N- versus O-Alkylation of 2,3′-Anhydrothymidine: Reaction of the Obtained Pyrimidinium Salts with Azide Ion

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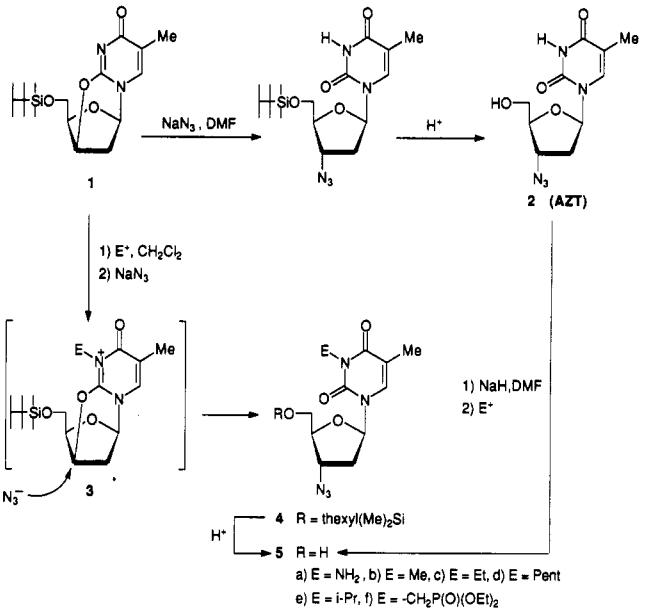
Reaction of 5′-*O*-(thexyldimethylsilyl)anhydrothymidine (1) with *O*-(mesitylenesulfonyl)hydroxylamine and CH_3OTf generates the pyrimidinium salts **3a** and **3b** which react with azide ion to give the N^3-substituted AZT derivatives **4a** and **4b**, respectively. In contrast, alkylation of **1** with pentyl triflate occurs at both the N^3 and O^4 positions leading, after treatment with NaN_3, to the expected AZT analog **4d** and the novel 3-substituted 2,3-dideoxyxylofuranosyl azide **7d**. In a further study, the extent to which competing O^4-alkylation occurs was found to be sensitive to steric factors, increasing in the order MeOTf < EtOTf < pentyl OTf < i-PrOTf. Formation of the alternate O^4-alkylated AZT derivatives **9** via an intramolecular Hilbert–Johnson process was not observed in these reactions. It was demonstrated, however, that reaction of the intermediate O^4-alkylated pyridinium salt **6c** with Me_4NCl does evolve toward the corresponding C-3′ chloro compound **14c**. Reaction of **1** with the less reactive alkylating agent $(EtO)_2P(O)CH_2OTf$ is more complicated producing the O-alkylated product **7f** and the novel dimer **19**.

Introduction

Since discovery of the anti-HIV activity of AZT (**2**)[1] a wide range of 2′,3′-dideoxynucleosides have been prepared and evaluated in the search for new therapeutic agents which will provide more effective protection against infection and progression of the AIDS syndrome. In this regard, a number of alterations of the pyrimidine and purine base component have been studied,[2] but to our knowledge, no systematic study of the influence of substitution at the N^3 position of the thymine base on HIV replication has been made.[3] Recent work from our laboratory showed that analogs of AZT substituted at the N^3 position are active against HIV and are substantially less toxic than AZT itself.[4] This series of analogs, illustrated by compounds **5a–f** (Scheme I), were typically prepared by reaction of the N^3 anion of AZT (NaH, DMF) with *O*-(mesitylenesulfonyl)hydroxylamine (MSH) or with the appropriate alkyl halide/triflate (DMF, 25 °C, 3 h).[5,6] In an effort to develop an alternative route to these compounds, which does not involve AZT as an intermediate, the idea emerged that they could be accessed directly through quaternization of the N^3 imino ether nitrogen in anhydronucleoside **1**, followed by reaction of the in situ generated salt **3** with NaN_3. In this paper, we describe a study of this "one-pot" protocol which, interestingly, produces both the desired AZT analogs **4a–e** and the novel 1′-azido-substituted 2′-deoxyxylose derivatives **7c–f** and **19** (Schemes II and III).

Scheme I



Results and Discussion

The starting 5′-*O*-(thexyldimethylsilyl)anhydronucleoside **1** was prepared in three steps from thymidine as previously reported.[7] As an initial goal, the synthesis of compound **5a** (RP67042)[4] was studied, Scheme II. The reaction of **1** with MSH in CH_2Cl_2 at 0 °C was rapid, resulting in complete disappearance of starting material (TLC analysis; silica gel) and formation of a colorless precipitate in less than 2 h.[8,9] After a change of solvent to DMF the intermediate salt **3a** was reacted with NaN_3 overnight at 0 °C. A very clean reaction occurred from

(1) Mitsuya, H.; Broder, S. *Proc. Natl. Acad. Sci. U.S.A.* **1986**, *83*, 1911.

(2) Nasr, M.; Litterest, C.; McGowan, J. *Antiviral Res.* **1990**, *14*, 125.

(3) During the preparation of this manuscript a paper appeared on the preparation of a series of N^3-substituted derivatives of AZT: Kitade, Y.; Suzuki, A.; Hirota, K.; Maki, Y.; Nakane, H.; Ono, K.; Baba, M.; Shigeta, S. *Chem. Pharm. Bull.* **1992**, *4*, 920.

(4) (a) Grierson, D. S.; Lu, W.-Y.; Maillard, M. C.; Monneret, C. G. EP-437382-A (Rhone-Pôulenc Sante) "New thymidine derivatives for treating AIDS are less toxic to bone marrow than 3′-deoxy-3′-fluorothymidine". (b) Maillard, M.; Florent, J.-C.; Lemâitre, M.; Begassat, F.; Bugnicourt, A.; Ferrieux, C.; Rombi, C.; Pacaud, E.; Thierry, D.; Glukman, E.; Zerial, A.; Monneret, C.; Grierson, D. S. *Bioorg. Med. Chem. Lett.*, **1992**, *2*, 1469.

(5) For alternative procedures for the preparation of *N*-3-aminopyrimidines, see: (a) Maeda, M.; Kawazoe, Y. *Chem. Pharm. Bull.* **1975**, *23*, 844. (b) Huang, G.-F.; Okamoto, T.; Maeda, M.; Kawazoe, Y. *Tetrahedron Lett.* **1973**, 4541.

(6) For references on the alkylation of the base component in pyrimidine nucleosides, see: Ueda, T. In *Chemistry of Nucleosides and Nucleotides*; Townsend, L. B., Ed.: Plenum Press: New York, 1988; Vol. 1, p 9.

(7) Maillard, M.; Faraj, A.; Frappier, F.; Florent, J.-C.; Grierson, D. S.; Monneret, C. *Tetrahedron Lett.* **1989**, *30*, 1955.

(8) (a) Ikeda, M.; Minamikawa, J.; Tamura, Y. *Synthesis* **1977**, 1. (b) Vlaovic, D.; Milic, B. L.; Mackenzie, K. *J. Chem. Res., Synop.* **1989**, 156.

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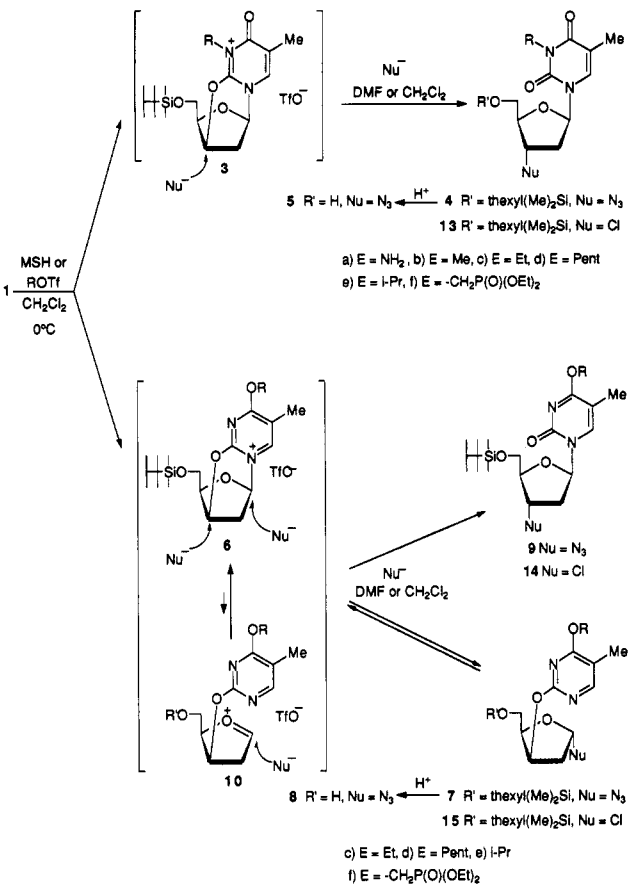
Scheme II



which the N^3-amino AZT derivative **4a** was isolated in 90% yield after flash column chromatography. Subsequent treatment of this intermediate with Dowex 50WX2 (H^+) resin in methanol effected 5′-O deprotection giving N^3-amino AZT (**5a**) in 73% yield. As expected, only minor alterations were observed in the ^1H and ^{13}C NMR spectra of this product relative to AZT (**2**). However, the occurence of a strong parent ion and fragments for N^3-aminothymine + H (m/z 142) and the azidosugar component were characteristic in its CI mass spectrum. In a similar fashion, the reaction of **1** with methyl triflate[10] in CH_2Cl_2 (20 °C, 1 h) followed by NaN_3 in DMF furnished the N^3-methyl compound **5b** in 59% overall yield after deprotection. Methyl triflate rather than methyl iodide was employed in this reaction in order to avoid opening of the quaternized intermediate **3b** by iodide ion.[11]

