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An Efficient Method for the Stereoselective Synthesis of β-D- and α-D-Ribofuranosides from 2,3,5-Tri-*O*-benzyl-D-ribofuranose by the Use of [Catecholato(2−)-*O*,*O*']oxotitanium and Trifluoromethanesulfonic Anhydride

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β-D-Ribofuranosides are stereoselectively synthesized in high yields directly from 2,3,5-tri-*O*-benzyl-D-ribofuranose and trimethylsilylated nucleophiles by the use of [catecholato(2−)-*O*,*O*']oxotitanium and trifluoromethanesulfonic anhydride, while α-D-ribofuranosides are prepared predominantly in high yields in the coexistence of lithium perchlorate.

The carbohydrate parts of glycoproteins, glycolipids, antibiotics, and immunodeterminants play biologically significant roles and the development of efficient and stereocontrolled construction of the glycosidic linkages is one of the most important problems in carbohydrate chemistry. Much effort has been devoted to the stereoselective synthesis of glycopyranosides and a large number of methods have been reported although stereoselective synthesis of glycofuranosides appears to be a more difficult problem. Most of the stereoselective synthesis of ribofuranosides are carried out starting from 1-*O*-acetyl-D-ribofuranoses,[1] D-ribofuranosyl fluorides[2] or 1-chloro-D-ribofuranuronic acids.[3] While, there have been reported a few methods concerning the glycosylation reaction starting from easily available 2,3,5-tri-*O*-protected D-ribofuranoses; for example, stereoselective synthesis of α-D- and β-D-ribofuranosyl disaccharides from protected ribofuranoses under basic conditions (NaH and *t*-BuOK).[4]

In our previous paper,[5] we reported one-pot glycosylation reactions employing 2,3,5-tri-*O*-benzyl-D-ribofuranose (**1**); that is, the stereoselective synthesis of α-D-ribofuranosides starting from **1** and alcohols or trimethylsilylated nucleophiles was achieved with the diphosphonium salt, prepared from tributylphosphine oxide and trifluoromethanesulfonic anhydride (triflic anhydride). Furthermore, the stereoselective synthesis of β-D-ribofuranosides was carried out by the combined use of [catecholato(2−)-*O*-*O*']oxotitanium (**2**) and triflic anhydride from the above-mentioned starting materials.[6]

In this paper, we would like to describe in full an efficient method for the highly stereoselective synthesis of β-D- and α-D-ribofuranosides from **1** and alcohols or trimethylsilylated nucleophiles with the combined use of **2** and triflic anhydride or together with an additive, lithium perchlorate, under mild conditions.

Results and Discussion

Synthesis of β-D-Ribofuranosides. First, glycosylation reaction of **1** with cyclohexyl trimethylsilyl ether was tried by using various titanium oxide species and triflic anhydride in the presence of *N*,*N*-diisopropylethylamine. The corresponding ribofuranoside was obtained in 95% yield (α/β=12/88) when **2** was employed. On the other hand, no ribofuranoside was obtained by the use of $(i\text{-PrO})_2\text{Ti=O}$ or $(\text{PhO})_2\text{Ti=O}$. Then, the effect of various bases and solvents on the above glycosylation reaction was further examined in order to achieve higher stereoselectivity and yield. The effect of bases is shown in Table 1. The combined use of *N*,*N*-diisopropylethylamine and cesium fluoride gave a better result (yield 95%, α/β=5/95), whereas no satisfactory result was observed when the above bases were used independently. Concerning the effect of solvents, a better yield (95%) was achieved when the reaction was carried out in dichloromethane, and a better stereoselectivity (α/β=2/98) was attained in diethyl ether.

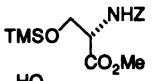
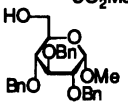
In a similar manner, the reaction with several alcohols or trimethylsilylated nucleophiles afforded the corresponding β-D-ribofuranosides[7] in high yields; for example, 3β-cholestanyl trimethylsilyl ether (88% yield, α/β=1/99) and phenyl trimethylsilyl ether (72% yield, α/β=9/91) (see Table 2). Meanwhile, the corresponding ribofuranosides were not obtained at all when acetonitrile was used as a solvent.

