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Practical Synthesis of 2′-Deoxy-4′-thioribonucleosides: Substrates for the Synthesis of 4′-ThioDNA

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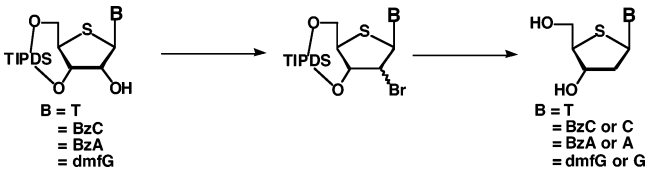

We report herein a practical synthesis of 4′-thiothymidine (**15**) and appropriately protected 2′-deoxy-4′-thiocytidine (**16**), -thioadenosine (**27**), and -thioguanosine (**29**) derivatives, substrates for the synthesis of 4′-thioDNA, from the corresponding 4′-thioribonucleosides. 2′-Deoxy-4′-thiopyrimidine nucleosides were synthesized using a radical reaction of the corresponding 2′-α-bromo derivatives, which were prepared via 2,2′-*O*-anhydro derivatives. 2′-Deoxy-4′-thiopurine nucleosides were synthesized using the same radical reaction of the corresponding 2′-*β*-bromo derivatives.

We have recently been studying the synthesis of a series of 4′-thioribonucleosides with the aim of developing a nucleoside antimetabolite as well as a functional RNA molecule.[1,2] In our preceding papers, we reported the stereoselective synthesis, via the Pummerer reaction,[3] of 4′-thioribonucleosides, which we have since incorporated into oligoribonucleotides by chemical and enzymatic approaches to give 4′-thioRNA.[2] Because the 4′-thioRNA showed high nuclease resistance and hybridization properties,[2a] we thought that the RNA molecule would be a promising candidate for functional RNAs such as antisense, ribozyme, RNA aptamer,[2b] and short interfering RNA.[2c]

Unlike the 4′-thioRNAs, the properties of oligodeoxyribonucleotides containing 2′-deoxy-4′-thioribonucleosides (4′-thioDNA) have not been well elucidated. Walker and co-workers reported the synthesis of 4′-thioDNAs consisting of 2′-deoxy-4′-thiopyrimidine nucleoside units, and their preliminary properties, including nuclease resistance and hybridization ability.[4] However since then, nothing has been published on the use of 4′-thioDNA as a functional DNA molecule despite the favorable properties of 4′-thioDNA. This is probably due in large part to the difficulty of synthesizing 2′-deoxy-4′-thioribonucleosides.[5,6] Haraguchi et al. have recently reported the stereoselective synthesis of 2′-deoxy-4′-thioribonucleosides based on electrophilic glycosidation of 4-thiofuranoid glycals.[7] Although this method involves interesting chemistry, the reactions were all carried out on a very small scale.

In view of the above background information, we decided to develop a practical synthesis of 2′-deoxy-4′-thioribonucleoside derivatives, which are substrates for the synthesis of 4′-thioDNA. Since our synthetic method using the Pummerer reaction can now be carried out on a large scale,[1a,8] deoxygenation of the 2′-hydroxyl groups of the resulting 4′-thioribonucleoside derivatives seemed to be the most straightforward and promising method for our purpose.

Two groups have independently reported the synthesis of 2′-deoxy-4′-thioribonucleosides from the corresponding 4′-thioribonucleosides using the radical deoxygenation. Jeong et al. reported the synthesis of the 2′-deoxy-4′-thiouridine derivative in a brief communication.[9] In their paper, the 2′-deoxy derivative was obtained in 79% yield by treatment of the corresponding 4′-thioribo derivative with phenyl chlorothionoformate [PhOC(S)Cl], followed by tributyltin hydride (Bu_3SnH) and triethylborane (Et_3B).[10] In contrast, the reaction with the 2-chloro-4′-thioadenosine derivative under the following conditions [*N*,*N*′-thiocarbonyldiimidazole, and then Bu_3SnH, 2,2′-azobisisobutyronitrile (AIBN), toluene, reflux] afforded the 2′-deoxy congener in poor yield.[11] With these results in mind, we first examined the radical deoxygenation of

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(1) (a) Minakawa, N.; Kaga, D.; Kato, Y.; Endo, K.; Tanaka, M.; Sasaki, T.; Matsuda, A. *J. Chem. Soc*., *Perkin Trans. 1* **2002**, 2182−2189. (b) Kaga, D.; Minakawa, N.; Matsuda, A. *Nucleosides Nucleotides Nucleic Acids* **2005** in press.