The reaction of **1** with the bulkier alkylating agent pentyl triflate[10] (CH_2Cl_2, 0 °C) followed by NaN_3 was more complex, giving rise to formation of a 1:2 mixture of two products. The minor and chromatographically more polar component corresponded to the expected N^3-pentyl-substituted derivative **4d** (25% yield). The major, less polar product, isolated in 58% yield, was shown on the basis of the parent ion peak at m/z 480 in its CI mass spectrum and a strong fragment peak at m/z 197 for the alkylated base component to be isomeric with **4d**. It was readily apparent from the ^{13}C NMR data that O^4- rather than N^3-alkylation of the pyrimidine base had occurred in the first step leading to this product. However, the very marked downfield position of the C-4 (δ 162) and C-6 (δ 157) absorptions relative to the same signals in the spectrum of **4d** (C-4, δ 151; C-6, δ 133) was difficult to accomodate with the structure **9d** which would result from reaction at C-3′ of the O^4-alkylated pyrimidine salt **6d** with azide ion. The abnormally downfield positions of the C-3′ absorption (δ 75) and H-3′ (δ 5.7) were also inconsistent with 3′-azido substitution as in **9d**. Comparison of the NMR data with that reported for the three other 1′ and 3′ configurational isomers of AZT[12] did not lead to a good correlation which forced us to consider that the structure of this major isomer corresponded to **7d**. Treatment of **7d** with Dowex resin (H^+) effected 5′-O deprotection giving crystalline **8d**, thereby providing the opportunity to confirm its structure by X-ray diffraction. Monoclinic crystals ($P2_1$) were obtained in which two independent molecules (A and B) of **8d** were present in the asymmetric unit. These two molecules are assembled in a dimeric type structure through two H-bonds established between the 5′-hydroxyl group of one component and the N^1 nitrogen atom of the thymine base of the other ($O^{5'H}$---N^1 = 2.883(2), 2.890(2) Å; $H^{O5'}$---N^1 = 1.92, 1.76 Å; angle $O^{5'}$--$H^{O5'}$--N^1 = 166.0°, 177.7°). This permits the thymine bases to align themselves in parallel planes separated by an average distance of 3.4 Å. In both molecules the O^4 pentyl side chain is deployed in the plane of the base. However, in molecule A the chain is bent and in molecule B it is fully extended. The structure of **8d** (form B) is presented in Figure 1 (correct absolute configuration). One can immediately see that the azide group is indeed substituted at C-1′ and that it is trans to the substituent at C-3′. Torsion angle measurements reveal that the furanose ring exists in an envelope form with the C-4′ carbon below the plane of the other four atoms by 0.53(1) Å and that the thymine base component is pointing out and away from the sugar ring ($C^{4'}$–$C^{3'}$–O^2–C^2 = 106° and 167°).

To further examine the influence of the alkylating agent in promoting the formation of **7** the reactions of **1** with ethyl and isopropyl triflates[10] were studied. In both instances the alkylation step was followed by treatment with Amberlite IR 400 (N_3^-) resin[13] in CH_2Cl_2 (0 °C) to avoid solvent changes. In the EtOTf experiment formation of a nearly 1:1 mixture of compounds **4c** and **7c** was observed. These products were separated by flash column chromatography and then 5′-O deprotected using the Dowex resin to afford the O^4-ethyl derivative **8c** and N^3-ethyl AZT (**5c**) in 33 and 34% overall yields, respectively. As might be expected, the corresponding reaction with i-PrOTf favored formation of the O^4-alkylation product **7e**. Determination of the **4e**/**7e** ratio was complicated in this case by the presence of a significant proportion of the corresponding 5′-O deprotected products **5e** and **8e** as well as the 5′-O-isopropyl ethers **11e** and **12e**.[14] Therefore, the crude reaction mixture was reacted with tetrabutylammonium fluoride (TBAF) in THF prior to column chromatography. In this way compounds **5e** and **8e**, an

(9) We thank Dr. K. Mackenzie, University of Bristol, for helpful comments concerning the preparation and handling of MSH which was made according to ref 8 with the exception that the product was thoroughly dried in vacuo over P_2O_5 (0.05 mmHg, −20 °C, 3 h) before use. The product was generally prepared on a scale no greater than 5 g and used immediately. When storage was necessary the material was kept at −20 °C over P_2O_5. MSH may decompose explosively and should be handled with due care.

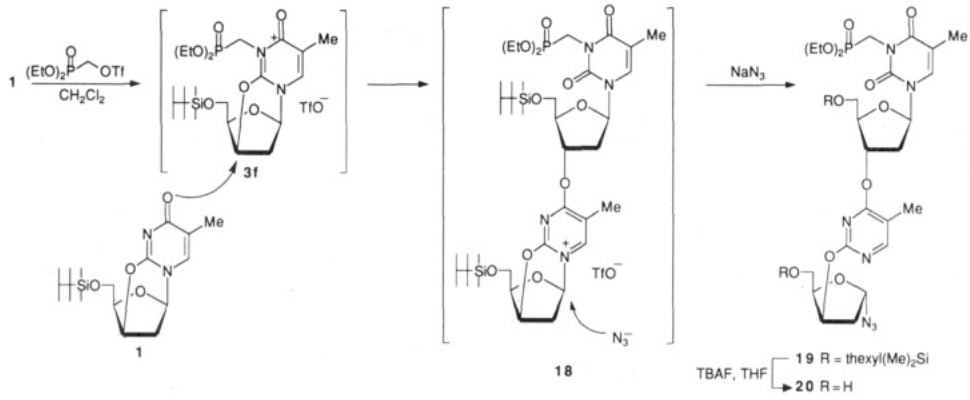
(10) Beard, C. D.; Baum, K.; Grakauskas, V. *J. Org. Chem.* **1973**, *38*, 3673.

(11) Kikugawa, K.; Ichino, M.; Ukita, T. *Chem. Pharm. Bull.* **1969**, *17*, 785.

(12) (a) Wengel, J.; Lau, J.; Pedersen, E. B.; Nielsen, C. M. *J. Org. Chem.* **1991**, *56*, 3591. (b) Wengel, J.; Pedersen, E. B. *Synthesis* **1991**, 451.

(13) Hassner, A.; Stern, M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 478.

Scheme III



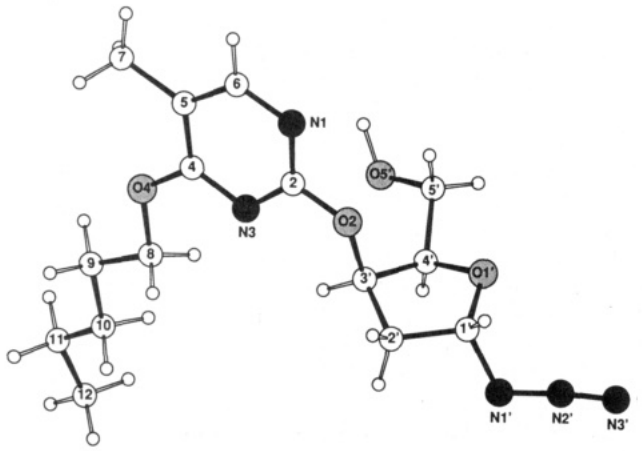
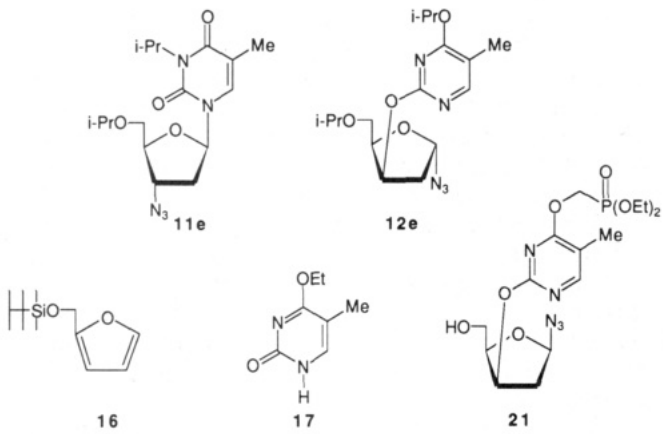


Figure 1. ORTEP representation of compound **8d** (form B).



inseparable 1:4.1 mixture, were obtained in 62% yield, along with a 1:6.2 mixture of **11e** and **12e** (28%).

As determined from the ^{1}H spectra on NMR tube scale reactions of **1** with each triflate ($CDCl_3$, 0 °C, 2 h) the isolated yields of **4c–e** and **7c–e** were found to correlate well with the proportion of intermediate salts **3** and **6** generated during the alkylation step. In the ^{1}H spectra for N^3-alkylated salts **3** the signals for H-6 (δ 7.3–7.4), H-1′ (δ 6.1–6.2), and H-3′ (δ 5.7–5.8) are displaced 0.3, 0.4, and 0.6 ppm downfield from the corresponding signals in the spectrum of **1**. Although the C-1′ absorption is also

(14) Formation of these side products undoubtedly results from the use of an excess of the unstable triflate reagent (freshly prepared and vacuum transferred immediately before use[10]) which partially decomposes to triflic acid. Slight 5′-O deprotection was sometimes observed in the reactions of **2** with the other more stable triflates, presumably for the same reasons.

Table I. Proportion of N^3- versus O^4-Alkylation of Anhydronucleoside 1

entry	alkylating agent	pyrimidinium salts (ratio[a])	product (isolated yield,[b] %)
1	MSH		**5a** (66)
2	CH_3OTf	**3b:6b** (5.5:1)	**5b** (59), **8b** (–)
3	C_2H_5OTf	**3c:6c** (1:1.3)	**5c** (34), **8c** (33)
4	$C_5H_{11}OTf$	**3d:6d** (1:2.0)	**5d** (22), **8d** (47)
5	$(CH_3)_2OTf$	**3e:6e** (1:4.0)	**5e** + **8e** (62)[c]
6	$(EtO)_2P(O)CH_2OTf$		**20** (38), **8f** + **21** (17)[d]

[a] Estimated from the ^{1}H NMR spectrum of the intermediate salt mixtures. [b] Overall yield of deprotected products from **1** after separation by flash column chromatography. [c] Inseparable 1:4.1 mixture of **5e** and **8e** obtained. [d] **8f** and epimer **21** obtained as a 7:3 mixture.

observed to lower field for salts **3**, $\Delta\delta$ is small compared to the pronounced shift in C-3′ (δ 85 for **3** versus δ 76 for **1**). In contrast, C-3′ in **6** (δ 81) does not show such a marked downfield movement compared to **3**. The ^{1}H spectra of salts **6** also reflect the change in charge distribution on the pyrimidine ring with respect to **3**. Thus, H-6 (δ 8.3–8.4), H-1′ (δ 6.3–6.4), and H-3′ (δ 5.4–5.5) show, respectively, 1.3, 0.6, and 0.3 ppm shifts downfield from **1**. A subsequent reexamination of the reaction of methyl triflate with **1** revealed that both N^3- and O^4-alkylation occurs to the extent of about 5.5 to 1. These results, summarized in Table I, show that there is a clear trend toward increased O^4-alkylation of **1** with increasing size of ROTf.

