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Synthesis and antiviral activities of 1′-carbon-substituted 4′-thiothymidines

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Abstract—4-Thiofuranoid glycals substituted at the 1-position with methyl (**5**), (*t*-butyldimethylsilyloxy)methyl (**7**), and acetoxymethyl (**8**) groups were prepared from the 3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl) (TIPDS)-4-thiofuranoid glycal (**3**) by way of LDA-lithiation. *N*-Iodosuccimide-initiated electrophilic glycosidation between silylated thymine and these 1-carbon-substituted 4-thioglycals gave the respective β-anomers (**9**, **10**, and **13**) stereoselectively. Tin radical-mediated removal of the 2′-iodine atom from these products provided the corresponding 1′-branched 4′-thiothymidine derivatives (**11**, **12**, and **14**) in good yields. The 1′-hydroxymethyl derivative (**15**) served as a precursor for the preparation of the formyl (**16**), cyanoethenyl (**17**), and cyano (**19**) derivatives. Among the deprotected 1′-branched 4′-thiothymidines (**20**–**25**), the 1′-methyl analogue **20** showed the most potent anti-HSV-1 activity, but it was much less active than the parent compound 4′-thiothymidine.

1. Introduction

Nucleoside analogues have been recognized as an important class of biologically active compounds, especially, the carbon-branched sugar derivatives possess potent antiviral activities.[1] In 1991, it was reported that the simple replacement of the furanose ring-oxygen with a sulfur atom leads to promising antiviral and antitumor nucleosides such as 4′-thiothymidine (**1**) and 2′-deoxy-4′-thiocytidine (**2**) (Fig. 1).[2,3] This discovery has stimulated the synthesis of 4′-thionucleosides.[4] The synthesis of these nucleosides has been carried out by way of Vorbrüggen-type or Pummerer-type glycosidation. A major drawback of these methods is the lack of β-stereoselectivity that is crucial for these 4′-thionucleosides to be active.

Recently, we reported a highly β-selective entry to 4′-thionucleosides based on an electrophilic glycosidation using 4-thiofuranoid glycal as a glycosyl donor.[5–9] In this paper, we focus on the synthesis 1′-carbon-substituted 4′-thiothymidines and disclose their antiviral activities.

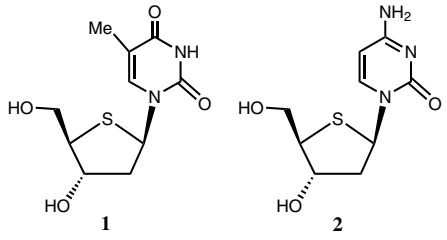

Figure 1. 4′-Thiothymidine and 2′-deoxy-4′thiocytidine.

2. Results and discussion

As reported briefly in our recent communications,[7,8] the 1-methyl-4-thiofuranoid glycal (**5**) was prepared in 73% yield by alpha-lithiation[10] of 3,5-*O*-(tetraisopropyldisiloxane-1.3-diyl) (TIPDS)-4-thiofuranoid glycal (**3**) with LDA followed by methylation of the 1-lithiated species

Keywords: Glycal; Lithiation; Glycosidation; Nucleoside.
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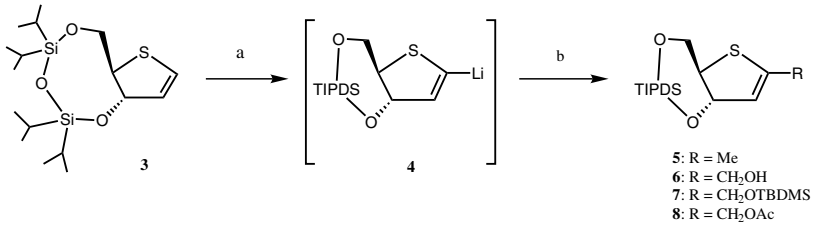


Scheme 1. Reagents: (a) LDA; (b) MeI (for **5**) or (1) DMF/$NaBH_4$, (2) TBDMSCI (for **7**) or (1) DMF/$NaBH_4$, (2) Ac_2O (for **8**).

(**4**) with MeI (Scheme 1). Likewise, the 1-hydroxymethyl derivative **6** was prepared by reacting **4** with DMF and subsequent reduction with $NaBH_4$ in 72% yield. Compounds **7** and **8** were obtained simply by conventional silylation or acetylation of **6**.

Electrophilic glycosidation between **5** and bis(trimethylsilyl)thymine was carried out by using *N*-iodosuccimide (NIS) as an electrophilic reagent in CH_3CN at 0 °C (Scheme 2). That the product (**9**, 57%) obtained from this reaction has the desired β-configuration was confirmed by NOE experiments (the observed NOE correlations: H-6/H-3′ and H-6/H-2′). In the case of **7**, the 1′-(*t*-butyldimethylsilyl)oxymethyl derivative **10** was also obtained stereoselectively in 70% yield. Removal of the iodine atom at the 2′-position of these products was performed by reacting with Bu_3SnH in the presence of Et_3B as a radical initiator to give the 1′-carbon-substituted 4′-thiothymidines (**11** and **12**) in excellent yields.

We have experienced in previous studies[8,9] that the above electrophilic glycosidation does not work for 4-thiofuranoid glycals having an electron-withdrawing group at the 1-position.[11] Therefore, as an alternative route to synthesize other 1′-carbon-substituted 4′-thiothymidines, chemical transformation of the 1′-hydroxymethylthymidine (**15**) was next investigated. Compound **15** was prepared from the 1-acetoxymethyl glycal **8** by following the aforementioned procedures and finally by deacetylation (**8** → **13** → **14** → **15**) (Fig. 2).

As shown in Scheme 3, oxidation of **15** with Dess–Martin periodinane furnished the 1′-carbaldehyde **16** in 91% yield. The Wittig reaction of **16** with $Bu_3P{=}CHCN$ gave the 1′-cyanoethenyl nucleoside **17** in 91% yield. The 1′-cyano derivative **19** was prepared by dehydration of the oxime intermediate (**18**) with Ac_2O at 100 °C.

