Allylic Substitution of 3′,4′-Unsaturated Nucleosides: Organosilicon-Based Stereoselective Access to 4′-*C*-Branched 2′,3′-Didehydro-2′,3′-dideoxyribonucleosides

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Reactions of organosilicon reagents (such as allyltrimethylsilane, silyl enol ethers, cyanotrimethylsilane) with 3′,4′-unsaturated nucleosides (of uracil, N^4-acetylcytosine, and hypoxanthine) having an allyl ester structure were investigated in the presence of a Lewis acid in CH_2Cl_2. In the cases of uracil and N^4-acetylcytosine derivatives, $SnCl_4$ appeared to be suitable, whereas the use of $EtAlCl_2$ was necessary for the hypoxanthine derivatives. The main pathway of these reactions was found to be α-face-selective S_N2' allylic substitution, irrespective of the configuration of 2′-*O*-acyl leaving group. As a result, a new stereoselective operation for C−C bonds formation leading to 4′-carbon-substituted 2′,3′-didehydro-2′,3′-dideoxyribonucleosides has been disclosed for the first time. Stereochemistry of these 4′-*C*-branched products can be assigned on the basis of ^{1}H NMR spectroscopy in terms of the anisotropic shift of H-5 of the pyrimidine base (or H-8 of the hypoxanthine), which is caused by the 5′-*O*-(*tert*-butyldiphenylsilyl) protecting group.

Introduction

Although a variety of unsaturated-sugar nucleosides have long been known,[1−5] their use in synthetic chemistry has attracted scant attention, presumably due to their anticipated propensity to undergo further elimination to yield resonance-stabilized furan derivatives.

Consequently, most reactions carried out with regard to these compounds had been limited to simple electrophilic additions by which only non-carbon substituents can be introduced.[6]

We have demonstrated through a series of publications that this class of compounds serve as useful substrates for constructing C−C bonds in the sugar portion.[7]

In this paper, we describe details of our previous study concerning Lewis acid-assisted stereoselective reaction between 3′,4′-unsaturated uracil nucleosides and organosilicon reagents, which proceeds with S_N2' allylic substitution to provide an entry to 4′-*C*-branched 2′,3′-didehydro-2′,3′-dideoxy derivatives.[8] Application of this method to N^4-acetylcytosine and hypoxanthine derivatives is also described. The reaction sequence is generalized in Scheme 1.

Preparation of 3′,4′-Unsaturated Nucleosides of Uracil, N^4-Acetylcytosine, and Hypoxanthine. Among methods available for the preparation of unsaturated-sugar nucleosides, procedures for 3′,4′-unsaturated derivatives are particularly few in number.[4] We have already reported that a phenyl selenide anion generated from $(PhSe)_2$ and $LiAlH_4$ is highly nucleophilic and, thus, serves as a useful species for introducing a phenylseleno group into various positions of the sugar moiety of uracil nucleosides.[9] Since the resulting products readily un-

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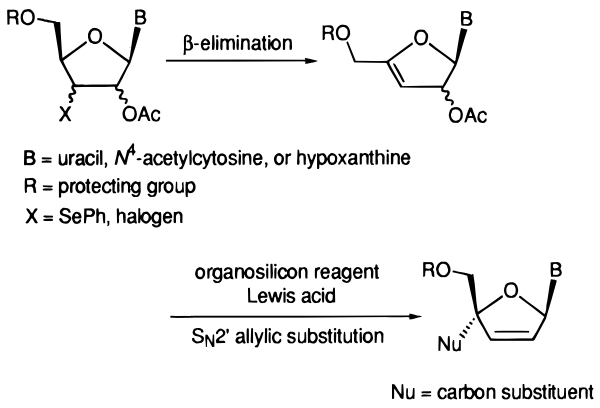
Scheme 1



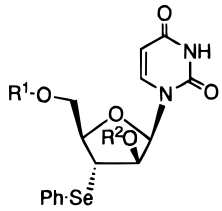
dergo selenoxide *syn*-elimination upon oxidative treatment,[10] the whole sequence constitutes a general entry to various types of unsaturated-sugar uracil nucleosides.[9c]

Compound **1** was prepared from 1-(2,3-anhydro-5-*O*-trityl-β-D-lyxofuranosyl)uracil through oxirane ring cleavage with $(PhSe)_2/LiAlH_4$ and subsequent detritylation. Selective silylation of **1** gave **2**, which was further acetylated to yield **3**. As reported in our previous study,[9c] there is a significant difference in regiochemical outcome of selenoxide elimination between **2a** and **3a**,[11] both carrying two *syn*-β-hydrogens (H-4′ and H-2′): although two possible elimination pathways occur equally in the case of the selenoxide derived from **2a**, the oxidative elimination of **3a** results in the exclusive formation of an allyl acetate **4a** (88%).

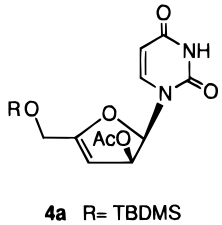
Preparation of the 5′-*O*-(*tert*-butyldiphenylsilyl: TBDPS) derivative (**4b**) was carried out by applying the above procedure for **4a**. Thus, when **3b** was treated with *m*-CPBA in CH_2Cl_2 and the resulting selenoxide was kept neat at 30−40 °C, **4b** was obtained in 90% yield.

Conventional dehydrohalogenation was applicable to N^4-acetylcytosine and hypoxanthine cases, since introduction of the "3′-up" halogeno substituent can be accomplished, starting from cytidine or inosine, according to the published procedure. Compound **5** has been synthesized from N^4-acetylcytidine by reacting with AcBr in CH_3CN without chromatographic purification.[12] When **5** was treated with DBU in CH_3CN, the desired **6a** was isolated in 71% yield. Compound **6b** was prepared from **6a** by a sequential reactions: deacetylation, 5′-*O*-selective silylation, and then reacetylation of the 2′-hydroxyl group. Dehydrohalogenation of the 3′,5′-di-*O*-acetyl derivative **8a**, prepared from **7**,[4b] under similar conditions gave **9a** in 95% yield. Benzoylation of **7** with benzoic anhydride in CH_3CN in the presence of diisopropylethylamine and DMAP directly produced the elimination product **9b** in 40% yield, instead of **8b**. Compound **9c** was prepared from **9a** in a similar manner to the conversion of **6a** to **6b**.

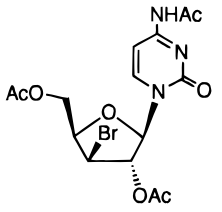
Lewis Acid-Assisted Allylic Substitution of 3′,4′-Unsaturated Uracil Nucleosides by the Use of Organosilicon Reagents. A variety of organometallic reagents are known to react with allylic substrates.[13]



1 $R^1 = R^2 = H$
2a R^1 = TBDMS, $R^2 = H$
2b R^1 = TBDPS, $R^2 = H$
3a R^1 = TBDMS, R^2 = Ac
3b R^1 = TBDPS, R^2 = Ac



4a R= TBDMS
4b R= TBDPS



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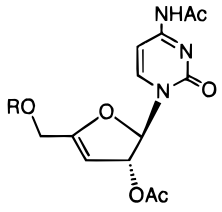
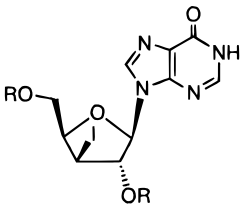
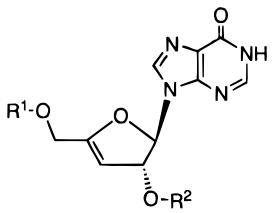


6a R= Ac
6b R= TBDPS



7 R= H
8a R= Ac
8b R= COPh



9a $R^1 = R^2$ = Ac
9b $R^1 = R^2$ = COPh
9c R^1 = TBDPS, R^2 = Ac

As our 3′,4′-unsaturated nucleosides (**4**, **6**, and **9**) have an allyl ester structure, we reasoned that reaction of these compounds with organometallic reagents could provide a route for constructing C−C bonds at the 4′-position of 2′,3′-didehydro-2′,3′-dideoxyribonucleosides of potential anti-HIV activity.[14,15] There are, however, several concerns involved in this approach: (1) anticipated occurrence of further elimination which leads to furan derivatives, (2) regioselectivity of organometallic reagents employed (γ- *vs.* α-attack to this allyl acetate system), and (3) stereoselectivity of C−C bond formation at the 4′-position.

Although Gilman reagents (R_2CuLi) are widely used for γ-selective alkylation of allyl acetates,[16] **4a** underwent simple deacetylation upon reaction with Me_2CuLi (3

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(11) For physical data of **2a**, **3a**, and **4a**, see ref 9c.

(12) Marumoto, R.; Honjo, M. *Chem. Pharm. Bull.* **1974**, *22*, 128−134.

(13) For a review concerning nucleophilic substitution of allylic compounds with organometallic reagents: Magid, R. M. *Tetrahedron* **1980**, *36*, 1901−1930.

(14) Several 2′,3′-didehydro-2′,3′-dideoxynucleosides, such as 3′-deoxy-2′,3′-didehydrothymidine (D4T), show promising anti-HIV activity. For a recent review: De Clercq, E. *Acquired Immune Defic. Syndr.* **1991**, *4*, 207−218.

(15) There have been only two methods available for constructing C−C bonds at the 4′-position of nucleosides: (a) Youssefyeh, R.; Tegg, D.; Verheyden, J. P. H.; Jones, G. H.; Moffatt, J. G. *Tetrahedron Lett.* **1977**, 435−438. (b) Secrist, J. A., III; Winter, W. J., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 2554−2555.