Two features of these reactions are immediately striking: First, that O^4-alkylation competes, even predominates with the larger triflates, and second, that subsequent reaction of salts **3** and **6** with azide ion is both regio- and stereospecific.[15] Normally, alkylation of the N^3 position in the thymine ring is highly favored.[6] However, in its anhydro form, the thymine ring in **1** is effectively divided into two independently reacting components: an O-alkyl imidate function (N^3–C(2)–O^2) and a β-enamino ketone (N^1–C(6,5,4)–O^4). The alkylation of N,N-disubstituted β-enamino ketones is known to be facile, occuring almost exclusively at the oxygen center to give conjugated iminium salts,[16] whereas alkylation of imino ethers occurs at the nitrogen. Competition between these reaction modes can thus occur, and the steric bulk of the alkylating agent

(15) For complimentary cases where regiospecific introduction of a nucleophile at the anomeric center (i.e., glycoside bond formation) is achieved in an intramolecular sense, see: (a) Stork, G.; Kim, G. J. *Am. Chem. Soc.* **1992**, *114*, 1087. (b) Bols, M. *J. Chem. Soc., Chem. Commun.* **1992**, 913. (c) Barresi, F.; Hindsgaul, O. *J. Am. Chem. Soc.* **1991**, *113*, 9376.

(16) Meyers, A. I.; Reine, A. H.; Gault, R. *Tetrahedron Lett.* **1967**, 4049.

appears to be a factor which distinguishes the reactivity of the two systems.

In considering the site of azide reaction with intermediate **6**, a parallel can be drawn with the Hilbert–Johnson reaction in which a pyrimidinium salt analogous to **6** is generated through condensation of a 2,4-dialkoxypyrimidine with a glycosyl chloride.[17] It has been shown that the chloride ion produced in this process reacts in a second step with the imino ether system of this intermediate to liberate the C-2 carbonyl function of the nucleoside product. In our "intramolecular" case the equivalent reaction would convert intermediate **6** into the 3′-chloride **14**, Scheme II. It is remarkable, therefore, that the reaction of **6** with azide ion leads to **7** rather than O^4-alkyl AZT **9**. A probable explanation for this is that charge buildup on N^1 weakens the N^1–C-1′ bond making it more susceptible to reaction under kinetic control with highly nucleophilic azide ion. Solvent, DMF or CH_2Cl_2, does not seem to influence the regiochemistry of this reaction. Formation of the alternative product **9** would thus require conditions that would promote the reversion of **7** back to salt **6** and its subsequent reaction with azide ion at C-3′.[18] Similar arguments involving charge buildup at N^3 in intermediate **3** can be invoked to explain the unique formation of the N^3-substituted AZT derivatives **4** through C-3′ rather than C-1′ attack.

Another intermediate which may play an important role in the formation of compounds **7** from the pyrimidinium salts **6** is the oxonium ion **10**. If this species is present to any appreciable extent in the reaction medium formation of an anomeric mixture of C-1′ azide substituted products might be expected. The observed formation of a single isomer in the reaction of **6** with N_3^- thus favors an S_N2 type mechanism, but it does not exclude the participation of **10** as a transient intermediate in which access to the upper face is blocked by the O^2,O^4-dialkylthymine unit.[19]

The specificity for azide ion to react at C-1′ of **6** under the conditions employed suggests that the first step in the Hilbert–Johnson reaction involves an equilibrium between an intermediate pyridinium salt and the 2,4-dialkoxypyrimidine and glycosyl halide starting materials. One would further anticipate this equilibrium to be positioned well over toward the more stable pyrimidinium salt which would undergo subsequent and irreversible conversion into the nucleoside product. To examine this possibility within the context of the present study anhydronucleoside **1** was reacted with ethyl triflate (CH_2Cl_2, 0 °C) followed by treatment with thoroughly dried tetramethylammonium chloride in acetonitrile over powdered 4-Å sieves. Indeed, after 4 days at room temperature two new components were isolated (Scheme II), the first corresponding to N^3-ethyl 3′-chloride **13c** (40%) and the other to O^4-ethyl analog **14c** (12%), and not the unstable 1′-chloride **15**. An extremely polar residue also isolated was shown to be identical in its ^1H and ^{13}C NMR data with salt **6c** (ca. 45%). On repeating the reaction at higher temperature (4 d at 40 °C followed by 2 d at 80 °C), **13c** was again obtained (41%) together with the O^4-ethyl derivative **14c** in marginally improved yield (18%). However, two additional products, furan **16** (23%) and O^4-ethylthymine **17** (28%), were also isolated (overall material balance = 92%). Formation of **16** and **17** is believed to result from elimination reactions taking place either on the salt **6c** itself or the 1′-chloride **15**. These results, and in particular the recovery of significant quantities of intermediate **6c**, indicate that the displacement of the C-3′ oxygen substituent in **6c** by Cl^- is the rate-limiting step. A relatively slow reaction of Cl^- with the secondary C-3′ center in **6c** is in keeping with previous work on the Hilbert–Johnson reaction.[20]

Finally, reaction of **1** with the less reactive alkylating agent (diethylphosphono)methyltriflate[21] was studied. In this case, the rate of alkylation was notably slower. After 8 h at room temperature the solvent was exchanged for DMF and the intermediate mixture of N^3- and O^4-alkylated salts reacted with NaN_3 overnight. Two new products were isolated in approximately 1:1 ratio by flash column chromatography. The less polar component was identified from its spectral data as O^4-alkylated derivative **7f** (18%), Scheme II. The more polar product, however, was not the expected N^3-[(diethylphosphono)methyl] AZT derivative **4f** but the dimeric nucleoside **19** (40%), Scheme III. The NMR spectra of **19** (^1H, ^{13}C, ^1H–^1H, and ^1H–^{13}C 2D-correlation spectra) clearly exhibited the presence of two thymine rings, two sugar rings, and a single (diethylphosphono)methyl substituent linked at the N^3 rather than O^4 position. The ^{13}C spectrum showed one set of thymine ring signals characteristic of the N^3-alkylated products **4** while the other set closely matched the by now familiar pattern of the O^4-alkylated derivatives **7**, thus indicating that the N^3-alkylated portion of the molecule was linked to the other half of the dimeric structure at its O^4-position. This view was corroborated by the position of H-1′ (δ 5.67), H-3′ (δ 5.55), and H-6 (δ 8.02) of one set of signals which was strongly characteristic of the deoxyxylofuranosyl azide pattern found in **7**. Whereas H-1′ (δ 6.44) of the second sugar ring was close to the H-1′ region of N^3-alkylated products **4** (δ 6.1–6.2), the H-3′ signal (δ 5.55), consistent with 3′-O substitution, showed a significant displacement downfield from the normal position in **4** (δ 4.3–4.4). The FAB mass spectrum of **19** exhibited a parent ion at m/z 949 (MNa^+) and appropriate peaks for loss of the 5′-O protecting groups and cleavage of the O^4–C-3′ link between the two halves of the dimeric structure.

The mechanism leading to formation of **19**, Scheme III, is pictured to involve initial formation of the N^3-alkylated salt **3f** which, in the absence of added N_3^- ion and because the alkylation step is slow, reacts with a remaining molecule of the starting anhydronucleoside **1**, present in the medium. In view of the steric bulk of the salt **3f** it is not surprising that it "alkylates" **1** exclusively at the O^4 position leading to dimeric intermediate **18**. C-1′ attack of azide ion in the manner now established for O^4-alkylated salts **6** then converts **18** into the product **19**. It is interesting to observe that whereas the N^3-alkylated salt **3f** is sufficiently reactive to alkylate a second molecule of anhydronucleoside **1**, when present in the reaction mixture, no such reaction was observed for the O^4-alkylated salt **6f** which gave rise only to the monomeric product **7f**. Attempts to 5′-O deprotect **7f** and **19** with Dowex 50WX2 (H^+) resin in methanol led to decomposition. However, the use of TBAF in THF

(17) (a) Hilbert, G. E.; Johnson, T. B. *J. Am. Chem. Soc.* **1930**, *52*, 4489. (b) Ueda, T.; Ohtsuka, H. *Chem. Pharm. Bull.* **1973**, *21*, 1451 and 1530. (c) Pliml, J.; Prystas, M. *Adv. Hetereocycl. Chem.*, **1967**, *8*, 115.

(18) Studies directed toward the preparation of AZT by reaction of derivatives of type **7** (Nu = OBz) with azide ion under Lewis acid conditions are currently in progress in the laboratory of Prof. D. Liotta, Emory University. Private communication.

(19) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155.

(20) Prystas, M.; Sorm, F. *Collect. Czech. Chem. Commun.* **1966**, *31*, 1035.