(2) (a) Hoshika, S.; Minakawa, N.; Matsuda, A. *Nucleic Acids Res.* **2004**, *32*, 3815−3825. (b) Kato, Y.; Minakawa, N.; Komatsu, Y. Kamiya, H.; Ogawa, N.; Harashima, H.; Matsuda, A. *Nucleic Acids Res.* **2005** *33*, 2942−2951. (c) Hoshika, S.; Minakawa, N.; Kamiya, H.; Harashima, H.; Matsuda, A. *FEBS Lett*. **2005**, *579*, 3115−3118.

(3) (a) Naka, T.; Nishizono, N.; Minakawa, N.; Matsuda, A. *Tetrahedron Lett*. **1999**, *40*, 6297−6300. (b) Naka, T.; Minakawa, N.; Abe, H.; Kaga, D.; Matsuda, A. *J. Am. Chem. Soc*. **2000**, *122*, 7233−7243.

(4) (a) Hancox, E. L.; Connolly, B. A.; Walker, R. T. *Nucleic Acids Res.* **1993**, *21*, 3485−3491. (b) Jones, G. D.; Lesnik, E. A.; Owens, S. R.; Risen, L. M.; Walker, R. T. *Nucleic Acids Res.* **1996**, *24*, 4117−4122. (c) Jones, G. D.; Altmann, K.-H.; Hüsken, D.; Walker, R. T. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 1275−1278.

(5) A preferable *β*-anomer synthesis of the 2′-deoxy-4′-thioribonucleoside derivative has been achieved by glycosidation of 3-*O*-carbamoyl-2-deoxythiosugar and 5-ethyluracil with assistance of the 3-*O*-carbamoyl group; see: Shaw-Ponter, S.; Mills, G.; Robertson, M.; Bostwick, R. D.; Hardy, G. W.; Young, R. J. *Tetrahedron Lett*. **1996**, *37*, 1867−1870.

(6) For examples: (a) Secrist, J. A.; Tiwari, K. N.; Riordan, J. M.; Montgomery, J. A. *J. Med. Chem*. **1991**, *34*, 2361−2366. (b) Dyson, M. R.; Coe, P. L.; Walker, R. T. *J. Med. Chem*. **1991**, *34*, 2782−2786.

(7) (a) Haraguchi, K.; Nishikawa, A.; Sasakura, E.; Tanaka, H.; Nakamura, K. T.; Miyasaka, T. *Tetrahedron Lett*. **1998**, *39*, 3713−3716. (b) Haraguchi, K.; Takahashi, H.; Shiina, N.; Horii, C.; Yoshimura, Y.; Nishikawa, A.; Sasakura, E.; Nakamura, K. T.; Tanaka, H. *J. Org. Chem*. **2002**, *67*, 5919−5927.

(8) Minakawa, N.; Kato, Y.; Uetake, K.; Kaga, D.; Matsuda, A. *Tetrahedron* **2003**, *59*, 1699−1702.

(9) Joeng, L. S.; Nicklaus, M. C.; George, C.; Marquez, V. E. *Tetrahedron Lett*. **1994**, *35*, 7573−7576.

(10) The radical reaction was presumably conducted at room temperature because Et_3B was used as a radical initiator.

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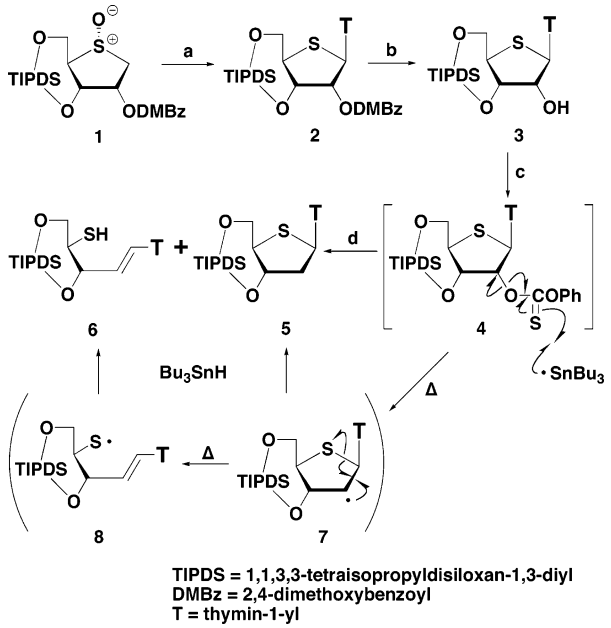
SCHEME 1[a]