Synthesis of α-D-Ribofuranosides. The effect of several additives in the above mentioned reaction was further studied in order to perform the stereoselective α-D-glycosylation reaction. We have already reported several successful methods for the synthesis of α-D-ribofuranosides using trityl perchlorate or the combination of tin(IV) chloride and tin(II) triflate in the

Table 1. Effect of Bases and Solvents

Entry	Solvent	Base	Yield/%	α/β
1	CH_2Cl_2	$^i\text{Pr}_2\text{NEt}$	95	12/88
2	CH_2Cl_2	2,6-Lutidine	92	7/93
3	CH_2Cl_2	CsF	71	6/94
4	CH_2Cl_2	2,6-Lutidine+CsF	93	6/94
5	CH_2Cl_2	$^i\text{Pr}_2\text{NEt}$+CsF	95	5/95
6	Et_2O	$^i\text{Pr}_2\text{NEt}$+CsF	92	2/98
7	Toluene	$^i\text{Pr}_2\text{NEt}$+CsF	92	3/97

Table 2. Synthesis of β-D-Ribofuranosides

Entry	ROTMS or ROH	Yield/%	α/β
1	MeOTMS	92[a]	4/96
2	Cyclohexyl-OTMS	95[b]	5/95
3	3β-Cholestanyl-OTMS	88[a]	1/99
4	Octadecyl-OTMS	86[b]	7/93
5	PhOTMS	72[b]	9/91
6		97[b]	20/80
7[d]		94[c]	11/89

a) Et_2O. b) CH_2Cl_2. c) Toluene. d) When methyl 2,3,4-tri-*O*-benzyl-6-*O*TMS-α-D-giucopyranoside was employed, the corresponding ribofuranoside was obtained in 94% yield (α/β=20/80).

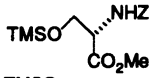
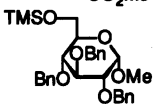
coexistence of lithium perchlorate from 1-*O*-acetylribofuranose and alcohols or trimethylsilylated nucleophiles. Accordingly, the glycosylation reaction of **1** with 3β-cholestanyl trimethylsilyl ether was tried in the coexistence of lithium perchlorate under the above reaction conditions and the corresponding α-D-ribofuranoside was obtained in 70% yield (α/β=99/1). Both yield and stereoselectivity were improved by further examination of the reaction conditions as bases and solvents (see Table 3). Concerning the effect of bases, the best stereoselectivity (α/β=>99/1) was obtained by the use of *N*,*N*-diisopropylethylamine or 2,6-lutidine. The yield and stereoselectivity were apparently influenced by the kind of solvents: The yield decreased in the following order; diethyl ether > dichloromethane, 1,2-dichloroethane > toluene, and the stereoselectivity decreased in the following order; dichloromethane, 1,2-dichloroethane > toluene > diethyl ether. Finally, the best result (yield 71%, α/β=>99/1) was attained when the reaction was carried out in dichloromethane or 1,2-dichloroethane in the coexistence of lithium perchlorate and *N*,*N*-diisopropylethylamine. Similarly, various α-D-ribofuranosides were successfully synthesized under the above mentioned procedures; for example, cyclohexyl trimethylsilyl ether (84% yield, α/β=98/2) and methyl 2,3,4-tri-*O*-benzyl-6-*O*-trimethylsilyl-α-D-glucopyranoside (90% yield, α/β=97/3) (see Table 4).

At present, the reaction is assumed to proceed via the

Table 3. Effect of Bases and Solvents

Entry	Solvent	Base	Yield/%	α/β
1	CH_2Cl_2	$^iPr_2NEt$+CsF	70	99/ 1
2	CH_2Cl_2	$^iPr_2NEt$	71	>99/ 1
3	CH_2Cl_2	2,6-Lutidine	67	>99/ 1
4	CH_2Cl_2	CsF	36	88/12
5	Et_2O	$^iPr_2NEt$	80	68/32
6	Toluene	$^iPr_2NEt$	59	95/ 5
7	1,2-Dichloroethane	$^iPr_2NEt$	71	>99/ 1

Table 4. Synthesis of α-D-Ribofuranosides

Entry	ROTMS	Yield/%	α/β
1	MeOTMS	94	82/18
2	Cyclohexyl-OTMS	84	98/ 2
3	3β-Cholestanyl-OTMS	71	99/ 1
4	Octadecyl-OTMS	72	98/ 2
5		83	80/20
6		90	97/ 3

intermediate **4** formed from **1** and **3**[8] together with **2** and *N*,*N*-diisopropylethylammonium triflate. Since the α-side of the anomeric center in the intermediate **4** is blocked by the internal chelation between the positively charged titanium(IV) atom and the oxygen atom located at 2-position of the ribofuranose, nucleophiles would exclusively approach from the β-side to form β-D-ribofuranosides accompanied with elimination of **2**.[9] On the other hand, in the coexistence of lithium perchlorate, the intermediate **5** would be formed readily from **4** and lithium perchlorate together with **2** and lithium triflate. In the intermediate **5**, the β-side of the anomeric center is blocked by the perchlorate anion and the anomeric carbon is attacked from the α-side by trimethylsilylated nucleophiles to form α-D-ribofuranosides (see Scheme 1).

