# Novel Glycosidation Method Using 2,6-Anhydro-2-thio Sugars for Stereocontrolled Synthesis of 2,6-Dideoxy-α- and -β-glycosides

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**Abstract:** Powerful and highly stereocontrolled *O*-glycosidation methods using several kinds of 2,6-anhydro-2-thio sugars as glycosyl donors have been developed for the synthesis of both 2,6-dideoxy-α- and -β-glycosides which frequently occur in biologically important natural products. Both glycosidations of phenyl 3,4-di-*O*-acetyl-2,6-anhydro-1,2-dithio-D-altropyranoside (**2**) and 3,4-di-*O*-acetyl-2,6-anhydro-1-fluoro-2-thio-D-altropyranoside (**3**) with alcohols exclusively gave the corresponding 2,6-anhydro-2-thio-α-glycosides. In contrast, the glycosidations of 1,3,4-tri-*O*-acetyl-2,6-anhydro-2-thio-D-altropyranose (**4**) with alcohols afforded the corresponding 2,6-anhydro-2-thio-β-glycosides with high stereocontrol. Furthermore, a novel method for the controlled block synthesis of 2,6-dideoxy oligosaccharides by the combined use of the activated 2,6-anhydro-2-thio sugar **23** and the deactivated 2,6-anhydro-2-sulfinyl sugar **24**, both of which have the same thiophenyl leaving group at the anomeric positions, has been demonstrated. The 2,6-anhydro-2-thio-α- and -β-glycosides obtained by the present methods were effectively converted into the corresponding 2,6-dideoxy-α- and -β-glycosides by both hydrogenolysis using Raney-Ni as a catalyst and reductive desulfurization using $Bu_3SnH$ and AIBN.

## Introduction

Over the past years, glycosubstances including glycoproteins, glycolipids, many antibiotics, and some immunodeterminants have been the subject of considerable interest in bioorganic chemistry, pharmacology, glycobiology, as well as in glycotechnology. The development of selective and efficient glycosidation methods to construct the glycosubstances is now becoming more and more important not only in carbohydrate chemistry but also in organic synthesis.[1] Although many types of 2-deoxy-α- and -β-glycosides frequently appear in naturally occurring bioactive substances such as aureolic acid antibiotics, anthracycline antibiotics, cardiac glycosides, avermectins, erythromycins, and recently discovered enediyne antibiotics (Figure 1),[2] the stereocontrolled and effective glycosidation of the 2-deoxy sugar, especially, the β-stereoselective glycosidation, has been a long standing problem in this field.[1r,3] The main reasons why highly stereocontrolled and effective glycosidation of the 2-deoxy sugar is difficult are the lack of stereodirecting anchimeric assistance from the C-2 position and the low stability of the glycoside bond of the 2-deoxy sugar in acidic conditions due to the lack of an electron-withdrawing C-2 substituent. In this context, glycals are now recognized to be one of the most versatile glycosyl donors for the synthesis of 2-deoxy-α-glycosides.[4] On the other hand, for the 2-deoxy-β-glycoside synthesis, an effect on the anomeric stereoselectivity due to the participation by the *p*-methoxybenzoyl group attached to the C-3 position of the 2-deoxy sugar was reported in analogy with the neighboring group-assisted method.[5] The use of 2-bromo-2-deoxyglycosyl bromides, which have a bromide as a temporary participating group at the C-2 position of the glycosyl donor, was introduced for the β-stereoselective glycosidation.[3,6] Furthermore, thiophenyl,[7] selenophenyl,[8] and *N*-formylamino[9] groups were also employed as other effective temporary participating groups at

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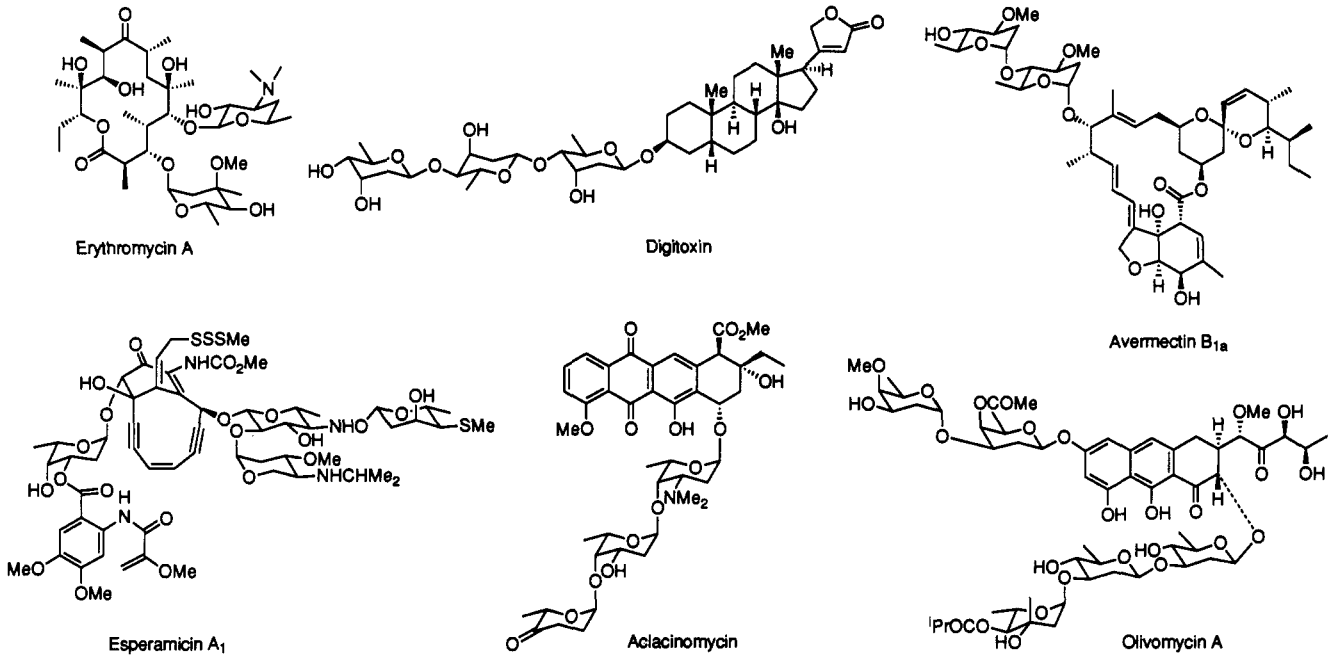


**Figure 1.** Some bioactive natural products having 2-deoxy (2,6-dideoxy) sugar(s).

the C-2 position which could be easily removed after glycoside formation. Alternatively, the stereoselective syntheses of 2-deoxy-$\beta$-glycosides using alkoxy-substituted anomeric radicals have been reported.[10] Very recently, van Boom et al.[11] announced that the *N*-iodosuccinimide (NIS)–TfOH-mediated stereospecific glycosidation of ethyl (or phenyl) 2-*O*-(phenoxythiocarbonyl)-1-thioglycosides and Hashimoto et al.[12] described the use of 2-deoxy-2-[(*p*-methoxyphenyl)thio]glycopyranosyl *N,N,N',N'*-tetramethylphosphoramidites as glycosyl donors for the synthesis of the 2-deoxy-$\beta$-glycosides. As a novel and effective method, we originally designed conformationally rigid 2,6-anhydro-2-thio glycosyl donors, which had a thio-bridge between the C-2 and C-6 positions, for the highly stereocontrolled synthesis of both the 2,6-dideoxy-$\alpha$- and -$\beta$-glycosides. The 2,6-dideoxy sugar is a very common and important class of 2-deoxy sugars in bioactive natural products, especially in the antitumor antibiotics as shown in Figure 1. The designed 2,6-anhydro-2-thio glycosyl donor has the following novel distinctive features (Figure 2): (1) the 2,6-anhydro-2-thio glycosyl donor has a very rigid structure due to the 2,6-anhydro-2-thio bridge; (2) the 2,6-anhydro-2-thio glycosyl donor could be a good precursor of the 2,6-dideoxy glycoside; and (3) the stereoselectivity of the glycosidation would not be affected by the anomeric effect[13] in the same manner as the more usual chair conformers because of its unusual boat conformation. In this paper, we report a full account on the novel and highly stereocontrolled glycosidation methods using the 2,6-anhydro-2-thio glycosyl donors for effective synthesis of both 2,6-dideoxy-$\alpha$- and -$\beta$-glycosides.[14]

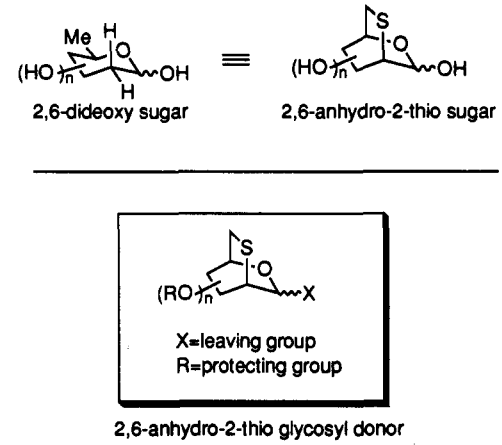


**Figure 2.** 2,6-Dideoxy sugar and 2,6-anhydro-2-thio sugar.

## Results and Discussion

**Synthesis of the 2,6-Anhydro-2-thio Glycosyl Donors.** The synthetic approach for the designed 2,6-anhydro-2-thio glycosyl donors **2**–**4** began with the conversion of methyl 4,6-*O*-benzylidene-$\alpha$-D-glucopyranoside into the 2,6-anhydro-2-thio sugar derivative **1** according to the literature.[15] It was found that **1** was obtained in good overall yield even on a large scale preparation and that no purifications were required for the first four steps. Different types of the C-1 activated 2,6-anhydro-2-thio glycosyl donors **2**–**4** were synthesized from the 2,6-anhydro-2-thio sugar **1** as shown in Scheme 1. Thus, conversion of the methyl glycoside of **1** into the phenylthio glycoside was achieved by Nicolaou's method[16] using $Me_3SiSPh$ and TMSOTf in $CH_2Cl_2$ to give **2** in 90% yield as a mixture of anomers ($\alpha/\beta$ = 83/17). Treatment of **2** with *N*-bromosuccinimide (NBS) and (diethylamido)sulfur

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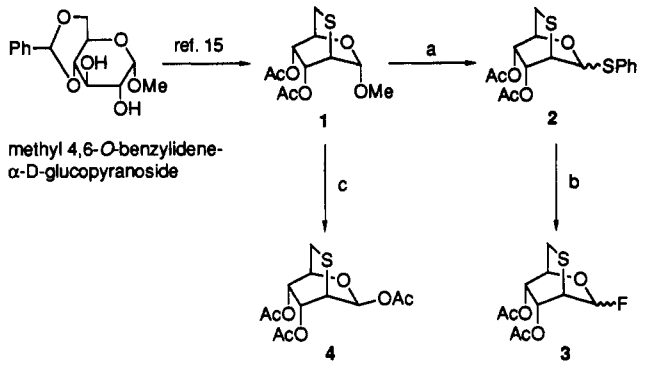
**Scheme 1**[a]




[a] (a) $Me_3SiSPh$, TMSOTf, $CH_2Cl_2$, 0 °C, 30 min, 90%; (b) NBS, DAST, $CH_2Cl_2$, −25 °C, 10 min, 84%; (c) $Ac_2O$, concd $H_2SO_4$, 0 °C, 10 min, 86%.

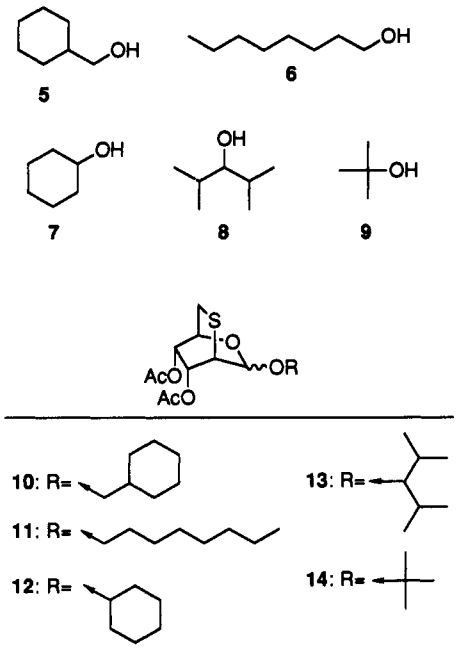



**Figure 3.** Glycosyl acceptors (alcohols) and 2,6-anhydro-2-thio glycosides.

trifluoride (DAST) in $CH_2Cl_2$[17] gave the corresponding fluoride **3** in 84% yield as an anomeric mixture ($\alpha/\beta = 92/8$). Since the fluoride **3** was not very stable for a long time on acidic silica gel, quick purification by silica gel column chromatography was important to get a high yield of pure **3**. On the other hand, acetolysis of **1** with concd $H_2SO_4$ (or TMSOTf) in $Ac_2O$ afforded the triacetate **4** in 86% yield as a $\beta$-anomer. The 2,6-anhydro-2-thio glycosyl donors **2** and **3** were used for the following glycosidation reactions as an anomeric mixture.