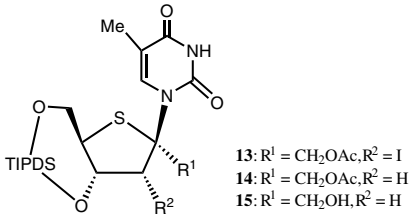
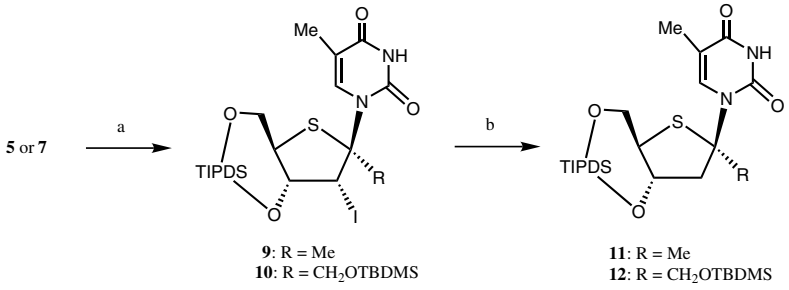


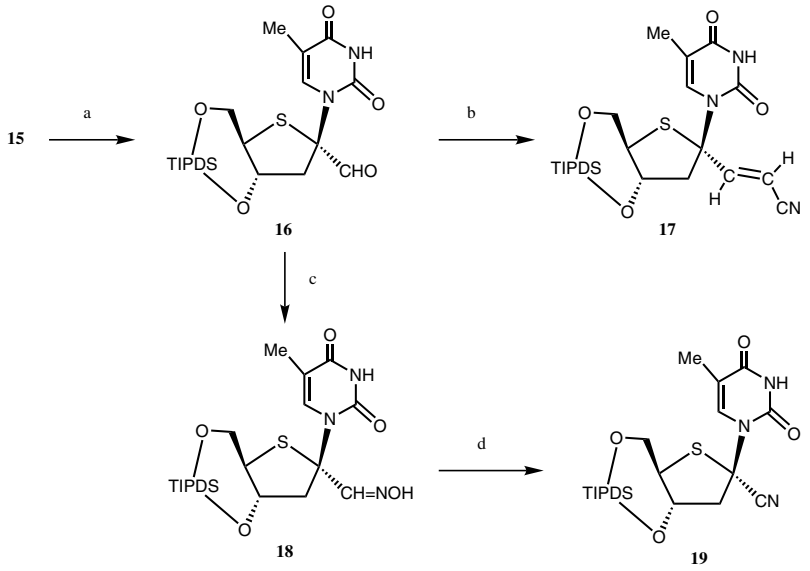
Figure 2. Synthesis of 1′-hydroxymethyl-4′-thiothymidine derivative.

Compounds (**11**, **12**, **16**, **17**, and **19**) synthesized in this study were desilylated by reacting with Bu_4NF to give the corresponding free nucleosides (**20**–**23**). The isolation procedure for 1′-cyano-4′-thiothymidine (**25**) deserves a comment. When the desilylated mixture containing **25** was subjected to silica gel column chromatography (8% CH_3OH in CH_2Cl_2), the iminoether **24** was isolated. This problem could be overcome by chromatographic purification using neutral silica gel (ICN Silica™) to furnish the 1′-cyanonucleoside **25**.

Finally, antiviral activities of 1′-carbon-substituted 4′-thiothymidines (**20**–**25**) were evaluated against herpes simplex virus type I (HSV-1) and human immunodeficiency virus type I (HIV-1) (Fig. 3), the results of which are summarized in Table 1. The anti-HSV-1 activity of the parent compound 4′-thiothymidine (**1**) is also included. The 1′-methyl analogue (**20**) showed anti-HVS-1 activity with ED_{50} of 4 μM, but its potency was 500 times less than that of **1**. No anti-HIV activity was observed for **21**–**25**.



Scheme 2. Reagents: (a) thymine, BSA, *N*-iodosuccimide/CH_3CN; (b) Bu_3SnH, Et_3B, O_2, PhMe.



Scheme 3. Reagents: (a) Dess–Martin periodinane; (b) $Bu_3P{=}CHCN$; (c) $HONH_2$; (d) Ac_2O.

Table 1. Antiviral activities of 1′-carbon-substituted 4′-thiothymidines

Compound (R)	HSV-1[a]		HIV-1[b,c]	
	ED_{50} (μg/mL)	CC_{50} (μg/mL)	ED_{50} (μM)	CC_{50} (μM)
20 (Me)	4	86.8	>34.1	>34.1
21 (CH_2OH)	>100	>100	>100	>100
22 (CHO)	20	>100	>95.1	>95.1
23 (CH=CHCN)	>100	>100	>100	>100
24 (C(OMe)=NH)	100	>100	>100	>100
25 (CN)	20	>100	>100	>100
4′-Thiothymidine	0.008	8.73	—	—

[a] EC_{50} value was determined by the CPE inhibition method.
[b] Data represent mean values for two separate experiments.
[c] Inhibitory concentration required to achieve 50% protection of MT-4 cells against the cytopathic-effect of HIV-1.

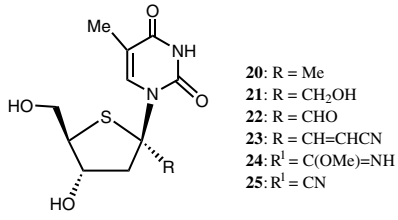


Figure 3. 1′-Carbon-substituted-4′-thiothymidines.

In summary, we have developed a synthetic method for novel 1′-carbon-substituted 4′-thiothymidines. This method consists of three step sequences; (1) preparation of 1-carbon-substituted 4-thiofuranoid glycal, (2) stereoselective electrophilic glycosydation to these 1-substituted glycals, and (3) tin radical-mediated removal of 2′-iodo substituent. Among the 1′-branched 4′-thiothymidines (**20**–**25**), the 1′-methyl analogue **20** showed the most potent anti-HSV-1 activity, but it was much less active than the parent compound 4′-thiothymidine. This data indicates that introduction of carbon-substituent into the anomeric position of 4′-thiothymidine gave detrimental effect for the antiviral activity. This would be attributed to the unfavorable direction of torsion angle around the glycosyl bond or sugar conformation for recognition by the enzymes, which convert these nucleoside analogues into active intermediate triphosphates.

3. Experimental

3.1. General

Melting points are uncorrected. ^1H NMR and ^{13}C NMR were measured on a JEOL JNM-LA 500 (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 on a JEOL JMS-700. Ultraviolet spectra (UV) were recorded on a JASCO V-530 spectrophotometer. Column chromatography was carried out on silica gel (Micro Bead Silica Gel PSQ 100B, Fuji Silysia Chemical Ltd). Thin layer chromatography (TLC) was performed on silica gel (precoated silica gel plate F_{254}, Merck). ICN silica gel was purchased from MP Biomedicals., Inc. Where necessary, analytical samples were purified by high-performance liquid chromatography (HPLC). HPLC was

carried out on a Shimadzu LC-6AD with a Shim-pack PREP-SIL (H)·KIT column (2 × 25 cm). THF was distilled from benzophenone ketyl.

3.2. Biological assay

3.2.1. Anti-HSV-1 activity.[12] Antiviral activity against HSV-1 was examined by cytopathic-effect (CPE) inhibition method. Briefly, HEL cells grown in 96 multi-wells were infected with about 100 plaque forming units of HSV-1. After 30 min of virus adsorption, virus inoculum was discarded, and the infected cells were incubated with various concentrations of the test compounds at 37 °C for two to three days. The CPE in each well were determined by microscopic examination. The antiviral activity was expressed as ED_{50} at which HSV-induced CPE were suppressed at least 50%.

