetane formation required for the Wittig methylenation could be difficult because of the ring strain, and the rather stable betaine could pick up a hydrogen from the excess of methyltriphenylphosphonium bromide to form the phosphonium salt **6**. From these considerations, we improved the yield of **7** to be almost quantitative when equimolar amounts of the phosphonium bromide and BuLi (each 3 equiv. of **5**) was used. Desilylation of **7** with tetrabutylammonium fluoride (TBAF) furnished **8** in quantitative yield. Further treatment of **8** with formic acid gave 3'-deoxy-3'-methylidene-5-methyluridine (**9**) as a foam.



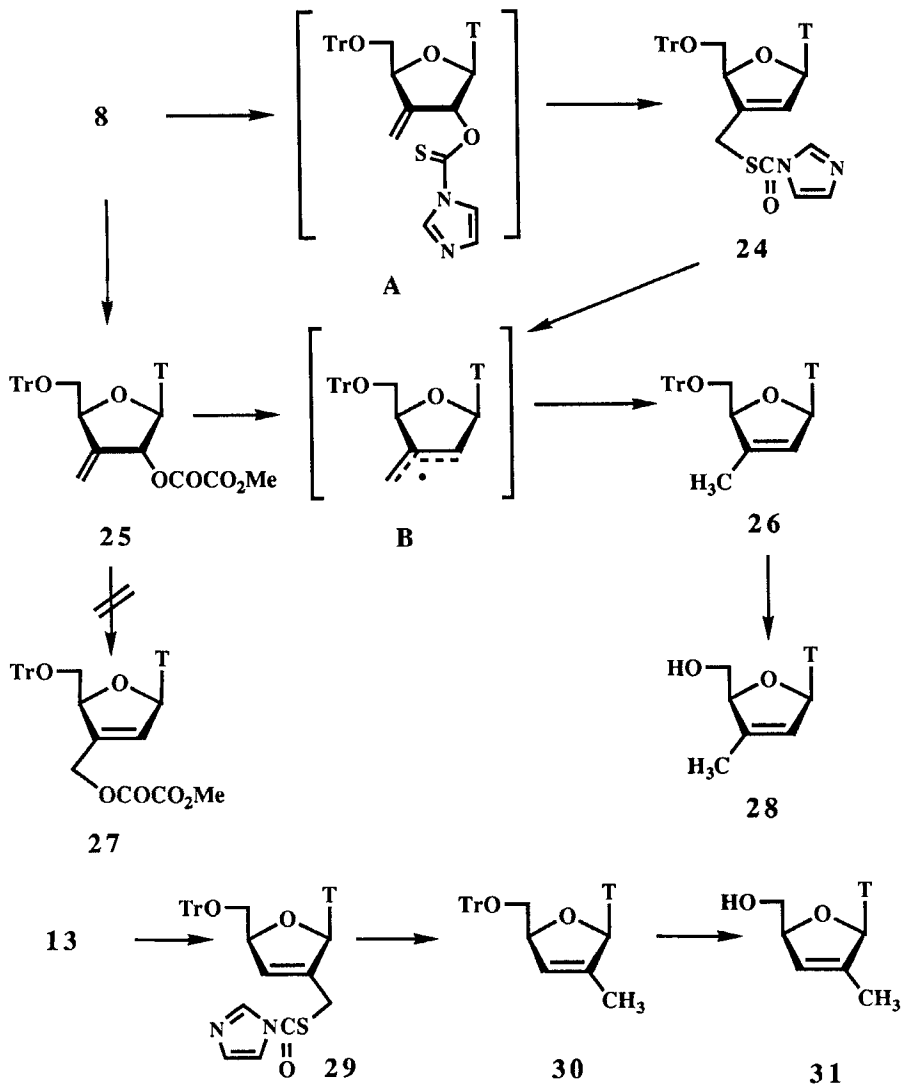
BzC = N^4-benzoylcytosin-1-yl

Scheme 2

Similarly, 3'-*O*-TBS derivative **3** was converted into the 2'-keto nucleoside **10**, which was used for the Wittig methylenation with methylenetriphenylphosphorane to afford again the desired 2'-methylidene nucleoside **12** in 40% yield along with the 2'-phosphonium salt **11**. Compound **11** could also transformed to **12** by treatment with NaH in THF. Desilylation of **12** with TBAF gave 2'-deoxy-2'-methylidene-5'-*O*-trityl-5-methyluridine (**13**).

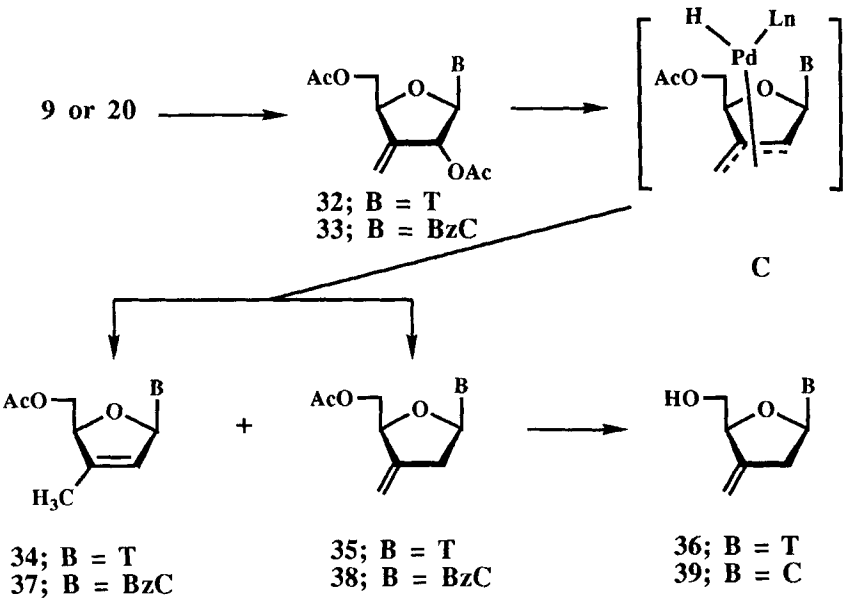
Synthesis of 3'-deoxy-3'-methylidenecytidine (**20**)[4] and N^4-benzoyl DMDC (**23**) were outlined in Scheme 2. N^4-Benzoylcytidine (**14**)[15] was silylated with TBSCl as described above to give 2',5'-di-*O*-TBS and 3',5'-di-*O*-TBS derivatives **15** and **16** in 53 and 31% yields, respectively, after separation by silica gel column chromatography. Oxidation of **15** as described above afforded 3'-keto nucleoside **17**, which was then converted into the corresponding 3'-deoxy-3'-methylidene derivative **18** in good overall yield. Desilylation of **18** with TBAF gave **19**, which was treated with NH_3 / MeOH to furnish **20** as a hydrochloride. Conversion of **16** into 2'-deoxy-2'-methylidene nucleoside **23** was done similarly.

Deoxygenation of the 2'-hydroxyl group in **8** was next examined.[10] Upon treatment of **8** with 1,1'-thiocarbonyldiimidazole in DMF for 24 h at room temperature, one



Scheme 3

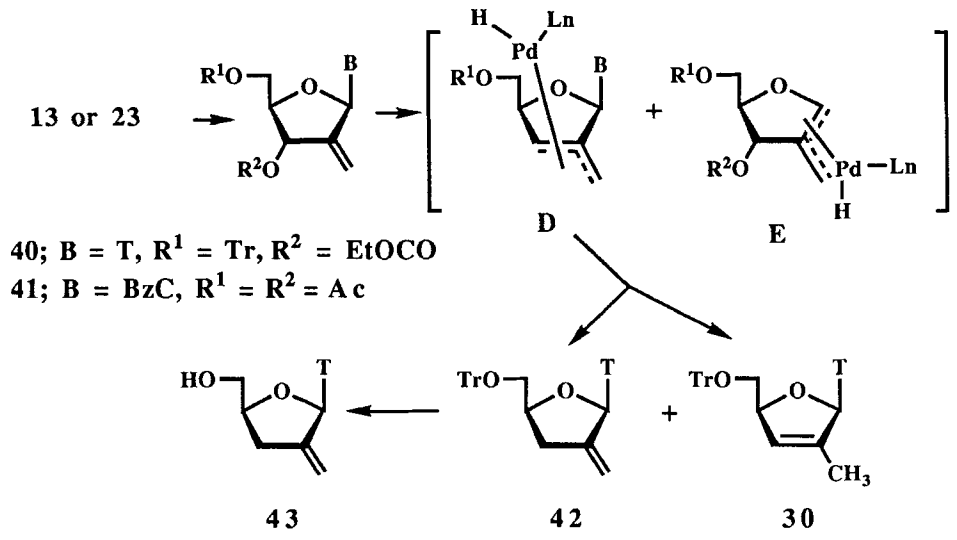
nucleosidic product was obtained as crystals from the reaction mixture in 84% yield. The ^{1}H NMR showed that two protons at 3.62 and 3.98 ppm as each doublet ($J_{a,b}$ = 15.4 Hz) appeared instead of the 3'-methylidene protons, which appeared at 5.20 and 5.53 ppm as each broad triplet in **8**. The 1'-proton of this nucleoside appeared at 5.95 ppm as a singlet, while the 1'-proton of **8** appeared at 5.80 ppm as a doublet ($J_{1',2'}$ = 6.2 Hz). Therefore, the structure of this nucleoside was assigned as 3'-[(imidazol-1-yl)carbonylthiomethyl] derivative **24** rather than an expected 2'-*O*-[(imidazol-1-yl)thiocarbonyl] derivative **A**



Scheme 4

(Scheme 3), as a result of the allylic rearrangement of the intermediate **A**. The desulfurization of **24** with Bu_3SnH and 2,2'-azobis(isobutyronitrile) (AIBN) in hot toluene gave 2',3'-didehydro-2',3'-dideoxy-3'-methyl-5'-*O*-trityl-5-methyluridine (**26**) in 83% yield. When 2'-*O*-methyloxalyl ester **25**, which was readily prepared from **8** with methyloxalyl chloride in CH_3CN in the presence of 4-dimethylaminopyridine (DMAP), was heated in benzene with Bu_3SnH and AIBN, the same nucleoside **26** was obtained in 95% yield.[16] When **25** was heated in benzene without addition of Bu_3SnH, the formation of the rearranged product **27** was not observed. Thus, both radical reactions starting from **24** and **25** proceeded through the same allylic radical intermediate **B** to form **26**, exclusively. Although the glycosyl linkage of **26** was rather unstable upon treatment with acid, the trityl group of **26** could be deblocked by the treatment with 97% formic acid[17] for 3 min at room temperature, and then the reaction mixture was quickly lyophylized to give the 3'-methyl derivative of D4T, **28** in 54% yield.

2'-Deoxy-2'-methylidene-5'-*O*-trityl-5-methyluridine (**13**) was likewise treated with 1,1'-thiocarbonyldiimidazole in DMF for 18 h at room temperature, and the resulting allylic rearranged product **29** was heated with Bu_3SnH in the presence of AIBN in toluene to give 2',3'-didehydro-2',3'-dideoxy-2'-methyl-5'-*O*-trityl-5'-methyluridine (**30**) in quantitative yield from **13**. Deprotection of **30** with formic acid furnished **31** in 67%



Scheme 5

yield. Thus, the radical deoxygenation of **24**, **25**, and **29** exclusively gave the 2',3'-didehydro-2',3'-dideoxy derivatives **26** and **30** but not the deoxygenated methylidene derivatives such as **36** and **43** as shown in Scheme 4 and 5.

Tsuji *et al.* has reported that allylic esters such as allyl acetate and allyl carbonate were smoothly deoxygenated by formic acid in the presence of palladium-catalyst.[18-20] We adopted this method for our systems.[10] A starting material, 2',3'-di-*O*-acetyl-3'-deoxy-3'-methylidene-5-methyluridine (**32**), was prepared from **9** with Ac_2O in the presence of Et_3N and DMAP in CH_3CN.[21] Reduction of **32** with $LiBH_4$ as a hydride donor in the presence of Ph_3P and a catalytic amount of $(PhCN)_2PdCl_2$ in THF at room temperature gave a mixture of 5'-*O*-acetyl-2',3'-didehydro-2',3'-dideoxy-3'-methyl-5-methyluridine (**34**) and 5'-*O*-acetyl-2',3'-dideoxy-3'-methylidene-5-methyluridine (**35**) in 50% total yield in a ratio of 3 : 1, which were not separable from each other by silica gel column chromatography. The structure of **35** was readily identified from the ^1H NMR spectrum of the mixture. The presence of the H-1'-proton at 6.25 ppm as a triplet, a set of 3'-methylidene protons at 5.10 and 5.23 ppm as both doublet of doublets, and a set of 2'a,b protons at 3.14 and 2.56 ppm as both multiplet is consistent with the 2',3'-dideoxy-3'-methylidene structure of **35**. The structure of **34** was also identified from the ^1H NMR spectrum, where a singlet peak at 1.26 ppm is due to the 3'-*C*-methyl protons. Further confirmation of the structure of **34** was done by comparison of the ^1H NMR spectra with

TABLE 1. The Palladium-Catalyzed Deoxygenation of **32** and **33**

entry	compd	catalyst	reducing agent	reaction conditions	total yield %	ratio endo : exo
1	**32**	$(PhCN)_2PdCl_2$ Ph_3P	$LiBH_4$	THF, rt	50	75 : 25
2	**32**	$(PhCN)_2PdCl_2$ Bu_3P	HCO_2^- HN^+Et_3	CH_3CN, 80 °C	44	12 : 88
3	**32**	$Pd(OAc)_2$ Bu_3P	HCO_2^- HN^+Et_3	CH_3CN, 80 °C	76	10 : 90
4	**32**	$Pd_2(DBA)\cdot CHCl_3$ Bu_3P	HCO_2^- HN^+Et_3	CH_3CN, 80 °C	78	5 : 95
5	**33**	$Pd(OAc)_2$ Bu_3P	HCO_2^- HN^+Et_3	CH_3CN, 80 °C	80	10 : 90
6	**33**	$Pd_2(DBA)\cdot CHCl_3$ Bu_3P	HCO_2^- HN^+Et_3	CH_3CN, 80 °C	77	5 : 95

5'-*O*-acetylated product of **28**. The mass spectral data of the mixture **34** and **35** showed a molecular ion peak at *m/z* 280 further supported both structures. The ratio was calculated by the integration of the peaks corresponding to H-1' of the both nucleosides in the ^1H NMR spectrum. Thus, the reduction of **32** proceeded via a π-allyl palladium complex **C** and the product ratio was set by regioselectivity of the hydride attack.

