Synthesis and Anti-HIV Activity of 4′-Substituted 4′-Thiothymidines: A New Entry Based on Nucleophilic Substitution of the 4′-Acetoxy Group

Kazuhiro Haraguchi,*[,†] Hisashi Shimada,[†] Hiromichi Tanaka,[†] Takayuki Hamasaki,[‡] Masanori Baba,[‡] Elizabeth A. Gullen,[§] Ginger E. Dutschman,[§] and Yung-Chi Cheng[§]

School of Pharmaceutical Sciences, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142-8555, Japan, Division of Antiviral Chemotherapy, Center for Chronic Viral Diseases, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima 890-8544, Japan, and Department of Pharmacology, School of Medicine, Yale University, New Haven, Connecticut 06520

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Diacetoxylation of 1-(2,5-dideoxy-β-L-*glycero*-pent-4-eno-4-thiofuranosyl)thymine (**13**) with $Pb(OAc)_4$ allowed introduction of an acetoxy leaving group to the 4′-position. Nucleophilic substitution of the resulting 4′-acetoxy derivative (**14**) with silicon reagents enabled us to prepare the 4′-phenylthio (**17a**), 4′-azido (**18a**), 4′-methoxy (**20a**), and 4′-allyl (**21a**) analogues of 4′-thiothymidine. 4′-Cyano (**25a**) and 4′-ethynyl (**31**) nucleosides were also synthesized from 3′,5′-bis-*O*-TBDMS derivative (**24**). Among novel 4′-substituted 4′-thiothymidines, the 4′-azido (**33**), 4′-cyano (**36**), and 4′-ethynyl (**37**) derivatives were found to show potent inhibitory activity against HIV-1 and HIV-2. It is noteworthy that **36** and **37** were also inhibitory against replication of HIV variant resistant to 3TC ($HIV\text{-}1_{M184V}$), being as potent as against $HIV\text{-}1_{IIIB}$.

Introduction

Nucleoside analogues are recognized as an important class of biologically active compounds, especially as antiviral and antitumor agents.[1] Among the sugar-modified nucleosides, 4′-thionucleosides, in which the oxygen atom in the furanose ring is replaced with sulfur atom, have attracted much attention since the discovery that 4′-thiothymidine (**1**) and 4′-thio-2′-deoxycytidine (**2**) possess potent antiviral and antitumor activities (Figure 1).[2]

Although many reports have dealt with the synthesis of 4′-thionucleoside analogues, the availability of their 4′-substituted derivatives has been quite limited,[3–5] 2′-deoxy-4′-methyl-4′-thiopyrimidine nucleosides (**I**) being the sole precedent.[6] In this instance, Vorbrüggen-type glycosidation was applied to the reaction between a 2-deoxy-4-methyl-4-thiofuranosyl derivative and a pyrimidine base, but the undesired α-anomer was also formed.

Recently, it has been reported that 4′-substituted nucleoside such as the 4′-azido (**3**), 4′-methoxy (**4**), 4′-cyano (**5**), and 4′-ethynyl (**6**) analogues of thymidine exhibit potent anti-HIV activity.[7] These findings motivated us to synthesize their 4′-thio counterparts. We describe here a novel method for the synthesis of 4′-thiothymidines having a variety of 4′-substituents and their inhibitory activity against HIV.

The present method consists of the following two reactions shown in Scheme 1: (1) $Pb(OAc)_4$-mediated vicinal diacetoxylation of a 4′,5′-unsaturated 4′-thiothymidine derivative **II** and (2) nucleophilic substitution of the resulting 4′-acetoxy analogue **III** with silicon reagents to furnish the target molecule **IV**.

Results and Discussion

Preparation of 4′,5′-Unsaturated 4′-Thiothymidine (13), the Substrate for Vicinal Diacetoxylation. Compound **13**, 1-(2,5-dideoxy-β-L-*glycero*-pent-4-eno-4-thiofuranosyl)thymine, was prepared from the TIPDS (1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-protected 4-thiofuranoid glycal (**7**) on the basis of electrophilic glycosidation. We have already reported that PhSeCl-mediated glycosidation between **7** and silylated uracil gave both the β- and α-anomers in a ratio of $\beta/\alpha = 18/1$.[8] When the present reaction of **7** with silylated thymine was carried out using *N*-iodosuccinimide (NIS) as an electrophile, the β-anomer (**8**) was obtained exclusively in 75% yield (Scheme 2). Subsequent radical reduction of **8** with $Bu_3SnH/Et_3B/O_2$ gave the 4′-thiothymidine derivative (**9**) in 98% yield. Compound **9** was desilylated with Bu_4NF in the presence of Ac_2O to give the 3′,5′-di-*O*-acetyl derivative (**10**, 93%). Deacetylation of **10** followed by iodination with I_2/PPh_3 gave 5′-deoxy-5′-iodo-4′-thiothymidine (**11**, 81%). Attempted elimination of HI from **11** by treatment with NaOMe/MeOH resulted in an intractable mixture of products. Therefore, **11** was converted to its 3′-acetate, and the elimination was effected by reacting it with DBN in CH_3CN at room temperature. This gave the 4′,5′-

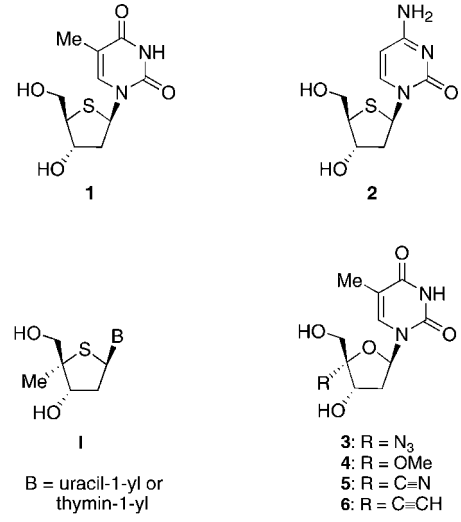

Figure 1. 4′-Thionucleosides **1**, **2**, **I**, and 4′-substituted thymidines **3**–**6**.

* Corresponding author. Tel: 81-3-3784-8187. Fax: 81-3-3784-8252. E-mail: harakazu@pharm.showa-u.ac.jp.
† Showa University.
‡ Kagoshima University.
§ Yale University.

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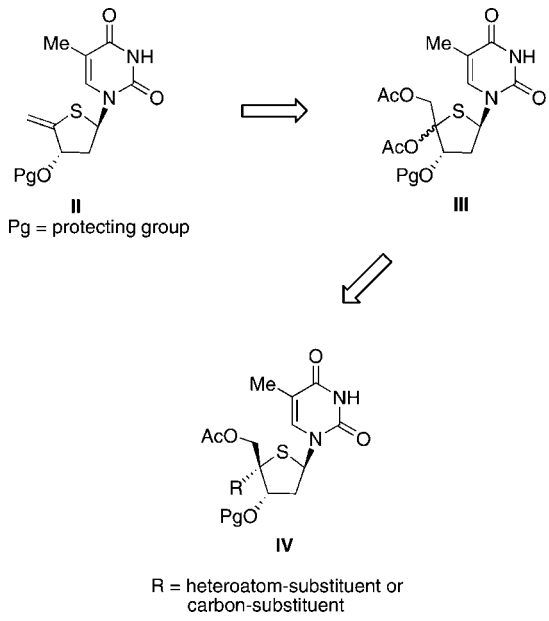
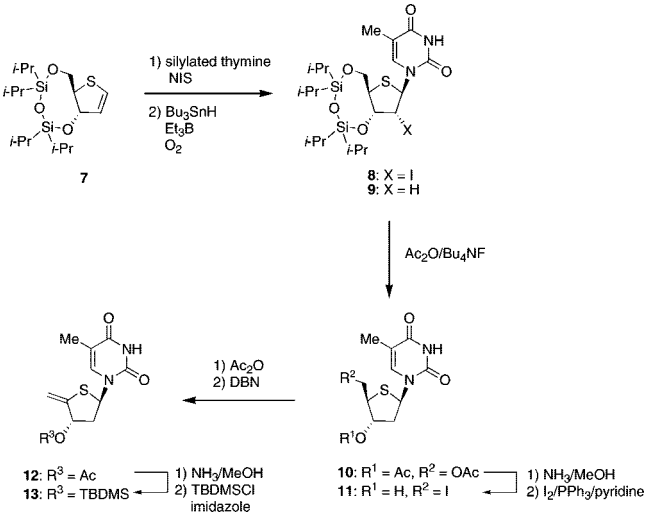
Scheme 1. Synthetic Scheme for 4′-Substituted 4′-Thiothymidines



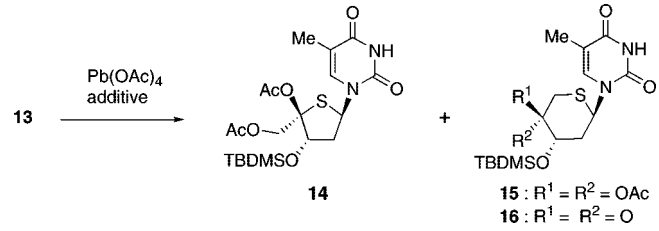
Scheme 2. Synthesis of 4′,5′-Unsaturated 4′-Thiothymidines **12** and **13**



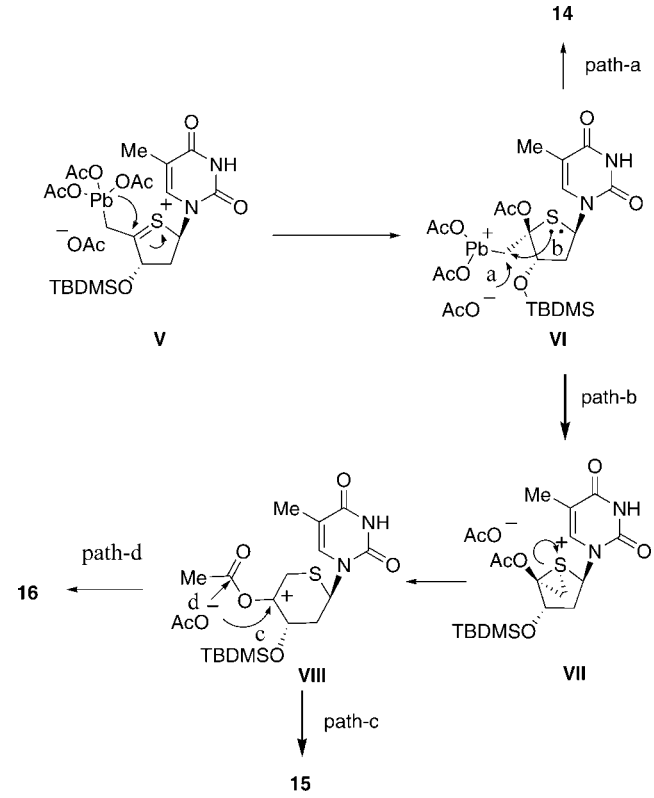
unsaturated derivative **12** in 83% yield. The corresponding 3′-*O*-TBDMS derivative **13** was also prepared in 72% yield from **12**.

