New Synthetic Methods and Reagents for Complex Carbohydrates. VII. Syntheses and Glycosylation Reactions of Glycopyranosyl Dimethylphosphinothioate Series Having a Nonparticipating Group at the C-2 Position

Takashi YAMANOI, Kazumi NAKAMURA, Shuji SADA, Masahiro GOTO, Yoji FURUSAWA, Masaaki TAKANO, Ayumi FUJIOKA, Kenji YANAGIHARA, Yuzuru SATOH, Hideaki HOSOKAWA, and Toshiyuki INAZU*
The Noguchi Institute, 1-8-1, Kaga, Itabashi-ku, Tokyo 173
(Received February 1, 1993)

Several glycopyranosyl dimethylphosphinothioates having a nonparticipating group at the C-2 position could be easily prepared by reactions of the corresponding glycopyranose and dimethylphosphinothioyl chloride using butyllithium as a base in tetrahydrofuran. These dimethylphosphinothioates are stable at room temperature and gave the corresponding α-glycosides, predominantly in good yields, by reactions with alcohols using silver perchlorate as an activator in the presence of molecular seives 4A in benzene at room temperature. Also, the combined use of iodine and a catalytic amount of triphenylmethyl perchlorate was effective for this glycosidation as a new activating system instead of silver perchlorate. Further, the synthetic intermediates of H-disaccharide and the Lewis X antigen were prepared using the present method.

The stereoselective synthesis of oligosaccharides is an important problem in carbohydrate chemistry.[1] The classical Koenig–Knorr glycosylation reaction, using unstable acylated glycosyl halide as a glycosyl donor, has been widely used for a long time. Recently, in order to improve the stability of the glycosyl donor as well as the stereoselectivity of glycoside formation, many new methods have been reported, which are the so-called "non-Koenig–Knorr" reaction. Glycosyl donors, such as glycosyl fluoride,[2] glycosyl trichloroacetimidate,[3] pentenyl glycoside,[4] and thioglycoside,[5] having a nonparticipating group at the C-2 position were used. Several glycosyl donors using phosphorus containing leaving groups have been reported as a new class of glycosyl donors; such as: glycosyl phosphorodithioate,[6] glycosyl diphenyl phosphate,[7] and so on.[8] We have also reported on the glycosyl dimethylphosphinothioate method for α-D-glucopyranosylation,[9] 2-amino-2-deoxy-β-D-glucopyranosylation,[10] 2-deoxy-β-D-glucopyranosylation,[11] and β-mannopyranosylation,[12] during the course of our continuous investigation to apply dimethylphoshinothioyl (Mpt) chloride[13] to synthetic carbohydrate chemistry.[14] Mpt-Cl was a useful reagent for protecting the amino group and coupling the amino acids in peptide synthesis.[13,15]

In this paper we describe the syntheses and glycosidation of a glycopyranosyl dimethylphosphinothioate series having a nonparticipating equatorial group at the C-2 position.

Results and Discussion

First, we examined the reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**1**)[16] and Mpt-Cl. Because of the poor reactivity of Mpt-Cl with alcohol,[15] the reaction in the presence of triethylamine in dichloromethane gave no product. According to the literature concerning how to obtain the stereoselective glycosyl acetate[17] and phosphate,[18] we attempted a reaction of **1** and Mpt-Cl using butyllithium and thallium ethoxide in tetrahydrofuran (THF). In the case of *n*-BuLi, the desired 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl dimethylphosphinothioate (**2**) was obtained in good yields. It was found that the anomer ratios were dependent on the reaction temperature. The reaction at −30 °C gave **2α** selectively in 96% yield. Although the reaction using TlOEt gave **2β** with high selectivity, the yield was poor.

By using *n*-BuLi and Mpt-Cl, we could prepare 2,3,4-tri-*O*-benzyl-L-fucopyranosyl dimethylphosphinothioate (**3**), methyl 2,3,4-tri-*O*-benzyl-1-*O*-dimethylphosphinothioyl-D-glucopyranuronate (**4**), and 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranosyl dimethylphosphinothioate (**5**) from 2,3,4-tri-*O*-benzyl-L-fucopyranose

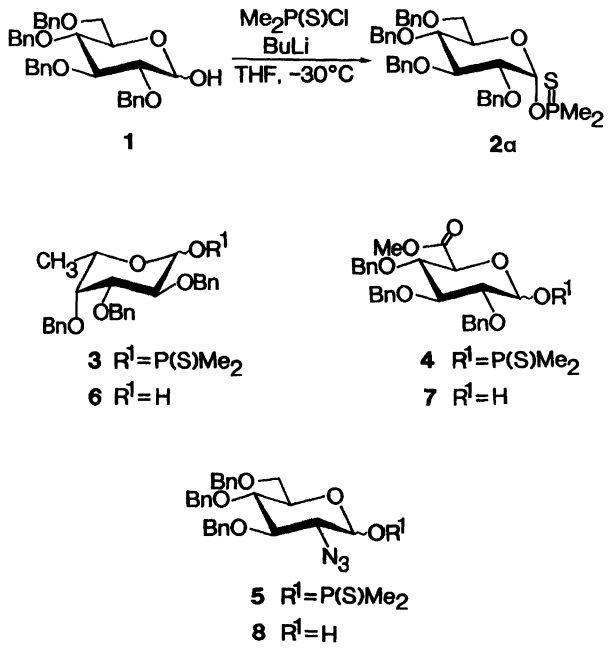


Fig. 1. Glycopyranosyl dimethylphosphinothioates (Bn=benzyl).

