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An Access to the β-Anomer of 4′-Thio-C-ribonucleosides: Hydroboration of 1-*C*-Aryl- or 1-*C*-Heteroaryl-4-thiofuranoid Glycals and Its Regiochemical Outcome

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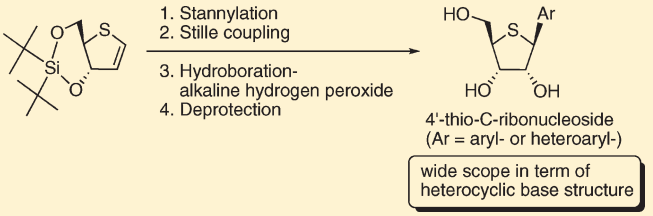
Supporting Information

ABSTRACT: We have developed a novel method for the synthesis of the β-anomer of 4′-thio-C-ribonucleosides from 3,5-*O*-(di-*tert*-butylsilylene)-4-thiofuranoid glycal. Palladium-catalyzed coupling of 1-tributylstannyl-4-thiofuranoid glycal with iodobenzene or a heteroaryl halide gave 1-C-phenyl- or 1-*C*-heteroaryl-glycals. Hydroboration of these glycals proceeded at the α-face, and subsequent alkaline hydrogen peroxide treatment of the resulting 2′-α-borane furnished the respective β-anomer of 4′-thio-C-ribonucleosides. These results demonstrate that this synthetic method has a wider scope in terms of heterocyclic base structure. During this study, unexpected Markovnikov-oriented hydroboration has been observed to lead to the respective 1′-α-boranes. These 1′-boranes were converted into either the ring-opened structure or the 2′-deoxy derivatives depending upon their stability.



INTRODUCTION

A class of compounds called "C-nucleosides" feature the ribofuranosyl moiety linked to a heterocyclic base through a carbon−carbon bond.[1] Besides naturally occurring C-nucleoside antibiotics,[1,2] several biologically active synthetic C-nucleosides are well-known. One example is tiazofurin (**1**, Figure 1),[3] which is metabolically converted to a NAD mimic and consequently strongly inhibits IMP-dehydrogenase.[4] An additional example, 9-deazaadenosine (**2**),[5] is highly cytotoxic against several lines of murine and human tumor cells.[6]

In the meantime, it has been reported that simple replacement of the furanose ring oxygen with a sulfur atom confers potent antiviral and antitumor activities on naturally occurring nucleosides, for example, 4′-thiothymidine (**3**) and 2′-deoxy-4′-thiocytidine (**4**) shown in Figure 2.[7] Although this finding stimulated the synthesis of thionucleosides of various types,[8,9] only one precedent[10] is available so far for 4′-thio-analogues of C-nucleosides, wherein highly reactive five-membered heterocyclic bases such as furan and thiophene derivatives were condensed with 1-*O*-acetyl-2,3,5-tri-*O*-benzyl-4-thio-D-ribofuranose.[11] In this context, we intended to develop a synthetic method for 4′-thio-C-ribonucleosides with a wider scope in terms of heterocyclic base structure.

RESULTS AND DISCUSSION

Our synthetic plan is shown in Scheme 1. 3,5-*O*-(Di-*tert*-butylsilylene)-4-thiofuranoid glycal **5**, previously used for our synthesis of 2′-deoxy-4′-thionucleosides,[9b] was selected as the starting material in the present study. After converting **5** into the 1-tributylstannyl derivative **6**, various types of aryl or heteroaryl groups can be introduced through Stille coupling to give **A**.[12] In our previous study on electrophilic glycosidation using **5** and NIS (or PhSeCl),[9b] a highly stereoselective formation of the β-anomer was observed as a result of the presence of the 3,5-*O*-DTBS (di-*tert*-butylsilylene) protecting group, which results in NIS approaching from the α-face of 4-thiofuranoid glycal.[13] Therefore, it might be reasonable to expect that hydroboration of **A** would take place from its α-face to ensure β-glycosidic stereochemistry in the product **B**. The depicted regiochemistry of **B** can be anticipated from the reported hydroboration of 1-*C*-aryl-furanoid glycals.[14] Finally, treatment of **B** with alkaline hydrogen peroxide should furnish the desired 4′-thio-C-ribonucleosides **C**.

Preparation of 1-*C*-Aryl (or Heteroaryl)-4-thiofuranoid Glycals. Because our previously reported method for the synthesis of **5** has involved utilization of 2-deoxy-D-ribose, an expensive starting material, and toxic mercuric acetate,[9b] a novel method shown in Scheme 2 was developed. Thus, the synthetic route utilized the cheaper starting material D-ribose, which was then converted to 1,4-anhydro-4-thio-D-ribitol **7** utilizing nontoxic reagents.[15] Deprotection of the isopropylidene group of **7** with 80% AcOH and subsequent protection of the resulting triol with the DTBS group gave **8** in 68% for 2 steps. Mesylation of **8** gave **9** in 98% yield. Finally, elimination of MsOH from **9** was

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carried out by treatment with DBN in DMF at 150 °C for 30 min to furnish **5** in 56% yield.

Stannylation at the C-1 of **5** was performed by lithiation of **5** with BuLi and subsequent treatment of the resulting 1-lithiated species with Bu_3SnCl, giving **6** in 84% yield (Scheme 3).[16] When **6** was reacted with iodobenzene in the presence of $(Ph_3P)_4Pd$ (10 mol %) and CuI (20 mol %) in THF under reflux conditions, the desired cross-coupling product 1-*C*-phenyl-glycal (**10**) could be obtained in 81% yield. Under the identical reaction conditions, 1-*C*-naphthyl- (**11**) (88%), 1-*C*-quinolyl- (**12**), and 1-*C*-pyridinyl-4-thiofuranoid glycals (**13**) could be obtained (Figure 3).

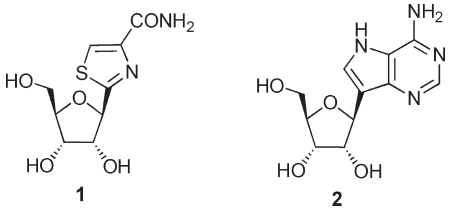


Figure 1. Synthetic C-nucleosides tiazofurine **1** and 9-deazaadenosine **2**.

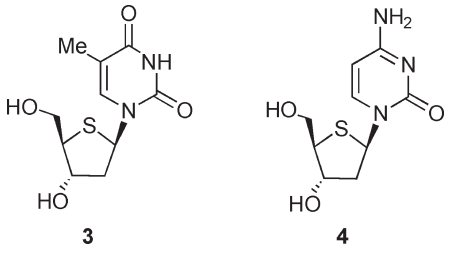


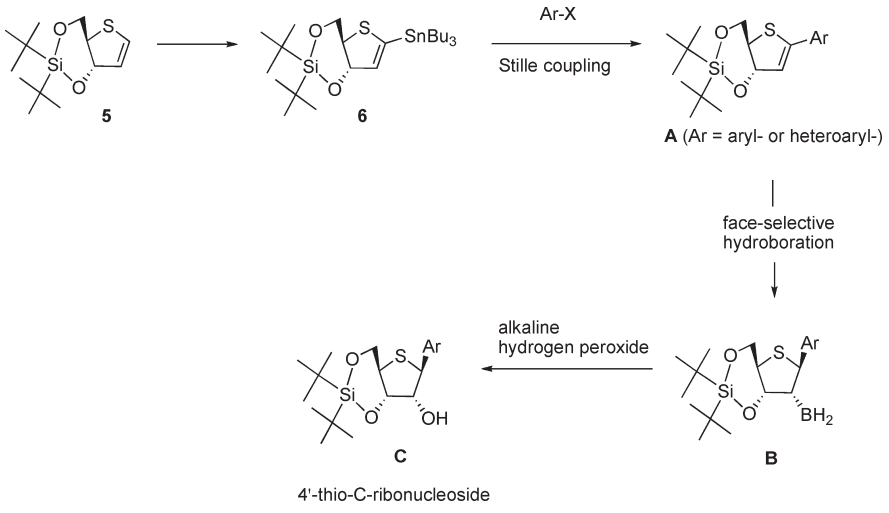
Figure 2. 4′-Thiothymidine **3** and 2′-deoxy-4′-thiocytidine **4**.

With the above result in mind, 5-iodoracil, which is the base moiety of pseudouridine, was reacted with **6** under the above reaction conditions (Figure 4). Unexpectedly, the coupling reaction failed to give the desired **14**, and instead **6** was recovered. Although we have no reasonable explanation for the result at the moment, 5-iodo-2,4-dimethoxypyrimidine was next reacted with **6**. In contrast to the above result, the dimethoxypyrimidine derivative successfully underwent coupling reaction to give the desired **15** in 88% yield. Next, coupling with 2,4-dibromothiazole[17] was examined. Although 2,4-dibromothiazole has two possible reaction sites, regioselective coupling at C-2 proceeded to give 1-*C*-(4-bromothiazol-2-yl)-4-thiofuranoid glycal **16** in 48% yield.[18]

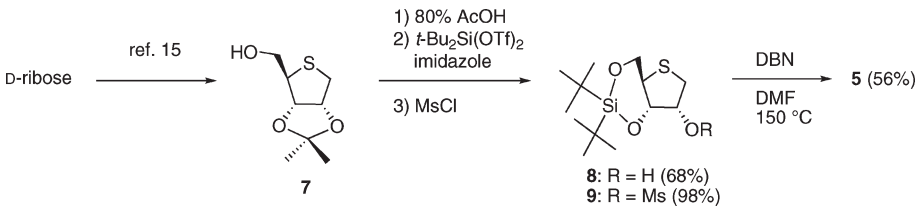
For the synthesis of **22**, a precursor for 4′-thio-9-deazaadenosine, 7-iodinated 4-pivaloylamino-3*H*,5*H*-pyrrolo[3,2-*d*]pyrimidine **21**, was prepared from **17**[19] (Scheme 4). Thus, **17** was chlorinated with $POCl_3$ to give **18** in 80% yield. The 4-chloro derivative **18** was subjected to ammonolysis to give **19** in 78% yield. After protection of the amino group of **19** with the pivaloyl group (80% isolated yield), the resulting **20** was iodinated by reaction with *N*-iodosuccinimide (NIS) in DMF at 80 °C to furnish **21** in 80% yield. When **21** was reacted with **6** under the conditions described for the synthesis of **10**, the expected coupling reaction proceeded to furnish **22** in 52% yield.

Hydroboration of 1-*C*-Phenyl- and 1-*C*-Heteroaryl-4-thiofuranoid Glycal: Synthesis of β-Anomer of 4′-Thio-C-nucleosides. When 1-*C*-phenyl-4-thiofuranoid glycal **10** was reacted with $BH_3 \cdot THF$ (5 equiv) in THF at 0 °C for 18 h, the expected hydroboration reaction proceeded to give an alkylborane **23** (Scheme 5).[20] To elucidate the structure of **23**, the reaction

Scheme 1. Synthetic Plan for 4′-Thio-C-ribonucleoside C from 4-Thiofuranoid Glycal 5



Scheme 2. Preparation of 4-Thiofuranoid Glycal 5



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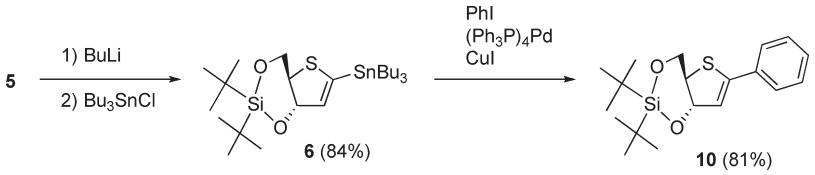
Scheme 3. Preparation of 1-*C*-Phenyl-4-thiofutanoid Glycal 10 by Stille Coupling of 1-Tributylstannyl Glycal 6 with PhI



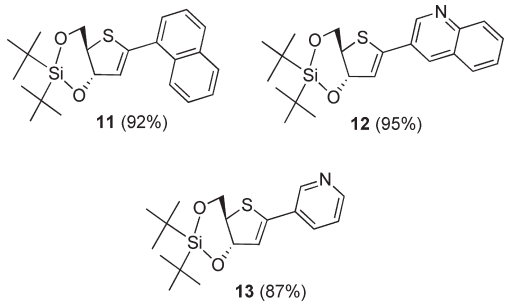


Figure 3. 1-*C*-Aryl- and 1-*C*-hereroaryl-4-thiofuranoid glycals **11**−**13**.

mixture was quenched with acetone pinacol. After chromatographic purification of the reaction mixture, the boronic acid pinacol ester **24** was isolated in 25% yield as a single stereoisomer. The depicted stereochemistry of **24** was determined on the basis of NOE experiments [H-1′/H-4′ (2.3%), H-2′/ H-Ph (1.9%) and H-3′/ H-Ph (1.4%)].[21] When the reaction solution was treated with 30% H_2O_2/1 M NaOH, a mixture of the desired 1′-*C*-phenyl-4′-thioribonucleoside derivative **25** and its partially desilylated product was obtained. The crude products were treated with Bu_4NF and then Ac_2O in one pot to provide the tri-*O*-acetate **26** (90% from **10**). The hydroboration reaction was found to be successfully applicable to glycal **11**−**13** to provide the respective 4′-thio-C-nucleosides **27**-**29** (Figure 5). The depicted structures of **27**−**29** were determined on the basis of NOE experiment as shown in Figure 5.

