Synthesis and Structure of 4-*O*,6-*O*-Glycosylidene Glycosides

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Interglycosidic spiro ortho esters (**9**−**20**) were efficiently prepared from methyl 2,6-di-*O*-benzylgluco- or galactopyranoside and various sugar lactones in the presence of methoxytrimethylsilane and a catalytic amount of trimethylsilyl triflate. All of the prepared sugar ortho esters possess perhydrospiro[2*H*-pyran-2,2′-pyrano[3,2-*d*][1,3]dioxin] ring systems commonly in their molecules and, remarkably, were afforded as single isomers. The configurations of the spiro centers in their molecules were determined or estimated by X-ray single crystallographic analysis and molecular modeling studies. By comparing the conformations of prepared ortho esters, we revealed that the difference in the stability between two possible isomers was principally caused from that between the spiro ring systems in their molecules in each case.

Introduction

The spiro ortho ester interlinkage between a glycosylidene group and the diol moiety of glycoside has been found in the orthosomycin family of antibiotics.[1,2] Since this unique ortho ester linkage[3,4] restricts conformation of the saccharide, it created interest also from the point of designing pseudo-saccharide molecules. For each interglycosidic ortho ester, two stereoisomers are possible around the spiro center, and X-ray crystallographic analysis is usually required for the determination of the absolute configuration of spiro carbon. Although the configurations of the spiro centers of several such compounds, including orthosomycins, have been determined by X-ray crystallographic analysis[3d,g,4a,5] or estimated by other spectral methods, the general knowledge about the predominance in the formation between two possible isomers of sugar ortho esters have not been reported.

Recently, we were interested in this unique type of linkage as the intermediate in our novel reductive glycosidic bond formation[6] and modified the process for the formation of these ortho esters.[6a,c] As described in a previous paper,[6a] we prepared sugar ortho esters (**9**−**11**) from D-sugar lactones (**1**−**3**) and methyl 2,3-di-*O*-benzylglucopyranoside (**7**) and revealed that only one of the two possible isomers was generated in each case. Yoshimura and co-workers had extensively studied interglycosidic ortho esters[3] for the purpose of synthesizing orthosomycin antibiotics and had also synthesized compound **9** as a single isomer.[3e] They determined the absolute configuration of the anomeric center of **9** to be *R* by X-ray crystallographic analysis after converting it into the acetylated derivative.[3g] In a previous paper, we estimated the configurations of the spiro centers of the other two ortho esters to be also *R* by the molecular modeling studies.[6a]

In this paper, we report the details of the preparation and the structure determination of various interglycosidic spiro ortho esters, including the above three ortho esters, which possess perhydrospiro[2*H*-pyran-2,2′-pyrano[3,2-*d*][1,3]dioxin] ring systems commonly in their molecules. Remarkably, all of the prepared ortho esters were afforded as single isomers. Considering the structures of formed ortho esters, we found generality among the configurations of spiro centers in the predominately generated isomers, which are also reported in detail in this report.

Preparation of Sugar Ortho Esters. Two decades ago, Yoshimura and co-workers reported the synthesis of interglycosidic spiro ortho esters from sugar lactones and silylated diols using TMSOTf as the catalyst[3a] in a modification of Noyori's method.[8] As we required a much more efficient method in the course of the study on our reductive glycosylation protocol,[6] we also modified the process for ortho ester preparation.[7,6a] Recently, Kurihara and Miyata have reported the efficient ketal formation from diols and ketones in the presence of excess amount

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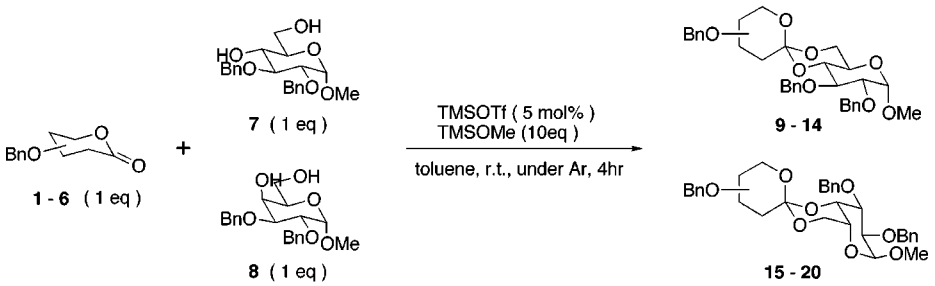
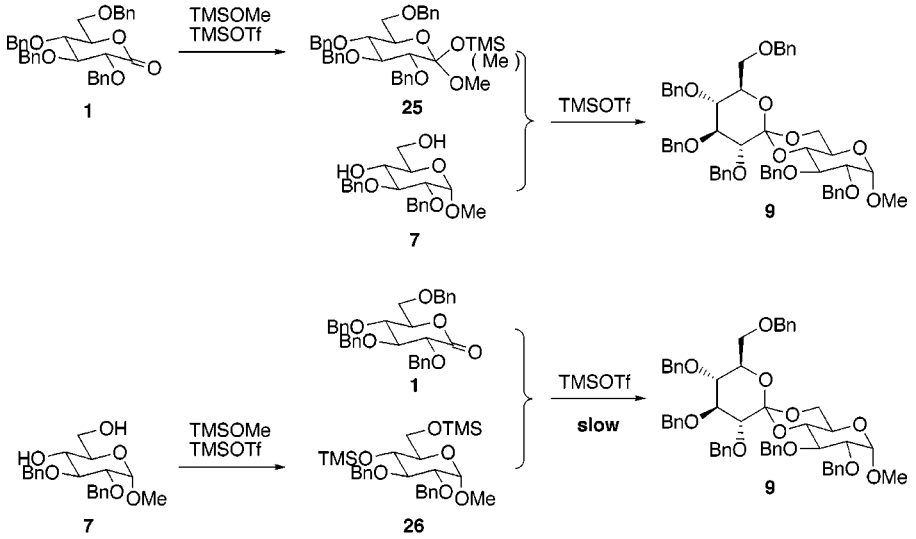
Scheme 1