(21) Andrew, S. S.; Phillion, D. P. *Tetrahedron Lett.* **1986**, *27*, 1477.

smoothly 5'-O deprotected **19** to dimer **20** in 96% yield. In contrast to this, TBAF deprotection of the monomeric product **7f** led to a 7:3 mixture of two isomeric deprotected products (95%) which were separated by HPLC. The major of the two products was shown to be **8f** while the minor component corresponds to its C-1' epimer **21**.[22] This unexpected result may conceivably arise from formation of a glycosyl fluoride under TBAF conditions. As this glycosyl fluoride would be relatively stable when compared, for example, to the corresponding chloride,[23] it is feasible that an intermediate pyrimidinium salt is not formed and that the liberated azide ion reacts directly with the C-1 center to produce the observed anomeric mixture of azides.[24]

Further work is in progress to explore the synthetic scope and mechanistic features of the reactions described in this paper. These results, as well as full details on the anti-HIV activity of 30 different N^3-substituted AZT derivatives, which display EC_{50} values of between 0.03 μM (**5a**) and 100 μM (**5b**), will be presented in the appropriate journal.

Experimental Section

General. NMR Spectra were recorded on Brucker WP-200, WP-250, or WP-400 instruments at 200, 250, or 400 MHz for ^1H and at 50.13 or 62.89 MHz for ^{13}C using deuterated solvents. Chemical shift data are reported in parts per million (δ in ppm) where s, d, dd, t, q, p, and m designate singlet, doublet, doublet of doublets, triplet, quartet, pentet, and multiplet, respectively. Infrared (IR) spectra were recorded on a Nicolet 205 FT IR spectrophotometer. Thin-layer chromatography (TLC) was performed using Merck 60 F_{254} (aluminum support, 0.2-mm thickness; Art. 5554) plates. Column chromatography over alumina was carried out with Merck neutral aluminum oxide 90 (Art. 1077) and flash column chromatography with Merck silica gel 60 (Art. 9385).[25] Mass spectra (MS) were recorded on an MS-9 AEI spectrometer for chemical ionization (CI) (isobutane as carrier gas unless otherwise stated) and a Kratos MS80RF spectrometer for fast atom bombardment (FAB) (4 kV, pos, thioglycerol). Elemental analyses were performed by the microanalysis laboratory at the ICSN.

Preparation of Compounds 4a–d, 7c–d, 7f, and 19. Typical Procedure. 3-Amino-3'-azido-3'-deoxy-5'-*O*-[dimethyl(1,1,2-trimethylpropyl)silyl]thymidine (4a). To a solution of anhydronucleoside 1 (100 mg, 0.272 mmol) in CH_2Cl_2 (2 mL) was added MSH[8,9] (58.7 mg, 0.272 mmol) at 0 °C under N_2. After 2 h the solvent was evaporated. The resulting solid residue was taken up in DMF (2 mL) and treated with NaN_3 (70.9 mg, 1.09 mmol) at 0 °C. After 16 h the solvent was removed in vacuo and the residue partitioned between CH_2Cl_2 and water. The organic phase was separated, dried (Na_2SO_4), and evaporated. Product **4a** was obtained as a colorless oil (104 mg; 90%) after flash column chromatography (silica gel; 25% EtOAc/heptane): IR (film) 2150, 1730–1680, 1480 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.15 (s, 6 H), 0.85–0.95 (m, 12 H), 1.65 (septet, J = 7 Hz, 1 H), 2.00 (s, 3 H), 2.17–2.30 (m, 1 H), 2.48 (dt, J = 14 and 5 Hz, 1 H), 3.80 (dd, J = 3 and 10 Hz, 1 H), 3.92–4.01 (m, 2 H), 4.23 (dt, J = 7 and 3 Hz, 1 H), 4.80 (br m, 2 H), 6.10 (t, J = 6 Hz, 1 H), 7.25 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ −3.41, −3.20, 13.25, 18.56, 20.35, 25.49, 34.11, 38.24, 60.37, 62.65, 84.70, 85.56, 109.52, 131.84, 148.41, 160.42; MS m/z (FAB) 447 (MNa^+), 425 (MH^+), 142.

3'-Azido-3'-deoxy-5'-*O*-[dimethyl(1,1,2-trimethylpropyl)silyl]-3-methylthymidine (4b). Compound 1 (100 mg, 0.272 mmol) was reacted with methyl triflate[10] (89.5 mg, 0.546 mmol) in CH_2Cl_2 (20 °C; 1 h) and, after solvent change to DMF, with NaN_3 (142 mg, 2.16 mmol). Product **4b** was obtained as a colorless oil (71 mg; 61%) after flash column chromatography (silica gel; 25% EtOAc/heptane): IR (film) 2102, 1700–1672, 1469 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.10 (s, 3 H), 0.87–0.90 (s, 12 H), 1.65 (septet, J = 7 Hz, 1 H), 1.95 (s, 3 H), 2.20 (dt, J = 14 and 6 Hz, 1 H), 2.45 (ddd, J = 4, 6 and 14 Hz, 1 H), 3.35 (s, 3 H), 3.75–3.95 (m, 3 H), 4.18–4.26 (m, 1 H), 6.25 (t, J = 6 Hz, 1 H), 7.35 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ −3.30, 13.34, 18.53, 20.32, 20.43, 25.44, 27.88, 34.09, 38.02, 60.40, 62.64, 84.45, 85.24, 110.10, 132.86, 151.31, 163.63; MS m/z (CI) 424 (MH^+), 141.

3'-Azido-3'-deoxy-5'-*O*-[dimethyl(1,1,2-trimethylpropyl)silyl]-3-ethylthymidine (4c) and 2,3-Dideoxy-5-*O*-[dimethyl(1,1,2-trimethylpropyl)silyl]-3-[(4-ethoxy-5-methyl-2-pyrimidinyl)oxy]-α-D-xylofuranosyl Azide (7c). Compound 1 (234 mg, 0.638 mmol) was reacted with ethyl triflate (166 μL, 1.28 mmol) in CH_2Cl_2 (0 °C; 1 h) followed by Amberlite IR 400 (N_3^-) resin[13] (2.04 g, ca. 5.11 mmol of N_3^-) for 16 h at 0 °C. Products **7c** (119 mg; 43%) and **4c** (99 mg; 36%) were isolated by flash column chromatography (silica gel; 10–20% EtOAc/heptane gradient) as colorless oils.

7c: IR (film) 2104, 1711, 1673, 1650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.00 and 0.06 (2 × s, 6 H), 0.74–0.81 (m, 12 H), 1.37 (t, J = 7 Hz, 3 H), 1.55 (septet, J = 7 Hz, 1 H), 2.03 (s, 3 H), 2.21 (ddd, J = 4, 6 and 14.5 Hz, 1 H), 2.39 (ddd, J = 3, 6 and 14.5 Hz, 1 H), 3.77–3.95 (m, 2 H), 4.31–4.43 (m, 3 H), 5.56–5.64 (m, 1 H), 5.67 (dd, J = 4 and 6 Hz, 1 H), 7.94 (s, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ −1.10, 13.52, 16.01, 19.99, 21.73, 26.46, 35.34, 41.11, 61.25, 62.97, 75.39, 77.77, 91.07, 110.64, 155.30, 160.74, 167.10; MS m/z (CI) 438 (MH^+), 155.

4c: IR (film) 2116, 1599, 1579, 1459 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.16 (s, 6 H), 0.88–0.91 (m, 12 H), 1.21 (t, J = 7 Hz, 3 H), 1.65 (septet, J = 7 Hz, 1 H), 1.93 (s, 3 H), 2.21 (dt, J = 14 and 6 Hz, 1 H), 2.44 (ddd, J = 4, 6 and 14 Hz, 1 H), 3.78 (dd, J = 3 and 12 Hz, 1 H), 3.81 (dd, J = 3 and 12 Hz, 1 H), 3.91–3.96 (m, 1 H), 3.99 (q, J = 7 Hz, 2H), 4.22 (dt, J = 7 and 4 Hz, 1 H), 6.21 (t, J = 7 Hz, 1 H), 7.30 (s, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ −2.97, 12.90, 13.31, 18.57, 20.38, 20.18, 25.51, 34.16, 36.58, 38.02, 60.45, 62.70, 84.42, 85.11, 110.38, 132.90, 150.12, 163.20; MS m/z (CI) 438 (MH^+), 155.

3'-Azido-3'-deoxy-5'-*O*-[dimethyl(1,1,2-trimethylpropyl)silyl]-3-pentylthymidine (4d) and 2,3-Dideoxy-5-*O*-[dimethyl(1,1,2-trimethylpropyl)silyl]-3-[(4-pentoxy-5-methyl-2-pyrimidinyl)oxy]-α-D-xylofuranosyl Azide (7d). Compound 1 (100 mg, 0.272 mmol) was reacted with pentyl triflate[10] (120 mg, 0.544 mmol) in CH_2Cl_2 (0 °C; 1 h) and, after solvent change to DMF, with NaN_3 (106 mg, 1.09 mmol). Products **7d** (76 mg; 58%) and **4d** (33 mg; 25%) were obtained as colorless oils after flash column chromatography (silica gel; 25% EtOAc/heptane).

7d: IR (film) 2110, 1605–1575, 1420 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.00 and 0.09 (2 × s, 6 H), 0.75–0.83 (m, 12 H), 0.95 (t, J = 7 Hz, 3 H), 1.35–1.45 (m, 4 H), 1.54 (septet, J = 7 Hz, 1 H), 1.77 (p, J = 7 Hz, 2 H), 2.04 (s, 3 H), 2.22 (ddd, J = 4, 6 and 14 Hz, 1 H), 2.40 (ddd, J = 4, 7 and 14 Hz, 1 H), 3.80–3.97 (m, 2 H), 4.28–4.41 (m, 3 H), 5.58–5.64 (m, 1 H), 5.67 (dd, J = 4 and 7 Hz, 1 H), 7.95 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ −3.37, 11.91, 14.07, 18.53, 20.31, 22.48, 25.13, 28.26, 28.53, 34.26, 40.17, 60.83, 66.87, 75.32, 81.84, 91.49, 111.50, 157.11, 162.87, 169.55; MS m/z (CI) 480 (MH^+), 197.