With the above result in mind, the glycal **22** was then subjected to hydroboration under the same conditions as used for **10** (Scheme 6), and the expected 4′-thio-9-deazaadenosine derivative **30** was obtained in 40% isolated yield as a single stereoisomer along with recovered **22** (19%). The depicted stereochemistry of **30** was determined on the basis of NOE experiments: H-1′/H-4′ (2.0%), H-6/H-2′ (0.6%), H-6/H-3′ (1.9%), HO-2′/H-4′ (3.1%).

In contrast to these results, the hydroboration/oxidation of **15** gave two kinds of products after acetylation of the reaction mixture (Scheme 7). The less polar compound was the desired **31** (isolated yield: 41%). NOE experiments revealed that **31** was the depicted β-D-ribofuranosyl *C*-glycoside; H-1′/H-4′ (2.2%), H-6/H-2′ (2.9%) and H-6/H-3′ (3.5%). On the other hand, the more polar product was found unexpectedly to be dimer of ring-opened furanose **32**, which was isolated as an epimeric mixture (major isomer/minor isomer = 5.5/1) in 16% isolated yield. A HMBC spectrum showed correlations as follows: H-6/C-1 and H-1/C(=O)CH_3. Additional supporting data are molecular ion peak 943 (M^+ + H), fragment ion peaks 883 (M^+ − OAc) and 824 (M^+ − 2OAc) observed in the MS spectrum.

To clarify the mechanism for the formation of **32**, the intermediate organoboranes in the reaction were trapped with acetone pinacol to provide **33** and **34** in 26% and 17% yield, respectively (Figure 6). The 1′-boronic acid pinacol ester **34** is derived from unusual Markovnikov-oriented hydroboration. On the basis of the formation of **34**, we postulated the mechanism for the formation of **32** in Scheme 8. Thus, the initially formed 1′-organoborane **35** is oxidized into **36** by treatment with alkaline hydrogen peroxide. The hemithioacetal **36** was then transformed into δ-ketothiol **37**, and reduction of the keto group−oxidation of the thiol group furnished dimeric **38**, which was isolated as the acetate **32**. The unexpected regiochemical outcome of the hydroboration of **15** could be explained by coordination of BH_3 to the oxygen atom of the methoxy group at the 2-position, which is visualized as the transition state **39** (Figure 7). The resulting 1′-borane **40** might be stabilized by a five-membered coordination structure.

A similar directing effect exerted by the heterocyclic base was observed in the hydroboration of **16**. Thus, **16** gave the target 4′-thiotiazofurin derivative **41** in 27% along with an anomeric mixture of 2′-deoxy counterparts (**42a** and **42b**, ratio of 1/1) in 33% yield (Figure 8).

As for the case of the hydroboration of **15**, 1′-organoborane **43** would form from **16** (Scheme 9). In contrast to the case of **40**, **43** would not be stabilized by cyclic coordination with base moiety due to its unfavorable four-membered structure. Therefore, the borane **43** would release H_2B^- to give thionium ion **44**, which is then transformed into **42a,b** by hydride reduction.

1-(2,4-Dimethoxypyrimidine-5-yl)-4′-thio-C-ribonucleoside **31** could be successfully transformed to 4′-thiopseudouridine **47** (Scheme 10). Thus, **31** was converted to tri-*O*-acetate **45**, which was then subjected to de-*O*-methylation by treatment with HI to give **46**.[22] Deprotection of **46** with NH_3/MeOH furnished **47** in 75% yield.

Finally, 2′-*O*-triethylsilylated 1-(3-bromothiazol-2-yl)-4′-thio-C-ribonucleoside **48** obtained from **41** was converted into the corresponding thiazole 4-carboxylic acid ethyl ester **49** by halogen−lithium exchange reaction and subsequent treatment of the resulting C4-lithio derivative with $ClCO_2Et$. Ester **49** can be transformed into 4′-thiotiazofurin **50** using a published procedure (Scheme 11).[23]

In conclusion, we have developed a novel method for the synthesis of the β-anomer of 4′-thio-C-ribonucleosides from 3,5-*O*-(di-*tert*-butylsilylene)-4-thiofuranoid glycal **5**. Pd-catalyzed coupling of 1-tributylstannyl-4-thiofuranoid glycal **6** with aryl halides or heteroaryl halides gave 1-*C*-aryl- **10** and **11** or 1-*C*-heteroaryl-glycals **11**−**13**, **15**, and **16**. Hydroboration of these glycals proceeded at the α-face, and subsequent alkaline hydrogen peroxide treatment of the resulting 2′-α-borane furnished the respective β-anomer of 4′-thio-C-ribonucleosides **26**−**31** and **41**. These results demonstrate that this synthetic method has a wider scope in terms of the heterocyclic base structure. During this study, unexpected Markovnikov-oriented hydroboration has

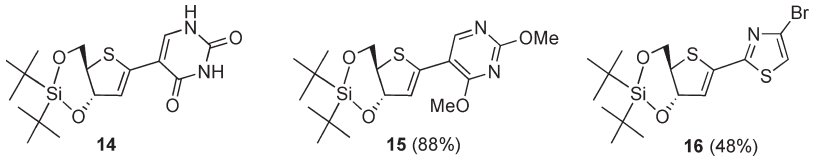
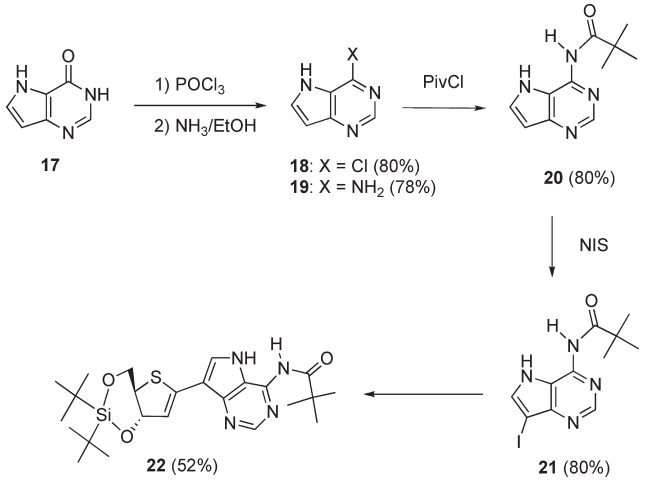


Figure 4. Structures of 1-*C*-hereroaryl-4-thiofuranoid glycals **14**−**16**.

Scheme 4. Preparation of 21 and Subsequent Coupling Leading to 22



been observed to lead to the respective 1′-α-boranes. These 1′-boranes were converted into ring-opened furanose **32** or 2′-deoxyribofuranosyl derivatives **42a,b**, depending upon their stability.

EXPERIMENTAL SECTION

Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded either at 400 or 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.

1,4-Anhydro-2-deoxy-3,5-*O*-(di-*tert*-butylsilylene)-4-thio-D-*erythro*-pento-1-enitol (5). To a DMF (15 mL) solution of **9** (1.78 g, 4.83 mmol) was added DBN (4.2 mL, 33.81 mmol) at rt, and the reaction mixture was stirred at 150 °C for 25 min. The reaction mixture was partitioned between AcOEt/saturated aqueous NH_4Cl, and silica gel column chromatography (hexane/AcOEt = 40/1) of the organic layer gave **5** (743.9 mg, 56%) as a solid: mp 68−69 °C; UV (MeOH) λ_{max} 242 nm (ε 4100) and λ_{min} 220 nm (ε 980); ^{1}H NMR ($CDCl_3$) δ 1.03 and 1.06 (18H, each as s), 3.81−3.87 (1H, m), 4.29 (1H, t, $J_{4,5a}$ = $J_{5a,5b}$ = 10.1 Hz), 4.33 (1H, dd, $J_{4,5b}$ = 0.6 and $J_{5a,5b}$ = 10.1 Hz), 5.11 (1H, ddd, $J_{1,3}$ = 2.5, $J_{2,3}$ = 2.7 and $J_{3,4}$ = 12.2 Hz), 5.86 (1H, dd, $J_{2,3}$ = 2.7 and $J_{1,2}$ = 6.1 Hz), 6.19 (1H, dd, $J_{1,3}$ = 2.5 and $J_{1,2}$ = 6.1 Hz); ^{13}C NMR ($CDCl_3$) δ 20.0, 22.7, 27.2, 27.5, 55.0, 67.6, 86.1, 124.8, 127.8. FAB-MS (*m*/*z*) 273 (M^+ + H) and 215 (M^+ − *t*-Bu). Anal. Calcd for $C_{13}H_{24}O_2SSi$: C, 57.30; H, 8.88. Found: C, 57.54; H, 9.10.

1,4-Anhydro-2-deoxy-3,5-*O*-(di-*tert*-butylsilylene)-1-tributylstannyl-4-thio-D-*erythro*-pento-1-enitol (6). To a THF (15 mL) solution of **5** (718 mg, 2.64 mmol) was added BuLi (2.6 M hexane solution) (1.2 mL, 3.17 mmol) at −70 °C, and the reaction mixture was stirred for 15 min. To the reaction mixture was added Bu_3SnCl (1.4 mL, 5.28 mL), and the mixture was stirred 15 min. The reaction mixture was partitioned between $CHCl_3$/saturated aqueous NH_4Cl, and silica gel column chromatography (hexane/AcOEt = 100/1) of the organic layer gave **6** (1.49 g, 84%) as a syrup: UV (MeOH) $\lambda_{shoulder}$ 262 nm (ε 1600), λ_{max} 251 nm (ε 2000) and λ_{min} 233 nm (ε 960); ^{1}H NMR ($CDCl_3$) δ 0.88−1.07 (27H, m), 1.03 and 1.06 (18H, each as s), 3.73 (1H, ddd, $J_{3,4}$ = 12.4, $J_{4,5a}$ = 11.2, $J_{4,5b}$ = 5.1 Hz), 4.26 (1H, dd, $J_{4,5a}$ = 11.2 and $J_{5a,5b}$ = 9.9 Hz), 4.32 (1H, dd, $J_{4,5b}$ = 5.1 and $J_{5a,5b}$ = 9.9 Hz), 5.09 (1H, dd, $J_{2,3}$ = 1.7 and $J_{3,4}$ = 12.4 Hz), 5.92 (1H, d, $J_{2,3}$ = 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ 10.1, 13.6, 13.7, 17.5, 20.0, 22.7, 27.2, 27.3, 27.51, 28.9, 55.9, 67.9, 87.4, 136.4, 138.7; FAB-MS (*m*/*z*) 561 (M^+ + H). Anal. Calcd for $C_{25}H_{50}O_2SSiSn$: C, 53.47; H, 8.98. Found: C, 53.54; H, 9.28.

3,5-*O*-(Di-*tert*-butylsilylene)-1,4-anhydro-4-thio-D-ribitol (8). An 80% AcOH (25 mL) solution of **7** (1.04 g, 5.47 mmol) was stirred at 70 °C for 8 h. The reaction mixture was evaporated to dryness and coevaporated with toluene. The crude product was treated with saturated methanolic ammonia (50 mL) at rt 10 h. The reaction mixture was evaporated to dryness, and silica gel column chromatography (4% MeOH in CH_2Cl_2) of the crude product gave the triol (821.6 mg, 100%) as a syrup. To a DMF (20 mL) solution of the triol were added imidazole (1.12 g, 16.41 mmol) and di-*tert*-butylsilyl bis-trifluoromethanesulfonate (2.2 mL, 6.02 mmmol) at 0 °C under Ar atmosphere, and the mixture was stirred at rt for 16 h. The reaction mixture was partitioned between AcOEt/H_2O, and silica gel column chromatograpy (hexane/AcOEt = 10/1) of the organic layer gave **8** (1.14 g, 68%) as a solid: mp 110−112 °C; ^{1}H NMR ($CDCl_3$) δ 1.03 and 1.06 (18H, each as s, *t*-Bu), 2.34 (1H, s, OH), 2.90 (1H, d, $J_{1a,1b}$ = 12.0 Hz), 3.08 (1H, ddd, J = 1.2, $J_{1b,2}$ = 5.4 and $J_{1a,1b}$ = 12.0 Hz), 3.60−3.67 (1H, m, H-4), 3.98−4.05 (1H, m, H-5a and H-5b), 4.34 (1H, dd, $J_{2,3}$ = 4.8 and $J_{3,4}$ = 10.0 Hz, H-3), 4.43 (1H, dd, $J_{1b,2}$ = 5.4 and $J_{2,3}$ = 4.8 Hz, H-2); ^{13}C NMR ($CDCl_3$) δ 20.2, 22.7, 27.2, 27.4, 32.7, 43.9, 68.7, 72.6, 76.7, 83.2; FAB-MS (*m*/*z*) 307 (M^+ + H). Anal. Calcd for $C_{13}H_{26}O_3SSi$: C, 53.75; H, 9.02. Found: C, 53.98; H, 9.07.