**Reactivity and Stereoselectivity of the Glycosidations of 2–4.** Glycosidations of **2**[14a] with several alcohols **5–9** listed in Figure 3 by Nicolaou's method using NBS[16] as an activator were first examined. The results in Table 1 clearly showed some excellent features of the present glycosidation reaction. The glycosidations of **2** with the primary alcohol, cyclohexylmethanol (**5**), as the glycosyl acceptor in several solvents, such as $CH_2Cl_2$, $(CH_2Cl)_2$, $Et_2O$, THF, MeCN, and PhMe, proceeded very rapidly (within 30 min) even at low temperature (−25 °C) to give the 2,6-anhydro-2-thio-$\alpha$-glycoside of **10** in excellent yields. Remarkably, the stereoselectivity of the glycosidations was quite $\alpha$-specific in all cases (entries 1–6 in Table 1). It was also made clear that the stereoselectivity of the glycosidations was completely independent of both solvent effect and the configuration of the anomeric center

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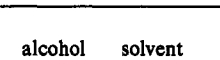
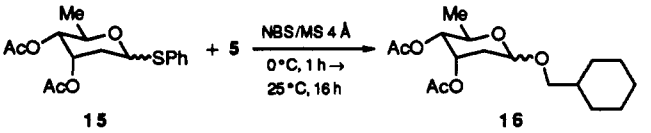
**Table 1.** Glycosidations of **2** with Several Alcohols by NBS[a]




| entry | alcohol | solvent | temp (°C) | time (min) | product | yield (%)[b] | $\alpha/\beta$[c] |
|---|---|---|---|---|---|---|---|
| 1 | **5** | $CH_2Cl_2$ | −25 | 15 | **10** | 94 | $\alpha$ |
| 2 | **5** | $(CH_2Cl)_2$ | −25 | 15 | **10** | 92 | $\alpha$ |
| 3 | **5** | $Et_2O$ | −25 | 30 | **10** | 96 | $\alpha$ |
| 4 | **5** | THF | −25 | 15 | **10** | 98 | $\alpha$ |
| 5 | **5** | MeCN | −25 | 15 | **10** | 97 | $\alpha$ |
| 6 | **5** | PhMe | −25 | 30 | **10** | 92 | $\alpha$ |
| 7 | **6** | MeCN | −40 | 15 | **11** | 91 | $\alpha$ |
| 8 | **7** | MeCN | −40 | 10 | **12** | 92 | $\alpha$ |
| 9 | **8** | MeCN | −40 | 10 | **13** | 96 | 97/3 |
| 10 | **9** | MeCN | −40 | 10 | **14** | 92 | 83/17 |

[a] All reactions were carried out by use of 2.0 equiv of alcohol and 1.1 equiv of NBS to the glycosyl donor. [b] Isolated yields after purification by column chromatography. [c] $\alpha:\beta$ Ratios were determined by $^1$H-NMR spectroscopy (270 MHz) and/or isolation of pure isomers.

**Table 2.** Glycosidations of **15** with **5** by NBS[a]




| entry | solvent | yield (%)[b] | $\alpha/\beta$[c] |
|---|---|---|---|
| 1 | $CH_2Cl_2$ | 91 | 51/49 |
| 2 | $(CH_2Cl)_2$ | 86 | 55/45 |
| 3 | $Et_2O$ | 95 | 42/58 |
| 4 | THF | 93 | 31/69 |
| 5 | MeCN | 78 | 50/50 |
| 6 | PhMe | 96 | 41/59 |

[a] All reactions were carried out by use of 2.0 equiv of alcohol and 1.1 equiv of NBS to the glycosyl donor. [b] Isolated yields after purification by column chromatography. [c] $\alpha:\beta$ Ratios were determined by $^1$H-NMR spectroscopy (270 MHz) and/or isolation of pure isomers.

of the phenyl thioglycoside **2**. Furthermore, some additional efficiencies were found in the glycosidations of **2** with several other alcohols, i.e., octanol (**6**), cyclohexanol (**7**), 2,4-dimethyl-3-pentanol (**8**) and *tert*-butyl alcohol (**9**) (entries 7–10 in Table 1). Even the hindered secondary alcohol **8** and the tertiary alcohol **9** were also smoothly glycosylated under similar conditions with high stereocontrol to give the corresponding $\alpha$-glycosides **13**-$\alpha$ and **14**-$\alpha$, respectively, in high yields. From the $^1$H-NMR analysis, it was found that *w*-coupling between H-1 and H-3 was clearly recognized for the 2,6-anhydro-2-thio-$\alpha$-glycosides so obtained. Our interest at this stage was to compare the 2,6-anhydro-2-thio glycosyl donor **2** and the 2,6-dideoxy glycosyl donor **15**,[18] both of which have the same configurations and C-1 leaving group and C-3 and C-4 hydroxyl protecting groups, from the view point of reactivity and stereoselectivity in their glycosidations with **5** by NBS. As shown in Table 2, the glycosidations of 2,6-dideoxy phenyl thioglycoside **15** with **5** at 25 °C in $CH_2Cl_2$, $(CH_2Cl)_2$, $Et_2O$, THF, MeCN, and PhMe gave the 2,6-dideoxy glycoside **16** in high yield. However, higher temperatures and longer reaction times were required and an anomeric mixture of **16** was produced with very low stereoselectivity in all examined cases. These results were in stark contrast to the efficiency observed when using the 2,6-anhydro-2-thio sugar. Therefore, we next examined the glycosidations of **2** with the alcohols **5–9** by another activating reagent, MeOTf,[19] in $CH_2Cl_2$. It was found that these glycosidations also proceeded smoothly to give the corresponding 2,6-anhydro-2-thio-$\alpha$-glycoside

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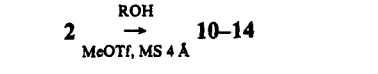
**Table 3.** Glycosidations of **2** with Several Alcohols by MeOTf[a]




| entry | alcohol | solvent | temp (°C) | time (h) | product | yield (%)[b] | $\alpha/\beta$[c] |
|---|---|---|---|---|---|---|---|
| 1 | **5** | $CH_2Cl_2$ | 25 | 12 | **10** | 92 | $\alpha$ |
| 2 | **6** | $CH_2Cl_2$ | 25 | 12 | **11** | 90 | $\alpha$ |
| 3 | **7** | $CH_2Cl_2$ | 25 | 12 | **12** | 91 | $\alpha$ |
| 4 | **8** | $CH_2Cl_2$ | 25 | 20 | **13** | 88 | 98/2 |
| 5 | **9** | $CH_2Cl_2$ | 25 | 20 | **14** | 89 | 90/10 |

[a] All reactions were carried out by use of 1.5 equiv of alcohol and 5.0 equiv of MeOTf to the glycosyl donor. [b] Isolated yields after purification by column chromatography. [c] $\alpha$:$\beta$ Ratios were determined by $^1$H-NMR spectroscopy (270 MHz) and/or isolation of pure isomers.

of **10** in high yield as shown in Table 3. Notably, the stereoselectivity of these glycosidations was very similar to that with NBS. Glycosidations of the 2,6-anhydro-2-thio fluoride **3** with the alcohols were next examined.[14b] The results summarized as entries 1–6 in Table 4 showed that the glycosidations of **3** and **5** with many kinds of activators such as $SnCl_2$–$AgClO_4$,[20] $SnCl_2$,[21] TMSOTf,[22] $Cp_2MCl_2$ (M=Zr, Hf)–$AgClO_4$,[23] or $AgBF_4$[24] proceeded under mild conditions to afford **10**-$\alpha$ with high stereocontrol and excellent yields. The stereoselectivity was highly independent of the glycosidation conditions including the activator and the solvent. Furthermore, it was found that the fluoride **3** was also smoothly coupled with the hindered alcohols **8** and **9** using only $SnCl_2$ as an activator to give the corresponding 2,6-anhydro-2-thio-$\alpha$-glycosides **13**-$\alpha$ and **14**-$\alpha$, in high yields, respectively (entries 8 and 9 in Table 4). On the other hand, in drastic contrast, the 2,6-anhydro-2-thio-$\beta$-glycosides were exclusively obtained by the glycosidations of the acetate **4** and the alcohols.[14c] The results indicated as entries 1–4 in Table 5 showed that the glycosidations of **4** with **5** in $CH_2Cl_2$ using several kinds of Lewis acids such as $SnCl_4$,[25] $Tf_2O$, TMSOTf,[26] and $TrClO_4$[27] proceeded nicely at low temperature (–10 °C) to give the 2,6-anhydro-2-thio-$\beta$-glycoside of **10** with high stereocontrol and excellent yields. The stereoselectivity of the glycosidations was highly independent of the activator, that is the examined Lewis acid. Furthermore, it was found that the alcohols **6**–**8** were also smoothly glycosylated with **4** by TMSOTf as an activator to afford the corresponding $\beta$-glycosides of **11**, **12**, and **13** in high yields, respectively. We next examined the solvent effect of the unexpected and high $\beta$-stereoselective glycosidation reactions. Therefore, the glycosidations of **4** with **5** by TMSOTf in several solvents, such as $(CH_2Cl)_2$, $Et_2O$, THF, MeCN, and PhMe, were tested. From the results shown as entries 8–12 in Table 5, it was interesting to note that the $\alpha$-glycoside of **10** was exclusively produced in $Et_2O$ and THF while the $\beta$-anomer was predominantly obtained in MeCN, PhMe, and $(CH_2Cl)_2$ as well as in $CH_2Cl_2$. Also, it was found that the ratio of the $\beta$-anomer was increased by a long reaction time even in the case of $Et_2O$ and THF, and the $\beta$-glycoside was produced in reasonable yield by treatment of the corresponding $\alpha$-glycoside with only the Lewis acids in $CH_2Cl_2$, MeCN, PhMe, and $(CH_2Cl)_2$. These results indicate that although these Lewis acids are considerably deactivated in $Et_2O$ and THF, they are strong enough in $CH_2Cl_2$, MeCN, PhMe, and $(CH_2Cl)_2$ to reverse the glycosidation reaction, and thermodynamic control is responsible for the high $\beta$-stereoselectivity.

### Mechanistic Considerations

From these results, the following mechanism for the highly stereocontrolled glycosidations using 2,6-anhydro-2-thio sugars as glycosyl donors was suggested. Since the configuration of the newly forming glycoside bond is completely independent of the configuration of the anomeric position of the glycosyl donor, these glycosidation reactions would proceed *via* a $S_N1$ type reaction pathway and involved the oxionium intermediate **A** as depicted in Figure 4. Two major interactions would be considered between the oxionium intermediate **A** and the approaching alcohol. One is the repulsive electronic interaction between the sulfur atom of the 2,6-anhydro-2-thio sugar and the alcohol approaching the anomeric center. The other is the steric interaction of the 1,3-diaxial repulsion between the C-3 substituent and the alcohol. When the glycosidation proceeds under kinetic conditions, the repulsive electronic interaction strongly impedes the reaction. Consequently, the alcohol predominantly attacks the $\alpha$-face of the anomeric center of the oxionium intermediate **A**, and the configuration of the formed glycoside bond is held during the reaction (path a in Figure 4). Indeed, no isomerization was observed when both of the obtained 2,6-anhydro-2-thio-$\alpha$- and -$\beta$-glycosides were exposed to the glycosidation conditions for the glycosyl donors **2** and **3**. In contrast, under thermodynamic conditions, even if the $\alpha$-bond formation preferentially occurs, the $\alpha$-glycoside bond is cleaved and then the thermodynamically stable $\beta$-glycoside bond that arises from the 1,3-diaxial interaction finally forms (path b in Figure 4). Interestingly, both effects strongly influence the stereoselectivity of the glycosidation of the 2,6-anhydro-2-thio glycosyl donor under any glycosidation conditions due to the very rigid conformation of the 2,6-anhydro-2-thio sugar.