3.2.2. Anti-HIV activity. The activity of these nucleoside analogues against HIV-1 replication was based on the inhibition of virus-infected cytopathogenicity in MT-4 cells, as described previously.[13] Briefly, the cells (1 × 105 cells/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. After a four 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.[14] The cytotoxicity of the compounds was evaluated in parallel with their antiviral activity, based on the viability of mock-infected cells.

3.3. Chemical synthesis

3.3.1. 1,4-Anhydro-2-deoxy-1-methyl-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-D-*erythro*-pento-1-enitol (5). To a THF (3.0 mL) solution of LDA (2.05 mmol) was added **3** (153 mg, 0.41 mmol) in THF (2.0 mL) at −70 °C under Ar atmosphere, and the mixture was stirred for 30 min. To this was added methyl iodide (0.25 mL, 4.09 mmol) and stirring was continued for further 30 min. The reaction mixture was partitioned between $CHCl_3$/satd NH_4Cl. Column chromatography (hexane/AcOEt = 400/1) of the organic layer gave **5** (115 mg, 73%) as a syrup: UV (MeOH) λ_{max} 237 nm (ε 7000); ^{1}H NMR ($CDCl_3$) δ 1.00–1.11 (28H, m, Si-*i*-Pr), 1.95 (3H, t, $J_{Me,2} = J_{Me,3} = 1.2$ Hz, Me), 3.82 (1H, dd, $J_{4,5a} = J_{5a,5b} = 11.0$ Hz, H-5a), 3.88–3.92 (1H, m, H-4), 4.04 (1H, dd, $J_{4,5b} = 3.6$ Hz and $J_{5a,5b} = 11.0$ Hz, H-5b), 5.25–5.26 (1H, m, H-3), 5.36–5.39 (1H, m, H-2); FAB-MS (*m*/*z*) 427 ($M^+ + K$). Anal. Calcd for $C_{18}H_{36}O_2SSi$: C, 55.62; H, 9.34. Found: C, 55.78; H, 9.55.

3.3.2. 1,4-Anhydro-2-deoxy-1-hydroxymethyl-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-D-*erythro*-pento-1-enitol (6). This compound was prepared by the same procedure for the synthesis of **5**, using the following substrate and reagents: LDA (1.87 mmol), **3** (140 mg, 0.37 mmol), DMF (0.17 mL, 2.24 mmol), and $NaBH_4$ (18.4 mg, 0.49 mmol), which gave **6** (109 mg, 72%) as a syrup: UV (MeOH) λ_{max} 238 nm (ε 7100); ^{1}H NMR ($CDCl_3 + D_2O$) δ 1.01–1.11 (28H, m, Si-*i*-Pr), 3.85 (1H, t, $J_{4,5a} = J_{5a,5b} = 11.2$ Hz, H-5a), 3.92 (1H, ddd, $J_{3,4} = 4.4$ Hz, $J_{4,5a} = 11.2$ Hz, and $J_{4,5b} = 4.0$ Hz, H-4), 4.07 (1H, dd, $J_{4,5b} = 4.0$ Hz and $J_{5a,5b} = 11.2$ Hz, H-5b), 4.25 and 4.30 (2H, each as dt, $J_{2,CH2} = J_{3,CH2} = 1.6$ Hz, and $J_{gem} = 14.4$ Hz, CH_2OH), 5.42 (1H, ddd,, $J_{CH2,3} = 1.6$ Hz, $J_{2,3} = 2.4$ Hz, and $J_{3,4} = 4.4$ Hz H-3), 5.54 (1H, dd, $J_{2,CH2} = 1.6$ Hz and $J_{2,3} = 2.4$ Hz, H-2); FAB-MS (*m*/*z*) 443 ($M^+ + K$). Anal. Calcd for $C_{18}H_{36}O_4SSi$: C, 53.42; H, 8.97. Found: C, 53.18; H, 9.11.

3.3.3. 1,4-Anhydro-1-(*t*-butyldimethylsilyloxymethyl)-2-deoxy-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-D-*erythro*-pento-1-enitol (7). A mixture of **6** (90.1 mg, 0.22 mmol), imidazole (45.5 mg, 0.67 mmol), and *t*-butyldimethylsilyl chloride (67.2 mg, 0.45 mmol) in DMF (3.0 mL) was stirred for 1 h. The reaction mixture was partitioned between AcOEt/H_2O. Column chromatography (hexane/AcOEt = 50/1) of the organic layer gave **7** (108 mg, 93%) as a syrup: UV (MeOH) $\lambda_{shoulder}$ 286 nm (ε 1300), λ_{max} 244 nm (ε 6200), λ_{min} 214 nm (ε 2400); ^{1}H NMR ($CDCl_3$) δ 0.08 (6H, s, Si-Me), 0.91 (9H, s, Si-*t*-Bu), 1.03–1.10 (28H, m, Si-*i*-Pr), 3.85 (1H, t, $J_{4,5a} = J_{5a,5b} = 9.6$ Hz, H-5a), 3.88–3.92 (1H, m, H-4), 4.06 (1H, dd, $J_{4,5b} = 2.0$ Hz and $J_{5a,5b} = 9.6$ Hz, H-5b), 4.27 and 4.33 (2H, each as dt, $J_{2,CH2} = J_{3,CH2} = 1.6$ Hz and $J_{gem} = 13.6$ Hz, CH_2OTBDMS), 5.38–5.41 (1H, m, H-3), 5.54 (1H, dd, $J_{2,CH2} = 1.6$ Hz and $J_{2,3} = 2.4$ Hz, H-2); FAB-MS (*m*/*z*) 557 ($M^+ + K$). Anal. Calcd for $C_{24}H_{50}O_4SSi_3 \cdot 1/2H_2O$: C, 54.60; H, 9.74. Found: C, 54.25; H, 9.73.