3,5-*O*-(Di-*tert*-butylsilylene)-2-*O*-methanesulfonyl-1,4-anhydro-4-thio-D-ribitol (9). To a pyridine (6 mL) solution of **8** (1.34 g, 4.37 mmol) was added MsCl (0.51 mL, 6.56 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred at rt for 8 h. The reaction mixture was partitioned between $CHCl_3$/saturated $NaHCO_3$, and silica gel column chromatograpy (hexane/AcOEt = 7/1) of the organic layer gave **9** (1.58 g, 98%) as a solid: mp 141−142 °C; ^{1}H NMR ($CDCl_3$) δ 1.02 and 1.06 (18H, each as s), 3.09 (3H, s), 3.10 (1H, d, $J_{1a,1b}$ = 13.2 Hz), 3.22 (1H, dd, $J_{1b,2}$ = 4.4 and $J_{1a,1b}$ = 13.2 Hz), 3.61−3.68 (1H, m, H-4), 3.99 (1H, dd, $J_{4,5a}$ = 10.4 and $J_{5a,5b}$ = 11.0 Hz), 4.12 (1H, dd, $J_{4,5b}$ = 3.6 and $J_{5a,5b}$ = 11.0 Hz), 4.34 (1H, dd, $J_{2,3}$ = 5.2 and $J_{3,4}$ = 10.2 Hz), 5.25 (1H, dd, $J_{1b,2}$ = 4.4 and $J_{2,3}$ = 5.2 Hz); ^{13}C NMR ($CDCl_3$) δ 20.1, 22.8, 26.9, 27.3, 32.2, 38.7, 43.9, 68.7, 81.0, 81.8; FAB-MS (*m*/*z*) 369 (M^+ + H). Anal. Calcd for $C_{14}H_{28}O_5S_2Si$: C, 45.62; H, 7.66. Found: C, 45.57; H, 7.68.

1,4-Anhydro-2-deoxy-3,5-*O*-(di-*tert*-butylsilylene)-1-*C*-phenyl-4-thio-D-*erythro*-pento-1-enitol (10). To a THF (10 mL) solution of **6** (434.4 mg, 0.77 mmol) were added PhI (0.17 mL, 1.54 mmol), $(Ph_3P)_4Pd$ (89 mg, 0.077 mmol), and CuI (28.6 mg, 0.15 mmol), and the mixture was stirred at 80 °C under Ar atmosphere for 8 h. The reaction mixture was chromatographed on silica gel (hexane/AcOEt = 150/1) to give **10** (218.3 mg, 81%) as a solid: mp 143−145 °C; UV (MeOH) λ_{max} 288 nm

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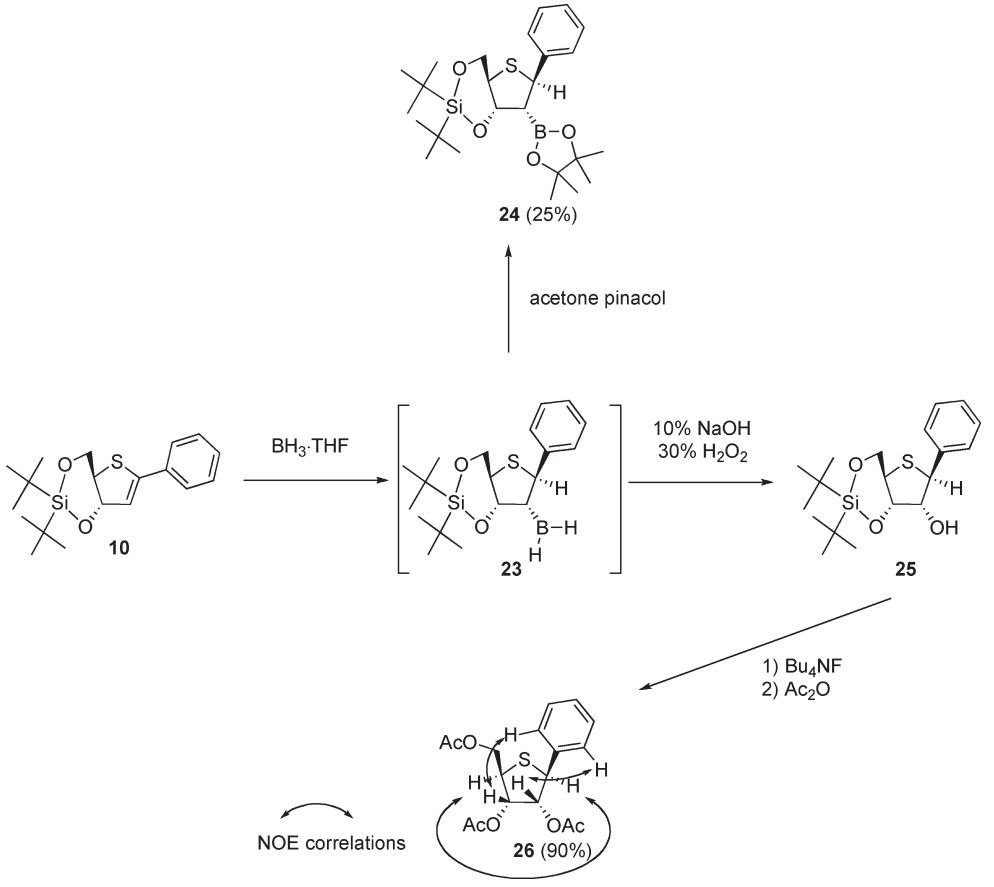
Scheme 5. Hydroboration of 10 with $BH_3 \cdot THF$



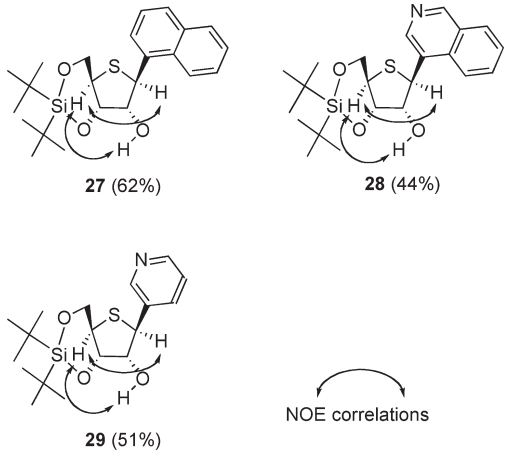
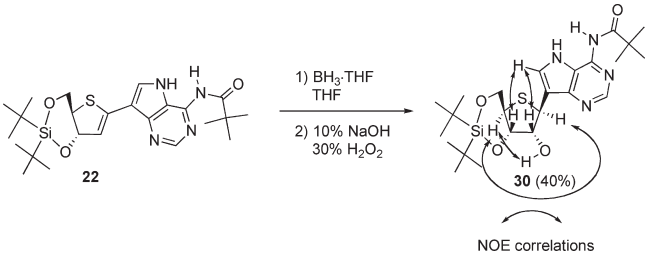


Figure 5. Structures of compounds **27**−**29**.

(ε 4900), 230 nm (ε 15300) and λ_{min} 264 nm (ε 2600); ^{1}H NMR ($CDCl_3$) δ 1.05 and 1.09 (18H, each as s), 3.99 (1H, ddd, $J_{3',4'}$ = 11.9, $J_{4',5'a}$ = 10.6 and $J_{4',5'b}$ = 5.5 Hz), 4.35 (1H, t, $J_{4',5'a}$ = $J_{5'a,5'b}$ = 10.6 Hz), 4.38 (1H, dd, $J_{4',5'b}$ = 5.5 and $J_{5'a,5'b}$ = 10.6 Hz), 5.30 (1H, dd, $J_{2',3'}$ = 1.8 and $J_{3',4'}$ = 11.9 Hz), 6.23 (1H, d, $J_{2',3'}$ = 1.8 Hz), 7.30−7.36 and 7.44−7.46 (5H, each as m); ^{13}C NMR ($CDCl_3$) δ 20.1, 22.7, 27.2, 27.5, 54.6, 67.5, 86.3, 122.2, 126.0, 128.5, 128.7, 133.7, 139.5; FAB-MS (m/z) 349 (M^+ + H). Anal. Calcd for $C_{19}H_{28}O_2SSi \cdot 1/3\ H_2O$: C, 64.36; H, 8.15. Found: C, 64.28; H, 8.07.

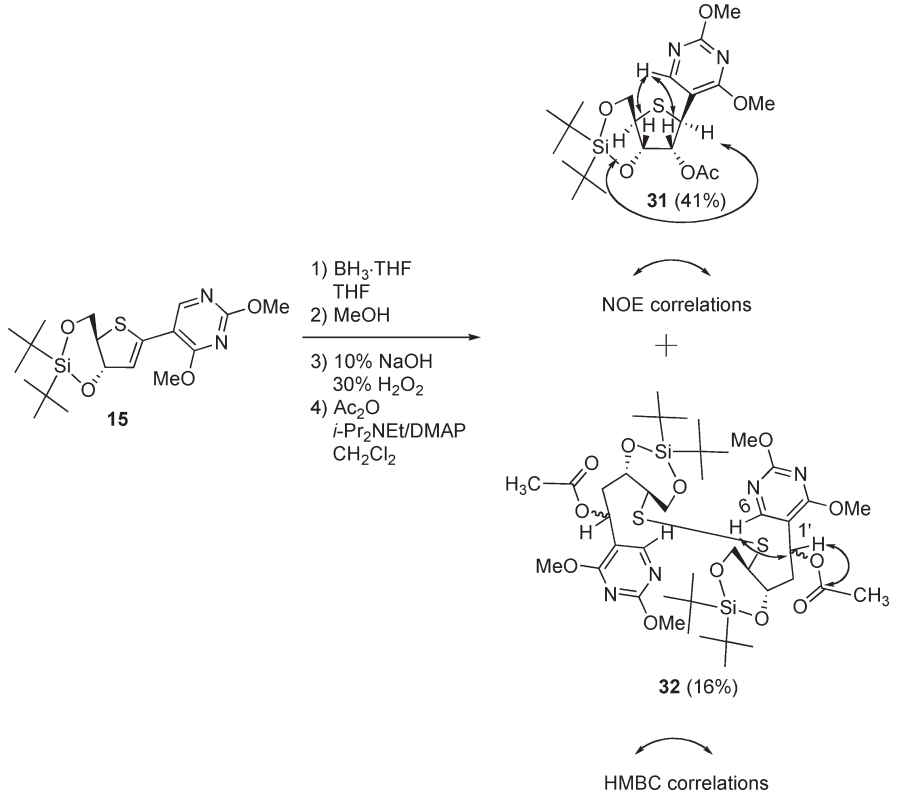
Scheme 6. Hydroboration of 22



1,4-Anhydro-2-deoxy-3,5-*O*-(di-*tert*-butylsilylene)-1-*C*-(naphthalen-1-yl)-4-thio-D-*erythro*-pento-1-enitol (11). To a THF (7 mL) solution of **6** (159.4 mg, 0.28 mmol) were added 1-iodonaphthalene (82 μL, 0.56 mmol), $(Ph_3P)_4Pd$ (32.4 mg, 0.028 mmol,) and CuI (3.6 mg, 0.056 mmol), and the mixture was stirred at 80 °C under Ar atmosphere for 16 h. The reaction mixture was chromatographed on silica gel (hexane/AcOEt = 150/1) to give **11** (102.7 mg, 92%) as a solid: mp 108−110 °C; ^{1}H NMR ($CDCl_3$) δ 1.08 and 1.12 (18H, each as s), 4.19 (1H, ddd, $J_{3',4'}$ = 11.9, $J_{4',5'a}$ = 10.0 and $J_{4',5'b}$ = 6.0 Hz), 4.39−4.43 (2H, m), 5.44 (1H, dd, $J_{2',3'}$ = 1.2 and $J_{3',4'}$ = 11.9 Hz), 6.05 (1H, d, $J_{2',3'}$ = 1.2 Hz), 7.41−7.45, 7.48−7.54, 7.80−7.86 and 8.26−8.28 (7H, each as m); ^{13}C NMR ($CDCl_3$) δ 20.1, 22.7, 55.9, 67.5, 86.6, 125.1, 125.4, 126.0, 126.3, 126.5, 127.1, 128.4, 129.0, 131.0, 132.8, 133.6, 138.2; FAB-MS (m/z) 399 (M^+ + H); FAB-HRMS (m/z) calcd for $C_{23}H_{31}O_2SSi$: 399.1814, found: 399.1802 (M^+ + H).

dx.doi.org/10.1021/jo201100n |J. Org. Chem. 2011, 76, 8658–8669

Scheme 7. Hydroboration of 15



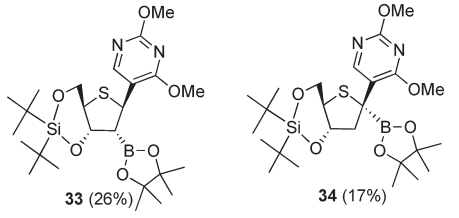


Figure 6. Structures of compounds **33** and **34**.