**Block Synthesis of 2,6-Dideoxy Oligosaccharide.** Our other work centered on the effective synthesis of 2,6-dideoxy oligosaccharides by combined use of an activated 2,6-anhydro-2-thio sugar and a deactivated 2,6-anhydro-2-thio sugar in the highly stereocontrolled glycosidation reactions.[14d] We expected that the high reactivity of the 2,6-anhydro-2-thio glycosyl donor under a variety of glycosidation conditions would result from the electron-donating nature of the sulfur at the C-2 position in the 2,6-anhydro-2-thio sugar and the rate of the glycosidation reaction would be strongly affected by the oxidation state of the sulfur. Therefore, the 2,6-anhydro-2-sulfinyl fluorides **17** and **18** and the 2,6-anhydro-2-sulfonyl fluoride **19** were prepared from the 2,6-anhydro-2-thio fluoride **3**-$\alpha$ by *m*CPBA oxidation in $CH_2Cl_2$. The stereochemistries of the sulfoxides of **17** and **18** were clearly determined by their $^1$H-NMR analyses based on the chemical shifts of H-1 and H-3.[15b] As expected, the glycosidations of **17**–**19** with cyclohexanol (**7**) under similar conditions ($SnCl_2$, $CH_2Cl_2$, –10 °C, 1.5 h, (entry 3 in Table 4)) as that for the 2,6-anhydro-2-thio fluoride **3** did not proceed and each unchanged glycosyl donor was recovered in nearly quantitative yield. Since both the 2,6-anhydro-2-sulfinyl glycosyl donors **17** and **18** showed similar low reactivity under the glycosidation conditions, the armed–disarmed phenomenon in this glycosidation reaction would come from the electronic effect of the C-2 substituent based on Fraser-Reid's explanation,[28] and not from the effect of neighboring participation of the C-2 substituent on the anomeric center. To demonstrate the potency of this favorable phenomenon for the block synthesis

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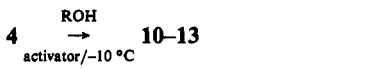
**Table 4.** Glycosidations of **3** with Alcohols under Several Conditions


| entry | alcohol[a] | activators (equiv) | solvent | temp (°C) | time (h) | product | yield (%)[b] | $\alpha/\beta$[c] |
|---|---|---|---|---|---|---|---|---|
| 1 | **5** | $SnCl_2$ (1.1)–$AgClO_4$ (1.1) | $Et_2O$ | −10 | 1.5 | **10** | 98 | 97/3 |
| 2 | **5** | $SnCl_2$ (1.1)–$ZnCl_2$ (1.1) | $Et_2O$ | −10 | 1.5 | **10** | 89 | 98/2 |
| 3 | **5** | $SnCl_2$ (1.1) | $Et_2O$ | −10 | 1.5 | **10** | 91 | $\alpha$ |
| 4 | **5** | TMSOTf (1.0) | $Et_2O$ | −10 | 1.5 | **10** | 90 | 92/8 |
| 5 | **5** | $Cp_2HfCl_2$ (5.0)–$AgClO_4$ (5.0) | $CH_2Cl_2$ | −10 → 25 | 1.5 | **10** | 95 | 93/7 |
| 6 | **5** | $Cp_2ZrCl_2$ (0.6)–$AgBF_4$ (1.2) | $CH_2Cl_2$ | −20 → 10 | 2 | **10** | 92 | 98/2 |
| 7 | **7** | $SnCl_2$ (1.1) | $Et_2O$ | −10 | 1.5 | **12** | 94 | 98/2 |
| 8 | **8** | $SnCl_2$ (1.1) | $Et_2O$ | −10 | 2.4 | **13** | 76 | 98/2 |
| 9 | **9** | $SnCl_2$ (1.1) | $Et_2O$ | −10 | 1.5 | **14** | 81 | 96/4 |

[a] All reactions were carried out by use of 2.0 equiv of alcohol to the glycosyl donor. [b] Isolated yields after purification by column chromatography. [c] $\alpha$:$\beta$ Ratios were determined by $^1$H-NMR spectroscopy (270 MHz) and/or isolation of pure isomers.

**Table 5.** Glycosidations of **4** with Alcohols under Several Conditions




| entry | alcohol[a] | activator (equiv) | solvent | time (min) | product | yield[b] | $\alpha/\beta$[c] |
|---|---|---|---|---|---|---|---|
| 1 | **5** | TMSOTf (1.1) | $CH_2Cl_2$ | 30 | **10** | 89 | 2/98 |
| 2 | **5** | $Tf_2O$ (1.1) | $CH_2Cl_2$ | 30 | **10** | 90 | 5/95 |
| 3 | **5** | $SnCl_4$ (1.1) | $CH_2Cl_2$ | 30 | **10** | 88 | 5/95 |
| 4 | **5** | $TrClO_4$ (2.2) | $CH_2Cl_2$ | 60 | **10** | 90 | 3/97 |
| 5 | **6** | TMSOTf (1.1) | $CH_2Cl_2$ | 30 | **11** | 95 | 2/98 |
| 6 | **7** | TMSOTf (1.1) | $CH_2Cl_2$ | 30 | **12** | 85 | 1/99 |
| 7 | **8** | TMSOTf (1.1) | $CH_2Cl_2$ | 30 | **13** | 76 | 5/95 |
| 8 | **5** | TMSOTf (1.1) | MeCN | 30 | **10** | 88 | 4/96 |
| 9 | **5** | TMSOTf (1.1) | PhMe | 30 | **10** | 84 | 4/96 |
| 10 | **5** | TMSOTf (1.1) | $(CH_2Cl)_2$ | 30 | **10** | 85 | 2/98 |
| 11 | **5** | TMSOTf (1.1) | $Et_2O$ | 60 | **10** | 88 | 94/6 |
| 12 | **5** | TMSOTf (1.1) | THF | 60 | **10** | 89 | 96/4 |

[a] All reactions were carried out by use of 2.0 equiv of alcohol to the glycosyl donor. [b] Isolated yields after purification by column chromatography. [c] $\alpha$:$\beta$ Ratios were determined by $^1$H-NMR spectroscopy (270 MHz) and/or isolation of pure isomers.

of 2,6-dideoxy oligosaccharides, the glycosidations of other pairs of activated and deactivated sugars were examined (Scheme 2).[29] The 2,6-anhydro-2-thio sugar **20** possessing an acetoxy group as a leaving group was coupled with the corresponding 2,6-anhydro-2-sulfinyl sugar **21** in the presence of TMSOTf in $CH_2Cl_2$ at −40 → −15 °C for 30 min to afford the disaccharide **22** in 81% yield. Although the combined use of NIS–TMSOTf was originally developed for effective activation of disarmed thioglycosyl donors having an acyloxy group at the C-2 position,[30,31] the glycosidation of the 2,6-anhydro-2-thio sugar **23** possessing a thiophenyl group at the anomeric center with the corresponding 2,6-anhydro-2-sulfinyl sugar **24** having the same leaving group by NIS–TMSOTf in $CH_2Cl_2$ at −40 °C for 15 min proceeded smoothly to give the disaccharide **25** in 89% yield. The self-coupling products of the deactivated sugars were not detected at all and the stereoselectivity of these glycosidations was highly $\alpha$-selective. Notably, although the glycosyl donor **20** had an acetoxy group as a leaving group at the anomeric center, the $\alpha$-glycoside **22** was exclusively formed because of the lack of the 1,3-diaxial interaction already mentioned. Furthermore, the obtained deactivated disaccharide **25** was easily converted into the activated disaccharide **26** by a standard reduction of the sulfoxide moiety using LAH in THF. After the protection of the hydroxyl group of **26** with an acetyl group, the resulting **27** was found to smoothly couple with cyclohexanol (**7**) by NBS in $CH_2Cl_2$ at −40 °C for 20 min to stereospecifically afford the 2,6-anhydro-2-thio $\alpha$-disaccharide **28** in 98% yield.

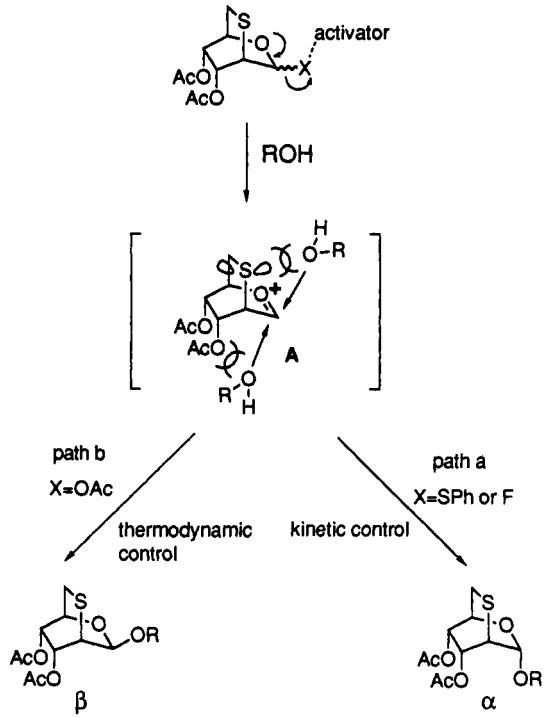



**Figure 4.** Presumed mechanism of the glycosidation of 2,6-anhydro-2-thio sugar.

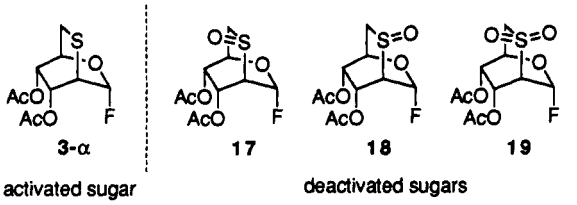



**Figure 5.** Activated (armed)-sugar and deactivated (disarmed)-sugars.

**Synthesis of 2,6-Dideoxy Glycosides from 2,6-Anhydro-2-thio Glycosides.** To accomplish the synthesis of both 2,6-dideoxy-$\alpha$- and -$\beta$-glycosides, the 2,6-anhydro-2-thio systems in the glycosides obtained by the present methods were effectively converted into the desired 2,6-dideoxy structures by two methods. The results are summarized in Table 6. The first one was the standard hydrogenolysis of the 2,6-anhydro-3,4-dihydroxy-2-thio glycosides, which were obtained by hydrolyses of the 3,4-di-*O*-acetyl-2,6-anhydro-2-thio glycosides **10–14**, using Raney-Ni (W4) as

(29) For 2,6-anhydro-2-thiomannopyranosides synthesis, see: Toshima, K.; Yoshida, T.; Mukaiyama, S.; Tatsuta, K. *Carbohydr. Res.* **1991**, *222*, 173.

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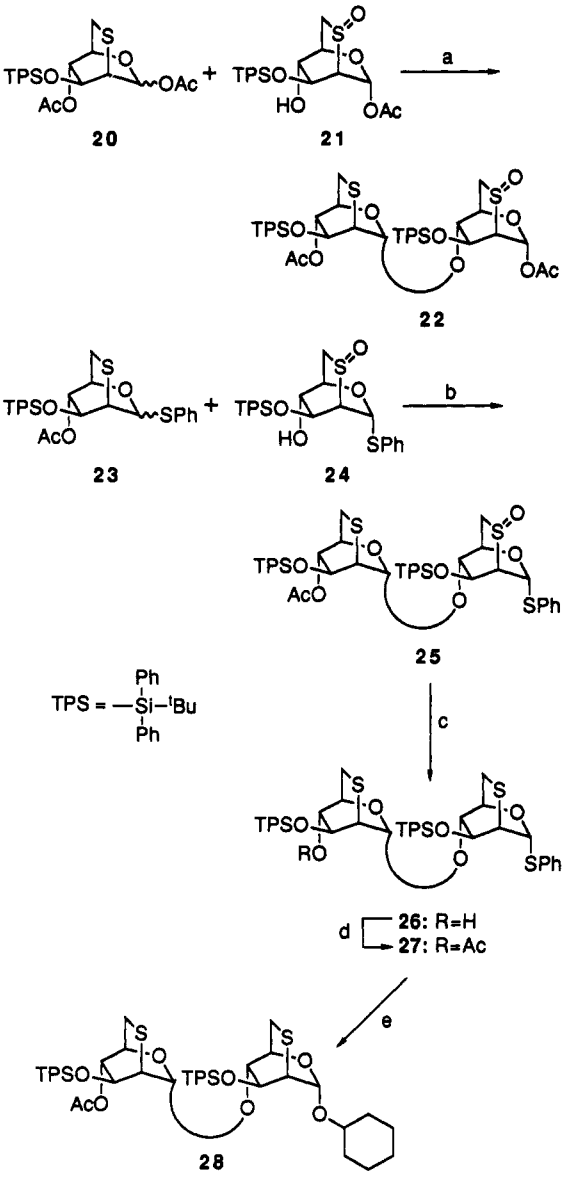
**Scheme 2**[a]




[a] (a) TMSOTf, $CH_2Cl_2$, MS 4 Å, −40 → −15 °C, 30 min, 81%; (b) NIS, TMSOTf, $CH_2Cl_2$, −40 °C, 15 min, 89%; (c) LAH, THF, 86%; (d) $Ac_2O$, 4-DMAP, Py, 90%; (e) **7**, NBS, −40 °C, 20 min, 98%.

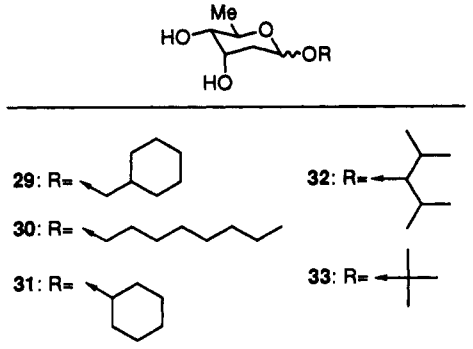
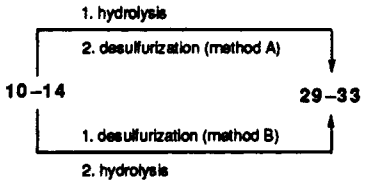



**Figure 6.** 2,6-Dideoxy glycosides.

a catalyst in EtOH at 40 °C. This protocol was quite effective not only for the 2,6-anhydro-3,4-dihydroxy-2-thio glycosides but also for the 3,4-di-*O*-acetyl-2,6-anhydro-2-thio glycosides. The second procedure was reductive desulfurization of the 3,4-di-*O*-acetyl-2,6-anhydro-2-thio glycosides using freshly distilled $Bu_3SnH$ and 2,2′-azobis(isobutyronitrile) (AIBN) in toluene under reflux. In the latter desulfurization reaction, even though a higher temperature and longer reaction time was required and small amounts of byproducts were sometimes produced along with the desired 2,6-dideoxy glycoside, this method would be useful for the chemoselective desulfurization in the presence of other functions affected by hydrogenolysis, such as a double bond.

