Synthesis of Novel Iso-4′-thionucleosides Using the Mitsunobu Reaction

Kohei Yamada, Shinji Sakata, and Yuichi Yoshimura*,†

Biochemicals Division, Yamasa Corporation, 2-10-1 Araoicho, Choshi, Chiba 288-0056, Japan

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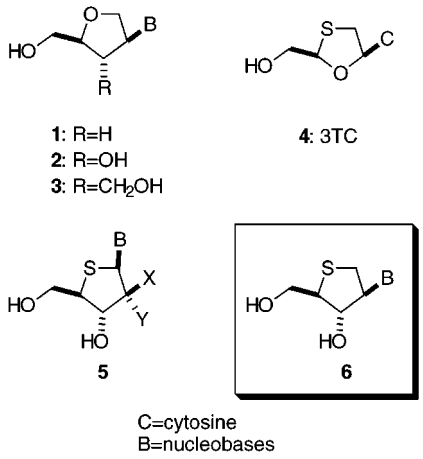
A novel class of isomeric 4′-thionucleosides with the base moiety at the 2′-position was synthesized from D-glucose. The coupling of 1,4-anhydro-4-thioarabitol (**13**) with various nucleobases using the Mitsunobu reaction was investigated. With both purines and N^3-benzoyluracils, the reaction predominantly gave β-isomers, suggesting that these were produced via an episulfonium intermediate. The β-anomers produced by the reaction of N^3-benzoyluracils included both *N*- and *O*-alkylated derivatives. Interestingly, only the reaction of N^3-benzoyluracil gave a mixture of *N*-alkylated adduct (**20d**) and *O*-alkylated bipyrimidinyl adduct (**22**), the structure of which was unambiguously determined by NMR spectroscopic data including HMBC and NOE. Deprotection of the Mitsunobu reaction products gave the desired iso-4′-thionucleosides.

Introduction

New compounds that are effective against human immunodeficiency virus (HIV), a causative agent of acquired immunodeficiency syndrome (AIDS), are urgently required. Nucleoside analogues, most of which act as inhibitors of reverse transcriptase (RT) coded by HIV, play an important role in the treatment of AIDS. To date, five nucleoside RT inhibitors, including some dideoxynucleosides (ddC, ddI, d4T), have been approved for clinical use. However, such dideoxynucleosides have shown limited stability: the glycosidic linkage of dideoxynucleosides is susceptible to both acidic and enzymatic hydrolysis. To circumvent this problem, a new class of dideoxynucleosides, isonucleosides (**1**: R = H; Chart 1), in which the base moiety is transposed from the natural 1′- to the 2′-position, were synthesized and shown to have potent anti-HIV activity and to be stable against hydrolysis of the glycosidic bond.[1] In addition to being anti-HIV agents, Tino[2] and Matsuda[3] independently reported that isonucleosides (**2**, R = OH; **3**, R = CH_2OH) had antiherpes virus and -hepatitis B virus (HBV) activity.

A new anti-HIV dideoxynucleoside, 2′-deoxy-3′-thiacytidine[4] (3TC, **4**), which has been used for the treatment of AIDS in clinical fields, has unique structural features: it is a synthetic L-nucleoside with an oxathiolane skeleton. From another perspective, 3TC is similar to 2′-isomeric-3′-oxo-4′-thio-β-D-cytidine or belongs to a novel class of iso-4′-thionucleosides. Thus, iso-4′-thionucleosides may be promising candidates as anti-HIV agents. However, despite such attractive structural features, there are few reports concerning iso-4′-thionucleosides.[5] This prompted us to design iso-4′-thionucleosides (**6**) as a hybrid constructive analogue of 2′-deoxynucleosides and 3TC.

Chart 1



Recently, we developed a new route to the synthesis of 4′-thionucleosides (**5**) with 2′-substituents,[6] and this may be applicable to the preparation of iso-4′-thionucleosides (**6**), using the same chiral synthon, 1,4-anhydro-4-thio-D-arabitol derivatives (**7**), as a starting material. We expected that it would be possible to introduce nucleobases at the 2-position of **7** with an "up" configuration, when the direct substitution reaction of the hydroxyl group proceeds with a retention of configuration. It has

† Tel: 479-22-0095 ext. 384. Fax: 479-22-9821. E-mail: chem2yms@choshinet.or.jp.

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(5) Jones, M. F.; Noble, S. A.; Robertson, C. A.; Storer, R. *Tetrahedron Lett.* **1991**, *32*, 247.

(6) (a) Yoshimura, Y.; Kitano, K.; Satoh, H.; Watanabe, M.; Miura, S.; Sakata, S.; Sasaki, T.; Matsuda, A. *J. Org. Chem.* **1996**, *61*, 822. (b) Yoshimura, Y.; Kitano, K.; Yamada, K.; Satoh, H.; Watanabe, M.; Miura, S.; Sakata, S.; Sasaki, T.; Matsuda, A. *J. Org. Chem.* **1997**, *62*, 3140. (c) Yoshimura, Y.; Watanabe, M.; Satoh, H.; Ashida, N.; Ijichi, K.; Sakata, S.; Machida, H.; Matsuda, A. *J. Med. Chem.* **1997**, *40*, 2177.

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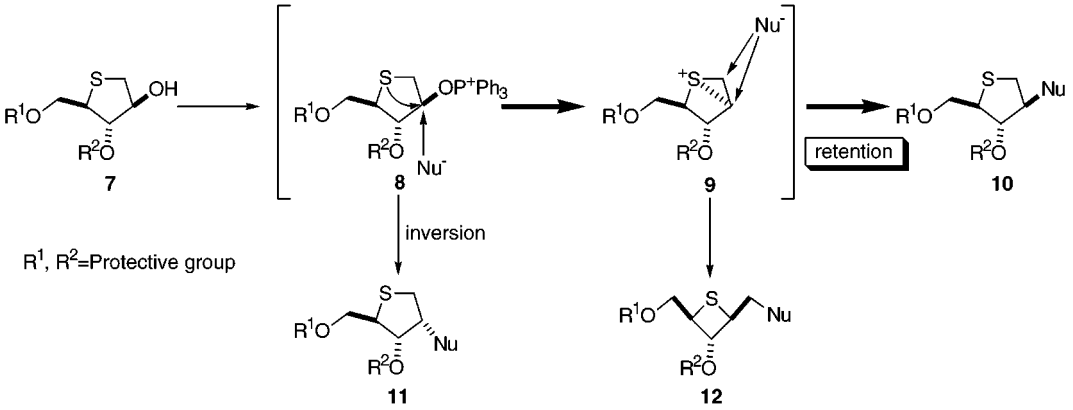
Scheme 1



been reported that some S_N2-type reactions at the β-position to the sulfur atom of tetrahydrothiopyran and tetrahydrothiophene derivatives proceeded with retention of configuration because of the formation of episulfonium intermediates.[7] This finding encouraged us to use the Mitsunobu reaction[8] to introduce nucleobases with an "up" configuration. In this report, we describe the coupling reaction of 1,4-anhydro-4-thio-D-arabitol derivative (**7**) with various nucleobases using the Mitsunobu reaction and the synthesis of iso-4′-thionucleosides.

Results and Discussion

We intended to use the Mitsunobu reaction to introduce nucleobases into the 2-position of 1,4-anhydro-4-thio-D-arabitol (**7**), which was readily obtained from D-glucose, as we reported previously.[6] If the Mitsunobu reaction proceeded via an episulfonium cation (**9**), as depicted in Scheme 1, the nucleobase moiety could be introduced at the 2-position with high β-stereoselectivity.

Initially, a coupling reaction of 3-*O*-benzyl derivative **13** with 6-chloropurine in THF was examined.[9,10] This reaction gave a mixture of two diastereoisomers[11] in 29% yield ($\beta/\alpha = 1.1$; see Table 1, entry 1). This result showed that the episulfonium intermediate (**9**), which gave rise to the formation of β-isomer, might compete with a direct S_N2 reaction (Scheme 1). In addition, thietane derivatives (**12**), which would be formed by nucleophilic attack at the 1-position of **9**, were not found in the reaction mixture. This also showed that nucleophilic ring-opening of the episulfonium cation (**9**) would take place regioselectively, controlled by the thermodynamic stability of the products.[7b]

Scheme 2

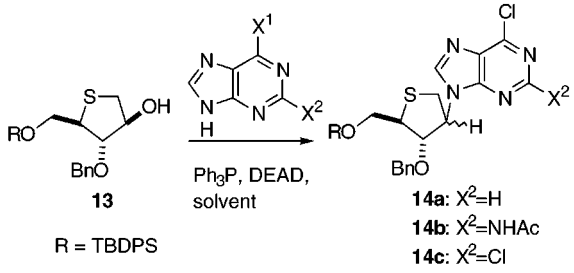


Table 1. Mitsunobu Reaction of 1,4-Anhydro-4-thio-D-arabitol Derivatives (13) with Purine Bases

entry	purine base	solvent	product	yield (%)[d]	β/α ratio
1	$X^1 = Cl$, $X^2 = H$	THF[a]	**14a**	29	1.1[e]
2	$X^1 = Cl$, $X^2 = H$	THF[b]	**14a**	24	1.4[e]
3	$X^1 = Cl$, $X^2 = H$	benzene[a]	**14a**	34	0.8[e]
4	$X^1 = Cl$, $X^2 = H$	CH_3CN[a]	**14a**	21	6.0[e]
5	$X^1 = Cl$, $X^2 = H$	CH_2Cl_2[a]	**14a**	22	1.2[e]
6	$X^1 = Cl$, $X^2 = H$	DMF[c]	**14a**	trace	
7	$X^1 = Cl$, $X^2 = NH_2$	THF[c]		NR	
8	$X^1 = X^2 = NH_2$	THF[c]		NR	
9	$X^1 = Cl$, $X^2 = NHAc$	THF[a]	**14b**	38	1.8[f]
10	$X^1 = X^2 = NHAc$	THF[a]		NR	
11	$X^1 = X^2 = Cl$	THF[a]	**14c**	33	3.1[e]

[a] Reaction was carried out at room temperature. [b] Reaction was carried out at 50 °C. [c] Reaction was carried out at 70 °C. [d] Isolated yields. [e] Isolated yields of two isomers. [f] β/α ratio was determined by ^1H NMR analysis.

On the other hand, we also attempted to react 6-chloropurine with a 2-*O*-mesylate of **13** in the presence of K_2CO_3 and 18-crown-6 in DMF. However, the formation of negligible amount of iso-4′-thionucleoside could only be observed even at the reflux temperature (data not shown). Thus, we tried to investigate the Mitsunobu coupling reaction of 3-*O*-benzyl derivative (**13**) with various purine bases in an appropriate solvent. The results are summarized in Table 1. The β-isomer was predominant ($\beta/\alpha = 6.0$) when acetonitrile was used; however, there was no improvement in the yield of **14a** (entry 4). In a previous report, the Mitsunobu reaction of **13** with diphenylphosphoryl azide gave a ribo-azide derivative, suggesting that a direct S_N2 reaction of azide anion, without the participation of episulfonium ion, had occurred from the α-side.[6b] In contrast, the same Mitsunobu reaction with 6-chloropurine gave predominantly the β-isomer or a mixture of α- and β-isomers. These results can be explained in terms of the potency of their

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(8) Mitsunobu, O. *Synthesis* **1981**, 1.