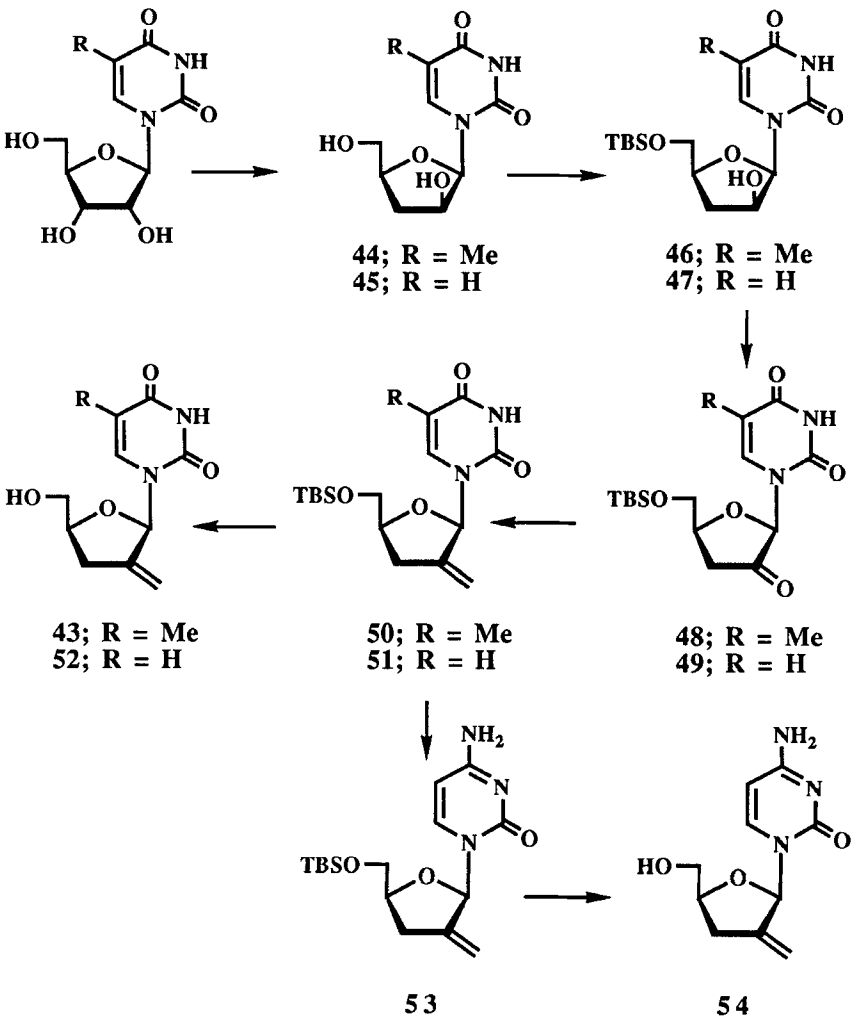
We examined the regioselectivity to use triethylammonium formate as a hydride source and the results are listed in Table 1. The use of triethylammonium formate in CH_3CN at 80 °C afforded a mixture of **34** and **35** (12 : 88) in 44% yield (entry 2). A combination of triethylammonium formate, Bu_3P, and $Pd(OAc)_2$ in CH_3CN for 15 min gave **34** and **35** in a ratio of 1 : 9 (76% yield, entry 3). More regioselective reduction was observed when **32** was treated with a mixture of triethylammonium formate, Bu_3P, and $Pd_2(DBA)_3\cdot CHCl_3$ in CH_3CN for 30 min to furnish a mixture of **34** and **35** (5 : 95) in 78% yield (entry 4). Thus, reduction of the allyl acetate **32** proceeded to give exclusively the *exo*-methylene compound **35** when the Pd^0 catalyst, $Pd_2(DBA)_3\cdot CHCl_3$ was used with formic acid as a hydride donor. Compounds **34** and **35** were not separable from each other by silica gel column chromatography. However, the mixture in the ratio of 5 : 95 was deblocked to furnish the target nucleoside 2'3'-dideoxy-3'-methylidene-5-methyluridine (**36**) in 98% yield, after separation by a silica gel column.

Synthesis of 2',3'-dideoxy-3'-methylidenecytidine (**39**) was done with the procedure described above. Treatment of 2',5'-di-*O*-acetyl-N^4-benzoyl-3'-deoxy-3'-methylidenecytidine (**33**) with a mixture of triethylammonium formate, Bu_3P, and $Pd_2(DBA)_3 \cdot CHCl_3$ in CH_3CN for 20 min furnished a mixture of **37** and **38** (5 : 95) in 77% yield (entry 6). Compound **38** was directly crystallized from the mixture and then deblocked with NH_3 / MeOH to give 2',3'-dideoxy-3'-methylidenecytidine (**39**) as a hydrochloride. Recently, Sharma and Bobek[11] reported the synthesis of **36** and **39** from reactions of the corresponding 2'-deoxy-3'-keto pyrimidine nucleosides with $Zn\text{-}CH_2Br_2\text{-}TiCl_4$ reagent, after our work was completed.[10] However, our method could be applicable to purine nucleosides, since 2'-deoxy-3'-keto purine nucleosides have never been synthesized because of their instability.

Next, we applied this palladium-catalyzed deoxygenation to the 2'-deoxy-2'-methylidene pyrimidine nucleosides (Scheme 6). When 3'-*O*-acetyl-2'-deoxy-2'-methylidene-5'-*O*-trityl-5-methyluridine was treated with a mixture of triethylammonium formate, Bu_3P, and $Pd_2(DBA)_3 \cdot CHCl_3$ in CH_3CN at reflux temperature, a complex mixture (data not shown) was obtained. Therefore, we prepared 3'-*O*-ethoxycarbonyl derivative **40** from **13**. Deoxygenation of **40** proceeded smoothly at 50 °C with triethylammonium formate in the presence of $Pd(OAc)_2$ and Bu_3P in THF to show one spot on TLC. However, ^{1}H-NMR spectrum of the product, purified by silica gel column chromatography, showed again a mixture of **30** and **42**. The structure of **42** was identified by the presence of the 2"-methylidene protons at 5.18 and 5.34 ppm each as a doublet, while **30** was consistent with the ^{1}H NMR spectrum of **30** prepared above. The product ratio of **30** and **42** was measured as 28 : 72 from the integration of the each H-1' (6.58 and 6.83 ppm, **30** and **42**, respectively). Further structure identification of **42** was done by treatment of the mixture with formic acid to produce 2',3'-dideoxy-2'-methylidene-5-methyluridine (**43**) as a crystal, while, during the deprotection, the acid unstable 2',3'-didehydro-2',3'-dideoxy-2'-methyl derivative was decomposed.

In applying the similar deoxygenation to cytidine derivatives, attempts to synthesize 3'-*O*-ethoxycarbonyl-5'-*O*-TBScytidine failed. Reaction of 3',5'-di-*O*-acetyl-N^4-benzoyl-2'-deoxy-2'-methylidenecytidine (**41**) with triethylammonium formate in the presence of $Pd(OAc)_2$ and Bu_3P in THF at 50 °C gave mainly N^4-benzoylcytosine (data not shown). Since it is known that an allyl carbonate is more reactive than an allyl acetate in the palladium-catalyzed reduction,[18-20] **40** reacted smoothly to produce the deoxygenated nucleosides **42** and **43** through a complex **D**, while **41** has the allyl acetate system in the structure and reacted via a π-allyl palladium complex **E** to give N^4-benzoylcytosine.

An alternative method for the synthesis of 2',3'-dideoxy-2'-methylidene pyrimidine nucleosides was then devised. Recently, Kawana *et al.* reported synthesis of 3'-deoxy-β-



Scheme 6

D-*threo*-pentofuranosyl nucleosides from the corresponding ribonucleosides by two-one-pot reactions including the deoxygenative [1,2]-hydride shift of the 3'-*O*-methanesulfonates.[22] First, we applied this method to 5-methyluridine to afford the desired nucleoside **44** in 50% overall yield. The 5'-hydroxyl group in **44** was protected by TBS group to give **46**, and then the 2'-hydroxyl group in **46** was oxidized with the CrO_3-pyridine-acetic anhydride system in CH_2Cl_2 to give the 2'-ketone **48** as crystals in 61% yield from **44**. The Wittig methylenation of **48** with methylenetriphenylphosphorane gave the 2'-methylidene **50** in 53% yield. In this reaction, it was observed that the ketone

48 was not consumed completely even with a longer reaction time or by addition of an excess of the ylide due to enolization. Separation of both nucleosides, **48** and **50**, was somewhat difficult by conventional column chromatographic techniques, but we finally found that Chromatotron worked. After deprotection of the 5'-*O*-TBS group with TBAF, one of the target nucleoside, 2',3'-dideoxy-2'-methylidene-5-methyluridine (**43**) was obtained as crystals, whose melting point and ^{1}H NMR spectrum were identical to those of **43** obtained from the palladium-catalyzed deoxygenation. Therefore, this route is an efficient alternative to the synthesis of **43**.

1-(3-Deoxy-β-D-*threo*-pentofuranosyl)uracil (**45**)[22] was also converted to its 2'-ketone **49**, and the methylenation of **49** was done as described above to give the 2'-methylidene derivative **51** in 22% from **45**. Again the yield of the methylenation step was low. Deprotection of the TBS group with TBAF gave 2',3'-dideoxy-2'-methylideneuridine (**52**). Conversion of **51** to the cytosine derivative by a conventional method via the O^4-triisopropylbenzenesulfonate of **51** with NH_4OH gave the desired **53** in 99% yield, of which the 5'-*O*-TBS group was removed by TBAF, furnishing 2',3'-dideoxy-2'-methylidenecytidine (**54**) as a hydrochloride.

Cytotoxicity of **9**, **20**, **28**, **31**, **36**, **39**, **43**, **52**, and **54** against mouse leukemic L1210 and human oral epidermoid carcinoma KB cells *in vitro* was examined as described previously.[3] Unlike the activity of DMDC (IC_{50} = 0.37 and 1.4 μg / ml for L1210 and KB cells, respectively), these nucleosides except **54** did not show any significant cytotoxicity to both cells up to 50 μg / ml, while **54** showed that IC_{50} values 5.6 μg / ml and 6.8 μg / ml for above cell lines, respectively.[23] Therefore, DMDC requires a methylidene group at the 2'-position and a hydroxyl group at the 3'-position in the molecule for significant antineoplastic activity. Recently, Stubbe *et al.* reported that 5'-diphosphate of DMDC potently and time-dependently inhibited ribonucleotide reductase from *E.* coli.[24] It is important for the inhibition of the enzyme that the radical at the 3'-position initially formed, which constitutes an allylic radical, is stabilized by the 2'-methylidene group. This observation is also consistent with this study. Since we found that DMDC 5'-triphosphate inhibited DNA polymerase α, DMDC has dual mechanisms to inhibit cell proliferation.[25] Inhibition of the cytopathogenicity of HIV-1 (MT-4 cells) by these nucleosides was also tested. None of them showed any significant inhibitory activity up to 100 μg / ml concentrations.[26]

Experimental Section

Melting points were measured on a Yanagimoto MP-3 micromelting point apparatus and are uncorrected. The ^{1}H NMR spectra were recorded on a JEOL JNM-FX 100 (100 MHz) or JEOL JNM-GX 270 (270 MHz) spectrometer with tetramethylsilane as an

internal standard. ^{31}P NMR spectra were recorded on a JEOL FX90Q spectrometer with triethyl phosphate as an internal standard. Chemical shifts are reported in parts per million (δ), and signals are expressed as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broad). All exchangeable protons were detected by addition of D_2O. UV absorption spectra were recorded with a Shimadzu UV-240 spectrophotometer. Mass spectra (MS) were measured on a JEOL JMX-DX303 spectrometer. TLC was done on Merck Kieselgel F254 precoated plates. The silica gel used for column chromatography was YMC gel 60A (70-230 mesh).