3.3.4. 1-Acetoxymethyl-1,4-anhydro-2-deoxy-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-D-*erythro*-pento-1-enitol (8). This compound was prepared by the same procedure for the synthesis of **5** using the following substrate and reagents: LDA (5.1 mmol), **3** (381.6 mg, 1.02 mmol), DMF (0.55 mL, 7.14 mmol), and $NaBH_4$ (57.9 mg, 1.53 mmol), which gave **6** (333.5 mg, 81%) as a syrup. To a CH_2Cl_2 (6 mL) solution of **6** were added *i*-Pr_2NEt (0.43 mL, 2.46 mmol), Ac_2O (0.15 mL, 1.64 mmol), and DMAP (50 mg, 0.41 mmol) at 0 °C. The mixture was stirred at rt for 1 h. The reaction mixture was partitioned between $CHCl_3$/satd $NaHCO_3$. Column chromatography (hexane/AcOEt = 40/1) of the organic layer gave **8** (287.1 mg, 78%) as a syrup: UV (MeOH) $\lambda_{shoulder}$ 257 nm (ε 2200), λ_{max} 240 nm (ε 4500), λ_{min} 215 nm (ε 1100); ^{1}H NMR ($CDCl_3$) δ 1.03–1.54 (28H, m, Si-*i*-Pr), 2.10 (3H, s, Ac), 3.88 (1H, dd, $J_{4,5a} = 10.8$ Hz and $J_{5a,5b} = 11.0$ Hz, H-5a), 3.91–3.96 (1H, m, H-4), 4.06 (1H, dd, $J_{4,5b} = 3.2$ Hz and $J_{5a,5b} = 11.0$ Hz, H-5b), 4.69 (1H, dt, $J_{2,CH2a} = J_{3,CH2a} = 1.2$ Hz and $J_{gem} = 13.2$ Hz, CH_{2a}OAc), 4.76 (1H, dt, $J_{2,CHb} = J_{3,CH2b} = 1.2$ Hz and $J_{gem} = 13.2$ Hz CH_{2b}OAc), 5.40 (1H, m, H-3), 5.56–5.57 (1H, m, H-2); FAB-MS (*m*/*z*) 387 (M^+−OAc). Anal. Calcd for $C_{20}H_{38}O_5SSi_2$: C, 53.77; H, 8.57. Found: C, 53.93; H, 8.83.

3.3.5. 1-[2-Deoxy-2-iodo-1-methyl-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]-thymine (9). To an CH_3CN (1.5 mL) solution of bis-*O*-trimethylsilylthymine, prepared from thymine (47.9 mg, 0.38 mmol) and BSA (0.19 mL, 0.75 mmol), were added

5 (96.6 mg, 0.25 mmol) in CH_3CN (2.0 mL)-CH_2Cl_2 (1.0 mL) and *N*-iodosuccimide (85.5 mg, 0.38 mmol) at 0 °C under Ar atmosphere. The reaction mixture was stirred for 2 h and then partitioned between $CHCl_3$/satd $NaHCO_3$. Column chromatography (hexane/AcOEt = 10/1) of the organic layer gave **9** (92.0 mg, 57%) as a foam: UV (MeOH) λ_{max} 269 nm (ε 10,600), λ_{min} 237 nm (ε 2700); ^{1}H NMR ($CDCl_3$) δ 0.89–1.07 (28H, m, Si-*i*-Pr), 1.95 (3H, d, $J_{Me,6}$ = 1.2 Hz, Me-5), 2.19 (3H, s, Me-1′), 3.27 (1H, dd, $J_{2',3'}$ = 4.0 Hz and $J_{3',4'}$ = 9.2 Hz, H-3′), 3.68–3.71 (1H, m, H-4′), 3.94 (1H, dd, $J_{4',5'a}$ = 1.6 Hz and $J_{5'a,5'b}$ = 12.8 Hz, H-5′a), 4.04 (1H, dd, $J_{4',5'b}$ = 3.2 Hz and $J_{5'a,5'b}$ = 12.8 Hz, H-5′b), 5.95 (1H, d, $J_{2',3'}$ = 4.0 Hz, H-2′), 8.06 (1H, br, NH), 8.62 (1H, d, $J_{Me,6}$ = 1.2 Hz, H-6); NOE experiment, H-6/H-2′ (1.0%), H-6/H-3′ (1.0%), H-2′/H-3′ (3.2%); FAB-MS (*m*/*z*) 641 (M^+ + H), 597 (M^+−*i*-Pr) and 515 (M^+−B). Anal. Calcd for $C_{23}H_{41}IN_2O_5SSi_2$: C, 43.11; H, 6.45; N, 4.37. Found: C, 43.14; H, 6.48; N, 4.16.

3.3.6. 1-[1-(*t*-Butyldimethylsilyloxymethyl)-2-deoxy-2-iodo-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]thymine (10). This compound was prepared by the same procedure for the synthesis of **9**, using the following substrate and reagents: thymine (26.5 mg, 0.21 mmol), BSA (0.10 mL, 0.42 mmol), **7** (72.1 mg, 0.14 mmol), *N*-iodosuccimide (47.2 mg, 0.21 mmol), which gave **10** (75.9 mg, 70%) as a syrup: UV (MeOH) λ_{max} 269 nm (ε 10,700), λ_{min} 237 nm (ε 3000); ^{1}H NMR ($CDCl_3$) δ −0.09 and 0.09 (6H, each as s, Si-Me), 0.78 (9H, s, Si-*i*-Bu), 0.91–0.98 and 1.03–1.06 (28H, each as m, Si-*i*-Pr), 1.92 (3H, d, $J_{Me,6}$ = 1.2 Hz, Me-5), 3.30 (1H, dd, $J_{2',3'}$ = 4.0 Hz and $J_{3',4'}$ = 9.4 Hz, H-3′), 3.57–3.60 (1H, m, H-4′), 3.92 (1H, d, $J_{5'a,5'b}$ = 12.8 Hz, H-5′a), 4.04 (1H, dd, $J_{4',5'b}$ = 2.8 Hz and $J_{5'a,5'b}$ = 12.8 Hz, H-5′b), 4.26 (1H, d, $J_{1''a,1''b}$ = 9.6 Hz, H-1″a), 4.65 (1H, d, $J_{1''a,1''b}$ = 9.6 Hz, H-1″b), 5.90 (1H, d, $J_{2',3'}$ = 4.0 Hz, H-2′), 8.47 (1H, d, $J_{Me,6}$ = 1.2 Hz, H-6), 8.64 (1H, br, NH); NOE experiment, H-6/H-2′ (1.0%), H-2′/H-3′ (10%); FAB-MS (*m*/*z*) 713 (M^+−*t*-Bu) and 645 (M^+−B). Anal. Calcd for $C_{29}H_{55}IN_2O_6SSi_3$·1/10AcOEt: C, 45.28; H, 7.21; N, 3.59. Found: C, 45.65; H, 7.38; N, 3.51.