Scheme 2



of *sec*- or *tert*-alkoxy silane and a catalytic amount of TMSOTf.[9] As the preparation of ortho esters from lactones seemed to be similar to that of ketals from ketones, we tried to apply their methods to the preparation of sugar ortho esters. Although a direct application of this method to the ortho ester formation was not effective, we revealed that sugar ortho esters were efficiently formed by using methoxy silane instead of *sec*- or *tert*-alkoxy silane (Scheme 1). To obtain high yields, it was required that the MeOH and hexamethyldisiloxane produced were removed from the reaction mixtures under reduced pressure during the course of the reactions.

By our improved method, we prepared the 12 sugar ortho esters listed in Table 1 in 71−90% yields. We used six sugar lactones, 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone (**1**),[10] 2,3,4,6-tetra-*O*-benzyl-D-galactono-1,5-lactone (**2**),[11] 2,3,4,6-tetra-*O*-benzyl-D-mannono-1,5-lactone (**3**),[11] 2,3,4-tri-*O*-benzyl-D-fucono-1,5-lactone (**4**), 2,3,4-tri-*O*-benzyl-L-fucono-1,5-lactone (**5**),[12] and 2,3,4-tri-*O*-benzyl-L-rhamnono-1,5-lactone (**6**), and two β-diol type glycosides, methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (**7**) and methyl 2,3-di-*O*-benzyl-α-D-galactopyranoside (**8**),[13] in this preparation. These starting materials are all known compounds except lactones **4** and **6**, which were prepared by the oxidation of corresponding hemiacetals[14,15] with DMSO/acetic anhydride. Remarkably, all the ortho esters in Table 1 were afforded as single isomers, despite the fact that two stereoisomers were possible around the spiro centers.

The role of TMSOMe under these reaction conditions is still not clear. While the reaction of the diol-type glycoside **7** with the sugar lactone **1** rapidly attained an equilibrium to afford the interglycosidic ortho ester **9** in the presence of TMSOMe and a catalytic amount of TMSOTf, the reaction of the corresponding trimethylsilylated diol **26** with **1** proceeded far more slowly in the presence of the same amount of catalyst (Scheme 2, below). Thus, we presume that TMSOMe may activate the carbonyl groups of sugar lactones instead of diol groups. It is plausible that the dimethyl or methyl trimethylsilyl ortho ester **25**[16] is produced under these reaction conditions and that the formed ortho ester **25** reacts more efficiently with **7** than the lactone **1** (Scheme 2, above).

Determination of the Absolute Configurations of the Spiro Centers in the Sugar Ortho Ester Molecules. All of the ortho esters listed in Table 1 possess perhydrospiro[2*H*-pyran-2,2′-pyrano[3,2-*d*][1,3]dioxin] ring systems commonly in their molecules and were afforded as single isomers. To determine the absolute configuration of the spiro centers of ortho esters, X-ray crystal-

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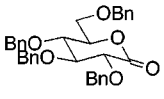
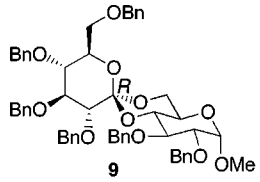
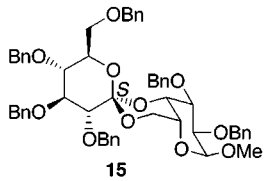
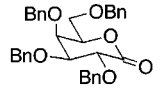
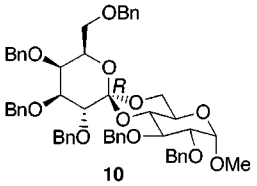
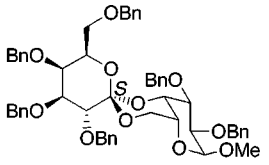
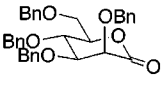
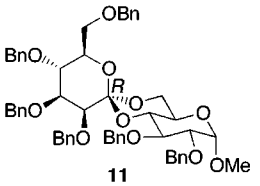
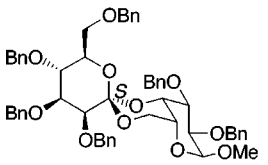
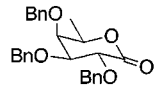
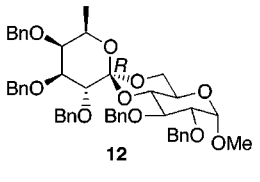
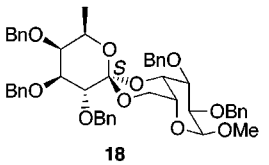
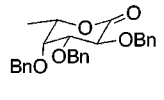
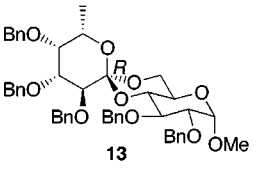
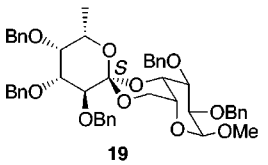
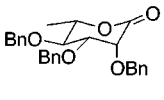
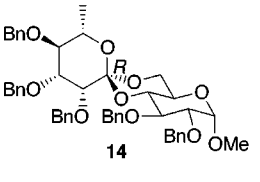
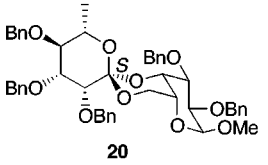
(15) Lai, W.; Martin, O. R. *Carbohydr. Res.* **1993**, *250*, 185.
(16) Dimethyl or methyl trimethylsilyl acetals of sugar lactones are known to be formed from sugar lactones and TMSOMe in the presence of TMSOTf: Yoshimura, J.; Horito, S.; Asano, K.; Hashimoto, H. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu*, *24th* (Japan), 1981; p 638.