5'-*O*-Trityl-5-methyluridine (1). A mixture of 5-methyluridine (51.65 g, 0.2 mol) and TrCl (61.22 g, 0.22 mol) in dry pyridine (500 ml) was stirred at 50 °C for 40 h. A further amount of TrCl (11.03 g, 0.04 mol) was added to the mixture and the whole was stirred at 100 °C for 8.5 h. The cooled mixture was concentrated to about a 1/3 volume and was diluted with EtOH (50 ml). The mixture was slowly poured into ice-water (2 l) with vigorous stirring. The resulting white precipitates were collected by filtration, washed well with water, and air-dried. The whole was crystallized from $CHCl_3$ to give **1** (70.53 g, 76.2%): mp 141-145 °C; MS *m/z* 500 (M^+); NMR (DMSO-d_6, 100 MHz) 11.30 (1H, br s, NH), 7.48 (1H, s, H-6), 7.41-7.18 (15H, m, Tr), 5.80 (1H, d, H-1', $J_{1',2'}$ = 4.4 Hz), 5.46, 5.15 (each 1H, d, 2'- or 3'-OH), 4.21-3.98 (3H, m, H-2',3',4'), 3.30 (2H, m, H-5'a,b), 1.43 (3H, s, 5-Me).

Silylation of 1. A mixture of **1** (5.32 g, 30 mmol), imidazole (2.25 g, 3.3 mmol), and *tert*-butyldimethylsilyl chloride (TBSCl, 4.97 g, 33 mmol) in dry DMF (60 ml) was stirred for 19 h at room temperature. The mixture was partitioned between EtOAc (300 ml) and H_2O (3 x 50 ml), the separated organic phase was dried (Na_2SO_4), and the solvent was removed *in vacuo*. The oily residue was purified by a silica gel column with hexane / EtOAc (4 : 1) to give 2',3'-di-*O*-TBS-5'-*O*-trityl-5-methyluridine (**4**, 1.75 g, 8%) as a foam. Successive elution of the column with hexane / EtOAc (2 : 1) to give 2'-*O*-TBS-5'-*O*-trityl-5-methyluridine (**2**, 8.30 g, 45%) as a foam, then 3'-*O*-TBS-5'-*O* trityl-5-methyluridine (**3**, 6.13 g, 33%) as a foam. Physical data for **4**: MS *m/z* 671 (M^+-*t*-Bu); NMR ($CDCl_3$, 100 MHz) 8.25 (1H, br s, NH), 7.82 (1H, d, H-6, $J_{6,Me}$ = 1.2 Hz), 7.56-7.30 (15H, m, Tr), 6.05 (1H, d, H-1', $J_{1',2'}$ = 5.4 Hz), 4.47-4.18 (3H, m, H-2',3',4'), 3.65 (1H, dd, H-5'a), 3.34 (1H, dd, H-5'b), 1.52 (3H, d, 5-Me), 0.99-0.85 (18H, m, *t*-Bu), 0.17-0.00 (12H, m, SiMe). Physical data for **2**: MS *m/z* 557 (M^+-*t*-Bu); NMR ($CDCl_3$, 100 MHz) 8.30 (1H, br s, NH), 7.64 (1H, d, H-6, $J_{6,Me}$ = 1.2 Hz), 7.48-7.26 (15H, m, Tr), 6.04 (1H, d, H-1', $J_{1',2'}$ = 5.4 Hz), 4.55-4.15 (3H, m, H-2',3',4'), 3.49 (1H, dd, H-5'a), 3.43 (1H, dd, H-5'b), 2.74 (1H, d, 3'-OH, J = 3.9 Hz), 1.37 (3H, d, 5-Me, $J_{Me,6}$ = 1.2 Hz), 0.93 (9H, t, *t*-Bu), 0.14 (6H, s, SiMe). *Anal.* Calcd for $C_{35}H_{42}N_2O_6Si \cdot 1/2\ H_2O$: C, 67.39; H, 6.95; N, 4.49. Found: C, 67.52; H, 7.09; N,

4.19. Physical data for **3**: MS *m/z* 557 (M^+-*t*-Bu); NMR ($CDCl_3$, 100 MHz) 8.35 (1H, br s, NH), 7.58 (1H, d, H-6, $J_{6,Me}$ = 1.2 Hz), 7.48-7.26 (15H, m, Tr), 5.97 (1H, d, H-1', $J_{1',2'}$ = 5.4 Hz), 4.45-4.02 (3H, m, H-2',3',4'), 3.55 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.2, $J_{5'a,b}$ = 10.8 Hz), 3.25 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.7, $J_{5'a,b}$ = 10.8 Hz), 2.85 (1H, d, 2'-OH, *J* = 7.6 Hz), 1.50 (3H, d, 5-Me, $J_{Me,6}$ = 1.0 Hz), 0.86 (9H, t, *t*-Bu), 0.06 (3H, s, SiMe), 0.04 (3H, s, SiMe). *Anal.* Calcd for $C_{35}H_{42}N_2O_6Si$: C, 68.38; H, 6.89; N, 4.56. Found: C, 68.27; H, 6.93; N, 4.44.

1-(3-Deoxy-2-*O*-TBS-5-*O*-trityl-β-D-*erythro*-3-pentofuran-3-urosyl)-5-methyluracil (5). A solution of **2** (3.07 g, 5 mmol) in CH_2Cl_2 (10 ml) was added to a preformed chromium complex [CrO_3 (2.5 g), pyridine (4 ml), and Ac_2O (2.5 ml) in CH_2Cl_2 (50 ml) containing molecular sieves (4 A, powder, 3 g)]. The reaction mixture was stirred for 6 h at room temperature and was poured dropwise into EtOAc (1000 ml). The suspension was filtered through a short silica gel column and the filtrate was concentrated to dryness. The residue was purified by a silica gel column with hexane / EtOAc (2 : 1) to give **5** (2.84 g, 92.6%) as a foam: MS *m/z* 555 (M^+-*t*-Bu); NMR ($CDCl_3$, 100 MHz) 8.04 (1H, br s, NH), 7.54 (1H, d, H-6, $J_{6,Me}$ = 1.2 Hz), 7.38-7.26 (15H, m, Tr), 6.26 (1H, d, H-1', $J_{1',2'}$ = 8.3 Hz), 4.64 (1H, d, H-2', $J_{2',1'}$ = 8.3 Hz), 4.25 (1H, m, H-4'), 3.62 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.2, $J_{5'a,b}$ = 10.5 Hz), 3.39 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.2, $J_{5'a,b}$ = 10.5 Hz), 1.40 (3H, d, 5-Me, $J_{Me,6}$ = 1.2 Hz), 0.91 (9H, t, *t*-Bu), 0.19 (3H, s, SiMe), 0.11 (3H, s, SiMe).

Wittig reaction of 5. a) A hexane solution of BuLi (1.53 M, 5.88 ml, 9 mmol) was added to a suspension of methyltriphenylphosphonium bromide (4.29 g, 12 mmol) in THF (50 ml) at 0 °C with stirring under argon and the mixture was further stirred for 15 min at room temperature. A solution of **5** (1.84 g, 3 mmol) in THF (10 ml) was added dropwise to the above ylide at 0 °C and the mixture was stirred for 1 h at room temperature. The mixture was neutralized with AcOH and the solvent was removed *in vacuo*. The residue was partitioned between EtOAc (200 ml) and H_2O (2 x 50 ml). The separated organic phase was dried (Na_2SO_4), concentrated *in vacuo*, and the residue was purified by a silica gel column with hexane / EtOAc (3 : 1) to afford 3'-deoxy-3'-methylidene-2'-*O*-TBS-5'-*O*-trityl-5-methyluridine (**7**, 454 mg, 24.8%) as a foam: MS *m/z* 553 (M^+-*t*-Bu); NMR ($CDCl_3$, 270 MHz) 7.93 (1H, br s, NH), 7.64 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz), 7.44-7.24 (15H, m, Tr), 5.95 (1H, d, H-1', $J_{1',2'}$ = 7.3 Hz), 5.38 (1H, br t, H-3"a), 5.17 (1H, br t, H-3"b), 4.97 (1H, m, H-2'), 4.68 (1H, m, H-4'), 3.40 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.6, $J_{5'a,b}$ = 10.3 Hz), 3.32 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.6, $J_{5'a,b}$ = 10.3 Hz), 1.34 (3H, d, 5-Me, $J_{Me,6}$ = 1.1 Hz), 0.94 (9H, s, *t*-Bu), 0.15 (3H, s, SiMe), 0.04 (3H, s, SiMe). Further elution of the column with EtOH / EtOAc (1 : 1) gave a crude **6** (2.2 g, 83%) as a foam: FAB-MS *m/z* 889 (M^++H); ^{31}P-NMR (DMSO-d_6) 21.84. b) A

hexane solution of BuLi (1.53 M, 5.88 ml, 9 mmol) was added to a suspension of methyltriphenylphosphonium bromide (3.22 g, 9 mmol) in THF (50 ml) at 0 °C with stirring under argon and the mixture was further stirred for 1 h at room temperature. A solution of **5** (1.84 g, 3 mmol) in THF (10 ml) was added dropwise to the above ylide at 0 °C and the mixture was stirred for 4 h at room temperature. The mixture was neutralized with aqueous 1 N NH_4Br and the whole was partitioned between EtOAc (200 ml) and H_2O (3 x 50 ml). The separated organic phase was dried (Na_2SO_4), concentrated *in vacuo*, and the residue was purified by a silica gel column with hexane / EtOAc (2 : 1) to afford **7** (1.81 g, 98.6%) as a foam.

Conversion of 6 into 7. Sodium hydride (60% dispersion, 238 mg) was added to a solution of **6** (2.0 g) in THF (25 ml) and the mixture was stirred for 6 h at room temperature under argon. Aqueous 1 N NH_4Br was added to the reaction mixture and the whole was partitioned between EtOAc and H_2O. The separated organic phase was dried (Na_2SO_4), concentrated to dryness, and was purified by a silica gel column to afford **7** (711 mg, 52%) as a foam.

3'-Deoxy-3'-methylidene-5'-*O*-trityl-5-methyluridine (8). A solution of **7** (711 mg, 1.16 mmol) in THF (20 ml) was treated with a 1 M THF solution of tetrabutylammonium fluoride (TBAF, 1.4 ml, 1.4 mmol) for 30 min at room temperature and the mixture was partitioned between EtOAc and H_2O. The organic phase was dried (Na_2SO_4) and purified by a short silica gel column with hexane / EtOAc (1 : 1) to give **8** (573 mg, 99%) as a foam: MS *m/z* 478 (M^+-H_2O), 253 (M^+-Tr); NMR ($CDCl_3$, 270 MHz) 8.11 (1H, br s, NH), 7.59 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz), 7.42-7.30 (15H, m, Tr), 5.80 (1H, d, H-1', $J_{1',2'}$ = 6.2 Hz), 5.53 (1H, br t, H-3"a), 5.20 (1H, br t, H-3"b), 4.87 (1H, m, H-2'), 4.80 (1H, m, H-4'), 3.36 (1H, dd, H-5'a), 3.34 (1H, dd, H-5'b), 3.13 (1H, d, 2'-OH, J = 5.5 Hz), 1.52 (3H, d, 5-Me, $J_{Me,6}$ = 1.1 Hz).

3'-Deoxy-3'-methylidene-5-methyluridine (9). Compound **8** (1.46 g, 2.94 mmol) was treated with 97% formic acid (10 ml) for 5 min at room temperature and the solvent was removed *in vacuo*. The residue was coevaporated several times with EtOH and treated with NH_3/MeOH (saturated at 0 °C, 20 ml) overnight at room temperature. Evaporation of the solvent and the residue was purified by a silica gel to afford **9** (662 mg, 88.8%) as a foam: MS *m/z* 255 (M^++H), 223 (M^+-H_2O); NMR ($CDCl_3$, 270 MHz) 7.64 (1H, s, H-6), 5.88 (1H, d, H-1', $J_{1',2'}$ = 6.2 Hz), 5.45 (1H, br s, H-3"a), 5.35 (1H, br s, H-3"b), 4.83 (1H, m, H-4'), 3.89 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.2, $J_{5'a,b}$ = 12.6 Hz), 3.79 (1H, dd, H-5'b, $J_{5'b,4'}$ = 4.0, $J_{5'a,b}$ = 12.6 Hz), 1.89 (3H, s, 5-Me). *Anal.* Calcd for $C_{11}H_{14}N_2O_5$: C, 51.97; H, 5.55; N, 11.02. Found: C, 51.87; H, 5.66; N, 10.83.