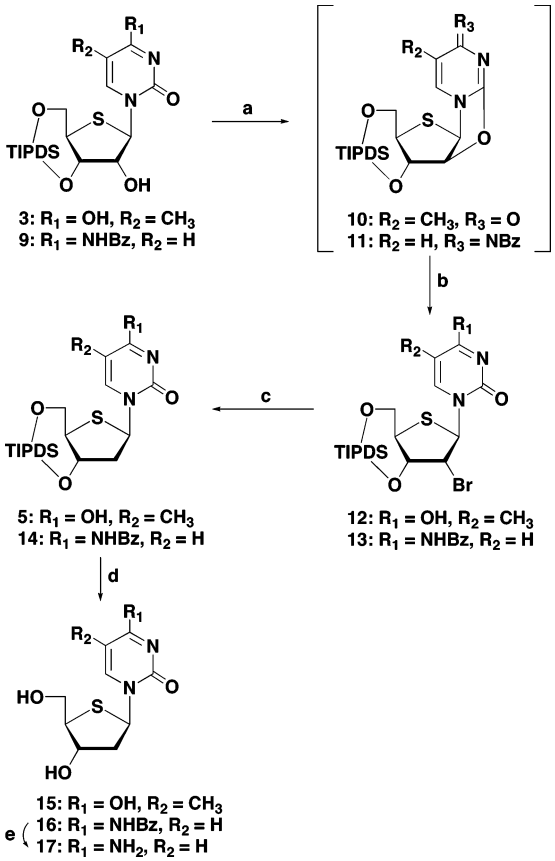


[a] Key: (a) thymine, TMSOTf, Et_3N, CH_2Cl_2−toluene; (b) $MeNH_2$ in MeOH; (c) PhOC(S)Cl, DMAP, CH_3CN; (d) Bu_3SnH, AIBN, toluene, 80 °C.

the 2′-hydroxyl group of 1-[3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]thymine (**3**) (Scheme 1).

When the Pummerer reaction of the sulfoxide **1** with silylated thymine was carried out, the desired 4′-thioribosylthymine derivative **2** was stereoselectively obtained in 81% yield. Treatment of **2** with methylamine gave **3**, a substrate for the radical deoxygenation. After conversion of **3** into the thionocarbonate [PhOC(S)Cl, (dimethylamino)pyridine (DMAP), CH_3CN, rt], the resulting **4**, after a water workup, was subjected to the standard radical deoxygenation conditions (Bu_3SnH, AIBN, toluene, 80 °C) to furnish the 4′-thiothymidine derivative **5** in 48% yield along with 35% of the unexpected compound **6**. In previous papers,[9,11] compounds such as **6** were not obtained.[12,13] Treatment of **3** with *N*,*N*′-thiocarbonyldiimidazole, followed by the radical deoxygenation under heating conditions also afforded the same results. In contrast, when the radical deoxygenation of **4** was conducted at room temperature using Et_3B as a radical initiator, **5** was obtained in only 10% yield after 24 h in our hands.[9,10] In the above reaction, approximately 40% of **4** was recovered, while the ring opening product **6** was not observed. From these results, it might be postulated that formation of the radical intermediate **7** from the thionocarbonate **4** through homolytic cleavage of the C−O bond required higher temperature; however, this reaction is accompanied by homolytic cleavage of the C−S bond

SCHEME 2[a]



[a] Key: (a) Tf_2O, DMAP, CH_2Cl_2; (b) LiBr, $BF_3{\cdot}Et_2O$, 1,4-dioxane, 50 °C; (c) Bu_3SnH, V70-L, CH_2Cl_2; (d) TBAF, THF; (e) $MeNH_2$ in MeOH.

to give the radical intermediate **8**. Consequently, the radical deoxygenation of **4** afforded **6** along with the desired **5**.