Table 1. Preparation of Sugar Ortho Esters from Sugar Lactones and Sugar Diols

Lactone	Ortho Ester with **7**	Yield[a]	Ortho Ester with **8**	Yield[a]
 **1**	 **9**	87 %	 **15**	90 %
 **2**	 **10**	82 %	 **16**	90 %
 **3**	 **11**	77 %	 **17**	81 %
 **4**	 **12**	71 %	 **18**	85 %
 **5**	 **13**	74 %	 **19**	88 %
 **6**	 **14**	73 %	 **20**	82 %

[a] These reactions were carried out at rt under Ar in toluene (initial concentration [lactone] = [**7** or **8**] = 100−200 mM, [TMSOMe] = 1−2 M (10 equiv), [TMSOTf] = 5−10 mM (5 mol %)). During the reaction, generated MeOH and TMSOTMS were removed under reduced pressure (5 mmHg, 1 h × 2). Yield is the isolated yield.

lographic analyses of the four ortho esters (**11**, **14**, **17**, **20**) were performed. As describe bellow, it was revealed that the prepared ortho esters could be classified into the following four groups: the ortho esters formed from D-sugar lactones (**1**, **2**, **3**, **4**) and **7**, the ones from L-sugar lactones (**5**, **6**) and **7**, the ones from D-sugar lactones and **8**, and the ones from L-sugar lactones and **8** from the point of the configurations of their ring systems. The analyzed four sugar ortho esters were regarded as the representatives of these groups.

Among them only ortho ester **11** was a crystalline compound suitable for X-ray analysis, which was obtained as colorless needles from an ether/hexane solution. The others were debenzylated by Pd/C−H_2 and then converted into penta- or hexaacetylated compounds (**21**−**23**) with Ac_2O/pyridine,[3g] which were also recrystallized from ether/hexane to afford colorless prisms. The X-ray single crystallographic structures of the four ortho esters are represented in Figure 1 by ball-and-stick models.[17] From the spatial relationship of the glycoside and the glycosylidene moieties, the configuration of the spiro centers of **11**, **14**, **17**, and **20** were determined as *R*, *R*, *S*, and *S*, respectively.

The configuration of the spiro centers of the other ortho esters were estimated by molecular modeling studies. We performed LOMD conformational searches[18] for two possible isomers of 12 ortho esters (total 24 molecules) using MacroModel 6.0[19] with the MM2* force field. As summarized in Table 2, it was suggested that one of the

(17) The X-ray analysis revealed that the prisms were formed from two different conformers in the cases of the ortho esters **14**, **17**, **20**. In Figure 1, one of the two conformers of each ortho ester was illustrated. The configurations of anomeric centers and the conformations of ring systems were the same between the two conformers in each case.

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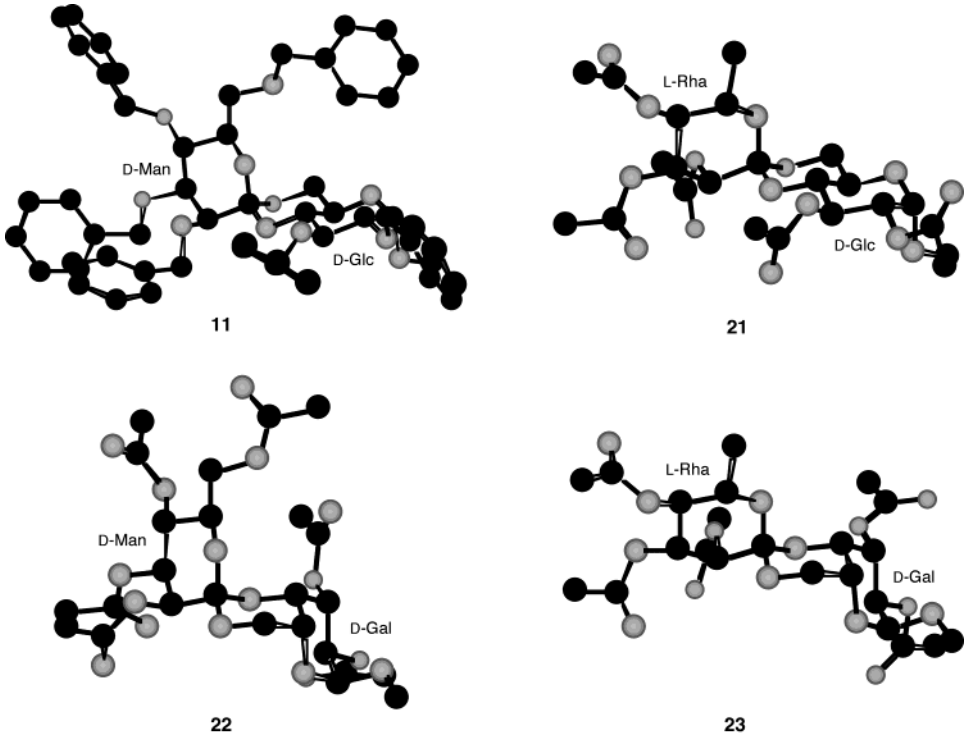


Figure 1. The X-ray single-crystal structure of sugar ortho esters. Hydrogen atoms were omitted. See ref 17.