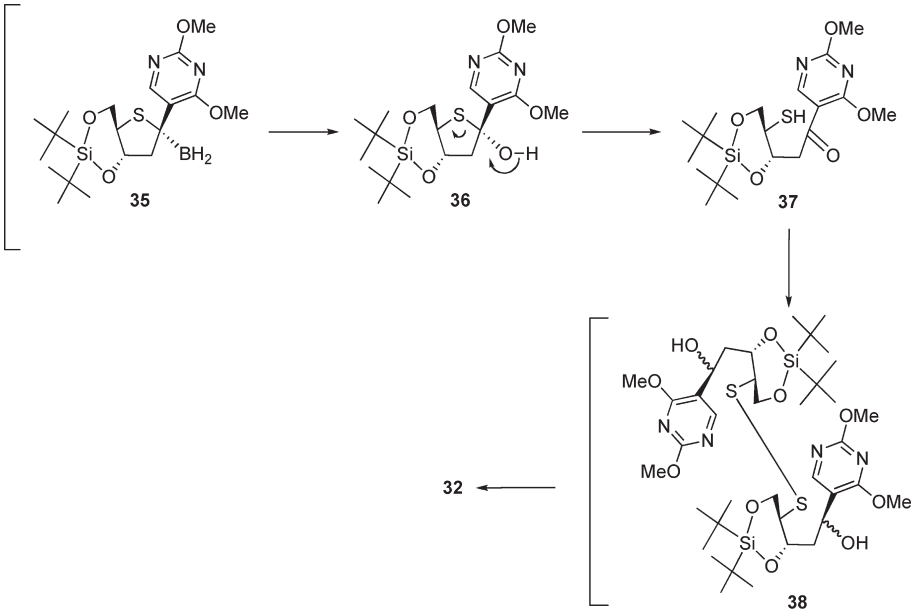
1,4-Anhydro-2-deoxy-3,5-*O*-(di-*tert*-butylsilylene)-1-*C*-(quinolin-3-yl)-4-thio-D-*erythro*-pento-1-enitol (12). To a THF (7.0 mL) solution of **6** (176.4 mg, 0.31 mmol) were added 3-bromoquinoline (84 μL, 0.62 mmol), $(Ph_3P)_4Pd$ (35.8 mg, 0.031 mmol), and CuI (3.6 mg, 0.062 mmol), and the mixture was stirred at 80 °C under Ar atmosphere for 17 h. The reaction mixture was chromatographed on silica gel (hexane/AcOEt = 40/1) to give **12** (117.8 mg, 95%) as a solid: mp 211−213 °C; ^{1}H NMR ($CDCl_3$) δ 1.06 and 1.10 (18H, each as s), 4.06 (1H, ddd, $J_{3',4'}$ = 12.0, $J_{4',5'a}$ = 10.0 and $J_{4',5'b}$ = 5.6 Hz), 4.38 (1H, t, $J_{4',5'a} = J_{5'a,5'b}$ = 10.0 Hz), 4.43 (1H, dd, $J_{4',5'b}$ = 5.6 and $J_{5'a,5'b}$ = 10.0 Hz), 5.38 (1H, dd, $J_{2',3'}$ = 2.0 and $J_{3',4'}$ = 12.0 Hz), 6.49 (1H, d, $J_{2',3'}$ = 2.0 Hz), 7.54−7.58, 7.69−7.74, 7.81−7.83, 8.05−8.10 and 9.07−9.08 (6H, each as m); ^{13}C NMR ($CDCl_3$) δ 20.1, 22.7, 54.7, 67.4, 86.5, 124.4, 126.8, 127.3, 127.5, 128.1, 129.3, 129.9, 132.8, 136.8, 147.7, 147.9; FAB-MS (m/z) 400 (M^+ + H); FAB-HRMS (m/z) calcd for $C_{22}H_{30}NO_2SSi$: 400.1767, found: 400.1772 (M^+ + H).

1,4-Anhydro-2-deoxy-3,5-*O*-(di-*tert*-butylsilylene)-1-*C*-(pyridin-3-yl)-4-thio-D-*erythro*-pento-1-enitol (13). To a THF (7.0 mL) solution of **6** (169.6 mg, 0.30 mmol) were added 3-iodopyridine (123.0 mg, 0.60 mmol), $(Ph_3P)_4Pd$ (34.7 mg, 0.03 mmol), and CuI (11.4 mg, 0.06 mmol), and the mixture was stirred at 80 °C under Ar atmosphere for 17 h. The reaction mixture was chromatographed on silica gel (hexane/AcOEt = 20/1) to give **13** (91.4 mg, 87%) as a solid: mp 133−135 °C; ^{1}H NMR ($CDCl_3$) δ 1.05 and 1.09 (18H, each as s), 4.02 (1H, ddd, $J_{3',4'}$ = 12.2, $J_{4',5'a}$ = 10.4 and $J_{4',5'b}$ = 5.6 Hz), 4.35 (1H, t, $J_{4',5'a} = J_{5'a,5'b}$ = 10.0 Hz), 4.39 (1H, dd, $J_{4',5'b}$ = 5.6 and $J_{5'a,5'b}$ = 10.0 Hz), 5.31 (1H, dd, $J_{2',3'}$ = 1.6 and $J_{3',4'}$ = 12.2 Hz), 6.32 (1H, d, $J_{2',3'}$ = 1.6 Hz), 7.28−7.30, 7.69−7.72, 8.53−8.55 and 8.71−8.72 (4H, each as m); ^{13}C NMR ($CDCl_3$) δ 20.0, 22.7, 55.2, 67.2, 86.3, 123.2, 124.1, 129.6, 133.2, 136.4, 147.2, 149.6; FAB-MS (m/z) 350 (M^+ + H); FAB-HRMS (m/z) calcd for $C_{18}H_{28}NO_2SSi$: 350.1610, found: 350.1604 (M^+ + H).

1,4-Anhydro-2-deoxy-3,5-*O*-(di-*tert*-butylsilylene)-1-(2,4-dimethoxypyrimidin-5-yl)-4-thio-D-*erythro*-pento-1-enitol (15). To a THF (4 mL) solution of **6** (210.2 mg, 0.37 mmol) were added 5-iododimethoxypyrimidine (196.9 mg, 0.74 mmol), $(Ph_3P)_4Pd$ (48.2 mg, 0.037 mmol), and CuI (14.1 mg, 0.074 mmol), and the mixture was stirred at 80 °C under Ar atmosphere for 8 h. The reaction mixture was chromatographed on silica gel (hexane/AcOEt = 30/1) to give **15** (134.1 mg, 88%) as foam: UV (MeOH) λ_{max} 291 nm (ε 7800), 249 nm (ε 13700), 232 nm (ε 13500) and λ_{min} 273 nm (ε 6700), 239 (ε 12200); ^{1}H NMR ($CDCl_3$) δ 1.04 and 1.09 (18H, each as s), 3.90 (1H, dt, $J_{3',4'} = J_{4',5'a}$ = 11.2 and $J_{4',5'b}$ = 5.4 Hz), 4.01 and 4.08 (6H, each as s, OMe), 4.32 (1H, t, $J_{4',5'a} = J_{5'a,5'b}$ = 11.2 Hz), 4.37 (1H, dd, $J_{4',5'b}$ = 5.4 and $J_{5'a,5'b}$ = 11.2 Hz), 5.27 (1H, dd, $J_{2',3'}$ = 2.0 and $J_{3',4'}$ = 11.2 Hz), 6.52 (1H, d, $J_{2',3'}$ = 2.0 Hz), 8.23 (1H, s, H-6); ^{13}C NMR ($CDCl_3$) δ 20.1, 22.7, 27.2, 27.4, 53.8, 54.3, 55.0, 67.3, 86.4, 109.7, 126.9, 130.4, 157.2, 164.3, 167.6; FAB-MS (m/z) 411 (M^+ + H) and 353 (M^+ − *t*-Bu). Anal. Calcd for $C_{19}H_{30}O_4N_2SSi$: C, 55.58; H, 7.36; N, 6.82. Found: C, 55.80; H, 7.50; N, 6.78.

1,4-Anhydro-2-deoxy-3,5-*O*-(di-*tert*-butylsilylene)-1-(4-bromothiazol-2-yl)-4-thio-D-*erythro*-pento-1-enitol (16). To a THF (6.0 mL) solution of **6** (490.3 mg, 0.87 mmol) were added 2,4-dibromothiazole (318.2 mg, 1.31 mmol), $(Ph_3P)_4Pd$ (100.5 mg, 0.087 mmol),

Scheme 8. Plausible Mechanism for the Formation of 32



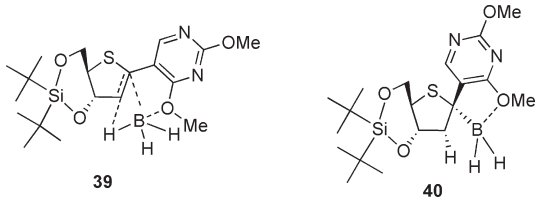


Figure 7. Transition state **39** for Markovnikov-oriented hydroboration of **15** leading to 1′-borane **40**.

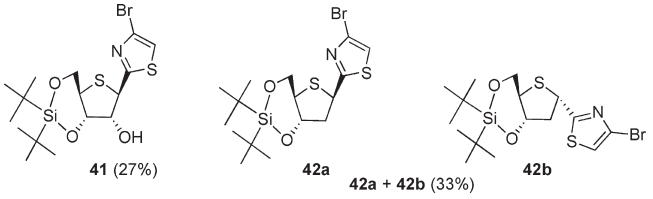
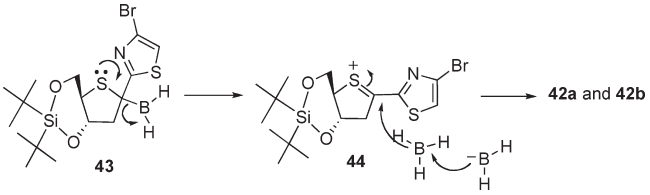


Figure 8. 4′-Thiotiazofurin derivative **41** and the 2′-deoxy counterparts **42a,b**.

and CuI (32.4 mg, 0.17 mmol), and the mixture was stirred at 80 °C under Ar atmosphere for 10 h. The reaction mixture was chromatographed on silica gel (hexane/AcOEt = 100/1) to give **16** (181.6 mg, 48%) as a solid: mp 157−159 °C; UV (MeOH) λ_{max} 391 nm (ε 6200), 289 (ε 6000) and λ_{min} 306 nm (ε 5700), 255 (ε 2200); ^{1}H NMR ($CDCl_3$) δ 1.03 and 1.07 (18H, each as s), 4.04 (1H, ddd, $J_{3',4'}$ = 12.2, $J_{4',5'a}$ = 10.0 and $J_{4',5'b}$ = 6.0 Hz), 4.33 (1H, t, $J_{4',5'a} = J_{5'a,5'b}$ = 10.0 Hz), 4.37 (1H, dd, $J_{4',5'b}$ = 6.0 and $J_{5'a,5'b}$ = 10.0 Hz), 5.31 (1H, dd, $J_{2',3'}$ = 2.0 and $J_{3',4'}$ = 12.2 Hz), 6.57 (1H, d, $J_{2',3'}$ = 2.0 Hz), 7.20 (1H, s); ^{13}C NMR ($CDCl_3$) δ 20.0, 22.7, 27.1, 27.4, 55.0, 67.1, 86.0, 117.6, 126.0, 128.4, 132.8, 162.2; FAB-MS (m/z) 434 and 435 (M^+ + H). Anal. Calcd for $C_{16}H_{24}BrNO_2S_2Si$: C, 44.23; H, 5.57; N, 3.22. Found: C, 44.13; H, 5.48; N, 3.03.