4d: IR (film) 2101, 1700–1672, 1454 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.17 (s, 6 H), 0.80–0.95 (m, 15 H), 1.25–1.38 (m, 4 H), 1.53–1.70 (m, 3 H), 1.94 (s, 3 H), 2.20 (dt, J = 14 and 7 Hz, 1 H), 2.45 (ddd, J = 4, 6 and 14 Hz, 1 H), 3.75–4.00 (m, 5 H), 4.25 (dt, J = 7 and 4 Hz, 1 H), 6.25 (t, J = 7 Hz, 1 H), 7.35 (s, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ −3.08, 13.33, 14.02, 18.62, 20.42, 20.51, 22.45, 25.56, 27.38, 29.21, 34.21, 38.07, 41.54, 60.47, 62.73, 84.47, 85.23, 110.32, 132.89, 150.89, 163.38; MS m/z (CI) 480 (MH^+), 197.

2,3-Dideoxy-3-[[4-[[(diethylphosphono)methyl]oxy]-5-methyl-2-pyrimidinyl]oxy]-5-*O*-[dimethyl(1,1,2-trimethylpropyl)silyl]-α-D-xylofuranosyl Azide (7f) and Dimer 19. Compound 1 (350 mg, 0.9552 mmol) was reacted with (diethylphosphono)methyl triflate[21] (573 mg, 1.91 mmol) in CH_2Cl_2 (20 °C; 8 h) and, after solvent change to DMF, with NaN_3 (372

(22) Jie, L.; Van Aerschot, A.; Balzarini, J.; Janssen, G.; Busson, R.; Hoogmartens, J.; De Clercq, E.; Herdewijn, P. *J. Med. Chem.* **1990**, *33*, 2481.

(23) Posner, G. H.; Haines, S. R. *Tetrahedron Lett.*, **1985**, *26*, 5 and references cited therein.

(24) Nicolaou, K. C.; Chucholowski, A.; Dolle, R. E.; Randall, J. L. *J. Chem. Soc., Chem. Commun.* **1984**, 1155.

(25) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

mg, 5.71 mmol) for 16 h at 0 °C. Products **7f** (94 mg; 18%) and **19** (177 mg; 40%) were obtained as colorless oils after column chromatography (neutral alumina; 60% EtOAc/heptane).

7f: IR (film) 2114, 1616–1569, 1417 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.01 and 0.05 (2 × s, 6 H), 0.74–0.80 (m, 12 H), 1.34 (t, J = 7 Hz, 6 H), 1.52 (septet, J = 7 Hz, 1 H), 1.98 (s, 1 H), 2.22 (ddd, J = 4, 6 and 14 Hz, 1 H), 2.36 (ddd, J = 3, 6 and 14 Hz, 1 H), 3.77–3.93 (m, 2 H), 4.13–4.25 (m, 4 H), 4.33 (q, J = 5 Hz, 1 H), 4.62–4.66 (m, 2 H), 5.56–5.62 (m, 1 H), 5.66 (dd, J = 4 and 6 Hz, 1 H), 7.98 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ −3.53, −3.40, 11.76, 16.52 (d, $^3J_{CP}$ = 4.5 Hz), 18.46, 20.25, 25.07, 34.17, 40.10, 59.35 (d, $^1J_{CP}$ = 168 Hz), 60.68, 62.85 (d, $^2J_{CP}$ = 5.5 Hz), 75.63, 81.63, 91.30, 111.47, 158.08, 162.56, 168.35; MS m/z (FAB) 582 (MNa^+), 560 (MH^+), 277.

19: IR (film) 2113, 1703, 1662, 1641, 1580, 1464 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) **N-alkylated portion** δ 0.00–0.22 (m, 6 H), 0.77–0.94 (m, 12 H), 1.31 (t, J = 6 Hz, 6 H), 1.67 (septet, J = 7 Hz, 1 H), 1.97 (s, 3 H), 2.12–2.26 (m, 1 H), 2.35 (ddd, J = 3, 6 and 14 Hz, 1 H), 3.80–3.95 (m, 3 H), 4.12–4.24 (m, 4 H), 4.42 (d, J = 12 Hz, 2 H), 5.52–5.58 (m, 1 H), 6.44 (dd, J = 6 and 9 Hz, 1 H), 7.55 (s, 1 H); **O-alkylated portion** δ 0.00–0.22 (m, 6 H), 0.77–0.94 (m, 12 H), 1.54 (septet, J = 7 Hz, 1 H), 2.07 (s, 3 H), 2.12–2.26 (m, 1 H), 2.56 (dd, J = 4 and 14 Hz, 1 H), 3.80–3.95 (m, 1 H), 4.05 (dd, J = 2.5 and 14 Hz, 1 H), 4.32 (q, J = 5 Hz, 1 H), 5.52–5.58 (m, 1 H), 5.67 (dd, J = 4 and 6 Hz, 1 H), 8.02 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) **N-alkylated portion** δ −3.57, −3.29, 13.21, 16.30 (d, $^3J_{CP}$ = 5.8 Hz), 18.41–18.52, 20.19–20.40, 24.95, 25.33, 34.00, 34.10, 36.40 (d, $^1J_{CP}$ = 155 Hz), 38.50, 62.54, 63.53, 77.12, 85.31, 85.68, 110.03, 133.25, 150.35, 162.39; **O-alkylated portion** δ −3.57, −3.29, 11.77, 18.41–18.52, 20.19–20.40, 24.95, 25.33, 34.00, 34.10, 40.15, 60.49, 75.35, 81.57, 91.26, 111.57, 158.04, 162.39, 167.99; MS m/z (FAB) 949 (MNa^+), 643, 582, 560, 517, 277.

Deprotection of Compounds 4a–d and 7c–d. Typical Procedure. 3-Amino-3'-azido-3'-deoxythymidine (5a). Dowex 50WX2 (H^+) beads (0.4 mL) were added to a solution of **4a** (74 mg, 0.174 mmol) in MeOH (2 mL). After 16 h the resin was removed by filtration and washed thoroughly with MeOH and the filtrate evaporated. Product **5a** was obtained as a colorless solid (36 mg; 73%) after flash column chromatography (silica gel; EtOAc): IR ($CHCl_3$) 3300, 2150, 1730–1680, 1480 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.95 (s, 3 H), 2.35–2.70 (m, 2 H), 3.00–3.50 (br m, 1 H), 3.80 (d, J = 10 Hz, 1 H), 3.93–4.04 (m, 2 H), 4.35–4.46 (m, 1 H), 4.50–5.00 (br m, 2 H), 6.10 (t, J = 6 Hz, 1 H), 7.45 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 13.09, 37.72, 59.83, 61.64, 84.81, 86.89, 109.43, 133.44, 148.49, 160.48; MS m/z (CI) 283 (MH^+), 142. Anal. Calcd for $C_{10}H_{14}N_6O_4$: C, 42.54; H, 5.00; N, 29.78. Found: C, 42.75; H, 4.92; N, 26.69.

3'-Azido-3'-deoxy-3-methylthymidine (5b). Silyl ether **4b** (130 mg, 0.307 mmol) was deprotected with Dowex resin to obtain **5b** as a colorless solid (76 mg; 88%) after flash column chromatography (silica gel; 70% EtOAc/heptane): IR ($CHCl_3$) 3450, 2125, 1686–1672 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.94 (s, 1 H), 2.40 (ddd, J = 5, 6 and 14 Hz, 1 H), 2.55 (ddd, J = 6, 7.5 and 14 Hz, 1 H), 2.74 (br m, 1 H), 3.34 (s, 3 H), 3.77–3.86 (m, 1 H), 3.95–4.03 (m, 2 H), 4.43 (dt, J = 7 and 5 Hz, 1 H), 6.05 (t, J = 6 Hz, 1 H), 7.37 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 13.36, 27.96, 37.44, 60.08, 62.13, 84.66, 87.75, 110.40, 134.73, 151.11, 163.60; MS m/z (CI) 282 (MH^+), 141. Anal. Calcd for $C_{11}H_{15}N_5O_4$: C, 46.96; H, 5.38; N, 24.91. Found: C, 47.28; H, 5.34; N, 25.07.

3'-Azido-3'-deoxy-3-ethylthymidine (5c). Silyl ether **4c** (130 mg, 0.297 mmol) was deprotected with Dowex resin to obtain **5c** as a colorless oil (84 mg; 96%) after flash column chromatography (silica gel; 55% EtOAc/heptane): IR (film) 3450, 2106, 1701, 1671, 1636, 1472, 1452 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.21 (t, J = 7 Hz, 3 H), 1.92 (d, J = 0.9 Hz, 3 H), 2.37–2.57 (m, 2 H), 3.41 (dd, J = 4 and 5.5 Hz, 1 H), 3.77–4.04 (m, 5 H), 4.41 (dt, J = 7 and 5 Hz, 1 H), 6.13 (t, J = 6 Hz, 1 H), 7.52 (d, J = 0.9 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.81, 13.24, 36.58, 37.56, 60.06, 61.94, 84.61, 86.93, 110.33, 134.66, 150.67, 163.31; MS m/z (CI) 296 (MH^+), 155. Anal. Calcd for $C_{12}H_{17}N_5O_4$: C, 48.81; H, 5.80; N, 23.72. Found: C, 48.87; H, 5.67; N, 23.56.

3'-Azido-3'-deoxy-3-pentylthymidine (5d). Silyl ether **4d** (167 mg, 0.348 mmol) was deprotected with Dowex resin to obtain **5d** as a colorless oil (101 mg; 86%) after flash column chromatography (silica gel; 40% EtOAc/heptane): IR (film) 3451, 2101, 1700–1672, 1454 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.88 (t, J = 7 Hz, 3 H), 1.20–1.43 (m, 4 H), 1.58 (p, J = 7 Hz, 2 H), 1.91 (s, 3 H), 2.31–2.59 (m, 2 H), 3.10 (br m, 1 H), 3.78–4.10 (m, 5 H), 4.40 (dt, J = 7 and 5 Hz, 1 H), 6.10 (t, J = 6 Hz, 1 H), 7.44 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 13.27, 13.95, 22.36, 27.25, 29.09, 37.54, 41.50, 60.02, 61.95, 84.60, 87.07, 110.29, 134.64, 150.83, 163.46; MS m/z (CI) 338 (MH^+). Anal. Calcd for $C_{15}H_{23}N_5O_4$: C, 53.38; H, 6.87; N, 20.76. Found: C, 53.15; H, 6.88; N, 21.01.