Table 2. Difference in Δ*E* between Favored Isomers and Disfavored Isomers of Sugar Ortho Esters

ortho ester	anomeric configuration	dioxane form	ΔΔ*E* (kcal)[a]	favored configuration
9	*R*	chair	4.2	*R*
	S	skew boat		
10	*R*	chair	4.9	*R*
	S	skew boat		
11	*R*	chair	5.0	*R*
	S	skew boat		
12	*R*	chair	3.4	*R*
	S	skew boat		
13	*R*	chair	6.4	*R*
	S	skew boat		
14	*R*	chair	7.8	*R*
	S	skew boat		
15	*R*	skew boat	9.8	
	S	chair		*S*
16	*R*	skew boat	10.0	
	S	chair		*S*
17	*R*	skew boat	7.3	
	S	chair		*S*
18	*R*	skew boat	8.0	
	S	chair		*S*
19	*R*	skew boat	6.1	
	S	chair		*S*
20	*R*	skew boat	4.7	
	S	chair		*S*

[a] LOMD[18] for sugar ortho esters were performed using MacroModel ver. 6.0[19] with the MM2*. ΔΔ*E* = Δ*E*(favored isomer) − Δ*E*(disfavored isomer).

possible isomers of each ortho ester was more stable by 3.4−10.0 kcal/mol than the other in each case. It was well explained by these differences that the prepared sugar ortho esters were all afforded as single isomers. From these results, we estimated the configuration of the spiro centers of the ortho esters **9**−**14** to be *R*, and that of **15**−**20** to be *S*. The configurations estimated by the calculations corresponded to the results of the X-ray analysis in the cases with the ortho esters **11**, **14**, **17**, **20**. The estimated configuration of the ortho ester **9** also corresponded to the results of X-ray analysis performed by Yoshimura and co-workers.

Discussion

From the above molecular modeling studies, it was estimated that *R*-isomers were commonly more stable than *S*-ones in the cases of the ortho esters (**9**−**14**) formed from **7**, and that *S*-isomers were energetically more favorable than *R*-ones in all the cases of the ortho esters (**15**−**20**) formed from **8**. Further, it was indicated by the calculations that the conformations of the ring systems of the favored or disfavored isomers were divided into the four types according to the groups described above. Namely, it was suggested for each prepared ortho ester that the conformations of the ring systems proposed for two possible isomers and the relative stability between them depended only on whether D- or L-sugar lactone was located in the glycosylidene moiety and on whether **7** or **8** was located in the diol moiety. In Figures 2 and 3, the typical four conformations of the ring systems of the energetically favored isomers (Figure 2) and those of disfavored ones (Figure 3) are illustrated.[20] The benzyl substituents on the molecules are omitted to show the shapes of the ring systems more clearly in Figures 2 and 3. The results of our four X-ray crystallographic analyses and that of Yoshimura and co-workers[3g] corresponded to these estimations from the points of the configurations

(19) Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendricson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440.

(20) LOMD for sugar ortho esters were continued until around 3000 conformers for each ortho ester were generated. Even if the steps in LOMD were not enough for the determination of the conformations of the whole molecules including benzyl protective groups, the conformations of the ring systems in the lower energy conformers were the same in each case.

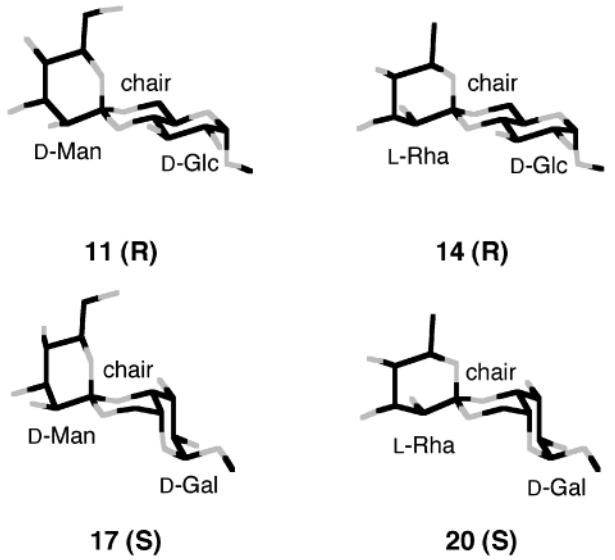


Figure 2. Typical four conformations for favored isomers calculated by LOMD[18] using MacroModel ver 6.0.[19] All of the benzyl groups and the hydrogen atoms on the molecules were omitted.