As an alternative method to prepare 2′-deoxy-4′-thioribonucleosides, we next envisioned the strategy of bromination at the 2′-position of 4′-thioribonucleoside derivatives, followed by radical reduction of the bromo group. As shown in Scheme 2, compound **3** was first converted into the 2,2′-*O*-anhydro derivative **10** by treatment with trifluoromethanesulfonic anhydride (Tf_2O) in CH_2Cl_2 in the presence of DMAP. The resulting **10** was then subjected to bromination conditions (LiBr, $BF_3{\cdot}Et_2O$ in dioxane)[14] to give **12** in 75% yield over two steps. When **12** was treated with Bu_3SnH in CH_2Cl_2 at room temperature in the presence of racemic 2,2′-azobis(2,4-dimethyl-4-methoxyvaleronitrile) (V70-L), the desired **5** was obtained in 94% yield without formation of **6**. Deprotection of the silyl group of **5** by tetrabutylammonium fluoride (TBAF) gave 4′-thiothymidine (**15**) in good yield. Likewise, compound **9**[1a] was converted into 2′-deoxy-4′-thiocytidine derivative **16**[15] via the bromide **13**. All reactions were conducted on a gram scale, and compound **15** and the *N*-benzoyl derivative **16** were finally obtained in more than 1 g. Analytical data of **15** and **17** prepared

(11) Tiwari, K. N.; Secrist, J. A.; Montgomery, J. A. *Nucleosides Nucleotides* **1994**, *13*, 1819−1828.

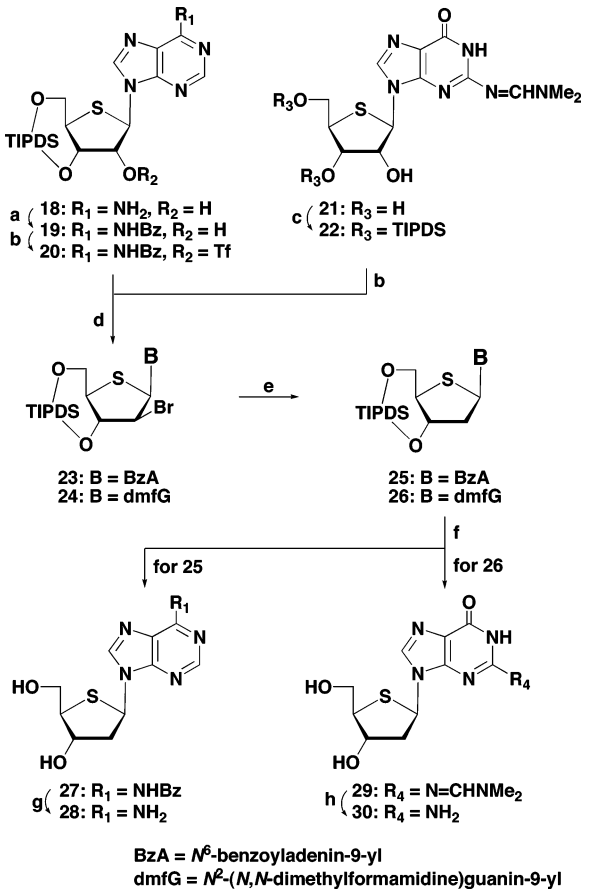
(12) After the report of ref 11, Secrist et al. presented the structure of the byproduct obtained in the reaction described in ref 11. However, this type of byproduct was not observed in our substrate; see: Secrist, J. A.; Parker, W. B.; Tiwari, K. N.; Messini, L.; Shaddix, S. C.; Rose, L. M.; Bennett, L. L.; Montgomery, J. A. *Nucleosides Nucleotides* **1995**, *14*, 675−686.

(13) Quite recently, Dong and Paquette reported a similar reaction, Dong, S.; Paquette, L. A. *J. Org. Chem.* **2005**, *70*, 1580−1596.

(14) Aoyama, Y.; Sekine, T.; Iwamoto, Y.; Kawashima, E.; Ishido, Y. *Nucleosides Nucleotides* **1996**, *15*, 733−738.

(15) Kumar, S.; Horton, J. R.; Jones, G. D.; Walker, R. T.; Roberts, R. J.; Cheng, X. *Nucleic Acids Res.* **1997**, *25*, 2773−2783.