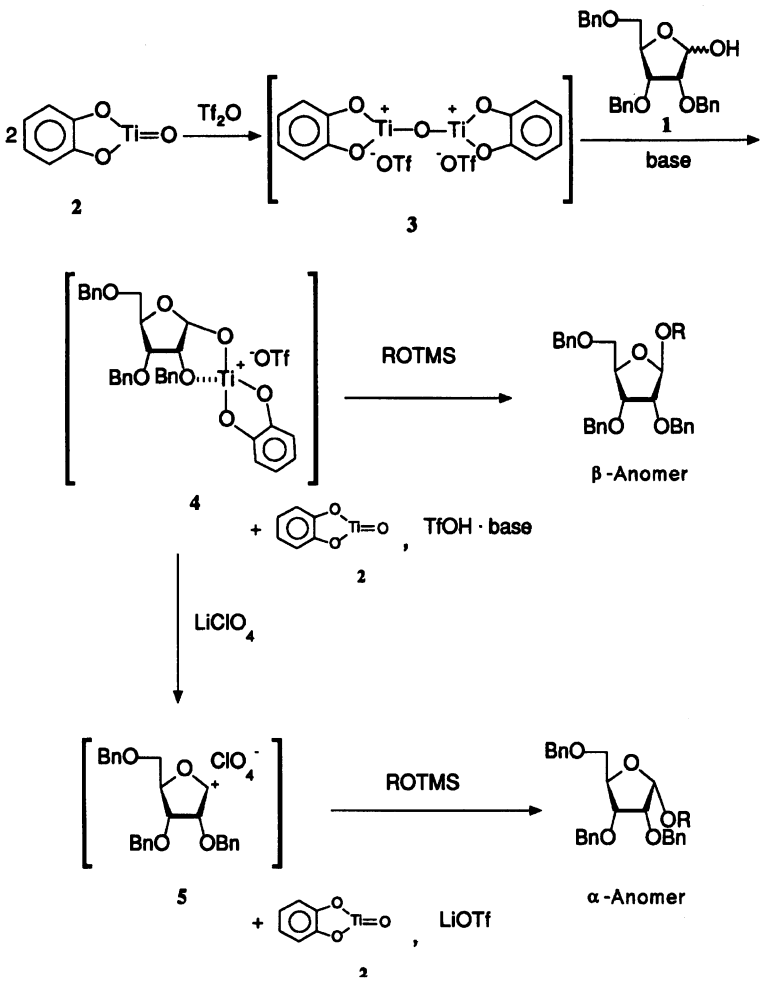
It is concluded that the combined use of **2** and triflic anhydride effectively promotes the stereoselective synthesis of β-D-ribofuranosides in high yields directly from **1** and alcohols or trimethylsilylated nucleophiles. Furthermore, α-D-ribofuranosides are obtained predominantly in high yields by the addition of lithium perchlorate to the above reaction system.

Experimental

All melting points are uncorrected. The IR spectra were determined on a Horiba FT-300 spectrometer. The ^1H NMR spectra were recorded with a JEOL JNM-EX270L, a JEOL JNM-GX400 or a Varian Unity 400 spectrometer with tetramethylsilane as an internal standard. Microanalyses were performed on a Yanako C, H, N analyzer. Optical rotations were measured with a JASCO DIP-360 digital polarimeter. Purification of products was performed by column chromatography on silica gel (Merck, Art. 7734 Kieselgel 60) or preparative TLC on silica gel (Wacogel B-5F).

2,3,5-Tri-*O*-benzyl-D-ribofuranose was prepared by the previously reported method.[10] Triflic anhydride was freshly distilled from P_2O_5. Dichloromethane and 1,2-dichloroethane were successively distilled from P_2O_5, and CaH_2, and stored over molecular sieves (MS). Diethyl ether was distilled from Na metal. Toluene was distilled from P_2O_5 and stored over MS.