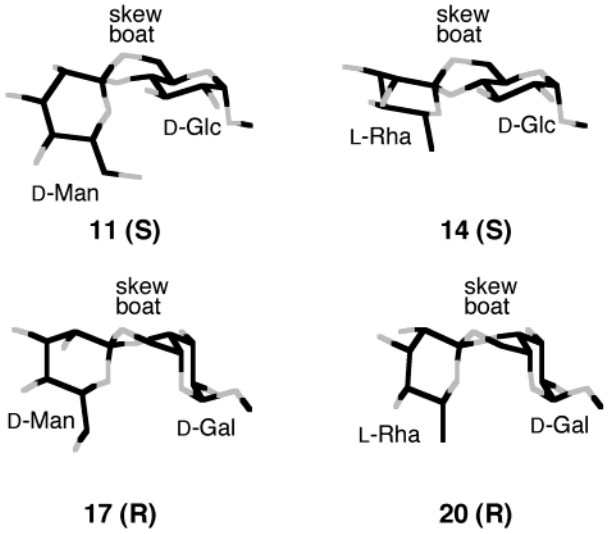


Figure 3. Typical four conformations for disfavored isomers calculated by LOMD[18] using MacroModel ver 6.0.[19] All of the benzyl groups and the hydrogen atoms on the molecules were omitted.

of anomeric carbons and the conformations of the ring systems in the molecules of the favored isomers and thus strongly supported these estimations. Especially, the result of the X-ray analysis of the mannosylidene ortho ester **11** and that of the glucosylidene ortho ester **9** clearly indicated that even the configurations of the two positions of the sugar lactones used did not affect the configurations of the adjacent spiro centers and the conformations of the ring systems in the molecules of the ortho esters formed.

These results indicate that the difference in stability of two possible isomers of each ortho ester is principally caused by that of the ring systems. To reveal the basis for these results, we compared the difference in the conformations of the ring systems between the favored and disfavored isomers of ortho esters estimated by calculations. As shown in Figure 2, the conformations of dioxane rings in the molecules of the four representative

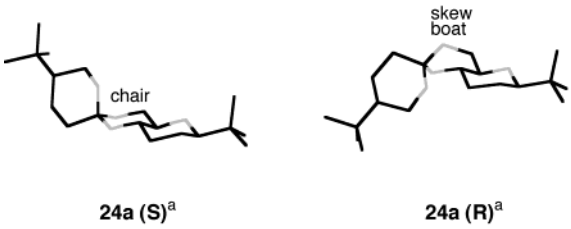
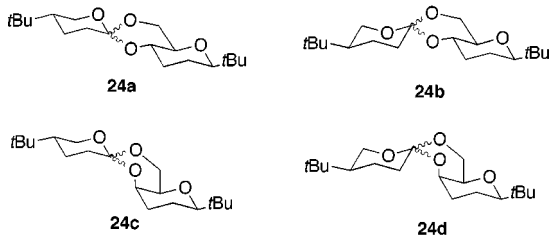


Figure 4. Proposed conformations for both isomers of **24a** calculated by LOMD[18] using MacroModel ver 6.0.[19] All of the hydrogen atoms were omitted. (a) See ref 23.

Scheme 3



favored isomers, which were located in the center of the molecules, were the chair forms. Contrary, in the cases of four disfavored isomers, the conformations of dioxane rings were the skew boat forms (Figure 3). It should be further noted that 5′-O of the favored isomers were in the axial positions of the chair formed dioxane rings but that 5′-O of the disfavored ones could not be in the axial positions of the central dioxane rings if the rings were chair formed. The conformational differences between two possible isomers can be simply explained by considering the anomeric effects derived from two oxygen atoms in dioxane rings.[21,22] It was expected that each 5′-O atom prefers to be located in the axial position of dioxane ring because of the overlapping between the n orbitals of two oxygen atoms in dioxane ring and the σ^* orbital of the C(1′)−O(5′) bond. By considering the relative stability of the chair form compared to the skew boat form, it was easy to explain that one of the two possible isomers was energetically more favorable than the other in each case.

To indicate that the differences in energy listed in Table 2 were principally caused from those of these ring systems more clearly, the molecular modeling studies on the isomers of 5,6′-di-*tert*-butyl-perhydrospiro[2*H*-pyran-2,2′-pyrano[3,2-*d*][1,3]dioxin] (**24a**−**d**) (Scheme 3) were performed. Figure 4 shows the calculated conformations of two possible isomers of (5*R*,4a′*R*,6′*R*,8a′*S*)-5,6′-di-*tert*-butyl-perhydrospiro[2*H*-pyran-2,2′-pyrano[3,2-*d*][1,3]-dioxin] (**24a**). These molecules could be regarded as the models for the sugar ortho esters formed from D-sugar lactones and **7**. It was suggested also in this case that one of the isomers in which the 5′-O atom was in the axial position of the chair form dioxane ring was more stable than the other[23] and that the dioxane ring in the molecule of the disfavored isomer formed a skew boat (Table 3, Figure 4). The conformational searches for the both

(21) (a) Lemieux, R. U. In *Molecular Rearrangements*; De Mayo, P., Ed.; Interscience: New York, 1964. (b) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: Berlin, 1983.

(22) Conformational analysis for ortho esters containing 1,3-dioxane ring systems in their molecules has been reported. (a) Pihlaja, K.; Heokkliä, J. *Acta Chem. Scand.* **1967**, *21*, 2390. (b) Eliel, E. L.; Nader, F. W. *J. Am. Chem. Soc.* **1970**, *92*, 584. (c) Salzner, U.; Schleyer, P. v. R. *J. Org. Chem.* **1994**, *59*, 2138.

