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Articles

Simple Entry to 3′-Substituted Analogues of Anti-HIV Agent Stavudine Based on an Anionic O → C Stannyl Migration

Hiroki Kumamoto and Hiromichi Tanaka*

School of Pharmaceutical Sciences, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142-8555, Japan

hirotnk@pharm.showa-u.ac.jp

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Reaction of 5′-*O*-protected derivatives of the anti-HIV agent stavudine (d4T) with LTMP was investigated with the aim to lithiate the vinylic hydrogens (H-3′ and H-2′). When the lithiation of the 5′-*O*-*tert*-butyldiphenylsilyl derivative **5** was carried out in the presence of HMPA, an anionic silyl migration took place to give the 3′-*C*-silylated product **4a**. The stannyl version of this reaction was found to be also possible, which has disclosed a highly simple entry to the d4T analogues variously substituted at the 3′-position by manipulating the 3′-*C*-stannyl d4T as a common intermediate.

Introduction

During our studies on lithiation (hydrogen−lithium exchange) of the base moiety of nucleosides,[1] we have recently observed that the 2′-position of 1′,2′-unsaturated uridine, 1-(2-deoxy-D-*erythro*-pent-1-enofuranosyl)uracil, undergoes lithiation in the case where the 6-position of the base is substituted with a silyl or stannyl group. As a result, an anionic migration of the silyl or stannyl group takes place from the 6-position to the 2′-position of the glycal portion (Scheme 1).[2] Although olefinic hydrogen atoms are generally not sufficiently acidic to undergo lithiation,[3] unless additional activation is provided by electron-withdrawing α-substituents[4] or by strain,[5] the successful result obtained in the above 1′,2′-unsaturated uridine prompted us to carry out the present study to see whether lithiation of simple vinylic hydrogens of the unsaturated-sugar nucleosides is feasible.

Stavudine (2′,3′-didehydro-3′-deoxythymidine: d4T, **1**) was selected as a substrate for the present lithiation. This was motivated by the fact that d4T has been noted to be a potent anti-HIV (human immunodeficiency virus) agent with reduced cytotoxicity in certain cells[6] and also that only a limited number of its analogues substituted either at the 3′- or 2′-position have been synthesized for evaluation of their anti-HIVactivity.[7−10]

(1) For a recent publication, see: Kato, K.; Hayakawa, H.; Tanaka, H.; Kumamoto, H.; Shindoh, S.; Shuto, S.; Miyasaka, T. *J. Org. Chem*. **1997**, *62*, 6833−6841.

(2) Kumamoto, H.; Shindoh, S.; Tanaka, H.; Itoh, Y.; Haraguchi, K.; Gen, E.; Kittaka, A.; Miyasaka, T.; Kondo, M.; Nakamura, K. T. *Tetrahedron* **2000**, *56*, 5363−5371.

(3) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: Oxford, 1974.

(4) (a) Eisch, J. J.; Galle, J. E. *J. Org. Chem*. **1979**, *44*, 3279−3280. (b) Schmidt, R. R.; Speer, H. *Synthesis* **1979**, 797−798.

(5) Applequist, D. E.; Saurborn, E. G. *J. Org. Chem*. **1972**, *37*, 1676−1677.

(6) Mansuri, M. M.; Hitchcock, M. J. M.; Buroker, R. A.; Bregman, C. L.; Ghazzouli, I.; Desiderio, J. V.; Starrett, J. E.; Sterzyski, R. Z.; Martin, J. C. *Antimicrob. Agents Chemother*. **1990**, *34*, 637−641.

(7) For the 3′-cyano derivative, see: Camarasa, M.-J.; Diaz-Ortiz, A.; Calvo-Mateo, A.; De las Heras, F. G.; Balzarini, J.; De Clercq, E. *J. Med. Chem*. **1989**, *32*, 1732−1738.

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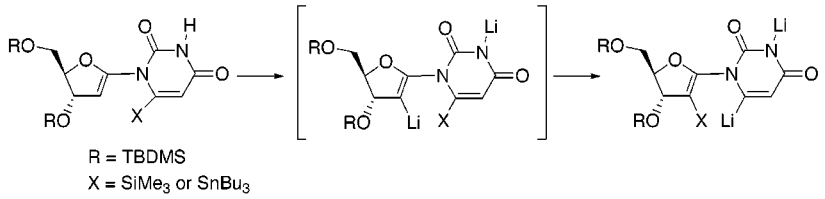
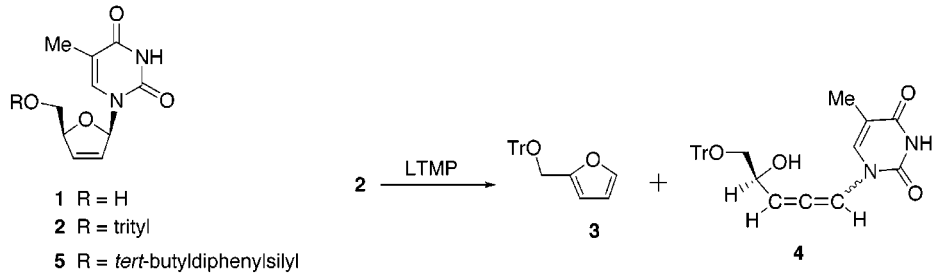
Scheme 1



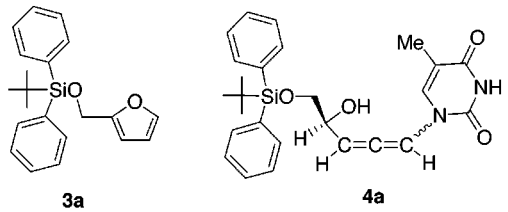
Scheme 2

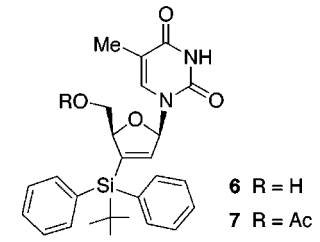


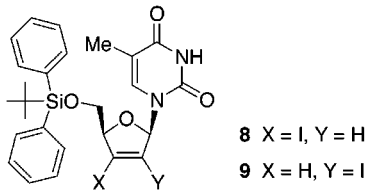
Lithiation of 5′-*O*-Protected d4T

One major concern involved in the lithiation of d4T was deprotonation of either H-1′ or H-4′ which occupies the allylic position.[11] In fact, when the 5′-*O*-tritylated substrate **2**[12] was reacted with LTMP (5 equiv) in THF (below −70 °C, for 15 min) and then worked up by adding aqueous NH_4Cl, the furan **3** was formed as the major product in 42% yield together with a 32% recovery of **2** (Scheme 2). An additional product was formed in this reaction (10% yield). The FAB-MS spectrum showed that this product [*m*/*z* 467 $M^+ + H$] has an isomeric structure to **2**. Characteristic IR absorption at 1974 cm^{-1} (KBr) in conjunction with the reported ^{13}C NMR data of N^1-(4-hydroxy-1,2-butadien-1-yl)thymine[13] confirmed the 1′,2′-allenic structure **4** (obtained as a single isomer, the absolute configuration about C1′ is not known).