(9) The Mitsunobu reaction of the 3-*O*-benzoyl derivative, instead of **13**, with 6-chloropurine gave an undesired α-isonucleoside, stereoselectively, the stereochemistry of which was determined by NOE experiments. This result suggests that the more electron-withdrawing benzoyl group at the 3-position makes the carbon at the 2-position electron deficient, thus potentiating the external nucleophilic attack.

(10) Contrary to our expectation, when tributylphosphine was used instead of triphenylphosphine, the reaction was not complete in THF at 50 °C even after 44 h. Only α-**14a** was obtained in 11% yield with a recovery of **13** in 32% yield.

(11) The undesired *N*7-adduct of 6-chloropurine was not obtained. Similarly, none of the *N*7-adducts were found in the reaction of the other purine bases. The structure of *N*9-adducts were confirmed by UV spectra after being converted to the deblocked compounds.

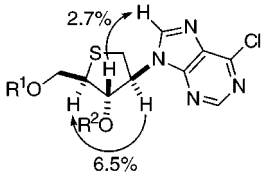


Figure 1.

nucleophilicities. The nucleophilic reaction of azide anion is faster than the formation of the strained episulfonium cation and, thus, proceeds via direct S_N2 reaction with inversion.[6b] On the other hand, the weak nucleophilicity of 6-chloropurine makes the formation of episulfonium cation energetically favorable. As a result, the reaction proceeds via competition between a direct S_N2 reaction and an episulfonium intermediate. In more polar acetonitrile, the latter path would be favored.

In the case of 2,6-dichloropurine, a similar result was obtained (33% yield, $\beta/\alpha = 3.1$, entry 11). The α,β-isomers (**14a**,**c**) could be easily separated on a silica gel column. On the other hand, the reactions with 2,6-diaminopurine or 2-amino-6-chloropurine did not proceed at all because they were scarcely soluble in THF (entries 7 and 8).[12] Accordingly, the reaction of 2-(acetylamino)-6-chloropurine gave **14b** in 38% yield, as an inseparable mixture of α,β-isomers ($\beta/\alpha = 1.8$, entry 9), which could be successfully separated in the next step.

The assignment of α- and β-stereochemistry was confirmed by NOE experiments. As shown in Figure 1, irradiation of H-2′ and H-3′ of β-**14a** enhanced the H-4′ and H-8 protons by 6.5% and 2.7%, respectively. The stereochemistry of β-**17** was also confirmed by ^{1}H NMR in comparison with the chemical shift of the H-2′ proton[13] of the corresponding α-**17** (data not shown).

The Mitsunobu adducts **14a**,**b** were converted to their corresponding adenine and guanine iso-4′-thionucleosides, as shown in Scheme 3. The benzyl group of the desirable β-isomer of **14a** was effectively removed by treatment with boron trichloride (BCl_3) in dichloromethane at −78 °C. Subsequently, compound β-**15** was desilylated by ammonium hydrogen fluoride in methanol and converted into iso-4′-thioadenosine β-**16** by amination of the 6-position with ethanolic ammonia. Likewise, the 2,6-diaminopurine derivative β-**18** and guanine derivative β-**19** were prepared. Debenzylation of a mixture of α- and β-isomers of **14b** under the conditions described above gave only the deprotected β-isomer (β-**17**) in 32% yield with unreacted α-isomer (α-**14b**) recovered in 8% yield. Although the α- and β-isomers of **14b** were effectively separated, the yields were relatively low. This is presumably due to complexation of the products with borane. However, attempts to recover further β-**14b** from the complex were not successful. The desirable β-isomer of **17** was desilylated and then converted into 2,6-diaminopurine derivative β-**18** by treatment with aqueous ammonia in methanol. In addition, guanine derivative β-**19** was synthesized by acidic hydrolysis of the 6-chloro moiety of β-**17** and subsequent deacetylation.

Next, we tried to prepare pyrimidine analogues using the above-mentioned reaction. In contrast to purine bases, the reaction with N^3-benzoyluracil derivatives[14] hardly proceeded at room temperature. However, the reaction at 70 °C gave pyrimidine isonucleosides in moderate yields. In the case of pyrimidine bases, a mixture of four isomers (α- and β-isomers of *N*-/*O*-alkylated derivatives) was produced, and these were difficult to separate. Fortunately, the α-isomers of the *N*-and *O*-alkyl compounds were not detected when acetonitrile was used as a solvent (e.g., α/β ratio of *N*-alkyl-5-fluorouracil derivative **20a**: α, 7%, and β, 11%, in THF vs α, ∼0%, and β, 18%, in acetonitrile). However, the reaction did not proceed regioselectively, and the product contained a mixture of *N*- and *O*-alkylated uracil (*N*/*O* ratio = 1.2−2.3), as shown in Table 2. These regioisomers could not be separated at this step on a silica gel column, with the exception of 5-fluorouracil derivative **20a**. Interestingly, only the reaction of N^3-benzoyluracil (R^3 = H) gave an *N*-alkylated product **20d** along with *O*-alkylated compound **22**, whose structure was unknown and determined later (*vide infra*).

As shown in Scheme 5, the desired *N*-alkylated 5-fluorouracil derivative **23a** was obtained in 91% yield by the debenzoylation of the *N*-alkyl-5-fluorouracil **20a**. Similarly, deprotection of the mixture of *N*,*O*-alkyl-5-methyluracil **20b**/**21b** and (*E*)-5-(bromovinyl)uracil **20c**/**21c** gave desired *N*-alkyluracils in yields of 46% and 59%, respectively. These were easily separated from their *O*-alkyluracils on a silica gel column at this step. Removal of the benzyl group and subsequent desilylation gave 5-fluorouracil **25a**, 5-methyluracil **25b**, and (*E*)-5-(bromovinyl)uracil derivative **25c** in yields of 85%, 74%, and 71%, respectively.

Assignment of *N*,*O*-regio- and α,β-stereochemistry was strictly determined on the basis of ^{1}H NMR and NOE spectra. For example, as shown in Figure 2, irradiation of H-3′ and H-2′ of *N*-alkyl compound **23b** enhanced the H-6 and H-4′ protons by 8.1% and 5.2%, respectively. In contrast, irradiation of H-4′ of *O*-alkyl compound **24b** enhanced the H-2′ proton by 2.5%, while irradiation of H-3′ did not enhance the H-6 proton. It has been reported that the resonance of the H-2′ proton in *O*-alkyl compounds shifted downfield compared with that in *N*-alkyl compounds.[3] This held true for all of the iso-4′-thionucleosides that we synthesized.

Furthermore, as shown in Scheme 6, the mixture of *N*,*O*-alkyl uracil **20d**/**22** was debenzoylated and aminated at the 4-position by treatment with 2,4,6-triisopropylbenzenesulfonyl chloride (TPSCl) in acetonitrile in the presence of triethylamine and 4-(dimethylamino)pyridine (DMAP), followed by aqueous ammonia, to give cytosine derivative **27** in 55% yield as a mixture with *O*-alkyl compound **28**. Treatment of **27**/**28** with BCl_3 at −78 °C gave **29** in 53% yield, which was successfully separated from *O*-alkyl compound **30**. Finally, iso-4′-thiocytidine **31** was synthesized in 69% yield by desilylation using NH_4F·HF in DMF. Likewise, *O*-alkyl compound **30** was converted into **32** in 79% yield.

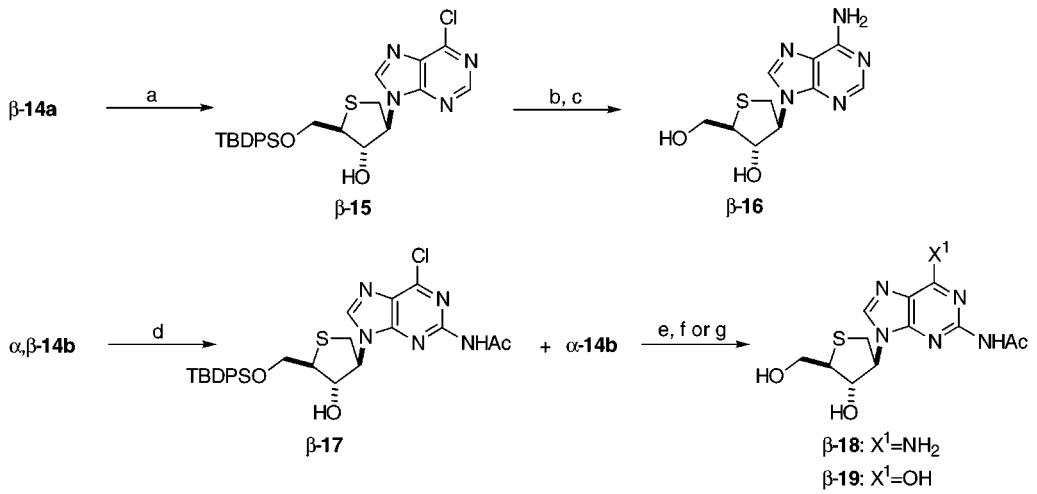
The spectral analysis of **32** revealed an unexpected structure. In the ^{1}H NMR spectrum of **32**, the chemical

(12) Although the reaction mixture became clear when DMF was used as a solvent, there was also no reaction (cf. Table 1, entry 6).

(13) In the ^{1}H NMR spectra of α- and β-**15**, the resonance of the H-2′ proton in the β-isomer was shifted upfield compared with that in the α-isomer.

(14) (a) Kametani, T.; Kigasawa, K.; Hiiragi, M.; Wakisaka, K.; Haga, S.; Nagamatsu, Y.; Sugi, H.; Fukawa, K.; Irino, O.; Yamamoto, T.; Nishimura, N.; Taguchi, A.; Okada, T.; Nakayama, M. *J. Med. Chem.* **1980**, *23*, 1324. (b) Cruickshank, K. A.; Jiricny, J.; Reese, C. B. *Tetrahedron Lett.* **1984**, *25*, 681.

Scheme 3[a]



[a] Reagents and conditions: (a) BCl_3, CH_2Cl_2, −78 °C, 87%; (b) NH_4·HF, MeOH; (c) NH_3, EtOH, 80 °C, 77% from *β*-**15**; (d) BCl_3, CH_2Cl_2, −78 °C, 32% (8% recovery of α-**14b**); (e) NH_4·HF, DMF; (f) NH_4OH, MeOH, 80 °C, yield a *β*-**18** in 66% from *β*-**17**; (g) TFA, H_2O and then NH_4OH, MeOH, 80 °C, yield of *β*-**19** in 80% from *β*-**17**.