Preparation of [Catecholato(2−)-*O*,*O*']oxotitanium. Under an argon atmosphere, a solution of (i-PrO)$_2$Ti=O (2.73 g, 15 mmol) and catechol (1.65 g, 15 mmol) in ben-



Scheme 1.

zene was heated for 2 h along with azeotropic removal of the resulting 2-propanol. After evaporation of the solvent, the residue was purified by dissolving in dichloromethane (15 ml) and reprecipitating with pentane (80 ml) to give **2** (1.95 g, 75%), mp >270°C. IR (KBr) 3430, 3390, 3060, 1480, 1260 cm^{-1}; ^1H NMR ($CDCl_3$) δ=5.50—7.50 (4H, m). Found: C, 39.41; H, 3.18; Ti, 26.0%. Calcd for $C_6H_4O_3Ti \cdot 0.5H_2O$: C, 39.81; H, 2.78; T, 26.5%.

Preparation of β-D-Ribofuranosides. A typical reaction procedure is described for the reaction of **1** and cyclohexyl trimethylsilyl ether: To a solution of **2** (0.58 mmol) in dichloromethane (5 ml) was added dropwise a solution of triflic anhydride (0.26 mmol) in dichloromethane (2 ml) at 0°C. After stirring for 1 h at 0°C and 1 h at room temperature, CsF (100 mg) was added to the reaction mixture. A solution containing 2,3,5-tri-*O*-benzyl-D-ribofuranose (0.13 mmol) and *N*,*N*-diisopropylethylamine (0.13 mmol) in dichloromethane (2 ml) was added at −23°C. Stirring was continued for 2 h, and then cyclohexyl trimethylsilyl ether (0.52 mmol) in dichloromethane (2 ml) was added dropwise. The solution was kept at 0°C for 8 h and washed with aqueous sodium hydrogencarbonate and dried over $MgSO_4$, and concentrated. The residue was purified by thin layer chromatography (silica gel) to give cyclohexyl 2,3,5-tri-*O*-benzyl-β-D-ribofuranoside (90%) and the corresponding α-anomer (5%): $[\alpha]_D^{24}$ −0.8° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=1.10—1.90 (10H, m), 3.52 (1H, dd, *J*=10.5 and 6.1 Hz, 5A-H), 3.56 (1H, m), 3.60 (1H, dd, *J*=10.5 and 4.0 Hz, 5B-H), 3.83 (1H, dd, *J*=4.8 and 1.3 Hz, 2-H), 4.01 (1H, dd, *J*=6.6 and 4.8 Hz, 3-H), 4.32 (1H, m, 4-H), 4.48 and 4.58 (2H, AB, *J*=11.7 Hz, C<u>H</u>$_2$Ph), 4.54 and 4.58 (2H, AB, *J*=12.1 Hz, C<u>H</u>$_2$Ph), 4.65 (2H, AB, *J*=12.3 Hz, C<u>H</u>$_2$Ph), 5.17 (1H, d, *J*=1.3 Hz, 1-H), 7.21—7.38 (15H, m); ^{13}C NMR ($CDCl_3$) δ=103.19 (C-1). Found: C, 76.20; H, 7.42%. Calcd for $C_{32}H_{38}O_5$: C, 76.46; H, 7.62%.

Physical properties of other products are presented:

Methyl 2,3,5-Tri-*O*-benzyl-β-D-ribofuranoside. $[\alpha]_D^{20}$ +20.0° (*c* 3.7, dioxane); ^1H NMR ($CDCl_3$) δ=3.30 (3H, s, OCH_3), 3.51 (1H, dd, *J*=10.6 and 5.9 Hz, 5A-H), 3.61 (1H, dd, *J*=10.6 and 3.9 Hz, 5B-H), 3.84 (1H, d, *J*=4.9 Hz, 2-H), 4.02 (1H, dd, *J*=4.9 and 7.1 Hz, 3-H), 4.35 (1H, m, 4-H), 4.44 and 4.54 (2H, AB, *J*=11.9 Hz, C<u>H</u>$_2$Ph), 4.53 and 4.57 (2H, AB, *J*=12.1 Hz, C<u>H</u>$_2$Ph), 4.60 and 4.66 (2H, AB, *J*=12.1 Hz, C<u>H</u>$_2$Ph), 4.91 (1H, s, 1-H), 7.25—7.37 (15H, m); ^{13}C NMR ($CDCl_3$) δ=106.30 (C-1); lit,[2] ^1H NMR ($CDCl_3$) δ=4.9 (1H, s, 1-H), ^{13}C NMR ($CDCl_3$) δ=106.3 (C-1), lit,[11] ^1H NMR ($CDCl_3$) δ=4.89 (1H, s, 1-H).