Vicinal Diacetoxylation of the 4′,5′-Unsaturated Derivatives (12 and 13). Vicinal diacetoxylation of **12** was first examined by reaction with $Pb(OAc)_4$ (3 equiv) in benzene at room temperature.[9] However, even after 24 h, most of **12** remained intact. Since the initial step of the diacetoxylation of olefins is considered to be electrophilic in nature, it is conceivable that the presence of an electronegative acetoxy group at the 3′-position of **12** decreases its reactivity toward $Pb(OAc)_4$.[10] In fact, **13** having a silyloxy group at the 3′-position showed a much higher reactivity. Thus, when the reaction with $Pb(OAc)_4$ (3 equiv) was carried out under conditions similar to those discussed above, the complete disappearance of **13** was observed after 10 h at room temperature. Three products were obtained from this reaction (Scheme 3). The major product was the 4′-acetoxy-4′-thionucleoside **14** (42%) with the α-L-configuration as evidenced by HMBC correlation (H-5′/5′-OCOMe) and NOE

Scheme 3. $Pb(OAc)_4$-Mediated Diacetoxylation of **13**



Scheme 4. Mechanism of Diacetoxylation of **13**



experiment (H-6/4′-OCOCH_3: 0.3%). The other two products were the ring-expanded compounds **15** (34%) and **16** (15%), their thiopyranosyl structures being evident from the observed HMBC correlations between H-5′ and C-1′.[11] A plausible reaction mechanism for the formation of these products is depicted in Scheme 4.

Electrophilic addition of the cationic species $(AcO)_3Pb^+$ to the enol thioether structure of **13** leads to the thiocarbenium intermediate **V**, which would prefer the depicted 5′-conformation due to the presence of the 3′-silyloxy group. There could be two possible origins for an acetoxy group to be introduced to the 4′-position: a ligand of the 5′-Pb substituent and the counteranion. By considering the advantage of intramolecular reaction as well as the fact that **14** was formed exclusively, we assume ligand transfer from the 5′-Pb substituent would be a likely pathway.

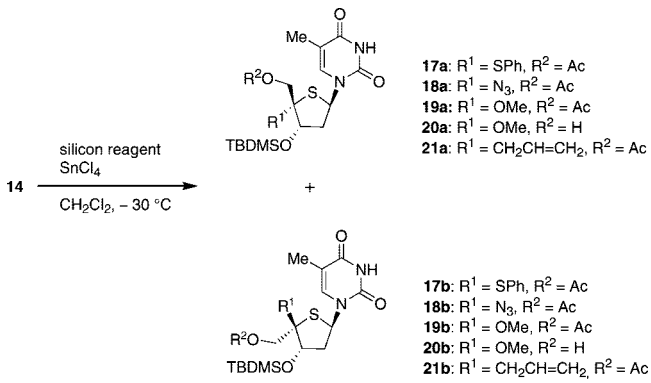
Upon departure of $Pb(OAc)_2$ from the resulting intermediate **VI**, there are two competing pathways depending upon the nucleophile. The attack of acetate anion (path a) forms **14**, while that of the sulfur atom (path b) leads to the formation of bicylo[3.1.0]sulfonium intermediate **VII** and then to the thiopyranosyl carbenium ion **VIII**. Finally, nucleophilic attack of acetate anion would take place either at the 4′-position of **VIII** leading to **15** (path c) or at the carbonyl carbon of the 4′-acetoxy group forming **16** (path d).

Table 1. Reaction of **13** with $Pb(OAc)_4$[a]

entry	solvent	additive (equiv)	yield (%) 14[b]	15[c]	16[c]	13[b]
1	benzene	–	42	34	15	0
2	THF	–	33	5	10	37
3	CH_2Cl_2	–	trace	19	58	0
4	benzene	Na_2CO_3(2.3)	56	28	14	0

[a] All reactions were carried out with $Pb(OAc)_4$ (3 equiv for entries 1–3 or 2.3 equiv for entry 4) at rt under Ar atmosphere overnight. [b] Isolated yield. [c] The yields of **15** and **16** were calculated by comparison of integration of H-1′ in ^{1}H NMR spectroscopy.

Scheme 5. 4′-Substituted 4′-Thiothymidines **17**−**21**

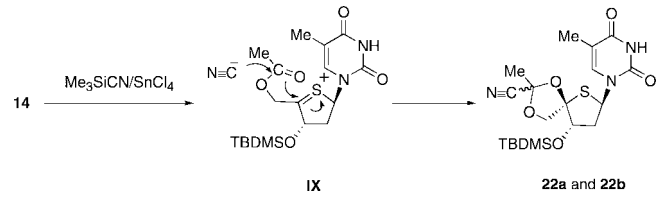


In Table 1 are shown several attempts to improve the yield of **14** with the aforementioned result being listed in entry 1. When THF was used as a solvent, a considerable amount of **13** was recovered (entry 2). Use of CH_2Cl_2 encouraged the ring expansion pathway, and **14** was formed in a trace amount (entry 3). A slight increase in the yield of **14** was observed upon carrying out the reaction in benzene in the presence of Na_2CO_3 as shown in entry 4.

Synthesis of 4′-Substituted 4′-Thiothymidines by Displacement of the 4′-Acetoxy Leaving Group. Displacement of the 4′-acetoxy group of **14** was carried out by using silicon reagents in combination with $SnCl_4$ in CH_2Cl_2 (Scheme 5). The reaction with Me_3SiSPh went to completion after 6 h at −30 °C to give the 4′-phenylthio-β-D-isomer (**17a**) in 74% yield as well as its 4′-epimer (**17b**, 12%). The stereochemistry of these products was assigned on the basis of NOE experiments: **17a**, H-3′/H-5′a (2.7%); Hβ-2′/H-5′b (1.4%); **17b**, H-6/SPh (2.1%).[12] The predominant formation of the 4′-substituted β-D-isomer over its α-L-counterpart was also seen in the reaction with Me_3SiN_3 (**18a**, 69%; **18b**, 30%) and with $Me_3SiCH_2CH{=}CH_2$ (**21a**/**21b** = 10/1, combined yield 53%). In contrast to the above stereochemical trend, the reaction of **14** with $Me_3SiOMe/SnCl_4$ resulted in the sole formation of the α-L-isomer (**19b**, 58%). The β-D-isomer (**19a**) was formed, as an inseparable mixture with **19b**, when $BF_3{\cdot}OEt_2$ was employed as a Lewis acid. Treatment of this mixture with NH_3/MeOH allowed isolation of each isomer, but the α-L-isomer appeared to be the major product (**20a**, 23%; **20b**, 44%).

In the case of the reaction between **14** and $Me_3SiCN/SnCl_4$, the spiro nucleosides were formed [**22a** (less polar product)/**22b** (more polar product) = 3/10, combined yield 92%], apparently as a result of nucleophilic attack of the carbonyl oxygen of the 5′-*O*-acetyl group at the 4′-position (Scheme 6). The fact that **22a** and **22b** have the same 4′-configuration supports conformational preference of the 5′-*O*-acetyl group of the thiocarbenium intermediate as depicted as **IX**, which is reminiscent of **V** in Scheme 4. The observed formation of **22** from **14** led us to prepare a 3′,5′-bis-*O*-silyl-protected substrate

Scheme 6. Reaction of **14** with Me_3SiCN



to introduce a cyano group to the 4′-position. The 4′-phenylthio derivative (**17**, a mixture of two 4′-epimers) prepared above was converted to the 4′-acetoxy-3′,5′-bis-*O*-TBDMS derivative (**24**) over three steps: deacetylation followed by silylation to give **23** (93%), and acetolysis of **23** with $Hg(OAc)_2$/AcOH to yield **24** (98%, **24a**/**24b** = 4.2/1).

When **24** was reacted with $Me_3SiCN/SnCl_4$ in CH_2Cl_2 at −30 °C, the desired 4′-cyano derivative **25** was obtained as a mixture of two 4′-epimers albeit in a low yield (**25a**/**25b** = 4.5/1, combined yield 29%) (Figure 2). In this reaction, two byproduct were obtained: the 4′-isonitrile (**26b**, 11%) with α-L-configuration and the elimination product **27** (27%). In terms of stereoselectivity, use of $BF_3{\cdot}OEt_2$ instead of $SnCl_4$ appeared to be effective, but the yield of **25** remained much the same (**25a**/**25b** = 20/1, combined yield 37%). Two 4′-isonitriles were also formed in this reaction (**26a**, 23%; **26b**, 9%).[13] The resulting product **25** was further converted to its 3′,5′-di-*O*-acetyl derivative which could be separated into the α-cyano (**28a**) and β-cyano nucleoside (**28b**).

An attempted introduction of an ethynyl group by reacting **24** with $Me_3SiC{\equiv}CAl(Cl)Et$ according to our recently published method[9] was unsuccessful, forming a complex mixture of products. Therefore, the crude 4′-cyano derivative (**25a**) containing **25b** and **26b** was transformed to the 4′-formyl derivative (**29**) by reacting with Dibal-H followed by acid hydrolysis (Figure 3). Conversion of the 4′-formyl group of **29** to an ethynyl group was carried out by reacting with $MeC(O)C(N_2)P(OMe)_2/K_2CO_3$ in MeOH.[14] The resulting product **30** was further converted to its 3′,5′-di-*O*-acetyl derivative (**31**) to provide an analytically pure sample (30% yield from **29**).

***anti*-HIV and *anti*-HBV Activity of 4′-Substituted 4′-Thiothymidines (32–37).** The 4′-substituted derivatives thus prepared were deprotected to yield the corresponding free 4′-

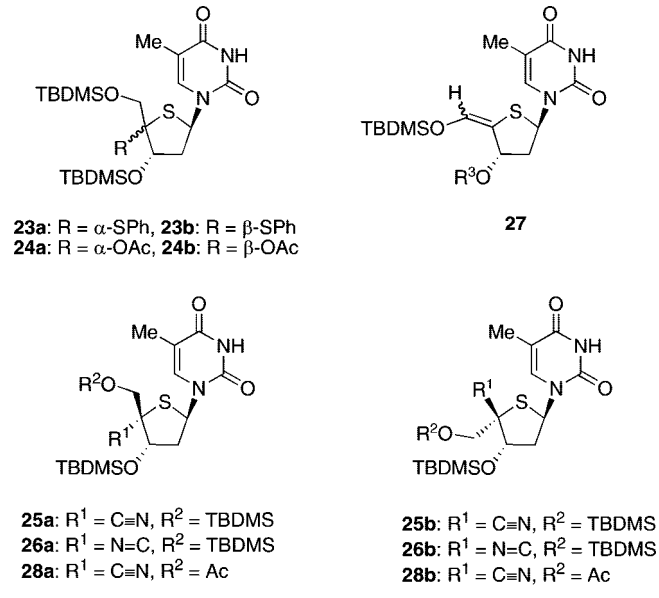


Figure 2. Compounds **23**−**28**.