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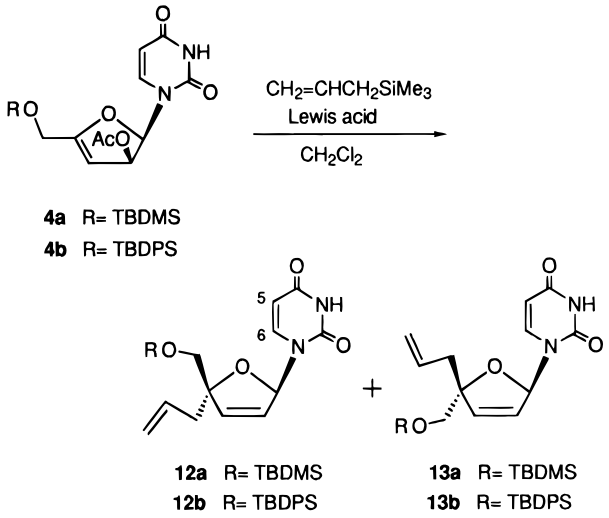
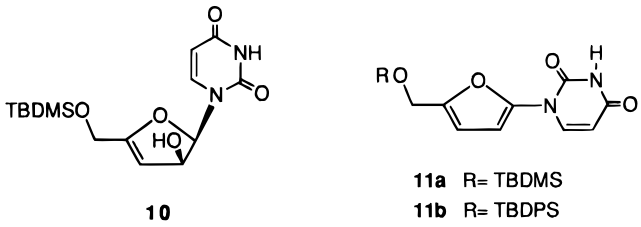
Scheme 2



equiv) in THF (0 °C, for 1 h) to give **10**[17] in 44% yield. Reaction of **4a** with another γ-selective organocopper reagent BuCu·BF_3[18] (3 equiv, in Et_2O, −78 °C to room temperature) also failed: 71% of the starting material was recovered. When Me_3Al (3 equiv) was reacted with **4a** (in CH_2Cl_2, −78 °C to room temperature),[19] only the furan derivative **11a** was isolated in 29% yield.[20]



On the other hand, when BF_3·OEt_2 (5 equiv) was added to a mixture of allyltrimethylsilane (5 equiv) and **4a** in CH_2Cl_2 at −78 °C and the mixture was allowed to warm to −40 °C, the expected γ-attack of the nucleophile took place to yield **12a** (23%) and its 4′-epimer **13a** (4%) (Scheme 2). Although a considerable amount of **11a** (10%) was isolated, no 2′-*C*-substituted product derived from α-attack of the nucleophile was formed. When **4b** was used in this reaction, a similar trend was seen: **12b** (33%), **13b** (14%), and **11b** (30%).[20,21] The use of 10 equiv of allyltrimethylsilane in this reaction of **4b** gave an improved stereoselectivity for the desired **12b** (**12b**: 53% *vs.* **13b:** 11%), but again **11b** was inevitably formed in 34% yield.

(17) In addition to **10**, an unknown product was also formed. For physical data of **10** see ref 9c.

(18) Yamamoto, Y.; Yamamoto, S.; Yatagai, H.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 2318-2325.

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(20) For physical data of **11a** see ref 9c. Physical data of **11b** are as follows: mp 136−137 °C (EtOH); UV (MeOH) λ_{max} 250 nm (ϵ 9700), λ_{min} 242 nm (ϵ 9600); ^{1}H NMR ($CDCl_3$) δ 1.05 (9H, s, SiBu-*t*), 4.63 (2H, s, H-5′), 5.79 (1H, dd, $J_{5,NH}$ = 2.4, $J_{5,6}$ = 8.1 Hz, H-5), 6.22 and 6.39 (2H, each as d, $J_{2',3'}$ = 3.4 Hz, H-2′ and H-3′), 7.22−7.45 (7H, m, H-6 and Ph), 7.60−7.71 (4H, m, Ph), 8.82 (1H, br, NH); MS *m*/*z* 389 (M^+ − Bu-*t*). Anal. Calcd for $C_{25}H_{26}N_2O_4Si$·1/4H_2O: C, 66.57; H, 5.92; N, 6.21. Found: C, 66.76; H, 5.88; N, 6.22.

(21) When the reaction temperature was maintained at −40 °C from the beginning, **11b** was obtained as the main product in 37% yield, together with **12b** (25%) and **13b** (5%). Premixing of allyltrimethylsilane and BF_3·OEt_2 gave a similar result, forming **11b** in 25% yield as well as **12b** (24%) and **13b** (12%).

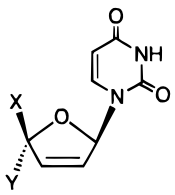
Table 1. Reaction of 4b with Organosilicon Reagents[a]

entry	reagent	reaction time (h)	products (isolated yield, %)
1	CH_2=$CHCH_2SiMe_3$	7	**12b** (74), **13b** (5)
2	CH_2=$C(Me)OSiMe_3$	1	**14** and **15** (*ca.* 6:1, 51)
3	$CH_2C(Ph)OSiMe_3$	0.5	**16** and **17** (*ca.* 6:1, 64), **20** (14)
4	1-[(trimethylsilyl)-oxy]cyclopentene	0.5	**18** (68), **19** (2), **21** (17)
5	$NCSiMe_3$	1	**22** and **23** (*ca.* 2:1, 64)

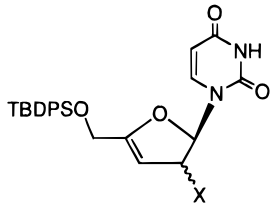
[a] All reactions were carried out at −78 °C in CH_2Cl_2 by the use of $SnCl_4$ (5 equiv) and an appropriate silicon reagent (10 equiv).

Stereochemical assignments of **12** and **13** were made on the basis of the following ^{1}H NMR observations. In the ^{1}H NMR spectrum of **12b** in $CDCl_3$, the resonance due to H-5 appeared at δ 5.13 ppm, which is significantly higher than that of its epimer **13b** (H-5, δ 5.69 ppm). Since there was virtually no difference in H-5 chemical shift between **12a** (δ 5.65 ppm) and **13a** (δ 5.68 ppm), both having a 5′-*O*-TBDMS group, the high-field shift observed in **12b** can be ascribable to the anisotropic effect of the 5′-*O*-TBDPS group. This consideration led us to assume their stereochemistry about C4′ as depicted, and this was further confirmed by X-ray analysis of **12a**.[22]

It was necessary to search for reaction conditions which allow a more efficient conversion of **4b** to **12b** while maintaining the above regioselectivity. We found that the use of $SnCl_4$, in place of BF_3·OEt_2, brings about several dramatic changes, which are in the following order: (1) the reaction goes to completion at −78 °C (for 7 h), (2) formation of the furan derivative (**11b**) can be eliminated completely, and (3) a high degree of stereoselectivity can be accomplished with an increased yield of the desired product (**12b**, 74%, *vs.* **13b**, 5%, entry 1 in Table 1). With this promising result in hand, we examined the applicability of other organosilicon reagents to the $SnCl_4$-assisted reaction of **4b**, the results of which are summarized in Table 1 for the preparation of **14**−**23**. The above result between allyltrimethylsilane and **4b** is also included.



14 X = CH_2OTBDPS, Y = acetonyl
15 X = acetonyl, Y = CH_2OTBDPS
16 X = CH_2OTBDPS, Y = phenacyl
17 X = phenacyl, Y = CH_2OTBDPS
18 X = CH_2OTBDPS, Y = cyclopentanon-2-yl
19 X = cyclopentanon-2-yl, Y = CH_2OTBDPS
22 X = CH_2OTBDPS, Y = CN
23 X = CN, Y = CH_2OTBDPS
24 X = CH_2OAc, Y = CN
25 X = CN, Y = CH_2OAc



20 X = phenacyl
21 X = cyclopentanon-2-yl

It may add merit to the present method that the organosilicon reagents employed can be extended to silyl enol ethers, since this class of reagents can be readily

Table 2. ^{1}H NMR Chemical Shift of H-5 in 4′-*c*-Branched 2′,3′-Didehydro-2′,3′-dideoxyuridines and Their 4′-Epimers (in $CDCl_3$, 400 MHz)

compd	H-5 chemical shift (δ in ppm)	compd	H-5 chemical shift (δ in ppm)	$\Delta\delta$
12a	5.65	**13a**	5.68	0.03
12b	5.13	**13b**	5.69	0.56
14	5.13	**15**	5.74	0.61
16	5.14	**17**	not assignable	
18	4.99 and 5.15	**19**	not assignable	
22	5.21	**23**	5.84	0.63

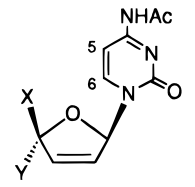
prepared either by enolate trapping or by hydrosilylation.[23] As shown in entries 2−4, the silyl enol ethers react uniformly faster than allyltrimethylsilane, although the stereoselectivity of their reactions remained only moderate, except the case of entry 4.[24] It should be mentioned that, in entries 3 and 4, α-attack of the nucleophile to this allylic system was also an observable event to give **20** (14%) and **21** (17%),[25] respectively, as an additional product. Entry 5 shows that introduction of a cyano group can be done by using cyanotrimethylsilane.