Table 3. Difference in Δ*E* between Favored Isomers and Disfavored Isomers of Model Ortho Esters

ortho ester	anomeric configuration	dioxane form	ΔΔ*E* (kcal)[a]	favored configuration
24a	*R*	skew boat	4.1	
	S	chair		*S*[b]
24b	*R*	skew boat	5.2	
	S	chair		*S*[b]
24c	*R*	chair	6.3	*R*[b]
	S	skew boat		
24d	*R*	chair	4.1	*R*[b]
	S	skew boat		

[a] LOMD[18] for sugar ortho esters were performed using MacroModel ver. 6.0[19] with the MM2*. ΔΔ*E* = Δ*E*(favored isomer) − Δ*E*(disfavored isomer). [b] See ref 23.

isomers of compounds **24b**, **24c**, and **24d**, which were regarded as models for the sugar ortho esters formed from the L-sugar lactones and **7**, from the D-sugar lactones and **8**, and from the L-sugar lactones and **8**, respectively, afforded results that were also compatible to those with the sugar ortho esters (Table 3, Figure 4).

Conclusion

We prepared the 12 sugar ortho esters (**9**−**20**), which possess perhydrospiro[2*H*-pyran-2,2′-pyrano[3,2-*d*][1,3]-dioxin] ring systems commonly in their molecules. Remarkably, all of the prepared ortho esters were obtainable as single structural isomers. The structures of the formed ortho esters were determined or estimated by the X-ray single crystallographic analysis and molecular modeling studies. By comparing the structures of these ortho esters, we revealed that one of the two possible isomers that were expected was more stable by the consideration of anomeric effects derived from the two oxygen atoms of the central dioxane ring generated predominately in each case.

Experimental Section

General. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded with a 400 MHz (^{1}H NMR) pulse Fourier transform NMR spectrometer in $CDCl_3$ solution with tetramethylsilane as an internal standard. Thin-layer chromatography (TLC) was performed on precoated plates (Merck TLC aluminum sheets silica 60 F_{254}) with detection by UV light or with phosphomolybdic acid in ethanol/H_2O followed by heating. Column chromatography was performed using SiO_2 (Wakogel C-200, Wako).

Calculations. Low-mode searches (LOMD)[18] were performed using MacroModel ver. 6.0[19] with the MM2* derivative of the MM2 force field on a Silicon Graphics IRIS-Indigo workstation. LOMD for the sugar ortho esters (**9**−**20**) were continued until around 3000 conformers for each ortho ester were generated. In the case of the model compounds (**24a**−**d**), the total steps in LOMD were 10 000, and 150−700 conformers were generated for each molecule.

Materials. Solvents were freshly distilled prior to use. TMSOMe was a commercial product and was used as received. TMSOTf was distilled under an inert atmosphere of argon. All of the starting substrates for the preparation of sugar lactones and percially protected sugar compounds were commercially available and were used as received or were purified by distillation, if necessary. 2,3,4,6-Tetra-*O*-benzyl-D-glucono-1,5-lactone (**1**),[10] 2,3,4,6-tetra-*O*-benzyl-D-galactono-1,5-lactone (**2**),[11] 2,3,4,6-tetra-*O*-benzyl-D-mannono-1,5-lactone (**3**),[11] 2,3,4-tri-*O*-benzyl-L-fucono-1,5-lactone (**5**),[12] methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (**7**), methyl 2,3-di-*O*-benzyl-α-D-galactopyranoside (**8**),[13] 2,3,4-tri-*O*-benzyl-D-fucopyranose (**27**),[15] and 2,3,4-tri-*O*-benzyl-L-rhamnopyranose (**28**)[14] were prepared according to the established methods.

2,3,4-Tri-*O*-benzyl-D-fucono-1,5-lactone (4) and 2,3,4-Tri-*O*-benzyl-L-rhamnono-1,5-lactone (6). Compound **27** (1.0 g, 2.2 mmol) was dissolved in dimethyl sulfoxide (24 mL) and acetic anhydride (12 mL), and the mixture was stirred under Ar at room temperature overnight. The resulting mixture was partitioned between EtOAc and water. The organic layer was washed several times with water to remove the acetic anhydride, dried over Na_2SO_4, filtered, and concentrated. The residue was chromatographed on silica gel (EtOAc/*n*-hexane 1:6) to afford **4** as a colorless oil (0.90 g, 90%): $[\alpha]^{21}_D$ + 87.8° (*c* 1.0, $CHCl_3$); IR (neat, cm^{-1}) 3036, 2938, 2869 1747, 1603, 1496; HRMS(EI) *m*/*z* calcd for $C_{27}H_{28}O_5$ 432.1937, found 432.1937 (M^+). According to the same procedure, **6** was prepared from corresponding hemiacetal **28** in 88% yield as a colorless oil: $[\alpha]^{21}_D$ −3.2° (*c* 1.1, $CHCl_3$); IR (neat, cm^{-1}) 3032, 2937, 2869, 1772, 1732, 1603, 1496; HRMS(EI) calcd for $C_{27}H_{28}O_5$ 432.1937, found 432.1938.