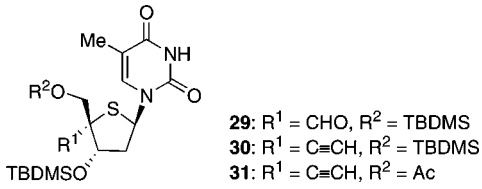


Figure 3. Compounds **29**−**31**.

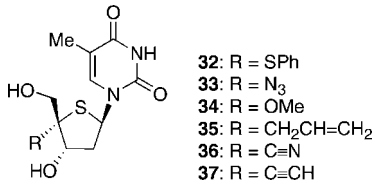


Figure 4. 4′-Substituted 4′-thiothymidines **32**−**37**.

Table 2. Inhibitory Effects of 4′-Substituted 4′-Thiothymidines (**32**–**37**) on HIV-1 and HIV-2 Replication in Cell Culture

		HIV-1		HIV-2 (EHO)	
compd	4′-substituent	EC_{50} (μM)[a]	CC_{50} (μM)[b]	EC_{50} (μM)[c]	CC_{50} (μM)[d]
32	SPh	>100	>100	>100	>100
33	N_3	0.02	40	0.024	>10
34	OMe	>4.0	>100	1.2	>100
35	$CH_2CH{=}CH_2$	>100	>100	>100	>100
36	C≡N	0.037	>100	0.023	>10
37	C≡CH	0.31	>100	0.13	>10

[a] Inhibitory concentration required to achieve 50% protection of MT-4 cells against the cytopathic effect of HIV-1_{IIIB}. [b] Cytotoxic concentration required to reduce the viability of mock-infected MT-4 cells by 50%. [c] Inhibitory concentration required to achieve 50% protection of M8166 cells against the cytopathic effect of HIV-2. [d] Cytotoxic concentration required to reduce the viability of mock-infected M8166 cells by 50%.

thiothymidines (**32**−**37**) (Figure 4). Table 2 summarizes the anti-HIV-1 activity, HIV-2 activity, and cytotoxicity of these compounds. Except for the 4′-phenylthio (**32**) and 4′-allyl (**35**) analogues, the compounds synthesized in this study showed inhibitory activity against HIV-1. Especially, the 4′-azido (**33**), 4′-cyano (**36**), and 4′-ethynyl (**37**) analogues exhibited potent anti-HIV activity, with EC_{50}'s of 0.02, 0.037, and 0.31 μM, respectively, although **33** showed a significant cytotoxicity to MT-4 cells. Compounds **33**, **36**, and **37** also showed inhibitory activity against HIV-2 as shown in Table 2. With regard to **36** and **37**, the activity against HIV-1 variant resistant to 3TC (HIV-1_{M184V}) was also tested. It was found that these compounds suppressed replication of HIV-1_{M184V} with an almost equal potency to HIV-1_{IIIB} (data not shown). These compounds did not show any anti-HBV activity up to 10 μM.[15]

Comparison of the selectivity indices (SI) was made between 4′-substituted 4′-thiothymidines (**33**, **34**, **36**, and **37**) and the corresponding thymidine derivatives (**3**−**6**) by employing the reported CC_{25}/EC_{50} values of **3**−**5**[1] or CC_{50}/EC_{50} value of **6**.[16] In the case of 4′-azido-, 4′-methoxy-, and 4′-ethynyl derivatives, comparable SI values were obtained: **3** (800) and **33** (670); **4** (>24) and **34** (>11); **6** (>120) and **37** (>322). Interestingly, 4′-cyano-4′-thiothymidine **36** was found to possess an SI value of 1586, which is three times better than that of 4′-cyanothymidine (**5**) (SI 500).

Conclusion

In conclusion, we have developed a novel synthetic approach to 4′-substituted 4′-thiothymidines on the basis of nucleophilic substitution. For the preparation of the substrate **14** having an acetoxy leaving group at the 4′-position, vicinal diacetoxylation of the 4′,5′-unsaturated 4′-thiothymidine **13** was employed. During this diacetoxylation reaction, ring-expansion to the thiopyranosides (**15** and **16**) was observed. Lewis acid assisted nucleophilic substitution of **14** furnished the desired compounds such as the 4′-phenylthio (**17a**), 4′-azido (**18a**), 4′-methoxy (**20a**), 4′-allyl (**21a**), and 4′-cyano (**28a**) analogues of 4′-thiothymidine. The 4′-ethynyl (**31**) analogue was also synthesized. Among the six deprotected 4′-substituted 4′-thiothymidines (**32**-**37**), the 4′-azido (**33**), 4′-cyano (**36**), and 4′-ethynyl (**37**) analogues showed inhibitory activity against HIV-1 as well as HIV-2. In particular, the 4′-cyano derivative **36** exhibited a potent anti-HIV-1 activity with EC_{50} 0.037 μM and did not show any cytotoxicity to MT-4 cells up to 100 μM. It is noteworthy that 4′-cyano (**36**) and 4′-ethynyl (**37**) analogues of 4′-thiothymidine were also inhibitory to replication of HIV-1 variant resistant to 3TC (HIV-1_{M184V}). By comparison with the reported SI value 4′-cyanothymidine, it was found that the 4′-thio counterpart (**36**) has a 3-fold better value. These facts suggest that replacement of the furanose oxygen with sulfur atom is a promising approach for development of new nucleoside antiviral agents. As have already been published from our laboratory,[3b,4,8] the present glycosidation method, electrophilic addition of nucleobases to 4-thiofuranoid glycals, is applicable to the preparation of cytosine and adenine 4′-thionucleosides. We are currently working along this line.

Experimental Section

Chemistry. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded either at 400 MHz or at 500 MHz. Chemical shifts are reported relative to Me_4Si. Mass spectra (MS) were taken in FAB mode with *m*-nitrobenzyl alcohol as a matrix. Column chromatography was carried out on silica gel. Thin-layer chromatography (TLC) was performed on silica gel. When necessary, analytical samples were purified by high-performance liquid chromatography (HPLC). THF was distilled from benzophenone ketyl.

Diaetoxylation of 13 with $Pb(OAc)_4$: 1-[4-*O*-Acetoxy-5-*O*-acetyl-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-α-L-*threo*-4-thiopentofuranosyl]thymine (14), 5,5-Bis-acetoxy-(4*S*)-*O*-(*tert*-butyldimethylsilyl)-(2*R*)-(thymin-1-yl)thiane (15), and (4*S*)-*O*-(*tert*-Butyldimethylsilyl)-(2*R*)-(thymin-1-yl)thian-5-one (16). To a benzene (50 mL) solution of **13** (1.45 g, 4.09 mmol) were added Na_2CO_3 (996.3 mg, 9.4 mmol) and $Pb(OAc)_4$ (4.2 g, 9.4 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred at rt overnight, quenched with saturated aq $NaHCO_3$, and filtered through a Celite pad. The filtrate was partitioned between $CHCl_3$/saturated aq $NaHCO_3$. Column chromatography (hexane/AcOEt = 2/1–1/1) of the organic layer gave **14** (1.08 g, 56%, foam) and a mixture of **15** and **16** (749.8 mg) [**15**: 530.8 mg (28%), **16**: 219 mg (14%), calculated by comparison of integration of H-1′]. Compounds **15** (foam, t_R 20.0 min) and **16** (solid, t_R 17.7 min) were separated by HPLC (hexace/EtOAc = 1/2).

Physical data of **14**: UV (MeOH) λ_{max} 269 nm (ϵ 10800), λ_{min} 236 nm (ϵ 2700). ^{1}H NMR ($CDCl_3$) δ 0.12 and 0.16 (6H, each as s), 0.93 (9H, s), 1.93 (3H, d, J = 1.2 Hz), 2.07 (3H, s), 2.13 (3H, s), 2.23 (1H, ddd, J = 10.0, 12.4, 3.2 Hz), 2.45 (1H, dd, J = 6.0, 12.4 Hz), 4.41 (1H, d, J = 12.0 Hz), 5.12 (1H, d, J = 12.0 Hz), 4.54 (1H, br), 6.62 (1H, dd, J = 10.0, 6.0 Hz), 7.27 (1H, d, J = 1.2 Hz), 8.95 (1H, br); NOE experiment H-6/CH_3CO-4′ (0.3%); HMBC H-5′/CH_3CO-5′; ^{13}C NMR ($CDCl_3$) δ −5.3, −4.7, 12.7, 17.7, 20.6, 21.6, 25.4, 41.7, 61.4, 61.5, 76.5, 100.3, 111.9, 135.6, 150.5, 163.6, 168.7, 169.7; FAB-MS (*m*/*z*) 435 and 473 (M^+ + H). Anal. Calcd for $C_{20}H_{32}N_2O_7SSi$: C, 50.83; H, 6.82; N, 5.93. Found: C, 50.93; H, 6.86; N, 5.87.

Physical data of **15**: UV (MeOH) λ_{max} 269 nm (ϵ 11100), λ_{min} 235 nm (ϵ2300); ^{1}H NMR ($CDCl_3$) δ 0.06 and 0.11 (6H, each as s), 0.91 (9H, s), 1.95 (3H, d, J = 1.2 Hz), 2.06 (3H, s), 2.11 (1H, ddd, J = 2.9, 13.4, 4.6 Hz), 2.20 (3H, s), 2.47 (1H, ddd, J = 12.2, 13.4, 2.0 Hz), 3.61 (2H, s), 4.91 (1H, d, J = 3.2 Hz), 6.21 (1H, dd,

J = 2.9, 12.2 Hz), 7.14 (1H, d, J = 1.2 Hz), 8.86 (1H, br); ^{13}C NMR ($CDCl_3$) δ −5.2, −4.6, 12.6, 17.8, 21.7, 21.8, 25.6, 29.3, 38.7, 48.5, 68.3, 100.0, 111.8, 135.6, 149.7, 163.2, 168.1, 168.5; HMBC C-1′/H-5′. Anal. Calcd for $C_{20}H_{32}N_2O_7SSi$: C, 50.83; H, 6.82; N, 5.93. Found: C, 50.83; H, 6.88; N, 5.83.