Although the elimination pathway leading to the furan was suppressed by using the 5′-*O*-*tert*-butyldiphenylsilyl derivative **5**, the results obtained were essentially the same as the case of **2**, forming **3a** (20%), **4a** (9%, as a single isomer), and the recovered **5** (60%). However, the presence of HMPA (10 equiv) in this LTMP (5 equiv) lithiation led to the formation of a new product **6** (36%). The structure of **6** is supported by the fact that, upon treatment with Ac_2O, the 5′-*O*-acetate **7** (91%) was obtained, and that the ^{13}C NMR spectrum of **6** showed the presence of a new quaternary ^{13}C-resonance (δ 143.9), in addition to those of the base moiety (δ 110.7, 150.7, and 163.7) and of the *tert*-butyldiphenylsilyl group (δ 18.7, 132.1, and 132.4). Its regiochemistry was confirmed by HMBC (heteronuclear multiple bond connectivity) experiment: this newly appeared ^{13}C-resonace showed correlations with both H-1′ and H-5′. Other products formed in this reaction were **3a** (4%), **4a** (9%), and the recovered **5** (18%).







We assumed that **6** had been formed through C3′-lithiation and subsequent migration of the 5′-*O*-silyl group, in which HMPA plays an essential role.[14] This was confirmed by the fact that the 3′-iodo derivative **8**, the preparation of which is described in the latter part of this paper, gave **6** (20%) upon reaction with BuLi (2 equiv) in the presence of HMPA (10 equiv). In a similar manner, the formation of **4a** (7%) was observed when the 2′-iodo derivative **9** was subjected to halogen−lithium exchange reaction.

(8) For the 3′-fluoro derivative, see: Van Aerschot, A.; Herdewijn, P.; Balzarini, J.; Pauwels, R.; De Clercq, E. *J. Med. Chem.* **1989**, *32*, 1743−1749.

(9) For the 2′-fluoro derivative, see: (a) Sterzycki, R. Z.; Ghazzouli, I.; Brankovan, V.; Martin, J. C.; Mansuri, M. M. *J. Med. Chem.* **1990**, *33*, 2150−2157. (b) Huang, J. T.; Chen, L.-C.; Wang, L.; Kim, M.-H.; Warshaw, J. A.; Armstrong, D.; Zhu, Q.-Y.; Chou, T.-C.; Watanabe, K. A.; Matulic-Adamic, J.; Su, T.-L.; Fox, J. J.; Polsky, B.; Baron, P. A.; Gold, J. W. M.; Hardy, W. D.; Zuckerman, E. *J. Med. Chem.* **1991**, *34*, 1640−1646.

(10) For the 2′- and 3′-methyl derivatives, see: Matsuda, A.; Okajima, H.; Masuda, A.; Kakefuda, A.; Yoshimura, Y.; Ueda, T. *Nucleosides Nucleotides* **1992**, *11*, 197−226.

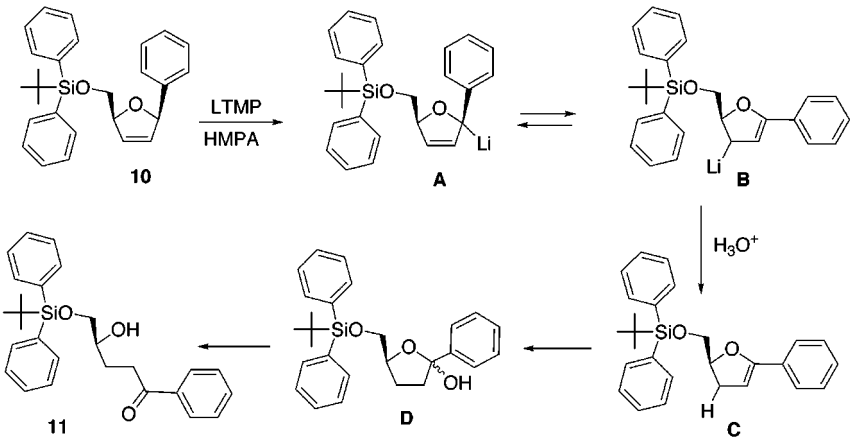
(11) For the lithiation of allylic ethers, see: (a) Evans, D. A.; Andrews, G. C.; Buckwalter, B. *J. Am. Chem. Soc.* **1974**, *96*, 5560−5561. (b) Still, W. C.; Macdonald, T. L. *J. Am. Chem. Soc.* **1974**, *96*, 5561−5563.

(12) Horwitz, J. P.; Chua, J.; Da Rooge, M. A.; Noel, M.; Klundt, I. L. *J. Org. Chem.* **1966**, *31*, 205−211.

(13) Phadtare, S.; Zemlicka, J. *J. Org. Chem.* **1989**, *54*, 3675−3679.

(14) A similar role of HMPA has been noted in our previous lithiation studies; see refs 1 and 2.

Scheme 3



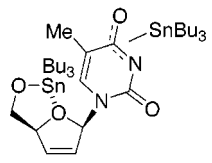
One would wonder how the olefinic hydrogen atoms (H-3′ and H-2′) of d4T undergo deprotonation in the presence of allylic hydrogens (H-4′ and H-1′). This question still remains to be addressed, but it is apparent that the base moiety, which can act as a Lewis base, plays an important role for the vinylic deprotonation. When the phenyl analogue **10**,[15] which cannot coordinate with a lithiating agent, was used as a substrate for the LTMP lithiation in the presence of HMPA, TLC analysis (hexane/EtOAc = 10:1) of the reaction mixture showed the formation of a product that runs faster (R_f 0.78) than **10** (R_f 0.56). Upon column chromatographic purification on silica gel, this product was converted to a polar substance (R_f 0.70 in hexane/EtOAc = 2:1), the structure of which appeared to be the phenyl ketone **11** (88% yield).

As shown in Scheme 3, the formation of **11** is considered to have initiated with deprotonation of H-1′ to form an allyllithium **A**, which would be largely ionic[16] and thus can exist as **B**. The above-mentioned faster running product is, therefore, assumed to be **C**. Hydration during column chromatography yields **D**, which in turn gives **11** as the final product. This mechanism is corroborated by the fact that, when the above lithiation mixture was quenched with MeOD, the isolated **11** was devoid of a signal corresponding to the H-3′ (δ 3.06−3.19). From this result, it would be possible to say at least that the vinylic deprotonation is not a feasible event by simple intermolecular reaction between LTMP and the substrate.

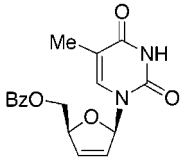
Lithiation-Based Stannylation of d4T

Encouraged by the above anionic silyl migration from the 5′-oxygen to the 3′-position, we next examined the possibility of carrying out a stannyl version of this migration. Vinylstannanes are useful intermediates for further transformations, for example, through the Stille reaction.[17] Stannylation of the 5′-hydroxyl group of **1** was carried out by transalkoxylation[18] using Bu_3SnOMe. Since the tin atom of trialkyltin alkoxides is known to coordinate with a neighboring oxygen,[19] the 5′-*O*-$SnBu_3$ bond resulting from **1** would be stabilized by the furanose ring oxygen.

While the reaction mixture remained heterogeneous upon reaction of **1** with 1 equiv of Bu_3SnOMe (neat, at 90 °C) even after prolonged reaction time, use of 2 equiv of the reagent gave a clear oily substance within 5 min. Its ^{119}Sn NMR spectrum in benzene-d_6 showed the presence of three resonances (δ 58.3, 86.3, and 107.5), one of which (δ 86.3) corresponds to that of $(Bu_3Sn)_2O$ formed from Bu_3SnOMe upon heating. The remaining two ^{119}Sn resonances, δ 58.3[20] and 107.5, were assigned to those bonded to the base moiety and 5′-oxygens, respectively, as depicted in **12**. Treatment of **12** with benzoyl chloride in benzene gave the 5′-*O*-benzoate **13**[21] in 91% yield. The ^{1}H NMR spectrum of **12** also suggested the presence of the 5′-*O*-Sn bond (H-5′, δ 3.68 and 3.93, each as ddd, $J_{Sn,H\text{-}5'}$ = 28.0 Hz) and that it consists of a single substance.