4-Chloro-3*H*,5*H*-pyrrolo[3,2-*d*]pyrimidine (18). A mixture of **17** (1.35 g, 10.0 mmol) and $POCl_3$ (18.6 mL, 200 mmol) was heated at 100 °C for 4 h. The reaction mixture was quenched with ice chips and

Scheme 9. Plausible Mechanism for the Formation of 42a,b



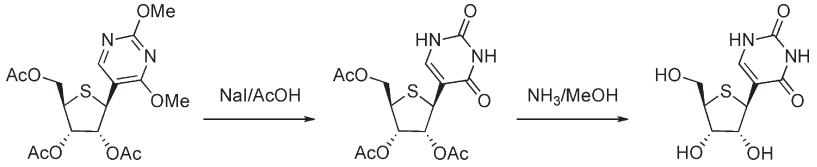
neutralized with $NaHCO_3$. The mixture was evaporated to dryness and the residual solid was collected by suction filtration to give **18** (1.23 g, 80%) as a solid: mp 195−197 °C; UV (MeOH) λ_{max} 275 nm (ε 7100) and λ_{min} 241 nm (ε 1500); ^{1}H NMR (DMSO-d_6) δ 6.73 (1H, s), 3.70 (1H, t, J = 2.8 Hz), 8.62 (1H, s), 12.44 (1H, br); ^{13}C NMR ($CDCl_3$) δ 102.3, 124.0, 134.4, 141.7, 149.1, 150.9; FAB-MS (m/z) 154 and 156 (M^+ + H). Anal. Calcd for $C_6H_4ClN_3 \cdot 1/10H_2O$: C, 46.33; H, 2.72; N, 27.01. Found: C, 46.46; H, 2.63; N, 27.34.

4-Amino-3*H*,5*H*-pyrrolo[3,2-*d*]pyrimidine (19). Ethanolic ammonia (200 mL) was added to **18** (1.23 g, 8.0 mmol) placed in sealed tube, and the suspension was heated under reflux for 24 h. The reaction mixture was evaporated to dryness, and the residue was chromatographed on silica gel (15% MeOH in CH_2Cl_2) to give **19** (829.9 mg, 78%) as a solid: mp 226−228 °C; UV (MeOH) λ_{max} 275 nm (ε 7100) and λ_{min} 241 nm (ε 1500); ^{1}H NMR (DMSO-d_6) δ 6.42 (1H, d, $J_{6,7}$ = 3.3 Hz), 7.67 (1H, d, $J_{6,7}$ = 3.3 Hz), 7.86 (2H, br), 8.31 (1H, s), 11.95 (1H, br); ^{13}C NMR ($CDCl_3$) δ 98.8, 113.0, 129.7, 140.5, 147.5, 151.4; FAB-MS (m/z) 135 (M^+ + H); FAB-HRMS (m/z) calcd for $C_6H_7N_4$: 135.0671, found: 135.0650 (M^+ + H).

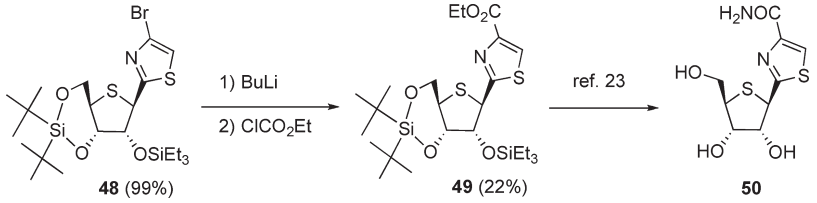
4-Pivaloylamino-3*H*,5*H*-pyrrolo[3,2-*d*]pyrimidine (20). To a CH_3CN (20 mL) solution of **19** (827 mg, 6.17 mmol) were added *i*-Pr_2NEt (4.3 mL, 24.68 mmol) and $(CH_3)_3COCl$ (2.3 mL, 18.51 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred for 20 h. The reaction mixture was quenched with MeOH and evaporated to dryness. Silica gel column chromatography (1% MeOH in CH_2Cl_2) of the residue gave **20** (1.08 g, 80%) as foam: UV (MeOH) $\lambda_{shoulder}$ 296 nm (ε 8200), λ_{max} 280 nm (ε 9400), 238 nm (ε 14700) and λ_{min} 253 nm (ε 3000),

dx.doi.org/10.1021/jo201100n |*J. Org. Chem.* 2011, 76, 8658–8669

Scheme 10. Synthesis of 4′-Thiopseudouridine 47 from 45



Scheme 11. Synthesis of 4′-Thiotiazofurin 50



224 nm (ε 8300); ^{1}H NMR ($CDCl_3$) δ 1.40 (9H, s), 6.72 (1H, t, $J_{6,7} = J_{7,NH} = 2.0$ Hz), 7.56 (1H, t, $J_{6,7} = J_{6,NH} = 2.0$ Hz), 8.51 (1H, br), 8.59 (1H, s); ^{13}C NMR ($CDCl_3$) δ 27.5, 39.9, 102.8, 115.4, 130.4, 142.0, 149.6, 152.4, 178.1; FAB-MS (m/z) 219 (M^+ + H). Anal. Calcd for $C_{11}H_{14}N_4OSSi \cdot 1/5CH_3OH$: C, 59.88; H, 6.64; N, 24.94. Found: C, 59.71; H, 6.54; N, 24.64.

4-Pivaloylamino-7-iodo-3*H*,5*H*-pyrrolo[3,2-*d*]pyrimidine (21). To a DMF (20 mL) solution of **20** (1.07 g, 4.90 mmol) was added *N*-iodosuccinimide (1.32 g, 5.88 mmol) at rt under Ar atmosphere, and the mixture was stirred at 80 °C for 1 h. The reaction mixture was partitioned between AcOEt/H_2O, and silica gel column chromatography (hexane/AcOEt = 2/1) of the organic layer gave **21** (1.35 g, 80%) as foam: UV (MeOH) λ_{max} 306 nm (ε 6140), 283 nm (ε 10200), 247 nm (ε 16500) and λ_{min} 297 nm (ε 6050), 261 nm (ε 5200), 231 nm (ε 8100); ^{1}H NMR ($CDCl_3$) δ 1.40 (9H, s, *t*-Bu), 7.64 (1H, d, $J_{6,NH} = 2.4$ Hz), 8.29 (1H, br), 8.68 (1H, s), 11.25 (1H, br); ^{13}C NMR ($CDCl_3$) δ 27.5, 40.0, 57.9, 115.6, 134.1, 142.4, 150.5, 152.3, 178.3; FAB-MS (m/z) 345 (M^+ + H). Anal. Calcd for $C_{11}H_{13}IN_4O \cdot 3/4H_2O$: C, 36.94; H, 8.37; N, 15.66. Found: C, 37.22; H, 3.69; N, 15.26.

1,4-Anhydro-2-deoxy-3,5-*O*-(di-*tert*-butylsilylene)-1-(4-*N*-pivaloylamino-pyrrolo[3,2-*d*]pyrimidin-7-yl)-4-thio-D-*erythro*-pento-1-enitol (22). To a THF (25.0 mL) solution of **6** (2.12 g, 3.78 mmol) were added **21** (1.69 g, 4.91 mmol), $(Ph_3P)_4Pd$ (566.2 mg, 0.49 mmol), and CuI (186.6 mg, 0.98 mmol), and the mixture was stirred at 80 °C under Ar atmosphere for 20 h. The reaction mixture was chromatographed on silica gel (hexane/AcOEt = 5/1) to give **22** (966.2 mg, 52%) as a solid: mp 179−180 °C; UV (MeOH) λ_{max} 323 nm (ε 4400), 264 nm (ε 22900), 237 nm (ε 21500) and λ_{min} 303 nm (ε 3700), 247 nm (ε 18100), 231 nm (ε 20100); ^{1}H NMR ($CDCl_3$) δ 1.04 and 1.09 (18H, each as s), 1.40 (9H, s), 3.96−4.03 (1H, m), 4.36 (1H, t, $J_{5'a,5'b} = J_{4',5'a} = 10.0$ Hz), 4.40 (1H, dd, $J_{5'a,5'b} = 10.0$ and $J_{4',5'b}$ 5.6 Hz), 5.39 (1H, dd, $J_{2',3'} = 1.8$ and $J_{3',4'} = 11.6$ Hz), 6.92 (1H, d, J = 1.8 Hz), 7.53 (1H, d, J = 2.4 Hz), 8.23 (1H, br), 8.66 (1H, s), 11.05 (1H, br); ^{13}C NMR ($CDCl_3$) δ 20.1, 22.7, 27.2, 27.47, 27.49, 27.8, 40.0, 53.9, 67.6, 86.5, 111.6, 116.4, 123.0, 128.4, 129.5, 142.4, 149.2, 150.1, 178.2; FAB-MS (m/z) 489 (M^+ + H). Anal. Calcd for $C_{24}H_{36}O_3N_4SSi$: C, 58.98; H, 7.42; N, 11.46. Found: C, 59.05; H, 7.49; N, 11.37.

Hydroboration of 10 and Quenching with Acetone Pinacol: Formation of 24. To a THF (2.5 mL) solution of **10** (38.3 mg, 0.11 mmol) was added $BH_3 \cdot$THF (1 M THF solution) (0.55 mL, 0.55 mmol) at 0 °C under Ar atmosphere, and the reaction mixture was stirred 18 h at rt. To the reaction mixture was added a THF (1.5 mL) solution of acetone cathecol (260 mg, 2.20 mmol), and the mixture stirred at 0 °C for 22 h at rt. ICN silica gel column chromatography (hexane/AcOEt = 300/1) of the reaction mixture gave **24** (13.2 mg, 25%) as a solid: mp 120−122 °C; UV (MeOH) $\lambda_{shoulder}$ 221 nm (ε 5400); ^{1}H NMR (500 MHz) (DMSO-d_6) δ 1.01 and 1.02 (18H, each as s), 1.23 and 1.24 (12H, each as s), 2.16 (1H, dd, $J_{1',2'} = 4.1$ and $J_{2',3'} = 8.6$ Hz), 3.66 (1H, ddd, $J_{3',4'} = 10.8$, $J_{4',5'a} = 9.8$ and $J_{4',5'b} = 4.6$ Hz), 3.95 (1H, dd, $J_{4',5'a} = 9.8$ and $J_{5'a,5'b} = 10.3$ Hz), 4.31 (1H, dd, $J_{4',5'b} = 4.6$ and $J_{5'a,5'b} = 10.3$ Hz), 4.49 (1H, d, $J_{1',2'} = 4.1$ Hz), 4.61 (1H, dd, $J_{2',3'} = 8.6$ and $J_{3',4'} = 10.8$ Hz), 7.21−7.25 and 7.30−7.36 (5H, each as m, Ph); NOE experiment: H-1′/H-4′ (2.3%), H-2′/ H-Ph (1.9%) and H-3′/ H-Ph (1.4%); ^{13}C NMR (DMSO-d_6) δ 19.7, 22.3, 24.0, 25.3, 26.8, 27.3, 48.3, 49.7, 68.2, 82.1, 83.4, 127.1, 127.2, 128.6, 143.8. FAB-MS (m/z) 476 and 477 (M^+ + H). Anal. Calcd for $C_{25}H_{41}BO_4SSi$: C, 63.01; H, 8.67. Found: C, 63.33; H, 8.78.