3-β-Cholestanyl 2,3,5-Tri-*O*-benzyl-β-D-ribofuranoside. Mp 83.5—84.0°C (EtOH). $[\alpha]_D^{26}$ +4.3° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=0.54—1.98 (47H, m), 3.52 (1H, dd, *J*=10.5 and 6.1 Hz, 5A-H), 3.59 (1H, dd, *J*=10.5 and 4.0 Hz, 5B-H), 3.83 (1H, dd, *J*=4.8 and 1.1 Hz, 2-H),

4.00 (1H, dd, J=6.8 and 4.8 Hz, 3-H), 4.31 (1H, m, 4-H), 4.46 and 4.56 (2H, AB, J=12.0 Hz, C$\underline{H}_2$Ph), 4.53 and 4.57 (2H, AB, J=12.1 Hz, C$\underline{H}_2$Ph), 4.65 (2H, AB, J=12.1 Hz, C$\underline{H}_2$Ph), 5.17 (1H, d, J=1.1 Hz, 1-H), 7.20—7.40 (15H, m); ^{13}C NMR ($CDCl_3$) δ=103.00 (C-1). Found: C, 80.44; H, 9.67%. Calcd for $C_{53}H_{74}O_5$: C, 80.46; H, 9.43%.

Octadecyl 2,3,5-Tri-*O*-benzyl-β-D-ribofuranoside. $[\alpha]_D^{23}$ +9.4° (c 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ=0.88 (3H, t, J=6.6 Hz, C$\underline{H}_3$), 1.26 (30H, s), 1.48 (2H, brs., $CH_2C\underline{H}_2CH_2O$), 3.32 (1H, dt, J=9.5 and 6.9 Hz, $CH_2C\underline{H}_2O$), 3.50 (1H, dd, J=10.6 and 5.9 Hz, 5A-H), 3.60 (1H, dd, J=10.6 and 3.6 Hz, 5B-H), 3.65 (1H, dt, J=9.5 and 6.9 Hz, $CH_2C\underline{H}_2O$), 3.85 (1H, dd, J=4.6 and 1.0 Hz, 2-H), 4.01 (1H, dd, J=6.9 and 4.6 Hz, 3-H), 4.45 and 4.56 (2H, AB, J=11.6 Hz, C$\underline{H}_2$Ph), 4.55 (2H, AB, J=12.2 Hz, C$\underline{H}_2$Ph), 4.62 and 4.68 (2H, AB, J=11.9 Hz, C$\underline{H}_2$Ph), 5.01 (1H, d, J=1.0 Hz, 1-H), 7.20—7.40 (15H, m); ^{13}C NMR ($CDCl_3$) δ=105.23 (C-1). Found: C, 78.25; H, 9.42%. Calcd for $C_{44}H_{64}O_5$: C, 78.53; H, 9.59%.

***N*-(Benzyloxycarbonyl)-*O*-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-L-serine Methyl Ester.** $[\alpha]_D^{26}$ +13.9° (c 1.1, $CHCl_3$); IR (neat) 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.37 (1H, dd, J=10.8 and 4.6 Hz, 5A-H), 3.56 (1H, dd, J=10.8 and 3.2 Hz, 5B-H), 3.62 (3H, s, $COOC\underline{H}_3$), 3.71 (1H, dd, J=10.4 and 3.9 Hz, $OC\underline{H}_2CH(NHZ)COOCH_3$), 3.83 (1H, d, J=4.6 Hz, 2-H), 4.00 (1H, dd, J=7.5 and 4.6 Hz, 3-H), 4.08 (1H, dd, J=10.4 and 3.9 Hz, $OC\underline{H}_2CH(NHZ)COOCH_3$), 4.24 (1H, m, 4-H), 4.34—4.64 (7H, m, 3C$\underline{H}_2$Ph and $OC\underline{H}_2CH(NHZ)COOCH_3$), 4.95 (1H, s, 1-H), 5.09 (2H, AB, J=12.0 Hz, $COOC\underline{H}_2$Ph), 6.05 (1H, d, J=8.4 Hz, N$\underline{H}$Z), 7.21—7.35 (20H, m); ^{13}C NMR ($CDCl_3$) δ=170.40, 155.99, and 105.27 (C-1). Found: C, 69.33; H, 6.35; N, 2.25%. Calcd for $C_{38}H_{41}NO_9$: C, 69.60; H, 6.30; N, 2.14%.