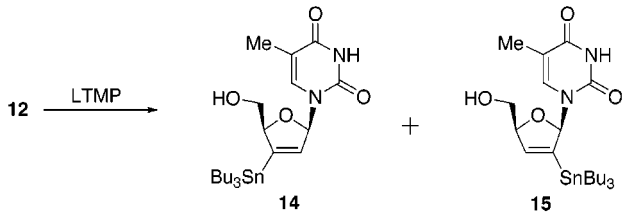
12



13

Anionic migration of the 5′-*O*-stannyl group in **12** was next examined (Scheme 4); the results are summarized

Scheme 4



in Table 1. Treatment of **12** with LTMP did produce the expected 3′-*C*-tributylstannyl derivative **14**, and an in-

(15) As described in the Experimental Section, **10** was prepared in 34% overall yield from the reported (β-D-ribofuranosyl)benzene: Matulic-Adamic, J.; Beigelman, L.; Portmann, S.; Egli, M.; Usman, N. *J. Org. Chem.* **1996**, *61*, 3909−3911.

(16) Allylic organolithium compounds are known to have ionic character: West, P.; Purmort, J. I.; McKinley, S. V. *J. Am. Chem. Soc.* **1968**, *90*, 797−798.

(17) For a review concerning the Stille reaction, see: Mitchell, T. N. *Synthesis* **1992**, 803−815.

(18) (a) Mack, M. G.; Parker, E. *Chem. Abstr.* **1956**, *50*, 10761. (b) Saigo, K.; Morikawa, A.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1656−1658.

(19) Such coordination has been applied for regioselective stannylation of carbohydrates: Ogawa, T.; Matsui, M. *Tetrahedron* **1981**, *37*, 2363−2369.

(20) The 5′-*O*-silyl derivative **5**, when treated with Bu_3SnOMe in a similar manner, gave a ^{119}Sn resonance at δ 60.1 ppm in benzene-d_6.

(21) Palomino, E.; Meltsner, B. R.; Horwitz, J. P. *J. Med. Chem.* **1990**, *33*, 258−263.

Table 1. Vinylic Stannylation of d4T (1) by Using 12 as a Substrate[a]

entry	HMPA (equiv)	TMEDA (equiv)	yield of **14**	yield of **15**	recovery of **1**[b]
1			6	10	16
2	10		43	10	not determined
3	15		50	8	20
4	15	5	60	9	8

[a] All reactions were carried out by using LTMP (5 equiv) in THF at below −70 °C for 15 min. Products other than **14**, **15**, and the recovered **1** were not isolated. [b] Compound **1** was recovered as its 5′-*O*-acetate.

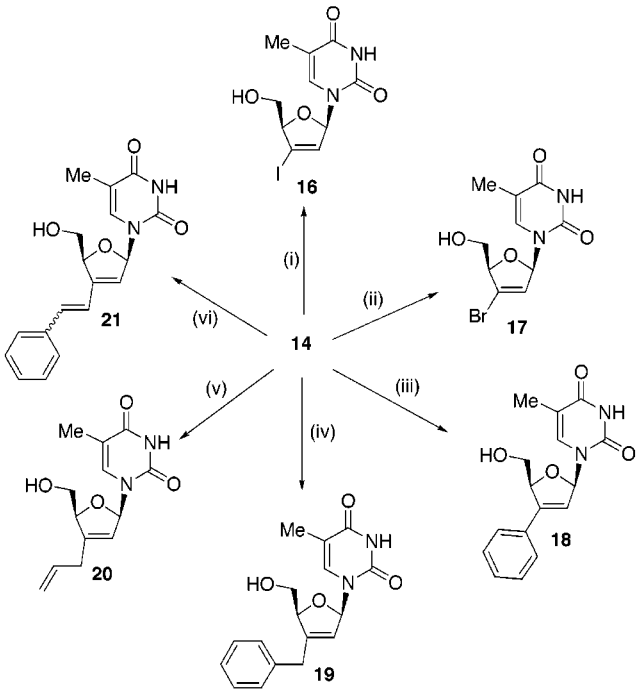
creased yield of **14** was seen again when HMPA was used as an additive (Table 1, entry 1 vs entry 2). A salient feature of this reaction, as compared with that of the silyl version, is the formation of the 2′-*C*-stannyl derivative **15**, instead of the allene derivative (**4a**). Compound **15** is assumed to be a product of an intermolecular anionic migration.[22] Therefore, this result may suggest that the stannyl group is highly susceptible to anionic migration, while that of the silyl group is too sluggish to trap the C2′-lithio intermediate in an intermolecular manner.

As shown in entry 4 (Table 1), a highest yield of 60% was attained for **14** by employing a combination of HMPA and TMEDA.

Synthesis of the 3′-Substituted Analogues of d4T

Simple application of the organotin chemistry[23] involving Sn−C (sp^2-hybridized) bonds to **14** provides access to a variety of 3′-substituted d4T analogues. The reactions shown in Scheme 5 were carried out uniformly at room temperature to give the 3′-halogeno (**16** and **17**) and the 3′-carbon-substituted (**18**−**21**) derivatives in 73−97% yields. These reactions would also be applicable to the

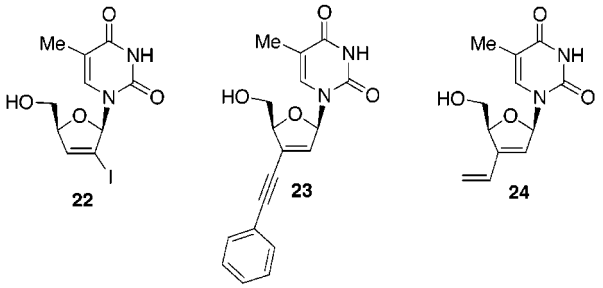
Scheme 5[a]



[a] Reagents, conditions, and yields: (i) iodine/THF, 1 h, 93%; (ii) NBS/THF, 4 h, 100%; (iii) PhI/$Pd(PPh_3)_4$/CuI/DMF, 12 h, 97%; (iv) $PhCH_2Br/Pd(PPh_3)_4$/CuI/DMF, 15 h, 78%; (v) $CH_2{=}CHCH_2Br/Pd(PPh_3)_4$/CuI/DMF, 3.5 h, 73%; (vi) $PhCH{=}CHBr/Pd(PPh_3)_4$/CuI/DMF, 4 h, 81%.

2′-*C*-stannyl derivative **15**. This was exemplified by the preparation of the 2′-iodo derivative **22** that was further silylated at the 5′-hydroxyl group to give **9** (62% yield from **15**).

In cases where organotin reagents are readily available, d4T analogues having carbon substituents can also be prepared by using the 2′-iodo derivative **16**. Thus, the 3′-*C*-(phenyl)ethynyl d4T (**23**) was prepared in 71% yield through the Stille reaction between **16** and tributyl(phenylethynyl)tin in the presence of $Pd(PPh_3)_4$ and CuI in DMF. Similarly, the 3′-*C*-vinyl derivative (**24**) was obtained in 63% yield by using tributyl(vinyl)tin.