SCHEME 3[a]



[a] Key: (a) BzCl, pyridine, then NaOMe in MeOH; (b) Tf_2O, DMAP, CH_2Cl_2; (c) $TIPDSCl_2$, pyridine; (d) Bu_4NBr, benzene; (e) Bu_3SnH, V70-L, CH_2Cl_2; (f) TBAF, THF; (g) $MeNH_2$ in MeOH; (h) NH_3 in EtOH, 80 °C.

from **16** were identical with those for the authentic samples.[6]

For the synthesis of the 4′-thiopurine derivatives, the synthetic route is illustrated in Scheme 3. Starting with **18**,[2a] **19** was prepared by treatment with an excess amount of benzoyl chloride, followed by brief treatment with sodium methoxide. After introduction of a trifluoromethanesulfonyl group on the 2′-hydroxyl group of **19**, bromination of **20** was examined. Among our attempts, treatment of **20** with Bu_4NBr in benzene at room temperature gave the best result, and **23** was obtained in 66% yield in two steps. Reduction of the bromo group proceeded smoothly under the radical conditions, and the 2′-deoxy-4′-thioadenosine derivative **27** was finally obtained in good yield. The 4′-thioguanosine derivative **29** was also prepared from **21** via protection, bromination, reduction, and deprotection steps. In these cases, all reactions were also conducted on gram scale to give **27** and **29** in sufficient quantities. The amino protective groups of **27** and **29** were deprotected to give 2′-deoxy-4′-thioadenosine (**28**) and 2′-deoxy-4′-thioguanosine (**30**), respectively. The analytical data of **28** and **30** were identical with the authentic data.[16]

(16) (a) Montgomery, J. A.; Secrist, J. A. 1991 PCT/US90/05252. (b) Draanen, N. A. V.; Freeman, G. A.; Short, S. A.; Harvey, R.; Jansen, R.; Szczech, G.; Koszalka, G. W. *J. Med. Chem*. **1996**, *39*, 538−542.

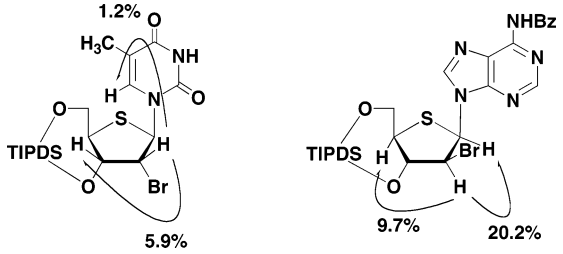


FIGURE 1. Structures of **12** and **23** confirmed by NOE experiments.

The configurations of the bromo groups of the pyrimidine (**12** and **13**) and purine (**23** and **24**) derivatives were confirmed by NOE experiments of **12** and **23** (Figure 1). Thus, NOEs were observed at H-6 (1.2%) and H-3′ (5.9%) upon irradiation of H-2′ of **12**. Therefore, it was determined that **12** had an α-bromo group at the 2′-position. In contrast, NOEs were observed at H-1′ (20.2%) and H-4′ (9.7%) upon irradiation of H-2′ of **23**, which indicated that there is a β-bromo group at the 2′-position. Conversion of **3** into the 2′-bromo derivative **12** proceeded with overall retention of configuration which can be explained by the formation of 2,2′-anhydro derivative **10**. In the reaction with **18**, the substitution proceeded via an S_N2-type reaction to give **23** with inversion of configuration.

Thus far, a number of reactions have been reported for 4′-thionucleosides derivatives, and unexpected results arising from the participation of the sulfur atom were observed in some cases.[13,17] In our reactions reported here, unexpected cleavage of the C−S bond in the sugar moiety to give **6** was observed during the radical deoxygenation on heating. This unfavorable C−S bond cleavage was avoided, however, when the radical reaction was carried out at room temperature. In contrast, participation of the sulfur atom would be negligible in the nucleophilic substitution at the C2′-position of 4′-thioribonucleoside derivative. These results agreed with those of the reactions of the O-congeners.

In conclusion, we have investigated the practical synthesis of the 2′-deoxy-4′-thioribonucleosides derivatives **15**, **16**, **27**, and **29** which would be easily converted into the corresponding phosphoramidite units for 4′-thioDNA synthesis. The desired compounds were synthesized from 4′-thioribonucleoside derivatives via bromination, followed by radical reduction at room temperature. Since four kinds of 2′-deoxy derivatives are now available on a gram scale, investigations of the synthesis and properties of 4′-thioDNA are in progress.