Phenyl 2,3,5-Tri-*O*-benzyl-β-D-ribofuranoside. Mp 76.0—77.0°C (hexane). $[\alpha]_D^{25}$ −20.3° (c 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ=3.53 (1H, dd, J=10.9 and 5.3 Hz, 5A-H), 3.61 (1H, dd, J=10.9 and 4.0 Hz, 5B-H), 4.12 (1H, dd, J=4.6 and 1.0 Hz, 2-H), 4.21 (1H, dd, J=6.6 and 4.6 Hz, 3-H), 4.40—4.73 (7H, m, 3C$\underline{H}_2$Ph and 4-H), 5.70 (1H, d, J=1.0 Hz, 1-H), 6.96—7.38 (20H, m); ^{13}C NMR ($CDCl_3$) δ=103.36 (C-1). Found: C, 77.11; H, 6.72%. Calcd for $C_{32}H_{32}O_5$: C, 77.40; H, 6.50%.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-α-D-glucopyranoside. $[\alpha]_D^{26}$ +13.8° (c 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ=3.29 (3H, s), 3.35—5.00 (24H, m), 5.06 (1H, s, 1-H), 7.15—7.40 (30H, m); ^{13}C NMR ($CDCl_3$) δ=105.78 (C-1). Found: C, 74.99; H, 6.85%. Calcd for $C_{54}H_{58}O_{10}$: C, 74.81; H, 6.74%; lit,[2] ^{1}H NMR ($CDCl_3$) δ=5.07 (1H, d, J=0.8 Hz, 1-H); ^{13}C NMR ($CDCl_3$) δ=105.87 (C-1).

Preparation of α-D-Ribofuranosides. A typical reaction procedure is described for the reaction of **1** and 3β-cholestanyl trimethylsilyl ether: To a stirred suspension of **2** (0.55 mmol) and lithium perchlorate (2 mmol) in dichloromethane (5 ml) was added dropwise a solution of triflic anhydride (0.25 mmol) in dichloromethane (2 ml) at 0°C. After stirring for 1 h at 0°C and 1 h at room temperature, a solution containing 2,3,5-tri-*O*-benzyl-D-ribofuranose (0.12 mmol) and *N*,*N*-diisopropylethylamine (0.25 mmol) in dichloromethane (2 ml) was added at −23°C. Stirring was continued for 1 h, and then 3β-cholestanyl trimethylsilyl ether (0.49 mmol) in dichloromethane (2 ml) was added dropwise. The solution was kept at 0°C for 8 h and washed with aqueous sodium hydrogencarbonate and dried over $MgSO_4$, and concentrated. The residue was purified by thin-layer chromatography (silica gel) to give 3β-cholestanyl 2,3,5-tri-*O*-benzyl-α-D-ribofuranoside (71%) and the corresponding β-anomer (trace). Mp 112.0—112.4°C (hexane); $[\alpha]_D^{26}$ +84.5° (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ=0.57—2.00 (47H, m), 3.36 (1H, dd, J=10.5 and 4.0 Hz, 5A-H), 3.44 (1H, dd, J=10.5 and 4.0 Hz, 5B-H), 3.58 (1H, m), 3.74 (1H, dd, J=7.0 and 4.2 Hz, 2-H), 3.82 (1H, dd, J=7.0 and 4.0 Hz, 3-H), 4.23 (1H, q, J=4.0 Hz, 4-H), 4.41 and 4.47 (2H, AB, J=12.1 Hz, C$\underline{H}_2$Ph), 4.53 and 4.72 (2H, AB, J=12.6 Hz, C$\underline{H}_2$Ph), 4.62 and 4.69 (2H, AB, J=12.5 Hz, C$\underline{H}_2$Ph), 5.15 (1H, d, J=4.2 Hz, 1-H), 7.20—7.40 (15H, m); ^{13}C NMR ($CDCl_3$) δ=99.70 (C-1). Found: C, 80.16; H, 9.59%. Calcd for $C_{53}H_{74}O_5$: C, 80.46; H, 9.43%.