3.3.7. 1-[2-Deoxy-1-methyl-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]thymine (11). To a toluene (2.5 mL) solution of **9** (48.2 mg, 0.25 mmol) was added tributyltin hydride (30 μL, 0.11 mmol) and triethylborane (38 μL, 0.038 mmol) at −40 °C, and the mixture was stirred under O_2 atmosphere for 2 h. Column chromatography (hexane/AcOEt = 10/1) of the reaction mixture gave **11** (36.3 mg, 94%) as a syrup: UV (MeOH) λ_{max} 272 nm (ε 9700), λ_{min} 238 nm (ε 2200); ^{1}H NMR ($CDCl_3$) δ 0.97–1.07 (28H, m, Si-*i*-Pr), 1.93 (3H, d, $J_{Me,6}$ = 1.2 Hz, Me-5), 1.98 (3H, s, Me-1′), 2.31 (1H, dd, $J_{2a',3'}$ = 12.0 Hz and $J_{2'a,2'b}$ = 13.8 Hz, H-2′a), 3.42–3.46 (1H, m, H-4′), 3.54 (1H, dd, $J_{2b',3'}$ = 4.8 Hz and $J_{2'a,2'b}$ = 13.8 Hz, H-2′b), 3.83 (1H, dd, $J_{4',5'a}$ = 3.2 Hz and $J_{5'a,5'b}$ = 12.6 Hz, H-5′a), 4.04 (1H, dd, $J_{4',5'b}$ = 3.2 Hz and $J_{5'a,5'b}$ = 12.6 Hz, H-5′b), 4.17–4.23 (1H, m, H-3′), 8.24 (1H, d, $J_{Me,6}$ = 1.2 Hz, H-6), 8.71 (1H, br, NH); FAB-MS (*m*/*z*) 389 (M^+−B). Anal. Calcd for $C_{23}H_{42}N_2O_5SSi_2$: C, 53.66; H, 8.22; N, 5.44. Found: C, 53.89; H, 8.41; N, 5.32.

3.3.8. 1-[1-(*t*-Butyldimethylsilyloxymethyl)-2-deoxy-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]thymine (12). This compound was prepared by the same procedure for the synthesis of **11**, using the following substrate and reagents: **10** (69.7 mg, 0.09 mmol), tributyltin hydride (38 μL, 0.14 mmol), triethylborane (47 μL, 0.047 mmol), which gave **12** (57.1 mg, 94%) as a syrup: UV (MeOH) λ_{max} 270 nm (ε 9800), λ_{min} 237 nm (ε 2100); ^{1}H NMR ($CDCl_3$) δ −0.06 and −0.02 (6H, each as s, Si-Me), 0.80 (9H, s, Si-*i*-Bu), 0.90–1.06 (28H, each as m, Si-*i*-Pr), 1.90 (3H, d, $J_{Me,6}$ = 0.8 Hz, Me-5), 2.27 (1H, dd, $J_{2'a,3'}$ = 10.8 Hz and $J_{2'a,2'b}$ = 13.8 Hz, H-2′a), 3.27–3.31 (1H, m, H-4′), 3.34 (1H, dd, $J_{2'b,3'}$ = 4.8 Hz and $J_{2'a,2'b}$ = 13.8 Hz, H-2′b), 3.80 (1H, d, $J_{4',5'a}$ = 3.6 Hz and $J_{5'a,5'b}$ = 12.8 Hz, H-5′a), 3.92 (1H, d, $J_{1''a,1''b}$ = 10.0 Hz, H-1″a), 4.02 (1H, dd, $J_{4',5'b}$ = 3.2 Hz and $J_{5'a,5'b}$ = 12.8 Hz, H-5′b), 4.25–4.31 (1H, m, H-3′), 4.37 (1H, d, $J_{1''a,1''b}$ = 10.0 Hz, H-1″b), 7.98 (1H, d, $J_{Me,6}$ = 0.8 Hz, H-6), 8.58 (1H, br, NH); FAB-MS (*m*/*z*) 601 (M^+−*i*-Pr) and 519 (M^+−B). Anal. Calcd for $C_{29}H_{56}N_2O_6SSi_3$: C, 53.99; H, 8.75; N, 4.34. Found: C, 54.35; H, 9.00; N, 4.27.

3.3.9. 1-[1-(Acetoxymethyl)-2-deoxy-2-iodo-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]thymine (13). This compound was prepared by the same procedure for the synthesis of **9**, using the following substrate and reagents: thymine (119.8 mg, 0.95 mmol), BSA (0.47 mL, 1.89 mmol), **8** (281.2 mg, 0.63 mmol), and *N*-iodosuccimide (212.6 mg, 0.95 mmol), which gave **13** (370.1 mg, 84%) as a foam: UV (MeOH) λ_{max} 267 nm (ε 11,000), λ_{min} 236 nm (ε 3000); ^{1}H NMR ($CDCl_3$) δ 0.83–1.07 (28H, each as m, Si-*i*-Pr), 1.95 (3H, d, $J_{Me,6}$ = 1.2 Hz, Me-5), 2.03 (3H, s, Ac), 3.29 (1H, dd, $J_{2',3'}$ = 4.0 Hz and $J_{3',4'}$ = 9.64 Hz, H-3′), 3.66–3.68 (1H, m, H-4′), 3.94 (1H, d, $J_{5'a,5'b}$ = 12.8 Hz, H-5′a), 4.05 (1H, dd, $J_{4',5'b}$ = 2.8 Hz and $J_{5'a,5'b}$ = 12.8 Hz, H-5′b), 4.86 (1H, d, $J_{1''a,1''b}$ = 11.2 Hz, H-1″a), 5.28 (1H, d, $J_{1''a,1''b}$ = 11.2 Hz, H-1″b), 5.87 (1H, d, $J_{2',3'}$ = 4.0 Hz, H-2′), 8.17 (1H, br, NH), 8.50 (1H, d, $J_{Me,6}$ = 1.2 Hz, H-6); NOE experiment, H-6/H-2′ (3.1%), CH_2OAc/H-4′ (0.9%), H-2′/H-3′ (10%); FAB-MS (*m*/*z*) 699 (M^+−H) and 573 (M^+−B). Anal. Calcd for $C_{25}H_{43}IN_2O_7SSi_2$: C, 42.97; H, 6.20; N, 4.01. Found: C, 43.32; H, 6.23; N, 3.90.

3.3.10. 1-[1-(Acetoxymethyl)-2-deoxy-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]thymine (14). This compound was prepared by the same procedure for the synthesis of **11**, using the following substrate and reagents: **13** (366.2 mg, 0.52 mmol), Bu_3SnH (0.21 mL, 0.78 mmol), Et_3B (0.26 mL, 0.26 mmol), which gave **14** (275 mg, 92%) as a foam: UV (MeOH) λ_{max} 269 nm (ε 10,000), λ_{min} 237 nm (ε 2600); ^{1}H NMR ($CDCl_3$) δ 0.91–1.08 (28H, each as m, Si-*i*-Pr), 1.93 (3H, d, $J_{Me,6}$ = 1.2 Hz, Me-5), 2.03 (3H, s, Ac), 2.34 (1H, dd, $J_{2'a,3'}$ = 11.6 Hz and $J_{2'a,2'b}$ = 14.0 Hz, H-2′a), 3.33–3.37 (1H, m, H-2′b and H-4′), 3.84 (1H, dd, $J_{4',5'a}$ = 2.8 Hz and $J_{5'a,5'b}$ = 12.8 Hz, H-5′a), 4.05 (1H,

dd, $J_{4',5'b}$ = 3.2 Hz and $J_{5'a,5'b}$ = 12.8 Hz, H-5′b), 4.24–4.30 (1H, m, H-3′), 4.57 (1H, d, $J_{1''a,1''b}$ = 11.2 Hz, H-1″a), 4.91 (1H, d, $J_{1''a,1''b}$ = 11.2 Hz, H-1″b), 8.01 (1H, d, $J_{Me,6}$ = 1.2 Hz, H-6), 8.19 (1H, br, NH); FAB-MS (*m/z*) 573 (M^+ + H) and 447 (M^+−B). Anal. Calcd for $C_{25}H_{44}N_2O_7SSi_2$: C, 52.42; H, 7.74; N, 4.89. Found: C, 52.43; H, 7.89; N, 4.80.