Scheme 4

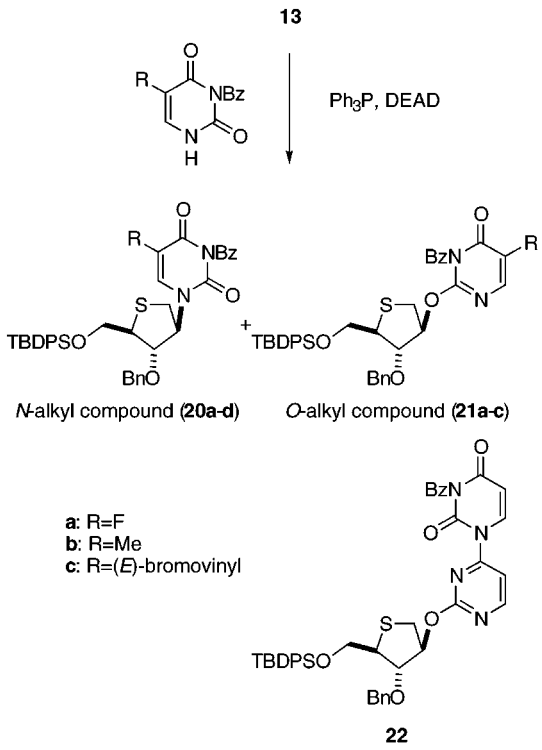


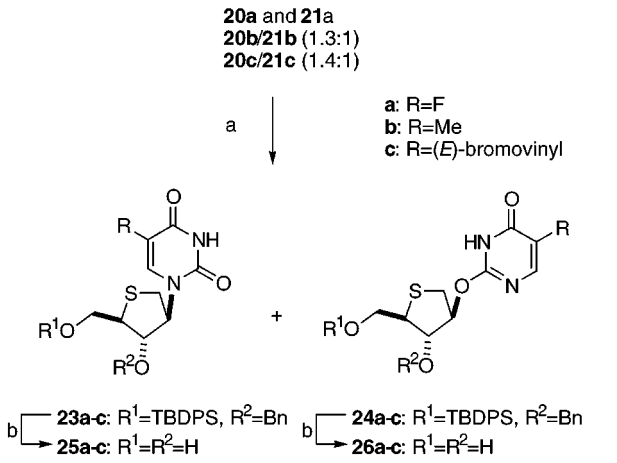
Table 2. Mitsunobu Reaction of 1,4-Anhydro-4-thio-D-arabitol Derivatives (13) with Pyrimidine Bases[a]

entry	pyrimidine base	product	yield (%)[b]	*N*/*O* ratio
1	R = F	**20a**/**21a**	26	2.3[c]
2	R = Me	**20b**/**21b**	36	1.3[d]
3	R = (*E*)-bromovinyl	**20c**/**21c**	40	1.4[d]
4	R = H	**20d**/**22**	39	1.2[d]

[a] Reaction was carried out at 70 °C. [b] Isolated yields. [c] Isolated yields of two regioisomers. [d] Ratio was determined by ^{1}H NMR analysis.

shift of the H-2′ proton (5.35 ppm) suggested a 2′-O^2-alkylated structure. Surprisingly, two sets of protons corresponding to the 5- and 6-positions of the pyrimidine ring were observed. One of the pyrimidines showed two

Scheme 5[a]



[a] Reagents and conditions: (a) NH_4OH, MeOH, THF, **23a** (91%), **24a** (49%), **23b** (46%), **24b** (39%), **23c** (59%), **24c** (39%); (b) (i) BCl_3, CH_2Cl_2, −78 °C, (ii) NH_4F·HF, DMF, **25a** (85%), **25b** (74%), **25c** (71%), **26a** (71%), **26b** (77%), **26c** (65%).

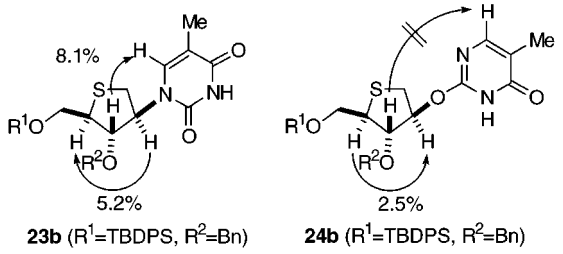
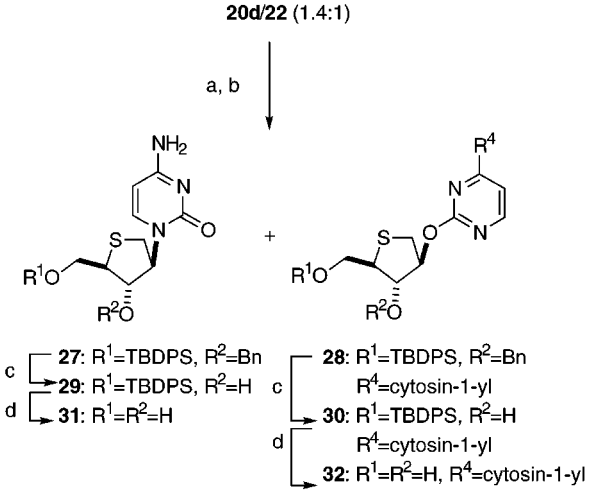


Figure 2.

doublet peaks at 8.29 and 5.99 ppm (J = 7.8 Hz). The other showed another set of doublets, which were shifted downfield, at 8.60 and 7.80 ppm (J = 5.4 Hz). The ^{13}C NMR spectrum of **32** also showed eight carbon peaks of two pyrimidines (see Experimental Section). These results clearly indicated that this compound had two pyrimidine moieties per molecule. This was also supported by the results of mass spectrum and elemental analysis. Moreover, the UV spectrum of **32** suggested that one pyrimidine ring combined with the other, i.e., a

Scheme 6[a]



[a] Reagents and conditions: (a) NH_4OH, MeOH, THF; (b) TPSCl, Et_3N, DMAP, CH_3CN, and then NH_4OH, 55% (**27**/**28** = 2.2) from **20d**/**22**; (c) BCl_3, CH_2Cl_2, −78 °C, **29** (53%), **30** (22%); (d) NH_4F·HF, DMF, **31** (69%), **32** (79%).

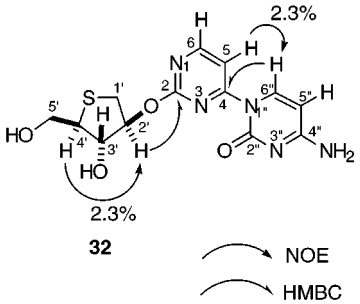
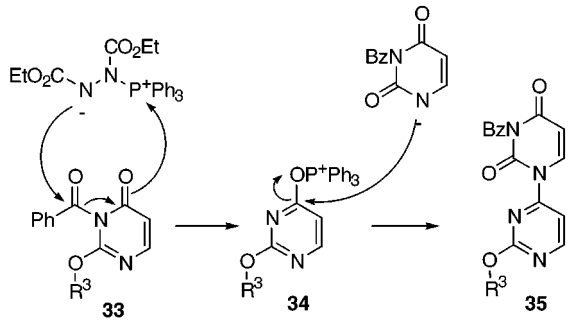


Figure 3.

4-$O^{2''}$- or 4-$N^{1''}$-alkylated structure. Finally, its regio- (at the 2′- and 4-positions, respectively) and stereochemistry (at the 2′-position) were determined by HMBC and NOE experiments. In the HMBC spectrum of **32**, a cross-peak of H-2′ to C-2 was observed, indicating a 2′-O^2-alkylated compound. Furthermore, the NOE experiment of **32**, in which irradiation of H-4′ enhanced the H-2′ proton by 2.3%, supported its β-stereochemistry at the 2′-position. On the other hand, a cross-peak of H-6″ to C-4 was also observed in the HMBC spectrum. This ruled out the 4-$O^{2''}$-alkylated structure, as did the NOE experiment: irradiation of H-5 of **32** enhanced the H-6″ proton by 2.3%. Thus, the structure of **32** was unambiguously determined, as depicted in Figure 3.

The bipyrimidinyl compound seemed to be produced by an extra Mitsunobu-type reaction as shown in Scheme 7. Initially, the *O*-alkylated derivative **33** was produced like those of other 5-substituted uracils. The second reaction then took place at the 4-position, when aromatization of the pyrimidine ring occurred along with cleavage of the N^3-benzoyl group. Presumably, this aromatization might cause differences in the reactivities of *O*- and *N*-alkylated derivatives in the extra Mitsunobu reaction at the 4-position. Although the O^2- and/or N^1-anion of the extra benzoyluracil might attack the 4-position of **34**, 4-$N^{1''}$-bipyrimidinyl compound **35**, in which substitution occurred at the softer N^1-site, was obtained. The 4-$N^{1''}$-bipyrimidinyl product **35** was not attacked by further N^3-benzoyluracil. It was not obvious that only

Scheme 7



the reaction of N^3-benzoyluracil gave the bipyrimidinyl compound.

In summary, the coupling of 1,4-anhydro-4-thio-D-arabitol (**13**) with various nucleobases using the Mitsunobu reaction was investigated. β-Adducts were predominantly formed when acetonitrile was used as a solvent. This result suggests that the reaction proceeded with retention of configuration via an episulfonium intermediate. This method could be effectively applied to the synthesis of iso-4′-thionucleosides. However, none of the compounds which we tested showed any antiviral activity (herpes simplex virus type 1 and type 2, varicella zoster virus, human cytomegalovirus, HIV) or cytotoxicity.[15]

Experimental Section

General Methods. Melting points are uncorrected. ^{1}H NMR spectra were recorded at 400 MHz (^{1}H) and at 100 MHz (^{13}C) using $CDCl_3$ or DMSO-d_6 with TMS as internal standard. Mass spectra were obtained by the fast atom bombardment (FAB) mode. Silica gel for chromatography was Merck Kieselgel 60.

(2*R*)-1,4-Anhydro-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-(6-chloropurin-9-yl)-2-deoxy-4-thio-D-ribitol (α-14a) and (2*S*)-1,4-Anhydro-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-(6-chloropurin-9-yl)-2-deoxy-4-thio-D-arabitol (*β*-14a). To a solution of **13**[6a,b] (1.20 g, 2.5 mmol) and triphenylphosphine (2.0 g, 7.5 mmol) in anhydrous THF (42 mL) were added 6-chloropurine (1.16 g, 7.5 mmol) and DEAD (1.2 mL, 7.5 mmol), and the mixture was stirred for 21 h at room temperature under argon. The reaction was quenched by addition of EtOH. After the solvent was evaporated under reduced pressure, the concentrated residue was purified by column chromatography over silica gel (3.6 × 19 cm, $CHCl_3$, and then 2.5 × 30 cm, 5−30% AcOEt in hexane) to give less polar α-**14a** (222 mg, 14%) and more polar *β*-**14a** (228 mg, 15%) as an amorphous foam, respectively.