Physical data of **16**: mp 207–209 °C; UV (MeOH) λ_{max} 269 nm (ϵ 11300), λ_{min} 236 nm (ϵ 2700); ^{1}H NMR ($CDCl_3$) δ 0.06 and 0.12 (6H, each as s), 0.94 (9H, s), 1.93 (3H, d, J = 1.2 Hz), 2.57 (1H, ddd, J = 3.2, 13.6, 4.4 Hz), 2.71 (1H, ddd, J = 11.6, 13.6, 2.0 Hz), 2.86 (1H, d, J = 12.4 Hz), 4.21 (1H, dd, J = 4.4, 2.0 Hz), 4.35 (1H, d, J = 12.4 Hz), 6.56 (1H, dd, J = 3.2, 11.6 Hz), 7.15 (1H, d, J = 1.2 Hz), 8.20 (1H, br); ^{13}C NMR ($CDCl_3$) δ −5.1, −5.07, 12.6, 18.0, 25.6, 32.7, 46.9, 48.8, 76.7, 112.3, 135.4, 149.7, 163.1, 201.8; HMBC C-1′/H-5′a and C-1′/H-5′b; FAB-MS (*m*/*z*) 371 (M^+ + H). Anal. Calcd for $C_{16}H_{26}N_2O_4SSi$: C, 51.86; H, 7.07; N, 7.56. Found: C, 51.98; H, 7.15; N, 7.49.

Reaction of 14 with Phenylthiotrimethylsilane: 1-[5-*O*-Acetyl-3-*O*-(*tert*-butyldimethylsilyl)-4-phenylthio-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (17a) and 1-[5-*O*-Acetyl-3-*O*-(*tert*-butyldimethylsilyl)-4-phenylthio-2-deoxy-α-L-*threo*-4-thiopentofuranosyl]thymine (17b). To a CH_2Cl_2 (12 mL) solution of **14** (497.5 mg, 1.05 mmol) were added phenylthiotrimethylsilane (0.99 mL, 5.25 mmol) and $SnCl_4$ (1.0 M CH_2Cl_2 solution) (3.2 mL, 3.2 mmol) at −30 °C under Ar atmosphere, and the mixture was stirred at −30 °C for 6 h. The reaction mixture was partitioned between $CHCl_3$/saturated aq $NaHCO_3$, and silica gel column chromatography (hexane/AcOEt = 3/1) of the organic layer gave a mixture of **17a** and **17b** (540.8 mg, 99%, **17a/17b** = 6.7/1, foam), which were separated by HPLC (hexane/AcOEt = 1/1) to give **17a** (t_R 12.4 min, 406.2 mg, 74%, foam) and **17b** (t_R 10.5 min, 65.9 mg, 12%, foam).

Physical data of **17a**: UV (MeOH) λ_{max} 269 nm (ϵ 13100), λ_{min} 241 nm (ϵ 5100); ^{1}H NMR ($CDCl_3$) δ 0.11 and 0.12 (6H, each as s), 0.95 (9H, s), 1.94 (3H, d, J = 1.0 Hz), 2.12 (3H, s), 2.24 (1H, ddd, J = 4.1, 5.1, 16.7 Hz), 2.90 (1H, ddd, J = 7.7, 8.8, 16.7 Hz), 4.31 (1H, d, J = 12.2 Hz), 4.38 (1H, d, J = 12.2 Hz), 4.66 (1H, dd, J = 5.1, 8.8 Hz), 6.32 (1H, dd, J = 4.1, 7.7 Hz), 7.33–7.42 and 7.59–7.61 (6H, each as m), 8.32 (1H, br); NOE experiment H-5′a/H-3′ (2.7%), H-PhS/H-1′ (2.4%), H-2′/H-5′b (1.4%), and H-3′/H-5′a (2.7%); ^{13}C NMR ($CDCl_3$) δ −5.1, −4.6, 12.8, 18.1, 20.8, 25.6, 41.8, 58.3, 65.1, 74.8, 75.7, 111.4, 128.7, 129.6, 130.4, 136.1, 136.1, 137.8, 150.6, 163.5, 169.8; FAB-MS (*m*/*z*) 523 (M^+ + H). Anal. Calcd for $C_{24}H_{34}N_2O_5S_2Si$: C, 55.14; H, 6.56; N, 5.36. Found: C, 54.79; H, 6.54; N, 5.32.

Physical data of **17b**: ^{1}H NMR ($CDCl_3$) δ–0.06 and 0.03 (6H, each as s), 0.87 (9H, s), 1.99 (3H, d, J = 1.2 Hz), 2.11 (3H, s), 2.46 (1H, ddd, J = 6.6, 2.0, 13.2 Hz), 2.87 (1H, ddd, J = 9.9, 3.4, 13.2 Hz), 4.21 (1H, d, J = 11.7 Hz), 4.40 (1H, d, J = 11.7 Hz), 4.49 (1H, dd, J = 2.0, 3.4 Hz), 6.72 (1H, dd, J = 6.6, 9.9 Hz), 7.37–7.49 and 7.52–7.57 (5H, each as m), 7.76 (1H, d, J = 1.2 Hz), 8.36 (1H, br); NOE experiment H-6/H-PhS-4′ (2.1%); ^{13}C NMR ($CDCl_3$) δ −5.3, −4.7, 12.8, 17.9, 20.8, 25.6, 42.5, 61.7, 65.8, 75.2, 78.4, 112.2, 129.4, 130.2, 130.9, 136.5, 136.6, 150.4, 163.1, 170.2; high-resolution FAB-MS (*m*/*z*) calcd for $C_{24}H_{35}N_2O_5S_2Si$ 523.1712 (M^+ + H), found 523.1762.

Reaction of 14 with Azidotrimethylsilane: 1-[5-*O*-Acetyl-4-azido-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (18a) and 1-[5-*O*-Acetyl-4-azido-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-α-L-*threo*-4-thiopentofuranosyl]thymine (18b). To a CH_2Cl_2 (6 mL) solution of **14** (104.0 mg, 0.22 mmol) were added azidotrimethylsilane (0.14 mL, 1.1 mmol) and $SnCl_4$ (1.0 M CH_2Cl_2 solution) (0.66 mL, 0.66 mmol) at −30 °C under Ar atmosphere, and the mixture was stirred at −30 °C for 7 h. The reaction mixture was partitioned between $CHCl_3$/saturated aq $NaHCO_3$, and silica gel column chromatography (hexane/AcOEt = 5/1–3/1) of the organic layer gave **18a** (68.9 mg, 69%, foam) and **18b** (30.3 mg, 30%, foam).

Physical data of **18a**: IR (neat) 2115 cm^{-1} (N_3); ^{1}H NMR ($CDCl_3$) δ 0.15 and 0.19 (6H, each as s), 0.96 (9H, s), 1.98 (3H, d, J = 1.2 Hz), 2.16 (3H, s), 2.21 (1H, ddd, J = 8.5, 3.9, 13.6 Hz), 2.51 (1H, ddd, J = 6.4, 4.2, 13.6 Hz), 4.18 (1H, d, J = 11.7 Hz), 4.40–4.44 (2H, m), 6.66 (1H, dd, J = 8.5, 6.4 Hz), 7.42 (1H, d, J = 1.2 Hz), 9.17 (1H, br); NOE experiment H-5′a/H-2′ (1.2%) and H-5′b/H-6 (0.4%); ^{13}C NMR ($CDCl_3$) δ −5.0, −4.9, 12.6, 18.1, 20.7, 25.7, 42.5, 59.8, 67.3, 77.7, 83.9, 112.2, 135.6, 150.4, 163.4, 170.2; FAB-MS (*m*/*z*) 456 (M^+ + H); high-resolution FAB-MS (*m*/*z*) calcd for $C_{18}H_{30}N_5O_5SSi$ 456.1737 (M^+ + H), found 456.1764.

Physical data of **18b**: IR (neat) 2120 cm^{-1} (N_3); ^{1}H NMR ($CDCl_3$) δ 0.12 and 0.14 (6H, each as s), 0.92 (9H, s), 1.98 (3H, d, J = 1.2 Hz), 2.13 (3H, s), 2.31 (1H, ddd, J = 10.1, 3.0, 13.3 Hz), 2.45 (1H, ddd, J = 6.6, 1.2, 13.3 Hz), 4.18–4.19 (1H, m), 4.42 (1H, d, J = 11.9 Hz), 4.62 (1H, d, J = 11.9 Hz), 6.75 (1H, dd, J = 10.1, 6.6 Hz), 7.37 (1H, d, J = 1.2 Hz), 8.88 (1H, br); NOE experiment H-1′/H-5′b (0.3%); ^{13}C NMR ($CDCl_3$) δ −5.1, −4.6, 12.8, 17.9, 20.6, 25.5, 42.5, 61.7, 66.2, 78.3, 87.4, 112.6, 135.6, 150.4, 163.2, 169.9; FAB-MS (*m*/*z*) 456 (M^+ + H); high-resolution FAB-MS (*m*/*z*) calcd for $C_{18}H_{30}N_5O_5SSi$ 456.1737 (M^+ + H), found 456.1771.

Reaction of 14 with Methoxytrimethylsilane: 1-[3-*O*-(*tert*-Butyldimethylsilyl)-4-methoxy-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (20a) and 1-[3-*O*-(*tert*-Butyldimethylsilyl)-4-methoxy-2-deoxy-α-L-*threo*-4-thiopentofuranosyl]thymine (20b). To a CH_2Cl_2 (2.0 mL) solution of **14** (35 mg, 0.074 mmol) were added methoxytrimethylsilane (51 μL, 0.37 mmol) and $BF_3 \cdot OEt_2$ (28 μL, 0.22 mmol) at −30 °C under Ar atmosphere, and the mixture was stirred at 0 °C for 12 h. The reaction mixture was partitioned between $CHCl_3$/saturated aq $NaHCO_3$. Silica gel column chromatography (hexane/AcOEt = 3/1) of the organic layer gave a mixture of **19a** and **19b** (26.8 mg, 81%). The mixture was treated with methanolic ammonia (6 mL) at rt for 20 h. The reaction mixture was evaporated to dryness and separated by preparative TLC (hexane/EtOAc = 2/1) to give **20a** (6.8 mg, 23%, foam) and **20b** (13 mg, 44%, foam).