In Table 2 are listed H-5 chemical shifts of **12**−**19**, **22**, and **23**. These data were used as a criterion to distinguish the requisite 4′-*C*-branched product from its 4′-epimer. In the case of the 4′-*C*-cyano derivatives (**22** and **23**), the stereochemistry was unambiguously determined. Thus, the inseparable mixture containing **22** and **23**, obtained in entry 5 in Table 1, was desilylated and then acetylated with Ac_2O in pyridine. This allowed chromatographic separation of **24** and **25**. The X-ray crystallographic analysis of **24**, derived from the main product **22**, gave the confirmation of its stereochemistry.[26]

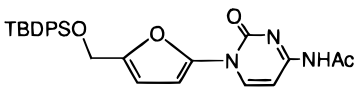
4′-*C*-Allylation and -Cyanation of 3′,4′-Unsaturated Nucleosides of *N*^{4}-Acetylcytosine and Hypoxanthine. Application of the $SnCl_4$-assisted C−C bond formation was first carried out by using *N*^{4}-acetylcytosine derivative **6a** and allyltrimethylsilane. In contrast to the case of **4b**, no reaction took place at −78 °C even after 6 h. However, by performing the reaction at −30 °C for 3 h, the 4′-*C*-allylated products **26** (65%) and **27** (15%) were obtained. These were converted to the respective 5′-*O*-TBDPS derivatives (**28** and **29**) by deacetylation followed by silylation, and their stereochemistry was assigned by comparing the chemical shifts of H-5 (**28**, δ 7.04 ppm, *vs.* **29**, δ 7.45 ppm). The assignments were also supported by the additional ^{1}H NMR evidence that H-5′ of **29** was observed as a singlet due to the absence of the bulky base moiety in the same face of the furanose ring (H-5′ of **28** appeared as two doublets: J_{gem} = 11.0 Hz). The observed stereochemical outcome of **6a** when combined with that of the aforementioned uracil case suggests that the nucleophile prefers attack from the less hindered α-face, irrespective of whether it is *syn* or *anti* to the 2′-*O*-acetyl leaving group. Quite unexpectedly, when this allylation was reexamined by employing **6b**, a complex mixture of products resulted, in which only characteristic fluorescent product attributable to **30** was detected by TLC (R_f 0.30, hexane/EtOAc = 1/2). Under similar reaction conditions, cyanotrimethylsilane also worked in the $SnCl_4$-assisted reaction of **6a** to give a mixture of **31** and **32** (*ca.* 10:1.3) in 90% yield. That the main product has the 4′-configuration depicted as **31** was unambiguously shown by coverting the mixture to the corresponding uracil derivatives **24** and **25**.

In contrast to the above results, allylation of the hypoxanthine derivative **9a** in the presence of $SnCl_4$ turned out to be unsuccessful: the furan **33** was formed as the main product. This was also the case for other Lewis acids, such as BF_3·OEt_2, TMSOTf, and Et_2AlCl. The use of oxophilic $TiCl_4$ gave a complex mixture of unknown products. We finally found that $EtAlCl_2$ effects 4′-*C*-allylation with a moderate yield of products. Thus, when **9a** was reacted with allyltrimethylsilane (5 equiv) in the presence of $EtAlCl_2$ (3 equiv) in CH_2Cl_2 at −78 °C and then the reaction mixture was gradually warmed to −30 °C, **34** and **35** (*ca.* 10:1) were formed as an inseparable mixture in 54% yield. Compound **9b** can also be used as a substrate under these conditions, forming an epimeric mixture of **36** and **37** in 68% combined yield. On the other hand, the elimination pathway leading to **38** (64%) was the sole observable event when the allylation was carried out by using **9c**. The $EtAlCl_2$-assisted reaction appeared not to be applicable to 4′-*C*-cyanation: treatment of **6a** with cyanotrimethylsilane (10 equiv) in the presence of $EtAlCl_2$ (5 equiv) under the identical reaction conditions gave a complex mixture of at least five products.

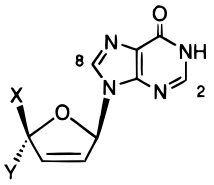
In an attempt to confirm stereochemistry of the 4′-*C*-allylated hypoxanthine nucleosides, protecting group manipulation leading to **39** and **40** was carried out and



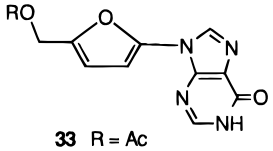
26 X = CH_2OAc, Y = $CH_2CH{=}CH_2$
27 X = $CH_2CH{=}CH_2$, Y = CH_2OAc
28 X = $CH_2OTBDPS$, Y = $CH_2CH{=}CH_2$
29 X = $CH_2CH{=}CH_2$, Y = $CH_2OTBDPS$
31 X = CH_2OAc, Y = CN
32 X = CN, Y = CH_2OAc



30



34 X = CH_2OAc, Y = $CH_2CH{=}CH_2$
35 X = $CH_2CH{=}CH_2$, Y = CH_2OAc
36 X = CH_2OCOPh, Y = $CH_2CH{=}CH_2$
37 X = $CH_2CH{=}CH_2$, Y = CH_2OCOPh
39 X = $CH_2OTBDPS$, Y = $CH_2CH{=}CH_2$
40 X = $CH_2CH{=}CH_2$, Y = $CH_2OTBDPS$



33 R = Ac
38 R = TBDPS

these 5′-*O*-TBDPS derivatives (inseparable mixture) were analyzed by ^{1}H NMR spectroscopy. While there was no

(22) The author has deposited atomic coordinates for **12a** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.

(23) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: London, 1988.

(24) Compounds **18** and **19** consist of two isomers about the α-carbon of the 1-oxocyclopent-2-yl moiety.

(25) The stereochemistry of **20** and **21** about the 2′-position is not known.

(26) Yamaguchi, K.; Haraguchi, K.; Tanaka, H.; Itoh, Y.; Miyasaka, T. *Acta Crystallogr.* **1992**, *C48*, 2277−2278.

significant change in H-2 and H-8 chemical shifts[27] between the minor products **35** (H-2, δ 8.24 ppm; H-8, δ 7.91 ppm) and **40** (H-2, δ 8.20 ppm; H-8, δ 7.93 ppm), an upfield shift was seen, particularly in the H-8 resonance, when such comparison was made between **34** (H-2, δ 8.24 ppm; H-8, δ 8.03 ppm) and **39** (H-2, δ 8.13 ppm; H-8, δ 7.67 ppm). These ^{1}H NMR observations are in accord with their depicted stereochemistry, although the observed difference of H-8 chemical shifts between **39** and **40** is rather small ($\Delta\delta = 0.26$) when compared with those difference of H-5 in uracil series in Table 2 ($\Delta\delta = 0.56-0.63$).

Conclusion

The present work has shown that the 3′,4′-unsaturated nucleosides, which had been considered to be highly susceptible to elimination, can act as an ordinary allyl ester under appropriate reaction conditions. Namely, by selection of a suitable Lewis acid and by reaction with organosilicon reagents, these substrates (**4**, **6**, and **9**) undergo S_N2' allylic substitution to effect C−C bond formation at the 4′-position.[28] Although $SnCl_4$ can be employed for both uracil and N^4-acetylcytosine derivatives (**4** and **6**), the use of $EtAlCl_2$ appeared to be crucial for hypoxanthine derivatives (**9a** and **9b**). Also, the presence of a 5′-*O*-acyl protecting group seems to be indispensable for the 4′-*C*-allylation of N^4-acetylcytosine and hypoxanthine derivatives.

The 4′-*C*-branched 2′,3′-didehydro-2′,3′-dideoxyribonucleosides synthesized in this study constitute a new class of nucleoside analogues with potential anti-HIV activity.[14] Biological evaluations of these compounds are in progress, and the results will be published separately.

Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were measured at 23 °C (internal standard, Me_4Si) either at 400 or 100 MHz. Mass spectra (MS) were taken either in the FAB mode (*m*-nitrobenzyl alcohol as a matrix) or in the EI mode. High-resolution mass spectrometry (HRMS) was performed in the FAB mode (*m*-nitrobenzyl alcohol plus KI as a matrix). Column chromatography was carried out on silica gel (silica gel 60, Merck). Thin layer chromatography (TLC) was performed on silica gel (precoated silica gel plate F_{254}, Merck).

1-(3-Deoxy-3-(phenylseleno)-β-D-arabinofuranosyl)-uracil (1). A solution of 1-[3-deoxy-3-(phenylseleno)-5-*O*-trityl-β-D-arabinofuranosyl]uracil[9c] (1.37 g, 2.19 mmol) in 80% aqueous AcOH (40 mL) was heated at 90 °C for 20 min. The reaction mixture was evaporated and then coevaporated with EtOH to remove trace amounts of AcOH. Silica gel column chromatography (3% EtOH in CH_2Cl_2) of the whole residue gave **1** (788.1 mg, 94%) as an analytically pure foam: UV (MeOH) λ_{max} 264 nm (ϵ 13100), λ_{min} 231 nm (ϵ 5000); ^{1}H NMR (DMSO-d_6, after addition of D_2O) δ 3.51 (1H, dd, $J_{2',3'} = 6.6$, $J_{3',4'} = 8.1$ Hz), 3.63 and 3.69 (2H, each as dd, $J_{4',5'} = 4.0$ and 3.3, $J_{gem} = 12.3$ Hz), 3.82−3.86 (1H, m), 4.27 (1H, t, $J_{1',2'} = 5.5$ Hz), 5.55 (1H, d, $J_{5,6} = 8.1$ Hz), 5.98 (1H, d), 7.33−7.35 and 7.59−7.61 (5H, each as m), 7.81 (1H, d); FAB-MS *m*/*z* 385 ($M^+ + H$). Anal. Calcd for $C_{15}H_{16}N_2O_5Se \cdot 1/4H_2O$: C, 46.46; H, 4.29; N, 7.22. Found: C, 46.70; H, 4.29; N, 6.97.