2,3-Dideoxy-3-[(4-ethoxy-5-methyl-2-pyrimidinyl)oxy]-α-D-xylofuranosyl Azide (8c). Silyl ether **7c** (100 mg, 0.229 mmol) was deprotected with Dowex resin to obtain **8c** as a colorless solid (52 mg; 77%) after flash column chromatography (silica gel; 55% EtOAc/heptane): IR ($CHCl_3$) 3223, 2099, 1609, 1580, 1636, 1427 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.41 (t, J = 7 Hz, 1 H), 2.05 (s, 3 H), 2.27 (ddd, J = 4, 6 and 14 Hz, 1 H), 2.42 (ddd, J = 3, 6 and 14 Hz, 1 H), 3.53–3.95 (m, 3 H), 4.37–4.48 (m, 3 H), 5.58 (dt, J = 6 and 3 Hz, 1 H), 5.76 (dd, J = 4 and 6 Hz, 1 H), 7.93 (s, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 11.90, 14.37, 40.24, 59.97, 62.90, 76.47, 81.66, 91.36, 112.34, 156.47, 163.00, 169.70; MS m/z (CI) 296 (MH^+), 155. Anal. Calcd for $C_{12}H_{17}N_5O_4$: C, 48.81; H, 5.80; N, 23.72. Found: C, 48.79; H, 5.76; N, 23.69.

2,3-Dideoxy-3-[(5-methyl-4-pentoxy-2-pyrimidinyl)oxy]-α-D-xylofuranosyl Azide (8d). Silyl ether **7d** (70 mg, 0.146 mmol) was deprotected with Dowex resin to obtain **8d** as a colorless solid (39 mg; 81%) after flash column chromatography (silica gel; 30% EtOAc/heptane): IR ($CHCl_3$) 3430, 2110, 1605–1575, 1420 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.92 (t, J = 7 Hz, 3 H), 1.33–1.48 (m, 4 H), 1.77 (p, J = 7 Hz, 2 H), 2.04 (s, 3 H), 2.28 (ddd, J = 4, 6 and 14 Hz, 1 H), 2.49 (ddd, J = 3, 6 and 14 Hz, 1 H), 3.10 (br m, 1 H), 3.68 (dd, J = 7 and 12 Hz, 1 H), 3.86 (dd, J = 5 and 12 Hz, 1 H), 4.34 (t, J = 7 Hz, 2 H), 4.36–4.43 (m, 1 H), 5.57 (dt, J = 6 and 3 Hz, 1 H), 5.75 (dd, J = 4 and 6 Hz, 1 H), 7.91 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 11.95, 14.06, 22.46, 28.22, 28.46, 40.27, 59.92, 67.22, 76.60, 81.69, 91.38, 112.50, 156.29, 162.93, 169.91; MS m/z (CI) 338 (MH^+), 197. Anal. Calcd for $C_{15}H_{23}N_5O_4$: C, 53.38; H, 6.87; N, 20.76. Found: C, 53.56; H, 6.78; N, 20.50.

Preparation of 3'-Azido-3'-deoxy-3-(1-methylethyl)thymidine (5e) + 2,3-Dideoxy-3-[[5-methyl-4-(1-methylethoxy)-2-pyrimidinyl]oxy]-α-D-xylofuranosyl Azide (8e) and 3'-Azido-3'-deoxy-3-(1-methylethyl)-5'-O-(1-methylethyl)thymidine (11e) + 2,3-Dideoxy-5-O-(1-methyl-3-[[5-methyl-4-(1-methylethoxy)-2-pyrimidinyl]oxy]-α-D-xylofuranosyl Azide (12e). To a solution of **1** (478 mg, 1.30 mmol) in CH_2Cl_2 (10 mL) at 0 °C under N_2 was added freshly prepared isopropyl triflate[10] (568 mg, 2.96 mmol) followed after 2 h by Amberlite IR 400 (N_3^-) resin[13] (3.50 g, ca. 8.75 mmol of N_3^-). The reaction mixture was warmed to 20 °C, and after 16 h the resin was removed by filtration and the filtrate evaporated. The residual oil was taken up in THF (10 mL) and deprotected with TBAF (1 M THF; 1.75 mL, 1.75 mmol) at 0 °C. After 3 h the solvent was removed in vacuo to afford, after flash column chromatography (silica gel; 15–50% EtOAc/heptane gradient), a 6.2:1 mixture of **12e** and **11e** (129 mg; 28%) as a colorless oil followed by a 4.1:1 mixture of **8e** and **5e** (251 mg; 62%), also a colorless oil.

8e/5e mixture: IR (film) 3360, 2111, 1699–1603, 1574 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) major product **8e** (80%) δ 1.33 (d, J = 7 Hz, 6 H), 1.99 (s, 3 H), 2.23 (ddd, J = 4, 6 and 15 Hz, 1 H), 2.46 (ddd, J = 3, 7 and 15 Hz, 1 H), 3.66–3.96 (m, 3 H), 4.34–4.40 (m, 1 H), 5.34 (septet, J = 6 Hz, 1 H), 5.49–5.55 (m, 1 H), 5.72 (dd, J = 4 and 6 Hz, 1 H), 7.88 (s, 1 H); minor product **5e** (20%) δ 1.41 (d, J = 7 Hz, 3 H), 2.35–2.65 (m, 2 H), 3.55–4.55 (m, 4 H), 5.15 (septet, J = 6 Hz, 1 H), 6.12 (t, J = 6 Hz, 1 H), 7.44 (s, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ major product **8e** δ 11.95, 21.90, 40.21, 59.90, 69.83, 76.32, 81.52, 91.33, 112.21, 156.46, 162.85, 169.17; MS m/z (CI) 310 (MH^+), 169. Anal. Calcd for $C_{13}H_{19}N_5O_4$: C, 50.48; H, 6.19; N, 22.64. Found (for isomeric mixture): C, 50.35; H, 6.04; N, 22.72.

12e/11e mixture: IR (film) 2111, 1603, 1570 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) major product **12e** (86%) δ 1.07 (d, J = 6 Hz, 3 H), 1.15 (d, J = 6 Hz, 3 H), 1.37 (d, J = 6 Hz, 6 H), 2.03 (s, 3 H), 2.27 (ddd, J = 3.5, 6 and 14.5 Hz, 1 H), 2.42 (ddd, J = 3.5, 6 and 14.5 Hz, 1 H), 3.59 (septet, J = 7 Hz, 1 H), 3.65–3.79 (m, 2 H), 4.47 (q, J = 5 Hz, 1 H), 5.37 (septet, J = 7 Hz, 1 H), 5.60–5.67 (m, 1 H), 5.72 (dd, J = 4 and 6.5 Hz, 1 H), 7.97 (s, 1 H); minor

product **11e** (14%) δ 1.22–1.25 (m, 6 H), 1.45 (d, J = 6 Hz, 6 H), 1.92 (s, 3 H), 2.26–2.48 (m, 2 H), 3.55–3.83 (m, 3 H), 3.99–4.04 (m, 1 H), 4.28 (q, J = 5.5 Hz, 1 H), 5.19 (septet, J = 7 Hz, 1 H), 6.28 (t, J = 6 Hz, 1 H), 7.61 (s, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) major product **12e** δ 11.91, 21.95, 40.05, 66.11, 69.48, 72.17, 75.47, 80.41, 91.43, 111.70, 157.31, 162.71, 168.82; MS m/z (CI) 352 (MH^+), 169. Anal. Calcd for $C_{16}H_{25}N_5O_4$: C, 54.69; H, 7.17; N, 19.93. Found (for isomeric mixture): C, 54.45; H, 7.11; N, 19.99.

Deprotection of 7f. Preparation of 2,3-Dideoxy-3-[[4-[[(diethylphosphono)methyl]oxy]-5-methyl-2-pyrimidinyl]-oxy]-α-D-xylofuranosyl Azide (8f) and 2,3-Dideoxy-3-[[4-[[(diethylphosphono)methyl]oxy]-5-methyl-2-pyrimidinyl]oxy]-β-D-xylofuranosyl Azide (21). TBAF (1 M THF; 460 μL, 0.46 mmol) was added to a solution of **7f** (0.140 g, 0.250 mmol) in THF (2 mL). After 1.5 h the reaction mixture was neutralized by addition of aqueous 1 N HCl and the solvent removed in vacuo to afford a 7:3 mixture of products **8f** and **21** (colorless oil; 99 mg; 95%) after short column chromatography (silica gel; 2% MeOH/EtOAc) to remove polar contaminants. Subsequent separation of **8f** from **21** was made by HPLC [Novopak C18 column (3.9 × 150 mm) (H_2O/MeOH/AcOH = 60/40/0.2); elution rate 1 mL/min].

8f (retention time = 6 min 30 s): IR (film) 3402, 2114, 1616–1569, 1417 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.35 (t, J = 7 Hz, 6 H), 2.12 (s, 3 H), 2.29 (ddd, J = 4, 6 and 14 Hz, 1 H), 2.49 (ddd, J = 4, 6 and 14 Hz, 1 H), 3.15 (br m, 1 H), 3.70 (dd, J = 6 and 12 Hz, 1 H), 3.87 (dd, J = 5 and 12 Hz, 1 H), 4.13–4.31 (m, 4 H), 4.36–4.44 (m, 1 H), 4.69 (d, J = 9 Hz, 2 H), 5.57–5.63 (m, 1 H), 5.76 (dd, J = 4 and 6 Hz, 1 H), 8.00 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 11.87, 16.55 (d, $^3J_{CP}$ = 5.7 Hz), 40.23, 59.65 (d, $^1J_{CP}$ = 171 Hz), 60.15, 62.98 (d, $^2J_{CP}$ = 6.0 Hz), 76.65, 81.53, 91.75, 112.49, 157.65, 162.77, 168.19; MS m/z (FAB) 440 (MNa^+), 418 (MH^+), 277. Anal. Calcd for $C_{15}H_{24}N_5O_7P$: C, 43.17; H, 5.80; N, 16.78. Found: C, 43.45; H, 5.62; N, 16.55.