Physical data of **20a**: ^{1}H NMR ($CDCl_3$) δ 0.10 and 0.13 (6H, each as s), 0.91 (9H, s), 1.96 (3H, d, J = 1.2 Hz), 2.21 (1H, ddd, J = 3.4, 5.8, 13.7 Hz), 2.27 (1H, dd, J = 5.6, 6.7 Hz), 2.65 (1H, ddd, J = 7.7, 9.8, 13.7 Hz), 3.50 (3H, s), 3.82 (1H, dd, J = 5.6, 11.7 Hz), 3.87 (1H, dd, J = 6.7, 11.7 Hz), 4.60 (1H, dd, J = 5.8, 9.8 Hz), 6.28 (1H, dd, J = 3.4, 7.7 Hz), 7.55 (1H, d, J = 1.2 Hz), 8.47 (1H, br); NOE experiment H-6/H-5′a (0.6%) and H-1′/OMe-4′ (0.8%); ^{13}C NMR ($CDCl_3$) δ −4.70, −4.66, 12.8, 18.1, 25.7, 42.4, 53.0, 57.8, 64.4, 76.1, 100.5, 111.6, 136.2, 150.3, 163.1; high-resolution FAB-MS (*m*/*z*) calcd for $C_{17}H_{31}N_2O_5SSi$ 403.1723 (M^+ + H), found 403.1755.

Physical data of **20b**: UV (MeOH) λ_{max} 271 nm (ϵ 10200), λ_{min} 237 nm (ϵ 2500); ^{1}H NMR ($CDCl_3$) δ 0.14 and 0.15 (6H, each as s), 0.93 (9H, s), 1.87 (1H, dd, J = 3.7, 8.0 Hz), 1.96 (3H, d, J = 1.2 Hz), 2.30 (1H, ddd, J = 9.6, 3.2, 13.1 Hz), 2.43 (1H, ddd, J = 7.1, 1.3, 13.1 Hz), 3.50 (3H, s), 3.88 (1H, dd, J = 3.4, 12.2 Hz), 4.39 (1H, dd, J = 7.8, 12.2 Hz), 4.38 (1H, dd, J = 1.3, 3.2 Hz), 6.63 (1H, dd, J = 9.6, 7.1 Hz), 7.32 (1H, d, J = 1.2 Hz), 8.46 (1H, br); NOE experiment H-6/OMe-4′ (1.2%); ^{13}C NMR ($CDCl_3$) δ −5.2, −4.6, 12.9, 17.9, 25.6, 42.5, 50.9, 58.6, 61.3, 78.0, 106.3, 112.1, 136.6, 150.4, 163.2; FAB-MS (*m*/*z*) 403 (M^+ + H). Anal. Calcd for $C_{17}H_{30}N_2O_5SSi$: C, 50.72; H, 7.51; N, 6.96. Found: C, 50.81; H, 7.60; N, 6.81.

Reaction of 14 with Allyltrimethylsilane: 1-[5-*O*-Acetyl-4-allyl-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (21a) and 1-[5-*O*-Acetyl-4-allyl-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-α-L-*threo*-4-thiopentofuranosyl]thymine (21b). To a CH_2Cl_2 (3 mL) solution of **14** (73.1 mg, 0.15 mmol) were added allyltrimethylsilane (0.24 mL, 1.50 mmol) and $SnCl_4$ (1.0 M CH_2Cl_2 solution) (0.45 mL, 0.45 mmol) at −30 °C under Ar atmosphere, and the mixture was stirred at −30 °C for 1.5 h. The reaction mixture was partitioned between $CHCl_3$/saturated aq $NaHCO_3$. Silica gel column chromatography (hexane/AcOEt = 5/1) of the organic layer gave a mixture of **21a** and **21b** (36.6 mg, 53%, **21a/21b** = 10/1, foam). Compounds **21a** (foam, t_R 27.5 min) and **21b** (syrup, t_R 23.6 min) were separated by HPLC (hexane/EtOAc = 2/1).

Physical data of **21a**: UV (MeOH) λ_{max} 270 nm (ϵ 10200), λ_{min} 236 nm (ϵ 2600); ^{1}H NMR ($CDCl_3$) δ 0.10 and 0.11 (6H, each as s), 0.94 (9H, s), 1.97 (3H, s), 2.13 (3H, s), 2.23 (1H, m), 2.46 (2H, m), 2.67 (2H, dd, J = 5.2, 11.2 Hz), 4.18 (1H, d, J = 9.2 Hz), 4.22 (1H, d, J = 9.2 Hz), 4.30 (1H, t, J = 2.8 Hz), 5.15 (1H, s), 5.18 (1H, d, J = 8.0 Hz), 5.77 (1H, m), 6.45 (1H, dd, J = 6.8, 5.2 Hz), 7.57 (1H, s), 8.12 (1H, br); NOE experiment H-5′/H-3′ (3.0%), H-5′a,b/H-6 (1.6%), and H-6/H-3′ (1.9%); ^{13}C NMR ($CDCl_3$) δ −5.0, −4.5, 12.7, 18.1, 20.9, 38.1, 42.9, 59.9, 64.8, 66.6, 75.8, 111.5, 119.5, 133.8, 136.0, 150.3, 163.0, 170.4; FAB-MS (*m*/*z*) 455 (M^+ + H); (+KI) 493 (M^+ + K). Anal. Calcd for $C_{21}H_{34}N_2O_5SSi$: C, 55.48; H, 7.54; N, 6.16. Found: C, 55.68; H, 7.75; N, 5.99.

Physical data of **21b**: ^{1}H NMR ($CDCl_3$) δ 0.09 and 0.10 (6H, each as s), 0.91 (9H, s), 1.97 (3H, s), 2.09 (3H, s), 2.15–2.21 (1H, m), 2.45–2.53 (2H, m), 2.64 (1H, dd, J = 7.5, 14.3 Hz), 4.23 (1H, d, J = 10.9 Hz), 4.26–4.31 (2H, m), 5.21 (1H, dd, J = 1.7, 17.2 Hz), 5.25 (1H, dd, J = 1.7, 10.3 Hz), 5.87–5.93 (1H, m), 6.40 (1H, t, J = 7.5 Hz), 7.52 (1H, d, J = 1.2 Hz), 8.04 (1H, br); NOE experiment H-6/CH_2═C*H*CH_2 (1.9%); ^{13}C NMR ($CDCl_3$) δ −5.0, −4.5, 12.8, 17.9, 20.9, 25.6, 29.7, 41.4, 43.1, 59.8, 64.0, 65.9, 111.6, 119.9, 132.9, 136.2, 150.2, 162.9, 170.3; FAB-MS (*m*/*z*) 455 (M^+ + H); (+KI) 493 (M^++ K); high-resolution FAB-MS (*m*/*z*) calcd for $C_{21}H_{35}N_2O_5SSi$ 455.2036 (M^+ + H), found 455.1993.

(3′*S*)-*O*-(*tert*-Butyldimethylsilyl)-(5′*R*)-(thymin-1-yl)-tetrahydrothiophene-2′-spiro-4-(2-cyano-2-methyl)-1,3-dioxolane (22a and 22b). To a CH_2Cl_2 (3 mL) solution of **14** (41 mg, 0.087 mmol) were added cyanotrimethylsilane (116 μL, 0.87 mmol) and $SnCl_4$ (1.0 M CH_2Cl_2 solution) (0.26 mL, 0.26 mmol) at −30 °C under Ar atmosphere, and the mixture was stirred at −30 °C for 3.5 h. The reaction mixture was partitioned between $CHCl_3$/saturated aq $NaHCO_3$. Silica gel column chromatography (hexane/AcOEt = 5/1) of the organic layer gave **22a** (less polar product: 8.5 mg, 22%, syrup and more polar product: 26 mg, 68%, syrup).

Physical data of **22a** (less polar product): IR 2231 cm^{-1} (CN). ^{1}H NMR ($CDCl_3$) δ 0.16 and 0.19 (6H, each as s), 0.92 (9H, s), 1.91 (3H, s), 1.97 (3H, d, J = 1.2 Hz), 2.17 (1H, ddd, J = 9.2, 12.8, 2.4 Hz), 2.55 (1H, dd, J = 6.8, 12.8 Hz), 4.41 (1H, d, J = 10.4 Hz), 4.50 (1H, d, J = 10.4 Hz), 4.58 (1H, d, J = 2.4 Hz), 6.71 (1H, dd, J = 9.2, 6.8 Hz), 7.45 (1H, d, J = 1.2 Hz), 8.55 (1H, br); NOE experiment H-5′b/H-3′ (4.1%); HMBC acetal-C/acetal-CH_3; ^{13}C NMR ($CDCl_3$) δ −4.9, −4.3, 12.9, 17.8, 25.2, 25.5, 43.1, 62.2, 72.7, 80.2, 101.3, 104.9, 112.5, 116.9, 136.0, 150.4, 163.1; high-resolution FAB-MS (*m*/*z*) calcd for $C_{19}H_{29}N_3O_5SSi$ 440.1675 (M^+ + H), found 440.1651.