Data for α-14a: ^{1}H NMR ($CDCl_3$) δ 8.66 (1H, s, H-2), 8.41 (1H, s, H-8), 7.72−7.67 (4H, m, Ar H), 7.45−7.37 (6H, m, Ar H), 7.19−7.12 (3H, m, Ar H), 7.00−6.98 (2H, m, Ar H), 5.27 (1H, ddd, H-2′, J = 3.9, 6.8, 10.7 Hz), 4.60 (1H, d, PhCH, J = 11.7 Hz), 4.40 (1H, d, H-3′, J = 3.9 Hz), 4.31 (1H, d, PhCH, J = 11.7 Hz), 3.78−3.71 (3H, m, H-4′, H-5′a,b), 3.52 (1H, t, H-1′a, J = 10.7 Hz), 3.21 (1H, dd, H-1′b, J = 6.8, 10.7 Hz), 1.10 (9H, s, *t*-Bu); FAB-MS *m*/*z* 615, 617 (M^+ + H). Anal. Calcd for $C_{33}H_{35}N_4O_2SSiCl$·0.25H_2O: C, 63.95; H, 5.77; N, 9.04. Found: C, 63.92; H, 5.80; N, 8.83.

Data for *β*-14a: ^{1}H NMR ($CDCl_3$) δ 8.59 (1H, s, H-2), 8.08 (1H, s, H-8), 7.69 (4H, dd, Ar H, J = 1.5, 7.8 Hz), 7.47−7.37 (6H, m, Ar H), 7.09−6.99 (3H, m, Ar H), 6.80 (2H, d, Ar H, J

(15) Antiviral activities, except against HIV, and cytotoxicity were assayed at the Biological Laboratory of Yamasa Corp. Anti-HIV activity was tested at the Rational Drug Design Laboratories, Fukushima, Japan. We greatly appreciate their assistance.

= 7.8 Hz), 5.01−4.95 (1H, m, H-2′), 4.74 (1H, dd, H-3′, *J* = 5.9, 8.3 Hz), 4.48 (1H, d, PhCH, *J* = 11.7 Hz), 4.19 (1H, d, PhCH, *J* = 11.7 Hz), 3.89 (1H, dd, H-5′a, *J* = 5.9, 10.8 Hz), 3.85 (1H, dd, H-5′b, *J* = 5.9, 10.8 Hz), 3.75 (1H, t, H-1′a, *J* = 11.2 Hz), 3.59 (1H, q, H-4′, *J* = 5.9 Hz), 3.08 (1H, dd, H-1′b, *J* = 6.8, 11.2 Hz), 1.11 (9H, s, *t*-Bu); FAB-MS *m*/*z* 615, 617 (M^+ + H). Anal. Calcd for $C_{33}H_{35}N_4O_2SSiCl$: C, 64.42; H, 5.73; N, 9.11. Found: C, 64.25; H, 5.90; N, 8.86.

(2*R*)-2-(2-(Acetylamino)-6-chloropurin-9-yl)-1,4-anhydro-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-ribitol and (2*S*)-2-(2-(Acetylamino)-6-chloropurin-9-yl)-1,4-anhydro-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (α,*β*-14b). Compound **13** (3.60 g, 2.84 mmol) was converted as described for the synthesis of α,*β*-**14a** to give α,*β*-**14b** (1.91 g, 38%, *β*/α = 1.8, as an amorphous foam): ^{1}H NMR ($CDCl_3$) *δ* 8.28 (0.36H, s, H-2), 7.95 (0.64H, s, H-8), 7.91 (0.64H, br s, NH), 7.88 (0.36H, br s, NH), 7.69−6.80 (15H, m, Ar H), 5.12−5.05 (0.36H, m, H-2′), 4.91−4.85 (0.64H, m, H-2′), 4.60 (0.36H, d, PhCH, *J* = 11.7 Hz), 4.54−4.48 (1.28H, m, PhCH, H-3′), 4.36−4.33 (0.72H, m, PhCH, H-3′), 4.22 (0.64H, d, PhCH, *J* = 12.2 Hz), 4.13−3.56 (3.64, m, H-4′ × 2, H-5′a,b × 2, 1′-Ha), 3.49 (0.36H, t, H-1′a, *J* = 10.3 Hz), 3.21 (0.36H, dd, H-1′b, *J* = 6.3, 10.3 Hz), 3.09 (0.64H, dd, H-1′b, *J* = 7.3, 11.2 Hz), 2.45 (1.92H, s, Ac), 2.44 (1.08H, s, Ac), 1.10 (9H, s, *t*-Bu); FAB-MS *m*/*z* 672, 674 (M^+ + H). Anal. Calcd for $C_{35}H_{38}N_5O_3SSiCl{\cdot}0.5H_2O$: C, 61.70; H, 5.77; N, 10.28. Found: C, 61.78; H, 5.74; N, 10.31.

(2*R*)-1,4-Anhydro-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-2-(2,6-dichloropurin-9-yl)-4-thio-D-ribitol (α-14c) and (2*S*)-1,4-Anhydro-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-2-(2,6-dichloropurin-9-yl)-4-thio-D-arabitol (*β*-14c). Compound **13** (120 mg, 0.25 mmol) was converted as described for the synthesis of α,*β*-**14a** to give less polar α-**14c** (12.7 mg, 8%) and more polar *β*-**14c** (40 mg, 25%) as a colorless oil, respectively.

Data for α-14c: ^{1}H NMR ($CDCl_3$) *δ* 8.31 (1H, s, H-8), 7.66−7.61 (4H, m, Ar H), 7.39−7.32 (6H, m, Ar H), 7.19−7.08 (3H, m, Ar H), 6.95−6.93 (2H, m, Ar H), 5.12−5.07 (1H, m, H-2′), 4.54 (1H, d, PhCH, *J* = 11.7 Hz), 4.35 (1H, d, H-3′, *J* = 3.9 Hz), 4.25 (1H, d, PhCH, *J* = 11.7 Hz), 3.71−3.59 (3H, m, 4′−H, H-5′a,b), 3.41 (1H, t, H-1′a, *J* = 10.3 Hz), 3.13 (1H, dd, H-1′b, *J* = 6.4, 10.3 Hz), 1.04 (9H, s, *t*-Bu); FAB-MS *m*/*z* 649, 651 (M^+ + H).

Data for *β*-14c: ^{1}H NMR ($CDCl_3$) *δ* 8.03 (1H, s, H-8), 7.70−7.68 (4H, m, Ar H), 7.47−7.39 (6H, m, Ar H), 7.07−7.01 (3H, m, Ar H), 6.87−6.85 (2H, m, Ar H), 4.93−4.87 (1H, m, H-2′), 4.63 (1H, dd, H-3′, *J* = 6.3, 8.3 Hz), 4.53 (1H, d, PhCH, *J* = 12.2 Hz), 4.24 (1H, d, PhCH, *J* = 12.2 Hz), 3.90 (1H, dd, H-5′a, *J* = 5.4, 10.7 Hz), 3.82 (1H, dd, H-5′b, *J* = 5.4 Hz, 10.7 Hz), 3.63 (1H, t, H-1′a, *J* = 10.7 Hz), 3.58−3.54 (1H, m, H-4′), 3.06 (1H, dd, H-1′b, *J* = 6.8, 10.7 Hz), 1.12 (9H, s, *t*-Bu); FAB-MS *m*/*z* 649, 651 (M^+ + H).

(2*S*)-1,4-Anhydro-5-*O*-(*tert*-butyldiphenylsilyl)-2-(6-chloropurin-9-yl)-2-deoxy-4-thio-D-arabitol (*β*-15). To a solution of *β*-**14a** (227 mg, 0.37 mmol) in CH_2Cl_2 (7.5 mL), was added slowly a solution of BCl_3 (3.0 mL of a 1 M CH_2Cl_2 solution, 3.0 mmol) at −78 °C under argon. After being stirred for 0.5 h at room temperature, the reaction was quenched by addition of pyridine−MeOH (4.5 mL, 2:1). The mixture was allowed to warm to room temperature and was stirred for 1 h. After the most of organic solvents were removed under reduced pressure, the remaining material was extracted with AcOEt (×2). The organic phase was washed with H_2O and brine and then dried (Na_2SO_4). After the solvent was evaporated under reduced pressure, the concentrated residue was purified by column chromatography over silica gel (1.5 × 11 cm, 10−30% AcOEt in hexane) to give *β*-**15** (169 mg, 87%) as an amorphous foam: ^{1}H NMR ($CDCl_3$) *δ* 8.65 (1H, s, H-2), 8.11 (1H, s, H-8), 7.61−7.57 (4H, m, Ar H), 7.41−7.31 (6H, m, Ar H), 4.91 (1H, dt, H-2′, *J* = 7.3, 10.3 Hz), 4.70 (1H, dd, H-3′, *J* = 8.3, 10.3 Hz), 3.89 (1H, dd, H-5′a, *J* = 5.4, 10.3 Hz), 3.83 (1H, dd, H-5′b, *J* = 7.8, 10.3 Hz), 3.53 (1H, t, H-1′a, *J* = 10.3 Hz), 3.48 (1H, dt, H-4′, *J* = 5.4, 8.3 Hz), 3.18 (1H, dd, H-1′b, *J* = 7.3, 10.3 Hz), 2.45−2.02 (1H, br, 3′-OH), 1.00 (9H, s, *t*-Bu); FAB-MS *m*/*z* 525, 527 (M^+ + H). Anal. Calcd for $C_{26}H_{29}N_4O_2SSiCl$: C, 59.47; H, 5.57; N, 10.67. Found: C, 59.40; H, 5.72; N, 10.37.

(2*S*)-2-(Adenin-9-yl)-1,4-anhydro-2-deoxy-4-thio-D-arabitol (*β*-16). A mixture of *β*-**15** (169 mg, 0.32 mmol) and $NH_4F{\cdot}HF$ (253 mg, 4.44 mmol) in MeOH (5.5 mL) was stirred for 40 h at room temperature. After concentration, the residue was passed through a short silica gel column. The eluate with 10% MeOH in $CHCl_3$ was collected and concentrated. The residue was dissolved in saturated methanolic ammonia (10 mL) and heated at 80 °C in a sealed tube for 20 h. After cooling, the solvent was removed under reduced pressure and the residue was purified by column chromatography over silica gel (1.5 × 5.5 cm, 1−10% MeOH in $CHCl_3$) to give *β*-**16** (66 mg, 77%) as crystals: mp 96 °C (dec, crystallized from MeOH); UV (MeOH) λ_{max} 261 nm; ^{1}H NMR (DMSO-d_6) *δ* 8.18 (1H, s, H-2 or H-8), 8.12 (1H, s, H-2 or H-8), 7.19 (2H, br s, NH_2), 5.56 (1H, d, 3′-OH, *J* = 6.8 Hz), 4.92 (1H, dd, 5′-OH, *J* = 4.4, 5.9 Hz), 4.81−4.74 (1H, m, H-2′), 4.43 (1H, dt, H-3′, *J* = 6.8, 8.3 Hz), 3.86 (1H, dt, H-5′a, *J* = 4.4, 10.8 Hz), 3.45−3.37 (1H, m, H-5′b), 3.39 (1H, t, H-1′a, *J* = 10.7 Hz), 3.24 (1H, dt, H-4′, *J* = 4.4, 8.3 Hz), 3.03 (1H, dd, H-1′b, *J* = 7.3, 10.7 Hz); FAB-MS *m*/*z* 268 (M^+ + H). Anal. Calcd for $C_{10}H_{13}N_5O_2S{\cdot}$ 0.33MeOH: C, 44.65; H, 5.20; N, 25.19. Found: C, 44.42; H, 4.96; N, 24.91.