**Table 6.** Synthesis of 2,6-Dideoxy Glycosides from 2,6-Anhydro-2-thio Glycosides




| entry | 2,6-anhydro-2-thio sugar | hydrolysis[a] yield (%) | desulfurization method[b] | time (h) | yield (%) | 2,6-dideoxy sugar |
|---|---|---|---|---|---|---|
| 1 | **10**-α | 90 | A | 0.5 | 80 | **29**-α |
| 2 | **10**-α | 93 | B | 5 | 71 | **29**-α |
| 3 | **10**-β | 91 | A | 0.5 | 74 | **29**-β |
| 4 | **10**-β | 95 | B | 2 | 86 | **29**-β |
| 5 | **11**-α | 98 | A | 1 | 81 | **30**-α |
| 6 | **11**-α | 94 | B | 5 | 72 | **30**-α |
| 7 | **11**-β | 89 | A | 1 | 80 | **30**-β |
| 8 | **11**-β | 90 | B | 4 | 73 | **30**-β |
| 9 | **12**-α | 91 | A | 3 | 80 | **31**-α |
| 10 | **12**-β | 92 | A | 3 | 75 | **31**-β |
| 11 | **13**-α | 91 | A | 0.5 | 84 | **32**-α |
| 12 | **13**-β | 95 | A | 0.5 | 81 | **32**-β |
| 13 | **14**-α | 85 | A | 1 | 83 | **33**-α |
| 14 | **14**-β | 85 | A | 1 | 80 | **33**-β |

[a] NaOMe, MeOH, rt, 30 min. [b] Method A: $H_2$, Raney-Ni (W4), EtOH, 40 °C. Method B: $Bu_3SnH$, AIBN, PhMe, reflux.

## Conclusions

The present novel *O*-glycosidation methods using several types of 2,6-anhydro-2-thio glycosyl donors offered a promising entry to the stereocontrolled synthesis of 2,6-dideoxy glycosides and oligosaccharides. Furthermore, this novel protocol gave a new trend in highly stereoselective glycosidation, that is, effective utilization of the constructional features of the glycosyl residue in the stereoselective glycosidation reaction. Some significant application of this method to natural product synthesis will be reported elsewhere in detail.[32]

## Experimental Section

**General Procedures.** The melting points were determined on a micro hot-stage Yanaco MP-S3 and were uncorrected. IR spectra were recorded on a BIO RAD DIGILAB FTS-65 spectrometer. Optical rotations were measured on a JASCO DIP-360 photoelectric polarimeter and $^1$H-NMR spectra were on a JEOL GSX270 spectrometer in $CDCl_3$ using TMS as internal standard unless otherwise noted. Silica gel TLC and column chromatography were performed on a Merck TLC 60F-254 and a Merck Kieselgel 60 or Fuji-Davison BW-820MH, respectively. Air- and/or moisture-sensitive reactions were carried out under an atmosphere of argon with oven-dried glassware. In general, organic solvents were purified and dried by the appropriate procedure, and evaporation and concentration were carried out under reduced pressure below 30 °C, unless otherwise noted.

**Phenyl 3,4-Di-*O*-acetyl-2,6-anhydro-1,2-dithio-D-altropyranoside (2).** To an ice-cold solution of methyl 3,4-di-*O*-acetyl-2,6-anhydro-2-thio-α-D-altropyranoside (**1**) (372 mg, 1.35 mmol) in dry $CH_2Cl_2$ (4.0 mL) were added $Me_3SiSPh$ (1.24 mL, 6.75 mmol) and TMSOTf (0.313 mL, 1.62 mmol) under argon. After the resulting solution was stirred under ice-cooling for 30 min, the reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL) and then the mixture was extracted with $CH_2Cl_2$ (5 mL × 3). The extracts were washed with saturated aqueous NaCl (10

(32) For our preliminary communications of those works, see: (a) Toshima, K.; Mukaiyama, S.; Yoshida, T.; Tamai, T.; Tatsuta, K.; *Tetrahedron Lett.* **1991**, *32*, 6155. (b) Toshima, K.; Nozaki, Y.; Nakata, M.; Tatsuta, K.; Kinoshita, M. *Tetrahedron Lett.* **1993**, *34*, 5761.

mL), dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (40 g of silica gel, 3:1 hexane–ethyl acetate) afforded phenyl thioglycoside **2** (430 mg, 90%, $\alpha/\beta = 83/17$) as crystals. $R_f$ 0.60 (1:1 hexane–ethyl acetate); $^1$H-NMR $\delta$ 2.09 (4/23H × 3, s), 2.11 (4/23H × 3, s), 2.17 (19/23H × 3, s), 2.20 (19/23H × 3, s), 2.80 (4/23H, dd, $J$ = 12.0 and 3.0 Hz), 2.83 (19/23H, dd, $J$ = 12.0 and 2.8 Hz), 3.25 (19/23H, dd, $J$ = 12.0 and 3.0 Hz), 3.25–3.3 (4/23H, m), 3.34 (19/23H, d, $J$ = 3.7 Hz), 3.68 (4/23H, dd, $J$ = 12.0 and 2.6 Hz), 4.33 (4/23H, dd, $J$ = 3.0 and 2.6 Hz), 4.41 (19/23H, ddd, $J$ = 3.0, 2.8, and 0.4 Hz), 5.09 (19/23H, dd, $J$ = 8.2 and 0.4 Hz), 5.14 (4/23H, d, $J$ = 8.2 Hz), 5.52 (19/23H, ddd, $J$ = 8.2, 3.7, and 1.0 Hz), 5.58 (4/23H, dd, $J$ = 8.2 and 4.0 Hz), 5.70 (19/23H, br s), 5.82 (4/23H, d, $J$ = 3.4), 7.2–7.6 (5H). Anal. Calcd for $C_{16}H_{18}O_5S_2$: C, 54.22; H, 5.12. Found: C, 53.97; H, 5.25.

**3,4-Di-*O*-acetyl-2,6-anhydro-1-fluoro-2-thio-D-altropyranoside (3).** To a solution of **2** (137 mg, 0.387 mmol) in dry $CH_2Cl_2$ (3.8 mL) were added (diethylamido)sulfur trifluoride (DAST) (0.0767 mL, 0.581 mmol) and NBS (89.6 mg, 0.503 mmol) at –25 °C under argon. After the resulting solution was stirred at –25 °C for 10 min, the reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL) and then the mixture was extracted with $CH_2Cl_2$ (5 mL × 3). The extracts were washed with saturated aqueous NaCl (10 mL), dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (10 g of silica gel, 10:1 toluene-acetone) afforded fluoride **3** (86.0 mg, 84%, $\alpha/\beta = 92/8$) as crystals: $R_f$ 0.44 (3:1 hexane–ethyl acetate); $^1$H-NMR $\delta$ 2.08 and 2.16 (each 23/25H × 3, each s), 2.11 and 2.12 (each 2/25H × 3, each s), 2.7–2.8 (2/25H, m), 2.73 (23/25H, ddd, $J$ = 12.0, 6.0, and 1.8 Hz), 3.06 (23/25H, dd, $J$ = 12.0 and 4.8 Hz), 3.11 (23/25H, ddd, $J$ = 2.1, 2.1, and 1.8 Hz), 3.2–3.25 (2/25H, m), 3.34 (2/25H, dd, $J$ = 11.8 and 2.4 Hz), 4.40 (2/25H, br t, $J$ = 2.4 Hz), 4.54 (23/25H, ddd, $J$ = 4.8, 1.8, and 1.8 Hz), 5.11 (23/25H, dd, $J$ = 9.0 and 1.8 Hz), 5.18 (2/25H, br d, $J$ = 8.2 Hz), 5.36 (23/25H, br d, $J$ = 9.0 Hz), 5.55–5.7 (2/25H, m), 5.92 (23/25H, ddd, $J$ = 66.4, 2.1 and 1.6 Hz), 5.94 (2/25H, $J$ = 67.0 and 3.8 Hz). Anal. Calcd for $C_{10}H_{13}FO_5S$: C, 45.45; H, 4.96. Found: C, 45.77; H, 4.82.

**1,3,4-Tri-*O*-acetyl-2,6-anhydro-2-thio-β-D-altropyanoside (4).** To an ice-cold solution of **1** (122 mg, 0.440 mmol) in acetic anhydride (2.4 mL) was added concd $H_2SO_4$ (0.0024 mL, 0.0440 mmol). After the resulting solution was stirred under ice-cooling for 10 min, the reaction was quenched with saturated aqueous $NaHCO_3$ (70 mL) and then the mixture was extracted with $CHCl_3$ (30 mL × 3). The extracts were washed with saturated aqueous NaCl (70 mL), dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (10 g of silica gel, 1:2 hexane–ether) afforded acetate **4** (115 mg, 86%, $\beta$ only) as a colorless syrup: $R_f$ 0.40 (2:1 hexane–acetone); $[\alpha]^{27}_D$ –5.2° (*c* 1.03, $CHCl_3$); $^1$H-NMR $\delta$ 2.11, 2.12 and 2.17 (each 3H, each s), 2.77 (1H, ddd, $J$ = 12.2, 3.4 and 1.0 Hz), 3.17 (1H, ddd, $J$ = 3.6, 3.6, and 1.0 Hz), 3.29 (1H, dd, $J$ = 12.2 and 3.0 Hz), 4.32 (1H, dd, $J$ = 3.4 and 3.0 Hz), 5.17 (1H, d, $J$ = 8.4 Hz), 5.61 (1H, dd, $J$ = 8.4 and 3.6 Hz), and 6.36 (1H, d, $J$ = 3.6 Hz). Anal. Calcd for $C_{12}H_{16}O_7S$: C, 47.36; H, 5.30. Found: C, 47.56; H, 5.34.

**Glycosidations of 2 by NBS. General Procedure.** To a mixture of **2** (0.1 mmol), alcohol (0.2 mmol), and powdered 4 Å molecular sieves (50 mg) in dry solvent (1 mL) described in Table 1 was added NBS (0.11 mmol) at –40 or –25 °C under argon. After the mixture was stirred at the same temperature for 10, 15, or 30 min, the reaction mixture was diluted with ether and then filtered to remove the molecular sieves. The filtrate was washed with saturated aqueous $NaHCO_3$ (10 mL) and saturated aqueous NaCl (10 mL), dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography gave the corresponding 2,6-anhydro-2-thio glycoside.

**Cyclohexylmethyl 3,4-Di-*O*-acetyl-2,6-anhydro-2-thio-α-D-altropyranoside (10-α). (A) In $CH_2Cl_2$.** Glycosidation of **2** (29.5 mg, 0.0832 mmol) and **5** (0.0194 mL, 0.166 mmol) in dry $CH_2Cl_2$ gave **10-α** (28.0 mg, 94%) as crystals: $R_f$ 0.33 (1:1 hexane–ether); $[\alpha]^{30}_D$ +88.2° (c 1.00, $CHCl_3$); mp 67.0–68.0 °C (hexane); $^1$H-NMR $\delta$ 0.9–1.1 (2H, m), 1.1–1.35 (3H, m), 1.5–1.9 (6H, m), 2.03 (3H, s), 2.12 (3H, s), 2.70 (1H, dd, $J$ = 12.0 and 2.0 Hz), 3.06 (1H, dd, $J$ = 2.6 and 1.2 Hz), 3.08 (1H, dd, $J$ = 12.0 and 4.0 Hz), 3.21 (1H, dd, $J$ = 8.6 and 6.0 Hz), 3.63 (1H, dd, $J$ = 8.6 and 6.0 Hz), 4.38 (1H, ddd, $J$ = 4.0, 2.0 and 1.6 Hz), 5.02 (1H, dd, $J$ = 8.2 and 1.6 Hz), 5.21 (1H, dd, $J$ = 1.2 and 1.2 Hz), 5.30 (1H, ddd, $J$ = 8.2, 2.6, and 1.2 Hz). Anal. Calcd for $C_{17}H_{26}O_6S$: C, 56.96; H, 7.31. Found: C, 56.75; H, 6.94. **(B) In $(CH_2Cl)_2$.** Glycosidation of **2** (22.2 mg, 0.0626 mmol) and **5** (0.0146 mL, 0.125 mmol) in dry $(CH_2Cl)_2$ gave **10-α** (20.3 mg, 92%). **(C) In $Et_2O$.** Glycosidation of **2** (18.6 mg, 0.0524 mmol) and **5** (0.0121 mL, 0.105 mmol) in dry $Et_2O$ gave **10-α** (18.0 mg, 96%). **(D) In THF.** Glycosidation of **2** (24.4 mg, 0.0688 mmol) and **5** (0.0160 mL, 0.137 mmol) in dry THF gave **10-α** (24.0 mg, 98%). **(E) In MeCN.** Glycosidation of **2** (31.0 mg, 0.0875 mmol) and **5** (0.0204 mL, 0.175 mmol) in dry MeCN gave **10-α** (30.5 mg, 97%). **(F) In PhMe.** Glycosidation of **2** (22.2 mg, 0.0626 mmol) and **5** (0.0120 mL, 0.125 mmol) in dry PhMe gave **10-α** (20.6 mg, 92%).