1-(3-*O*-TBS-5-*O*-trityl-β-D-*erythro*-2-pentofuran-2-ulosyl)-5-methyluracil (10). A solution of **3** (4.88 g, 8 mmol) in CH_2Cl_2 (30 ml) was added to a

preformed chromium complex [CrO_3 (3.97 g), pyridine (6.35 ml), and Ac_2O (3.97 ml) in CH_2Cl_2 (95 ml) containing molecular sieves (4 A, powder, 7 g)]. The reaction mixture was stirred for 3.5 h at room temperature and was poured dropwise to EtOAc (1500 ml). The suspension was filtered through a short silica gel column and the filtrate was concentrated to dryness. The residue was purified by a silica gel column with hexane / EtOAc (3 : 1) to give **10** (3.56 g, 73.2%) as a foam: MS *m/z* 555 (M^+-*t*-Bu); NMR ($CDCl_3$, 100 MHz) 8.30 (1H, br s, NH), 7.51-7.18 (15H, m, Tr), 7.07 (1H, d, H-6, $J_{6,Me}$ = 1.2 Hz), 5.12 (1H, s, H-1'), 4.71 (1H, d, H-3', $J_{3',4'}$ = 8.6 Hz), 4.08 (1H, m, H-4'), 3.58 (1H, dd, H-5'a), 3.35 (1H, dd, H-5'b), 1.90 (3H, d, 5-Me, $J_{Me,6}$ = 1.2 Hz), 0.77 (9H, t, *t*-Bu), 0.08 (3H, s, SiMe), 0.01 (3H, s, SiMe). *Anal.* Calcd for $C_{35}H_{40}N_2O_6Si \cdot H_2O$: C, 66.64; H, 6.71; N, 4.44. Found: C, 66.71; H, 6.44; N, 4.29.

Wittig reaction of 10. A hexane solution of BuLi (1.53 M, 5.88 ml, 9 mmol) was added to a suspension of methyltriphenylphosphonium bromide (4.29 g, 12 mmol) in THF (50 ml) at 0 °C with stirring under argon. After being stirred for 30 min, a solution of **10** (1.84 g, 3 mmol) in THF (10 ml) was added dropwise over 10 min at 0 °C. The mixture was stirred for further 2 h at 0 °C and aqueous 1 N NH_4Br was added to the mixture, which was then partitioned between EtOAc (200 ml) and H_2O (3 x 50 ml). The separated organic phase was dried (Na_2SO_4) and the solvent was removed *in vacuo*. The residue was purified by a silica gel column with hexane / EtOAc (2 : 1) to give 2'-deoxy-2'-methylidene-3'-*O*-TBS-5'-*O*-trityl-5-methyluridine (**12**, 732 mg, 40 %) as a foam. Successive elution of the column with EtOH / EtOAc (1 : 1) afforded the phosphonium salt **11** (2.31 g). Physical data of **12**: MS *m/z* 553 (M^+-*t*-Bu); NMR ($CDCl_3$, 270 MHz) 8.01 (1H, br s, NH), 7.43-7.24 (16H, m, Tr and H-6), 6.73 (1H, d, H-1', *J* = 1.8 Hz), 5.46 (1H, br t, H-2"a), 5.39 (1H, br t, H-2"b), 4.88 (1H, m, H-3'), 3.90 (1H, m, H-4'), 3.60 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.2, $J_{5'a,b}$ = 11.0 Hz), 3.35 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.9, $J_{5'a,b}$ = 11.0 Hz), 1.46 (3H, d, 5-Me, $J_{Me,6}$ = 1.2 Hz), 0.80 (9H, t, t-Bu), 0.06 (3H, s, SiMe), 0.16 (3H, s, SiMe). *Anal.* Calcd for $C_{36}H_{42}N_2O_5Si \cdot H_2O$: C, 68.75; H, 7.05; N, 4.45. Found: C, 69.01; H, 6.79; N, 4.39. Physical data of **11**: ^{31}P-NMR ($CDCl_3$) 20.21.

Conversion of 11 into 12. Sodium hydride (60%, 56.5 mg, 2.3 mmol) was added to a solution of **11** (900 mg, 1 mmol) in THF (20 ml) and the mixture was stirred for 23 h at room temperature under argon. The mixture was neutralized with AcOH and was partitioned between EtOAc (100 ml) and H_2O (3 x 30 ml). The separated organic phase was dried (Na_2SO_4) and the solvent was removed *in vacuo*. The residue was purified by a silica gel column with hexane / EtOAc (4 : 1) to give **12** (260 mg, 43 %) as a foam.

2'-Deoxy-2'-methylidene-5'-*O*-trityl-5-methyluridine (13). A THF solution of TBAF (1 M, 0.91 ml) was added to a solution of **12** (398 mg, 0.65 mmol) in

THF (5 ml) at room temperature. After being stirred for 1 h at room temperature, the solvent was removed *in vacuo* and the residue was purified by a silica gel column with hexane / EtOAc (1 : 1) to give **13** (320 mg, 99%) as a foam: MS *m/z* 253 (M^+-Tr); NMR ($CDCl_3$, 270 MHz) 8.23 (1H, br s, NH), 7.44-7.23 (15H, m, Tr), 7.24 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz), 6.71 (1H, d, H-1', J = 1.8 Hz), 5.60 (1H, br t, H-2"a), 5.41 (1H, br t, H-2"b), 4.81 (1H, m, H-3'), 3.87 (1H, m, H-4'), 3.58 (1H, dd, H-5'a, $J_{5'a,4'}$ = 3.3, $J_{5'a,b}$ = 10.6 Hz), 3.46 (1H, dd, H-5'b, $J_{5'b,4'}$ = 3.3, $J_{5'a,b}$ = 10.6 Hz), 1.95 (1H, d, 3'-OH), 1.53 (3H, d, 5-Me, $J_{Me,6}$ = 1.1 Hz).

Silylation of N^4-benzoylcytidine (14). TBSCl (3.32 g, 22 mmol) was added to a mixture of **14** (3.47 g, 10 mmol) and imidazole (1.50 g, 22 mmol) in DMF (20 ml) at 0 °C under argon. The reaction mixture was stirred for 1 h at room temperature and then diluted with EtOAc (100 ml), which was washed with H_2O (3 x 30 ml). The separated organic phase was dried (Na_2SO_4) and the solvent was removed *in vacuo*. The residue was purified by a silica gel column with hexane / EtOAc (2 : 1 to 1 : 1) to give N^4-benzoyl-2',5'-di-*O*-TBScytidine (**15**, 3.03 g, 52.6%, crystallized from EtOH): mp 152-154 °C; MS *m/z* 560 (M^+-Me); NMR ($CDCl_3$, 270 MHz) 8.65 (1H, br s, NH), 8.54 (1H, d, H-6, $J_{6,5}$ = 7.7 Hz), 7.92-7.89 (2H, m, Bz), 7.64-7.49 (3H, m, Bz), 7.53 (1H, d, H-5), 5.98 (1H, d, H-1', $J_{1',2'}$ = 2.2 Hz), 4.23 (1H, dd, H-2', $J_{2',3'}$ = 4.4 Hz), 4.20-4.06 (3H, m, H-3',4',5'a), 3.89 (1H, d, H-5'b, $J_{5'a,b}$ = 11.5 Hz), 2.46 (1H, d, 3'-OH), 0.97, 0.94 (each 9H, s, *t*-Bu), 0.28 (3H, s, SiMe), 0.17, 0.16 (9H, s, SiMe). *Anal.* calcd for $C_{28}H_{45}N_3O_6Si_2$: C, 58.40; H, 7.88; N, 7.30. Found: C, 58.35; H, 7.72; N, 7.11. Successive elution of the column with hexane / EtOAc (1 : 2 to 1 : 4) gave N^4-benzoyl-3',5'-di-*O*-TBScytidine (**16**, 1.78 g, 30.8%, crystallized from EtOH): mp 156-157 °C; MS *m/z* 560 (M^+-Me); NMR ($CDCl_3$, 100 MHz) 8.74 (1H, br s, NH), 8.37 (1H, d, H-6, $J_{6,5}$ = 7.6 Hz), 7.95-7.86 (2H, m, Bz), 7.64-7.27 (4H, m, Bz and H-5), 6.04 (1H, d, H-1', $J_{1',2'}$ = 2.9 Hz), 4.30-3.75 (5H, m, H-2',3',4',5'a,b), 0.97, 0.92 (each 9H, s, *t*-Bu), 0.15, 0.14 (each 3H, s, SiMe), 0.13 (6H, s, SiMe). *Anal.* calcd for $C_{28}H_{45}N_3O_6Si_2$: C, 58.40; H, 7.88; N, 7.30. Found: C, 58.26; H, 7.96; N, 7.19.

N^4-Benzoyl-1-(2,5-di-*O*-TBS-β-D-*erythro*-3-pentofuran-3-ulosyl)-cytosine (17). A solution of **15** (2.30 g, 4 mmol) in CH_2Cl_2 (20 ml) was added to a preformed chromium complex [CrO_3 (2.0 g), pyridine (3.24 ml), and Ac_2O (1.89 ml) in CH_2Cl_2 (50 ml) containing molecular sieves (4 A, powder, 3 g)]. The reaction mixture was stirred for 20 min at room temperature and was poured dropwise to EtOAc (800 ml). The suspension was filtered through a short silica gel column and the filtrate was washed with aqueous saturated $NaHCO_3$ solution and H_2O. The organic phase was dried (Na_2SO_4) and concentrated to dryness. The residue was purified by a silica gel column with hexane / EtOAc (3 : 1) to give **17** (1.99 g, 86.7%, crystallized from hexane / EtOAc):

mp >300 °C; MS *m/z* 558 (M^+-Me); NMR ($CDCl_3$, 100 MHz) 8.65 (1H, br s, NH), 8.22 (1H, d, H-6, $J_{6,5}$ = 7.6 Hz), 7.97-7.89 (2H, m, Bz), 7.64-7.45 (4H, d, Bz and H-5), 6.43 (1H, d, H-1', $J_{1',2'}$ = 7.6 Hz), 4.28-4.18 (2H, m, H-2', 4'), 3.95 (3H, m, H-4',5'a,b), 0.91, 0.86 (each 9H, s, *t*-Bu), 0.12, 0.08, 0.05, 0.01 (each 3H, s, SiMe). *Anal.* Calcd for $C_{28}H_{43}N_3O_6Si_2$: C, 58.61; H, 7.55; N, 7.32. Found: C, 58.70; H, 7.62; N, 7.38.

N^4-Benzoyl-3'-deoxy-3'-methylidene-2',5'-di-*O*-TBScytidine (18). Butyllithium (1.59 M hexane solution, 5.03 ml, 8 mmol) was added to a suspension of methyltriphenylphosphonium bromide (2.83 g, 8 mmol) in THF (30 ml) with stirring for 15 min at 0 °C and then 1 h at room temperature under argon. A solution of **17** (1.15 g, 2 mmol) in THF (20 ml) was added dropwise to the above ylide at 0 °C and the mixture was further stirred for 5 h at room temperature. Aqueous NH_4Br solution (1 M, 20 ml) was added to the mixture, and the whole was extracted with EtOAc (2 x 50 ml), which was washed with H_2O (2 x 30 ml). The separated organic phase was dried (Na_2SO_4) and concentrated to dryness. The residue was purified by a silica gel column with hexane / EtOAc (3 : 1) to give **18** (1.04 g, 90.5%, crystallized from hexane / EtOAc): mp 161-162.5 °C; NMR ($CDCl_3$, 100 MHz) 8.63 (1H, br s, NH), 8.37 (1H, d, H-6, $J_{6,5}$ = 7.6 Hz), 7.88-7.57 (2H, m, Bz), 7.44-7.24 (4H, m, Bz and H-5), 6.09 (1H, d, H-1', $J_{1',2'}$ = 5.1 Hz), 5.26 (1H, t, H-3"a, *J* = 2.0 Hz), 5.14 (1H, t, H3"b, *J* = 2.0 Hz), 4.72 (1H, m, H-4'), 4.57 (1H, m, H-2'), 4.07 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.2, $J_{5'a,b}$ = 11.5 Hz), 3.79 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.2 Hz), 0.95, 0.90 (each 9H, s, *t*-Bu), 0.13, 0.11, 0.03, 0.01 (each 3H, s, SiMe). *Anal.* Calcd for $C_{29}H_{45}N_3O_5Si_2$: C, 60.91; H, 7.93; N, 7.35. Found: C, 61.13; H, 8.08; N, 7.23.