1-[3-*O*-Acetyl-5-*O*-(*tert*-butyldiphenylsilyl)-3-deoxy-3-(phenylseleno)-β-D-arabinofuranosyl]uracil (3b). A pyridine (10 mL) solution of **1** (683.7 mg, 1.78 mmol) and TBDPSCl (0.93 mL, 3.57 mmol) was stirred overnight. After evaporation of the solvent, the whole residue was chromatographed on a silica gel column (2% EtOH in $CHCl_3$). This gave **2b**, which was dissolved in a mixture of Ac_2O (0.5 mL, 5.34 mmol) and pyridine (10 mL) and stirred overnight. Conventional workup followed by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3b** (929.3 mg, 79%) as an analytically pure foam: UV (MeOH) λ_{max} 264 nm (ϵ 11 900), λ_{min} 235 nm (ϵ 5500); ^{1}H NMR ($CDCl_3$) δ 1.08 (9H, s), 1.92 (3H, s), 3.76 (1H, dd, $J_{2',3'} = 8.1$, $J_{3',4'} = 9.5$ Hz), 3.86−3.89 (1H, m), 3.98 and 4.06 (2H, each as dd, $J_{4',5'} = 2.6$ and 2.2, $J_{gem} = 11.7$ Hz), 5.32 (1H, dd, $J_{5,NH} = 2.6$, $J_{5,6} = 8.1$ Hz), 5.59 (1H, dd), 6.10 (1H, d, $J_{1',2'} = 5.9$ Hz), 7.29−7.67 (10H, m), 7.83 (1H, d), 8.30 (1H, br); MS *m*/*z* 607 (M^+ − Bu-*t*). Anal. Calcd for $C_{33}H_{36}N_2O_6SeSi$: C, 59.73; H, 5.47; N, 4.22. Found: C, 59.71; H, 5.47; N, 4.10.

1-[2-*O*-Acetyl-5-*O*-(*tert*-butyldiphenylsilyl)-β-L-*glycero*-pent-3-enofuranosyl]uracil (4b). A mixture of **3b** (1.45 g, 2.19 mmol) and *m*-CPBA (453.5 mg, 2.6 mmol) in CH_2Cl_2 was stirred for 20 min at room temperature. After being quenched with Et_3N, the reaction mixture was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$. Silica gel short-column chromatography (5% EtOH in $CHCl_3$) of the organic layer gave the corresponding selenoxide. The selenoxide was kept standing neat at 30−40 °C overnight. The resulting mixture containing **4b** and benzeneselenenic acid was dissolved in benzene and then neutralized with Et_3N. Silica gel column chromatography (hexane/EtOAc = 2/1) of the mixture gave **4b** (994 mg, 90%) as an analytically pure foam: UV (MeOH) λ_{max} 258 nm (ϵ 9700), λ_{min} 236 nm (ϵ 4300); ^{1}H NMR ($CDCl_3$) δ 1.08 (9H, s), 1.98 (3H, s), 4.28 (2H, s), 5.27−5.28 (1H, m), 5.68 (1H, dd, $J_{5,NH} = 2.2$, $J_{5,6} = 8.1$ Hz), 5.81−5.84 (1H, m), 6.66 (1H, d, $J_{1',2'} = 6.7$ Hz), 7.10 (1H, d), 7.39−7.48 (6H, m), 7.64−7.69 (4H, m), 8.61 (1H, br); MS *m*/*z* 449 (M^+ − Bu-*t*), 389 (M^+ − Bu-*t*−AcOH). Anal. Calcd for $C_{27}H_{30}N_2O_6Si$: C, 64.02; H, 5.97; N, 5.53. Found: C, 63.74; H, 6.00; N, 5.30.

1-(2,5-Di-*O*-acetyl-β-D-*glycero*-pent-3-enofuranosyl)-N^4-acetylcytosine (6a). A mixture of **5** (864.5 mg, 2.0 mmol) and DBN (0.49 mL, 4.0 mmol) in CH_3CN (20 mL) was stirred overnight and then treated with AcOH. Conventional workup followed by silica gel column chromatography (2% EtOH in CH_2Cl_2) gave **6a** (500.7 mg, 71%) as a powder, which was crystallized from CH_2Cl_2−acetone (mp 122−125 °C): UV (MeOH) λ_{max} 249 nm (ϵ 13 300), λ_{min} 228 nm (ϵ 7000); ^{1}H NMR ($CDCl_3$) δ 2.11, 2.15, and 2.16 (9H, each as s), 2.27 and 2.30 (2H, each as d, $J_{gem} = 12.5$ Hz), 5.40 (1H, dd, $J_{2',3'} = 1.1$, $J_{1',2'} = 2.2$ Hz), 5.68−5.70 (1H, m), 6.55 (1H, d), 7.47 and 7.51 (2H, each as d, $J_{5,6} = 7.3$ Hz), 9.67 (1H, br); FAB-MS *m*/*z* 374 ($M^+ + Na$), 352 ($M^+ + H$). Anal. Calcd for $C_{15}H_{17}N_3O_7$: C, 51.28; H, 4.88; N, 11.96. Found: C, 50.97; H, 4.87; N, 11.95.

1-[2-*O*-Acetyl-5-*O*-(*tert*-butyldiphenylsilyl)-β-D-*glycero*-pent-3-enofuranosyl]-N^4-acetylcytosine (6b). Compound **6a** (91.8 mg, 0.26 mmol) was dissolved in NH_3/MeOH (7 mL) and kept at room temperature for 7 h. After evaporation, pyridine (4 mL) and TBDPSCl (81 μL, 0.31 mmol) were added to the residue and the mixture was stirred overnight. After workup, the reaction mixture was chromatographed on a silica gel column (6% EtOH in CH_2Cl_2), which gave 1-[5-*O*-(*tert*-butyldiphenylsilyl)-β-D-*glycero*-pent-3-enofuranosyl]cytosine (63.3 mg, 52%) as a foam. This product (59.7 mg, 0.13 mmol) was acetylated with Ac_2O (37 μL, 0.39 mmol) in pyridine (2 mL) overnight. Conventional workup followed by silica gel column chromatography (hexane/EtOAc = 1/2) gave **6b** (46.5 mg, 65%) as a syrup: UV (MeOH) λ_{max} 249 (ϵ 14 500) and 298 nm (ϵ 6400), λ_{min} 277 nm (ϵ 4600); ^{1}H NMR ($CDCl_3$) δ 1.09 (9H, s), 2.08 and 2.29 (6H, each as s), 4.30 and 4.35 (2H, each as d, $J_{gem} = 14.3$ Hz), 5.33−5.34 (1H, m), 5.60−5.61 (1H, m), 6.53 (1H, d, $J_{1',2'} = 1.5$ Hz), 7.36−7.52 and 7.66−7.69 (12H, each as m), 9.97 (1H, br); FAB-MS *m*/*z* 570 ($M^+ + Na$), 548 ($M^+ + H$). Anal. Calcd for $C_{29}H_{33}N_3O_6Si \cdot 1/4H_2O$: C, 63.08; H, 6.12; N, 7.61. Found: C, 63.07; H, 6.28; N, 7.21.

(27) The assignments of these two aromatic protons can be made by ^{1}H NMR spectroscopy: a slightly broad signal, which becomes sharp upon D_2O addition, is assignable to H-2.

(28) According to a reviewer's advice, a palladium-catalyzed allylic substitution was briefly examined by using **9b**, dimethyl sodiomalonate (2.5 equiv), and $Pd(PPh_3)_4$ (0.2 equiv) in THF. No reaction took place at room temperature, and heating of the reaction mixture at 60 °C overnight gave the corresponding furan derivative (20%) along with the recovered **9b** (32%).

9-(2,5-Di-*O*-acetyl-3-deoxy-3-iodo-*β*-D-xylofuranosyl)-hypoxanthine (8a). A mixture of 9-(3-deoxy-3-iodo-*β*-D-xylofuranosyl)hypoxanthine[4b] (1.04 g, 2.75 mmol) and Ac_2O (1.04 mL, 11.0 mmol) in pyridine (10 mL) was stirred overnight. Conventional workup followed by silica gel column chromatography (2% EtOH in CH_2Cl_2) gave **7a** (779.1 mg, 61%) as a foam: UV (MeOH) λ_{max} 245 nm (ϵ 11 500), λ_{min} 222 nm (ϵ 3200); ^{1}H NMR ($CDCl_3$) δ 2.13 and 2.18 (6H, each as s), 4.02−4.04 (1H, m), 4.32−4.46 (3H, m), 5.85 (1H, t, $J_{1',2'} = J_{2',3'} = 2.6$ Hz), 6.15 (1H, d, $J_{1',2'} = 2.6$ Hz), 8.22 and 8.33 (2H, each as s); FAB-MS *m*/*z* 463 ($M^+ + H$). Anal. Calcd for $C_{14}H_{15}IN_4O_6 \cdot 1/4EtOH$: C, 37.68; H, 3.51; N, 11.83. Found: C, 37.45; H, 3.38; N, 11.74.