(2*S*)-2-(2-(Acetylamino)-6-chloropurin-9-yl)-1,4-anhydro-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (*β*-17). To a solution of α,*β*-**14b** (1.91 g, 2.84 mmol) in CH_2Cl_2 (61 mL) was added slowly a solution of BCl_3 (25 mL of a 1 M CH_2Cl_2 solution, 25.0 mmol) at −78 °C under argon. After being stirred for 1.5 h at the same temperature, the reaction was quenched by addition of pyridine−MeOH (33 mL, 2:1). The mixture was allowed to warm to room temperature and was stirred for 1 h. After the solvents were removed under reduced pressure, the concentrated residue was purified by column chromatography over silica gel (3.4 × 16 cm, 20% MeOH in $CHCl_3$ and then 3.4 × 10 cm, 50% AcOEt in hexane) to give *β*-**17** (529 mg, 32%) as a white solid. Unreacted α-**14b** was recovered as a single isomer (145 mg, 8%): mp 180−184 °C; ^{1}H NMR ($CDCl_3$) *δ* 8.17 (1H, br s, NH), 8.14 (1H, s, H-8), 7.69−7.65 (4H, m, Ar H), 7.46−7.36 (6H, m, Ar H), 4.93−4.89 (1H, m, H-2′), 4.69 (1H, t, H-3′, *J* = 8.3 Hz), 3.93 (2H, d, H-5′a,b, *J* = 8.9 Hz), 3.61−3.56 (1H, m, H-4′), 3.45 (1H, t, H-1′a, *J* = 10.3 Hz), 3.29 (1H, dd, H-1′b, *J* = 7.3, 10.3 Hz), 2.99−2.45 (1H, br, 3′-OH), 1.05 (9H, s, *t*-Bu); FAB-MS *m*/*z* 582, 584 (M^+ + H). Anal. Calcd for $C_{28}H_{32}N_5O_3SSiCl{\cdot}0.2$hexane: C, 58.51; H, 5.85; N, 11.68. Found: C, 58.35; H, 5.80; N, 11.62.

(2*S*)-1,4-Anhydro-2-deoxy-2-(2,6-diaminopurin-9-yl)-4-thio-D-arabitol (*β*-18). A mixture of *β*-**17** (46 mg, 0.08 mmol) and $NH_4F{\cdot}HF$ (54 mg, 0.95 mmol) in DMF (1 mL) was stirred at room temperature overnight. After concentration, the residue was passed through a short silica gel column. The eluate with 20% MeOH in $CHCl_3$ was collected and concentrated. The residue was dissolved in MeOH (2 mL) and concentrated NH_4OH (4 mL). The mixture was heated at 60 °C in a sealed tube for 11 h. After cooling, the solvent was removed under reduced pressure and the residue was purified by column chromatography over silica gel (1 × 8 cm, 20% MeOH in $CHCl_3$) to give *β*-**18** (15 mg, 66%) as crystals: mp 207−209 °C (crystallized from MeOH); UV (MeOH) λ_{max} 258, 283 nm; ^{1}H NMR (DMSO-d_6) *δ* 7.77 (1H, s, H-8), 6.63 (2H, br s, NH_2), 5.76 (2H, br s, NH_2), 5.56 (1H, d, 3′-OH, *J* = 6.4 Hz), 4.91 (1H, t, 5′-OH, *J* = 4.4 Hz), 4.60 (1H, dt, H-2′, *J* = 7.3, 10.3 Hz), 4.37−4.31 (1H, m, H-3′), 3.88 (1H, dt, H-5′a, *J* = 4.4, 10.7 Hz), 3.46−3.38 (1H, m, H-5′b), 3.30−3.19 (2H, m, H-1′a, H-4′), 2.98 (1H, dd, H-1′b, *J* = 7.3, 10.3 Hz); FAB-MS *m*/*z* 283 (M^+ + H). Anal. Calcd for $C_{10}H_{14}N_6O_2S{\cdot}0.75$MeOH: C, 42.15; H, 5.59; N, 27.43. Found: C, 42.35; H, 5.49; N, 27.31

(2*S*)-1,4-Anhydro-2-deoxy-2-(guanin-9-yl)-4-thio-D-arabitol (*β*-19). A mixture of *β*-**17** (233 mg, 0.40 mmol) and $NH_4F{\cdot}HF$ (276 mg, 4,8 mmol) in DMF (5 mL) was stirred at room temperature overnight. After concentration, the residue was passed through a short silica gel column. The eluate with 20% MeOH in $CHCl_3$ was collected and concentrated. The residue was dissolved in TFA−H_2O (5 mL, 3:1) and stirred for

40 h at room temperature. After the solvent was removed under reduced pressure, the residue was dissolved in MeOH (10 mL) and concentrated NH_4OH (20 mL). The mixture was heated at 80 °C in a sealed tube for 5 h. After cooling, the solvent was removed under reduced pressure and the residue was applied to a column of adsorption resin (8 mL, Sepabeads SP206, Mitsubishi Chemical Corp., Tokyo, Japan). The eluate of 10% aqueous EtOH was collected and concentrated to give *β*-**19** (91 mg, 80%) as crystals: mp >250 °C (dec, crystallized from H_2O); UV (MeOH) λ_{max} 256 nm; ^{1}H NMR (DMSO-d_6) δ 10.60 (1H, br s, NH), 7.78 (1H, s, H-8), 6.45 (2H, br s, NH_2), 5.58 (1H, d, 3′-OH, J = 5.8 Hz), 4.92 (1H, br s, 5′-OH), 4.59 (1H, dt, H-2′, J = 7.3, 10.3 Hz), 4.32−4.26 (1H, m, H-3′), 3.88 (1H, br d, H-5′a, J = 10.7 Hz), 3.46−3.40 (1H, m, H-5′b), 3.23−3.17 (2H, m, H-1′a, H-4′), 2.97 (1H, dd, H-1′b, J = 7.3, 10.3 Hz); FAB-MS m/z 284 (M^+ + H). Anal. Calcd for $C_{10}H_{13}N_5O_3S\cdot 0.9H_2O$: C, 40.10; H, 5.01; N, 23.38. Found: C, 40.33; H, 5.31; N, 23.12.

(2*S*)-1,4-Anhydro-2-(*N*^{3}-benzoyl-5-fluorouracil-1-yl)-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (20a) and (2*S*)-1,4-Anhydro-2-*O*-(*N*^{3}-benzoyl-5-fluoropyrimidin-4-on-2-yl)-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (21a). A solution of DEAD (2.9 mL, 40% toluene solution, 6.3 mmol) was added to a mixture of **13** (1.91 g, 4.0 mmol), *N*^{3}-benzoyl-5-fluorouracil (1.40 g, 6.0 mmol), and triphenylphosphine (3.14 g, 4.0 mmol) in CH_3CN (64 mL) at 0 °C and stirred for 1 h at 70 °C. After cooling, the reaction was quenched by addition of EtOH. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography over silica gel (3.6 × 20 cm, 1% MeOH in $CHCl_3$, and then 3.6 × 20 cm, 10−20% AcOEt in hexane) to give less polar **21a** (213 mg, 8%) and more polar **20a** (497 mg, 18%) as an amorphous foam, respectively.

Data for 20a: ^{1}H NMR ($CDCl_3$) δ 7.87 (2H, dd, Ar H, J = 1.5, 8.8 Hz), 7.70−7.64 (5H, m, Ar H), 7.49−7.18 (14H, m, Ar H, H-6), 4.98−4.92 (1H, m, H-2′), 4.63 (1H, d, PhCH, J = 11.7 Hz), 4.42 (1H, d, PhCH, J = 11.7 Hz), 4.28 (1H, dd, H-3′, J = 5.9, 6.9 Hz), 3.87 (1H, dd, H-5′a, J = 5.9, 10.7 Hz), 3.81 (1H, dd, H-5′b, J = 5.9, 10.7 Hz), 3.53 (1H, q, H-4′, J = 5.9 Hz), 3.08 (1H, dd, H-1′a, J = 7.3, 11.7 Hz), 3.00 (1H, dd, H-1′b, J = 8.3, 11.7 Hz), 1.08 (9H, s, *t*-Bu); FAB-MS m/z 695 (M^+ + H). Anal. Calcd for $C_{39}H_{39}N_2O_5SSiF\cdot 0.75H_2O$: C, 66.12; H, 5.76; N, 3.95. Found: C, 66.18; H, 5.66; N, 3.96.

Data for 21a: ^{1}H NMR ($CDCl_3$) δ 8.30−8.12 (3H, m, Ar H, H-6), 7.71−7.21 (18H, m, Ar H), 5.73−5.70 (1H, m, H-2′), 4.68 (1H, d, PhCH, J = 12.2 Hz), 4.64 (1H, d, PhCH, J = 12.2 Hz), 4.47 (1H, t, H-3′, J = 2.9 Hz), 3.87 (1H, dd, H-5′a, J = 8.3, 10.3 Hz), 3.71 (1H, dd, H-5′b, J = 3.4, 10.3 Hz), 3.62−3.58 (1H, m, H-4′), 3.42 (1H, dd, H-1′a, J = 4.9, 12.2 Hz), 3.04 (1H, dd, H-1′b, J = 3.9, 12.2 Hz), 1.03 (9H, s, *t*-Bu); FAB-MS m/z 695 (M^+ + H). Anal. Calcd for $C_{39}H_{39}N_2O_5SSiF\cdot 0.5$hexane: C, 68.36; H, 6.28; N, 3.80. Found: C, 68.34; H, 6.42; N, 3.68.