3'-Deoxy-3'-methylidenecytidine Hydrochloride (20). A solution of **18** (286 mg, 0.5 mmol) in THF (10 ml) was treated with TBAF (1 M, 1.2 ml) for 1 h at room temperature and the solvent was removed *in vacuo*. The residue was purified by a silica gel column with 10% EtOH in $CHCl_3$ to give **19** as a foam, which was further treated with NH_3/MeOH (saturated at 0 °C, 10 ml) in a sealed tube overnight at room temperature. The solvent was removed *in vacuo* and 1 N HCl (0.5 ml) in EtOH (5 ml) was added. The mixture was concentrated to dryness and the residue was crystallized from EtOH to give **20** (100 mg, 73%): mp 189-190.5 °C; NMR (D_2O, 270 MHz) 8.05 (1H, d, H-6, $J_{6,5}$ = 8.1 Hz), 6.23 (1H, d, H-5, $J_{5,6}$ = 8.1 Hz), 5.91 (1H, d, H-1', $J_{1',2'}$ = 5.1 Hz), 5.47 (1H, br t, H-3"a), 5.36 (1H, br t, H-3"b), 4.89 (1H, m, H-4'), 3.92 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.9, $J_{5'a,b}$ = 12.8 Hz), 3.81 (1H, dd, H-5'b, $J_{5'b,4'}$ = 4.0, $J_{5'a,b}$ = 12.8 Hz). *Anal.* Calcd for $C_{10}H_{13}N_3O_4$·HCl: C, 43.56; H, 5.11; N, 15.24. Found: C, 43.51; H, 5.08; N, 15.06.

N^4-Benzoyl-1-(3,5-di-*O*-TBS-β-D-*erythro*-2-pentofuran-2-ulosyl)-cytosine (21). A solution of **16** (4.49 g, 7.8 mmol) in CH_2Cl_2 (50 ml) was added to a preformed chromium complex [CrO_3 (3.12 g), pyridine (5.05 ml), and Ac_2O (2.94 ml) in CH_2Cl_2 (100 ml) containing molecular sieves (4 A, powder, 4 g)]. The reaction mixture was stirred for 20 mim at room temperature and was poured dropwise into EtOAc (1200 ml). The suspension was filtered through a short silica gel column and the filtrate was washed with aqueous saturated $NaHCO_3$ solution and H_2O. The organic phase was dried (Na_2SO_4) and concentrated to dryness. The residue was purified by a silica gel column with EtOAc to give **21** (3.64 g, 81.2%, crystallized from hexane / EtOAc): mp >300 °C; MS *m/z* 558 (M^+-Me); NMR ($CDCl_3$, 270 MHz) 8.66 (1H, br s, NH), 7.88 (1H, d, H-6, $J_{6,5}$ = 7.0 Hz), 7.64-7.49 (6H, m, Bz and H-5), 5.24 (1H, s, H-1'), 4.80 (1H, d, H-3', $J_{3',4'}$ = 7.7 Hz), 4.21-3.81 (3H, m, H-4',5'a,b), 0.92, 0.91 (each 9H, s, *t*-Bu), 0.22, 0.17 (each 6H, s, SiMe). *Anal.* Calcd for $C_{28}H_{43}N_3O_6Si_2$: C, 58.61; H, 7.55; N, 7.32. Found: C, 58.64; H, 7.64; N, 7.36.

N^4-Benzoyl-2'-deoxy-2'-methylidene-3',5'-di-*O*-TBScytidine (22). Butyllithium (1.59 M hexane solution, 16.4 ml, 26 mmol) was added to a suspension of methyltriphenylphosphonium bromide (9.29 g, 26 mmol) in THF (100 ml) with stirring for 15 min at 0 °C and then 1 h at room temperature under argon. A solution of **21** (3.73 g, 6.5 mmol) in THF (20 ml) was added dropwise to the above ylide at 0 °C and the mixture was further stirred for 2.5 h at room temperature. Aqueous NH_4Br solution (1 M, 150 ml) was added to the mixture, and the whole was extracted with EtOAc (2 x 200 ml), which was washed with H_2O (2 x 70 ml). The separated organic phase was dried (Na_2SO_4) and concentrated to dryness. The residue was purified by a silica gel column with hexane / EtOAc (2 : 1) to give **22** (3.21 g, 86.2%, crystallized from hexane / EtOAc): mp 167-168.5 °C; MS *m/z* 571 (M^+); NMR ($CDCl_3$, 270 MHz) 8.61 (1H, br s, NH), 8.23 (1H, d, H-6, $J_{6,5}$ = 7.3 Hz), 7.89 (2H, d, Bz, *J* = 7.0 Hz), 7.64-7.49 (4H, m, Bz and H-5), 6.80 (1H, s, H-1'), 5.67 (1H, br s, H-2"a), 5.36 (1H, t, H-2"b, *J* = 1.7 Hz), 4.80 (1H, br d, H-3', $J_{3',4'}$ = 6.2 Hz), 4.04 (1H, br d, H-5'a, $J_{5'a,4'}$ = 1.5, $J_{5'a,b}$ = 12.1 Hz), 3.87-3.79 (2H, m, H-4',5'b), 0.97, 0.93 (each 9H, s, *t*-Bu), 0.14 (12H, s, SiMe). *Anal.* Calcd for $C_{29}H_{45}N_3O_5Si_2$: C, 60.91; H, 7.93; N, 7.35. Found: C, 60.82; H, 7.98; N, 7.28.

2',3'-Didehydro-2',3'-dideoxy-3'-[(imidazol-1-yl)carbonylthio-methyl]-5'-*O*-trityl-5-methyluridine (24). A mixture of **8** (700 mg, 1.41 mmol) and 1,1'-thiocarbonyldiimidazole (419 mg, 2.1 mmol) in DMF (5 ml) was stirred for 24 h at room temperature and was partitioned between EtOAc (100 ml) and H_2O (3 x 30 ml). The separated organic phase was dried (Na_2SO_4) and concentrated to dryness *in vacuo* to leave an oily residue, which was crystallized from hexane / EtOAc to give **24** (715 mg,

83.6%): mp 202-204 °C; MS *m/z* 480 (M^+-SCOim); NMR ($CDCl_3$, 270 MHz) 8.14 (1H, br s, NH), 7.96 (1H, s, im), 7.63 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz), 7.13 (1H, d, im), 7.04 (1H, m, im), 5.95 (1H, s, H-1'), 4.92 (1H, br s, H-4'), 3.98 (1H, d, H-3"a, $J_{3"a,b}$ = 15.4 Hz), 3.72 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.6, $J_{5'a,b}$ = 11.0 Hz), 3.62 (1H, d, H-3"b, $J_{3"a,b}$ = 15.4 Hz), 3.37 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.9, $J_{5'a,b}$ = 11.0 Hz), 1.14 (3H, d, 5-Me, $J_{Me,6}$ = 1.1 Hz). *Anal.* Calcd for $C_{34}H_{30}N_4O_5S$: C, 67.31; H, 4.98; N, 9.23. Found: C, 67.13; H, 4.95; N, 9.05.

3'-Deoxy-3'-methylidene-2'-*O*-methyloxalyl-5'-*O*-trityl-5-methyluridine (25). Methyloxalyl chloride (69 µl, 0.75 mmol) was added to a solution of **8** (248 mg, 0.5 mmol) and DMAP (92 mg, 0.75 mmol) in dry CH_3CN (5 ml) at 0 °C under argon. The mixture was stirred for 30 min at 0 °C and was diluted with EtOAc (50 ml). The whole was washed with H_2O (3 x 20 ml), dried (Na_2SO_4), and concentrated to dryness *in vacuo*. The white foam (**25**, 285 mg, 98%) was used to the next reaction without further purification: MS *m/z* 478 (M^+-$COCO_2Me$-H_2O); NMR ($CDCl_3$, 270 MHz) 8.12 (1H, br s, NH), 7.53 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz), 6.20 (1H, d, H-1', $J_{1',2'}$ = 5.5 Hz), 6.05 (1H, m, H-2'), 5.52 (1H, br s, H-3"a), 5.27 (1H, br s, H-3"b), 3.94 (3H, s, OCH_3), 3.45 (2H, dd, H-5'a,b), 1.41 (3H, d, 5-Me, $J_{Me,6}$ = 1.1 Hz).

2',3'-Didehydro-2',3'-dideoxy-3'-methyl-5'-*O*-trityl-5-methyluridine (26). a) A solution of **24** (303 mg, 0.5 mmol), AIBN (50 mg), and Bu_3SnH (466 µl, 1.5 mmol) in toluene (20 ml) was heated at 100 °C for 24 h. The solvent was removed *in vacuo* and the residue was purified by a silica gel column with $CHCl_3$ to give **26** (200 mg, 83.2%, crystallized from EtOAc / hexane): mp 120-125 °C; NMR ($CDCl_3$, 270 MHz) 8.01 (1H, br s, NH), 7.68 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz), 7.45-7.23 (15H, m, Tr), 6.99 (1H, m, H-1'), 5.55 (1H, br d, H-2', J = 1.5 Hz), 4.71 (1H, br s, H-4'), 3.65 (1H, dd, H-5'a, $J_{5'a,4'}$ = 1.8, $J_{5'a,b}$ = 10.6 Hz), 3.19 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.9, $J_{5'a,b}$ = 10.6 Hz), 1.78 (3H, d, 3'-Me, $J_{Me,2'}$ = 1.7 Hz), 1.26 (3H, br s, 5-Me). *Anal.* Calcd for $C_{30}H_{28}N_2O_4 \cdot 1/4\ H_2O$: C, 74.28; H, 5.92; N, 5.77. Found: C, 74.18; H, 5.99; N, 5.77. b) A solution of **25** (280 mg, 0.48 mmol), AIBN (50 mg), and Bu_3SnH (336 µl, 1.25 mmol) in benzene (20 ml) was heated under reflux for 1.5 h and the solvent was removed *in vacuo*. The residue was purified by a silica gel column as above to give **26** (218 mg, 95%, crystallized from hexane / EtOAc).

2',3'-Didehydro-2',3'-dideoxy-3'-methyl-5-methyluridine (28). Formic acid (97%, 2 ml) was added to a solution of **26** (301 mg, 0.63 mmol) in THF (0.5 ml). The mixture was stirred for 3 min at room temperature and then was diluted with H_2O (5 ml). The whole was quickly cooled to -78 °C and lyophilized. The residue was purified by a silica gel column with 2% EtOH in $CHCl_3$ to give **28** (80 mg, 53.7%, crystallized from EtOAc): mp 208-210 °C; MS *m/z* 238 (M^+); NMR ($CDCl_3$ + D_2O, 270

MHz) 7.52 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz), 7.94 (1H, m, H-1'), 5.46 (1H, br s, H-2'), 4.68 (1H, d, H-4'), 3.95 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.6, $J_{5'a,b}$ = 12.5 Hz), 3.82 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.6, $J_{5'a,b}$ = 12.5 Hz), 1.94 (3H, d, 3'-Me, J = 0.7 Hz), 1.87 (3H, d, 5-Me, $J_{Me,6}$ = 1.1 Hz). *Anal.* Calcd for $C_{11}H_{14}N_2O_4$: C, 55.46; H, 5.92; N, 11.76. Found: C, 55.58; H, 5.81; N, 11.67.

2',3'-Didehydro-2',3'-dideoxy-2'-[(imidazol-1-yl)carbonylthiomethyl]-5'-*O*-trityl-5-methyluridine (29). A mixture of **13** (312 mg, 0.63 mmol) and 1,1'-thiocarbonyldiimidazole (187 mg, 0.94 mmol) in DMF (3 ml) was stirred for 18 h at room temperature and was partitioned between EtOAc (50 ml) and H_2O (3 x 15 ml). The organic phase was dried (Na_2SO_4) and concentrated. The residue was purified by a silica gel column with $CHCl_3$ to give **29** (319 mg, 83.7%) as a foam: MS *m/z* 353 (M^+-SCOim-base); NMR ($CDCl_3$, 270 MHz) 8.24 (1H, br s, NH), 8.18 (1H, t, im), 7.40-7.21 (15H, m, Tr), 7.54 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz),7.43 (1H, t, im), 7.13 (1H, m, im), 7.04 (1H, m, H-1'), 6.37 (1H, br s, H-3'), 4.98 (1H, br s, H-4'), 3.93 (1H, d, H-2"a), 3.77 (1H, d, H-2"b), 3.46 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.6, $J_{5'a,b}$ = 10.6 Hz), 3.38 (1H, dd, H-5'b, $J_{5'b,4'}$ = 3.7, $J_{5'a,b}$ = 10.6 Hz), 1.51 (3H, d, 5-Me, $J_{Me,6}$ = 1.1 Hz).

2',3'-Didehydro-2',3'-dideoxy-2'-methyl-5'-*O*-trityl-5-methyluridine (30). A mixture of **29** (314 mg, 0.52 mmol), AIBN (10 mg), and Bu_3SnH (209 µl, 0.78 mmol) in toluene (5 ml) was heated for 6.5 h at 100 °C. The solvent was removed *in vacuo* and the residue was purified by a silica gel column with hexane / EtOAc (1 : 1) to afford **30** (249 mg, 99%) as a foam: MS *m/z* 355 (M^+-base); NMR ($CDCl_3$, 270 MHz) 8.00 (1H, br s, NH), 7.44-7.22 (16H, m, Tr and H-6), 6.87 (1H, m, H-1'), 5.93 (1H, m, H-3'), 4.94 (1H, br s, H-4'), 3.36 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.9, $J_{5'a,b}$ = 10.3 Hz), 3.30 (1H, dd, H-5'b, $J_{5'b,4'}$ = 4.4, $J_{5'a,b}$ = 10.3 Hz), 1.75 (3H, s, 2'-Me), 1.27 (3H, d, 5-Me, $J_{Me,6}$ = 1.1 Hz). *Anal.* Calcd for $C_{30}H_{28}N_2O_4 \cdot 2/3\ H_2O$: C, 73.15; H, 6.00; N, 5.69. Found: C, 73.18; H, 5.88; N, 5.43.