9-(2,5-Di-*O*-acetyl-*β*-D-*glycero*-pent-3-enofuranosyl)-hypoxanthine (9a). This compound was prepared from **8a** in 95% yield by the procedure described for the preparation of **6**. Crystallization from MeOH−CH_2Cl_2 gave an analytical sample (mp 120−122 °C): UV (MeOH) λ_{max} 244 nm (ϵ 11 000), λ_{min} 227 nm (ϵ 6400); ^{1}H NMR ($CDCl_3$) δ 2.12 and 2.14 (6H, each as s), 4.74 and 4.77 (2H, each as d, $J_{gem} = 15.4$ Hz), 5.47−5.48 (1H, m), 5.99−6.00 (1H, m), 6.57 (1H, d, $J_{1',2'} = 1.8$ Hz), 7.87 and 8.23 (2H, each as s); FAB-MS *m*/*z* 335 ($M^+ + H$). Anal. Calcd for $C_{14}H_{14}N_4O_6 \cdot 3/4H_2O$: C, 48.34; H, 4.49; N, 16.11. Found: C, 48.23; H, 4.17; N, 15.81.

9-(2,5-Di-*O*-benzoyl-*β*-D-*glycero*-pent-3-enofuranosyl)-hypoxanthine (9b). A mixture of 9-(3-deoxy-3-iodo-*β*-D-xylofuranosyl)hypoxanthine[4b] (3.20 g, 8.46 mmol), $(PhCO)_2O$ (7.66 g, 33.5 mmol), DMAP (84.6 mg), and diisopropylethylamine (7.37 mL, 42.3 mmol) in CH_3CN (25 mL) was stirred overnight. The reaction mixture was evaporated and partitioned between $CHCl_3$ and H_2O. Silica gel column chromatography (2% EtOH in CH_2Cl_2) of the organic layer gave **8b** (1.56 g, 40%) as a foam: UV (MeOH) λ_{max} 232 nm (ϵ 35 800), λ_{min} 214 nm (ϵ 19 000); ^{1}H NMR ($CDCl_3$) δ 5.02 and 5.06 (2H, each as d, $J_{gem} = 14.3$ Hz), 5.67−5.68 (1H, m), 6.28−6.29 (1H, m), 6.75 (1H, d, $J_{1',2'} = 2.2$ Hz), 7.44−7.49, 7.57−7.63, and 8.04−8.13 (10H, each as m), 7.98 and 8.18 (2H, each as s); FAB-MS *m*/*z* 459 ($M^+ + H$). Anal. Calcd for $C_{24}H_{18}N_4O_6 \cdot 1/2H_2O$: C, 61.67; H, 4.10; N, 11.99. Found: C, 61.38; H, 4.19; N, 11.71.

9-[2-*O*-Benzoyl-5-(*tert*-butyldiphenylsilyl)-*β*-D-*glycero*-pent-3-enofuranosyl]hypoxanthine (9c). This compound was obtained in 26% overall yield from **9a** by the procedure described for the preparation of **6b** from **6a**. Physical data of **9c** obtained as a foam are as follows: UV (MeOH) λ_{max} 245 nm (ϵ 11 000), λ_{min} 233 nm (ϵ 8600); ^{1}H NMR ($CDCl_3$) δ 1.08 (9H, s), 2.14 (3H, s), 4.28 and 4.35 (2H, each as d, $J_{gem} = 13.9$ Hz), 5.44−5.45 (1H, m), 5.91−5.92 (1H, m), 6.53 (1H, d, $J_{1',2'} = 1.8$ Hz), 7.36−7.49 and 7.62−7.68 (10H, each as m), 7.73 and 8.16 (2H, each as s); FAB-MS *m*/*z* 553 ($M^+ + Na$), 531 ($M^+ + H$). Anal. Calcd for $C_{28}H_{30}N_4O_5Si$: C, 63.38; H, 5.70; N, 10.56. Found: C, 63.25; H, 5.82; N, 10.28.

Reaction of 4a with Allyltrimethylsilane in the Presence of $BF_3 \cdot OEt_2$: Formation of 12a, 13a, and 11a. To a mixture of **4a** (86.2 mg, 0.23 mmol) and allyltrimethylsilane (0.36 mL, 2.25 mmol) in CH_2Cl_2 (4 mL) was added $BF_3 \cdot OEt_2$ (0.14 mL, 1.13 mmol) at −78 °C under positive pressure of dry Ar. The reaction mixture was allowed to warm gradually to −40 °C over 1 h with stirring and then further stirred at −40 °C for 2.5 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and then extracted with $CHCl_3$. TLC analysis (hexane/EtOAc = 1/1) of the extract showed the presence of three products (R_f values: **12a** 0.56; **13a** 0.46; **11a** 0.52), from which **12a** (25 mg, 30%) and **13a** (5 mg, 6%) were isolated by preparative TLC (hexane/EtOAc = 1/1).

Physical data of **12a** are as follows: mp 114−115 °C (Et_2O−hexane); UV (MeOH) λ_{max} 260 nm (ϵ 9200), λ_{min} 235 nm (ϵ 2900); ^{1}H NMR ($CDCl_3$) δ 0.07 (6H, s), 0.90 (9H, s), 2.17−2.39 (2H, m), 3.71 and 3.75 (2H, each as d, $J_{gem} = 11.0$ Hz), 5.09−5.14 (2H, m), 5.65 (1H, dd, $J_{5,NH} = 2.2$, $J_{5,6} = 8.1$ Hz), 5.68−5.79 (1H, m), 5.81 (1H, dd, $J = 1.1$ and 5.9 Hz), 6.14 (1H, dd, $J = 1.8$ and 5.9 Hz), 6.92−6.93 (1H, m), 7.92 (1H, d), 8.60 (1H, br); MS *m*/*z* 307 (M^+ − Bu-*t*). Anal. Calcd for $C_{18}H_{28}N_2O_4Si$: C, 59.33; H, 7.75; N, 7.69. Found: C, 59.27; H, 7.93; N, 7.74.

Physical data of **13a** obtained as a syrup are as follows: UV (MeOH) λ_{max} 259 nm, λ_{min} 230 nm; ^{1}H NMR ($CDCl_3$) δ 0.05 and 0.06 (6H, each as s), 0.89 (9H, s), 2.42−2.54 (2H, m), 3.56 and 3.63 (2H, each as d, $J_{gem} = 9.9$ Hz), 5.13 (1H, d, $J = 17.2$ Hz), 5.14 (1H, d, $J = 9.9$ Hz), 5.68 (1H, dd, $J_{5,NH} = 2.6$, $J_{5,6} = 8.1$ Hz), 5.73−5.75 (1H, m), 5.82 (1H, d, $J = 5.9$ Hz), 6.29 (1H, dd, $J = 1.8$ and 5.9 Hz), 6.93 (1H, m), 7.33 (1H, d), 8.27 (1H, br); FAB-MS *m*/*z* (M^+ − Bu-*t*); HRMS (*m*/*z*) calcd for $C_{18}H_{28}N_2O_4Si \cdot K$ 403.1455 [MK^+], found 403.1453 ($\sigma = 0.0009$).

Reaction of 4b with Organosilicon Reagents in the Presence of $SnCl_4$. Synthesis of 12b and 13b as a Typical Example. To a mixture of **4b** (50.7 mg, 0.1 mmol) and allyltrimethylsilane (0.16 mL, 1.0 mmol) in CH_2Cl_2 (2 mL) was added $SnCl_4$ (1 M CH_2Cl_2 solution, 0.5 mL, 0.5 mmol) at −78 °C under positive pressure of dry Ar. The reaction mixture was stirred at −78 °C for 7 h, quenched with saturated aqueous $NaHCO_3$, and then extracted with $CHCl_3$. Preparative TLC (hexane/EtOAc = 2/1) of the extract gave **12b** (36 mg, 74%) and a crude **13b** that contained an unidentified product having an acetyl group (confirmed by ^{1}H NMR spectroscopy). The latter was treated overnight with NH_3/MeOH, from which **13b** (2 mg, 5%) was isolated by preparative TLC (hexane/EtOAc = 2/1).

Physical data of **12b** obtained as a syrup are as follows: UV (MeOH) λ_{max} 260 nm (ϵ 9200), λ_{min} 235 nm (ϵ 2900); ^{1}H NMR ($CDCl_3$) δ 1.07 (9H, s), 2.29−2.36 (2H, m), 3.77 and 3.80 (2H, each as d, $J_{gem} = 11.4$ Hz), 5.05−5.11 (2H, m), 5.13 (1H, dd, $J_{5,NH} = 2.2$, $J_{5,6} = 8.4$ Hz), 5.66−5.70 (1H, m), 5.82 (1H, dd, $J = 5.9$ and 1.1 Hz), 6.21 (1H, dd, $J = 2.5$ and 1.1 Hz), 6.93−6.94 (1H, m), 7.36−7.47 (6H, m), 7.57−7.64 (5H, m), 8.90 (1H, br); MS *m*/*z* 431 (M^+ − Bu-*t*). Anal. Calcd for $C_{28}H_{32}N_2O_4Si \cdot 1/4H_2O$: C, 68.21; H, 6.64; N, 5.68. Found: C, 68.10; H, 6.83; N, 5.51.

Physical data of **13b** obtained as a syrup are as follows: UV (MeOH) λ_{max} 259 nm, λ_{min} 235 nm; ^{1}H NMR ($CDCl_3$) δ 1.06 (9H, s), 2.39−2.55 (2H, m), 3.61 and 3.65 (2H, each as d, $J_{gem} = 10.3$ Hz), 5.11 (1H, d, $J = 15.4$ Hz), 5,12 (1H, d, $J = 11.7$ Hz), 5.69 (1H, dd, $J_{5,NH} = 1.8$, $J_{5,6} = 8.1$ Hz), 5.68−5.78 (1H, m), 5.84 (1H, d, $J = 5.9$ Hz), 6.27 (1H, dd, $J = 1.5$ and 5.9 Hz), 6.96−6.97 (1H, m), 7.33−7.45 (7H, m), 7.64−7.66 (4H, m), 8.20 (1H, br); MS *m*/*z* 431 (M^+ − Bu-*t*); HRMS (*m*/*z*) calcd for $C_{28}H_{32}N_2O_4Si \cdot K$ 527.1768 [MK^+], found 527.1761 ($\sigma = 0.0020$).