Physical data of **22b** (more polar product): IR 2229 cm^{-1} (CN); ^{1}H NMR ($CDCl_3$) δ 0.13 and 0.14 (6H, each as s), 0.92 (9H, s), 1.85 (3H, s), 2.00 (3H, d, J = 1.2 Hz), 2.13 (1H, ddd, J = 9.2, 12.4, 3.2 Hz), 2.49 (1H, dd, J = 6.8, 12.4 Hz), 4.16 (1H, d, J = 3.2 Hz), 4.23 (1H, d, J = 10.4 Hz), 4.56 (1H, d, J = 10.4 Hz), 6.64 (1H, dd, J = 9.2, 6.8 Hz), 7.55 (1H, d, J = 1.2 Hz), 8.99 (1H, br); NOE experiment H-5′b/H-3′ (2.4%); HMBC acetal-C/acetal-*C*H_3, acetal-C/H-5′b and *C*N/acetal-C*H*$_3$; ^{13}C NMR ($CDCl_3$)δ 12.9, 17.9, 25.0, 25.5, 42.7, 61.7, 68.8, 79.6, 100.1, 104.6, 112.4, 116.4, 136.0, 150.3, 163.0; high-resolution FAB-MS (*m*/*z*) calcd for $C_{19}H_{29}N_3O_5SSi$ 440.1675 (M^+ + H), found 440.1668.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-4-phenylthio-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (23a) and 1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-4-phenylthio-2-deoxy-α-L-*threo*-4-thiopentofuranosyl]thymine (23b). Compound **17** (561.1 mg, 1.07 mmol) was treated with metanolic ammonia (35 mL), and the mixture was kept at rt. The reaction mixture was evaporated to dryness, and the residue was dried in vacuo overnight. To a DMF (10 mL) solution of the residue were added imidazole (437.1 mg, 6.42 mmol) and *tert*-butyldimethylsilyl chloride (645 mg, 4.28 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred at rt overnight. The reaction mixture was partitioned between AcOEt/H_2O. Silica gel column chromatography (hexane/AcOEt = 5/1) of the organic layer gave a mixture of **23a** and **23b** (589.9 mg, 93%, **23a**/**23b** = 12.1:1, foam): ^{1}H NMR ($CDCl_3$) δ (for **23a**) 0.03, 0.04, 0.11 and 0.12 (12H, each as s), 0.89 and 0.94 (18H, each as s), 1.93 (3H, d, J = 1.2 Hz), 2.16 (1H, ddd, J = 2.7, 5.7, 13.7 Hz), 2.93 (1H, ddd, J = 8.3, 9.9, 13.7 Hz), 3.67 (1H, d, J = 11.2 Hz), 4.00 (1H, d, J = 11.2 Hz), 4.84 (1H, dd, J = 5.7, 9.9 Hz), 6.28 (1H, dd, J = 2.7, 8.3 Hz), 7.29–7.40 and 7.54–7.57 (5H, each as m), 7.63 (1H, d, J = 1.2 Hz), 8.29 (1H, br), (selected data for **23b**) δ 2.40 (1H, ddd, J = 2.2,6.6, 13.2 Hz), 3.51 (1H, d, J = 10.5 Hz), 4.03 (1H, d, J = 10.5 Hz), 4.38 (1H, dd, J = 2.2, 2.9 Hz), 6.63 (1H, dd, J = 6.6, 9.8 Hz), 7.69 (1H, d, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ (for **23a**) −5.4, −5.4, −5.0, −4.6, 12.6, 18.1, 18.5, 25.7, 25.9, 41.6, 57.1, 64.5, 74.5, 77.8, 111.5, 129.1, 131.3, 136.3, 137.8, 150.7, 163.6; (selected data for **23b**) −5.2, −4.8, 12.7, 17.9, 18.4, 25.5, 42.5, 60.7, 65.2, 78.3, 78.7, 111.9, 128.9, 129.7, 132.3, 136.7, 136.7, 163.7; FAB-MS (*m*/*z*) 595 (M^+ + H). Anal. Calcd for $C_{28}H_{46}N_2O_4S_2Si_2$: C, 56.52; H, 7.79; N, 4.71. Found: C, 56.47; H, 7.85; N, 4.66.

1-[4-Acetoxy-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (24a) and 1-[4-Acetoxy-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-α-L-*threo*-4-thiopentofuranosyl]thymine (24b). To a AcOH (8.9 mL, 156 mmol) solution of **23** (596.4 mg, 1.00 mmol) was added $Hg(OAc)_2$ (701.1 mg, 2.2 mmol) ar rt under Ar atmosphere and the mixture was stirred at rt for 5 h. The reaction mixture was diluted with $CHCl_3$ and the solution was washed with H_2O, saturated aq $NaHCO_3$ and aq. KCN. Silica gel column chromatography (hexane/AcOEt = 4/1) of the organic layer gave a mixture of **24a** and **24b** (523 mg, 96%, **24a**/**24b** = 4.2/1, foam): ^{1}H NMR ($CDCl_3$)δ(for **24a**) 0.09, 0.11, 0.12 and 0.13 (12H, each as s), 0.92 and 0.93 (18H, each as s), 1.95 (3H, d, J = 1.2 Hz), 2.09 (3H, s), 2.04–2.10 (1H, m), 2.44 (1H, ddd, J = 7.1, 4.4, 13.1 Hz), 3.94 (1H, d, J = 11.0 Hz), 4.13 (1H, d, J = 11.0 Hz), 4.69 (1H, t, J = 4.4 Hz), 6.46 (1H, t, J = 7.1 Hz), 7.49 (1H, d, J = 1.2 Hz), 8.74 (1H, br): δ(selected data for **24b**) 0.04, 0.05, 0.14, 0.16 (12H, each as s), 0.89 and 0.94 (18H, each as s), 1.94 (3H, d, J = 1.2 Hz), 2.13 (3H, s), 4.13 (1H, d, J = 10.7 Hz), 4.37 (1H, d, J = 10.7 Hz), 4.55 (1H, br), 6.58 (1H, dd, J = 6.1, 9.9 Hz), 7.29 (1H, d, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$)δ: (for **24a**) −5.4, −4.7, 12.6, 18.1, 18.3, 21.5, 25.6, 25.8, 40.8, 59.5, 64.0, 74.2, 97.3, 111.5, 136.1, 150.5, 163.5, 169.9; (for **24b**)δ−5.4, −4.9, 12.9, 17.9, 25.5, 42.0, 59.9, 61.4, 76.0, 103.4, 111.8, 135.9, 150.5, 163.4, 168.7. FAB-MS (*m*/*z*) 545 (M^++H). *Anal*. Calcd for $C_{24}H_{44}N_2O_6SSi_2$: C, 52.91; H, 8.14; N, 5.14. Found: C, 53.06; H, 8.28; N, 5.14.

Reaction of 24 with cyanotrimethylsilane in the presence of $SnCl_4$: Formation of 1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-4-cyano-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (25a), 1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-4-cyano-2-deoxy-α-L-*threo*-4-thiopentofuranosyl]thymine (25b), 1-[-3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-4-isocyano-2-deoxy-α-L-*erythro*-4-thiopentofuranosyl]thymine (26b), and 1-[-3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-4,5-didehydro-β-D-*erythro*-4-thiopentofuranosyl]thymine (27). To a CH_2Cl_2 (3.5 mL) solution of **24** (81.7 mg, 0.15 mmol) were added cyanotrimethylsilane (0.1 mL, 0.75 mmol) and $SnCl_4$ (1.0 M CH_2Cl_2 solution) (0.45 mL, 0.45 mmol) at −30 °C under Ar atmosphere, and the mixture was stirred at −30 °C overnight. The reaction mixture was partitioned between $CHCl_3$/saturated aq $NaHCO_3$. Preparative TLC (hexane/AcOEt = 2/1) of the organic layer gave a mixture of **25** and **26b** (22.3 mg) [**25**; 14.0 mg (18%, **25a**: **25b** = 1: 0.22), **26b**; 8.3 mg (11%)], and **27** (19.6 mg, 27%, foam).

Physical data of **25** and **26b**: IR (neat) 2120 (*N*═C:) and 2240 cm^{-1} (CN); ^{1}H NMR ($CDCl_3$) δ (for **25a**) 0.11, 0.12, 0.13 and 0.15 (12H, each as s), 0.92 and 0.93 (18H, each as s), 1.96 (3H, d, J = 1.2 Hz), 2.24 (1H, ddd, J = 6.8, 4.4, 13.7 Hz), 2.50 (1H, ddd, J = 6.8, 5.4, 13.7 Hz), 3.79 (1H, d, J = 10.7 Hz), 3.95 (1H, d, J = 10.7 Hz), 4.63 (1H, dd, J = 4.6, 5.4 Hz), 6.48 (1H, t, J = 6.8 Hz), 7.30 (1H, d, J = 1.2 Hz), 8.89 (1H, br): δ (selected data for **25b**) 4.36 (1H, t, J = 4.1 Hz), 6.55 (1H, dd, J = 6.4, 8.1 Hz), 7.59 (1H, d, J = 1.2 Hz), 8.87 (1H, br); δ (selected data for **26b**) 0.91 and 0.92 (18H, each as s), 2.36 (1H, ddd, J = 8.9, 3.5, 13.5 Hz), 2.44 (1H, ddd, J = 6.9, 1.2, 13.5 Hz), 3.85 (1H, d, J = 9.8 Hz), 3.96 (1H, d, J = 9.8 Hz), 4.22 (1H, br), 6.63 (1H, dd, J = 8.9, 6.9 Hz), 7.67 (1H, d, J = 1.1 Hz), 8.58 (1H, br); ^{13}C NMR ($CDCl_3$) δ (for **25a**) −5.42, −5.36, −4.9, −4.7, 12.7, 18.0, 18.3, 25.6, 25.7,

41.4, 60.1, 60.2, 65.4, 74.2, 79.5, 99.7, 112.2, 118.0, 135.6, 150.3, 163.3; (selected data for **26b**) δ −5.5, −5.0, −4.4, 17.8, 18.4, 25.8, 25.9, 42.9, 61.4, 67.1, 79.5, 112.0, 137.3, 150.6, 163.6.

Physical data of **27**: UV (MeOH) λ_{max} 267 nm (ϵ 11900), λ_{min} 245 nm (ϵ 9100); ^{1}H NMR ($CDCl_3$) δ 0.08, 0.09 and 0.18 (12H, each as s), 0.89 and 0.95 (18H, each as s), 1.90–1.97 (1H, m), 1.94 (3H, s), 2.40 (1H, ddd, J = 6.1, 2.7, 12.7 Hz), 4.81–4.83 (1H, m), 6.63 (1H, s), 6.69 (1H, dd, J = 8.9, 6.1 Hz), 7.41 (1H, s), 8.51 (1H, br); ^{13}C NMR ($CDCl_3$) δ −5.3, −5.2, −4.64, −4.55, 12.7, 18.0, 18.2, 25.5, 25.7, 45.5, 61.1, 73.4, 111.7, 122.4, 133.7, 136.1, 150.3, 163.1; FAB-MS (*m*/*z*) 484 (M^+); (+KI) 523 (M^+ + K). Anal. Calcd for $C_{22}H_{40}N_2O_4SSi_2$: C, 54.50; H, 8.32; N, 5.78. Found: C, 54.87; H, 8.55; N, 5.84.

Reaction of 24 with cyanotrimethylsilane in the presence of $BF_3 \cdot OEt_2$: Formation of 25, 1-[-3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-4-isocyano-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (26a) and 26b/1-[3,5-Di-*O*-acetyl-4-cyano-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (28a), and 1-[3,5-Di-*O*-acetyl-4-cyano-2-deoxy-α-L-*threo*-4-thiopentofuranosyl]thymine (28b). To a CH_2Cl_2 (7.0 mL) solution of **24** (206.8 mg, 0.38 mmol) were added cyanotrimethylsilane (0.25 mL, 1.9 mmol) and $BF_3 \cdot OEt_2$ (0.14 mL, 1.14 mmol) at −30 °C under Ar atmosphere, and the mixture was stirred at −30 °C for 20 h. The reaction mixture was partitioned between $CHCl_3$/saturated aq $NaHCO_3$. Silica gel column chromatography (hexane/AcOEt = 4/1) of the organic layer gave a mixture of **25** and **26b** (89.7 mg) [**25**; 72.5 mg (37%, **25a**: **25b** = 1: 0.05), **26b**; 17.3 mg (9%)] and **26a** (44.1 mg, 23%, foam). To a THF (3.5 mL) solution of a mixture of **25** and **26b** was added Bu_4NF (1 M THF solution) (0.36 mL, 0.36 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred for 3 h. To the reaction mixture was added Ac_2O (35 μL, 0.37 mmol), and the mixture was stirred for 12 h. The reaction mixture was partitioned between $CHCl_3$/saturated aq $NaHCO_3$. Preparative TLC (hexane/AcOEt = 1/1) of the organic layer gave **28a** (31.4 mg, 61%, crystallized from benzene/CH_2Cl_2) and **28b** (1.6 mg, 3%, syrup).