21 (retention time = 10 min 12 s): IR (film) 3375, 2114, 1609–1569, 1417 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.35 (t, J = 7 Hz, 6 H), 1.99–2.15 (m, 1 H), 2.12 (s, 3 H), 2.31 (dd, J = 6 and 14 Hz, 1 H), 4.16–4.28 (m, 4 H), 4.28–4.38 (m, 2 H), 4.48 (dd, J = 4 and 11 Hz, 1 H), 4.69 (d, J = 9 Hz, 2 H), 4.77 (dd, J = 8 and 11 Hz, 1 H), 5.69 (t, J = 6 Hz, 1 H), 7.99 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 11.93, 16.60 (d, $^3J_{CP}$ = 5.2 Hz), 41.65, 59.71 (d, $^1J_{CP}$ = 171 Hz), 63.03 (d, $^2J_{CP}$ = 5.5 Hz), 64.36, 70.78, 80.81, 91.79, 112.30, 157.18, 163.20, 168.91; MS m/z (CI) 418 (MH^+), 277. Anal. Calcd for $C_{15}H_{24}N_5O_7P$: C, 43.17; H, 5.80; N, 16.78. Found: C, 43.29; H, 5.68; N, 16.47.

Deprotection of 19. Preparation of Dimer 20. TBAF (1 M THF; 300 μL, 0.300 mmol) was added to a solution of **19** (153 mg, 0.165 mmol) in THF (2 mL). After 1.5 h the reaction mixture was neutralized by addition of aqueous 1 N HCl and the solvent removed in vacuo to afford product **20** as a colorless solid (102 mg; 96%) after flash column chromatography (silica gel; 2% MeOH/EtOAc): IR ($CHCl_3$) 3371, 2113, 1703, 1662, 1641, 1580, 1464 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) **N-alkylated portion** δ 1.33 (t, J = 7 Hz, 6 H), 1.95 (s, 3 H), 2.38–2.57 (m, 2 H), 3.25 (br m, 1 H), 3.94–3.98 (m, 2 H), 4.14–4.25 (m, 5 H), 4.40 (d, J = 12.5 Hz, 2 H), 5.64 (m, 1 H), 6.34 (dd, J = 6 and 8 Hz, 1 H), 7.65 (s, 1 H); **O-alkylated portion** δ 2.07 (s, 3 H), 2.23–2.33 (m, 1 H), 2.38–2.57 (m, 1 H), 3.25 (br m, 1 H), 3.70 (dd, J = 7 and 12 Hz, 1 H), 3.86 (dd, J = 5 and 12 Hz, 1 H), 4.35–4.45 (m, 1 H), 5.53–5.67 (m, 1 H), 5.74 (dd, J = 4 and 6 Hz, 1 H), 8.00 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) **N-alkylated portion** δ 13.19, 16.32 (d, $^3J_{CP}$ = 5.7 Hz), 36.51 (d, $^1J_{CP}$ = 156 Hz), 38.12, 62.25, 62.80 (d, $^2J_{CP}$ = 5.2 Hz), 77.21, 85.27, 86.44, 110.19, 134.51, 150.49, 162.51, 162.59; **O-alkylated portion** δ 11.83, 40.20, 60.06, 76.58, 81.41, 91.30, 112.34, 157.61, 162.51, 162.59, 167.99; MS m/z (FAB) 664 (MNa^+), 642 (MH^+). Anal. Calcd for $C_{25}H_{36}N_7O_{11}P$: C, 46.80; H, 5.66; N, 15.28. Found: C, 47.17; H, 5.62; N, 14.98.

NMR Scale Preparations of Pyrimidinium Salts 3b–e/6b–e. Pyrimidinium Salts 3b/6b. Methyl triflate (37.0 mg, 225 μmol) was introduced to a solution of **1** (37.0 mg, 101 μmol) in $CDCl_3$ in a dry NMR tube at 0 °C. After 2.5 h the reaction mixture was examined on the spectrometer: ^{1}H NMR (250 MHz) major product **3b** (85%) δ −0.08 and 0.03 (2 × s, 6 H), 0.76–0.82 (m, 12 H), 1.55 (septet, J = 7 Hz, 1 H), 2.02 (s, 3 H), 2.75 (dt, J = 14 and 1.5 Hz, 1 H), 3.09 (d, J = 14 Hz, 1 H), 3.84 (dd, J = 7 and 11 Hz, 1 H), 4.02 (dd, J = 3 and 11 Hz, 1 H), 4.20 (s, 3 H), 4.44–4.47 (m, 1 H), 5.79 (s, 1 H), 6.16 (d, J = 1.5 Hz, 1 H), 7.68 (s, 1 H); minor product **6b** (15%) δ 2.15 (s, 3 H), 3.90 (s, 3 H), 5.50 (s, 1 H), 6.34 (d, J = 1.5 Hz, 1 H), 8.27 (s, 1 H); ^{13}C NMR (63 MHz) major product **3b** δ −3.67, −3.51, 12.89, 18.31, 18.46, 20.11, 20.43, 25.59, 29.31, 32.54, 33.98, 60.01, 84.81, 85.22, 90.31, 118.87, 136.37, 154.56, 159.20; minor product **6b** δ 11.70, 32.94, 60.16, 61.76, 80.69, 86.27, 90.93, 145.68.

Pyrimidinium salts 3c/6c. Ethyl triflate (41.2 mg, 231 μmol) was introduced to a solution of **1** (40.5 mg, 111 μmol) in $CDCl_3$ in a dry NMR tube at 0 °C. After 3 h the reaction mixture was examined on the spectrometer: ^{1}H NMR (250 MHz) minor product **3c** (43%) δ −0.05 to +0.05 (2 × s, 6 H), 0.78–0.84 (m, 12 H), 1.43–1.55 (m, 3 H), 2.02 (s, 3 H), 2.77 (br d, J = 14 Hz, 1 H), 3.14 (d, J = 14 Hz, 1 H), 3.76 (dd, J = 7 and 11.5 Hz, 1 H), 4.00 (dd, J = 4 and 11.5 Hz, 1 H), 4.43–4.46 (m, 1 H), 4.55–4.66 (m, 2 H), 5.82 (s, 1 H), 6.19 (d, J = 1.5 Hz, 1 H), 7.70 (s, 1 H); major product **6c** (57%) δ −0.05 to +0.05 (2 × s, 6 H), 0.78–0.84 (m, 12 H), 1.43–1.55 (m, 3 H), 2.14 (s, 3 H), 2.77 (br d, J = 14 Hz, 1 H), 2.90 (d, J = 14 Hz, 1 H), 3.66 (dd, J = 7 and 11.5 Hz, 1 H), 3.92 (dd, J = 4 and 11.5 Hz, 1 H), 4.43–4.46 (m, 1 H), 4.55–4.66 (m, 2 H), 5.49 (s, 1 H), 6.37 (d, J = 1.5 Hz, 1 H), 8.29 (s, 1 H); ^{13}C NMR (63 MHz) minor product **3c** δ −3.64, 12.36, 12.91, 18.37–18.46, 20.17–20.40, 25.38, 32.62, 34.12, 39.35, 60.08, 84.70, 85.47, 90.39, 119.32, 136.64, 154.20, 164.25; major product **6c** δ −3.64, 13.92, 18.37–18.46, 20.17–20.40, 25.38, 32.47, 34.02, 60.16, 67.20, 80.53, 86.27, 90.88, 119.24, 145.67, 155.85, 173.02.

Pyrimidinium Salts 3d/6d. Pentyl triflate (38.0 mg, 173 μmol) was introduced to a solution of **1** (39.5 mg, 108 μmol) in $CDCl_3$ in a dry NMR tube at 0 °C. After 2.5 h the reaction mixture was examined on the spectrometer: ^{1}H NMR (250 MHz) minor product **3d** (33%) δ −0.01 to +0.04 (m, 6 H), 0.73–0.97 (m, 15 H), 1.23–1.43 (m, 4 H), 1.53 (septet, J = 7 Hz, 1 H), 1.80 (p, J = 7 Hz, 2 H), 2.03 (s, 3 H), 2.78 (br d, J = 14 Hz, 1 H), 3.12 (d, J = 14 Hz, 1 H), 3.76 (dd, J = 7 and 11 Hz, 1 H), 3.98 (dd, J = 4 and 11 Hz, 1 H), 4.33–4.55 (m, 3 H), 5.82 (s, 1 H), 6.23 (d, J = 1.5 Hz, 1 H), 7.72 (s, 1 H); major product **6d** (67%) δ −0.01 to +0.04 (m, 6 H), 0.73–0.97 (m, 15 H), 1.23–1.43 (m, 4 H), 1.53 (septet, J = 7 Hz, 1 H), 1.80 (p, J = 7 Hz, 1 H), 2.15 (s, 3 H), 2.78 (br d, J = 14 Hz, 1 H), 2.90 (d, J = 14 Hz, 1 H), 3.66 (dd, J = 7 and 11 Hz, 1 H), 3.92 (dd, J = 4 and 11 Hz, 1 H), 4.33–4.55 (m, 3 H), 5.49 (s, 1 H), 6.39 (d, J = 1.5 Hz, 1 H), 8.30 (s, 1 H); ^{13}C NMR (63 MHz) minor product **3d** δ −3.60, 12.94, 13.88, 18.49, 20.21–20.33, 25.39–25.47, 22.01–29.80, 32.69, 34.13, 43.94, 60.18, 84.75, 85.56, 90.41, 118.05–120.40, 136.76, 154.18, 158.96; major product **6d** δ −3.60, 11.77, 13.88, 18.49, 20.21–20.33, 25.39–25.47, 22.01–29.80, 32.53, 34.13, 60.18, 71.22, 80.59, 86.25, 90.91, 118.05–120.40, 145.76, 155.87, 173.13.