4′-*C*-Acetonyl-5′-*O*-(*tert*-butyldiphenylsilyl)-2′,3′-didehydro-2′,3′-dideoxyuridine (14) and Its 4′-Epimer 15. These compounds were obtained as an epimeric mixture (foam): UV (MeOH) λ_{max} 260 nm (ϵ 8800), λ_{min} 235 nm (ϵ 3200); MS *m*/*z* 447 (M^+ − Bu-*t*). Anal. Calcd for $C_{28}H_{32}N_2O_5Si \cdot 1/2H_2O$: C, 65.48; H, 6.48; N, 5.45. Found: C, 65.75; H, 6.73; N, 5.21.

^{1}H NMR data of **14** are as follows: ^{1}H NMR ($CDCl_3$) δ 1.06 (9H, s), 2.17 (3H, s), 2.72 and 3.03 (2H, each as d, $J_{gem} = 16.5$ Hz), 3.85 (2H, s), 5.13 (1H, dd, $J_{5,NH} = 2.2$, $J_{5,6} = 8.1$ Hz), 5.81 (1H, dd, $J = 1.1$ and 6.0 Hz), 6.52 (1H, dd, $J = 2.2$ and 6.0 Hz), 6.98 (1H, m), 7.30−7.65 (11H, m), 9.16 (1H, br).

Selected ^{1}H NMR data of **15** are as follows: ^{1}H NMR ($CDCl_3$) δ 1.06 (9H, s), 2.15 (3H, s), 2.86 and 3.02 (2H, each as d, $J_{gem} = 15.7$ Hz), 4.05 (2H, s), 5.74 (1H, dd, $J_{5,NH} = 2.2$, $J_{5,6} = 8.1$ Hz), 5.79 (1H, dd, $J = 1.1$ and 6.0 Hz), 6.48 (1H, dd, $J = 2.0$ and 6.0 Hz), 6.94 (1H, m).

5′-*O*-(*tert*-Butyldiphenylsilyl)-2′,3′-didehydro-2′,3′-dideoxy-4′-*C*-phenacyluridine (16), Its 4′-Epimer 17, and 20. Compounds **16** and **17** were obtained as an epimeric mixture (foam): UV λ_{max} 249 nm (ϵ 17 400), λ_{min} 232 nm (ϵ 10 800); MS *m*/*z* 509 (M^+ − Bu-*t*). Anal. Calcd for $C_{33}H_{34}N_2O_5Si \cdot 1/4H_2O$: C, 69.39; H, 6.09; N, 4.90. Found: C, 69.35 ; H, 6.13; N, 4.62.

^{1}H NMR data of **16** are as follows: ^{1}H NMR ($CDCl_3$) δ 1.04 (9H, s), 3.28 and 3.59 (2H, each as d, $J_{gem} = 16.5$ Hz), 3.97 (2H, s), 5.14 (1H, dd, $J_{5,NH} = 1.8$, $J_{5,6} = 8.1$ Hz), 5.80 (1H, dd, $J = 1.5$ and 6.0 Hz), 6.66 (1H, dd, $J = 1.8$ and 6.0 Hz), 6.89−6.90 (1H, m), 7.31−7.95 (16H, m), 9.11 (1H, br).

Selected ^{1}H NMR data of **17** are as follows: ^{1}H NMR ($CDCl_3$) δ 0.96 (9H, s), 3.27 and 3.66 (2H, each as d, $J_{gem} = 16.9$ Hz), 5.58 (1H, dd, $J_{5,NH} = 2.2$, $J_{5,6} = 8.1$ Hz), 5.77 (1H, dd, $J = 1.5$ and 6.0 Hz), 6.61 (1H, dd, $J = 1.8$ and 6.0 Hz), 6.90−6.91 (1H, m).

Physical data of **20** obtained as a syrup are as follows: UV (MeOH) $\lambda_{shoulder}$ 275 nm; ^{1}H NMR ($CDCl_3$) δ 1.07 (9H, s), 3.14−

3.21 (1H, m), 3.39−3.44 (2H, m), 4.25 (2H, d, $J_{3',5'}$ = 1.5 Hz), 5.16−5.17 (1H, m), 5.68 (1H, dd, $J_{5,NH}$ = 2.2, $J_{5,6}$ = 8.2 Hz), 6.32 (1H, d, $J_{1',2'}$ = 2.9 Hz), 7.36−7.49, 7.58−7.69, and 7.84−7.94 (15H, each as m), 8.80 (1H, br); MS *m*/*z* 509 (M^+ − Bu-*t*); HRMS (*m*/*z*) calcd for $C_{33}H_{34}N_2O_5Si$·K 605.1874 [MK^+], found 605.1880 (σ = 0.0015).

5′-*O*-(*tert*-Butyldiphenylsilyl)-4′-*C*-(1-oxocyclopent-2-yl)-2′,3′-didehydro-2′,3′-dideoxyuridine (18), Its 4′-Epimer 19, and 21. Physical data of **18** (a mixture of two diastereomers, *ca.* 10:8.1 about C2 of the cyclopentanone ring) obtained as a foam are as follows: UV (MeOH) λ_{max} 260 nm (ϵ 9200), λ_{min} 236 nm (ϵ 3100); ^{1}H NMR ($CDCl_3$) δ 1.07 and 1.09 (9H, each as s), 1.21−2.55 (7H, m), 3.85 and 4.30 (2H, each as d, J_{gem} = 11.4 Hz), 4.99 and 5.15 (1H, each as dd, $J_{5,NH}$ = 1.8, $J_{5,6}$ = 8.1 Hz), 5.83 and 5.90 (1H, each as dd, *J* = 1.3 and 5.8 Hz), 6.21 and 6.41 (1H, each as dd, *J* = 2.2 and 5.8 Hz), 6.88−6.89 and 7.01−7.02 (1H, each as m), 7.35−7.66 (11H, m), 9.20 and 9.23 (1H, each as br); MS *m*/*z* 473 (M^+ − Bu-*t*). Anal. Calcd for $C_{30}H_{34}N_2O_5Si$: C, 67.91; H, 6.46; N, 5.28. Found: C, 67.76; H, 6.57; N, 5.11.

Physical data of **19** (a mixture of two diastereomers, *ca.* 10:1.4, about C2 of the cyclopentanone ring) obtained as a syrup are as follows: UV (MeOH) λ_{max} 255 nm, λ_{min} 235 nm; ^{1}H NMR ($CDCl_3$) of the major diastereomer δ 1.04 (9H, s), 1.93−2.51 (7H, m), 3.72 and 3.75 (2H, each as d, J_{gem} = 10.2 Hz), 5.74 (1H, dd, $J_{5,NH}$ = 2.2, $J_{5,6}$ = 8.1 Hz), 5.85 (1H, dd, *J* = 1.5 and 6.0 Hz), 6.58 (1H, dd, *J* = 1.8 and 6.0 Hz), 6.91−6.92 (1H, m), 7.37−7.45 and 7.59−7.68 (10H, each as m), 7.73 (1H, d); MS *m*/*z* 473 (M^+ − Bu-*t*).

Physical data of **21** (a mixture of two diastereomers, *ca.* 10:8.1) obtained as a syrup are as follows: UV (MeOH) λ_{max} 254 nm, λ_{min} 235 nm; ^{1}H NMR ($CDCl_3$) δ 1.06 and 1.07 (9H, each as s), 1.65−2.36 (7H, m), 3.05−3.06 and 3.37−3.38 (1H, each as m), 4.24−4.25 (2H, m), 4.78 and 5.26 (1H, each as d, $J_{2',3'}$ = 2.6 and 1.5 Hz), 5.65 (1H, dd, $J_{5,NH}$ = 1.8, $J_{5,6}$ = 8.4 Hz), 6.31 and 6.40 (1H, each as d, $J_{1',2'}$ = 3.3 Hz), 7.30 and 7.31 (1H, each as d), 7.35−7.47 and 7.57−7.69 (10H, m), 8.81 (1H, br); MS *m*/*z* 473 (M^+ − Bu-*t*); HRMS (*m*/*z*) calcd for $C_{30}H_{34}N_2O_5Si$·K 569.1874 [MK^+], found 569.1863 (σ = 0.0013).

5′-*O*-(*tert*-Butyldiphenylsilyl)-4′-*C*-cyano-2′,3′-didehydro-2′,3′-dideoxyuridine (22) and Its 4′-Epimer 23. These compounds were obtained as an epimeric mixture (foam): UV (MeOH) λ_{max} 258 nm (ϵ 9100), λ_{min} 235 nm (ϵ 3200); MS *m*/*z* 416 (M^+ − Bu-*t*). Anal. Calcd for $C_{26}H_{27}N_3O_4Si$·1/5EtOAc: C, 65.53; H, 5.89; N, 8.55. Found: C, 65.26; H, 6.02; N, 8.31.

^{1}H NMR data of **22** are as follows: ^{1}H NMR ($CDCl_3$) δ 1.10 (9H, s), 4.01 and 4.05 (2H, each as d, J_{gem} = 11.0 Hz), 5.21 (1H, dd, $J_{5,NH}$ = 1.5, $J_{5,6}$ = 8.1 Hz), 6.14 (1H, dd, *J* = 2.6 and 5.9 Hz), 6.31 (1H, dd, *J* = 1.8 and 5.9 Hz), 7.23−7.24 (1H, m), 7.22 (1H, d), 7.38−7.67 (10H, m), 9.19 (1H, br).