Conclusion

In the present study, it has been shown that the vinylic lithiation of d4T (**1**) either at the 3′-position and at the 2′-position is a feasible event by employing LTMP in the presence of HMPA. When the 5′-hydroxyl group of **1** was protected with a *tert*-butyldiphenylsilyl group, the C3′-lithiated species underwent migration of the silyl group to give the 3′-*C*-silyl derivative (**6**), while the C2′-lithiated species was further transformed to the allene derivative (**4a**) as a result of furanose ring opening.

The stannyl version of this migration, carried out by using the bis-stannyl derivative (**12**) as a substrate, gave the 3′-*C*-stannyl derivative (**14**) as well as the 2′-*C*-stannyl derivative (**15**). The synthetic usefulness of these stannyl derivatives was demonstrated by the conversion of either **14** or the 3′-iodo derivative (**16**) to a variety of the 3′-substituted analogues of d4T.

Experimental Section

Melting points are uncorrected. NMR was measured at 500 MHz. Chemical shifts are reported relative to Me_4Si for ^1H NMR and ^{13}C NMR, while Me_4Sn was used for those of ^{119}Sn NMR. Mass spectra (MS) were taken in FAB mode (*m*-nitrobenzyl alcohol as a matrix). Column chromatography was carried out on silica gel (silica gel 60). Thin-layer chromatography (TLC) was performed on silica gel (precoated silica gel plate F_{254}). HPLC was carried out on a 2 × 25 cm column. THF was distilled from benzophenone ketyl. HMPA and 2,2,6,6-tetramethylpiperidine were distilled from CaH_2.

Lithiation of 5′-*O*-Trityl-d4T (2) with LTMP. To a THF (7.5 mL) solution of 2,2,6,6-tetramethylpiperidine (682 μL, 4.04 mmol) was added BuLi (1.5 M in hexane, 2.7 mL, 4.04 mmol) below −70 °C under positive pressure of dry Ar. The resulting LTMP solution was stirred for 5 min. To this was added dropwise a THF (7.5 mL) solution of **2** (377 mg, 0.81 mmol) while the temperature was kept below −70 °C. The reaction

(22) When an equimolar mixture of **12** and 2′,3′-didehydro-2′,3′-dideoxy-5′-*O*-triisopropylsilyluridine (5′-*O*-TIPS-d4U) was reacted with LTMP in the presence of HMPA, the 2′-*C*-tributylstannyl derivative of the latter substrate was obtained, albeit in a low yield (2%), along with **14** (35%), **15** (11%), and 3′-*C*-triisopropylsilyl-d4U (12%).

(23) Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987.

mixture was stirred for 15 min and then treated with saturated aqueous NH_4Cl. Extraction with EtOAc followed by silica gel column chromatography (hexane/EtOAc = 4/1) gave **3** (114 mg, 42%) as a solid. Further elution with hexane/EtOAc = 1/2 gave a mixture of **2** and **4**, each of which was separated by HPLC (hexane/EtOAc = 2/3): **2** (t_R 12.5 min, foam, 121 mg, 32%), **4** (t_R 15 min, foam, 37 mg, 10%). For physical data of **3**, see ref 12. Physical data of **4** are as follows: UV (MeOH) λ_{max} 287 nm (ϵ 10 200), λ_{min} 250 nm (ϵ 4700); IR (KBr) 1974 cm^{-1} (C=C=C); ^1H NMR ($CDCl_3$) δ 1.79 (3H, d, J = 1.2 Hz), 3.27 (1H, dd, J = 6.1, 9.5 Hz), 3.35 (1H, dd, J = 4.6, 9.5 Hz), 4.40−4.43 (1H, m), 6.11 (1H, dd, J = 5.2 and 6.1 Hz), 7.11−7.12 (1H, q, J = 1.2 Hz), 7.24−7.34 (9H, m), 7.41−7.44 (7H, m); ^{13}C NMR ($CDCl_3$) δ 12.3 (q), 66.9 (d), 69.1 (t), 87.1 (s), 99.1 (t), 107.6 (t), 112.1 (s), 127.2 (t), 127.9 (t), 128.6 (t), 135.7 (t), 143.4 (s), 148.7 (s), 163.1 (s), 194.5 (s); FAB-MS m/z 467 (M^+ + H). Anal. Calcd for $C_{29}H_{26}N_2O_4 \cdot {}^3/_4H_2O$: C, 72.56; H, 5.77; N, 5.84. Found: C, 72.76; H, 5.71; N, 5.57.

5′-*O*-(*tert*-Butyldiphenylsilyl)-2′,3′-didehydro-3′-deoxythymidine (5). A mixture of **1** (615 mg, 2.74 mmol), imidazole (373 mg, 5.48 mmol), and *tert*-butyldiphenylsilyl chloride (1.43 mL, 5.48 mmol) in DMF (10 mL) was stirred at room temperature for 15 h. The reaction mixture was treated with saturated aqueous $NaHCO_3$ and extracted with EtOAc. Silica gel column chromatography (hexane/EtOAc = 2/1) of the extract gave **5** (991 mg, 78%) as a foam: UV (MeOH) λ_{max} 265 nm (ϵ 8700), λ_{min} 237 nm (ϵ 2500); ^1H NMR ($CDCl_3$) δ 1.08 (9H, s), 1.48 (3H, d, J = 1.3 Hz), 3.88 (1H, dd, J = 4.2, 11.3 Hz), 3.92 (1H, dd, J = 3.8, 11.3 Hz), 4.29−4.94 (1H, m), 5.85−5.87 (1H, m), 6.35−6.37 (1H, m), 6.98−7.00 (1H, m), 7.15 (1H, d, J = 1.3 Hz), 7.34−7.45 (6H, m), 7.62−7.70 (4H, m), 8.19 (1H, br); FAB-MS m/z 463 (M^+ + H). Anal. Calcd for $C_{26}H_{30}N_2O_4Si \cdot {}^1/_5H_2O$: C, 66.98; H, 6.57; N, 6.01. Found: C, 66.96; H, 6.45; N, 5.98.

Lithiation of 5′-*O*-(*tert*-Butyldiphenylsilyl)-d4T (5) with LTMP in the Presence of HMPA. To a THF (10 mL) solution of 2,2,6,6-tetramethylpiperidine (970 μL, 5.73 mmol) was added BuLi (1.5 M in hexane, 3.8 mL, 5.73 mmol) below −70 °C under positive pressure of dry Ar. After the LTMP solution was stirred for 5 min, HMPA (2.0 mL, 11.5 mmol) was added, and the whole was stirred for a further 5 min. To this was added dropwise a solution of **5** (377 mg, 0.81 mmol) in THF (10 mL) while the temperature was kept below −70 °C. The reaction mixture was stirred for 15 min and then treated with saturated aqueous NH_4Cl. Extraction with EtOAc followed by silica gel column chromatography (hexane/EtOAc = 4:1) gave **3a** (14 mg, 4%) as a solid. Elution with hexane/EtOAc = 1:1 gave a mixture of **5** and **4a**, each of which was separated by HPLC (hexane/EtOAc = 1/1): **5** (t_R 14.9 min, foam, 95 mg, 18%), **4a** (t_R 17.7 min, foam, 47 mg, 9%). Further elution with hexane/EtOAc = 1/2 gave **6** (189 mg, 36%) as a foam.