Physical properties of other products are presented:

Methyl 2,3,5-Tri-*O*-benzyl-α-D-ribofuranoside. $[\alpha]_D^{23}$ +78.0° (c 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ=3.25 (3H, s, OCH_3), 3.35 (1H, dd, J=10.4 and 4.2 Hz, 5A-H), 3.41 (1H, dd, J=10.4 and 4.2 Hz, 5B-H), 3.77 (1H, dd, J=6.8 and 4.2 Hz, 2-H), 3.82 (1H, dd, J=6.8 and 2.9 Hz, 3-H), 4.25 (1H, m, 4-H), 4.42 and 4.49 (2H, AB, J=12.1 Hz, C$\underline{H}_2$Ph), 4.58 and 4.64 (2H, AB, J=12.5 Hz, C$\underline{H}_2$Ph), 4.61 and 4.68 (2H, AB, J=12.8 Hz, C$\underline{H}_2$Ph), 4.87 (1H, d, J=4.2 Hz, 1-H), 7.20—7.35 (15H, m); ^{13}C NMR ($CDCl_3$) δ=102.43 (C-1); lit,[2] ^{1}H NMR ($CDCl_3$) δ=4.8 (1H, d, J=3—4 Hz, 1-H); ^{13}C NMR ($CDCl_3$) δ=102.4 (C-1), lit,[11] $[\alpha]_D^{24}$ +77.6° (c 1.4, $CHCl_3$), ^{1}H NMR ($CDCl_3$) δ=4.86 (1H, d, J=4 Hz, 1-H).

Cyclohexyl 2,3,5-Tri-*O*-benzyl-α-D-ribofuranoside. $[\alpha]_D^{30}$ +97.9° (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ=1.12—2.02 (10H, m), 3.37 (1H, dd, J=10.5 and 4.2 Hz, 5A-H), 3.46 (1H, dd, J=10.5 and 3.7 Hz, 5B-H), 3.61 (1H, m), 3.76 (1H, dd, J=6.8 and 4.0 Hz, 2-H), 3.84 (1H, dd, J=6.8 and 4.0 Hz, 3-H), 4.24 (1H, q, J=4.0 Hz, 4-H), 4.41 and 4.47 (2H, AB, J=12.3 Hz, C$\underline{H}_2$Ph), 4.52 and 4.72 (2H, AB, J=12.6 Hz, C$\underline{H}_2$Ph), 4.61 and 4.72 (2H, AB, J=12.3 Hz, C$\underline{H}_2$Ph), 5.17 (1H, d, J=4.0 Hz, 1-H), 7.20—7.40 (15H, m); ^{13}C NMR ($CDCl_3$) δ=99.70 (C-1). Found: C, 76.25; H, 7.58%. Calcd for $C_{32}H_{38}O_5$: C, 76.46; H, 7.62%.

Octadecyl 2,3,5-Tri-*O*-benzyl-α-D-ribofuranoside. $[\alpha]_D^{23}$ +60.8° (c 1.23, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ=0.88 (3H, t, J=6.6 Hz, C$\underline{H}_3$), 1.26 (30H, s), 1.67 (2H, brs., $CH_2C\underline{H}_2CH_2O$), 3.35 (1H, dd, J=10.6 and 4.0 Hz, 5A-H), 3.45 (1H, dd, J=10.6 and 4.0 Hz, 5B-H), 3.52 (1H, m, $CH_2C\underline{H}_2O$), 3.70—3.86 (3H, m, 2-H, 3-H, and $CH_2C\underline{H}_2O$), 4.23 (1H, dd, J=7.6 and 4.0 Hz, 4-H), 4.41 and 4.48 (2H, AB, J=12.2 Hz, C$\underline{H}_2$Ph), 4.53 and 4.69 (2H, AB, J=12.5 Hz, C$\underline{H}_2$Ph), 4.61 and 4.67 (2H, AB, J=12.2 Hz, C$\underline{H}_2$Ph), 5.00 (1H, d, J=4.3 Hz, 1-H), 7.12—7.56 (15H, m); ^{13}C NMR ($CDCl_3$) δ=101.24 (C-1). Found: C, 78.25; H, 9.42%. Calcd for $C_{44}H_{64}O_5$: C, 78.43; H, 9.53%.