Physical data of **26a**: IR (neat) 2117 cm^{-1} (*N* = C:); UV (MeOH) λ_{max} 270 nm (ϵ 10600), λ_{min} 236 nm (ϵ 2600); ^{1}H NMR ($CDCl_3$) δ 0.13, 0.145, 0.149, 0.16 (12H, each as s), 0.93 and 0.94 (18H, each as s), 1.99 (3H, d, J = 0.7 Hz), 2.45 (1H, ddd, J = 9.8, 2.7, 13.2 Hz), 2.54 (1H, dd, J = 6.7, 13.2 Hz), 3.84 (1H, d, J = 10.2 Hz), 4.00 (1H, d, J = 10.2 Hz), 4.54 (1H, br), 6.72 (1H, dd, J = 6.7, 9.8 Hz), 7.52 (1H, d, J = 0.7 Hz), 8.62 (1H, br); NOE experiment: H-3′/ H-5′b (1.7%); ^{13}C NMR ($CDCl_3$) δ −5.3, −5.3, −5.1, −4.6, 12.9, 17.9, 18.4, 25.5, 25.8, 42.6, 61.8, 64.8, 78.3, 82.0, 113.0, 135.9, 150.4, 162.1, 163.1; FAB-MS (*m*/*z*) 359 (M^+ − NC − B + H), 485 (M^+ − NC); (+KI) 550 (M^++K). Anal. Calcd for $C_{23}H_{41}N_3O_4SSi_2$: C, 53.97; H, 8.07; N, 8.21. Found: C, 54.26; H, 8.30; N, 7.85.

Physical data of **28a**: mp 190–191 °C; IR (neat) 2243 cm^{-1} (CN); UV (MeOH) λ_{max} 268 nm (ϵ 10900), λ_{min} 236 nm (ϵ 2900); ^{1}H NMR ($CDCl_3$) δ 1.99 (3H, d, J = 1.2 Hz), 2.19 and 2.24 (6H, each as s), 2.56 (1H, ddd, J = 7.1, 5.0, 14.4 Hz), 2.69 (1H, ddd, J = 7.1, 5.0, 14.4 Hz), 4.44 (1H, d, J = 11.7 Hz), 4.50 (1H, d, J = 11.7 Hz), 5.58 (1H, t, J = 5.0 Hz), 6.53 (1H, t, J = 7.1 Hz), 7.31 (1H, d, J = 1.2 Hz), 8.79 (1H, br); NOE experiment H-6/CH_2-5′ (1.0%), H-2′a/ H-5′a (0.7%) and H-2′a/ H-5′b (0.4%); ^{13}C NMR ($CDCl_3$) δ 12.7, 20.5, 20.8, 29.7, 38.2, 54.7, 60.6, 74.5, 113.0, 116.1, 134.8, 150.2, 162.8, 169.5, 169.9; FAB-MS (*m*/*z*) 368 (M^+ + H). Anal. Calcd for $C_{15}H_{17}N_3O_6S$: C, 49.04; H,4.66; N, 11.44. Found: C, 49.00; H, 4.53; N, 11.04.

Physical data of **28b**: IR (neat) 2235 cm^{-1} (CN); ^{1}H NMR ($CDCl_3$) δ 2.01 (3H, d, J = 1.2 Hz), 2.14 and 2.18 (6H, each as s), 2.56 (1H, ddd, J = 9.8, 3.7, 14.6 Hz), 2.79 (1H, ddd, J = 6.8, 1.2, 14.6 Hz), 4.24 (1H, d, J = 11.2 Hz), 4.51 (1H, d, J = 11.2 Hz), 5.81 (1H, dd, J = 3.7, 1.2 Hz), 6.81 (1H, dd, J = 9.8, 6.8 Hz), 7.48 (1H, d, J = 1.2 Hz), 8.17 (1H, br); ^{13}C NMR ($CDCl_3$) δ 12.9, 20.4, 20.7, 29.7, 41.2, 54.6, 61.6, 62.5, 113.8, 118.9, 134.8, 150.2, 162.4, 168.9, 169.6; FAB-MS (*m*/*z*) 368 (M^+ + H); high-resolution FAB-MS (*m*/*z*) calcd for $C_{15}H_{18}N_3O_6S$ 368.0952 (M^+ + H), found 368.0895.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-4-formyl-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (29)To a toluene (6.0 mL) solution of a mixture of **25** and **26b** [148.2 mg; **25**,115.5 mg (0.23 mmol); **26b**, 32.7 mg (0.064 mmol)] was added DIBAL-H (0.99 M toluene solution) (0.88 mL, 0.87 mmol) at −70 °C under Ar atmosphere, and the mixture was stirred at −70 °C for 4 h. To the reaction mixture was added 10 M H_2SO_4 (30 drops), and the mixture was stirred at rt for 30 min. The reaction mixture was partitioned between $CHCl_3/H_2O$, and the organic layer was washed with saturated aq $NaHCO_3$. Silica gel column chromatography (hexane/AcOEt = 4/1) of the organic layer gave **29** (50.2 mg, 42%, foam): UV (MeOH) λ_{max} 270 nm (ϵ 9900), λ_{min} 236 nm (ϵ 2500); ^{1}H NMR ($CDCl_3$) δ 0.08, 0.09, 0.13 and 0.14 (12H, each as s), 0.89 and 0.93 (18H, each as s), 1.97 (3H s, J = 1.2 Hz), 2.34 (1H, ddd, J = 7.0, 5.6, 13.4 Hz), 2.52 (1H, ddd, J = 7.0, 5.6, 13.4 Hz), 3.86 (1H, d, J = 11.2 Hz), 4.09 (1H, d, J = 11.2 Hz), 4.80 (1H, t, J = 5.6 Hz), 6.56 (1H, t, J = 7.0 Hz), 7.58 (1H, d, J = 1.2 Hz), 8.57 (1H, br), 9.65 (1H, s); NOE experiment H-6/Ha-5′ (0.6%) and CHO/ H-1′ (0.9%); ^{13}C NMR ($CDCl_3$) δ −5.4, −5.3, −5.2, −4.7, 12.7, 17.9, 18.5, 25.5, 25.9, 43.8, 60.5, 62.9, 71.0, 76.7, 111.9, 135.7, 150.3, 163.0, 195.9; FAB-MS (*m*/*z*) 515 (M^+ + H). Anal. Calcd for $C_{23}H_{42}N_2O_5SSi_2$: C, 53.66; H,8.22; N, 5.44. Found: C, 53.85; H, 8.37; N, 5.40.

1-[3,5-Di-*O*-acetyl-4-ethynyl-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (31). To a MeOH (5.0 mL) solution of **29** (103.5 mg, 0.2 mmol) were added dimethyl 1-diazo-2-oxopropylphosphonate (96.1 mg, 0.5 mmol) and K_2CO_3 (110.6 mg, 0.8 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred at rt for 16 h. The reaction mixture was neutralized with AcOH and evaporated to dryness. The residue was partitioned between $CHCl_3$/saturated aq $NaHCO_3$. Silica gel column chromatography (hexane/AcOEt = 4/1) of the organic layer gave a crude product of **30** (41.8 mg). To a THF (2.0 mL) solution of the crude product was added Bu_4NF (1 M THF solution) (0.17 mL, 0.17 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred at 0 °C for 1 h. To the reaction mixture was added Ac_2O (20 μL, 0.21 mmol) at 0 °C, and the mixture was stirred at rt for 16 h. The reaction mixture was partitioned between $CHCl_3$/saturated aq $NaHCO_3$. Silica gel column chromatography (hexane/AcOEt = 1/1) of the organic layer gave **31** (21.8 mg, 30%, foam): IR (neat) 2117 cm^{-1} (C≡CH); UV (MeOH) λ_{max} 269 nm (ϵ 10700), λ_{min} 236 nm (ϵ 3600); ^{1}H NMR ($CDCl_3$) δ 1.99 (3H, d, J = 1.2 Hz), 2.17 and 2.18 (6H, each as s), 2.42 (1H, ddd, J = 7.2, 5.1, 14.2 Hz), 2.60 (1H, s), 2.67 (1H, ddd, J = 7.2, 5.1, 14.2 Hz), 4.36 (1H, d, J = 11.4 Hz), 4.45 (1H, d, J = 11.4 Hz), 5.50 (1H, t, J = 5.1 Hz), 6.59 (1H, t, J = 7.1 Hz), 7.50 (1H, d, J = 1.2 Hz), 8.39 (1H, br); ^{13}C NMR ($CDCl_3$)δ: 12.8, 20.8, 20.9, 39.0, 56.2, 59.9, 67.0, 75.0, 75.9, 79.4, 112.4, 135.3, 150.3, 162.8, 169.8, 170.2; FAB-MS (*m*/*z*) 367 (M^+ + H) and 307 (M^+ − OAc). Anal. Calcd for $C_{16}H_{18}N_3O_6S \cdot {}^1/_2$-AcOEt: C, 52.67; H,5.40; N, 6.83. Found: C, 53.02; H, 5.55; N, 6.94.

1-[4-Phenylthio-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (32). To a THF (4 mL) solution of **17a** (91.7 mg, 0.18 mmol) was added $Bu_4NF \cdot 3H_2O$ (70.6 mg, 0.27 mmol) at 0 °C, and the mixture was stirred at 0 °C for 3 h. Silica gel column chromatography (2–4% MeOH in CH_2Cl_2) of the reaction mixture gave a 1-[5-*O*-acetyl-4-phenylthio-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine. The product was treated with methanolic ammonia (6 mL) at rt for 5 h. The reaction mixture was evaporated to dryness. Silica gel column chromatography (4% MeOH in CH_2Cl_2) of the residue gave **32** (66 mg, 100%) as syrup, which was triturated from Et_2O: mp 100–102 °C; UV (MeOH) λ_{max} 269 nm (ϵ 12600), λ_{min} 242 nm (ϵ 5200); ^{1}H NMR (CD_3OD) δ 1.86 (3H, d, J = 1.2 Hz), 2.41 (1H, ddd, J = 3.6, 5.1, 13.4 Hz), 2.80 (1H, ddd, J = 7.3, 9.5, 13.4 Hz), 3.70 (1H, d, J = 12.2 Hz), 3.89 (1H, d, J = 12.2 Hz), 4.69 (1H, dd, J = 5.1, 9.5 Hz), 6.18 (1H, dd, J = 3.6, 7.3 Hz), 7.32–7.41 and 7.62–7.65 (5H, each as m), 8.19 (1H, d, J = 1.2 Hz); ^{13}C NMR (CD_3OD) δ 12.5, 42.8, 59.8, 66.0, 75.4, 78.3, 111.5, 129.7, 130.3, 132.4, 138.8, 139.3, 152.6, 166.2; FAB-MS (*m*/*z*) 367 (M^+ + H). Anal. Calcd for $C_{16}H_{18}N_2O_4S_2$: C, 52.44; H, 4.95; N, 7.64. Found: C, 52.71; H, 5.08; N, 7.48.