Experimental Section

1-[2-α-Bromo-2-deoxy-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]thymine (12). To a solution of **3** (1.4 g, 2.6 mmol) in dry CH_2Cl_2 (26 mL) containing DMAP (1.3 g, 11 mmol) was added Tf_2O (0.88 mL, 5.2 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. The reaction was quenched by addition of saturated aqueous $NaHCO_3$. The reaction mixture was partitioned between AcOEt

(17) For examples: (a) Hancox, E. L.; Walker, R. T. *Nucleosides Nucleotides* **1996**, *15*, 135−148. (b) Otter, G. P.; Elzagheid, M. I.; Jones, G. D.; MacCulloch, A. C.; Walker, R. T.; Oivanen, M.; Klika, K. D. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2343−2349. (c) Miller, J. A.; Pugh, A. W.; Ullah, G. M. *Nucleosides Nucleotides Nucleic Acids* **2000**, *19*, 1475−1486.

and H_2O. The separated organic layer was washed with saturated aqueous $NaHCO_3$ (three times), followed by brine. The organic layer was dried (Na_2SO_4) and concentrated in vacuo to give crude **10**. The resulting **10** was dissolved in dry 1,4-dioxane (26 mL), then $BF_3{\cdot}Et_2O$ (47%, an Et_2O solution, 0.49 mL, 3.9 mmol) and LiBr (340 mg, 3.9 mmol) were added to the solution. The mixture was heated at 50 °C for 30 min. The reaction was quenched by addition of H_2O. The reaction mixture was partitioned between AcOEt and H_2O. The separated organic layer was washed with saturated aqueous $NaHCO_3$, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by a silica gel column, eluted with hexane/AcOEt (9:1−5:1), to give **12** (1.1 g, 75%, as a white solid): ^{1}H NMR ($CDCl_3$) δ 9.11 (s, 1 H), 8.09 (s, 1 H), 6.04 (s, 1 H), 4.37 (d, 1 H, J = 4.8 Hz), 4.13 (m, 2 H), 4.03 (d, 1 H, J = 12.9 Hz), 3.72 (d, 1 H, J = 9.1 Hz), 1.93 (s, 3 H), 0.96−1.12 (m, 28 H); ^{13}C NMR ($CDCl_3$) δ 163.6, 150.6, 136.3, 110.6, 71.2, 65.9, 58.9, 58.0, 51.7, 17.5, 17.4, 17.3, 17.1, 16.9, 16.8, 13.3, 13.1, 12.6, 12.5; FAB-LRMS m/z 581 (MH^+); FAB-HRMS calcd for $C_{22}H_{40}{}^{79}BrN_2O_5SSi_2$ (MH^+) 579.1380, found 579.1387.

1-[2-Deoxy-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-riofuranosyl]thymine (5). To a solution of **12** (1.1 g, 1.9 mmol) in dry CH_2Cl_2 (9.5 mL) containing 2,2′-azobis-(2,4-dimethyl-4-methoxyvaleronitrile) (racemic form) (120 mg, 0.39 mmol) was added tributyltin hydride (0.80 mL, 2.5 mmol), and the mixture was stirred at room temperature for 15 min. The mixture was concentrated in vacuo, and the residue was purified by silica gel column, eluted with hexane/AcOEt (9:1−1:1), to give **5** (1.0 g, 94%, as a yellow form): ^{1}H NMR ($CDCl_3$) δ 9.78 (s, 1 H), 7.89 (s, 1 H), 6.07 (d, 1 H, J = 7.6 Hz), 4.45 (m, 1 H), 4.13 (dd, 1 H, J = 3.1 and 12.9 Hz), 3.95 (d, 1 H, J = 12.9 Hz), 3.32 (m, 1 H), 2.48 (m, 1 H), 2.25 (m, 1 H), 1.92 (s, 3 H), 0.88−1.15 (m, 28 H); ^{13}C NMR ($CDCl_3$) δ 163.8, 150.8, 136.5, 110.7, 70.9, 58.0, 57.1, 54.8, 43.0, 17.5, 17.3, 17.1, 17.0, 16.9, 13.4, 13.2, 12.9, 12.6, 12.4; FAB-LRMS m/z 501 (MH^+); FAB-HRMS calcd for $C_{22}H_{41}N_2O_5SSi_2$ (MH^+) 501.2275, found 501.2265.