(2*S*)-1,4-Anhydro-2-(*N*^{3}-benzoyl-5-methyluracil-1-yl)-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (20b) and (2*S*)-1,4-Anhydro-2-*O*-(*N*^{3}-benzoyl-5-methylpyrimidin-4-on-2-yl)-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (21b). Compound **13** (720 mg, 1.5 mmol) was converted as described for the synthesis of **20a** to give a mixture of **20b** and **21b** (367 mg, 36%, **20b**/**21b** = 1.3) as an amorphous foam: ^{1}H NMR ($CDCl_3$) δ 7.88−7.06 (21H, m, Ar H, H-6), 5.56−5.53 (0.43H, m, H-2′), 4.96−4.90 (0.57H, m, H-2′), 4.68 (0.43H, d, PhCH, J = 12.2 Hz), 4.62 (0.43H, d, PhCH, J = 12.2 Hz), 4.60 (0.57H, d, PhCH, J = 12.2 Hz), 4.43 (0.57H, d, PhCH, J = 12.2 Hz), 4.37 (0.57H, dd, H-3′, J = 5.9, 7.3 Hz), 4.32 (0.43H, t, H-3′, J = 3.4 Hz), 3.88 (0.57H, dd, H-5′a, J = 5.9, 10.7 Hz), 3.79 (0.57H, dd, H-5′b, J = 5.9, 10.7 Hz), 3.74−3.66 (0.86H, m, H-5′a,b), 3.63−3.59 (0.43H, m, H-4′), 3.52 (0.57H, q, H-4′, J = 5.9 Hz), 3.55 (0.43H, dd, H-1′a, J = 4.9, 12.2 Hz), 3.12 (0.57H, dd, H-1′a, J = 9.3, 11.2 Hz), 3.04 (0.57H, dd, H-1′b, J = 7.3, 11.2 Hz), 2.95 (0.43H, dd, H-1′b, J = 3.4, 12.2 Hz), 1.96 (1.29H, d, 5-Me, J = 1.0 Hz), 1.83 (1.71H, s, 5-Me), 1.07 (5.13H, s, *t*-Bu), 1.03 (3.87H, s, *t*-Bu); FAB-MS m/z 691 (M^+ + H).

(2*S*)-1,4-Anhydro-2-(*N*^{3}-benzoyl-5-(*E*)-(bromovinyl)uracil-1-yl)-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (20c) and (2*S*)-1,4-Anhydro-2-*O*-(*N*^{3}-benzoyl-5-(*E*)-(bromovinyl)pyrimidin-4-on-2-yl)-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (21c). Compound **13** (960 mg, 2.0 mmol) was converted as described for the synthesis of **20a** to give a mixture of **20c** and **21c** (630 mg, 40%, **20c**/**21c** = 1.5) as an amorphous foam: ^{1}H NMR ($CDCl_3$) δ 7.88−7.16 (22H, m, Ar H, H-6, 5-vinyl H), 6.79 (0.4H, d, 5-vinyl H, J = 13.2 Hz), 6.45 (0.6H, d, 5-vinyl H, J = 13.7 Hz), 5.60−5.55 (0.4H, m, H-2′), 5.00−4.93 (0.6H, m, H-2′), 4.69 (0.4H, d, PhCH, J = 11.7 Hz), 4.61 (1H, d, PhCH, J = 11.7 Hz), 4.42 (0.6H, d, PhCH, J = 11.7 Hz), 4.36−4.31 (1H, m, H-3′), 3.87 (0.6H, dd, H-5′a, J = 5.9, 10.7 Hz), 3.81 (0.6H, dd, H-5′b, J = 5.9, 10.7 Hz), 3.71−3.51 (1.8H, m, H-5′a,b, H-4′×2), 3.36 (0.4H, dd, H-1′a, J = 4.9, 12.2 Hz), 3.08 (1.2H, d, H-1′a,b, J = 8.3 Hz), 2.95 (0.4H, dd, H-1′b, J = 3.4, 12.2 Hz), 1.08 (5.4H, s, *t*-Bu), 1.04 (3.6H, s, *t*-Bu); FAB-MS m/z 781, 783 (M^+ + H).

(2*S*)-1,4-Anhydro-2-(*N*^{3}-benzoyluracil-1-yl)-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (20d) and (2*S*)-1,4-Anhydro-2-*O*-(4-(*N*^{3}-benzoyluracil-1-yl)pyrimidin-2-yl)-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (22). Compound **13** (1.91 g, 4.0 mmol) was converted as described for the synthesis of **20a** to give a mixture of **20d** and **22** (1.10 g, 39%, **20d**/**22** = 1.2) as an amorphous foam: ^{1}H NMR ($CDCl_3$) δ 8.54 (0.45H, d, H-6, J = 5.4 Hz), 8.44 (0.45H, d, H-6″, J = 8.3 Hz), 7.97−7.17 (21H, m, Ar H, H-6, H-5), 6.02 (0.45H, d, H-5″, J = 8.3 Hz), 5.71−5.68 (0.45H, m, H-2′), 5.65 (0.55H, d, H-5, J = 7.8 Hz), 4.95−4.89 (0.55H, m, H-2′), 4.72 (0.45H, d, PhCH, J = 11.7 Hz), 4.67 (0.45H, d, PhCH, J = 11.7 Hz), 4.59 (0.55H, d, PhCH, J = 11.7 Hz), 4.48−4.45 (1H, m, PhCH, H-3′), 4.37 (0.55H, dd, H-3′, J = 5.4, 6.9 Hz), 3.95−3.49 (3H, m, H-5′a,b × 2, H-4′ × 2), 3.40 (0.45H, dd, H-1′a, J = 5.4, 11.7 Hz), 3.12−3.09 (1.1H, m, H-1′a,b), 3.05 (0.45H, dd, H-1′b, J = 4.4, 11.7 Hz), 1.06 (4.95H, s, *t*-Bu), 1.02 (4.05H, s, *t*-Bu); FAB-MS m/z 677 (M^+ + H) and 771 (M^+ + H).

(2*S*)-1,4-Anhydro-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-2-(5-fluorouracil-1-yl)-4-thio-D-arabitol (23a). To a solution of **20a** (490 mg, 0.71 mmol) in MeOH−THF (18 mL, 4:5) was added concentrated NH_4OH (9 mL) and stirred for 2 h at room temperature. After the solvent was evaporated under reduced pressure, the concentrated residue was purified by column chromatography over silica gel (2.2 × 18 cm, 20−30% AcOEt in hexane) to give **23a** (379 mg, 91%) as an amorphous foam: ^{1}H NMR ($CDCl_3$) δ 8.49−8.40 (1H, br, NH), 7.68 (4H, dd, Ar H, J = 1.5, 7.8 Hz), 7.48−7.38 (7H, m, Ar H), 7.28−7.24 (2H, m, Ar H), 7.17−7.14 (3H, m, Ar H, H-6), 4.91−4.85 (1H, m, H-2′), 4.62 (1H, d, PhCH, J = 12.2 Hz), 4.40 (1H, d, PhCH, J = 12.2 Hz), 4.26 (1H, dd, H-3′, J = 5.4, 7.3 Hz), 3.84 (2H, d, H-5′a,b, J = 5.4 Hz), 3.53 (1H, q, H-4′, J = 5.4 Hz), 3.05 (1H, dd, H-1′a, J = 7.8, 11.2 Hz), 2.96 (1H, dd, H-1′b, J = 8.8, 11.2 Hz), 1.10 (9H, s, *t*-Bu); FAB-MS m/z 591 (M^+ + H). Anal. Calcd for $C_{32}H_{35}N_2O_4SSiF\cdot 1.25$AcOEt: C, 63.40; H, 6.47; N, 4.00. Found: C, 63.18; H, 6.58; N, 3.99.

(2*S*)-1,4-Anhydro-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-2-(5-methyluracil-1-yl)-4-thio-D-arabitol (23b) and (2*S*)-1,4-Anhydro-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-2-*O*-(5-methylpyrimidin-4(3*H*)-on-2-yl)-4-thio-D-arabitol (24b). A mixture of compound **20b** and **21b** (360 mg, 0.52 mmol) was converted as described for the synthesis of **23a** to give less polar **24b** (119 mg, 39%) and more polar **23b** (141 mg, 46%) as an amorphous foam, respectively.

Data for 23b: ^{1}H NMR ($CDCl_3$) δ 8.30 (1H, br s, NH), 7.68 (4H, dd, Ar H, J = 1.5, 8.3 Hz), 7.47−7.37 (6H, m, Ar H), 7.25−7.23 (3H, m, Ar H), 7.13−7.11 (2H, m, Ar H), 6.91 (1H, d, H-6, J = 1.0 Hz), 4.92−4.85 (1H, m, H-2′), 4.58 (1H, d, PhCH, J = 12.2 Hz), 4.39 (1H, d, PhCH, J = 12.2 Hz), 4.34 (1H, dd, H-3′, J = 5.9, 7.8 Hz), 3.87 (1H, dd, H-5′a, J = 5.9, 10.3 Hz), 3.82 (1H, dd, H-5′b, J = 5.9, 10.3 Hz), 3.52 (1H, q, H-4′, J = 5.9 Hz), 3.08 (1H, dd, H-1′a, J = 9.3, 11.2 Hz), 3.00 (1H, dd, H-1′b, J = 7.3, 11.2 Hz), 1.78 (3H, d, 5-Me, J = 1.0 Hz), 1.09 (9H, s,

t-Bu); FAB-MS *m*/*z* 587 ($M^+ + H$). Anal. Calcd for $C_{33}H_{38}N_2O_4SSi$: C, 67.54; H, 6.53; N, 4.77. Found: C, 67.27; H, 6.65; N, 4.50.

Data for 24b: ^{1}H NMR ($CDCl_3$) δ 9.57 (1H, br s, NH), 7.65−7.61 (4H, m, Ar H), 7.50 (1H, s, H-6), 7.46−7.27 (11H, m, Ar H), 5.55−5.52 (1H, m, H-2′), 4.68 (1H, d, PhCH, J = 12.2 Hz), 4.64 (1H, d, PhCH, J = 12.2 Hz), 4.31 (1H, t, H-3′, J = 3.4 Hz), 3.75 (1H, dd, H-5′a, J = 8.3, 10.7 Hz), 3.69 (1H, dd, H-5′b, J = 5.9, 10.7 Hz), 3.59 (1H, ddd, H-4′, J = 3.4, 5.9, 8.3 Hz), 3.36 (1H, dd, H-1′a, J = 4.9, 12.2 Hz), 2.95 (1H, dd, H-1′b, J = 3.9, 12.2 Hz), 1.92 (3H, s, 5-Me), 1.03 (9H, s, *t*-Bu); FAB-MS *m*/*z* 587 ($M^+ + H$). Anal. Calcd for $C_{33}H_{38}N_2O_4SSi$: C, 67.54; H, 6.53; N, 4.77. Found: C, 67.51; H, 6.56; N, 4.53.

(2*S*)-1,4-Anhydro-3-*O*-benzyl-2-(5-(*E*)-(bromovinyl)uracil-1-yl)-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (23c) and (2*S*)-1,4-Anhydro-3-*O*-benzyl-2-*O*-(5-(*E*)-(bromovinyl)pyrimidin-4(3*H*)-on-2-yl)-5-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-4-thio-D-arabitol (24c). A mixture of compounds **20c** and **21c** (630 mg, 0.81 mmol) was converted as described for the synthesis of **23a** to give less polar **24c** (212 mg, 39%) and more polar **23c** (324 mg, 59%) as an amorphous foam, respectively.