2',3'-Didehydro-2',3'-dideoxy-2'-methyl-5-methyluridine (31). Formic acid (97%, 2 ml) was added to a solution of **30** (260 mg, 0.54 mmol) in THF (0.5 ml). The mixture was stirred for 3 min at room temperature and then was diluted with H_2O (5 ml). The whole was quickly cooled to -78 °C and lyophilized. The residue was purified by a silica gel column with 4% EtOH in $CHCl_3$ to give **31** (86 mg, 66.7%) as a foam: MS *m/z* 238 (M^+); NMR ($CDCl_3$, 270 MHz) 8.34 (1H, br s, NH), 7.41 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz), 6.83 (1H, dd, H-1', $J_{1',4'}$ = 2.6, $J_{1',3'}$ = 1.5 Hz), 5.92 (1H, dd, H-3', $J_{3',4'}$ = 3.3, $J_{1',3'}$ = 1.5 Hz), 4.87 (1H, br s, H-4'), 3.91 (After addition of D_2O, 1H, dd, H-5'a, $J_{5'a,4'}$ = 2.6, $J_{5'a,b}$ = 12.5 Hz), 3.74 (After addition of D_2O, 1H, dd, H-5'b, $J_{5'b,4'}$ = 3.3, $J_{5'a,b}$ = 12.5 Hz), 2.40 (1H, br s, 5'-OH), 1.88 (3H, s, 5-Me, $J_{Me,6}$ = 1.1 Hz),

1.72 (3H, s, 2'-Me). *Anal.* Calcd for $C_{11}H_{14}N_2O_4 \cdot 1/2\ H_2O$: C, 53.44; H, 6.12; N, 11.32. Found: C, 53.81; H, 5.95; N, 10.99.

2',5'-Di-*O*-acetyl-3'-deoxy-3'-methylidene-5-methyluridine (32). Acetic anhydride (190 µl, 2 mmol) was added to a solution of **9** (203 mg, 0.8 mmol) and DMAP (5 mg) in CH_3CN (5 ml). After being stirred for 1 h at room temperature, MeOH (1 ml) was added to the mixture, which was evaporated and coevaporated several times with EtOH. The residue was purified by a silica gel column with 5% EtOH in $CHCl_3$ to give **32** (265 mg, 98%) as a foam: MS *m/z* 338 (M^+); NMR ($CDCl_3$, 100 MHz) 8.22 (1H, br s, NH), 7.22 (1H, d, H-6, $J_{6,Me}$ = 1.2 Hz), 6.02 (1H, d, H-1', $J_{1',2'}$ = 5.4 Hz), 5.66 (1H, m, H-2'), 5.45 (1H, br t, H-3"a), 5.32 (1H, br t, H-3"b), 4.90 (1H, m, H-4'), 4.38 (1H, d, H-5'a), 4.34 (1H, s, H-5'b), 2.14 (6H, s, Ac), 1.95 (3H, d, 5-Me, $J_{Me,6}$ = 1.2 Hz).

2',5'-Di-*O*-Acetyl-N^4-benzoyl-3'-deoxy-3'-methylidenecytidine (33). A THF solution of TBAF (1 M, 4.43 ml) was added to a solution of **18** (1.01 g, 1.77 mmol) in THF (18 ml). The mixture was stirred for 1 h at room temperature and the solvent was removed *in vacuo*. The residue **19** was dissolved in a mixture of pyridine (10 ml) and Ac_2O (1 ml) and the mixture was stirred for 1 h at room temperature. MeOH (5 ml) was added to the mixture and the whole was concentrated to dryness. The residue was partitioned between EtOAc and H_2O and the organic phase was dried (Na_2SO_4). The solvent was removed *in vacuo* and the residue was crystallized from hexane / EtOAc to give **33** (642 mg, 84.9% from **18**): mp 153-154 °C; NMR ($CDCl_3$, 100 MHz) 8.68 (1H, br s, NH), 8.00 (1H, d, H-6, $J_{6,5}$ = 7.6 Hz), 7.94-7.85 (2H, m, Bz), 7.69-7.39 (4H, m, Bz and H-5), 6.14 (1H, d, H-1', $J_{1',2'}$ = 3.9 Hz), 5.70 (1H, dd, H-2', $J_{1',2'}$ = 3.9, $J_{2',3"}$ = 1.7 Hz), 5.53 (1H, t, H-3"a, J = 1.7 Hz), 5.32 (1H, t, H3"b, J = 1.7 Hz), 5.01 (1H, m, H-4'), 4.53 (1H, dd, H-5'a, $J_{5'a,4'}$ = 4.6, $J_{5'a,b}$ = 12.5 Hz), 4.36 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.9 Hz), 2.15, 2.13 (each 3H, s, Ac). *Anal.* Calcd for $C_{21}H_{21}N_3O_7$: C, 59.01; H, 4.95; N, 9.83. Found: C, 59.14; H, 4.99; N, 9.66.

Palladium-catalyzed deoxygenation of 32. Entry 1) A mixture of **32** (85 mg, 0.25 mmol), Ph_3P (66 mg, 0.25 mmol), $LiBH_4$ (16 mg, 0.75 mmol), and $(PhCN)_2PdCl_2$ (5 mg) in THF (5 ml) was stirred for 4 h at room temperature under argon. The solvent was removed *in vacuo* and the residue was suspended in EtOH. Insoluble materials were removed by filtration through a Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by a silica gel column with hexane / EtOAc (1 : 1) to give a mixture of **34** and **35** (35 mg, 50% as a glass, in a ratio of 75 : 25 from its ^{1}H-NMR (270 MHz). Entry 2) A mixture of **32** (85 mg, 0.25 mmol), Bu_3P (13 µl, 0.05 mmol), Et_3N (105 µl, 0.75 mmol), formic acid (99%, 32 µl, 0.75 mmol), and $(PhCN)_2PdCl_2$ (5 mg) in CH_3CN (2 ml) was heated under reflux for 1 h under argon.

The same work-up and purification were done as above to give a mixture of **34** and **35** (30 mg, 44% as a glass, in a ratio of 12 : 88). Entry 3) A mixture of **32** (85 mg, 0.25 mmol), Bu_3P (13 μl, 0.05 mmol), Et_3N (70 μl, 0.5 mmol), formic acid (99%, 21 μl, 0.5 mmol), and $Pd(OAc)_2$ (5 mg) in CH_3CN (2 ml) was heated under reflux for 15 min under argon. The same work-up and purification were done as above to give a mixture of **34** and **35** (54 mg, 76% as a glass, in a ratio of 10 : 90). Entry 4) A mixture of **32** (169 mg, 0.5 mmol), Bu_3P (25 μl, 0.1 mmol), Et_3N (140 μl, 1 mmol), formic acid (99%, 38 μl, 1 mmol), and $Pd_2(DBA)_3 \cdot CHCl_3$ (6 mg) in CH_3CN (8 ml) was heated under reflux for 30 min with stirring under argon. The same work-up and purification were done as above to give a mixture of **34** and **35** (109 mg, 77.8% as a glass, in a ratio of 5 : 95). Physical data for **35**: NMR ($CDCl_3$, 270 MHz) 9.50 (1H, br s, NH), 7.33 (1H, d, H-6, $J_{6,Me}$ = 1.2 Hz), 6.25 (1H, t, H-1', $J_{1',2'a} = J_{1',2'b}$ = 6.6 Hz), 5.23 (1H, dd, H-3"a, J = 2.2, J = 4.6 Hz), 5.10 (1H, dd, H-3'b, J = 2.2, J = 4.6 Hz), 4.71 (1H, m, H-4'), 4.34 (2H, d, H-5'a,b), 3.14 (1H, ddd, H-2'a, J = 1.2, $J_{1',2'a}$ = 6.6, $J_{2'a,b}$ = 16.6 Hz), 2.56 (1H, m, H-2'b), 1.95 (3H, d, 5-Me, $J_{Me,6}$ = 1.2 Hz). The assignment was done with the spectra of the mixture.

5'-*O*-Acetyl-2',3'-didehydro-2',3'-dideoxy-3'-methyl-5-methyluridine (34). Et_3N (6.6 μl, 0.047 mmol) was added to a mixture of **28** (7.5 mg, 0.032 mmol), Ac_2O (4.5 μl, 0.047 mmol), and DMAP (3 mg) in CH_3CN (2 ml). The mixture was stirred for 1.5 h at room temperature. The solvent was removed *in vacuo* and the residue was partitioned between EtOAc (10 ml) and H_2O (2 x 5 ml). The organic phase was dried (Na_2SO_4) and concentrated to dryness. The residue was purified by a silica gel column with hexane / EtOAc (1 : 4) to give **34** (8 mg, 91%) as a solid: MS *m/z* 280 (M^+); NMR ($CDCl_3$, 270 MHz) 8.53 (1H, br s, NH), 7.27 (1H, d, H-6, $J_{6,Me}$ = 1.5 Hz), 6.93 (1H, m, H-1', $J_{1',2'}$ = 1.8 Hz), 5.52 (1H, d, H-2', $J_{2',1'}$ = 1.8 Hz), 4.82 (1H, m, H-4'), 4.36 (1H, dd, H-5'a, $J_{5'a,4'}$ = 3.3, $J_{5'a,b}$ = 12.5 Hz), 4.29 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.6, $J_{5'a,b}$ = 12.5 Hz), 2.10 (3H, s, Ac), 1.92 (3H, d, 5-Me or 3'-Me), 1.89 (3H, d, 5-Me or 3'-Me).

2',3'-Dideoxy-3'-methylidene-5-methyluridine (36). A solution of **35** (54 mg, 0.19 mmol) in MeOH (3 ml) containing Et_3N (0.1 ml) was stirred for 24 h at room temperature and the solvent was removed *in vacuo*. The residue was coevaporated several times with EtOH and was purified by a silica gel column with 10% EtOH in $CHCl_3$ to give **36** (45 mg, 98%) as a foam: NMR (D_2O, 270 MHz) 7.64 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz), 6.25 (1H, dd, H-1', J = 7.1, J = 5.3 Hz), 5.30 (1H, d, H-3"a, J = 2.2 Hz), 5.14 (1H, d, H-3"b, J = 2.2 Hz), 4.65 (1H, br s, H-4'), 3.90 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.9, $J_{5'a,5'b}$ = 12.5 Hz), 3.79 (1H, dd, H-5'b, $J_{5'b,4'}$ = 4.0 Hz), 3.21 (1H, m, H-2'a), 2.84 (1H, m, H-2'b), 1.87 (3H, d, 5-Me). *Anal.* Calcd for $C_{11}H_{14}N_2O_4$: C, 55.46; H, 5.92; N, 11.76. Found: C, 55.19; H, 6.12; N, 11.38.

Palladium-catalyzed deoxygenation of 33. Entry 6) A mixture of **33** (171 mg, 0.4 mmol), Bu_3P (20 µl, 0.08 mmol), Et_3N (112 µl, 0.8 mmol), formic acid (99%, 31 µl, 0.8 mmol), and $Pd_2(DBA)\cdot CHCl_3$ (5 mg) in CH_3CN (5 ml) was heated under reflux for 20 min under argon. The solvent was removed *in vacuo* and the residue was suspended in EtOH. Insoluble materials were removed by filtration through a Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by a silica gel column with hexane / EtOAc (1 : 1) to give a mixture of **37** and **38** (113 mg, 76.5% as a glass, in a ratio of 5 : 95 from its ^{1}H-NMR). 5'-*O*-Acetyl-N^4-benzoyl-2',3'-dideoxy-3'-methylidenecytidine (**38**, 89 mg, 60%) was crystallized from hexane / EtOAc from the mixture: mp >300 °C; MS *m/z* 280 (M^+); NMR ($CDCl_3$, 270 MHz) 8.85 (1H, br s, NH), 8.16 (1H, d, H-6, $J_{6,5}$ = 7.3 Hz), 7.90 (2H, d, Bz, J = 7.7 Hz), 7.64-7.49 (4H, m, Bz and H-5), 6.19 (1H, t, H-1', $J_{1',2'a} = J_{1',2'b}$ = 6.2 Hz), 5.20 (1H, d, H-3"a, J = 2.2 Hz), 5.07 (1H, d, H-3'b, J = 2.2 Hz), 4.82 (1H, br s, H-4'), 4.43 (1H, dd, H-5'a, $J_{5'a,4'}$ = 5.1, $J_{5'a,b}$ = 12.1 Hz), 4.36 (1H, dd, H-5'b, $J_{5'b,4'}$ = 3.1 Hz), 3.42 (1H, dd, H-2'a, $J_{2'a,1'}$ = 6.2, $J_{2'a,b}$ = 16.9 Hz), 2.65 (1H, m, H-2'b), 2.11 (3H, s, Ac).