^{1}H NMR data of **23** are as follows: ^{1}H NMR ($CDCl_3$) δ 1.09 (9H, s), 3.77 and 3.93 (2H, each as d, J_{gem} = 10.3 Hz), 5.84 (1H, d, $J_{5,6}$ = 8.1 Hz), 6.14 (1H, dd, *J* = 5.7 Hz), 6.40 (1H, dd, *J* = 1.7 and 5.7 Hz), 7.08−7.09 (1H, m), 7.19 (1H, d), 7.38−7.67 (10H, m), 9.19 (1H, br).

5′-*O*-Acetyl-4′-*C*-cyano-2′,3′-didehydro-2′,3′-dideoxyuridine (24) and Its 4′-Epimer 25. A mixture of **22** and **23** (78 mg, 0.16 mmol) in THF (3 mL) was reacted with $Bu_4NF{\cdot}3H_2O$ (101 mg, 0.32 mmol) for 2 h. The reaction mixture was treated with MeOH and then evaporated. Silica gel column chromatography (2% EtOH in $CHCl_3$) of the residue gave the corresponding free nucleoside (37.2 mg, 99%) as a mixture. The free nucleoside (34.5 mg, 0.15 mmol) was acetylated with Ac_2O (35 μL, 0.38 mmol) in pyridine (2 mL) overnight. Preparative TLC (CH_2Cl_2/EtOH = 50/1) of the reaction mixture gave **24** (21.8 mg, 55%, crystals) and **25** (8.1 mg, 21%, syrup).

Physical data of **24** are as follows: mp 161−164 °C (CH_2Cl_2); UV (MeOH) λ_{max} 257 nm (ϵ 9800), λ_{min} 229 nm (ϵ 2900); ^{1}H NMR ($CDCl_3$ containing CD_3OD) δ 2.15 (3H, s), 4.36 and 4.54 (2H, each as d, J_{gem} = 12.1 Hz), 5.75 (1H, d, $J_{5,6}$ = 8.1 Hz), 6.27 (1H, dd, *J* = 1.1 and 5.9 Hz), 6.40 (1H, dd, *J* = 2.2 and 5.9 Hz), 7.18−7.19 (1H, m), 7.27 (1H, d); MS *m*/*z* 277 (M^+). Anal. Calcd for $C_{12}H_{11}N_3O_5{\cdot}1/6H_2O$: C, 51.43; H, 4.08; N, 14.99. Found: C, 51.68; H, 3.89; N, 14.65.

Physical data of **25** obtained as a syrup are as follows: UV (MeOH) λ_{max} 257 nm (ϵ 9600), λ_{min} 228 nm (ϵ 2800); ^{1}H NMR ($CDCl_3$) δ 2.15 (3H, s), 4.27 and 4.48 (2H, each as d, J_{gem} = 11.7 Hz), 5.86 (1H, d, $J_{5,6}$ = 8.1 Hz), 6.23 (1H, dd, *J* = 1.5 and 5.9 Hz), 6.38 (1H, dd, *J* = 1.8 and 5.9 Hz), 7.15 (1H, d), 7.17−7.18 (1H, m), 9.03 (1H, br); MS *m*/*z* 277 (M^+). Anal. Calcd for $C_{12}H_{11}N_3O_5{\cdot}1/3EtOH$: C, 52.00; H, 4.48; N, 14.36. Found: C, 51.65; H, 4.35; N, 14.42.

4′-*C*-Allyl-N^4,$O^{5'}$-diacetyl-2′,3′-didehydro-2′,3′-dideoxycytidine (26) and Its 4′-Epimer 27. Compounds **26** (65%) and **27** (15%) were obtained from **6a** by the procedure described for the preparation of **12b** and **13b** from **4b** by using allyltrimethylsilane (5 equiv) and $SnCl_4$ (3 equiv). The reaction was carried out initially at −78 °C, and then the reaction mixture was allowed to warm gradually to −30 °C overnight.

Physical data of **26** obtained as a syrup are as follows: UV (MeOH) λ_{max} 247 (ϵ 14 700) and 298 nm (ϵ 6600), λ_{min} 227 (ϵ 6100) and 273 nm (ϵ 4700); ^{1}H NMR ($CDCl_3$) δ 2.02 and 2.28 (6H, each as s), 2.37−2.50 (2H, m), 4.04 and 4.49 (2H, each as d, J_{gem} = 12.1 Hz), 5.12−5.17 (2H, m), 5.68−5.79 (1H, m), 6.07 (2H, s), 6.85 (1H, s), 7.42 and 8.09 (2H, each as d, $J_{5,6}$ = 7.3 Hz), 9.91 (1H, br); FAB-MS *m*/*z* 356 (M^+ + Na), 334 (M^+ + H). Anal. Calcd for $C_{16}H_{19}N_3O_5{\cdot}1/2H_2O$: C, 56.30; H, 5.91; N, 12.31. Found: C, 56.19; H, 5.80; N, 12.19.

Physical data of **27** obtained as a syrup are as follows: UV (MeOH) λ_{max} 248 (ϵ 15 600) and 298 nm (ϵ 7200), λ_{min} 227 (ϵ 5700) and 273 nm (ϵ 4600); ^{1}H NMR ($CDCl_3$) δ 2.08 and 2.28 (6H, each as s), 2.49−2.60 (2H, m), 4.08 and 4.28 (2H, each as d, J_{gem} = 11.7 Hz), 5.17−5.21 (2H, m), 5.68−5.79 (1H, m), 6.09 (1H, dd, *J* = 1.5 and 6.0 Hz), 6.15 (1H, dd, *J* = 1.8 and 6.0 Hz), 6.93−6.94 (1H, m), 7.40 and 7.83 (2H, each as d, $J_{5,6}$ = 7.7 Hz), 9.43 (1H, br); FAB-MS *m*/*z* 356 (M^+ + Na), 334 (M^+ + H). Anal. Calcd for $C_{16}H_{19}N_3O_5{\cdot}2/3MeOH$: C, 56.43; H, 6.15; N, 11.85. Found: C, 56.14; H, 6.02; N, 11.72.

***N*^{4}-Acetyl-4′-*C*-allyl-5′-*O*-(*tert*-butyldiphenylsilyl)-2′,3′-didehydro-2′,3′-dideoxycytidine (28) and Its 4′-Epimer 29.** These compounds were prepared from **26** or **27**. The procedure is given below by the preparation **28** from **26**. A solution of **26** (103.2 mg, 0.3 mmol) in NH_3/MeOH (10 mL) was kept at room temperature overnight. After evaporation, pyridine (6 mL) and TBDPSCl (0.36 mL, 1.25 mmol) were added to the residue. The reaction mixture was stirred overnight. Conventional workup followed by preparative TLC (CH_2Cl_2/EtOH = 20/1) gave 4′-*C*-allyl-5′-*O*-(*tert*-butyldiphenylsilyl)-2′,3′-didehydro-2′,3′-dideoxycytidine (52.2 mg, 36%) as a syrup. This product (31.5 mg, 0.065 mmol) was acetylated with Ac_2O (12.3 μL, 0.13 mmol) in pyridine (2 mL) for 3 h. Preparative TLC (hexane/EtOAc = 1/2) of the reaction mixture gave **28** (25.4 mg, 76%) as a solid.

Physical data of **28** are as follows: UV (MeOH) λ_{max} 247 (ϵ 14 700) and 298 nm (ϵ 6600), λ_{min} 227 (ϵ 6100) and 273 nm (ϵ 4700); ^{1}H NMR ($CDCl_3$) δ 1.07 (9H, s), 2.25 (3H, s), 2.28−2.43 (2H, m), 3.74 and 3.83 (2H, each as d, J_{gem} = 11.0 Hz), 5.05−5.14 (2H, m), 5.63−5.78 (1H, m), 5.98 (1H, dd, *J* = 1.1 and 5.9 Hz), 6.07 (1H, dd, *J* = 1.8 and 5.9 Hz), 6.91−6.92 (1H, m), 7.32−7.49 and 7.60−7.65 (10H, each as m), 7.04 and 8.05 (2H, each as d, $J_{5,6}$ = 7.3 Hz), 9.48 (1H, br); FAB-MS *m*/*z* 552 (M^+ + Na), 530 (M^+ + H). Anal. Calcd for $C_{30}H_{35}N_3O_4Si{\cdot}1/2H_2O$: C, 56.30; H, 5.91; N, 12.31. Found: C, 56.14; H, 5.80; N, 12.19.

Physical data of **29** obtained as a syrup are as follows: UV (MeOH) λ_{max} 248 (ϵ 15 600) and 298 nm (ϵ 7200), λ_{min} 227 (ϵ 5700) and 273 nm (ϵ 4600); ^{1}H NMR ($CDCl_3$) δ 1.06 (9H, s), 2.28 (3H, s), 2.50−2.64 (2H, m), 3.66 (2H, s), 5.12−5.16 (2H, m), 5.66−5.76 (1H, m), 6.05 (1H, d, *J* = 5.9 Hz), 6.21 (1H, dd, *J* = 1.8 and 5.9 Hz), 6.88−6.89 (1H, m), 7.37−7.43 and 7.60−7.66 (10H, each as m), 7.45 and 7.89 (2H, each as d, $J_{5,6}$ = 7.3 Hz), 9.56 (1H, br); FAB-MS *m*/*z* 552 (M^+ + Na), 530 (M^+ + H). Anal. Calcd for $C_{30}H_{35}N_3O_4Si{\cdot}2/3MeOH$: C, 56.43; H, 6.15; N, 11.85. Found: C, 56.14; H, 6.02; N, 11.72.