***n*-Octyl 3,4-Di-*O*-acetyl-2,6-anhydro-2-thio-α-D-altropyranoside (11-α).** Glycosidation of **2** (20.4 mg, 0.0576 mmol) and **6** (0.0182 mL, 0.115 mmol) in dry MeCN gave **11-α** (19.6 mg, 91%) as a colorless syrup: $R_f$ 0.41 (3:1 hexane–ethyl acetate); $[\alpha]^{25}_D$ +86.4° (*c* 0.90, $CHCl_3$); $^1$H-NMR $\delta$ 0.88 (3H, t, $J$ = 6.4 Hz), 1.15–1.7 (12H, m), 2.04 and 2.14 (each 3H, each s), 2.71 (1H, dd, $J$ = 11.8 and 2.2 Hz), 3.08 (1H, dd, $J$ = 11.8 and 4.0 Hz), 3.09 (1H, dd, $J$ = 3.0 and 1.6 Hz), 3.40 (1H, dt, $J$ = 8.6 and 6.2 Hz), 3.80 (1H, dt, $J$ = 8.6 and 6.6 Hz), 4.38 (1H, ddd, $J$ = 4.0, 2.2, and 1.6 Hz), 5.01 (1H, dd, $J$ = 8.8 and 1.6 Hz), 5.23 (1H, dd, $J$ = 1.6 and 1.6 Hz), 5.30 (1H, ddd, $J$ = 8.8, 3.0, and 1.6 Hz). Anal. Calcd for $C_{18}H_{30}O_6S$: C, 57.73; H, 8.07. Found: C, 57.79; H, 7.73.

**Cyclohexyl 3,4-Di-*O*-acetyl-2,6-anhdyro-2-thio-α-D-altropyranoside (12-α).** Glycosidation of **2** (22.2 mg, 0.0626 mmol) and **7** (0.0130 mL, 0.125 mmol) in dry MeCN gave **12-α** (19.8 mg, 92%) as crystals: $R_f$ 0.36 (3:1 hexane–ethyl acetate); $[\alpha]^{27}_D$ +120.5° (*c* 0.81, $CHCl_3$); mp 106–107 °C (ethyl acetate–hexane); $^1$H-NMR $\delta$ 1.15–1.95 (10H, m), 2.04 and 2.13 (each 3H, each s), 2.70 (1H, dd, $J$ = 11.8 and 2.2 Hz), 3.07 (1H, dd, $J$ = 3.4 and 1.4 Hz), 3.08 (1H, dd, $J$ = 11.8 and 3.9 Hz), 3.55–3.7 (1H, m), 4.37 (1H, ddd, $J$ = 3.9, 2.2, and 1.2 Hz), 5.01 (1H, dd, $J$ = 8.4 and 1.2 Hz), 5.30 (1H, ddd, $J$ = 8.4, 3.4, and 1.4 Hz), 5.38 (1H, dd, $J$ = 1.4 and 1.4 Hz). Anal. Calcd for $C_{16}H_{24}O_6S$: C, 55.80; H, 7.02. Found: C, 55.96; H, 6.80.

**2,4-Dimethyl-3-pentyl 3,4-Di-*O*-acetyl-2,6-anhydro-2-thio-D-altropyranoside (13).** Glycosidation of **2** (20.2 mg, 0.0570 mmol) and **8** (0.0160 mL, 0.114 mmol) in dry MeCN gave **13-α** (19.2 mg, 93%) as needles and **13-β** (0.6 mg, 2.9%) as a colorless syrup. **13-α**: $R_f$ 0.50 (10:1 toluene–ethyl acetate); $[\alpha]^{22}_D$ +100.5° (*c* 0.75, $CHCl_3$); mp 66.5–67.0 °C (hexane); $^1$H-NMR $\delta$ 0.88, 0.89, 1.00, and 1.01 (each 3H, each d, $J$ = 7.0 Hz), 1.7–1.9 (2H, m), 2.02 and 2.11 (each 3H, each s), 2.69 (1H, dd, $J$ = 11.8 and 2.0 Hz), 3.02 (1H, dd, $J$ = 11.8 and 4.0 Hz), 3.06 (1H, t, $J$ = 7.0 Hz), 3.10 (1H, dd, $J$ = 2.8 and 1.6 Hz), 4.34 (1H, ddd, $J$ = 4.0, 2.0, and 1.6 Hz), 5.01 (1H, dd, $J$ = 9.0 and 1.6 Hz), 5.28 (1H, dd, $J$ = 1.6 and 1.2 Hz), 5.30 (1H, ddd, $J$ = 9.0, 2.8, and 1.2 Hz). Anal. Calcd for $C_{17}H_{28}O_6S$: C, 56.65; H, 7.83. Found: C, 56.72; H, 7.68. **13-β**: $R_f$ 0.42 (10:1 toluene–ethyl acetate); $[\alpha]^{26}_D$ +23.5° (*c* 0.34, $CHCl_3$); $^1$H-NMR $\delta$ 0.89 (6H, br d, $J$ = 6.8 Hz), 1.00 and 1.01 (each 3H, each d, $J$ = 6.8 Hz), 1.8–2.0 (2H, m), 2.09 and 2.10 (each 3H, each s), 2.68 (1H, br dd, $J$ = 11.8 and 3.0 Hz), 3.08 (1H, ddd, $J$ = 3.8, 3.6, and 0.8 Hz), 3.22 (1H, t, $J$ = 5.4 Hz), 3.37 (1H, dd, $J$ = 11.8 and 2.6 Hz), 4.26 (1H, dd, $J$ = 3.0 and 2.6 Hz), 5.14 (1H, d, $J$ = 8.2 Hz), 5.22 (1H, d, $J$ = 3.6 Hz), 5.58 (1H, dd, $J$ = 8.2 and 3.8 Hz). Anal. Calcd for $C_{17}H_{28}O_6S$: C, 56.65; H, 7.83. Found: C, 56.89; H, 8.19.

***tert*-Butyl 3,4-Di-*O*-acetyl-2,6-anhydro-2-thio-D-altropyranoside (14).** Glycosidation of **2** (22.0 mg, 0.0620 mmol) and **9** (0.0116 mL, 0.124 mmol) in dry MeCN gave **14** (18.2 mg, 92%, $\alpha/\beta = 83/17$)) as a mixture of anomers: $R_f$ 0.42 (10:1 toluene–ethyl acetate); $^1$H-NMR $\delta$ 1.24 (83/100H × 9, s), 1.31 (17/100H × 9, s), 2.04 and 2.15 (each 83/100H × 3, each s), 2.11 and 2.13 (each 17/100H × 3, each s), 2.66 (17/100H, ddd, $J$ = 11.8, 3.8, and 0.8 Hz), 2.69 (83/100H, dd, $J$ = 12.0 and 3.6 Hz), 2.88 (17/100H, dd, $J$ = 4.0, 3.6 and 0.8 Hz), 3.08 (83/100H, br d, $J$ = 3.8 Hz), 3.11 (83/100H, dd, $J$ = 12.0 and 3.0 Hz), 3.33 (17/100H, dd, $J$ = 11.8 and 2.4 Hz), 4.22 (17/100H, br dd, $J$ = 3.8 and 2.4 Hz), 4.38 (83/100H, ddd, $J$ = 3.6, 3.0, and 1.0 Hz), 4.95 (83/100H, dd, $J$ = 8.4 and 1.0 Hz), 5.17 (17/100H, dd, $J$ = 8.4 and 0.6 Hz), 5.29 (83/100H, ddd, $J$ = 8.4, 3.8, and 1.6 Hz), 5.43 (17/100H, d, $J$ = 3.6 Hz), 5.41 (83/100H, dd, $J$ = 1.6 and 1.4 Hz), 5.58 (17/100H, dd, $J$ = 8.4 and 4.0 Hz). Anal. Calcd for $C_{14}H_{22}O_6S$: C, 52.81; H, 6.96. Found: C, 52.89; H, 6.55.

**Glycosidations of 3 and 5. (A) With $SnCl_2$–$AgClO_4$.** To a mixture of **3** (15.0 mg, 0.0568 mmol), **5** (0.0132 mL, 0.114 mmol), and powdered 4 Å molecular sieves (28 mg) in dry $Et_2O$ (0.56 mL) were added $SnCl_2$ (11.8 mg, 0.0624 mmol) and $AgClO_4$ (0.013 mg, 0.0624 mmol) at –10 °C under argon. After the resulting mixture was stirred at –10 °C for 1.5 h, the reaction mixture was diluted with ether (0.56 mL) and then filtered. The filterate was washed with saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous NaCl (5 mL), dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2.4 g of silica gel, 10:1 toluene–acetone) gave **10** (20.0 mg, 98%, $\alpha/\beta = 97/3$) as crystals. **10-β**: $R_f$ 0.56 (10:1 toluene–acetone); $[\alpha]^{27}_D$ –10.7° (*c* 1.05, $CHCl_3$); mp 137.5–138.5 °C (ethyl acetate–hexane);

$^1$H-NMR δ 0.85–1.9 (11H, m), 2.11 and 2.12 (each 3H, each s), 2.68 (1H, ddd, $J$ = 11.8, 3.4, and 1.0 Hz), 3.07 (1H, ddd, $J$ = 3.8, 3.6 and 1.0 Hz), 3.29 (1H, dd, $J$ = 11.8 and 2.6 Hz), 3.36 (1H, dd, $J$ = 9.6 and 6.2 Hz), 3.68 (1H, dd, $J$ = 9.6 and 6.8 Hz), 4.25 (1H, dd, $J$ = 3.4 and 2.6 Hz), 5.16 (1H, d, $J$ = 3.6 Hz), 5.17 (1H, d, $J$ = 8.2 Hz), 5.59 (1H, dd, $J$ = 8.2 and 3.8 Hz). Anal. Calcd for $C_{17}H_{26}O_6S$: C, 56.96; H, 7.31. Found: C, 56.69; H, 6.94. **(B) With $SnCl_2$–$ZnCl_2$.** To a mixture of **3** (14.6 mg, 0.0552 mmol), **5** (0.0128 mL, 0.110 mmol), and powdered 4 Å molecular sieves (28 mg) in dry $Et_2O$ (0.56 mL) were added $SnCl_2$ (11.6 mg, 0.0668 mmol) and $ZnCl_2$ (0.0081 mg, 0.0668 mmol) at –10 °C under argon. After the resulting mixture was stirred at –10 °C for 1.5 h, the reaction mixture was worked up and purified as described above to give **10** (17.6 mg, 89%, α/β = 98/2). **(C) With $SnCl_2$.** To a mixture of **3** (15.0 mg, 0.0568 mmol), **5** (0.0134 mL, 0.114 mmol), and powdered 4 Å molecular sieves (28 mg) in dry $Et_2O$ (0.56 mL) was added $SnCl_2$ (11.8 mg, 0.0624 mmol) at –10 °C under argon. After the resulting mixture was stirred at –10 °C for 1.5 h, the reaction mixture was worked up and purified as described above to give **10**-α (20.0 mg, 91%). **(D) With TMSOTf.** To a mixture of **3** (15.0 mg, 0.0568 mmol), **5** (0.0134 mL, 0.114 mmol), and powdered 4 Å molecular sieves (28 mg) in dry $Et_2O$ (0.56 mL) was added TMSOTf (0.0110 mL, 0.0568 mmol) at –10 °C under argon. After the resulting mixture was stirred at –10 °C for 1.5 h, the reaction mixture was worked up and purified as described above to give **10** (18.4 mg, 90%, α/β = 92/8). **(E) With $Cp_2HfCl_2$–$AgClO_4$.** To a mixture of **3** (15.0 mg, 0.0568 mmol), **5** (0.0134 mL, 0.114 mmol), and powdered 4 Å molecular sieves (28 mg) in dry $CH_2Cl_2$ (0.56 mL) were added $Cp_2HfCl_2$ (108 mg, 0.282 mmol) and $AgClO_4$ (58.4 mg, 0.282 mmol) at –10 °C under argon. After the resulting mixture was stirred at –10 → 25 °C for 1.5 h, the reaction mixture was worked up and purified as described above to give **10** (19.4 mg, 95%, α/β = 93/7). **(E) With $Cp_2ZrCl_2$–$AgBF_4$.** To a mixture of **3** (15.0 mg, 0.0568 mmol), **5** (0.0134 mL, 0.114 mmol), and powdered 4 Å molecular sieves (28 mg) in dry $CH_2Cl_2$ (0.56 mL) were added $Cp_2ZrCl_2$ (10.0 mg, 0.034 mmol) and $AgBF_4$ (13.2 mg, 0.0682 mmol) at –20 °C under argon. After the resulting mixture was stirred at –20 → 10 °C for 2 h, the reaction mixture was worked up and purified as described above to give **10** (18.8 mg, 92%, α/β = 98/2).