Physical data of **3a** are as follows: mp 129−131 °C; ^1H NMR ($CDCl_3$) δ 4.64 (2H, s), 6.13 (1H, dd, J = 0.6, 3.3 Hz), 6.29 (1H, dd, J = 1.8, 3.3 Hz), 7.35−7.45 (7H, m), 7.65−7.73 (4H, m); FAB-MS m/z 375 (M^+ + K). Anal. Calcd for $C_{21}H_{24}O_2Si$: C, 74.96; H, 7.19. Found: C, 74.76; H, 7.39.

Physical data of **4a** are as follows: UV (MeOH) λ_{max} 286 nm (ϵ 10 500), λ_{min} 248 nm (ϵ 4500); IR (neat) 1975 cm^{-1} (C=C=C); ^1H NMR ($CDCl_3$) δ 1.09 (9H, s), 1.87 (3H, d, J = 1.2 Hz), 3.71 (1H, dd, J = 6.1, 10.2 Hz), 3.79 (1H, dd, J = 4.4, 10.2 Hz), 4.37−4.41 (1H, m), 6.11 (1H, t, J = 6.1 Hz), 7.14 (1H, q, J = 1.2 Hz), 7.33 (1H, dd, J = 2.4, 6.1 Hz), 7.38−7.47 (6H, m), 7.64−7.67 (4H, m); ^{13}C NMR ($CDCl_3$) δ 12.4 (q), 19.3 (s), 26.8 (q), 67.3 (t), 70.3 (d), 98.8 (d), 107.1 (d), 112.1 (s), 127.9 (d), 130.0 (d), 135.5 (d), 132.7 (s), 135.6 (d), 148.9 (s), 163.5 (s), 194.8 (s); FAB-MS m/z 463 (M^+ + H). Anal. Calcd for $C_{26}H_{30}N_2O_4Si$: C, 67.50; H, 6.54; N, 6.06. Found: C, 67.23; H, 6.47; N, 5.99.

Physical data of **6** are as follows: UV (MeOH) λ_{max} 266 nm (ϵ 10 400), λ_{min} 240 nm (ϵ 3700); ^1H NMR ($CDCl_3$) δ 1.17 (9H, s), 1.52−1.55 (1H, br), 1.87 (3H, d, J = 1.1 Hz), 3.15−3.20 (1H, m), 3.52−3.57 (1H, m), 5.05−5.08 (1H, m), 6.34 (1H, t, J = 1.6 Hz), 7.11 (1H, dd, J = 1.6, 3.4 Hz), 7.38−7.51 (6H, m), 7.57 (1H, q, J = 1.1 Hz), 7.62−7.66 (4H, m), 8.39 (1H, br); ^{13}C NMR ($CDCl_3$) δ 12.6 (q), 18.7 (s), 28.1 (q), 63.5 (t), 90.1 (t), 92.8 (d), 110.7 (s), 128.1 (d), 128.2 (d), 130.1 (d), 130.2 (d), 132.1 (s), 132.4 (s), 135.9 (d), 136.2 (d), 136.8 (d), 139.2 (d), 143.9 (s), 150.7 (s), 163.7 (s); FAB-MS m/z 463 (M^+ + H). Anal. Calcd for $C_{26}H_{30}N_2O_4Si \cdot {}^1/_5H_2O$: C, 66.98; H, 6.57; N, 6.01. Found: C, 66.81; H, 6.52; N, 5.83.

5′-*O*-Acetyl-3′-*C*-(*tert*-butyldiphenylsilyl)-2′,3′-didehydro-3′-deoxythymidine (7). A mixture of **6** (81 mg, 0.18 mmol) and Ac_2O (83 μL, 0.88 mmol) in pyridine (5 mL) was stirred for 3 h at room temperature. After evaporation of the solvent, the residue was chromatographed on a silica gel column (hexane/EtOAc = 2/1). This gave **7** (83 mg, 91%) as a foam: UV (MeOH) λ_{max} 265 nm (ϵ 10 500), λ_{min} 239 nm (ϵ 3600); ^1H NMR ($CDCl_3$) δ 1.16 (9H, s), 1.82 (3H, s), 1.93 (3H, d, J = 1.3 Hz), 3.51 (1H, dd, J = 4.1, 12.6 Hz), 3.92 (1H, dd, J = 2.5, 12.6 Hz), 5.13−5.16 (1H, m), 6.41 (1H, t, J = 1.6 Hz), 7.07 (1H, dd, J = 1.6, 3.7 Hz), 7.30 (1H, q, J = 1.3 Hz), 7.38−7.49 (6H, m), 7.58−7.68 (4H, m), 8.36 (1H, br); FAB-MS m/z 505 (M^+ + H). Anal. Calcd for $C_{28}H_{32}N_2O_5Si$: C, 66.64; H, 6.39; N, 5.55. Found: C, 66.37; H, 6.47; N, 5.50.

Preparation of (2,3-Didehydro-2,3-dideoxy-β-D-ribofuranosyl)benzene (10). To a suspension of (β-D-ribofuranosyl)benzene[15] (1.29 g, 6.14 mmol) in CH_3CN (40 mL) was added dropwise 2-acetoxyisobutyryl bromide[24] (3.14 mL, 21.5 mmol) while the temperature was maintained at 0 °C. The mixture was stirred for 1 h at 0 °C and then for 2 h at room temperature. The reaction mixture was partitioned between saturated aqueous $NaHCO_3$ and EtOAc. The organic layer was dried ($MgSO_4$), evaporated, and dissolved in CH_3CN/THF = 1:1 (30 mL). Freshly prepared zinc−copper couple[25] (2.7 g) and AcOH (1 mL) were added to the solution, and the whole was stirred vigorously under Ar atmosphere for 48 h. The reaction mixture was filtered through Celite, and the filtrate was partitioned between saturated aqueous $NaHCO_3$ and EtOAc. The organic layer was dried ($MgSO_4$) and evaporated to dryness. The residue was dissolved in NH_3/MeOH, kept standing at room temperature for 4 days, and then evaporated to dryness. To this were added DMF (5 mL), *tert*-butyldiphenylsilyl chloride (2.9 mL, 11.5 mmol), and imidazole (1.01 g, 14.86 mmol), and the mixture was stirred for 1.5 h. The reaction mixture was partitioned between saturated aqueous $NaHCO_3$ and EtOAc. Silica gel column chromatography (hexane/EtOAc = 25:1) of the organic layer followed by HPLC (hexane/EtOAc = 10:1) purification gave **10** (t_R 8.9 min, 877 mg, 34% for four steps) as an oil: ^1H NMR ($CDCl_3$) δ 1.06 (9H, s), 3.77 (1H, dd, J = 5.6, 10.5 Hz), 3.85 (1H, dd, J = 5.0, 10.5 Hz), 4.99−5.03 (1H, m), 5.78−5.79 (1H, m), 5.91 (1H, ddd, J = 1.5, 2.1, 6.1 Hz), 6.01 (1H, ddd, J = 1.5, 2.4, 6.1 Hz), 7.24−7.44 (11H, m), 7.66−7.69 (4H, m); FAB-MS m/z 453 (M^+ + H). Anal. Calcd for $C_{27}H_{30}O_2Si \cdot {}^1/_4H_2O$: C, 77.37; H, 7.34. Found: C, 77.70; H, 7.35.