1-[4-Azido-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (33). To a THF (3 mL) solution of **18a** (60.2 mg, 0.13 mmol) was added $Bu_4NF \cdot 3H_2O$ (52.3 mg, 0.20 mmol) at 0 °C, and the mixture was stirred for 1 h. Silica gel column chromatography (3% MeOH in CH_2Cl_2) of the reaction mixture gave 1-[5-*O*-acetyl-4-azido-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine. The product was treated with methanolic ammonia (6 mL) at rt for 6 h. The reaction mixture was evaporated to dryness. Silica gel column chromatography (3% MeOH in CH_2Cl_2) of the residue gave **33** (30.9 mg, 79%) as syrup, which was triturated from Et_2O: IR (KBr) 2117 cm^{-1} (N_3); mp 100–102 °C; UV (MeOH) λ_{max} 270 nm (ϵ 12800), λ_{min} 237 nm (ϵ 4100); ^1H NMR (CD_3OD) δ 1.91 (3H, d, $J = 1.0$ Hz), 2.41–2.54 (2H, m), 3.77 (1H, d, $J = 11.7$ Hz), 3.82 (1H, d, $J = 11.7$ Hz), 4.48 (1H, dd, $J = 5.1, 7.1$ Hz), 6.41 (1H, d, $J = 6.1$), 7.88 (1H, d, $J = 1.0$ Hz); ^{13}C NMR (CD_3OD) δ 13.0, 42.0, 60.4, 67.8, 77.5, 88.1, 112.7, 138.9, 153.0, 166.5; FAB-MS (*m/z*) 300 ($M^+ + H$). Anal. Calcd for $C_{10}H_{13}N_5O_4S \cdot {}^1/_2AcOMe$: C, 41.07; H, 4.79; N, 20.82. Found: C, 41.00; H, 4.44; N, 21.22.

1-[2-Deoxy-4-methoxy-β-D-*erythro*-4-thiopentofuranosyl] thymine (34). To a THF (3.0 mL) solution of **20a** (49.5 mg, 0.12 mmol) was added $Bu_4NF \cdot 3H_2O$ (47.1 mg, 0.18 mmol) at 0 °C, and the mixture was stirred for 1 h. Silica gel column chromatography (3% MeOH in CH_2Cl_2) of the reaction mixture gave **34** (30.7 mg, 89%), which was triturated from Et_2O: mp 85–87 °C; UV (MeOH) λ_{max} 271 nm (ϵ 10200), λ_{min} 238 nm (ϵ 2480); ^1H NMR (CD_3OD) δ 1.90 (3H, d, $J = 1.0$ Hz), 2.33 (1H, ddd, $J = 3.4, 5.6, 10.7$ Hz), 2.58 (1H, ddd, $J = 7.3, 10.0, 10.7$ Hz), 3.46 (3H, s), 3.84 (1H, d, $J = 10.5$ Hz), 3.94 (1H, d, $J = 10.5$ Hz), 4.51 (1H, dd, $J = 5.6, 10.0$ Hz), 6.15 (1H, dd, $J = 3.4, 7.3$ Hz), 8.00 (1H, d, $J = 1.0$ Hz); ^{13}C NMR (CD_3OD) δ 12.6, 42.0, 53.1, 58.8, 63.0, 75.1, 101.9, 111.7, 138.9, 152.6, 166.2; FAB-MS (*m/z*) 289 ($M^+ + H$). Anal. Calcd for $C_{11}H_{16}N_2O_5S$: C, 45.82; H, 5.59; N, 9.72. Found: C, 45.95; H, 5.57; N, 9.41.

1-[4-Allyl-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (35). To a THF (3.5 mL) solution of **21a** (93.4 mg, 0.21 mmol) was added $Bu_4NF \cdot 3H_2O$ (100.2 mg, 0.38 mmol) at 0 °C, and the mixture was stirred for 2 h. Silica gel column chromatography (2% MeOH in CH_2Cl_2) of the reaction mixture gave 5′-*O*-acetyl derivative. The acetate was treated with methanolic ammonia (2.5 mL) at rt for 7 h. The reaction mixture was evaporated to dryness. Silica gel column chromatography of the crude product gave **35** (38.8 mg, 46%) as syrup, which was triturated from Et_2O: mp 86–88 °C; UV (MeOH) λ_{max} 272 nm (ϵ 9800), λ_{min} 237 nm (ϵ 2600); ^1H NMR (CD_3OD) δ 1.90 (3H, d, $J = 1.0$ Hz), 2.40–2.43 (2H, m), 2.54–2.56 (2H, m), 3.68 (2H, s), 4.38 (1H, t, $J = 4.4$ Hz), 5.09 (1H, dd, $J = 2.4, 10.0$ Hz), 5.15 (1H, dd, $J = 2.4, 16.8$ Hz), 5.81–5.91 (1H, m), 6.36 (1H, t, $J = 7.2$ Hz), 8.10 (1H, d, $J = 1.2$ Hz); ^{13}C NMR (CD_3OD) δ 13.0, 39.3, 44.1, 61.5, 67.3, 68.1, 76.4, 112.2, 119.3, 136.5, 139.7, 153.1, 166.7; FAB-MS (*m/z*) 299 ($M^+ + H$). Anal. Calcd for $C_{13}H_{19}N_2O_4S$: C, 52.33; H, 6.08; N, 9.39. Found: C, 52.10; H, 5.98; N, 9.05.

1-[4-Cyano-2-deoxy-β-D-*erythro*-4-thiopentofuranosyl]thymine (36). Compound **28a** was treated with methanolic ammonia (8 mL) at rt for 9 h. The reaction mixture was evaporated to dryness. Silica gel column chromatography (3% MeOH in CH_2Cl_2) of the residue gave **36** (21.5 mg, 77%) as syrup, which was triturated from Et_2O: IR (KBr) 2223 cm^{-1} (C≡N); mp 234–237 (dec) °C; UV (MeOH) λ_{max} 270 nm (ϵ 10500), λ_{min} 236 nm (ϵ 2500); ^1H NMR (CD_3OD) δ 1.90 (3H, d, $J = 1.2$ Hz), 2.46–2.58 (2H, m), 3.91 (1H, d, $J = 11.7$ Hz), 3.95 (1H, d, $J = 11.7$ Hz), 4.59 (1H, dd, $J = 4.9, 6.6$ Hz), 6.43 (1H, t, $J = 6.6$ Hz), 7.82 (1H, d, $J = 1.2$ Hz); ^{13}C NMR (CD_3OD) δ 12.5, 41.9, 61.16, 61.23, 66.0, 75.0, 112.3, 119.8, 138.3, 152.4, 166.0; FAB-MS (*m/z*) 284 ($M^+ + H$). Anal. Calcd for $C_{11}H_{13}N_3O_4S$: C, 46.63; H, 4.63; N, 14.83. Found: C, 46.70; H, 4.60; N, 14.47.

1-[2-Deoxy-4-ethynyl-β-D-*erythro*-4-thiopentofuranosyl]thymine (37). Compound **31** (25.5 mg, 0.07 mmol) was treated with methanolic ammonia (5 mL) at rt for 5 h. The reaction mixture was evaporated to dryness. Silica gel column chromatography (3% MeOH in CH_2Cl_2) of the residue gave **37** (16.7 mg, 84%) as syrup, which was triturated from Et_2O: IR (KBr) 2103 cm^{-1} (C≡CH); mp 229–231 °C; UV (MeOH) λ_{max} 270 nm (ϵ 10100), λ_{min} 237 nm (ϵ 2500); ^1H NMR (CD_3OD) δ 1.90 (3H, d, $J = 1.2$ Hz), 2.40 (1H, ddd, $J = 4.6, 5.1, 13.4$ Hz), 2.58 (1H, ddd, $J = 6.8, 7.9, 13.4$ Hz), 2.95 (1H, s), 3.79 (1H, d, $J = 11.7$ Hz), 3.87 (1H, d, $J = 11.7$ Hz), 4.41 (1H, dd, $J = 4.6, 7.9$ Hz), 6.31 (1H, dd, $J = 5.1, 6.8$ Hz), 8.11 (1H, t, $J = 1.2$ Hz); ^{13}C NMR (CD_3OD) δ 12.5, 42.7, 60.3, 61.5, 66.8, 75.1, 77.2, 82.8, 111.6, 139.0, 152.6, 166.2; FAB-MS (*m/z*) 283 ($M^+ + H$) and 267 ($M^+ - OH$). Anal. Calcd for $C_{12}H_{14}N_2O_4S_2 \cdot {}^1/_4H_2O$: C, 50.25; H, 5.10; N, 9.77. Found: C, 50.21; H, 4.96; N, 9.90.

Anti-HIV Assay. MT-4 cells[17] were maintained in RPMI 1640 medium supplemented with 10% heat-inactivated fetal bovine serum (FBS), 100U/mL of penicillin G, and 100 mg/mL of streptomycin. The III_B strain of HIV-1 was used throughout the experiment. The virus was propagated and titrated in MT-4 cells. Virus stocks were stored at −80 °C until use.

The anti-HIV-1 activity of the test compounds was determined by the inhibition of either virus-induced cytopathogenicity in MT-4 cells.[18] Briefly, MT-4 cells (1×10^5cells/mL) were infected with HIV-1 at a multiplicity of infection (MOI) of 0.02 and were cultured in the presence of various concentrations of the test compounds. In the case of HIV-2, M8166 cells (1×10^5) were infected at a MOI of 0.1. After a 4-day incubation at 37 °C, the number of viable cells was monitored by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) method.[19] The cytotoxicity of the compounds was evaluated in parallel with their antiviral activity, based on the viability of mock-infected cells, as determined by the MTT method.

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Supporting Information Available: Experimental procedures and full characterization for compounds **8**−**13**. This material is available free of charge via the Internet at http://pubs.acs.org.

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