1-[2,3,5-Tri-*O*-acetyl-4-thio-β-D-ribofuranosyl]benzene (26). To a THF (2.5 mL) solution of **10** (42.9 mg, 0.12 mmol) was added $BH_3 \cdot$THF (1 M THF solution) (0.6 mL, 0.60 mmol) at 0 °C under Ar atmosphere, and the reaction mixture was stirred for 15 h. To the reaction mixture was added MeOH (89 μL, 2.2 mmol), and the mixture stirred at 0 °C. After 1 h, 10% NaOH (0.18 mL, 0.44 mmol) and 30% H_2O_2 (37 μL, 0.33 mmol) was added at 0 °C, and the mixture was stirred for 24 h at rt. The reaction mixture was partitioned between $CHCl_3/H_2O$ and the organic layer was evaporated to dryness and dried in vacuo overnight. To a stirred THF (3.0 mL) solution of the crude product was added Bu_4NF (1 M THF solution) (0.33 mL, 0.33 mmol) at 0 °C under Ar atmosphere. After stirring for 11 h, Ac_2O (52 μL, 0.55 mmol) was added to the reaction mixture, and the mixture was stirred for 10 h at rt. The reaction mixture was partitioned between $CHCl_3$/saturated aqueous $NaHCO_3$ and column chromatography (hexane/AcOEt = 7/1) of the organic layer gave **26** (34.8 mg, 90%) as a syrup: UV (MeOH) $\lambda_{shoulder}$ 250 nm (ε 370); ^{1}H NMR ($CDCl_3$) δ 1.97, 2.14, and 2.14 (18H, each as s), 3.66 (1H, ddd, $J_{3',4'} = 3.2$, $J_{4',5'a} = 6.8$ and $J_{4',5'b} = 6.0$ Hz), 4.27 (1H, dd, $J_{4',5'a} = 6.8$ and $J_{5'a,5'b} = 11.4$ Hz), 4.36 (1H, dd, $J_{4',5'b} = 6.0$ and $J_{5'a,5'b} = 11.4$ Hz), 4.63 (1H, d, $J_{1',2'} = 8.1$ Hz), 5.41 (1H, dd, $J_{1',2'} = 8.1$ and $J_{2',3'} = 3.2$ Hz), 5.52 (1H, t, $J_{2',3'} = J_{3',4'} = 3.2$ Hz), 7.27−7.36 and 7.45−7.47 (5H, each as m, Ph); NOE experiment: H-1′/H-4′ (1.1%) and H-2′/ H-5′a (2.0%); ^{13}C NMR ($CDCl_3$) δ 20.5, 20.8, 46.5, 50.8, 65.0, 74.3, 78.3, 128.0, 128.1, 128.7, 136.7, 169.7, 169.8, 170.5. FAB-MS (m/z) 353 (M^+ + H). Anal. Calcd for $C_{17}H_{20}O_6S$: C, 57.94; H, 5.72. Found: C, 57.83; H, 5.77.

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1-[3,5-*O*-(Di-*tert*-butylsilylene)-4-thio-β-D-ribofuranosyl]-naphthalene (27). To a THF (6.0 mL) solution of **11** (105.3 mg, 0.26 mmol) was added BH_3·THF (1 M THF solution) (1.3 mL, 1.30 mmol) at 0 °C under Ar atmosphere, and the reaction mixture was stirred 4 h. To the reaction mixture was added MeOH (0.20 mL, 5.2 mmol), and the mixture stirred at 0 °C for 1 h. The reaction mixture was evaporated to dryness, and silica gel column chromatography (hexane/AcOEt = 20/1) of the residue gave the organoborane. To a THF (5.0 mL) solution of the organoborane was added 9.9% NaOH (0.42 mL, 1.04 mmol) and 30% H_2O_2 (88 μL, 0.78 mmol) was added at 0 °C, and the mixture was stirred for 7 h. The reaction mixture was partitioned between AcOEt/H_2O and the organic layer was washed with saturated NH_4Cl and saturated $NaHCO_3$. Silica gel column chromatography (hexane/AcOEt = 40/1) of the organic layer gave **27** (67 mg, 62%) as a solid: mp 102−104 °C; ^{1}H NMR ($CDCl_3$) δ 1.02 and 1.05 (18H, each as s), 2.06 (1H, br), 3.89 (1H, ddd, $J_{3',4'}$ = 9.8, $J_{4',5'a}$ = 10.0 and $J_{4',5'b}$ = 3.6 Hz), 4.18 (1H, t, $J_{4',5'a}$ = $J_{5'a,5'b}$ = 10.0 Hz), 4.21 (1H, dd, $J_{4',5'b}$ = 3.6 and $J_{5'a,5'b}$ = 10.0 Hz), 4.40−4.42 (1H, m), 4.47 (1H, dd, $J_{2',3'}$ = 5.2 and $J_{3',4'}$ = 9.8 Hz), 5.31 (1H, s), 7.45−7.49, 7.51−7.54, 7.57−7.62, 7.77−7.79, 7.87−7.90, 8.22−8.24 (7H, each as m); NOE experiment: H-1′/H-4′ (1.7%) and HO-2′/H-4′ (3.3%); ^{13}C NMR ($CDCl_3$) δ 20.5, 23.0, 27.5, 27.6, 45.1, 51.0, 68.9, 79.3, 81.7, 123.4, 125.52, 125.53, 126.2, 126.9, 128.4, 129.1, 131.6, 134.0, 136.0; FAB-MS (*m*/*z*) 417 (M^+ + H); FAB-HRMS (*m*/*z*) calcd for $C_{23}H_{33}O_3SSi$: 417.1920, found: 417.1932 (M^+ + H).

3-[3,5-*O*-(Di-*tert*-butylsilylene)-4-thio-β-D-ribofuranosyl]-quinoline (28). To a THF (5.0 mL) solution of **12** (80.9 mg, 0.034 mmol) was added BH_3·THF (1 M THF solution) (1.0 mL, 1.00 mmol) at 0 °C under Ar atmosphere, and the reaction mixture was stirred 6 h. To the reaction mixture was added MeOH (0.15 mL, 4.0 mmol), and the mixture stirred at 0 °C for 1 h. The reaction mixture was evaporated to dryness, and silica gel column chromatography (hexane/AcOEt = 3/1) of the residue gave the organoborane. To a THF (5.0 mL) solution of the organoborane were added 9.9% NaOH (0.32 mL, 0.80 mmol) and 30% H_2O_2 (68 μL, 0.60 mmol) at 0 °C, and the mixture was stirred for 8 h. The reaction mixture was partitioned between AcOEt/H_2O, and the organic layer was washed with saturated NH_4Cl and saturated $NaHCO_3$. Silica gel column chromatography (hexane/AcOEt = 3/1) of the organic layer gave **28** (36.7 mg, 44%) as a syrup: ^{1}H NMR ($CDCl_3$) δ 1.05 and 1.07 (18H, each as s), 2.63 (1H, br), 3.83−3.90 (1H, m), 4.20 (1H, dd, $J_{4',5'a}$ = 10.0 and $J_{5'a,5'b}$ = 11.2 Hz), 4.30 (1H, dd, $J_{4',5'b}$ = 6.4 and $J_{5'a,5'b}$ = 11.2 Hz), 4.29 (1H, d, $J_{2',3'}$ = 4.4), 4.46 (1H, dd, $J_{2',3'}$ = 4.4 and $J_{3',4'}$ = 10.0 Hz), 4.69 (1H, s), 7.54−7.59, 7.72−7.76, 7.82−7.84, 8.09−8.12, 8.18−8.19, 8.97−8.98 (6H, each as m); NOE experiment: H-1′/H-4′ (1.5%), HO-2′/H-4′ (3.5%); ^{13}C NMR ($CDCl_3$) δ 20.2, 22.8, 25.8, 27.2, 27.4, 46.0, 52.2, 68.3, 68.3, 79.7, 81.6, 127.2, 127.6, 127.8, 129.2, 129.7, 133.3, 134.8, 147.4, 150.7; FAB-MS (*m*/*z*) 418 (M^+ + H); FAB-HRMS (*m*/*z*) calcd for $C_{22}H_{32}NO_3SSi$: 418.1863, found: 418.1863 (M^+ + H).

3-[3,5-*O*-(Di-*tert*-butylsilylene)-4-thio-β-D-ribofuranosyl]-pyridine (29). To a THF (5.0 mL) solution of **13** (78.8 mg, 0.23 mmol) was added BH_3·THF (1 M THF solution) (1.2 mL, 1.15 mmol) at 0 °C under Ar atmosphere, and the reaction mixture was stirred 8 h. To the reaction mixture was added MeOH (0.17 mL, 4.6 mmol), and the mixture stirred at 0 °C for 1 h. The reaction mixture was evaporated to dryness, and silica gel column chromatography (hexane/AcOEt = 1/1) of the residue gave the organoborane. To a THF (5.0 mL) solution of the organoborane were added 9.9% NaOH (0.37 mL, 0.19 mmol) and 30% H_2O_2 (78 μL, 0.69 mmol) at 0 °C, and the mixture was stirred for 8 h. The reaction mixture was partitioned between AcOEt/H_2O, and the organic layer was washed with saturated NH_4Cl and saturated $NaHCO_3$. Silica gel column chromatography (hexane/AcOEt = 3/1) of the organic layer gave **29** (43 mg, 51%) as a solid: mp 129−131 °C; ^{1}H NMR ($CDCl_3$) δ 1.04 and 1.07 (18H, each as s), 2.62 (1H, br), 3.82 (1H, ddd, $J_{3',4'}$ = 10.0, $J_{4',5'a}$ = 10.4 and $J_{4',5'b}$ = 4.8 Hz), 4.20−4.23 (1H, m), 4.42 (1H, dd, $J_{2',3'}$ = 4.8 and $J_{3',4'}$ = 10.0 Hz), 4.49 (1H, s), 7.48−7.52, 7.98−7.99, 8.52−8.54, 8.69 (6H, each as m); NOE experiment: H-1′/H-4′ (2.0%), HO-2′/H-4′ (3.0%); ^{13}C NMR ($CDCl_3$) δ 20.2, 22.8, 27.2, 27.3, 46.2, 51.3, 67.9, 79.3, 81.5, 125.2, 138.8, 139.2, 146.5, 147.3; FAB-MS (*m*/*z*) 368 (M^+ + H); FAB-HRMS (*m*/*z*) calcd for $C_{18}H_{30}NO_3SSi$: 368.1716, found: 368.1717 (M^+ + H).

7-[3,5-*O*-(Di-*tert*-butylsilylene)-4-thio-β-D-ribofuranosyl]-4-pivaloylamino-3*H*,5*H*-pyrrolo[3,2-*d*]pyrimidine (30). To a THF (2.5 mL) solution of **22** (48.9 mg, 0.1 mmol) was added BH_3·THF (1 M THF solution) (0.5 mL, 0.5 mmol) at 0 °C under Ar atmosphere, and the reaction mixture was stirred 18 h. To the reaction mixture was added MeOH (81 μL, 2.0 mmol), and the mixture stirred at 0 °C for 1 h. The reaction mixture was evaporated to dryness, and silica gel column chromatography (hexane/AcOEt = 2/1) of the residue gave **19** (9.4 mg, 19%) and the organoborane. To a THF (2.5 mL) solution of the organoborane (26.8 mg) were added 9.9% NaOH (40 μL, 0.10 mmol) and 30% H_2O_2 (8.7 μL, 0.015 mmol) at 0 °C, and the mixture was stirred for 2 h. The reaction mixture was partitioned between AcOEt/H_2O, and the organic layer was washed with saturated NH_4Cl and saturated $NaHCO_3$. Silica gel column chromatography (hexane/AcOEt = 1/1) of the organic layer gave **30** (20 mg, 40%, syrup): UV (MeOH) $\lambda_{shoulder}$ 301 nm (ε 6100), λ_{max} 283 nm (ε 9500), 243 nm (ε 20000) and λ_{min} 260 nm (ε 4500), 227 nm (ε 8900); ^{1}H NMR ($CDCl_3$) δ 1.04 and 1.06 (18H, each as s), 1.39 (9H, s), 3.02 (1H, br), 3.84 (1H, ddd, $J_{3',4'}$ = 11.2, $J_{4',5'a}$ = 10.0 and $J_{4',5'b}$ = 4.8 Hz), 4.16 (1H, dd, $J_{4',5'a}$ = 10.0 and $J_{5'a,5'b}$ = 11.2 Hz), 4.41 (1H, dd, $J_{4',5'b}$ = 4.8 and $J_{5'a,5'b}$ = 11.2 Hz), 4.57 (1H, d, $J_{2',3'}$ = 3.6 Hz), 4.65 (1H, dd, $J_{2',3'}$ = 3.6 and $J_{3',4'}$ = 11.2 Hz), 4.84 (1H, s), 7.55 (1H, d, $J_{NH,6}$ = 2.8 Hz), 8.25 (1H, br), 8.59 (1H, s), 10.84 (1H, br); NOE experiment: H-1′/H-4′ (2.0%), H-6/H-2′ (0.6%), H-6/H-3′ (1.9%), HO-2′/H-4′ (3.1%); ^{13}C NMR ($CDCl_3$) δ 20.2, 22.7, 27.2, 27.4, 27.5, 39.9, 44.9, 45.0, 68.8, 78.5, 81.3, 116.5, 116.6, 129.2, 142.2, 149.2, 149.3, 178.2; FAB-MS (*m*/*z*) 507 (M^+ + H). Anal. Calcd for $C_{24}H_{38}N_4O_4SSi$·1/4$CH_3CO_2C_2H_5$: C, 56.78; H, 7.62; N, 10.60. Found: C, 57.00; H, 7.60; N, 10.60.