**12**: To a mixture of **3** (12.2 mg, 0.0462 mmol), **7** (0.0096 mL, 0.0924 mmol) and powdered 4 Å molecular sieves (23 mg) in dry $Et_2O$ (0.46 mL) was added $SnCl_2$ (9.6 mg, 0.0508 mmol) at –10 °C under argon. After the resulting mixture was stirred at –10 °C for 1.5 h, the reaction mixture was worked up and purified as described above to give **12** (15.0 mg, 94%, α/β = 98/2). **12**-β: $R_f$ 0.50 (10:1 toluene–acetone); $[\alpha]^{27}_D$ –23.6° ($c$ 1.06, $CHCl_3$); mp 165–166 °C (ethyl acetate–hexane, needles); $^1$H-NMR δ 1.15–2.1 (10H, m), 2.11 and 2.12 (each 3H, each s), 2.68 (1H, br dd, $J$ = 12.0 and 3.4 Hz), 3.02 (1H, ddd, $J$ = 4.2 and 3.6 Hz), 3.33 (1H, dd, $J$ = 12.0 and 2.8 Hz), 3.74 (1H, m), 4.25 (1H, dd, $J$ = 3.4 and 2.8 Hz), 5.16 (1H, d, $J$ = 8.2 Hz), 5.34 (1H, d, $J$ = 3.6 Hz), 5.58 (1H, dd, $J$ = 8.2 and 4.2 Hz). Anal. Calcd for $C_{16}H_{24}O_6S$: C, 55.80; H, 7.02. Found: C, 55.87; H, 6.69.

**13**: To a mixture of **3** (20.0 mg, 0.0756 mmol), **8** (0.0212 mL, 0.151 mmol), and powdered 4 Å molecular sieves (38 mg) in dry $Et_2O$ (0.76 mL) was added $SnCl_2$ (15.8 mg, 0.0832 mmol) at –10 °C under argon. After the resulting mixture was stirred at –10 °C for 2.4 h, the reaction mixture was worked up and purified as described above to give **13** (20.8 mg, 76%, α/β = 98/2).

**14**: To a mixture of **3** (15.6 mg, 0.0590 mmol), **9** (0.0112 mL, 0.118 mmol) and powdered 4 Å molecular sieves (30 mg) in dry $Et_2O$ (0.6 mL) was added $SnCl_2$ (12.4 mg, 0.065 mmol) at –10 °C under argon. After the resulting mixture was stirred at –10 °C for 1.5 h, the reaction mixture was worked up and purified as described above to give **14** (15.2 mg, 81%, α/β = 96/4).

**Glycosidations of 4 by Lewis acid. General Procedure.** To a mixture of **4** (0.1 mmol) and alcohol (0.2 mmol) in dry solvent (1 mL) described in Table 5 was added a Lewis acid (0.11 or 0.22 mmol) at –10 °C under argon. After the mixture was stirred at –10 °C for 30 or 60 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL) and then the resulting mixture was extracted with $CHCl_3$ (10 mL × 3). The extracts were washed with saturated aqueous NaCl (10 mL), dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography gave the corresponding 2,6-anhydro-2-thio glycoside.

**10: (A) with TMSOTf in $CH_2Cl_2$.** Glycosidation of **4** (93.0 mg, 0.306 mmol) and **5** (0.072 mL, 0.612 mmol) by TMSOTf (0.0644 mL, 0.336 mmol) for 30 min gave **10** (96.6 mg, 89%, α/β = 2/98). **(B) With $Tf_2O$ in $CH_2Cl_2$.** Glycosidation of **4** (18.0 mg, 0.0592 mmol) and **5** (0.0138 mL, 0.118 mmol) by $Tf_2O$ (0.011 mL, 0.0651 mmol) for 30 min gave **10** (19.0 mg, 90%, α/β = 5/95). **(C) With $SnCl_4$ in $CH_2Cl_2$.** Glycosidation of **4** (52.0 mg, 0.171 mmol) and **5** (0.040 mL, 0.342 mmol) by 1.0 M $SnCl_4$–$CH_2Cl_2$ (0.188 mL, 0.188 mmol) for 30 min gave **10** (53.9 mg, 88%, α/β = 5/95). **(D) With $TrClO_4$ in $CH_2Cl_2$.** Glycosidation of **4** (30.6 mg, 0.101 mmol) and **5** (0.024 mL, 0.201 mmol) by $TrClO_4$ (75.9 mg, 0.221 mmol) for 1 h gave **10** (32.4 mg, 90%, α/β = 3/97).

**11**: Glycosidation of **4** (26.0 mg, 0.0855 mmol) and **6** (0.027 mL, 0.171 mmol) by TMSOTf (0.018 mL, 0.094 mmol) for 30 min gave **11** (30.5 mg, 95%, α/β = 2/98). **11**-β: $R_f$ 0.47 (10:1 toluene–acetone); $[\alpha]^{27}_D$ –11.2° ($c$ 1.09, $CHCl_3$); $^1$H-NMR δ 0.88 (3H, t, $J$ = 7.2 Hz), 1.2–1.7 (12H, m), 2.11 (6H, br s), 2.69 (1H, br dd, $J$ = 11.8 and 3.7 Hz), 3.06 (1H, ddd, $J$ = 4.2, 3.6, and 0.6 Hz), 3.30 (1H, dd, $J$ = 11.8 and 2.6 Hz), 3.58 and 3.87 (each 1H, each dt, $J$ = 9.8 and 6.4 Hz), 4.26 (1H, dd, $J$ = 3.7 and 2.6 Hz), 5.18 (1H, d, $J$ = 8.4 Hz), 5.19 (1H, d, $J$ = 3.6 Hz), 5.59 (1H, dd, $J$ = 8.4 and 4.2 Hz). Anal. Calcd for $C_{18}H_{30}O_6S$: C, 57.73; H, 8.07. Found: C, 57.73; H, 7.81.

**12**: Glycosidation of **4** (22.2 mg, 0.0730 mmol) and **7** (0.0154 mL, 0.146 mmol) by TMSOTf (0.0154 mL, 0.0803 mmol) for 30 min gave **12** (21.3 mg, 85%, α/β = 1/99).

**13**: Glycosidation of **4** (41.8 mg, 0.137 mmol) and **8** (0.0386 mL, 0.275 mmol) by TMSOTf (0.0289 mL, 0.151 mmol) for 30 min gave **13** (39.4 mg, 76%, α/β = 5/95).

**3,4-Di-*O*-acetyl-2,6-anhydro-1-fluoro-2-sulfinyl-α-D-altropyranosides (17 and 18).** To an ice-cold solution of **3**-α (44.0 mg, 0.166 mmol) in dry $CH_2Cl_2$ (0.88 mL) was added *m*CPBA (31.5 mg, 0.183 mmol). After the mixture was stirred under ice-cooling for 30 min, the reaction was quenched with saturated aqueous $NaHCO_3$ (1 mL) and then the resulting mixture was extracted with $CHCl_3$ (1 mL × 3). The extracts were washed with saturated aqueous NaCl (3 mL), dired over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (1 g of silica gel, 1:3 hexane–ethyl acetate) gave **17** (14.7 mg, 31%) and **18** (31.1 mg, 67%) as crystals. **17**: $R_f$ 0.46 (1:3 hexane–ethyl acetate); IR ($CHCl_3$) 1057 cm$^{-1}$ (sulfoxide); $[\alpha]^{27}_D$ –120.3° ($c$ 0.66, $CHCl_3$); mp 182.5–183.0 °C (ethyl acetate–hexane); $^1$H-NMR δ 2.13 (3H, s), 2.15 (3H, s), 2.39 (1H, d, $J$ = 14.0 Hz), 3.78 (1H, br s), 3.80 (1H, dd, $J$ = 14.0 and 5.9 Hz), 4.56 (1H, dd, $J$ = 5.9 and 2.5 Hz), 5.42 (1H, dd, $J$ = 8.4 and 2.5 Hz), 5.68 (1H, br ddd, $J$ = 62.8, 2.0 and 1.0 Hz), 5.80 (1H, ddd, $J$ = 8.4, 2.2 and 1.0 Hz). Anal. Calcd for $C_{10}H_{13}FO_6S$: C, 42.86; H, 4.68. Found: C, 42.59; H, 4.77. **18**: $R_f$ 0.43 (1:3 hexane–ethyl acetate); IR ($CHCl_3$) 1050 cm$^{-1}$ (sulfoxide); $[\alpha]^{27}_D$ –71.6° ($c$ 0.74, $CHCl_3$); mp 165.0–165.5 °C (ethyl acetate–hexane, needles); $^1$H-NMR δ 2.13 (3H, s), 2.17 (3H, s), 2.88 (1H, dd, $J$ = 14.8 and 6.0 Hz), 3.27 (1H, dd, $J$ = 14.8 and 3.9 Hz), 3.83 (1H, br s), 4.75 (1H, br d, $J$ = 8.4 Hz), 4.78 (1H, dd, $J$ = 6.0 and 3.9 Hz), 5.02 (1H, dd, $J$ = 8.4 and 2.2 Hz), 6.20 (1H, ddd, $J$ = 63.4, 2.4 and 1.6 Hz). Anal. Calcd for $C_{10}H_{13}FO_6S$: C, 42.86; H, 4.68. Found: C, 42.88; H, 4.51.

**3,4-Di-*O*-acetyl-2,6-anhydro-1-fluoro-2-sulfonyl-α-D-altropyranoside (19).** To an ice-cold solution of **3**-α (87.0 mg, 0.330 mmol) in dry $CH_2Cl_2$ (1.7 mL) was added *m*CPBA (119 mg, 0.693 mmol). After the mixture was stirred at 26 °C for 3 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (2 mL) and then the resulting mixture was extracted with $CHCl_3$ (2 mL × 3). The extracts were washed with saturated aqueous NaCl (8 mL), dreid over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (3 g of silica gel, 3:2 hexane–ethyl acetate) gave **19** (89.3 mg, 95%) as needles: $R_f$ 0.85 (1:3 hexane–ethyl acetate); $[\alpha]^{27}_D$ –72.5° ($c$ 1.09, $CHCl_3$); mp 193.0–194.0 °C (chloroform–hexane, needles); $^1$H-NMR δ 2.14 (3H, s), 2.16 (3H, s), 3.25 (1H, dd, $J$ = 14.0 and 1.2 Hz), 3.64 (1H, ddd, $J$ = 14.0, 6.0, and 1.1 Hz), 3.68 (1H, br s), 4.85 (1H, br d, $J$ = 6.0 Hz), 5.37 (1H, dd, $J$ = 8.4 and 2.2 Hz), 5.73 (1H, br d, $J$ = 8.4 Hz), 6.21 (1H, ddd, $J$ = 62.0, 2.1, and 1.2 Hz). Anal. Calcd for $C_{10}H_{13}FO_7S$: C, 40.54; H, 4.42. Found: C, 40.29; H, 4.29.

**1-*O*-Acetyl-4-*O*-(4-*O*-acetyl-2,6-anhydro-3-*O*-(*tert*-butyldiphenylsilyl)-2-thio-α-D-mannopyranosyl)-2,6-anhydro-3-*O*-(*tert*-butyldiphenylsilyl)-2-sulfinyl-α-D-mannopyranose (22).** To a suspension of **20** (82.0 mg, 0.164 mmol), **21** (54.0 mg, 0.114 mmol), and 4 Å molecular sieves (82 mg) in dry $CH_2Cl_2$ (1.2 mL) was added TMSOTf (0.035 mL, 0.180 mmol) at –40 °C under argon, and the mixture was allowed to warm to –15 °C for 30 min with stirring. The reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL) and then the resulting mixture was extracted with $CHCl_3$ (5 mL × 3). The extracts were washed with saturated aqueous NaCl (10 mL), dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (20 g of silica gel, 1:1 hexane–ethyl acetate) gave **22** (84.1 mg, 81%) as needles: $R_f$ 0.29 (1:2 hexane–ethyl acetate); $[\alpha]^{29}_D$ –23.8° ($c$ 0.74, $CHCl_3$); mp

211.2–212.6 °C (chloroform–hexane, needles); $^1$H-NMR δ 1.03 (9H, s), 1.05 (9H, s), 1.31 (3H, s), 1.80 (3H, s). 2.26 (1H, dd, $J$ = 3.2 and 2.1 Hz), 2.7–2.85 (3H, m), 3.31 (1H, br s), 3.34 (1H, br d, $J$ = 14.0 Hz), 3.59 (1H, dd, $J$ = 5.2 and 2.2 Hz), 4.10 (1H, br s), 4.32 (1H, br d, $J$ = 5.2 Hz), 4.52 (1H, dd, $J$ = 2.6 and 2.2 Hz), 4.55–4.65 (2H, m), 4.56 (1H, d, $J$ = 2.1 Hz). 6.44 (1H, d, $J$ = 2.2 Hz), 7.15–7.7 (20H). Anal. Calcd for $C_{48}H_{58}O_{10}S_2Si_2$: C, 62.99; H, 6.39. Found: C, 62.79; H, 6.15.