Lithiation of 10 with LTMP in the Presence of HMPA: Formation of 11. This reaction was carried out by using **10** (330 mg, 0.8 mmol) by the same procedure described for the case of **5**. Compound **11** (305 mg, 88%) was isolated as an oil by silica gel column chromatography (hexane/EtOAc = 1:3): ^1H NMR ($CDCl_3$) δ 1.07 (9H, s), 1.77−1.85 and 1.88−1.95 (2H, each as m), 2.63 (1H, br), 3.06−3.19 (2H, m), 3.56 (1H, dd, J = 7.0, 10.2 Hz), 3.71 (1H, dd, J = 3.7, 10.2 Hz), 3.79−3.83 (1H, m), 7.35−7.47 (8H, m), 7.52−7.56 (1H, m), 7.65−7.67 (4H, m), 7.95−7.98 (2H, m); FAB-MS m/z 433 (M^+ + H). Anal. Calcd for $C_{27}H_{32}O_3Si$: C, 74.96; H, 7.46. Found: C, 74.79; H, 7.49.

Preparation of the Bis-tributylstannyl-d4T (12) and Its Benzoylation To Form 13. A mixture of **1** (132 mg, 0.59 mmol) and Bu_3SnOMe (340 μL, 1.18 mmol) was heated at 90

(24) The use of 2-acetoxyisobutyryl bromide, and then Zn/Cu couple, has been reported for the preparation of 2′,3′-didehydro-2′,3′-dideoxyribonucleosides: Robins, M. J.; Hansske, F.; Low, N. H.; Park, J. I. *Tetrahedron Lett.* **1984**, *25*, 367−370. (b) Bhat, V.; Ugarkar, B. G. *Synth. Commun.* **1992**, *22*, 1481−1486.

(25) Mansuri, M. M.; Starrett, J. E., Jr.; Wos, J. A.; Tortolani, D. R.; Brodfuehrer, P. R.; Howell, H. G.; Martin, J. C. *J. Org. Chem.* **1989**, *54*, 4780−4785.

°C for 90 min with stirring. The resulting oily substance (**12**) was kept under reduced pressure for 30 min. NMR data of **12** are as follows: ^{119}Sn NMR (benzene-d_6) δ 58.3, 86.3, 107.5; partial ^{1}H NMR data (benzene-d_6) δ 2.01 (3H, m), 3.68 (1H, ddd, J = 4.4, 11.2, 28.0 Hz), 3.93 (1H, ddd, J = 3.6, 11.2, 28.0 Hz), 4.63−4.64 (1H, m), 5.20−5.22 (1H, m), 5.77−5.80 (1H, m), 7.34−7.37 (1H, m), 7.56−7.57 (1H, m).

The above prepared **12** was dissolved in benzene (3 mL), and reacted with benzoyl chloride (137 μL, 1.18 mmol) for 1 h at room temperature. The reaction mixture was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$. Silica gel column chromatography ($CHCl_3$/MeOH = 20:1) of the organic layer gave **13** (176 mg, 91%) as a solid. For physical data of **13**, see ref 21.

LTMP Lithiation of 12: Formation of 2′,3′-Didehydro-3′-deoxy-3′-*C*-(tributylstannyl)thymidine (14) and Its 2′-*C*-Stannylated isomer (15). Compound **12** used in this reaction was prepared from 1.0 g (4.46 mmol) of **1**. To a THF (20 mL) solution of 2,2,6,6-tetramethylpiperidine (3.76 mL, 22.3 mmol) and HMPA (11.6 mL, 66.9 mmol) was added BuLi (1.5 M in hexane, 15 mL, 22.3 mmol) below −70 °C under positive pressure of dry Ar. After the mixture was stirred for 5 min, TMEDA (3.37 mL, 22.3 mmol) was added to the LTMP solution and the whole was stirred for a further 5 min. To this was added dropwise a solution of the above prepared **12** in THF (20 mL) while the temperature was kept below −70 °C. The reaction mixture was stirred for 15 min and then partitioned between EtOAc and saturated aqueous NH_4Cl. The aqueous layer was evaporated, dried, and treated with Ac_2O (4.2 mL, 44.6 mmol) in pyridine (40 mL) at room temperature for 3 h. Silica gel column chromatography (hexane/EtOAc = 1:2) of the reaction mixture gave the 5′-*O*-acetate[25] (95 mg, 8%) of **1**. The EtOAc layer was subjected to silica gel column chromatography (hexane/EtOAc = 5:2) to give **14** (1.38 g, 60%) as an oil. Elution with hexane/EtOAc = 1:1 gave **15** (206 mg, 9%) as an oil. Physical data of **14**: UV (MeOH) λ_{max} 267 nm (ϵ 7600), λ_{min} 238 nm (ϵ 1900); ^{1}H NMR ($CDCl_3$) δ 0.85−0.99 (9H, m), 1.03−1.14, 1.27−1.51, and 1.52−1.62 (18H, each as m), 1.85 (3H, d, J = 1.1 Hz), 2.17−2.20 (1H, m), 3.72 (1H, ddd, J = 4.0, 5.1, 12.2 Hz), 3.94 (1H, ddd, J = 2.9, 6.1, 12.2 Hz), 4.97−5.00 (1H, m), 5.74−5.81 (1H, m), 6.95−6.98 (1H, m), 7.37 (1H, q, J = 1.1 Hz), 8.19 (1H, br); FAB-MS m/z 513 (M^+ + H). Anal. Calcd for $C_{22}H_{38}N_2O_4Sn$: C, 51.48; H, 7.46; N, 5.46. Found: C, 51.60; H, 7.66; N, 5.34. Physical data of **15**: UV (MeOH) λ_{max} 267 nm (ϵ 9100), λ_{min} 238 nm (ϵ 2600); ^{1}H NMR ($CDCl_3$) δ 0.80−1.03 and 1.20−1.68 (27H, each as m), 1.83 (3H, d, J = 1.1 Hz), 2.92−2.95 (1H, m), 3.77 (1H, ddd, J = 3.5, 6.1, 12.5 Hz), 3.96 (1H, ddd, J = 2.8, 6.1, 12.5 Hz), 4.86−4.89 (1H, m), 6.26−6.32 (1H, m), 7.13−7.15 (1H, m), 7.36 (1H, q, J = 1.1 Hz), 8.48 (1H, br); FAB-MS m/z 513 (M^+ + H). Anal. Calcd for $C_{22}H_{38}N_2O_4Sn$: C, 51.48; H, 7.46; N, 5.46. Found: C, 51.34; H, 7.65; N, 5.34.

2′,3′-Didehydro-3′-deoxy-3′-iodothymidine (16). A mixture of **14** (100 mg, 0.19 mmol) and iodine (73 mg, 0.29 mmol as I_2) in THF (4 mL) was stirred for 1 h at room temperature. The reaction mixture was partitioned between $CHCl_3$ and saturated aqueous $Na_2S_2O_3$. Silica gel column chromatography ($CHCl_3$/MeOH = 30:1) of the organic layer gave **16** (62 mg, 93%) as a solid: mp 104−108 °C; UV (MeOH) λ_{max} 264 nm (ϵ 10 900), λ_{min} 238 nm (ϵ 4000); ^{1}H NMR ($CDCl_3$) δ 1.87 (3H, d, J = 1.3 Hz), 2.25 (1H, br), 3.95 (1H, ddd, J = 2.0, 5.3, 12.8 Hz), 4.08 (1H, ddd, J = 2.3, 5.7, 12.8 Hz), 4.75−4.78 (1H, m), 6.21 (1H, t, J = 1.6 Hz), 6.97 (1H, dd, J = 1.6, 3.7 Hz), 7.58 (1H, q, J = 1.3 Hz), 8.25 (1H, br); FAB-MS m/z 351 (M^+ + H). Anal. Calcd for $C_{10}H_{11}IN_2O_4$: C, 34.31; H, 3.17; N, 8.00. Found: C, 34.39; H, 3.03; N, 7.92.