Hydroboration of 15: Formation of 31 and 32. To a THF (2.0 mL) solution of **15** (41.9 mg, 0.10 mmol) was added BH_3·THF (1 M THF solution) (0.5 mL, 0.50 mmol) at 0 °C under Ar atmosphere, and the reaction mixture was stirred for 4 h. To the reaction mixture was added MeOH (76 μL, 2.0 mmol), and the mixture stirred at 0 °C. After 2 h of stirring, 10% NaOH (0.16 mL, 0.4 mmol) and 30% H_2O_2 (34 μL, 0.3 mmol) were added at 0 °C, and the mixture was stirred for 4 h. The reaction mixture was partitioned between $CHCl_3/H_2O$, and the organic layer was evaporated to dryness. The crude product was reacted with Ac_2O (28 μL, 0.3 mmol), *i*-PrNEt$_2$ (70 μL, 0.4 mmol), and DMAP (2.4 mg, 0.02 mmol) in CH_2Cl_2 (2.5 mL) for 3 h at rt. The reaction mixture was partitioned between $CHCl_3$/saturated $NaHCO_3$, and column chromatography (hexane/AcOEt = 7/1) of the organic layer gave **31** (19.5 mg, 41%, syrup) and **32** (15.0 mg, 16%, syrup).

Physical data of **31**: UV (MeOH) λ_{max} 267 nm (ε 5100) and λ_{min} 245 nm (ε 2800); ^{1}H NMR ($CDCl_3$) δ 1.00 and 1.02 (18H, each as s), 2.16 (3H, s), 3.72−3.79 (1H, m), 3.99 and 4.02 (6H, each as s), 4.07 (1H, t, $J_{4',5'a}$ = $J_{5'a,5'b}$ = 10.0 Hz), 4.25 (1H, dd, $J_{2',3'}$ = 3.8 and $J_{3',4'}$ = 10.0 Hz), 4.38 (1H, dd, $J_{4',5'b}$ = 4.8 and $J_{5'a,5'b}$ = 10.0 Hz), 4.43 (1H, s), 5.51 (1H, d, $J_{2',3'}$ = 3.8 Hz), 8.38 (1H, s); NOE experiment: H-1′/H-4′ (2.2%), H-6/H-2′ (2.9%) and H-6/H-3′ (3.5%); ^{13}C NMR ($CDCl_3$) δ 20.0, 21.1, 22.7, 26.9, 27.2, 44.7, 45.3, 54.3, 54.9, 68.4, 77.7, 79.7, 113.6, 157.3, 164.9, 168.2, 169.3; FAB-MS (*m*/*z*) 471 (M^+ + H). Anal. Calcd for $C_{21}H_{34}N_2O_6SSi$: C, 53.59; H, 7.28; N, 5.95. Found: C, 53.91; H, 7.40; N, 5.62.

Physical data of **32**: UV (MeOH) λ_{max} 263 nm (ε 5600) and λ_{min} 241 nm (ε 2700); ^{1}H NMR ($CDCl_3$) (major isomer) δ 0.93 and 0.99 (18H, each as s), 2.06 (3H, s), 2.00−2.10 (1H, m, H-2′a), 2.70 (1H, dt, $J_{1',2'b}$ = $J_{2'a,2'b}$ = 8.6 and $J_{1',2'b}$ = 5.2 Hz), 2.76 (1H, dd, $J_{3',4'}$ = 1.5, $J_{4',5'a}$ = 11.0 and $J_{4',5'b}$ = 4.4 Hz), 3.70 (1H, dt, $J_{2'a,3'}$ = $J_{2'b,3'}$ = 8.2 and $J_{3',4'}$ = 1.5 Hz), 3.96 (1H, t, $J_{4',5'a}$ = $J_{5'a,5'b}$ = 11.0 Hz), 3.99 and 4.00 (6H, each as s),

4.21 (1H, dd, $J_{4',5'b}$ = 4.4 and $J_{5'a,5'b}$ = 11.0 Hz), 6.12 (1H, dd, $J_{1',2'a}$ = 5.2 and $J_{1',2'b}$ = 8.6 Hz), 8.24 (1H, s); (minor isomer) δ 1.00 and 1.02 (18H, each as s), 2.13 (3H, s), 6.01 (1H, dd, $J_{1',2'a}$ = 4.4 and $J_{1',2'b}$ = 7.4 Hz); HMBC experiment: C-1′/H-6 and H-1′/ C(=O)CH_3; ^{13}C NMR ($CDCl_3$) δ 19.7, 21.2, 22.5, 26.9, 27.2, 39.5, 54.1, 54.6, 54.9, 67.5, 67.7, 73.4, 112.7, 157.8, 165.1, 168.9, 169.9; FAB-MS (m/z) 943 (M^+ + H). Anal. Calcd for $C_{42}H_{70}N_4O_{12}S_2Si_2$: C, 53.48; H, 7.48; N, 5.94. Found: C, 53.64; H, 7.55; N, 5.60.

Hydroboration of 15 and Quenching with Acetone Cathecol: Formation of 33 and 34. To a THF (2.5 mL) solution of **15** (35.3 mg, 0.086 mmol) was added BH_3·THF (1 M THF solution) (0.43 mL, 0.43 mmol) at 0 °C under Ar atmosphere, and the reaction mixture was stirred for 7 h at rt. To the reaction mixture was added a THF (2.0 mL) solution of acetone cathecol (203.3 mg, 1.72 mmol), and the mixture stirred for 18 h at rt. Silica gel column chromatography (hexane/AcOEt = 40/1) of the reaction mixture gave a mixture of **33** and **34**. Preparative TLC of the mixture gave **33** (12.2 mg, 26%, solid) and **34** (7.8 mg, 17%, solid).

Physical data of **33**: mp 84−86 °C; ^{1}H NMR (CD_3Cl) δ 1.03 and 1.04 (18H, each as s), 1.31 and 1.32 (12H, each as s), 2.21 (1H, dd, $J_{1',2'}$ = 2.4 and $J_{2',3'}$ = 8.0 Hz), 3.73 (1H, ddd, $J_{3',4'}$ = 10.8, $J_{4',5'a}$ = 9.8 and $J_{4',5'b}$ = 4.6 Hz), 3.98 and 4.00 (6H, each as s, OMe), 4.00 (1H, t, $J_{4',5'a}$ = $J_{5'a,5'b}$ = 10.2 Hz), 4.34 (1H, dd, $J_{4',5'b}$ = 4.8 and $J_{5'a,5'b}$ = 10.2 Hz), 4.47 (1H, dd, $J_{2',3'}$ = 8.0 and $J_{3',4'}$ = 9.4 Hz), 4.59 (1H, d, $J_{1',2'}$ = 2.4 Hz), 8.38 (1H, s); NOE experiment: H-1′/H-4′ (1.8%), H-2′/ H-2 (5.6%) and H-3′/ H-2 (3.0%); ^{13}C NMR (CD_3Cl) δ 20.1, 22.8, 24.6, 25.4, 27.1, 39.2, 48.7, 54.0, 54.8, 69.3, 81.7, 83.7, 118.0, 155.8, 164.3, 168.3; FAB-MS (m/z) 539 (M^+ + H); FAB-HRMS (m/z) calcd for $C_{25}H_{44}BN_2O_6SSi$: 539.2782, found: 539.2729 (M^+ + H).

Physical data of **34**: mp 159−161 °C; ^{1}H NMR (CD_3Cl) δ 0.98 and 1.00 (18H, each as s), 1.24 and 1.26 (12H, each as s), 2.26 (1H, dd, $J_{2'a,3'}$ = 5.2 and $J_{2'a,2'b}$ = 12.4 Hz), 2.40 (1H, dd, $J_{2'b,3'}$ = $J_{2'a,2'b}$ = 12.4 Hz), 3.32 (1H, ddd, $J_{3',4'}$ = 11.7, $J_{4',5'a}$ = 7.8 and $J_{4',5'b}$ = 4.4 Hz), 3.98 and 3.99 (6H, each as s), 3.95−4.05 (2H, m), 4.33 (1H, dd, $J_{4',5'b}$ = 4.8 and $J_{5'a,5'b}$ = 12.4 Hz), 8.61 (1H, s); NOE experiment: H-2′/H-2 (1.0%) and H-3′/ H-2 (1.4%); ^{13}C NMR (CD_3Cl) δ 19.9, 22.7, 24.3, 27.1, 27.4, 29.7, 43.3, 48.7, 53.8, 54.7, 69.0, 79.4, 84.1, 118.6, 156.9, 164.2, 167.9; FAB-MS (m/z) 539 (M^+ + H); FAB-HRMS (m/z) calcd for $C_{25}H_{44}BN_2O_6SSi$: 539.2782, found: 539.2729 (M^+ + H).

Hydroboration of 16: Formation of 41, 42a, and 42b. To a THF (2.5 mL) solution of **16** (35.9 mg, 0.083 mmol) was added BH_3·THF (1 M THF solution) (0.42 mL, 0.42 mmol) at 0 °C under Ar atmosphere, and the reaction mixture was stirred for 8 h at rt. To the reaction mixture was added MeOH (63 μL, 1.66 mmol), and the mixture stirred at 0 °C. After be stirring for 1 h, 9.9% NaOH (0.13 mL, 0.33 mmol) and 30% H_2O_2 (28 μL, 0.25 mmol) was added at 0 °C, and the mixture was stirred for 14 h at rt. The reaction mixture was partitioned between $CHCl_3$/H_2O and column chromatography (hexane/AcOEt = 30/1−20/1) of the organic layer gave **41** (10 mg, 27%, syrup) and **42a,b** (12 mg, 33%, solid). Compounds **42a** (solid, t_R 10.6 min) and **42b** (solid, t_R 11.1 min) were separated by HPLC (hexane/ethyl acetate =20/1).

Physical data of **41**: UV (MeOH) λ_{max} 256 nm (ε 4000) and λ_{min} 233 nm (ε 2700); ^{1}H NMR ($CDCl_3$) δ 1.03 and 1.04 (18H, each as s), 2.48 (1H, br), 3.83 (1H, ddd, $J_{3',4'}$ = 4.8, $J_{4',5'a}$ = 10.0 and $J_{4',5'b}$ = 11.2 Hz), 4.12 (1H, dd, $J_{4',5'a}$ = 10.0 and $J_{5'a,5'b}$ = 11.2 Hz), 4.26 (1H, dd, $J_{4',5'b}$ = 3.6 and $J_{5'a,5'b}$ = 11.2 Hz), 4.40 (1H, dd, $J_{2',3'}$ = 4.8 and $J_{3',4'}$ = 10.0 Hz), 4.57 (1H, d, $J_{2',3'}$ = 4.8 Hz), 4.71 (1H, d, $J_{1',2'}$ = 0.4 Hz), 7.20 (1H, s), 7.26 (1H, s); NOE experiment: H-1′/H-4′ (1.3%) and HO-2′/ H-4′ (1.6%); ^{13}C NMR ($CDCl_3$) δ 20.2, 22.7, 27.2, 27.3, 44.9, 50.8, 68.4, 78.8, 81.0, 118.4, 125.6, 173.1; FAB-MS (m/z) 451 and 453 (M^+ + H). Anal. Calcd for $C_{16}H_{26}BrNO_3S_2Si$·1/2$CH_3CO_2C_2H_5$: C, 43.54; H, 6.09; N, 2.82. Found: C, 43.81; H, 5.79; N, 3.10.

Physical data of **42a**: mp 110−112 °C; UV (MeOH) λ_{max} 257 nm (ε 3470) and λ_{min} 231 nm (ε 1950); ^{1}H NMR ($CDCl_3$) δ 1.02 and 1.05 (18H, each as s), 2.32 (1H, dt, $J_{1',2'}$ = 8.8, $J_{2'a,3'}$ = $J_{2'a,2'b}$ = 12.4 Hz), 2.70 (1H, dd, $J_{2'b,3'}$ = 5.2 and $J_{2'a,2'b}$ = 12.8 Hz), 3.43 (1H, ddd, $J_{3',4'}$ = 9.8, $J_{4',5'a}$ = 11.0 and $J_{4',5'b}$ = 4.8 Hz), 4.32 (1H, ddd, $J_{2'a,3'}$ = 12.4, $J_{2'b,3'}$ = 5.2 and $J_{3',4'}$ = 9.8 Hz), 4.36 (1H, dd, $J_{4',5'b}$ = 4.8 and $J_{5'a,5'b}$ = 10.8 Hz), 4.75 (1H, d, $J_{1',2'a}$ = 8.8 Hz), 7.19 (1H, s); NOE experiment: H-1′/H-4′ (1.1%) and H-1′/ H-2′a (5.7%); ^{13}C NMR ($CDCl_3$) δ 19.9, 22.7, 27.0, 27.3, 42.5, 42.5, 49.3, 68.7, 78.6, 118.0, 125.2, 177.1; FAB-MS (m/z) 436 and 438 (M^+ + H). Anal. Calcd for $C_{16}H_{26}BrNO_2S_2Si$·1/2AcOEt: C, 44.99; H, 6.29; N, 2.91. Found: C, 44.62; H, 6.10; N, 2.86.