**Phenyl 4-*O*-(4-*O*-Acetyl-2,6-anhydro-3-*O*-(*tert*-butyldiphenylsilyl))-2-thio-α-D-mannopyranosyl)-2,6-anhydro-3-*O*-(*tert*-butyldiphenylsilyl)-2-sulfinyl-1-thio-α-D-mannopyranoside (25).** To a solution of **23** (65.7 mg, 0.119 mmol) and **24** (43.6 mg, 0.0831 mmol) in dry $CH_2Cl_2$ (0.85 mL) were added NIS (30.5 mg, 0.137 mmol) and TMSOTf (0.0253 mL, 0.131 mmol) at –40 °C under argon. After the resulting solution was stirred at –40 °C for 15 min, the reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL) and then the mixture was extracted with $CHCl_3$ (5 mL × 3). The extracts were washed with saturated aqueous $Na_2S_2O_3$ (10 mL) and saturated aqueous NaCl (10 mL), dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (16 g of silica gel, 1:1 hexane–ethyl acetate) gave **25** (71.3 mg, 89%) as a white form: $R_f$ 0.30 (1:1 hexane–ethyl acetate); $[\alpha]^{29}_D$ –15.1° ($c$ 1.06, $CHCl_3$); $^1$H-NMR δ 1.02 (9H, s), 1.06 (9H, s), 1.81 (3H, s), 2.25 (1H, dd, $J$ = 3.8 and 2.0 Hz), 2.72 (1H, dd, $J$ = 14.4 and 5.6 Hz), 2.75–2.9 (2H, m), 3.30 (1H, br s), 3.33 (1H, dd, $J$ = 14.4 and 1.4 Hz), 3.66 (1H, dd, $J$ = 4.8 and 1.5 Hz), 4.09 (1H, br m), 4.43 (1H, br d, $J$ = 5.6 Hz), 4.47 (1H, d, $J$ = 2.0 Hz), 4.53 (1H, d, $J$ = 4.8 Hz), 4.64 (1H, dd, $J$ = 2.3 and 1.9 Hz), 4.77 (1H, dd, $J$ = 3.8 and 2.3 Hz), 5.86 (1H, d, $J$ = 2.0 Hz), 7.25–7.8 (25H). Anal. Calcd for $C_{52}H_{60}O_8S_3Si_2$: C, 64.70; H, 6.26. Found: C, 64.96; H, 6.55.

**Phenyl 2,6-Anhydro-4-*O*-(2,6-anhydro-3-*O*-(*tert*-butyldiphenylsilyl)-2-thio-α-D-mannopyranosyl)-3-*O*-(*tert*-butyldiphenylsilyl)-1,2-dithio-α-D-mannopyranoside (26).** To an ice-cold solution of **25** (14.5 mg, 0.0150 mmol) in dry THF (0.3 mL) was added 1 M LAH–THF (0.0225 mL, 0.0225 mmol) under argon. After the resulting mixture was stirred under ice-cooling for 1 h, the reaction was quenched with $H_2O$ (1.1 mL). The mixture was filtered and then the filtrate was concentrated *in vacuo*. Purification of the residue by flash column chromatography (3 g of silica gel, 1:4 hexane–ethyl acetate) gave **26** (11.7 mg, 86%) as a white form: $R_f$ 0.46 (2:1 hexane–ethyl acetate); $[\alpha]^{30}_D$ +10.8° ($c$ 1.09, $CHCl_3$); $^1$H-NMR δ 1.03 (9H, s), 1.04 (9H, s), 2.25 (1H, dd, $J$ = 4.8 and 3.0 Hz), 2.67 (1H, br d, $J$ = 11.4 Hz), 2.74 (1H, dd, $J$ = 11.9 and 1.7 Hz), 2.85 (1H, dd, $J$ = 11.4 and 6.0 Hz), 2.87 (1H, dd, $J$ = 4.0 and 2.1 Hz), 3.06 (1H, dd, $J$ = 11.9 and 4.4 Hz), 3.39 (1H, br s), 3.4–3.45 (2H, m), 4.15 (1H, br d, $J$ = 6.0 Hz), 4.35 (1H, $J$ = 4.4 and 1.7 Hz), 4.48 (1H, d, $J$ = 3.0 Hz), 4.59 (1H, d, $J$ = 4.8 Hz), 4.6–4.7 (1H, m), 5.54 (1H, d, $J$ = 2.1 Hz), 7.1–7.8 (25H). Anal. Calcd for $C_{50}H_{58}O_6S_3Si_2$: C, 66.19; H, 6.44. Found: C, 66.38; H, 6.37.

**Phenyl 4-*O*-(4-*O*-Acetyl-2,6-anhydro-3-*O*-(*tert*-butyldiphenylsilyl)-2-thio-α-D-mannopyranosyl)-2,6-anhydro-3-*O*-(*tert*-butyldiphenylsilyl)-1,2-dithio-α-D-mannopyranoside (27).** To an ice-cold solution of **26** (35.1 mg, 0.0387 mmol) in dry pyridine (0.71 mL) was added acetic anhydride (0.177 mL) and 4-DMAP (0.6 mg, 0.0039 mmol). After the resulting solution was stirred under ice-cooling for 30 min, the mixture was poured into $H_2O$ (0.3 mL) and then extracted with ethyl acetate (0.5 mL × 3). The extracts were washed with saturated aqueous NaCl (1 mL), dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (9 g of silica gel, 20:1 toluene–ether) gave **27** (33.0 mg, 90%) as a colorless syrup: $R_f$ 0.31 (4:1 hexane–ethyl acetate); $[\alpha]^{30}_D$ +10.9° ($c$ 0.11, $CHCl_3$); $^1$H-NMR δ 1.05 (9H, s), 1.08 (9H, s), 1.76 (3H, s), 2.38 (1H, dd, $J$ = 3.8 and 2.0 Hz), 2.73 (1H, dd, $J$ = 2.9 and 1.7 Hz), 2.80 (1H, br d, $J$ = 11.9 Hz), 2.81 (1H, br d, $J$ = 11.9 Hz), 2.89 (1H, dd, $J$ = 11.9 and 4.1 Hz), 3.04 (1H, dd, $J$ = 11.9 and 4.0 Hz), 3.69 (1H, d, $J$ = 3.2 Hz), 4.10 (1H, m), 4.29 (1H, m), 4.55 (1H, dd, $J$ = 3.2 and 2.9 Hz), 4.64 (1H, dd, $J$ = 3.0 and 1.5 Hz), 4.72 (1H, dd, $J$ = 3.8 and 3.0 Hz), 5.00 (1H, d, $J$ = 2.0 Hz), 5.54 (1H, d, $J$ = 1.7 Hz), 7.25–7.8 (15H). Anal. Calcd for $C_{52}H_{60}O_7S_3Si_2$: C, 65.79; H, 6.37. Found: C, 65.85; H, 6.11.

**Cyclohexyl 4-*O*-(4-*O*-Acetyl-2,6-anhydro-3-*O*-(*tert*-butyldiphenylsilyl)-2-thio-α-D-mannopyranosyl)-2,6-anhydro-3-*O*-(*tert*-butyldiphenylsilyl)-2-thio-α-D-mannopyranoside (28).** To a mixture of **27** (55.0 mg, 0.0580 mmol), **7** (0.0120 mL, 0.116 mmol), and powdered 4 Å molecular sieves (28.6 mg) in dry $CH_2Cl_2$ (0.58 mL) was added NBS (11.4 mg, 0.0638 mmol) at –40 °C under argon. After the resulting mixture was stirred at the same temperature for 20 min, the mixture was diluted with ether (1 mL) and then filtered to remove the molecular sieves. The filterate was washed with saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous NaCl (5 mL), dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (12 g of silica gel, 6:1 hexane–ethyl acetate) gave **28** (53.4 mg, 98%) as crystals: $R_f$ 0.26 (6:1 hexane–ethyl acetate); $[\alpha]^{30}_D$ –13.3° ($c$ 0.90, $CHCl_3$); mp 117.5–118 °C (ether–hexane); $^1$H-NMR δ 1.0–1.6 (10H, m), 1.05 (9H, s), 1.06 (9H, s), 1.78 (3H, s), 2.33 (1H, dd, $J$ = 3.8 and 2.0 Hz), 2.50 (1H, dd, $J$ = 2.9 and 1.8 Hz), 2.70 (1H, dd, $J$ = 11.2 and 2.0 Hz), 2.78 (1H, dd, $J$ = 11.8 and 2.0 Hz), 2.86 (1H, dd, $J$ = 11.8 and 4.2 Hz), 2.88 (1H, dd, $J$ = 11.2 and 3.6 Hz), 3.35–3.45 (1H, m), 3.61 (1H, d, $J$ = 3.7 Hz), 4.10 (1H, m), 4.25 (1H, m), 4.55–4.65 (2H, m), 4.66 (1H, dd, $J$ = 3.8 and 3.0 Hz), 5.04 (1H, d, $J$ = 2.0 Hz), 5.12 (1H, d, $J$ = 1.8 Hz), 7.25–7.8 (20H). Anal. Calcd for $C_{52}H_{66}O_8S_2Si_2$: C, 66.49; H, 7.08. Found: C, 65.50; H, 6.79.

**Synthesis of 2,6-Dideoxy Glycosides from 2,6-Anhydro-2-thio Glycosides. General Procedure. (1) Hydrolysis:** To an ice-cold solution of 3,4-di-*O*-acetyl-2,6-anhydro-2-thio glycoside or 3,4-di-*O*-acetyl-2,6-dideoxy glycoside (0.1 mmol) in dry MeOH (1 mL) was added 5 N NaOMe–MeOH (0.3 mmol). After the resulting solution was stirred at room temperature for 30 min, the reaction mixture was made neutral with solid $CO_2$ and then concentrated. The residue was diluted with water (5 mL) and extracted with $CHCl_3$ (3 mL × 3). The extracts were washed with saturated aqueous NaCl (5 mL), dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification of the residue by flash column chromatography gave the corresponding 3,4-dihydroxy glycoside. **(2) Desulfurization: Method A.** To a solution of 2,6-anhydro-3,4-dihydroxy-2-thio glycoside (0.1 mmol) in EtOH (or EtOH–dioxane (4:1)) (0.5 mL) was added a catalytic amount of Raney-Ni (W4). After the reaction mixture was vigorously stirred at 40 °C for 0.5–2 h under $H_2$, the mixture was filtered and the catalyst was washed with MeOH. The combined filtrate and washings were concentrated *in vacuo*. Purification of the residue by flash column chromatography gave the corresponding 2,6-dideoxy-3,4-dihydroxy glycoside. **Method B.** To a solution of 3,4-di-*O*-acetyl-2,6-anhydro-2-thio glycoside (0.1 mmol) in dry toluene (1 mL) was added freshly distilled $Bu_3SnH$ (0.5 mmol) and a catalytic amount of AIBN under argon. After the resulting mixture was stirred at 110 °C for 1–5 h under argon, the mixture was cooled and concentrated *in vacuo*. Purification of the residue by flash column chromatography gave the corresponding 3,4-di-*O*-acetyl-2,6-dideoxy glycoside.

**Cyclohexylmethyl 2,6-Dideoxy-α-D-*ribo*-hexopyranoside (29-α). 10-α** (60.0 mg, 0.167 mmol) gave **29-α** (29.4 mg, 72% overall yield) as a colorless syrup through method A: $R_f$ 0.29 (1:2 hexane–ether); $[\alpha]^{20}_D$ +121° ($c$ 1.13, $CHCl_3$); $^1$H-NMR δ 0.85–1.85 (11H, m), 1.32 (3H, d, $J$ = 6.2 Hz), 1.90 (1H, ddd, $J$ = 14.8, 3.4, and 3.4 Hz), 2.18 (1H, ddd, $J$ = 14.8, 3.4, and 1.4 Hz), 2.49 (1H, d, $J$ = 10.6 Hz), 3.13 (1H, ddd, $J$ = 10.6, 10.2, and 3.6 Hz), 3.18 (1H, dd, $J$ = 9.6 and 6.0 Hz), 3.51 (1H, dd, $J$ = 9.6 and 6.4 Hz), 3.57 (1H, d, $J$ = 10.0 Hz), 3.69 (1H, dq, $J$ = 10.2 and 6.2 Hz), 3.94 (1H, dddd, $J$ = 10.0, 3.6, 3.4, and 3.4 Hz), 4.84 (1H, br d, $J$ = 3.4 Hz). Anal. Calcd for $C_{13}H_{24}O_4$: C, 63.91; H, 9.90. Found: C, 63.70; H, 9.56. **10-α** (42.3 mg, 0.118 mmol) gave **29-α** (18.4 mg, 66% overall yield) through method B.