Data for 23c: ^{1}H NMR ($CDCl_3$) δ 8.39 (1H, br s, NH), 7.69−7.67 (4H, m, Ar H), 7.48−7.38 (6H, m, Ar H), 7.33 (1H, d, 5-vinyl H, J = 13.7 Hz), 7.26−7.22 (3H, m, Ar H), 7.13−7.10 (2H, m, Ar H), 7.03 (1H, s, H-6), 6.43 (1H, d, 5-vinyl H, J = 13.7 Hz), 4.91−4.85 (1H, m, H-2′), 4.60 (1H, d, PhCH, J = 12.2 Hz), 4.38 (1H, d, PhCH, J = 12.2 Hz), 4.33 (1H, dd, H-3′, J = 5.9, 7.3 Hz), 3.89−3.81 (2H, m, H-5′a,b), 3.52 (1H, q, H-4′, J = 5.9 Hz), 3.07−3.02 (2H, m, H-1′a,b), 1.10 (9H, s, *t*-Bu); FAB-MS *m*/*z* 677, 679 ($M^+ + H$). Anal. Calcd for $C_{34}H_{37}N_2O_4SSiBr\cdot 0.5AcOEt$: C, 59.91; H, 5.73; N, 3.88. Found: C, 60.04; H, 5.99; N, 3.73.

Data for 24c: ^{1}H NMR ($CDCl_3$) δ 9.95 (1H, br s, NH), 7.66−7.59 (5H, m, Ar H, H-6), 7.52 (1H, d, 5-vinyl H, J = 13.7 Hz), 7.45−7.22 (11H, m, Ar H), 6.77 (1H, d, 5-vinyl H, J = 13.7 Hz), 5.60−5.57 (1H, m, H-2′), 4.69 (1H, d, PhCH, J = 11.7 Hz), 4.63 (1H, d, PhCH, J = 11.7 Hz), 4.31 (1H, t, H-3′, J = 2.9 Hz), 3.72 (2H, d, H-5′a,b, J = 7.3 Hz), 3.61 (1H, dt, H-4′, J = 2,9, 7.3 Hz), 3.36 (1H, dd, H-1′a, J = 4.9, 11.7 Hz), 2.95 (1H, dd, H-1′b, J = 3.9, 11.7 Hz), 1.03 (9H, s, *t*-Bu); FAB-MS *m*/*z* 677, 679 ($M^+ + H$).

(2*S*)-1,4-Anhydro-2-deoxy-2-(5-fluorouracil-1-yl)-4-thio-D-arabitol (25a). A solution of BCl_3 (3.5 mL of a 1 M CH_2Cl_2 solution, 3.5 mmol) was added slowly to a solution of **23a** (372 mg, 0.63 mmol) in CH_2Cl_2 (13 mL) at −78 °C. After being stirred for 1 h at the same temperature, the reaction was quenched by addition of pyridine−MeOH (5 mL, 2:1). The mixture was allowed to warm to room temperature and was stirred for 1 h. After the solvents were removed under reduced pressure, the whole was extracted with $CHCl_3$ (×2). The organic phase was washed with H_2O and brine and then dried (Na_2SO_4). After the solvent was removed under reduced pressure, the residue was dissolved in DMF (9 mL) and $NH_4F\cdot HF$ (410 mg, 7.2 mmol) was added to the solution. After the mixture was stirred at room temperature overnight, the solvent was removed under reduced pressure. The residue was purified by column chromatography over silica gel (1.5 × 12 cm, 20% MeOH in $CHCl_3$) to give **25a** (141 mg, 85%) as crystals: mp 266−268 °C (crystallized from MeOH); UV (MeOH) λ_{max} 273 nm; ^{1}H NMR (DMSO-d_6) δ 12.10−11.55 (1H, br, NH), 8.17 (1H, d, H-6, J = 7.3 Hz), 5.73−5.41 (1H, br, 3′-OH), 5.10−4.74 (1H, br, 5′-OH), 4.69−4.62 (1H, m, H-2′), 4.03 (1H, t, H-3′, J = 9.3 Hz), 3.87 (1H, dd, H-5′a, J = 3.4, 10.7 Hz), 3.42−3.37 (1H, m, H-5′b), 3.14 (1H, dt, H-4′, J = 3.4, 9.3 Hz), 2.91 (1H, t, H-1′a, J = 10.7 Hz), 2.80 (1H, dd, H-1′b, J = 7.3, 10.7 Hz); FAB-MS *m*/*z* 263 ($M^+ + H$). Anal. Calcd for $C_9H_{11}N_2O_4SF$: C, 41.22; H, 4.23; N, 10.68. Found: C, 41.37; H, 4.28; N, 10.50.

(2*S*)-1,4-Anhydro-2-deoxy-2-*O*-(5-fluoropyrimidin-4(3*H*)-on-2-yl)-4-thio-D-arabitol (26a). Compound **24a** (70 mg, 0.12 mmol), which was obtained by the debenzoylation of **21a**, was converted as described for the synthesis of **25a** to give **26a** (22 mg, 71%) as a white solid: mp 169−170 °C; UV (MeOH) λ_{max} 270 nm; ^{1}H NMR (DMSO-d_6) δ 7.82 (1H, d, H-6, J = 3.4 Hz), 5.77−5.35 (1H, br, 3′-OH), 5.26 (1H, q, H-2′, J = 4.9 Hz), 4.90 (1H, br s, 5′-OH), 4.12 (1H, t, H-3′, J = 4.9 Hz), 3.71−3.68 (1H, m, H-5′a), 3.44−3.40 (1H, m, H-5′b), 3.21−3.02 (2H, m, H-1′a, H-4′), 2.81 (1H, dd, H-1′b, J = 4.9, 11.2 Hz); FAB-MS *m*/*z* 263 ($M^+ + H$). Anal. Calcd for $C_9H_{11}N_2O_4SF\cdot 0.25H_2O$: C, 40.52; H, 4.35; N, 10.50. Found: C, 40.60; H, 4.39; N, 10.39.

(2*S*)-1,4-Anhydro-2-deoxy-2-(5-methyluracil-1-yl)-4-thio-D-arabitol (25b). Compound **23b** (257 mg, 0.46 mmol) was converted as described for the synthesis of **25a** to give **25b** (99 mg, 74%) as a white solid: mp 268−270 °C (dec); UV (MeOH) λ_{max} 271 nm; ^{1}H NMR (DMSO-d_6) δ 11.05−11.48 (1H, br, NH), 7.63 (1H, s, H-6), 5.51 (1H, d, 3′-OH, J = 6.4 Hz), 4.88 (1H, dd, 5′-OH, J = 4.4, 6.3 Hz), 4.70−4.63 (1H, m, H-2′), 4.04 (1H, dt, H-3′, J = 6.4, 10.3 Hz), 3.87 (1H, dt, H-5′a, J = 4.4, 10.7 Hz), 3.44−3.37 (1H, m, H-5′b), 3.17−3.12 (1H, m, H-4′), 2.90 (1H, dd, H-1′a, J = 10.3, 11.2 Hz), 2.80 (1H, dd, H-1′b, J = 7.3, 10.3 Hz), 1.77 (3H, s, 5-Me); FAB-MS *m*/*z* 259 ($M^+ + H$). Anal. Calcd for $C_{10}H_{14}N_2O_4S\cdot 0.5MeOH$: C, 45.97; H, 5.88; N, 10.21. Found: C, 45.92; H, 5.69; N, 10.16.

(2*S*)-1,4-Anhydro-2-deoxy-2-*O*-(5-methylpyrimidin-4(3*H*)-on-2-yl)-4-thio-D-arabitol (26b). Compound **24b** (130 mg, 0.22 mmol) was converted as described for the synthesis of **25a** to give **26b** (43 mg, 77%) as a white solid: mp 109−111 °C; UV (MeOH) λ_{max} 271 nm; ^{1}H NMR (DMSO-d_6) δ 12.50−12.10 (1H, br, NH), 7.58 (1H, s, H-6), 5.68−5.34 (1H, br, 3′-OH), 5.29 (1H, q, H-2′, J = 4.9 Hz), 4.90 (1H, br s, 5′-OH), 4.12 (1H, t, H-3′, J = 4.9 Hz), 3.74−3.69 (1H, m, H-5′a), 3.40−3.34 (1H, m, H-5′b), 3.21−3.16 (2H, m, H-1′a, H-4′), 2.80 (1H, dd, H-1′b, J = 4.9, 11.7 Hz), 1.83 (3H, s, 5-Me); FAB-MS *m*/*z* 259 ($M^+ + H$). Anal. Calcd for $C_{10}H_{14}N_2O_4S\cdot 0.75MeOH$: C, 45.73; H, 6.07; N, 9.92. Found: C, 45.48; H, 5.77; N, 10.20.

(2*S*)-1,4-Anhydro-2-(5-(*E*)-(bromovinyl)uracil-1-yl)-2-deoxy-4-thio-D-arabitol (25c). Compound **23c** (132 mg, 0.23 mmol) was converted as described for the synthesis of **25a** to give **25c** (42 mg, 71%) as a white solid: mp 173−174 °C; UV (MeOH) λ_{max} 252, 297 nm; ^{1}H NMR (DMSO-d_6) δ 11.54 (1H, br s, NH), 8.01 (1H, s, H-6), 7.26 (1H, d, 5-vinyl H, J = 13.2 Hz), 6.84 (1H, d, 5-vinyl H, J = 13.2 Hz), 5.58 (1H, d, 3′-OH, J = 5.9 Hz), 4.91 (1H, t, 5′-OH, J = 4.9 Hz), 4.69 (1H, dt, H-2′, J = 7.3, 10.7 Hz), 4.07−4.01 (1H, m, H-3′), 3.89−3.84 (1H, m, H-5′a), 3.43−3.38 (1H, m, H-5′b), 3.15 (1H, dt, H-4′, J = 3.4, 8.3 Hz), 2.90 (1H, t, H-1′a, J = 10.7 Hz), 2.83 (1H, dd, H-1′b, J = 7.3, 10.3 Hz); FAB-MS *m*/*z* 349, 351 ($M^+ + H$). Anal. Calcd for $C_{11}H_{13}N_2O_4SBr$: C, 37.83; H, 3.75; N, 8.02. Found: C, 37.69; H, 3.94; N, 7.98.

(2*S*)-1,4-Anhydro-2-*O*-(5-(*E*)-(bromovinyl)pyrimidin-4(3*H*)-on-2-yl)-2-deoxy-4-thio-D-arabitol (26c). Compound **24c** (53 mg, 0.08 mmol) was converted as described for the synthesis of **25a** to give **26c** (18 mg, 65%) as a white solid: mp 82−86 °C (dec); UV (MeOH) λ_{max} 255, 302 nm; ^{1}H NMR (DMSO-d_6) δ 13.20−12.40 (1H, br, NH), 7.89 (1H, s, H-6), 7.44 (1H, d, 5-vinyl H, J = 13.2 Hz), 6.96 (1H, d, 5-vinyl H, J = 13.2 Hz), 5.74−5.40 (1H, br, 3′-OH), 5.35 (1H, q, H-2′, J = 4.9 Hz), 4.91 (1H, t, 5′-OH, J = 4.9 Hz), 4.14 (1H, t, H-3′, J = 4.9 Hz), 3.73−3.68 (1H, m, H-5′a), 3.51−3.38 (1H, m, H-5′b), 3.21−3.16 (2H, m, H-1′a, H-4′), 2.83 (1H, dd, H-1′b, J = 4.9, 11.7 Hz); FAB-MS *m*/*z* 349, 351 ($M^+ + H$). Anal. Calcd for $C_{11}H_{13}N_2O_4SBr\cdot 0.45H_2O$: C, 36.98; H, 3.92; N, 7.84. Found: C, 36.69; H, 3.62; N, 7.60.