***N*-(Benzyloxycarbonyl)-*O*-(2,3,5-tri-*O*-benzyl-α-D-ribofuranosyl)-L-serine Methyl Ester.** $[\alpha]_D^{27}$ +53.2° (c 1.0, $CHCl_3$); IR (neat) 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.34 (1H, dd, J=10.5 and 3.9 Hz, 5A-H), 3.41 (1H, dd, J=10.5 and 3.7 Hz, 5B-H), 3.67 (3H, s, $COOC\underline{H}_3$), 3.81 (1H, dd, J=6.3 and 4.0 Hz, 2-H), 3.85 (1H, dd, J=6.3 and 2.8 Hz, 3-H), 3.91 (1H, dd, J=10.5 and 3.2 Hz, $OC\underline{H}_2CH(NHZ)COOCH_3$), 4.12 (1H, dd, J=10.5 and 3.2

Hz, $OC\underline{H}_2CH(NHZ)COOCH_3$), 4.21 (1H, m 4-H), 4.38—4.68 (7H, m, $3C\underline{H}_2Ph$ and $OC\underline{H}_2CH(NHZ)COOCH_3$), 4.95 (1H, d, J=4.0 Hz, 1-H), 5.05 and 5.12 (2H, AB, J=12.3 Hz, $COOC\underline{H}_2Ph$), 6.41 (1H, d, J=9.2 Hz, $N\underline{H}Z$), 7.18—7.34 (20H, m); ^{13}C NMR ($CDCl_3$) δ=170.92, 156.35, and 101.08 (C-1). Found: C, 69.41; H, 6.08; N, 2.38%. Clacd for $C_{38}H_{41}NO_9$: C, 69.60; H, 6.30; N, 2.14%.

Phenyl 2,3,5-Tri-*O*-benzyl-α-D-ribofuranoside. $[\alpha]_D^{27}$ +124.6° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=3.39 (1H, dd, J=10.6 and 3.7 Hz, 5A-H), 3.49 (1H, dd, J=10.6 and 3.8 Hz, 5B-H), 4.00 (2H, m, 2-H, and 3-H), 4.37 (1H, m, 4-H), 4.41 and 4.51 (2H, AB, J=12.1 Hz, $C\underline{H}_2Ph$), 4.62 and 4.77 (2H, AB, J=12.5 Hz, $C\underline{H}_2Ph$), 4.71 (2H, AB, J=12.3 Hz, $C\underline{H}_2Ph$), 5.63 (1H, d, J=4.4 Hz, 1-H), 7.15—7.40 (20H, m); ^{13}C NMR ($CDCl_3$) δ=99.83 (C-1). Found: C, 77.18; H, 6.41%. Calcd for $C_{32}H_{32}O_5$: C, 77.40; H, 6.50%.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,5-tri-*O*-benzyl-α-D-ribofuranosyl)-α-D-glucopyranoside. $[\alpha]_D^{26}$ +82.0° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=3.33 (3H, s, OCH_3), 3.40 (1H, dd, J=10.7 and 4.0 Hz), 3.45 (1H, dd, J=9.5 and 3.7 Hz), 3.46 (1H, dd, J=10.7 and 3.4 Hz), 3.66 (1H, dd, J=11.3 and 0.5 Hz), 3.70—3.78 (2H, m), 3.86—3.90 (2H, m), 3.95 (1H, dd, J=9.5 and 8.6 Hz), 4.15 (1H, dd, J=11.3 and 3.4 Hz), 4.21 (1H, m), 4.40—4.76 (9H, m), 4.73 (2H, s), 4.74 (2H, AB, J=11.0 Hz), 5.14 (1H, d, J=2.3 Hz), 7.15—7.38 (30H, m); ^{13}C NMR ($CDCl_3$) δ=102.07 (C-1). Found: C, 74.51; H, 6.46%. Calcd for $C_{54}H_{58}O_{10}$: C, 74.81; H, 6.74%. lit,[2] ^1H NMR ($CDCl_3$) δ=5.14 (1H, d, J=3—5 Hz, 1-H); ^{13}C NMR ($CDCl_3$) δ=102.0 (C-1).

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7) The configuration of the anomeric center was determined by the ^1H NMR and ^{13}C NMR spectra. The vicinal coupling constants of the β-anomeric protons were the small value (J=0—1 Hz). The chemical shifts of the β-anomeric carbons were at lower field compared with the α-anomeric carbons.

8) In analogous to the case of the diphosphonium salt prepared from tributylphosphine oxide and triflic anhydride, we assumed the intermediate **3** would be formed from **2** and triflic anhydride.

9) No isomerization of α-D-ribofuranosides to β-D-ribofuranosides was observed under the present reaction conditions.

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