3.3.11. 1-[2-Deoxy-1-hydroxymethyl-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]thymine (15). Compound **14** (259 mg, 0.45 mmol) was treated with methanolic ammonia (15 mL) at rt overnight. The reaction mixture was evaporated to dryness. Column chromatography (1.5% MeOH in CH_2Cl_2) of the residue gave **15** (226.9 mg, 95%) as a foam: UV (MeOH) λ_{max} 271 nm (ε 9800), λ_{min} 238 nm (ε 2100); ^{1}H NMR ($CDCl_3$) δ 0.93–1.07 (28 H, each as m, Si-*i*-Pr), 1.89 (3H, d, $J_{Me,6}$ = 1.2 Hz, Me-5), 2.41 (1H, dd, $J_{2'a,3'}$ = 11.6 Hz and $J_{2'a,2'b}$ = 14.0 Hz, H-2′a), 3.22 (1H, dd, $J_{2'b,3'}$ = 5.2 Hz and $J_{2'a,2'b}$ = 14.0 Hz, H-2′b), 3.31–3.33 (1H, m, H-4′), 3.86 (1H, dd, $J_{4',5'a}$ = 2.4 Hz and $J_{5'a,5'b}$ = 13.0 Hz, H-5′a), 4.02 (1H, d, $J_{1''a,1''b}$ = 11.6 Hz, H-1″a), 4.06 (1H, dd, $J_{4',5'b}$ = 3.2 Hz and $J_{5'a,5'b}$ = 13.0 Hz, H-5′b), 4.25 (1H, d, $J_{1''a,1''b}$ = 11.6 Hz, H-1″b), 4.25–4.30 (1H, m, H-3′), 8.01 (1H, d, $J_{Me,6}$ = 1.2 Hz, H-6), 8.19 (1H, br, NH); FAB-MS (*m/z*) 531 (M^+ + H) and 405 (M^+−B). Anal. Calcd for $C_{23}H_{42}N_2O_6SSi_2$: C, 52.04; H, 7.98; N, 5.28. Found: C, 51.99; H, 8.19; N, 5.46.

3.3.12. 1-[2-Deoxy-1-formyl-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]thymine (16). To a CH_2Cl_2 (4.0 mL) solution of **15** (83.7 mg, 0.16 mmol) was added Dess–Martin periodinane (101.8 mg, 0.24 mmol) at 0 °C, and the mixture was stirred for 3 h. The reaction mixture was partitioned between $CHCl_3$/satd $NaHCO_3$. Column chromatography (hexane/AcOEt = 5/1) of the organic layer gave **16** (79.0 mg, 93%) as a foam: UV (MeOH) λ_{max} 269 nm (ε 9700), λ_{min} 237 nm (ε 2500); ^{1}H NMR ($CDCl_3$) δ 0.91–1.10 (28H, each as m, Si-*i*-Pr), 1.95 (3H, d, $J_{Me,6}$ = 1.2 Hz, Me-5), 2.48 (1H, dd, $J_{2'a,3'}$ = 5.6 Hz and $J_{2'a,2'b}$ = 13.8 Hz, H-2′a), 2.96 (1H, dd, $J_{2'b,3'}$ = 12.4 Hz and $J_{2'a,2'b}$ = 13.8 Hz, H-2′b), 3.31–3.34 (1H, m, H-4′), 3.95 (1H, d, $J_{5'a,5'b}$ = 13.2 Hz, H-5′a), 4.13 (1H, dd, $J_{4',5'b}$ = 3.2 Hz and $J_{5'a,5'b}$ = 13.2 Hz, H-5′b), 4.30–4.37 (1H, m, H-3′), 8.17 (1H, d, $J_{Me,6}$ = 1.2 Hz, H-6), 9.17 (1H, br, NH), 9.20 (1H, s, CHO); FAB-MS (*m/z*) 529 (M^+ + H). Anal. Calcd for $C_{23}H_{40}N_2O_6SSi_2$: C, 52.24; H, 7.62; N, 5.30. Found: C, 52.20; H, 7.74; N, 5.22.

3.3.13. 1-[1-(*E*)-Cyanoethenyl-2-deoxy-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]thymine (17). To a THF (4.0 mL) solution of **16** (72.1 mg, 0.14 mmol) was added cyanomethylenetributylphosphorane (101.4 mg, 0.42 mmol) at 0 °C, and the mixture was stirred at rt overnight. The reaction mixture was partitioned between $CHCl_3$/satd NH_4Cl. Column chromatography (hexane/AcOEt = 5/1) of the organic layer gave **17** (73.4 mg, 95%) as a foam: UV (MeOH) λ_{max} 266 nm (ε 11,600), λ_{min} 240 nm (ε 6300); ^{1}H NMR ($CDCl_3$) δ 0.90–1.08 (28H, each as m, Si-*i*-Pr), 1.95 (3H, d, $J_{Me,6}$ = 0.8 Hz, Me-5), 2.44 (1H, dd, $J_{2'a,3'}$ = 12.0 Hz and $J_{2'a,2'b}$ = 13.6 Hz, H-2′a), 3.30 (1H, dd, $J_{2'b,3'}$ = 4.8 Hz and $J_{2'a,2'b}$ = 13.6 Hz, H-2′b), 3.45–3.47 (1H, m, H-4′), 3.90 (1H, dd, $J_{4',5'a}$ = 2.0 Hz and $J_{5'a,5'b}$ = 12.8 Hz, H-5′a), 4.07 (1H, dd, $J_{4',5'b}$ = 3.2 Hz and $J_{5'a,5'b}$ = 13.2 Hz, H-5′b), 4.22–4.29 (1H, m, H-3′), 5.24 (1H, d, $J_{1'',1'''}$ = 16.4 Hz, H-1″), 6.90 (1H, d, $J_{1'',1'''}$ = 16.4 Hz, H-1‴), 8.20 (1H, d, $J_{Me,6}$ = 1.2 Hz, H-6), 8.89 (1H, br, NH); FAB-MS (*m/z*) 552 (M^+ + H), 508 (M^+−*i*-Pr), 426 (M^+−B). Anal. Calcd for $C_{25}H_{41}N_3O_5SSi_2$: C, 54.41; H, 7.49; N, 7.61. Found: C, 54.68; H, 7.64; N, 7.47.