2',3'-Dideoxy-3'-methylidenecytidine Hydrochloride (39). A solution of **38** (181 mg, 0.49 mmol) in MeOH (3 ml) containing NaOMe (1 M, 50 µl) was stirred for 5 h at room temperature and the mixture was acidified by HCl (1 M, 1 ml). The mixture was diluted with H_2O and was washed with $CHCl_3$. The separated H_2O phase was concentrated to dryness and coevaporated several times with EtOH. The resulting powder was collected by filtration to give **39** (79 mg, 60%) as a hydrochloride: mp 164.5-166 °C; NMR (D_2O, 270 MHz) 8.05 (1H, d, H-6, $J_{6,5}$ = 7.8 Hz), 6.24 (1H, dd, H-1', J = 7.3, J = 4.4 Hz), 6.18 (1H, d, H-5), 5.30 (1H, dd, H-3"a, J = 2.2, J = 4.4 Hz), 5.14 (1H, dd, H-3"b, J = 2.2, J = 4.4 Hz), 4.72 (1H, m, H-4'), 3.91 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.9, $J_{5'a,b}$ = 12.5 Hz), 3.79 (1H, dd, H-5'b, $J_{5'b,4'}$ = 4.4 Hz), 3.29 (1H, m, H-2'a), 2.85 (1H, m, H-2'b). *Anal.* Calcd for $C_{10}H_{13}N_3O_3\cdot HCl\cdot 1/2\ H_2O$: C, 44.70; H, 5.63; N, 15.64. Found: C, 44.45; H, 5.24; N, 15.85.

2'-Deoxy-3'-*O*-ethoxycarbonyl-2'-methylidene-5'-*O*-trityl-5-methyluridine (40). Ethyl chloroformate (105 µl, 1.1 mmol) was added to a solution of **13** (497 mg, 1 mmol) and *N,N*-diisopropylethylamine (210 µl, 1.2 mmol) in CH_2Cl_2 (5 ml) at 0 °C. The mixture was stirred for 2 h at 0 °C and then for 2 h at room temperature. Ethyl chloroformate (50 µl, 0.5 mmol) and *N,N*-diisopropylethylamine (105 µl, 0.6 mmol) were added to the mixture, which was further stirred overnight at room temperature. The solvent was removed *in vacuo* and the residue was taken up in EtOAc, which was washed with H_2O. The separated organic phase was dried (Na_2SO_4) and concentrated to dryness. The residue was purified by a silica gel column with hexane / EtOAc (2 : 1) to give **40** (437 mg, 77%) as a foam: NMR ($CDCl_3$, 100 MHz) 8.15 (1H,

br s, NH), 7.46-7.24 (16H, m, Tr and H-6), 6.79 (1H, br d, H-1'), 5.87 (1H, br s, H-2"a), 5.77 (1H, dd, H-3'), 5.37 (1H, br s, H-2"b), 4.21 (3H, m, H-4' and OCH_2CH_3), 3.48 (2H, m, H-5'a,b), 1.33 (6H, m, 5-Me and OCH_2CH_3).

3',5'-Di-*O*-Acetyl-N^4-benzoyl-2'-deoxy-2'-methylidenecytidine (41). A THF solution of TBAF (1 M, 6.25 ml) was added to a solution of **22** (1.43 g, 2.5 mmol) in THF (30 ml). The mixture was stirred for 1 h at room temperature and the solvent was removed *in vacuo*. The residue **23** was dissolved in a mixture of pyridine (20 ml) and Ac_2O (2 ml) and the mixture was stirred overnight at room temperature. MeOH (5 ml) was added to the mixture and the whole was concentrated to dryness. The residue was partitioned between EtOAc and H_2O and the organic phase was dried (Na_2SO_4). The solvent was removed *in vacuo* and the residue was crystallized from hexane / EtOAc to give **41** (923 mg, 86.4% from **22**): mp 133-135 °C; MS *m/z* 427 (M^+); NMR ($CDCl_3$, 100 MHz) 8.75 (1H, br s, NH), 7.96-7.77 (3H, m, Bz and H-6), 7.64-7.42 (4H, m, Bz and H-5), 6.89 (1H, br d, H-1'), 5.70 (1H, dd, H-3'), 5.60 (1H, br t, H-2"a), 5.46 (1H, br t, H-2"b), 4.42-4.25 (3H, m, H-4',5'a,b), 2.15, 2.13 (each 3H, s, Ac). *Anal.* Calcd for $C_{21}H_{21}N_3O_7$: C, 59.01; H, 4.95; N, 9.83. Found: C, 58.95; H, 5.01; N, 9.69.

Palladium-catalyzed deoxygenation of 40. A mixture of **40** (57 mg, 0.1 mmol), Bu_3P (5 µl, 0.02 mmol), Et_3N (28 µl, 0.2 mmol), formic acid (99%, 7.6 µl, 0.2 mmol) and $Pd(OAc)_2$ (1 mg) in THF (4 ml) was heated at 50 °C for 3 h under argon. The solvent was removed *in vacuo* and the residue was suspended in EtOH. Insoluble materials were removed by filtration through a Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by a silica gel column with 1% EtOH in $CHCl_3$ to give a mixture of **30** and **42** (41 mg, 85% as a glass) in a ratio of 28 : 72 from their integration of the H-1' proton signals of ^{1}H-NMR ($CDCl_3$, 270 MHz); 6.83 ppm (multiplet) for **30** and 6.59 ppm (broad singlet) for **42**. Deprotection of the mixture with formic acid gave **43** (see below).

1-(3-Deoxy-β-D-*threo*-pentofuranosyl)thymine (44). Pivaloyl chloride (18.4 ml, 150 mmol) was added dropwise to a solution of 5-methyluridine (15.56 g, 60 mmol) in pyridine (200 ml) at 0 °C under argon. After being stirred for 1 h at 0 °C, MsCl (18.4 ml, 240 mmol) was added to the mixture. The mixture was stirred for 3 h at room temperature and ice-water (about 100 ml) was added. The whole was extracted with EtOAc (400 ml), which was washed with H_2O (2 x 150 ml), aqueous saturated $NaHCO_3$ (3 x 150 ml) and brine (150 ml). The separated organic phase was dried (Na_2SO_4), concentrated *in vacuo*, and coevaporated two times with toluene. The residue was dissolved in MeOH (150 ml) and a MeOH solution of KOH (13.53 g, 240 mmol in 120 ml) and $NaBH_4$ (4.58 g, 120 mmol) was successively added to the above solution at 0 °C. The mixture was stirred overnight at room temperature and was adjusted about pH 3-4 by

addition of a MeOH solution (80 ml) of conc. HCl (23.6 ml, 72 mmol) at 0 °C. Insoluble materials were removed by filtration and the filtrate was concentrated *in vacuo*. The residue was purified by a silica gel column with 4% MeOH in $CHCl_3$ to afford **44** (7.31 g, 50.3%, crystallized from EtOH-Et_2O): mp 164-166 °C; NMR (DMSO-d_6, 270 MHz) 11.21 (1H, br s, NH), 7.64 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz), 5.85 (1H, d, H-1', $J_{1',2'}$ = 5.0 Hz), 5.32 (1H, br s, 2'-OH), 5.08 (1H, br s, 5'-OH), 4.31 (1H, ddd, H-2', $J_{2',1'}$ = 5.0, $J_{2',3'a}$ = 6.3, $J_{2',3'b}$ = 5.5 Hz), 3.97 (1H, dddd, H-4', $J_{4',3'a}$ = 7.2, $J_{4',3'b}$ = 7.4, $J_{4',5'a}$ = 4.7, $J_{4',5'b}$ = 3.9 Hz), 3.62 (1H, dd, H-5'a, $J_{5'a,b}$ = 12.1 Hz), 3.54 (1H, dd, H-5'b), 2.20 (1H, ddd, H-3'a, $J_{3'a,b}$ = 13.3 Hz), 1.76 (3H, d, 5-Me), 1.75 (1H, ddd, H-3'b). *Anal.* Calcd for $C_{10}H_{14}N_5O_2$: C, 49.59; H, 5.83; N, 11.56. Found: C, 49.37; H, 5.85; N, 11.42.

1-(3-Deoxy-5-*O*-TBS-β-D-*threo*-pentofuranosyl)thymine (46). A DMF (20 ml) solution of TBSCl (3.62 g, 24 mmol) was added dropwise over 30 min to a solution of **44** (4.85 g, 20 mmol) and imidazole (2.04 g, 30 mmol) in DMF (100 ml) at 0 °C under argon. After being stirred for 3 h at 0 °C, H_2O (ca 5 ml) was added to the mixture and the solvent was removed *in vacuo*. The residue was partitioned between EtOAc (200 ml) and H_2O (3 x 150 ml) and the separated organic phase was dried (Na_2SO_4). The solvent was removed *in vacuo* and the residue was purified by a silica gel column with 1-2% MeOH in $CHCl_3$ to afford **46** (5.83 g, 81.8%, crystallized from hexane / EtOAc): mp 189.5-190 °C; MS *m/z* 357 (M^++1); NMR ($CDCl_3$, 100 MHz) 9.15 (1H, br s, NH), 7.48 (1H, d, H-6, $J_{6,Me}$ = 1.5 Hz), 5.89 (1H, d, H-1', $J_{1',2'}$ = 1.5 Hz), 4.38-4.35 (3H, m, H-2', 4', 2'-OH), 4.01 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.0, $J_{5'a,b}$ = 11.4 Hz), 3.66 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.2 Hz), 2.57-2.47 (1H, m, H-3'a), 2.09-2.02 (1H, m, H-3'b), 1.89 (3H, d, 5-Me), 0.96 (9H, s, *t*-Bu), 0.18 (3H, s, SiMe), 0.16 (3H, s, SiMe). *Anal.* Calcd for $C_{16}H_{28}N_2O_5Si \cdot 1/2\ H_2O$: C, 52.58; H, 7.72; N, 7.66. Found: C, 52.28; H, 7.92; N, 7.86.

1-(3-Deoxy-5-*O*-TBS-β-D-*threo*-pentofuranosyl)uracil (47). A DMF (15 ml) solution of TBSCl (2.08 g, 13.8 mmol) was added dropwise over 30 min to a solution of **45** (2.62 g, 11.5 mmol) and imidazole (1.17 g, 17.3 mmol) in DMF (80 ml) at 0 °C under argon. After being stirred for 7 h at 0 °C, H_2O (ca 5 ml) was added to the mixture and the solvent was removed *in vacuo*. The residue was purified as above to afford **47** (3.52 g, 89.3%, crystallized from EtOAc): mp 153-154 °C; MS *m/z* 343 (M^++1); NMR ($CDCl_3$, 270 MHz) 8.95 (1H, br s, NH), 7.76 (1H, d, H-6, $J_{6,5}$ = 8.3 Hz), 5.92 (1H, d, H-1', $J_{1',2'}$ = 3.4 Hz), 5.65 (1H, dd, H-5, $J_{5,NH}$ = 2.0 Hz), 4.41-4.34 (2H, m, H-2', 4'), 4.22 (1H, d, 2'-OH), 4.02 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.0, $J_{5'a,b}$ = 11.2 Hz), 3.65 (1H, dd, H-5'b, $J_{5'b,4'}$ = 1.5 Hz), 2.49 (1H, ddd, H-3'a, $J_{3'a,2'}$ = 5.4, $J_{3'a,4'}$ = 2.0, $J_{3'a,b}$ = 14.2 Hz), 2.08 (1H, ddd, H-3'b, $J_{3'b,2'}$ = 2.9, $J_{3b,4'}$ = 3.9 Hz), 0.95 (9H, s,

t-Bu), 0.16 (6H, s, SiMe). *Anal.* Calcd for $C_{15}H_{26}N_2O_5Si$: C, 52.61; H, 7.65; N, 8.18. Found: C, 52.39; H, 7.72; N, 8.18.

1-(3-Deoxy-5-*O*-TBS-β-D-*glycero*-pentofuran-2-ulosyl)thymine (48). A solution of **46** (5.70 g, 16 mmol) in CH_2Cl_2 (40 ml) was added to a preformed chromium complex [CrO_3 (6.40 g), pyridine (10.26 ml), and Ac_2O (6.04 ml) in CH_2Cl_2 (200 ml) containing molecular sieves (4 A, powder, 4 g)] at 0 °C. The reaction mixture was stirred for 30 min at 0 °C and was poured dropwise to EtOAc (1750 ml). The suspension was filtered through a short silica gel column and the filtrate was concentrated to dryness. The residue was crystallized from hexane / EtOAc to give **48** (4.21 g, 74.1%): mp 129-130 °C; MS *m/z* 355 (M^++1); NMR ($CDCl_3$, 270 MHz) 8.41 (1H, br s, NH), 6.94 (1H, d, H-6, $J_{6,Me}$ = 1.2 Hz), 5.40 (1H, s, H-1'), 4.55-4.35 (1H, m, H-4'), 4.09-3.74 (2H, m, H-5'a,b), 2.89 (1H, dd, H-3'a, $J_{3'a,4'}$ = 8.1, $J_{3'a,b}$ = 18.8 Hz), 2.59 (1H, dd, H-3'b, $J_{3'b,4'}$ = 7.3 Hz), 1.90 (3H, d, 5-Me), 0.90 (9H, s, *t*-Bu), 0.02 (6H, s, SiMe). *Anal.* Calcd for $C_{16}H_{26}N_2O_5Si$: C, 54.22; H, 7.39; N, 7.90. Found: C, 54.31; H, 7.46; N, 7.75.