5′-*O*-(*tert*-Butyldiphenylsilyl)-3′-iodo-d4T (8). A mixture of **16** (84 mg, 0.24 mmol), *tert*-butyldiphenylsilyl chloride (125 μL, 0.48 mmol), and imidazole (49 mg, 0.72 mmol) in DMF (3.0 mL) was stirred for 1 h at room temperature. The reaction mixture was partitioned between EtOAc and saturated aqueous $NaHCO_3$. Silica gel column chromatography (hexane/EtOAc = 2:1) of the organic layer gave **8** (102 mg, 72%) as a foam: UV (MeOH) λ_{max} 265 nm (ϵ 6800), λ_{min} 239 nm (ϵ 2500); ^{1}H NMR ($CDCl_3$) δ 1.11 (3H, d, J = 1.3 Hz), 1.12 (9H, s), 4.11 (1H, dd, J = 1.3, 11.9 Hz), 4.17 (1H, dd, J = 2.6, 11.9 Hz), 4.77−4.80 (1H, m), 6.28 (1H, t, J = 1.5 Hz), 6.95 (1H, dd, J = 1.5, 4.2 Hz), 7.24 (1H, q, J = 1.3 Hz), 7.33−7.44 (6H, m), 7.63−7.70 (4H, m), 8.13 (1H, br); FAB-MS m/z 589 (M^+ + H). Anal. Calcd for $C_{26}H_{29}IN_2O_4Si$: C, 53.06; H, 4.97; N, 4.76. Found: C, 53.05; H, 4.90; N, 4.56.

3′-Bromo-2′,3′-didehydro-3′-deoxythymidine (17). A mixture of **14** (185 mg, 0.36 mmol) and NBS (95 mg, 0.54 mmol) in THF (5 mL) was stirred for 4 h at room temperature. The reaction mixture was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$. Silica gel column chromatography ($CHCl_3$/MeOH = 20:1) of the organic layer gave **17** (108 mg, 100%) as a foam: UV (MeOH) λ_{max} 264 nm (ϵ 9700), λ_{min} 236 nm (ϵ 2800); ^{1}H NMR ($CDCl_3$) δ 1.88 (3H, d, J = 1.3 Hz), 2.35−2.38 (1H, m), 3.96 (1H, ddd, J = 2.2, 5.0, 12.8 Hz), 4.04 (1H, ddd, J = 2.0, 5.7, 12.8 Hz), 4.78−4.80 (1H, m), 6.02 (1H, t, J = 1.7 Hz), 6.98 (1H, dd, J = 1.7, 3.7 Hz), 7.62 (1H, q, J = 1.3 Hz), 8.64 (1H, br). Anal. Calcd for $C_{10}H_{11}BrN_2O_4$: C, 39.62; H, 3.66; N, 9.24. Found: C, 39.67; H, 3.49; N, 9.01. This compound gave no assignable ion peak in FAB-MS and thus was converted to its 5′-*O*-acetate [FAB-MS m/z 345 and 347 (M^+ + H)] by a conventional procedure.

2′,3′-Didehydro-3′-deoxy-3′-*C*-phenylthymidine (18). A mixture of **14** (167 mg, 0.33 mmol), PhI (110 μL, 0.99 mmol), $Pd(PPh_3)_4$ (38 mg, 0.033 mmol), and CuI (12 mg, 0.066 mmol) in DMF (1.85 mL) was stirred at room temperature for 12 h under positive pressure of dry Ar. The reaction mixture was partitioned between EtOAc and saturated aqueous $NaHCO_3$. Silica gel column chromatography (hexane/EtOAc = 1:6) of the organic layer gave **18** (95 mg, 97%) as a foam: UV (MeOH) λ_{max} 254 nm (ϵ 17 800), λ_{min} 224 nm (ϵ 6800); ^{1}H NMR ($CDCl_3$) δ 1.84 (3H, d, J = 1.3 Hz), 3.25 (1H, br), 3.90−3.94 (1H, m), 4.01−4.10 (1H, m), 5.35−5.36 (1H, m), 5.98 (1H, t, J = 1.6 Hz), 7.15 (1H, dd, J = 1.6, 3.1 Hz), 7.36−7.45 (5H, m), 7.68 (1H, q, J = 1.3 Hz), 9.22 (1H, br); FAB-MS m/z 301 (M^+ + H). Anal. Calcd for $C_{16}H_{16}N_2O_4$: C, 63.99; H, 5.37; N, 9.33. Found: C, 63.73; H, 5.17; N, 9.41.

3′-*C*-Benzyl-2′,3′-didehydro-3′-deoxythymidine (19). This compound was prepared from **14** (355 mg, 0.65 mmol) by the procedure described for the preparation of **18**. The following amounts of reagents were used: benzyl bromide (195 μL, 1.63 mmol), $Pd(PPh_3)_4$ (75 mg, 0.065 mmol), and CuI (25 mg, 0.13 mmol) in DMF (2.0 mL). Compound **19** (160 mg, 78%) was obtained as a foam after silica gel column chromatography (hexane/EtOAc = 1:6): UV (MeOH) λ_{max} 265 nm (ϵ 9900), λ_{min} 234 nm (ϵ 2500); ^{1}H NMR ($CDCl_3$) δ 1.82 (3H, d, J = 1.2 Hz), 3.27 (1H, m), 3.43 (1H, d, J = 16.6 Hz), 3.68 (1H, d, J = 16.6 Hz), 3.84 (1H, ddd, J = 2.4, 6.3, 12.8 Hz), 3.95 (1H, ddd, J = 2.4, 5.5, 12.8 Hz), 4.67−4.70 (1H, m), 5.31−5.32 (1H, m), 6.97−6.98 (1H, m), 7.22−7.27 (3H, m), 7.31−7.35 (2H, m), 7.52 (1H, q, J = 1.2 Hz), 8.81 (1H, br); FAB-MS m/z 315 (M^+ + H). Anal. Calcd for $C_{17}H_{18}N_2O_4 \cdot {}^1/_5H_2O$: C, 64.21; H, 5.83; N, 8.81. Found: C, 63.95; H, 5.62; N, 8.53.

3′-*C*-Allyl-2′,3′-didehydro-3′-deoxythymidine (20). This compound was prepared from **14** (307 mg, 0.60 mmol) by the procedure described for the preparation of **18**. The following amounts of reagents were used: allyl bromide (155 μL, 1.8 mmol), $Pd(PPh_3)_4$ (70 mg, 0.06 mmol), and CuI (22 mg, 0.12 mmol) in DMF (2.0 mL). Compound **20** (110 mg, 73%) was obtained as a foam after silica gel column chromatography (hexane/EtOAc = 1:4): UV (MeOH) λ_{max} 269 nm (ϵ 15 100), λ_{min} 239 nm (ϵ 12 600); ^{1}H NMR ($CDCl_3$) δ 1.87 (3H, d, J = 1.1 Hz), 2.17−2.21 (1H, m), 2.88−2.94 (1H, m), 3.04−3.10 (1H, m), 3.81−3.86 (1H, m), 3.93−3.98 (1H, m), 4.73−4.74 (1H, m), 5.18−5.21 (1H, m), 5.21−5.24 (1H, m), 5.46−5.50 (1H, m), 5.83−5.93 (1H, m), 6.95−6.96 (1H, m), 7.51 (1H, q, J = 1.1 Hz), 8.10 (1H, br); FAB-MS m/z 265 (M^+ + H). Anal. Calcd for $C_{13}H_{16}N_2O_4 \cdot {}^1/_4H_2O$: C, 58.09; H, 6.19; N, 10.42. Found: C, 57.82; H, 6.19; N, 10.11.