3.3.14. 1-[2-Cyano-2-deoxy-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]thymine (19). To a pyridine (2.5 mL) solution of **16** (95.2 mg, 0.18 mmol) was added hydroxylamine hydrochloride (25 mg, 0.366 mmol) at 0 °C, and the mixture was stirred for 6 h. The reaction mixture was partitioned between $CHCl_3$/satd $NaHCO_3$. Column chromatography (hexane/AcOEt = 2/1) of the organic layer gave the oxime[18] (94.3 mg, 96%, foam). A mixture of the oxime[18] and Ac_2O (3.0 mL) was heated at 130 °C under Ar atmosphere for 11 h. The reaction mixture was evaporated to dryness and partitioned between $CHCl_3$/satd $NaHCO_3$. The organic layer was evaporated to dryness, and the residue was treated with methanolic ammonia at rt for 1 h. Purification of the reaction mixture by preparative TLC (hexane/AcOEt = 2/1) gave **19** (52.4 mg, 59%) as a syrup; UV (MeOH) λ_{max} 265 nm (ε 9700), λ_{min} 235 nm (ε 2900); ^{1}H NMR ($CDCl_3$) δ 0.90–1.08 (28H, each as m, Si-*i*-Pr), 1.95 (3H, d, $J_{Me,6}$ = 1.2 Hz, Me-5), 2.83 (1H, dd, $J_{2'a,3'}$ = 12.4 Hz and $J_{2'a,2'b}$ = 14.0 Hz, H-2′a), 3.19 (1H, dd, $J_{2'b,3'}$ = 4.8 Hz and $J_{2'a,2'b}$ = 14.0 Hz, H-2′b), 3.59–3.61 (1H, m, H-4′), 3.93 (1H, d, $J_{5'a,5'b}$ = 12.4 Hz, H-5′a), 4.10 (1H, dd, $J_{4',5'b}$ = 3.2 Hz and $J_{5'a,5'b}$ = 12.4 Hz, H-5′b), 4.17–4.23 (1H, m, H-3′), 8.03 (1H, d, $J_{Me,6}$ = 1.2 Hz, H-6), 8.51 (1H, br, NH); FAB-MS (*m/z*) 525 (M^+ + H); IR (neat) 2240 (cm^{-1}) (CN); Anal. Calcd for $C_{23}H_{39}N_3O_5SSi_2$: C, 52.54; H, 7.48; N, 7.99. Found: C, 52.90; H, 7.64; N, 7.81.

3.3.15. 1-[2-Deoxy-1-methyl-4-thio-β-D-ribofuranosyl]-thymine (20). To a THF (3.0 mL) solution of **11** (46.5 mg, 0.09 mmol) was added $Bu_4NF{\cdot}3H_2O$ (60.1 mg, 0.23 mmol) at 0 °C, and the mixture was stirred for 1 h. Column chromatography (8% MeOH in CH_2Cl_2) of the reaction mixture gave **20** (20.9 mg, 85%) as a syrup, which was crystallized from EtOH: mp 169–171 °C; UV (MeOH) λ_{max} 271 nm (ε 12,200), λ_{min} 237 nm (ε 2500); ^{1}H NMR (CD_3OD) δ 1.89 (3H, s, Me-5), 1.97 (3H, s, Me-1′), 2.42 (1H, dd, $J_{2'a,3'}$ = 7.6 Hz and $J_{2'a,2'b}$ = 13.6 Hz, H-2′a), 3.09 (1H, dd, $J_{2'b,3'}$ = 4.8 Hz and $J_{2'a,2'b}$ = 13.6 Hz, H-2′b), 3.43–3.83 (1H, m, H-4′), 3.57 (1H, dd, $J_{4',5'a}$ = 6.0 Hz and $J_{5'a,5'b}$ = 11.6 Hz, H-5′a), 3.65 (1H, dd, $J_{4',5'b}$ = 5.6 Hz and $J_{5'a,5'b}$ = 11.6 Hz, H-5′b), 4.20–4.24 (1H, m, H-3′), 8.21 (1H, s, H-6); FAB-MS (*m/z*) 273 (M^+ + H); Anal. Calcd for $C_{11}H_{16}N_2O_4S$: C, 48.52; H, 5.92; N, 10.29. Found: C, 48.42; H, 5.85; N, 10.16.

3.3.16. 1-[2-Deoxy-1-hydroxymethyl-4-thio-β-D-ribofuranosyl]thymine (21). This compound was prepared by

the same procedure for the synthesis of **20**, using **12** (63.5 mg, 0.098 mmol) and $Bu_4NF{\cdot}3H_2O$ (89.7 mg, 0.34 mmol), which gave **21** (23.2 mg, 82%) as a solid, which was crystallized from EtOH: mp 178–181 °C; UV (MeOH) λ_{max} 271 nm (ε 10,500), λ_{min} 237 nm (ε 2300); ^{1}H NMR (CD_3OD) δ 1.89 (3H, s, Me-5), 2.61–2.65 (1H, m, CH_2-2′), 3.54–3.55 (1H, m, H-4′), 3.54–3.55 (1H, m, CH_2-5′), 4.04 (1H, d, $J_{1''a,1''b}$ = 11.2 Hz, H-1″a), 4.14 (1H, d, $J_{1''a,1''b}$ = 11.2 Hz, H-1″b), 4.39–4.40 (1H, m, H-3′), 7.83 (1H, s, H-6); FAB-MS (*m*/*z*) 289 (M^+ + H). Anal. Calcd for $C_{11}H_{16}N_2O_5S{\cdot}1/4H_2O$: C, 45.12; H, 5.68; N, 9.57. Found: C, 45.38; H, 5.44; N, 9.45.

3.3.17. 1-[2-Deoxy-1-formyl-4-thio-β-D-ribofuranosyl]-thymine (22). This compound was prepared by the same procedure for the synthesis of **20** using **16** (27.5 mg, 0.052 mmol) and $Bu_4NF{\cdot}3H_2O$ (34.0 mg, 0.13 mmol), which gave **22** (10.2 mg, 68%) as a solid: mp 107–109 °C; UV (MeOH) λ_{max} 269 nm (ε 10,900), λ_{min} 236 nm (ε 2800); ^{1}H NMR (CD_3OD) δ 1.89 (3H, s, Me-5), 2.39 (1H, dd, $J_{2'a,3'}$ = 4.0 Hz and $J_{2'a,2'b}$ = 13.2 Hz, H-2′a), 2.82 (1H, dd, $J_{2'b,3'}$ = 7.6 Hz and $J_{2'a,2'b}$ = 13.2 Hz, H-2′b), 3.35–3.40 (1H, m, H-4′), 3.73 (1H, dd, $J_{4',5'a}$ = 6.0 Hz and $J_{5'a,5'b}$ = 11.6 Hz, H-5′a), 3.81 (1H, dd, $J_{4',5'b}$ = 5.6 Hz and $J_{5'a,5'b}$ = 11.6 Hz, H-5′b), 4.31–4.32 (1H, m, H-3′), 7.97 (1H, s, H-6), 9.31 (1H, s, CHO); FAB-MS (*m*/*z*) 325 (M^+ + K). Anal. Calcd for $C_{11}H_{14}N_2O_5S{\cdot}1.1H_2O$: C, 43.15; H, 4.97; N, 9.15. Found: C, 43.15; H, 5.12; N, 8.75.