Physical data of **42b**: mp 103−105 °C; UV (MeOH) λ_{max} 335 nm (ε 1370), 257 nm (ε 3440) and λ_{min} 298 nm (ε 510) and 230 nm (ε 2230); ^{1}H NMR ($CDCl_3$) δ 1.01 and 1.07 (18H, each as s), 2.06 (1H, dd, $J_{1',2'a}$ = 10.8 and $J_{2'a,2'b}$ = 12.2 Hz), 2.92 (1H, ddd, $J_{1',2'b}$ = 7.2, $J_{2'b,3'}$ = 5.2 and $J_{2'a,2'b}$ = 12.2 Hz), 3.58 (1H, ddd, $J_{3',4'}$ = 9.4, $J_{4',5'a}$ = 11.1 and $J_{4',5'b}$ = 4.8 Hz), 3.99 (1H, dd, $J_{4',5'a}$ = 11.0 and $J_{5'a,5'b}$ = 10.0 Hz), 4.25−4.30 (1H, m), 4.30 (1H, dd, $J_{4',5'b}$ = 4.8 and $J_{5'a,5'b}$ = 10.0 Hz), 4.77 (1H, dd, $J_{1',2'a}$ = 10.8 and $J_{1',2'b}$ = 7.2 Hz), 7.18 (1H, s); NOE experiment: H-1′/H-2′ β (4.7%), H-1′/ H-3′ (4.7%) and H-2′α/H-4′(4.0%); ^{13}C NMR ($CDCl_3$) δ 19.9, 22.7, 27.0, 27.4, 42.1, 43.6, 49.5, 68.3, 80.4, 117.4, 124.7, 175.0; FAB-MS (m/z) 436 and 438 (M^+ + H). Anal. Calcd for $C_{16}H_{26}BrNO_2S_2Si$: C, 44.03; H, 6.00; N, 3.21. Found: C, 44.37; H, 5.98; N, 3.02.

5-[2,3,5-Tri-*O*-acetyl-4-thio-β-D-ribofuranosyl]-2,4-dimethoxypyrimidine (45). To a stirred THF (2.0 mL) solution of **31** was added Bu_4NF (1 M THF solution) (0.12 mL, 0.12 mmol) at 0 °C under Ar atmosphere. After 7.5 h of stirring, Ac_2O (25 μL, 0.27 mmol) was added to the reaction mixture, and the mixture was stirred overnight at rt. The reaction mixture was partitioned between $CHCl_3$/saturated aqueous $NaHCO_3$, and silica gel column chromatography (hexane/AcOEt = 3/1) of the organic layer gave **45** (20.4 mg, 93%) as a syrup: UV (MeOH) λ_{max} 266 nm (ε 5200) and λ_{min} 246 nm (ε 3000); ^{1}H NMR ($CDCl_3$) δ 2.03 and 2.12 (9H, each as s), 3.68 (1H, dt, $J_{3',4'}$ = 4.4 and $J_{4',5'}$ = 6.0 Hz), 3.99 and 4.04 (6H, each as s), 4.28 (2H, d, $J_{4',5'}$ = 6.0 Hz), 4.65 (1H, d, $J_{1',2'}$ = 6.8 Hz), 5.46 (1H, dd, $J_{2',3'}$ = 3.6 and $J_{3',4'}$ = 4.4 Hz), 5.71 (1H, dd, $J_{1',2'}$ = 6.8 and $J_{2',3'}$ = 3.6 Hz), 8.34 (1H, s); ^{13}C NMR ($CDCl_3$) δ 20.6, 20.7, 43.3, 46.2, 54.2, 54.9, 64.5, 74.2, 75.2, 110.9, 157.6, 165.0, 168.8, 169.7, 169.8, 170.5; FAB-MS (m/z) 415 (M^+ + H). Anal. Calcd for $C_{17}H_{22}N_2O_8S$: C, 49.27; H, 5.35; N, 6.76. Found: C, 49.06; H, 5.42; N, 6.48.

5-[2,3,5-Tri-*O*-acetyl-4-thio-β-D-ribofuranosyl]uracil (46). To an AcOH (32.0 mL) solution of **45** (168.2 mg, 0.41 mmol) was added NaI (121.6 mg, 0.82 mmol) at rt under Ar atmosphere, and the reaction mixture was stirred under reflux for 45 min. The reaction mixture was evaporated to dryness, and silica gel column chromatography ($CHCl_3$/MeOH = 20/1) of the residue gave **46** (135.8 mg, 87%) as a solid: mp 94−96 °C; UV (MeOH) λ_{max} 264 nm (ε 6600) and λ_{min} 235 nm (ε 2300); ^{1}H NMR (CD_3OD) δ 1.94, 1.97, and 1.99 (9H, each as s) 3.54−3.62 (1H, m), 4.16 (1H, dd, $J_{4',5'a}$ = 5.7 and $J_{5'a,5'b}$ = 11.7 Hz), 4.25 (1H, dd, $J_{4',5'b}$ = 6.8 and $J_{5'a,5'b}$ = 11.7 Hz), 4.38 (1H, d, $J_{1',2'}$ = 6.4 Hz), 5.30 (1H, dd, $J_{2',3'}$ = 3.7 and $J_{3',4'}$ = 4.2 Hz), 5.58 (1H, dd, $J_{1',2'}$ = 3.7 and $J_{2',3'}$ = 3.7 Hz), 7.51 (1H, d, $J_{6,1'}$ = 0.7 Hz); ^{13}C NMR ($CDCl_3$) δ 20.8, 20.9, 42.9, 45.8, 65.2, 74.5, 75.9, 111.5, 140.4, 152.3, 163.1, 169.99, 170.05, 171.06; FAB-MS (m/z) 287 (M^+ + H). Anal. Calcd for $C_{15}H_{18}N_2O_8S$: C, 46.62; H, 4.69; N, 7.25. Found: C, 46.89; H, 4.61; N, 6.98.

5-[4-Thio-β-D-ribofuranosyl]uracil (47). Compound **46** (100.2 mg, 0.26 mmol) was treated with methanolic ammonia (15 mL) at rt for 12 h. The reaction mixture was evaporated to dryness, and silica gel column chromatography ((($CHCl_3$/MeOH = 5/1) of the residue gave crude product, which was purified by reversed pase HPLC (H_2O/CH_3CN = 98/2; t_R 20 min) to give **47** (50.9 mg, 75%) as a solid: mp 256−259 °C (dec.); UV (MeOH) λ_{max} 264 nm (ε 6600) and λ_{min} 236 nm (ε 2500); ^{1}H NMR (D_2O) δ 3.28 (1H, m), 3.58 (1H, dd, $J_{4',5'a}$ = 6.1 and $J_{5'a,5'b}$ = 11.7 Hz), 3.71 (1H, dd, $J_{4',5'b}$ = 6.4 and $J_{5'a,5'b}$ = 11.7 Hz),

4.04 (1H, t, $J_{2',3'} = J_{3',4'} = 4.1$ Hz), 4.13 (1H, d, $J_{1',2'} = 6.3$ Hz), 4.26 (1H, dd, $J_{1',2'} = 6.3$ and $J_{2',3'} = 3.9$ Hz), 7.61 (1H, s); ^{13}C NMR ($CDCl_3$) δ 46.5, 52.9, 64.7, 76.2, 78.7, 113.1, 141.9, 153.1, 165.9; FAB-MS (m/z) 261 ($M^+ + H$). Anal. Calcd for $C_9H_{12}N_2O_5S$: C, 41.53; H, 4.65; N, 10.76. Found: C, 41.70; H, 4.65; N, 10.40.

4-Bromo-2-[2-(triethylsilyl)-3,5-*O*-(di-*tert*-butylsilylene)-4-thio-D-*erythro*-pentofuranosyl]thiazole (48). To a DMF (2.0 mL) solution of **41** (13.2 mg, 0.029 mmol) were added imidazole (8.2 mg, 0.12 mmol) and Et_3SiCl (15.2 μL, 0.087 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred at rt for 12 h. The reaction mixture was partitioned between AcOEt/H_2O, and silica gel column chromatography (hexane/AcOEt = 100/1) of the organic layer gave **48** (16.3 mg, 99%) as a syrup: UV (MeOH) λ_{max} 258 nm (ε 3700) and λ_{min} 233 nm (ε 2000); ^{1}H NMR ($CDCl_3$) δ 0.73 (6H, q, J = 4.4 Hz, $SiCH_2$), 1.01−1.04 (27H, m), 3.86 (1H, ddd, $J_{3',4'} = 4.8$, $J_{4',5'a} = 11.0$ and $J_{4',5'b} = 11.2$ Hz), 4.08 (1H, dd, $J_{4',5'a} = 9.6$ and $J_{5'a,5'b} = 11.4$ Hz), 4.14 (1H, dd, $J_{4',5'b} = 3.2$ and $J_{5'a,5'b} = 11.4$ Hz), 4.36 (1H, dd, $J_{2',3'} = 4.8$ and $J_{3',4'} = 10.0$ Hz), 4.43 (1H, d, $J_{1',2'} = 0.8$ Hz), 4.54 (1H, d, $J_{2',3'} = 4.8$ Hz), 7.17 (1H, s), 7.26 (1H, s); ^{13}C NMR ($CDCl_3$) δ 4.8, 6.7, 20.1, 22.7, 27.0, 27.3, 27.4, 4.1, 53.1, 68.7, 79.7, 80.3, 118.3, 125.6, 173.9; FAB-MS (m/z) 566 and 568 ($M^+ + H$). Anal. Calcd for $C_{22}H_{40}BrNO_3S_2Si_2 \cdot 1/2CH_3CO_2C_2H_5$: C, 47.19; H, 7.26; N, 2.29. Found: C, 47.56; H, 7.11; N, 2.19.

2-[2-(Triethylsilyl)-3,5-*O*-(di-*tert*-butylsilylene)-4-thio-D-*erythro*-pentofuranosyl]-4-ethoxycarbonylthiazole (49). To a THF (1.5 mL) solution of **48** (16.7 mg, 0.029 mmol) was added *tert*-BuLi (1.55 M, hexane solution) (21 μL, 0.032 mmol) at −70 °C under Ar atmosphere, and the mixture was stirred for 5 min. To the reaction mixture was added $ClCO_2Et$ (8.3 μL, 0.087 mmol), and the mixture was stirred for 10 min. The reaction mixture was partitioned between $CHCl_3$/saturated aqueous NH_4Cl, and preparative TLC (hexane/AcOEt = 20/1) of the organic layer gave **49** (3.6 mg, 22%) as a syrup: ^{1}H NMR ($CDCl_3$) δ 0.72 (2H, q, $J_{CH_2,CH_3} = 8.0$ Hz), 1.01 and 1.02 (18H, each as s), 1.02 (3H, t, $J_{CH_2,CH_3} = 8.0$ Hz), 1.38 (3H, t, $J_{CH_2,CH_3} = 7.2$ Hz), 3.87−3.92(1H, m), 4.10 (1H, dd, $J_{4',5'a} = 10.0$ and $J_{5'a,5'b} = 10.0$ Hz), 4.17 (1H, dd, $J_{4',5'b} = 3.2$ and $J_{5'a,5'b} = 10.0$ Hz), 4.33−4.40 (3H, m), 4.44 (1H, s), 4.56 (1H, d, $J_{2',3'} = 3.2$ Hz), 7.26 (1H, s); ^{13}C NMR ($CDCl_3$) δ 4.8, 6.7, 14.1, 14.3, 20.2, 22.7, 27.0, 27.3, 29.7, 44.4, 53.3, 61.6, 68.6, 79.6, 80.4, 130.2, 131.0, 149.3, 161.4, 178.9; FAB-MS (m/z) 560 ($M^+ + H$). FAB-HRMS (m/z) calcd for $C_{25}H_{46}NO_5S_2Si_2$: 560.2356, found: 560.2375 (M^+).

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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