4′-*C*-Cyano-N^4,$O^{5'}$-diacetyl-2′,3′-didehydro-2′,3′-dideoxycytidine (31) and Its 4′-Epimer 32. These compounds (an epimeric mixture) were obtained from **6a** by the procedure described for the preparation of **12b** and **13b** from **4b** by using cyanotrimethylsilane (10 equiv) and $SnCl_4$ (5 equiv). The reaction was carried out initially at −78 °C (2 h) and then was allowed to warm gradually to −30 °C over 3 h, and finally the reaction mixture was stirred at −30 °C overnight. A mixture of **31** and **32** (*ca.* 10:1.3, combined yield 90%) was obtained

by silica gel column chromatography (2% EtOH in CH_2Cl_2): UV (MeOH) λ_{max} 250 (ϵ 15 900) and 298 nm (ϵ 6400), λ_{min} 227 (ϵ 5300) and 276 nm (ϵ 4600); FAB-MS m/z 319 ($M^+ + H$). Anal. Calcd for $C_{14}H_{14}N_4O_5 \cdot 2/5EtOH$: C, 52.64; H, 4.91; N, 16.64. Found: C, 52.75; H, 4.61; N, 16.46.

^1H NMR data of the major product **31** are as follows: ^1H NMR ($CDCl_3$) δ 2.12 and 2.30 (6H, each as s), 4.35 and 4.65 (2H, each as d, J_{gem} = 12.1 Hz), 6.30 (1H, dd, J = 1.8 and 5.9 Hz), 6.40 (1H, dd, J = 1.1 and 5.9 Hz), 7.22−7.23 (1H, m), 7.49 (1H, d, J = 7.3 Hz), 7.73 (1H, d), 10.11 (1H, br).

2-(Acetoxymethyl)-5-(hypoxanthin-9-yl)furan (33). Physical data of this compound are as follows: mp 250−252 °C (MeOH); UV (MeOH) λ_{max} 240 nm (ϵ 23 700), λ_{min} 204 nm (ϵ 8600); ^1H NMR ($CDCl_3$) δ 2.06 (3H, s), 5.09 (2H, s), 6.73 and 6.76 (2H, each as d, $J_{3,4}$ = 3.3 Hz), 8.12 (1H, br), 8.39 (1H, s), 12.59 (1H, br). FAB-MS m/z 275 ($M^+ + H$). Anal. Calcd for $C_{12}H_{10}N_4O_4 \cdot 1/4H_2O$: C, 51.71; H, 3.80; N, 20.10. Found: C, 52.07; H, 3.65; N, 19.97.

5′-*O*-Acetyl-4′-*C*-allyl-2′,3′-didehydro-2′,3′-dideoxyinosine (34) and Its 4′-Epimer 35. These compounds (an epimeric mixture) were obtained from **9a** by the procedure described for the preparation of **12b** and **13b** from **4b** by using allyltrimethylsilane (5 equiv) and $EtAlCl_2$ (3 equiv). The reaction was carried out initially at −78 °C, and then the reaction mixture was allowed to warm gradually to −30 °C overnight. Compounds **34** and **35** (combined yield: 44%) were obtained by preparative TLC (CH_2Cl_2/EtOH = 20/1): UV (MeOH) λ_{max} 248 nm (ϵ 11 800), λ_{min} 222 nm (ϵ 3700); FAB-MS m/z 339 ($M^+ + Na$), 317 ($M^+ + H$). Anal. Calcd for $C_{15}H_{16}N_4O_4 \cdot 1/2EtOH$: C, 56.63; H, 5.64; N, 16.57. Found: C, 56.29; H, 5.38; N, 16.80.

^1H NMR data of the major product (**34**) are as follows: ^1H NMR ($CDCl_3$) δ 2.06 (3H, s), 2.40−2.53 (2H, m), 4.07 and 4.13 (2H, each as d, J_{gem} = 12.1 Hz), 5.16−5.20 (2H, m), 5.73−5.81 (1H, m), 6.12 (1H, d, J = 5.9 Hz), 6.29 (1H, dd, J = 1.8 and 5.9 Hz), 6.99−7.00 (1H, m), 8.03 and 8.24 (2H, each as s).

Selected ^1H NMR data of the minor product (**35**) are as follows: ^1H NMR ($CDCl_3$) δ 2.10 (3H, s), 5.07−5.15 (1H, m), 5.58−5.68 (1H, m), 7.03−7.04 (1H, m), 7.91 and 8.24 (2H, each as s).

4′-*C*-Allyl-5′-*O*-benzoyl-2′,3′-didehydro-2′,3′-dideoxyinosine (36) and Its 4′-Epimer 37. These compounds (an epimeric mixture) were obtained from **9b** by the procedure described for the preparation of **12b** and **13b** from **4b** by using allyltrimethylsilane (5 equiv) and $EtAlCl_2$ (3 equiv). The reaction was carried out initially at −78 °C, and then the reaction mixture was allowed to warm gradually to −30 °C overnight. A mixture of **36** and **37** (*ca.* 10:3.1, combined yield 68%) was obtained by preparative TLC (CH_2Cl_2/EtOH = 30/1): UV (MeOH) λ_{max} 234 nm (ϵ 18 100), λ_{min} 216 nm (ϵ 9800); FAB-MS m/z 401 ($M^+ + Na$), 379 ($M^+ + H$). Anal. Calcd for $C_{20}H_{18}N_4O_4 \cdot 1/4EtOH$: C, 63.14; H, 5.04; N, 14.37. Found: C, 62.96; H, 4.94; N, 14.06.

^1H NMR data of the major product (**36**) are as follows: ^1H NMR ($CDCl_3$) δ 2.53−2.64 (2H, m), 4.31 and 4.69 (2H, each as d, J_{gem} = 12.1 Hz), 5.20−5.24 (2H, m), 5.80−5.90 (1H, m), 6.13 (1H, dd, J = 1.1 and 6.1 Hz), 6.38 (1H, dd, J = 1.8 and 6.1 Hz), 6.98−6.99 (1H, m), 7.44−7.57 and 7.92−7.96 (10H, each as m), 7.88 and 8.20 (2H, each as s).

Selected ^1H NMR data of the minor product (**37**) are as follows: ^1H NMR ($CDCl_3$) δ 4.35 and 4.59 (2H, each as d, J_{gem} = 11.7 Hz), 5.20−5.24 (2H, m), 5.65−5.75 (1H, m), 7.10−7.11 (1H, m), 7.58−7.61 and 8.04−8.14 (10H, each as m), 7.92 and 8.25 (2H, each as s).

2-(*tert*-Butyldiphenylsilyl)-5-(hypoxanthin-9-yl)furan (38). Physical data of this compound are as follows: mp 265−268 °C (EtOH); UV (MeOH) λ_{max} 220 (ϵ 18 000) and 240 nm (ϵ 15 300), λ_{min} 231 nm (ϵ 14 200); ^1H NMR ($CDCl_3$) δ 1.07 (9H, s), 4.70 (2H, s), 6.32 and 6.61 (2H, each as d, $J_{3,4}$ = 3.3 Hz), 7.37−7.45 and 7.58−7.70 (10H, each as m), 7.96 and 8.24 (2H, each as s); FAB-MS m/z 471 ($M^+ + H$). Anal. Calcd for $C_{26}H_{25}N_4O_3Si \cdot 1/2H_2O$: C, 65.25; H, 5.48; N, 11.71. Found: C, 65.23; H, 5.58; N, 11.77.

4′-*C*-Allyl-5′-*O*-(*tert*-butyldiphenylsilyl)-2′,3′-didehydro-2′,3′-dideoxyinosine (39) and Its 4′-Epimer 40. These compounds (an epimeric mixture, syrup) were obtained in 41% overall yield from an inseparable mixture of **36** and **37** by debenzoylation (NaOMe/MeOH) followed by silylation (TBDPSCl/imidazole/DMF): UV (MeOH) λ_{max} 247 nm (ϵ 11 500), λ_{min} 232 nm (ϵ 7500); FAB-MS m/z 535 ($M^+ + Na$), 513 ($M^+ + H$). Anal. Calcd for $C_{29}H_{32}N_4O_3Si \cdot 2/3EtOH$: C, 67.04; H, 6.68; N, 10.31. Found: C, 67.31; H, 6.57; N, 9.93.

^1H NMR data of the major product (**39**) are as follows: ^1H NMR ($CDCl_3$) δ 1.06 (9H, s), 2.51−2.62 (2H, m), 3.65 and 3.72 (2H, each as d, J_{gem} = 10.3 Hz), 5.12−5.17 (2H, m), 5.72−5.81 (1H, m), 5.98 (1H, d, J = 5.9 Hz), 6.37 (1H, dd, J = 1.8 and 5.9 Hz), 6.94−6.95 (1H, m), 7.31−7.47 and 7.54−7.66 (10H, each as m), 7.67 and 8.13 (2H, each as s).

Selected ^1H NMR data of the minor product (**40**) are as follows: ^1H NMR ($CDCl_3$) δ 1.08 (9H, s), 5.05−5.09 (2H, m), 5.58−5.67 (1H, m), 7.04−7.05 (1H, m), 7.93 and 8.20 (2H, each as s).

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Supporting Information Available: ^1H NMR spectra of compounds **13a**,**b**, **20**, and **21** (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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