(2*S*)-1,4-Anhydro-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-(cytosin-1-yl)-2-deoxy-4-thio-D-arabitol (27) and (2*S*)-1,4-Anhydro-3-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-2-*O*-(4-(cytosin-1-yl)pyrimidin-2-yl)-2-deoxy-4-thio-D-arabitol (28). To a solution of **20d** and **22** (1.10 g, 1.54 mmol) in MeOH−THF (45 mL, 3:4) was added concentrated NH_4OH (23 mL), and the mixture was stirred for 2 h at room temperature. After concentration, the residue was passed through a short silica gel column. The eluate with 10−50% AcOEt in hexane was collected and concentrated. The residue was dissolved in CH_3CN (34 mL), and DMAP (295 mg, 2.42 mmol), TPSCl (733 mg, 2.42 mmol), and triethylamine (0.34 mL, 2.42 mmol) were added to the solution at 0 °C. After the mixture was stirred at room temperature for 2 h, concentrated NH_4OH was added at 0 °C, and then the new mixture stirred for 1.5 h at room

temperature. After the solvents were removed under reduced pressure, the residue was purified by column chromatography over silica gel (3.6 × 18 cm, 1−10% MeOH in $CHCl_3$) to give a mixture of **27** and **28** (507 mg, 55%, **27**/**28** = 2.2) as an amorphous foam: ^{1}H NMR ($CDCl_3$) δ 9.82−9.47 (0.62H, br, NH_2), 9.27−8.88 (1.38H, br, NH_2), 8.56 (0.31H, d, H-6″, J = 5.9 Hz), 8.36 (0.69H, d, H-6, J = 7.8 Hz), 7.94 (0.31H, d, H-6, J = 5.4 Hz), 7.67−7.10 (15.31H, m, Ar H, H-5″), 6.30 (0.69H, d, H-5, J = 7.8 Hz), 6.28 (0.31H, d, H-5, J = 5.4 Hz), 5.69−5.65 (0.31H, m, H-2′), 4.83−4.78 (0.69H, m, H-2′), 4.70 (0.31H, d, PhCH, J = 12.2 Hz), 4.67 (0.31H, d, PhCH, J = 12.2 Hz), 4.57 (0.69H, d, PhCH, J = 12.2 Hz), 4.45 (0.31H, t, H-3′, J = 3.9 Hz), 4.39 (0.69H, d, PhCH, J = 12.2 Hz), 4.36 (0.69H, t, H-3′, J = 6.8 Hz), 3.91 (0.31H, dd, H-5′a, J = 7.8, 10.3 Hz), 3.85−3.74 (1.69H, m, H-5′a,b, H-5′b), 3.59 (0.31H, dt, H-4′, J = 3.9, 10.3 Hz), 3.54−3.49 (0.69H, m, H-4′), 3.52 (0.31H, dd, H-1′a, J = 5.9, 11.7 Hz), 3.38 (0.69H, dd, H-1′a, J = 5.4, 11.7 Hz), 3.14−3.00 (1H, m, H-1′b×2), 1.07 (9H, s, *t*-Bu); FAB-MS m/z 572 (M^+ + H) and 666 (M^+ + H).

(2*S*)-1,4-Anhydro-5-*O*-(*tert*-butyldiphenylsilyl)-2-(cytosin-1-yl)-2-deoxy-4-thio-D-arabitol (29) and (2*S*)-1,4-Anhydro-5-*O*-(*tert*-butyldiphenylsilyl)-2-*O*-[4-(cytosin-1-yl)pyrimidin-2-yl]-2-deoxy-4-thio-D-arabitol (30). To a solution of **27** and **28** (500 mg, 0.83 mmol) in CH_2Cl_2 (16 mL) was added slowly a solution of BCl_3 (5.3 mL of a 1 M CH_2Cl_2 solution, 5.3 mmol) at −78 °C. After being stirred for 1.5 h at the same temperature, the reaction was quenched by addition of pyridine−MeOH (5.5 mL, 2:1). The mixture was allowed to warm to room temperature and was stirred for 1 h. After the most of organic solvents were removed under reduced pressure, the whole was extracted with $CHCl_3$ (×2). The organic phase was washed with H_2O and brine and then dried (Na_2SO_4). After the solvent was evaporated under reduced pressure, the concentrated residue was purified by column chromatography over silica gel (2.8 × 20 cm, 1−10% MeOH in $CHCl_3$, and then 2.8 × 5 cm, AcOEt) to give less polar **30** (104 mg, 22%) and more polar **29** (256 mg, 53%) as an amorphous foam, respectively.

Data for 29: ^{1}H NMR ($CDCl_3$ + D_2O) δ 7.69−7.62 (4H, m, Ar H), 7.41−7.31 (7H, m, Ar H), 5.99 (1H, d, H-5, J = 7.8 Hz), 4.95−4.88 (1H, m, H-2′), 4.21 (1H, t, H-3′, J = 8.8 Hz), 4.02 (1H, dd, H-5′a, J = 4.9, 10.3 Hz), 3.82 (1H, dd, H-5′b, J = 7.3, 10.3 Hz), 3.55−3.50 (1H, m, H-4′), 2.97 (1H, dd, H-1′a, J = 7.8, 10.3 Hz), 2.76 (1H, t, H-1′b, J = 10.3 Hz), 1.04 (9H, s, *t*-Bu); FAB-MS m/z 482 (M^+ + H). Anal. Calcd for $C_{25}H_{31}N_3O_3SSi\cdot 0.7H_2O$: C, 60.75; H, 6.61; N, 8.50. Found: C, 60.72; H, 6.41; N, 8.35.

Data for 30: ^{1}H NMR ($CDCl_3$) δ 9.46−8.84 (2H, br, NH_2), 8.52−8.42 (2H, m, H-6, H-6″), 7.71 (1H, d, H-5, J = 5.4 Hz), 7.68−7.65 (4H, m, Ar H), 7.43−7.26 (6H, m, Ar H), 5.58 (1H, d, H-5″, J = 7.3 Hz), 5.57−5.52 (1H, m, H-2′), 4.44 (1H, t, H-3′, J = 6.8 Hz), 3.96 (1H, dd, H-5′a, J = 6.8, 10.3 Hz), 3.84 (1H, dd, H-5′b, J = 6.8, 10.3 Hz), 3.51 (1H, q, H-4′, J = 3.5 Hz), 3.32 (1H, dd, H-1′a, J = 6.8, 10.7 Hz), 2.92 (1H, dd, H-1′b, J = 7.8, 10.7 Hz), 1.04 (9H, s, *t*-Bu); FAB-MS m/z 576 (M^+ + H). Anal. Calcd for $C_{29}H_{33}N_5O_4SSi\cdot 0.5AcOEt$: C, 60.07; H, 6.02; N, 11.30. Found: C, 59.78; H, 6.05; N, 11.25.

(2*S*)-1,4-Anhydro-2-(cytosin-1-yl)-2-deoxy-4-thio-D-arabitol (31). A mixture of **29** (234 mg, 0.50 mmol) and $NH_4F\cdot HF$ (342 mg, 6.00 mmol) in DMF (7.6 mL) was stirred at room temperature overnight. After concentration, the residue was purified by column chromatography over silica gel (1.5 × 12 cm, 10−20% MeOH in $CHCl_3$) to give **31** (84 mg, 69%) as crystals: mp 239−241 °C (crystallized from MeOH); UV (MeOH) λ_{max} 276 nm; ^{1}H NMR (DMSO-d_6) δ 7.60 (1H, d, H-6, J = 7.3 Hz), 7.05 (1H, br s, NH), 7.00 (1H, br s, NH), 5.67 (1H, d, H-5, J = 7.3 Hz), 5.38 (1H, d, 3′-OH, J = 6.8 Hz), 4.85 (1H, dd, 5′-OH, J = 4.4, 6.4 Hz), 4.63 (1H, dt, H-2′, J = 7.8, 10.7 Hz), 4.12−4.06 (1H, m, H-3′), 3.86 (1H, dt, H-5′a, J = 4.4, 10.3 Hz), 3.39 (1H, ddd, H-5′b, J = 6.4, 8.3, 10.3 Hz), 3.18−3.12 (1H, m, H-4′), 2.85 (1H, t, H-1′a, J = 10.7 Hz), 2.80 (1H, dd, H-1′b, J = 7.8, 10.7 Hz); FAB-MS m/z 244 (M^+ + H). Anal. Calcd for $C_9H_{13}N_3O_3S$: C, 44.43; H, 5.39; N, 17.27. Found: C, 44.23; H, 5.36; N, 17.03.

(2*S*)-1,4-Anhydro-2-*O*-(4-(cytosin-1-yl)pyrimidin-2-yl)-2-deoxy-4-thio-D-arabitol (32). Compound **30** (85.4 mg, 0.15 mmol) was converted as described for the synthesis of **31** to give **33** (39.8 mg, 79%) as a white solid: mp 145 °C (dec); UV (MeOH) λ_{max} 253, 300 nm; ^{1}H NMR (DMSO-d_6) δ 8.60 (1H, d, H-6, J = 5.4 Hz), 8.29 (1H, d, H-6″, J = 7.8 Hz), 7.80 (1H, d, H-5, J = 5.4 Hz), 7.70 (1H, br s, NH), 7.66 (1H, br s, NH), 5.99 (1H, d, H-5″, J = 7.8 Hz), 5.54 (1H, d, 3′-OH, J = 4.9 Hz), 5.35 (1H, q, H-2′, J = 4.9 Hz), 4.91 (1H, t, 5′-OH, J = 5.4 Hz), 4.17 (1H, q, H-3′, J = 4.9 Hz), 3.77−3.72 (1H, m, H-5′a), 3.43−3.38 (1H, m, H-5′b), 3.28−3.18 (2H, m, H-4′, H-1′a), 2.83 (1H, dd, H-1′b, J = 4.9, 11.2 Hz); ^{13}C NMR (DMSO-d_6−D_2O) δ 166.24 (C-4″), 164.30 (C-2), 161.40 (C-6), 160.25 (C-4), 155.00 (C-2″), 142.35 (C-6″), 110.81 (C-5), 97.64 (C-5″), 83.41 (C-2′), 76.89 (C-3′), 64.13 (C-5′), 53.68 (C-4′), 31.69 (C-1′); FAB-MS m/z 338 (M^+ + H). Anal. Calcd for $C_{13}H_{15}N_5O_4S\cdot 1.0H_2O$: C, 43.94; H, 4.82; N, 19.71. Found: C, 43.76; H, 4.32; N, 19.44.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR, HMBC, and NOE spectral charts of **32** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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