Pyrimidinium Salts 3e/6e. Isopropyl triflate (52.0 mg, 271 μmol) was introduced to a solution of **1** (33.5 mg, 91.4 μmol) in $CDCl_3$ in a dry NMR tube at 0 °C. After 3 h the reaction mixture was examined on the spectrometer: ^{1}H NMR (250 MHz) minor product **3e** (20%) δ 1.56 (d, J = 6 Hz, 1 H), 2.02 (s, 3 H), 5.79 (s, 1 H), 6.35 (d, J = 1.5 Hz, 1 H), 7.65 (s, 1 H); major product **6e** (80%) δ −0.01 and 0.04 (2 × s, 6 H), 0.78–0.85 (m, 12 H), 1.41 (septet, J = 7 Hz, 1 H), 1.55 (d, J = 6 Hz, 6 H), 2.12 (s, 3 H), 2.78 (br d, J = 14 Hz, 1 H), 2.90 (d, J = 14 Hz, 1 H), 3.64 (dd, J = 7 and 11 Hz, 1 H), 3.92 (dd, J = 4 and 11 Hz, 1 H), 4.41–4.47 (m, 1 H), 5.20 (septet, J = 6 Hz, 1 H), 5.48 (s, 1 H), 6.35 (d, J = 1.5 Hz, 1 H, 8.25 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) minor product **3e** δ 13.05, 32.83, 53.45, 60.12, 84.42, 85.23, 90.53, 136.64; major product **6e** δ −3.65, 11.80, 18.45, 20.21–20.32, 21.48, 23.07, 25.38, 32.47, 34.16, 60.12, 75.92, 80.48, 86.24, 90.81, 119.28–120.34, 145.53, 155.85, 172.65.

Reaction of Pyrimidinium Salts 3c/6c with Cl$^-$ at Room Temperature. 3′-Chloro-3′-deoxy-5′-*O*-[dimethyl(1,1,2-trimethylpropyl)silyl]-3-ethylthymidine (13c) and 3′-Chloro-3′-deoxy-5′-*O*-[dimethyl(1,1,2-trimethylpropyl)silyl]-*O*^{4}-ethylthymidine (14c). To a solution of **1** (514 mg, 1.40 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added ethyl triflate (365 μL, 2.82 mmol). After 2 h the reaction mixture was transferred under N_2 to a vigorously stirred suspension of dry Me_4NCl (0.92 g, 8.4 mmol) and powdered 4-Å sieves (3.5 g) in dry acetonitrile (50 mL) at 20 °C. After 4 d the reaction mixture was filtered and the filtrate evaporated. The residue was flash column chromatographed (silica gel; 15% EtOAc/heptane to 10% MeOH/EtOAc gradient) to afford successively **13c** (258 mg, 40%) and

14c (79 mg, 12%) as colorless oils followed by a colorless solid (275 mg, ca. 45%) identical in ^1H and ^{13}C NMR data with salt 6c.

13c: IR (film) 1705, 1671, 1641 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.17 (s, 6 H), 0.89 (s, 12 H), 1.22 (t, J = 7 Hz, 3 H), 1.65 (septet, J = 5.5 Hz, 1 H), 2.43 (dt, J = 14 and 6 Hz, 1 H), 2.62 (ddd, J = 5, 6 and 14 Hz, 1 H), 3.84 (dd, J = 2.5 and 11 Hz, 1 H), 3.93 (dd, J = 2 and 11 Hz, 1 H), 4.01 (q, J = 7 Hz, 2 H), 4.18 (dt, J = 5 and 2 Hz, 1 H), 4.43 (dt, J = 7 and 4.5 Hz, 1 H), 6.37 (t, J = 6 Hz, 1 H), 7.39 (s, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ −2.94, 12.89, 13.30, 18.54, 20.35, 20.47, 25.51, 34.14, 36.55, 42.08, 54.58, 62.07, 84.96, 87.78, 110.34, 132.93, 150.70, 163.19; MS m/z (CI) 431 and 433 (MH^+), 155. Anal. Calcd for $C_{20}H_{35}N_2O_4SiCl$: C, 55.73; H, 8.18; N, 6.50. Found: C, 55.93; H, 7.95; N, 6.45.

14c: IR (film) 1674, 1538 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.11 (s, 6 H), 0.82 (s, 12 H), 1.32 (t, J = 7 Hz, 3 H), 1.58 (septet, J = 7 Hz, 1 H), 1.89 (s, 3 H), 2.39 (dt, J = 14 and 6.5 Hz, 1 H), 2.71 (dt, J = 14 and 6.5 Hz, 1 H), 3.80 (dd, J = 2 and 12 Hz, 1 H), 3.92 (dd, J = 1.5 and 12 Hz, 1 H), 4.11–4.14 (m, 1 H), 4.30 (q, J = 6 Hz, 1 H), 4.39 (q, J = 7 Hz, 2 H), 6.25 (t, J = 5.5 Hz, 1 H), 7.66 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ −3.49, −3.35, 12.33, 14.23, 18.48, 20.19, 20.35, 25.37, 33.96, 42.66, 53.76, 61.59, 63.26, 85.72, 87.91, 104.46, 138.85, 155.80, 170.47; MS m/z (CI) 433 and 431 (MH^+), 155. Anal. Calcd for $C_{20}H_{35}N_2O_4SiCl$: C, 55.73; H, 8.18; N, 6.50. Found: C, 55.78; H, 7.96; N, 6.57.

Reaction of Salts 3c/6c with Cl^- at Elevated Temperature. 2-[[[Dimethyl(1,1,2-trimethylpropyl)silyl]oxy]methyl]-furan (16) and 4-Ethoxy-5-methyl-2(1*H*)-pyrimidinone (17). To a solution of 1 (521 mg, 1.42 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added ethyl triflate (400 μL, 3.09 mmol). After 2 h the reaction mixture was transferred under N_2 to a vigorously stirred suspension of dry Me_4NCl (1.16 g, 10.6 mmol) and powdered 4-Å sieves (4.30 g) in dry acetonitrile (50 mL) at 20 °C. After 30 min the reaction mixture was heated at 40 °C for 4 d and then 80 °C for 2 d and finally cooled, filtered, and evaporated. The residual oil was flash column chromatographed (15% EtOAc/heptane to 10% MeOH/EtOAc gradient) to afford successively **16** (79 mg, 23%), **13c** (250 mg, 41%), and **14c** (112 mg, 18%) as colorless oils followed by **17** (62 mg, 28%) and residual salt **6c** (31 mg, ca. 5%) as colorless solids.

16: IR (film) 2960, 2868, 1466, 1253, 1151, 1075, 832 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.14 (s, 6 H), 0.88–0.92 (m, 12 H), 1.65 (septet, J = 7 Hz), 4.64 (s, 2 H), 6.24 (d, J = 3 Hz, 1 H), 6.32 (d, J = 2 Hz, 1 H), 7.38 (s, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ −3.21, 18.59, 20.40, 34.25, 58.06, 107.13, 110.24, 142.01, 154.62; MS m/z (EI) 225 ($M - CH_3$)$^+$, 155, 81. Anal. Calcd for $C_{13}H_{24}O_2Si$: C, 64.95; H, 10.06. Found: C, 65.09; H, 10.23.

17:[26] IR (Nujol) 3212, 1731, 1664, 1626, 1541 cm^{-1}; ^1H NMR (250 MHz, CD_3OD) δ 1.38 (t, J = 7 Hz, 3 H), 1.94 (s, 3 H), 4.42 (q, J = 7 Hz, 2H), 7.48 (s, 1 H); ^{13}C NMR (63 MHz, CD_3OD) δ 11.84, 14.42, 64.30, 106.24, 142.97, 160.64, 173.61; MS (EI) 154 (M^+). Anal. Calcd for $C_7H_{10}N_2O_2$: C, 54.54; H, 6.54; N, 18.17. Found: C, 54.60; H, 6.52; N, 18.35.

X-ray Crystallographic Analysis of 8d. $C_{15}H_{23}N_5O_4$, MW = 337.38. Crystal of 0.09 × 0.25 × 0.31 mm, monoclinic, space group $P2_1$ with a = 14.803(11) Å, b = 7.825(5) Å, c = 16.030(10) Å, β = 104.91(3)°, V = 1794.3 Å^3, Z = 4 (two molecules in the asymmetric unit), d_{calc} = 1.25 g cm^{-3}, λ (Cu Kα) = 1.5418 Å, μ = 0.73 mm^{-1} (absorption ignored).

Intensity data were measured on an Enraf-Nonius CAD-4 diffractometer using graphite-monochromated Cu Kα radiation and the $\theta-2\theta$ scans, up to θ = 65°. Of the 6083 collected reflections ($-17 \le h \le 16$, k:0 → 9, l:0 → 18), 3286 were unique (R_{int} = 0.047) and 2465 were considered as observed having $I \ge 3\sigma(I)$. Cell parameters were refined from 25 well-centered reflections with $11.4 < \theta < 17.9°$. The structure was solved by direct methods using SHELX86[27] and refined by least-squares using SHELX76[28] to an R value of 0.056, Rw = 0.083 (with $w = 1/\sigma^2(F_o) + 0.0045F_o^2$). Most of the hydrogen atoms were located on successive difference maps; however, they were included in the refinement at theoretical positions (d C–H = 1.00 Å), except those for the hydroxyl groups 5'-OH which were refined. They were assigned an isotropic thermal factor equivalent to that of the bonded atom (+10%). The residual electron density in the final difference map was located between −0.22 and 0.39 e Å^{-3}.

The authors have deposited atomic coordinates, bond lengths, bond and torsion angles, and anisotropic thermal factors for this structure at 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.

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Supplementary Material Available: ^1H spectra for compounds **4a-d**, **7c**, **7d**, **7f**, and **19** as well as a more detailed experimental section giving the NMR peak assignments for all products described (26 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.

(26) For a preparation of this compound see: Wittenburg, E. *J. Prakt. Chem.* **1966**, *33*, 165.

(27) Sheldrick, G. M. (1986). SHELX86. Program for the solution of Crystal Structures; University of Gottingen, Germany.

(28) Sheldrick, G. M. (1976). SHELX76. Program for Crystal Structure Determination; University of Cambridge, England.