3.3.18. 1-[1-(*E*)-Cyanoethenyl-2-deoxy-4-thio-β-D-ribofuranosyl]thymine (23). This compound was prepared by the same procedure for the synthesis of **20**, using **17** (23.2 mg, 0.04 mmol) and $Bu_4NF{\cdot}3H_2O$ (26.1 mg, 0.1 mmol), which gave **23** (10.1 mg, 81%) as a solid, which was crystallized from MeOH: mp 112–114 °C; UV (MeOH) λ_{max} 265 nm (ε 12,000), λ_{min} 238 nm (ε 5800); ^{1}H NMR (CD_3OD) δ 1.92 (3H, s, Me-5), 2.62 (1H, dd, $J_{2'a,3'}$ = 7.2 Hz and $J_{2'a,2'b}$ = 13.8 Hz, H-2′a), 2.94 (1H, dd, $J_{2'b,3'}$ = 4.4 Hz and $J_{2'a,2'b}$ = 13.8 Hz, H-2′b), 3.46–3.50 (1H, m, H-4′), 3.69 (1H, dd, $J_{4',5'a}$ = 5.2 Hz and $J_{5'a,5'b}$ = 11.8 Hz, H-5′a), 3.65 (1H, dd, $J_{4',5'b}$ = 5.2 Hz and $J_{5'a,5'b}$ = 11.8 Hz, H-5′b), 4.28–4.32 (1H, m, H-3′), 5.43 (1H, d, $J_{1'',1'''}$ = 16.0 Hz, H-1‴), 7.14 (1H, d, $J_{1'',1'''}$ = 16.0 Hz, H-1″), 8.24 (1H, s, H-6); FAB-MS (*m*/*z*) 310 (M^+ + H) and 185 (M^+−B). Anal. Calcd for $C_{13}H_{15}N_3O_4S{\cdot}1/4H_2O$: C, 49.75; H, 4.98; N, 13.38. Found: C, 49.86; H, 5.05; N, 13.05.

3.3.19. 1-[2-Deoxy-(1-methoxyimino)-4-thio-β-D-ribofuranosyl]thymine (24). To a THF (3.5 mL) solution of **19** (61.3 mg, 0.12 mmol) was added $Bu_4NF{\cdot}3H_2O$ (78.4 mg, 0.3 mmol) at 0 °C, and the mixture was stirred for 1 h. Silica gel column chromatography (8% MeOH in CH_2Cl_2) of the reaction mixture gave a mixture of desilylated products. A mixture of this products, *i*-Pr_2NEt (84 μL, 0.48 mmol), Ac_2O (34 μL, 0.36 mmol), and DMAP (7.3 mg, 0.06 mmol) in CH_2Cl_2 (3 mL) was stirred at rt overnight. The reaction mixture was partitioned between $CHCl_3$/satd $NaHCO_3$. Purification of the organic layer by preparative TLC (CH_2Cl_2/MeOH = 20/1) gave di-*O*-acetate of **24** (23.2 mg, 48%) as a syrup. This acetate was treated with methanolic ammonia (6 mL) at rt for 2 h. The reaction mixture was evaporated to give crude **24** (19 mg, 97%), which was crystallized from acetone: mp 138–140 °C; UV (MeOH) λ_{max} 269 nm (ε 10,100), λ_{min} 236 nm (ε 2400); ^{1}H NMR (CD_3OD) δ 1.92 (3H, d, $J_{Me\text{-}5,6}$ = 0.8 Hz, Me-5), 2.74–2.86 (2H, m, H-2′), 3.47–3.50 (1H, m, H-4′), 3.69 (3H, s, OMe), 3.66–3.72 (1H, m, H-5′a), 3.75 (1H, dd, $J_{4',5'b}$ = 4.8 Hz and $J_{5'a,5'b}$ = 11.6 Hz, H-5′b), 4.24–4.32 (1H, m, H-3′), 8.02 (1H, s, H-6); FAB-MS (*m*/*z*) 315 (M^+ + H). Anal. Calcd for $C_{12}H_{17}N_3O_5S$: C, 45.70; H, 5.43; N, 13.33. Found: C, 45.72; H, 5.38; N, 12.99.

3.3.20. 1-[Cyano-2-deoxy-4-thio-β-D-ribofuranosyl]thymine (25). This compound was prepared by the same procedure for the synthesis of **20**, using, **19** (50.1 mg, 0.095 mmol) and $Bu_4NF{\cdot}3H_2O$ (62.8 mg, 0.24 mmol). The reaction mixture was chromatographed on a ICN silica gel (4% MeOH in CH_2Cl_2) gave **25** (24.1 mg, 90%) as a syrup, which was crystallized from acetone–CH_2Cl_2: mp 131–133 °C: UV (MeOH) λ_{max} 264 nm (ε 10,400), λ_{min} 234 nm (ε 3000); ^{1}H NMR (DMSO-d_6) δ 1.81 (3H, d, $J_{Me,6}$ = 0.9 Hz, Me-5), 2.84 (1H, dd, $J_{2'a,3'}$ = 4.9 Hz and $J_{2'a,2'b}$ = 13.7 Hz, H-2′a), 2.89 (1H, dd, $J_{2'b,3'}$ = 3.7 Hz and $J_{2'a,2'b}$ = 13.7 Hz, H-2′b), 3.57–3.41 (1H, m, H-4′), 3.43–3.51 (2H, m, CH_2-5′), 4.35–4.38 (1H, m, H-3′), 5.09 (1H, t, $J_{5',OH}$ = 4.9 Hz, OH-5′), 5.59 (1H, d, $J_{3',OH}$ = 3.7 Hz, OH-3′), 7.82 (1H, d, $J_{Me,6}$ = 0.9 Hz, H-6), 11.71 (1H, br, NH); FAB-MS (*m*/*z*) 284 (M^+ + H). Anal. Calcd for $C_{11}H_{13}N_3O_4S{\cdot}1/2CH_2Cl_2$: C, 45.09; H, 4.61; N, 13.71. Found: C, 44.76; H, 4.54; N, 13.31.

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