**Cyclohexylmethyl 2,6-Dideoxy-β-D-*ribo*-hexopyranoside (29-β). 10-β** (101.7 mg, 0.284 mmol) gave **29-β** (46.4 mg, 67% overall yield) as a colorless syrup through method A: $R_f$ 0.39 (1:1 hexane–ethyl acetate); $[\alpha]^{27}_D$ –32.3° ($c$ 1.61, $CHCl_3$); $^1$H-NMR δ 0.8–1.85 (12H, m), 1.30 (3H, d, $J$ = 6.2 Hz), 2.10 (1H, ddd, $J$ = 13.9, 3.6, and 2.0 Hz), 2.22 (1H, d, $J$ = 6.8 Hz), 2.43 (1H, br s), 3.22 (1H, dd, $J$ = 9.8 and 6.9 Hz), 3.32 (1H, ddd, $J$ = 9.6, 6.8 and 3.6 Hz), 3.68 (1H, dd, $J$ = 9.8 and 6.0 Hz), 3.72 (1H, dq, $J$ = 9.6 and 6.2 Hz), 4.12 (1H, br m), 4.77 (1H, dd, $J$ = 9.7 and 2.0 Hz). Anal. Calcd for $C_{13}H_{24}O_4$: C, 63.91; H, 9.90. Found: C, 63.58; H, 9.60. **10-β** (30.3 mg, 0.0845 mmol) gave **29-β** (16.2 mg, 82% overall yield) through method B.

***n*-Octyl 2,6-Dideoxy-α-D-*ribo*-hexopyranoside (30-α). 11-α** (30.3 mg, 0.0809 mmol) gave **30-α** (16.6 mg, 79% overall yield) as a colorless syrup through method A: $R_f$ 0.47 (1:1 hexane–ethyl acetate); $[\alpha]^{24}_D$ +108° ($c$ 0.97, $CHCl_3$); $^1$H-NMR δ 0.89 (3H, t, $J$ = 6.8 Hz), 1.2–1.65 (10H, m), 1.32 (3H, d, $J$ = 6.2 Hz), 1.91 (1H, ddd, $J$ = 14.6, 3.4 and 3.4 Hz), 2.18 (1H, ddd, $J$ = 14.6, 3.4 and 1.2 Hz), 2.51 (1H, d, $J$ = 10.4 Hz), 3.13 (1H, ddd, $J$ = 10.2, 10.2, and 3.6 Hz), 3.37 (1H, dt, $J$ = 9.6 and 6.6 Hz), 3.58 (1H, d, $J$ = 10.2 Hz), 3.70 (1H, dt, $J$ = 9.6 and 6.8 Hz), 3.71 (1H, dq, $J$ = 10.2 and 6.2 Hz), 3.95 (1H, dddd, $J$ = 10.4, 3.6, 3.4, and 3.4 Hz), 4.87 (1H, br d, $J$ = 3.4 Hz). Anal. Calcd for $C_{14}H_{28}O_4$: C, 64.58; H, 10.84. Found: C, 64.58; H, 10.71. **11-α** (54.9 mg, 0.118 mmol) gave **30-α** (27.1 mg, 67% overall yield) through method B.

***n*-Octyl 2,6-Dideoxy-β-D-*ribo*-hexopyranoside (30-β). 11-β** (45.4 mg, 0.121 mmol) gave **30-β** (22.5 mg, 71% overall yield) as a colorless syrup through method A: $R_f$ 0.40 (2:1 hexane–acetone); $[\alpha]^{25}_D$ –27.4° ($c$ 0.73,

$CHCl_3$); $^1$H-NMR $\delta$ 0.88 (3H, t, $J$ = 6.8 Hz), 1.2–1.65 (10H, m), 1.31 (3H, d, $J$ = 6.4 Hz), 1.73 (1H, ddd, $J$ = 13.0, 9.6, and 3.0 Hz), 2.05 (1H, d, $J$ = 7.4 Hz), 2.11 (1H, ddd, $J$ = 13.0, 3.2, and 2.2 Hz), 2.29 (1H, br s), 3.32 (1H, ddd, $J$ = 9.4, 7.4, and 3.0 Hz), 3.42 (1H, dt, $J$ = 9.6 and 6.8 Hz), 3.73 (1H, dq, $J$ = 9.4 and 6.4 Hz), 3.85 (1H, dt, $J$ = 9.6 and 7.0 Hz), 4.12 (1H, br s), 4.80 (1H, dd, $J$ = 9.6 and 2.2 Hz). Anal. Calcd for $C_{14}H_{28}O_4$: C, 64.58; H, 10.84. Found: C, 64.37; H, 10.80. **11-$\beta$** (86.4 mg, 0.118 mmol) gave **30-$\beta$** (39.0 mg, 66% overall yield) through method B.

**Cyclohexyl 2,6-Dideoxy-$\alpha$-D-*ribo*-hexopyranoside (31-$\alpha$).** **12-$\alpha$** (65.2 mg, 0.189 mmol) gave **31-$\alpha$** (31.8 mg, 73% overall yield) as crystals through method A: $R_f$ 0.33 (1:1 hexane–ethyl acetate); $[\alpha]^{24}_D$ +147° ($c$ 0.72, $CHCl_3$); mp 70.0–71.0 °C (hexane); $^1$H-NMR $\delta$ 1.2–1.95 (10H, m), 1.31 (3H, d, $J$ = 6.2 Hz), 1.91 (1H, ddd, $J$ = 14.4, 3.2, and 3.2 Hz), 2.13 (1H, ddd, $J$ = 14.4, 3.4, and 1.0 Hz), 2.56 (1H, d, $J$ = 10.6 Hz), 3.13 (1H, ddd, $J$ = 10.4, 10.4, and 3.4 Hz), 3.63 (1H, m), 3.74 (1H, d, $J$ = 10.4 Hz), 3.78 (1H, dq, J = 10.4 and 6.2 Hz), 3.95 (1H, dddd, $J$ = 10.6, 3.4, 3.4, and 3.2 Hz), 5.05 (1H, br d, $J$ = 3.2 Hz). Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.22; H, 9.76.

**Cyclohexyl 2,6-Dideoxy-$\beta$-D-*ribo*-hexopyranoside (31-$\beta$).** **12-$\beta$** (64.7 mg, 0.188 mmol) gave **31-$\beta$** (29.9 mg, 69% overall yield) as a colorless syrup through method A: $R_f$ 0.27 (2:1 hexane–acetone); $[\alpha]^{24}_D$ –38.8° ($c$ 0.34, $CHCl_3$); $^1$H-NMR $\delta$ 1.15–2.05 (11H, m), 1.30 (3H, d, $J$ = 6.2 Hz), 1.98 (1H, d, $J$ = 7.2 Hz), 2.06 (1H, ddd, $J$ = 14.0, 3.6, and 2.4 Hz), 2.23 (1H, br s), 3.33 (1H, ddd, $J$ = 9.6, 7.2, and 3.6 Hz), 3.63 (1H, m), 3.72 (1H, dq, $J$ = 9.6 and 6.2 Hz), 4.12 (1H, br m), 4.95 (1H, dd, $J$ = 9.8 and 2.4 Hz). Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.55; H, 9.61.

**2,4-Dimethyl-3-pentyl 2,6-Dideoxy-$\alpha$-D-*ribo*-hexopyranoside (32-$\alpha$).** **13-$\alpha$** (39.7 mg, 0.110 mmol) gave **32-$\alpha$** (20.7 mg, 76% overall yield) as a colorless syrup through method A: $R_f$ 0.27 (1:2 hexane–ether); $[\alpha]^{25}_D$ +135° ($c$ 0.99, $CHCl_3$); $^1$H-NMR $\delta$ 0.92 (6H, d, $J$ = 6.4 Hz), 0.93 and 0.98 (each 3H, each d, $J$ = 6.4 Hz), 1.31 (3H, d, $J$ = 6.2 Hz), 1.8–1.95 (3H, m), 2.29 (1H, ddd, $J$ = 14.4, 3.6, and 1.4 Hz), 2.47 (1H, br d, $J$ = 10.6 Hz), 3.1–3.2 (1H, m), 3.13 (1H, dd, $J$ = 5.6 and 4.0 Hz), 3.61 (1H, d, $J$ = 10.0 Hz), 3.92 (1H, dq, $J$ = 9.7 and 6.2 Hz), 3.98 (1H, dddd, $J$ = 10.0, 3.6, 3.6 and 3.4 Hz), 4.92 (1H, br d, $J$ = 3.6 Hz). Anal. Calcd for $C_{13}H_{26}O_4$: C, 63.39; H, 10.64. Found: C, 63.62; H, 10.48.

**2,4-Dimethyl-3-pentyl 2,6-Dideoxy-$\beta$-D-*ribo*-hexopyranoside (32-$\beta$).** **13-$\beta$** (20.0 mg, 0.0554 mmol) gave **32-$\beta$** (13.7 mg, 77% overall yield) as crystals through method A: $R_f$ 0.33 (1:2 hexane-ether); $[\alpha]^{25}_D$ –17.3° ($c$ 0.52, $CHCl_3$); mp 34.0–35.0 °C (hexane); $^1$H-NMR $\delta$ 0.91 and 0.92 (each 3H, each d, $J$ = 6.2 Hz), 0.93 (6H, d, $J$ = 6.2 Hz), 1.28 (3H, d, $J$ = 6.2 Hz), 1.65–1.9 (3H, m), 1.90 (1H, d, $J$ = 6.6 Hz), 2.16 (1H, br s), 2.17 (1H, ddd, $J$ = 14.0, 3.4 and 2.2 Hz), 3.06 (1H, t, $J$ = 5.8 Hz), 3.30 (1H, ddd, $J$ = 9.6, 6.6, and 3.6 Hz), 3.67 (1H, dq, $J$ = 9.6 and 6.2 Hz), 4.12 (1H, br ddd, $J$ = 3.6, 3.4, and 3.4 Hz), 4.76 (1H, dd, $J$ = 9.6 and 2.2 Hz). Anal. Calcd for $C_{13}H_{26}O_4$: C, 63.39; H, 10.64. Found: C, 63.51; H, 10.32.

***tert*-Butyl 2,6-Dideoxy-$\alpha$-D-*ribo*-hexopyranoside (33-$\alpha$) and $\beta$-Anomer (33-$\beta$).** An anomer mixture of **14** (112.0 mg, 0.352 mmol) gave the corresponding 2,6-anhydro-3,4-dihydroxy-2-thio-$\alpha$- and -$\beta$-glycosides (69.9 mg, 85%) as a chromatographically separatable mixture by a hydrolysis. The 2,6-anhydro-3,4-dihydroxy-2-thio-$\alpha$-glycoside (47.9 mg, 0.204 mmol) gave **33-$\alpha$** (34.5 mg, 83%) as a colorless syrup by method A: $R_f$ 0.24 (1:1 hexane–ether); $[\alpha]^{26}_D$ +141° ($c$ 0.88, $CHCl_3$); $^1$H-NMR $\delta$ 1.27 (9H, s), 1.275 (3H, d, $J$ = 6.2 Hz), 1.89 (1H, ddd, $J$ = 14.4, 3.2, and 3.2 Hz), 2.05 (1H, ddd, $J$ = 14.4, 3.4, and 1.4 Hz), 2.49 (1H, d, $J$ = 10.4 Hz), 3.11 (1H, ddd, $J$ = 10.0, 9.8, and 3.5 Hz), 3.82 (1H, d, $J$ = 10.0 Hz), 3.90 (1H, dq, $J$ = 9.8 and 6.2 Hz), 3.94 (1H, dddd, $J$ = 10.4, 3.5, 3.4, and 3.2 Hz), 5.20 (1H, br d, $J$ = 3.2 Hz). Anal. Calcd for $C_{10}H_{20}O_4$: C, 58.80; H, 9.87. Found: C, 58.89; H, 10.02. The 2,6-anhydro-3,4-dihydroxy-2-thio-$\beta$-glycoside (25.9 mg, 0.111 mmol) gave **33-$\beta$** (18.1 mg, 80%) as a colorless syrup by method A: $R_f$ 0.18 (1:1 hexane–ethyl acetate); $[\alpha]^{29}_D$ –23.5° ($c$ 0.57, $CHCl_3$); $^1$H-NMR $\delta$ 1.26 (9H, s), 1.29 (3H, d, $J$ = 6.2 Hz), 1.78 (1H, ddd, $J$ = 14.0, 9.6 and 2.9 Hz), 1.97 (1H, ddd, $J$ = 14.0, 3.0 and 3.0 Hz), 2.04 (1H, br d, $J$ = 6.2 Hz), 2.33 (1H, br s), 3.25–3.4 (1H, br m), 3.73 (1H, dq, $J$ = 9.6 and 6.2 Hz), 4.11 (1H, br ddd, $J$ = 3.0, 3.0, and 2.9 Hz), 5.03 (1H, dd, $J$ = 9.6 and 3.0 Hz). Anal. Calcd for $C_{10}H_{20}O_4$: C, 58.80; H, 9.87. Found: C, 58.86; H, 9.80.

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