1-(3-Deoxy-5-*O*-TBS-β-D-*glycero*-pentofuran-2-ulosyl)uracil (49). Compound **47** (3.43 g, 10 mmol) was oxidized as described above to give **49** (2.11 g, 61.9%, crystallized from hexane / EtOAc): mp 124-125 °C; MS *m/z* 341 (M^++1); NMR ($CDCl_3$, 270 MHz) 8.61 (1H, br s, NH), 7.25 (1H, d, H-6, $J_{6,5}$ = 8.1 Hz), 5.72 (1H, dd, H-5, $J_{5,NH}$ = 2.2 Hz), 5.50 (1H, s, H-1'), 4.53 (2H, dddd, H-4', $J_{4',3'a} = J_{4',3'b}$ = 7.7, $J_{4',5'a}$ = 3.4, $J_{4',5'b}$ = 4.3 Hz), 3.96 (1H, dd, H-5'a, $J_{5'a,4'}$ = 3.4, $J_{5'a,b}$ = 11.1 Hz), 3.81 (1H, dd, H-5'b, $J_{5'b,4'}$ = 4.3 Hz), 2.89 (1H, dd, H-3'a, $J_{3'a,4'}$ = 7.7, $J_{3'a,b}$ = 18.7 Hz), 2.62 (1H, dd, H-3'b, $J_{3b,4'}$ = 7.7 Hz), 0.90 (9H, s, *t*-Bu), 0.08 (6H, s, SiMe). *Anal.* Calcd for $C_{15}H_{24}N_2O_5Si$: C, 52.92; H, 7.11; N, 8.23. Found: C, 52.75; H, 7.16; N, 8.27.

2',3'-Dideoxy-2'-methylidene-5'-*O*-TBS-5-methyluridine (50). BuLi (1.55 M hexane solution, 1.94 ml, 3 mmol) was added to a suspension of methyltriphenylphosphonium bromide (1.18 g, 3.3 mmol) in THF (20 ml) with stirring for 20 min at 0 °C and then further 40 min more at room temperature under argon. A solution of **48** (355 mg, 1 mmol) in THF (10 ml) was added dropwise to the above ylide at 0 °C and the mixture was stirred for 2 h more at room temperature. Aqueous NH_4Br solution (1 M, 20 ml) was added to the mixture, and the whole was extracted with EtOAc (30 ml), which was washed with H_2O (2 x 10 ml). The separated organic phase was dried (Na_2SO_4) and concentrated to dryness. The residue was purified by Chromatotron (1 mm thick, Harrison Res., Palo Alto, CA) with hexane / EtOAc (3 : 1) to give **50** (186 mg, 52.8%, crystallized from hexane / EtOAc): mp 148-148.5 °C; MS *m/z* 337 (M^+-Me); NMR ($CDCl_3$, 270 MHz) 8.38 (1H, br s, NH), 7.17 (1H, d, H-6, $J_{6,Me}$ = 1.5 Hz), 6.55 (1H,

m, H-1'), 5.29 (1H, m, H-2"a), 5.14 (1H, m, H-2"b), 4.19-4.15 (1H, m, H-4'), 3.93 (1H, dd, H-5'a, $J_{5'a,4'}$ = 3.2, $J_{5'a,b}$ = 11.2 Hz), 3.72 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.9 Hz), 2.85-2.77 (1H, m, H-3'a), 2.66 (1H, dd, H-3'b, $J_{3'b,4'}$ = 6.8, $J_{3'a,b}$ = 16.1 Hz), 1.90 (3H, d, 5-Me), 0.92 (9H, s, *t*-Bu), 0.09 (6H, s, SiMe). *Anal.* Calcd for $C_{17}H_{28}N_2O_4Si$: C, 57.92; H, 8.01; N, 7.95. Found: C, 57.92; H, 7.97; N, 7.94.

2',3'-Dideoxy-2'-methylidene-5'-*O*-TBSuridine (51). Compound **49** (1.02 g, 3 mmol) was converted as above to give **51** (409 mg, 40.2 %, crystallized from hexane / EtOAc), after silica gel column chromatographic purification with hexane / EtOAc (3 : 1): mp 123.5-125 °C; MS *m/z* 323 (M^+-Me); NMR ($CDCl_3$, 270 MHz) 8.50 (1H, br s, NH), 7.72 (1H, d, H-6, $J_{6,5}$ = 8.3 Hz), 6.55 (1H, m, H-1'), 5.67 (1H, dd, H-5, $J_{5,NH}$ = 2.4 Hz), 5.28 (1H, m, H-2"a), 5.24 (1H, m, H-2"b), 4.23 (1H, dddd, H-4', $J_{4',3'a}$ = 8.6, $J_{4',3'b}$ = 6.8, $J_{4',5'a}$ = 2.9, $J_{4',5'b}$ = 2.4 Hz), 3.98 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.9, $J_{5'a,b}$ = 11.7 Hz), 3.70 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.4 Hz), 2.88-2.80 (1H, m, H-3'a), 2.63 (1H, dd, H-3'b, $J_{3'b,4'}$ = 6.8, $J_{3'a,b}$ = 16.1 Hz), 0.92 (9H, s, *t*-Bu), 0.09 (6H, s, SiMe). *Anal.* Calcd for $C_{16}H_{26}N_2O_4Si$: C, 56.78; H, 7.74; N, 8.28. Found: C, 56.74; H, 7.73; N, 8.27.

2',3'-Dideoxy-2'-methylidene-5-methyluridine (43). a) A THF solution of TBAF (1 M, 1.61 ml) was added to a solution of **50** (163 mg, 0.46 mmol) in THF (4 ml) containing AcOH (92 µl). The mixture was stirred for 9 h at room temperature and was concentrated to dryness. The residue was purified by a silica gel column with hexane / EtOAc (1 : 4 to 1 : 5) to give **43** (104 mg, 95%, crystallized from hexane / EtOAc): mp 135-136 °C; MS *m/z* 238 (M^+); NMR ($CDCl_3$, 270 MHz) 8.67 (1H, br s, NH), 7.11 (1H, d, H-6, $J_{6,Me}$ = 1.1 Hz), 6.53 (1H, m, H-1'), 5.35 (1H, m, H-2"a), 5.15 (1H, m, H-2"b), 4.24 (1H, dddd, H-4', $J_{4',3'a}$ = 2.4, $J_{4',3'b}$ = 6.8, $J_{4',5'a}$ = 2.9, $J_{4',5'b}$ = 3.9 Hz), 3.97 (1H, ddd, H-5'a, $J_{5'a,4'}$ = 2.9, $J_{5'a,b}$ = 12.7, $J_{5'a,OH}$ = 5.4 Hz), 3.68 (1H, ddd, H-5'b, $J_{5'b,4'}$ = 3.9, $J_{5'b,OH}$ = 6.8 Hz), 2.89-2.81 (1H, m, H-3'a), 2.70 (1H, dd, H-3'b, $J_{3'b,4'}$ = 6.8, $J_{3'a,b}$ = 16.6 Hz), 2.57 (1H, dt, 5'-OH), 1.89 (3H, d, 5-Me). *Anal.* Calcd for $C_{11}H_{14}N_2O_4$: C, 55.46; H, 5.92; N, 11.76. Found: C, 55.48; H, 5.94; N, 11.67. b) A mixture of **30** and **42** (33 mg), obtained from the deoxygenation of **40** in THF, was treated with formic acid (97%, 1 ml) for 15 min at room temperature. The solvent was removed *in vacuo* and was coevaporated several times with EtOH. The residue was purified by a silica gel column with 4% EtOH in $CHCl_3$ to give **43** (11 mg, 92%, crystallized from hexane / EtOAc); mp 133-135 °C. When this compound was admixed with **43** prepared above, no depression of melting point was observed. The ^{1}H-NMR spectrum taken in $CDCl_3$ was identical with that of **43** prepared above.

2',3'-Dideoxy-2'-methylideneuridine (52). Compound **51** (150 mg, 0.44 mmol) was desilylated as above to give **52** (95 mg, 96%) as a powder: MS *m/z* 224 (M^+);

NMR (DMSO-d_6, 270 MHz) 11.35 (1H, br s, NH), 7.59 (1H, d, H-6, $J_{6,5}$ = 8.3 Hz), 6.37 (1H, br s, H-1'), 5.63 (1H, dd, H-5, $J_{5,NH}$ = 2.4 Hz), 5.26 (1H, dd, H-2"a, $J_{2"a,1'}$ = 2.0, $J_{2"a,b}$ = 4.4 Hz), 5.07 (1H, dd, H-2"b, $J_{2"b,1'}$ = 2.4 Hz), 4.96 (1H, t, 5'-OH, $J_{OH,5'a}$ = $J_{OH,5'b}$ = 5.4 Hz), 4.10 (1H, ddd, H-4', $J_{4',3'a,b}$ = 8.3, $J_{4',5'a}$ = 3.4, $J_{4',5'b}$ = 4.4 Hz), 3.60 (1H, ddd, H-5'a, $J_{5'a,4'}$ = 3.4, $J_{5'a,b}$ = 11.7, $J_{5'a,OH}$ = 5.4 Hz), 3.50 (1H, ddd, H-5'b, $J_{5'b,4'}$ = 4.4 Hz), 2.67 (2H, d, H-3'a,b). *Anal.* Calcd for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.39; N, 12.58. Found: C, 53.73; H, 5.54; N, 12.41.

2',3'-Dideoxy-2'-methylidene-5'-*O*-TBScytidine (53). Triethylamine (200 µl, 1.43 mmol) was added to a mixture of **51** (243 mg, 0.72 mmol), 2,4,6-triisopropylbenzenesulfonyl chloride (434 mg, 1.43 mmol), and DMAP (175 mg, 1.43 mmol) in CH_3CN (12 ml) under argon. The mixture was stirred for 4 h at room temperature and conc. NH_4OH (28%, 7 ml) was added to the mixture, which was further stirred for 2.5 h at room temperature. The solvent was concentrated to dryness and the residue was purified by a silica gel column with 4% EtOH in $CHCl_3$ to give **53** (240 mg, 99.2 %)as a foam: MS *m/z* 322 (M^+-Me); NMR ($CDCl_3$, 270 MHz) 7.80 (1H, d, H-6, $J_{6,5}$ = 7.3 Hz), 6.67 (1H, s, H-1'), 5.77 (1H, d, H-5), 5.31 (1H, m, H-2"a), 5.20 (1H, m, H-2"b), 4.20 (1H, dddd, H-4', $J_{4',3'a}$ = 8.8, $J_{4',3'b}$ = 6.8, $J_{4',5'a}$ = 2.9, $J_{4',5'b}$ = 2.4 Hz), 3.97 (1H, dd, H-5'a, $J_{5'a,4'}$ = 2.9, $J_{5'a,b}$ = 11.2 Hz), 3.71 (1H, dd, H-5'b, $J_{5'b,4'}$ = 2.4 Hz), 2.82-2.75 (1H, m, H-3'a), 2.59 (1H, dd, H-3'b, $J_{3'b,4'}$ = 6.8, $J_{3'a,b}$ = 16.1 Hz), 0.91 (9H, s, *t*-Bu), 0.09 (6H, s, SiMe). High-resolution MS *m/z*: M^+ Calcd for $C_{16}H_{27}N_3O_3Si$: 337.1822. Found: 337.1797.

2',3'-Dideoxy-2'-methylidenecytidine Hydrochloride (54). Compound **53** (257 mg, 0.76 mmol) was desilylated as above. The product was purified by a silica gel column with 10% MeOH in $CHCl_3$, and was dissolved in EtOH (5 ml) and 1 N HCl (0.87 ml). The solution was concentrated to dryness and coevaporated several times with EtOH to give **54** (96 mg, 51.2%) as a hydrochloride: mp 209-211 °C; NMR (DMSO-d_6, 270 MHz) 9.85 (1H, br s, 4-NH), 8.77 (1H, br s, 4-NH), 8.03 (1H, d, H-6, $J_{6,5}$ = 7.8 Hz), 6.38 (1H, s, H-1'), 6.13 (1H, d, H-5), 5.31 (1H, d, H-2"a, $J_{2"a,b}$ = 2.0 Hz), 5.22 (1H, d, H-2"b), 4.17 (1H, ddd, H-4', $J_{4',3'a,b}$ = 7.8, $J_{4',5'a}$ = 3.4, $J_{4',5'b}$ = 3.9 Hz), 3.63 (1H, dd, H-5'a, $J_{5'a,b}$ = 11.7 Hz), 3.51 (1H, dd, H-5'b), 2.69 (2H, d, H-3'a,b). *Anal.* Calcd for $C_{10}H_{13}N_3O_3$·HCl: C, 46.25; H, 5.43; N, 16.18. Found: C, 46.12; H, 5.44; N, 16.03.

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