Preparation of Sugar Ortho Esters. To a solution of lactone **1** (400 mg, 0.74 mmol) and diol **8** (277 mg, 0.74 mmol) in toluene (5 mL) was added TMSOMe (1.0 mL, 7.4 mmol) and TMSOTf (7 μL, 5 mol %) at room temperature under Ar. After 1 h of stirring, the solvent was removed under reduced pressure (5 mmHg, 1 h). The reaction vessel was leaked with Ar, and the remainder was again dissolved in toluene. TMSOMe (1.0 mL, 7.4 mmol) and TMSOTf (7 μL, 5 mol %) was added to the solution, and the mixture was stirred for further 30 min. The solvent was removed under reduced pressure again. The remainder was dissolved in toluene containing 5% Et_3N, and the mixture was applied to a silica gel column chromatography (ether/hexane 1:3 then 1:2) to afford **15** as a colorless syrup (598 mg, 90%). According to the same procedure, other sugar ortho esters were prepared in the yields listed in Table 1.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyrano-sylidene)-α-D-glucopyranoside (9): colorless syrup; $[\alpha]^{22}_D$ +38.0° (*c* 0.91, $CHCl_3$); IR (neat, cm^{-1}) 2920, 2857, 1711, 1603, 1456, 1377; MS(FAB) *m*/*z* 933 (M + K)$^+$, 917 (M + Na)$^+$, 895 (M + H)$^+$, 826 (M − Bn + Na)$^+$; HRMS(FAB) calcd for $C_{55}H_{58}O_{11}Na$ 917.3877, found 917.3892.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4,6-tetra-*O*-benzyl-D-galactopyrano-sylidene)-α-D-glucopyranoside (10): colorless syrup; $[\alpha]^{22}_D$ +31.6° (*c* 1.0, $CHCl_3$); IR (neat, cm^{-1}) 3063, 2920, 1726, 1604, 1587; MS(FAB) *m*/*z* 933 (M + K)$^+$, 917 (M + Na)$^+$, 895 (M + H)$^+$, 826 (M − Bn + Na)$^+$; HRMS(FAB) calcd for $C_{55}H_{58}O_{11}Na$ 917.3877, found 917.3866.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4,6-tetra-*O*-benzyl-D-mannopyrano-sylidene)-α-D-glucopyranoside (11): colorless needle; mp 107.5−108.5 °C; $[\alpha]^{21}_D$ −6.9° (*c* 1.0, $CHCl_3$); IR (KBr, cm^{-1}) 3374, 2930, 2857, 2361, 2339, 1711, 1460, 1377; MS(FAB) *m*/*z* 933 (M + K)$^+$, 917 (M + Na)$^+$, 895 (M + H)$^+$, 826 (M − Bn + Na)$^+$; HRMS(FAB) calcd for $C_{55}H_{58}O_{11}Na$ 917.3877, found 917.3894. Anal. Calcd for $C_{55}H_{58}O_{11}$: C, 73.81; H, 6.53. Found: C, 73.84; H, 6.53.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4-tri-*O*-benzyl-D-fucopyranosyl-idene)-α-D-glucopyranoside (12): colorless syrup; $[\alpha]^{20}_D$ +26.7° (*c* 1.1, $CHCl_3$); IR (neat, cm^{-1}) 3373, 2926, 1711, 1460, 1377; MS(FAB) *m*/*z* 827 (M + K)$^+$, 811 (M + Na)$^+$, 789 (M + H)$^+$; HRMS(FAB) calcd for $C_{48}H_{52}O_{10}Na$ 811.3458, found 811.3472.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4-tri-*O*-benzyl-L-fucopyranosyl-idene)-α-D-glucopyranoside (13): colorless syrup; $[\alpha]^{20}_D$ −32.9° (*c* 1.1, $CHCl_3$); IR (neat, cm^{-1}) 3347, 2855, 2359, 1462, 1377; MS(FAB) *m*/*z* 827 (M + K)$^+$, 811 (M + Na)$^+$, 789 (M + H)$^+$; HRMS(FAB) calcd for $C_{48}H_{52}O_{10}Na$ 811.3458, found 811.3474.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4-tri-*O*-benzyl-L-rhamnopyranosyl-idene)-α-D-glucopyranoside (14): colorless syrup; $[\alpha]^{21}_D$ +9.5° (*c* 1.1, $CHCl_3$); IR (neat, cm^{-1}) 3378, 2924, 2361, 1462, 1377; MS(FAB) *m*/*z* 827 (M + K)$^+$, 811 (M + Na)$^+$,

(23) In the case of compound **24a**, the configuration of the spiro carbon in the favored isomer should be indicated as *S*, because the substituents on the ring system are different from that of sugar ortho esters.