***N*^{6}-Benzoyl-9-[2-β-bromo-2-deoxy-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]adenine (23).** To a solution of **19** (1.4 g, 2.2 mmol) in dry CH_2Cl_2 (22 mL) containing DMAP (1.1 g, 8.8 mmol) was added Tf_2O (0.73 mL, 4.3 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 min. The reaction was quenched by addition of saturated aqueous $NaHCO_3$. The reaction mixture was partitioned between AcOEt and H_2O. The separated organic layer was washed with saturated aqueous $NaHCO_3$ (three times), followed by brine. The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The resulting crude **20** was coevaporated with toluene and then dissolved in dry benzene (37 mL). To this solution, tetrabutylammonium bromide (1.4 g, 4.3 mmol) was added, and the reaction mixture was stirred at room temperature for 1 h. The reaction was quenched by addition of H_2O. The reaction mixture was partitioned between AcOEt and H_2O. The separated organic layer was washed with saturated $NaHCO_3$, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by silica gel column, eluted with hexane/AcOEt (3:1−1:1), to give **23** (1.0 g, 66%, as a yellow form): ^{1}H NMR ($CDCl_3$) δ 9.02 (s, 1 H), 8.84 (s, 1 H), 8.46 (s, 1 H), 8.03 (m, 1 H), 7.63 (m, 1 H), 7.55 (m, 2 H), 6.24 (d, 1 H, J = 6.6 Hz), 4.82 (dd, 1 H, J = 10.7 and 9.4 Hz), 4.41 (dd, 1 H, J = 6.6 and 10.7 Hz), 4.25 (dd, 1 H, J = 2.9 and 11.1 Hz), 4.17 (dd, 1 H, J = 2.8 and 11.1 Hz), 3.48 (ddd, 1 H, J = 9.4, 2.9 and 2.8 Hz), 1.05−1.22 (m, 28 H); ^{13}C NMR ($CDCl_3$) δ 164.4, 152.7, 152.6, 152.3, 149.6, 142.4, 133.7, 132.7, 128.8, 127.7, 122.6, 60.0, 57.2, 55.4, 50.4, 17.5, 17.4, 17.3, 17.2, 17.1, 13.8, 13.2, 12.6; FAB-LRMS m/z 694 (MH^+); FAB-HRMS calcd for $C_{29}H_{42}{}^{79}BrN_5O_4SSi_2$ (MH^+) 692.1758, found 692.1761.

***N*^{6}-Benzoyl-9-[2-deoxy-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-thio-β-D-ribofuranosyl]adenine (25).** In the similar manner as described for **5**, **23** (2.6 g, 3.8 mmol) in dry CH_2Cl_2 (20 mL) containing 2,2′-azobis(2,4-dimethyl-4-methoxyvaleronitrile) (racemic form) (0.23 g, 0.76 mmol) was treated with tributyltin hydride (1.5 mL, 5.6 mmol) to give **25** (2.0 g, 84%, as a white form): ^{1}H NMR ($CDCl_3$) δ 9.01 (s, 1 H), 8.81 (s, 1 H), 8.54 (s, 1 H), 8.02 (m, 1 H), 7.62 (m, 1 H), 7.53 (m, 2 H), 6.12 (d, 1 H, J = 6.5 Hz), 4.71 (m, 1 H), 4.17 (dd, 1 H, J = 2.9 and 12.6 Hz), 4.02 (dd, 1 H, J = 2.6 and 12.6 Hz), 3.47 (ddd, 1 H, J = 8.8, 2.6 and 2.9 Hz), 2.57−2.69 (m, 2 H), 0.91−1.15 (m, 28 H); ^{13}C NMR ($CDCl_3$) δ 164.4, 152.5, 151.3, 149.4, 142.1, 133.6, 132.7, 128.8, 127.7, 123.4, 72.0, 58.9, 55.2, 54.6, 43.6, 17.5, 17.4, 17.3, 17.2, 17.1, 17.0, 13.4, 13.0, 12.6, 12.5; FAB-LRMS m/z 614 (MH^+); FAB-HRMS calcd for $C_{29}H_{43}N_5O_4SSi_2$ (MH^+) 614.2653, found 614.2682.

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Supporting Information Available: Experimental procedures and spectral data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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