2′,3′-Didehydro-3′-deoxy-3′-*C*-(*β*-styryl)thymidine (21). This compound was prepared from **14** (314 mg, 0.61 mmol) by the procedure described for the preparation of **18**. The following amounts of reagents were used: β-bromostyrene (195 μL, 1.53 mmol, E/Z = 7:1), $Pd(PPh_3)_4$ (70 mg, 0.06 mmol), and CuI (23 mg, 0.12 mmol) in DMF (2.5 mL). Compound **21** (161 mg,

81%, E/Z = 6:1) was obtained as a foam after silica gel column chromatography (hexane/EtOAc = 1:6): UV (MeOH) λ_{max} 287 nm (ϵ 34 000), λ_{min} 239 nm (ϵ 5600); ^{1}H NMR ($CDCl_3$) of (*E*)-isomer δ 1.88 (3H, d, J = 1.3 Hz), 2.34 (1H, br), 4.07−4.09 (2H, m), 5.18−5.19 (1H, m), 5.84−5.85 (1H, m), 6.76 and 6.92 (2H, each as d, J = 16.7 Hz), 7.05−7.06 (1H, m), 7.30−7.39 (3H, m), 7.45−7.47 (2H, m), 7.59 (1H, q, J = 1.3 Hz), 8.25 (1H, br); ^{1}H NMR ($CDCl_3$) of (*Z*)-isomer δ 1.87 (3H, d, J = 1.1 Hz), 2.43−2.44 (1H, m), 3.61−3.66 (1H, m), 4.87−4.88 (1H, m), 5.55−5.56 (1H, m), 6.15 (1H, dd, J = 1.1, 12.0 Hz), 6.84 (1H, d, J = 12.0 Hz), 6.96−6.97 (1H, m), 7.28−7.39 (3H, m), 7.44−7.47 (2H, m), 8.33 (1H, br); FAB-MS m/z 365 (M^+ + K). Anal. Calcd for $C_{18}H_{18}N_2O_4 \cdot {}^3/_4H_2O$: C, 63.61; H, 5.78; N, 8.24. Found: C, 64.00; H, 5.61; N, 7.98.

Preparation of 2′-Iodo-d4T (22) and Subsequent Silylation: Formation of the 5′-*O*-Silylated Derivative (9). Compound **22** was prepared from **15** (265 mg, 0.52 mmol) by the procedure described for the preparation of **16**. After the extractive workup, the solvent was removed. The resulting residue was treated with *tert*-butyldiphenylsilyl chloride (268 μL, 1.03 mmol) and imidazole (105 mg, 1.55 mmol) in DMF (3.0 mL) as described for the preparation of **8**. Compound **9** (188 mg, 62% yield from **15**) was obtained as a foam after silica gel column chromatography (hexane/EtOAc = 1:1): UV (MeOH) λ_{max} 264 nm (ϵ 8300), λ_{min} 239 nm (ϵ 3400); ^{1}H NMR ($CDCl_3$) δ 1.10 (9H, s), 1.43 (3H, d, J = 1.3 Hz), 3.90 (1H, dd, J = 3.9, 11.5 Hz), 3.94 (1H, dd, J = 3.8, 11.5 Hz), 4.87−4.90 (1H, m), 6.64 (1H, t, J = 2.0 Hz), 6.91 (1H, dd, J = 2.0, 4.0 Hz), 7.03 (1H, q, J = 1.3 Hz), 7.36−7.46 (6H, m), 7.61−7.66 (4H, m), 7.98 (1H, br); FAB-MS m/z 627 (M^+ + K). Anal. Calcd for $C_{26}H_{29}IN_2O_4Si$: C, 53.06; H, 4.97; N, 4.76. Found: C, 53.05; H, 4.91; N, 4.54.

2′,3′-Didehydro-3′-deoxy-3′-*C*-(phenylethynyl)thymidine (23). This compound was prepared from **16** (126 mg, 0.36 mmol) by the procedure described for the preparation of **18**. The following amounts of reagents were used: tributyl(phenylethynyl)tin (282 μL, 0.72 mmol), $Pd(PPh_3)_4$ (42 mg, 0.036 mmol), and CuI (14 mg, 0.07 mmol) in DMF (2.0 mL). The reaction was carried out at room temperature for 41 h. Compound **23** (83 mg, 71%) was obtained as a foam after silica gel column chromatography (hexane/EtOAc = 1:4): UV (MeOH) λ_{max} 289 nm (ϵ 28 900) and 273 nm (ϵ 37 300), λ_{min} 284 nm (ϵ 23 400) and 232 nm (ϵ 9500); ^{1}H NMR ($CDCl_3$) δ 1.88 (3H, d, J = 1.1 Hz), 2.53 (1H, br), 4.04−4.05 (2H, m), 4.90−4.93 (1H, m), 6.05−6.06 (1H, m), 7.15−7.17 (1H, m), 7.35−7.40 (3H, m), 7.49−7.52 (2H, m), 7.60 (1H, q, J = 1.1 Hz), 8.43 (1H, br); FAB-MS m/z 325 (M^+ + H). Anal. Calcd for $C_{18}H_{16}N_2O_4$: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.39; H, 4.79; N, 8.61.

2′,3′-Didehydro-3′-deoxy-3′-*C*-vinylthymidine (24). This compound was prepared from **16** (260 mg, 0.74 mmol) by the procedure described for the preparation of **18**. The following amounts of reagents were used: tributyl(vinyl)tin (434 μL, 1.48 mmol), $Pd(PPh_3)_4$ (86 mg, 0.074 mmol), and CuI (28 mg, 0.15 mmol) in DMF (2.0 mL). The reaction was carried out at room temperature for 41 h. Compound **24** (116 mg, 63%) was obtained as a syrup after silica gel column chromatography (EtOAc): UV (MeOH) λ_{max} 265 nm (ϵ 6800), λ_{min} 245 nm (ϵ 4500); ^{1}H NMR ($CDCl_3$) δ 1.86 (3H, d, J = 1.1 Hz), 2.44−2.47 (1H, m), 4.00−4.01 (1H, m), 5.07−5.08 (1H, m), 5.44 (1H, d, J = 11.2 Hz), 5.47 (1H, d, J = 17.8 Hz), 5.75−5.76 (1H, m), 6.55 (1H, dd, J = 11.2, 17.8 Hz), 7.00−7.01 (1H, m), 7.55 (1H, q, J = 1.1 Hz), 8.37 (1H, br); FAB-MS m/z 250 (M^+ + H). Anal. Calcd for $C_{12}H_{14}N_2O_4 \cdot {}^1/_4H_2O$: C, 56.58; H, 5.73; N, 11.00. Found: C, 56.30; H, 5.59; N, 10.61.

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