789 (M + H)$^+$; HRMS(FAB) calcd for $C_{48}H_{52}O_{10}Na$ 811.3458, found 811.3442.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyrano-sylidene)-α-D-galactopyranoside (15): colorless syrup; $[\alpha]^{20}_D$ +76.5° (*c* 1.1, $CHCl_3$); IR (neat, cm^{-1}) 3063, 2361, 2340, 1736, 1604, 1497; MS(FAB) *m*/*z* 933 (M + K)$^+$, 917 (M + Na)$^+$, 895 (M + H)$^+$, 826 (M − Bn + Na)$^+$; HRMS(FAB) calcd for $C_{55}H_{58}O_{11}Na$ 917.3877, found 917.3865.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4,6-tetra-*O*-benzyl-D-galactopyrano-sylidene)-α-D-galactopyranoside (16): colorless powder; mp 108.5−109.5 °C; $[\alpha]^{21}_D$ +73.6° (*c* 1.0, $CHCl_3$); IR (neat, cm^{-1}) 3348, 2924, 2855, 1711, 1462, 1377; MS(FAB) *m*/*z* 933 (M + K)$^+$, 917 (M + Na)$^+$, 895 (M + H)$^+$, 826 (M − Bn + Na)$^+$; HRMS(FAB) calcd for $C_{55}H_{58}O_{11}Na$ 917.3877, found 917.3866. Anal. Calcd for $C_{55}H_{58}O_{11}$: C, 73.81; H, 6.53. Found: C, 73.89; H, 6.56.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4,6-tetra-*O*-benzyl-D-mannopyrano-sylidene)-α-D-galactopyranoside (17): colorless syrup; $[\alpha]^{20}_D$ +18.2° (*c* 1.1, $CHCl_3$); IR (neat, cm^{-1}) 3373, 2926, 1711, 1460, 1377; MS(FAB) *m*/*z* 933 (M + K)$^+$, 917 (M + Na)$^+$, 895 (M + H)$^+$, 826 (M − Bn + Na)$^+$; HRMS(FAB) calcd for $C_{55}H_{58}O_{11}Na$ 917.3877, found 917.3884.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4-tri-*O*-benzyl-D-fucopyranosyl-idene)-α-D-galactopyranoside (18): colorless syrup; $[\alpha]^{20}_D$ +86.4° (*c* 1.1, $CHCl_3$); IR (neat, cm^{-1}) 3347, 2855, 2359, 1462, 1377; MS(FAB) *m*/*z* 827 (M + K)$^+$, 811 (M + Na)$^+$, 789 (M + H)$^+$; HRMS(FAB) calcd for $C_{48}H_{52}O_{10}Na$ 811.3458, found 811.3474.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4-tri-*O*-benzyl-L-fucopyranosyl-idene)-α-D-galactopyranoside (19): colorless syrup; $[\alpha]^{21}_D$ +6.1° (*c* 0.7, $CHCl_3$); IR (neat, cm^{-1}) 3380, 2926, 1725, 1462, 1377; MS(FAB) *m*/*z* 827 (M + K)$^+$, 811 (M + Na)$^+$, 789 (M + H)$^+$; HRMS(FAB) calcd for $C_{48}H_{52}O_{10}Na$ 811.3458, found 811.3456.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4-tri-*O*-benzyl-L-rhamnopyranosyl-idene)-α-D-galactopyranoside (20): colorless powder; mp 93.5−95.0 °C; $[\alpha]^{19}_D$ +52.1° (*c* 1.1, $CHCl_3$); IR (neat, cm^{-1}) 3409, 2926, 2359, 1711, 1458, 1377; MS(FAB) *m*/*z* 827 (M + K)$^+$, 811 (M + Na)$^+$, 789 (M + H)$^+$; HRMS(FAB) calcd for $C_{48}H_{52}O_{10}Na$ 811.3458, found 811.3448. Anal. Calcd for $C_{48}H_{52}O_{10}$: C, 73.08; H, 6.64. Found: C, 72.88; H, 6.71.

Preparation of Acetylated Sugar Ortho Esters. Benzyl-protected sugar ortho esters (**14**, **17**, **20**) were debenzylated by Pd/C under H_2 atmosphere according to the method reported by Yoshimura and co-workers.[3g] The resulting compounds were treated with acetic anhydride/pyridine (1:1) to afford acetylated ortho esters in 85−95% yields.

Methyl 2,3-di-*O*-acetyl-4,6-*O*-(2,3,4-tri-*O*-acetyl-D-rhamnopyranosyl-idene)-α-D-glucopyranoside (21): colorless prisms; mp 165−166 °C; $[\alpha]^{24}_D$ +39.2° (*c* 1.0, $CHCl_3$); IR (KBr, cm^{-1}) 1757, 1372, 1213; MS(EI) *m*/*z* 548 (M)$^+$, 517(M − OMe)$^+$, 488 (M − AcOH)$^+$. Anal. Calcd for $C_{23}H_{32}O_{15}$: C, 50.36; H, 5.88. Found: C, 50.35; H, 5.90.

Methyl 2,3-di-*O*-acetyl-4,6-*O*-(2,3,4,6-tetra-*O*-acetyl-D-mannopyrano-sylidene)-α-D-galactopyranoside (22): colorless prisms; mp 147−148 °C; $[\alpha]^{24}_D$ +144.1° (*c* 1.0, $CHCl_3$); IR (KBr, cm^{-1}) 1754, 1373, 1221; MS(EI) *m*/*z* 606 (M)$^+$, 575 (M − OMe)$^+$, 546 (M − AcOH)$^+$. Anal. Calcd for $C_{25}H_{34}O_{17}$: C, 49.51; H, 5.65. Found: C, 49.02; H, 5.59.

Methyl 2,3-di-*O*-acetyl-4,6-*O*-(2,3,4-tri-*O*-acetyl-D-rhamnopyranosyl-idene)-α-D-galactopyranoside (23): colorless prisms; mp 198−200 °C; $[\alpha]^{27}_D$ +111.5° (*c* 1.0, $CHCl_3$); IR (KBr, cm^{-1}) 1750, 1373, 1227; MS(EI) *m*/*z* 548 (M)$^+$, 517 (M − OMe)$^+$, 488 (M − AcOH)$^+$. Anal. Calcd for $C_{23}H_{32}O_{15}$: C, 50.36; H, 5.88. Found: C, 50.32; H, 5.90.

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Supporting Information Available: X-ray data for **11**, **21**−**23** and the peak assignments in ^{1}H and ^{13}C NMR spectra for **4**, **6**, and **9**−**23**. This material is available free of charge via the Internet at http://pubs.acs.org.

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