Table 1. Syntheses of Several Glycopyranosyl Dimethylphosphinothioates

Compound	Solvent	Base	Temp/°C	Product	Yield/%	α/β Ratio[a)]
1	CH_2Cl_2	Et_3N	R.T.	**2**	No reaction	
1	THF	*n*-BuLi	66	**2**	90	40/60
1	THF	*n*-BuLi	0	**2**	99	50/50
1	THF	*n*-BuLi	−30	**2**	96	α(>98%)
1	THF–Benzene	TlOEt	R.T.	**2**	30	9/91
6	THF	*n*-BuLi	−30	**3**	90	86/14
7	THF	*n*-BuLi	−30	**4**	80	40/60[b)]
7	THF	*n*-BuLi	−70	**4**	79	69/31[b)]
8	THF	*n*-BuLi	−30	**5**	67	58/42[b)]

a) Determined by ^{1}H NMR spectra. b) Determined by the isolated yield.

Table 2. Properties of Glycopyranosyl Dimethylphosphinothioates

Compound	Mp/°C	$[\alpha]_D^{24}$/degree	^{1}H NMR spectra of H-1/ppm[a)] ($J_{1,2}$, J_{HCP}/Hz)	^{13}C NMR spectra of C-1/ppm[b)] (J_{COP}/Hz)
2α	62—64	+37.4 (*c* 1, $CHCl_3$)	6.18 (3.4, 12.0)	92.28 (5.5)
2β	84—85	−0.7 (*c* 1.35, $CHCl_3$)	5.38 (8.1, 11.5)	96.62 (8.3)
3α	oil	−80.0 (*c* 4.06, $CHCl_3$)	6.13 (3.4, 14.8)	93.50 (5.5)
3β	oil	+27.8 (*c* 0.89, $CHCl_3$)	5.31 (11.7, 12.1)	96.82 (7.3)
4α	103—104	+86.5 (*c* 1.11, PhH)	6.18 (3.4, 12.7)	92.24 (4.5)
4β	106—107	+4.5 (*c* 1.11, PhH)	5.45 (11.7, 11.7)	96.26 (7.4)
5α	98—99.5	+80.5 (*c* 2.77, $CHCl_3$)	6.04 (3.7, 12.0)	93.29 (5.5)
5β	oil	−18.2 (*c* 1.65, $CHCl_3$)	5.27 (8.1, 11.5)	95.46 (5.5)

a) Signals were observed in double–doublet in all cases. b) Signals were observed in doublet in all cases.

(**6**),[19] methyl 2,3,4-tri-*O*-benzyl-D-glucopyranuronate (**7**),[20] 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranose (**8**)[21] in 90, 80, and 67% yields, respectively as shown in Table 1 (Fig. 1).

It is noted that these glycosyl dimethylphosphinothioates are stable compounds after being on the shelf for several months without receiving any special care. The physical data concerning these glycosyl dimethylphosphinothioates are given in Table 2.

Although the anomer selectivity of **3** was similar to those of **2**, **4** and **5** were obtained with low selectivities. Based on these findings, we assumed the mechanism of stereoselectivity to be as follows. The five-membered chelate ring shown in Fig. 2 might be formed by a coordination of the oxygen atom in the benzyloxy group at the C-2 position and the 1-*O*-lithium cation at low temperature. Consequently, **2** and **3** were obtained with high α-selectivity. In the case of **4**, the coordination of the 6-carbonyl group and the lithium cation would decreased the α-selectivity. Compound **5** could not be synthesized selectively, due to the absence of a benzyloxy group at the C-2 position.

Secondly, we investigated the glucosidation of 3β-cholestanol using compound **2α**. We considered that a silver cation would promote glycosidation using the dimethylphosphinothioates, as shown in Fig. 3. Based on this hypothesis, we examined the glucosidation using several kinds of silver salts and mercury salt, such as silver perchlorate, silver oxide, silver carbonate, silver *p*-toluenesulfonate, silver trifluoromethanesulfonate,

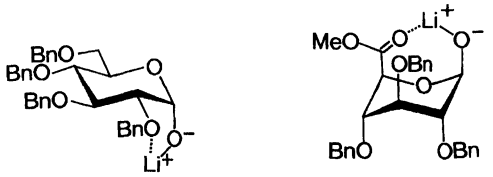


Fig. 2. Coordination of the oxygen atom in the benzyloxy group and the 1-*O*-lithium cation.

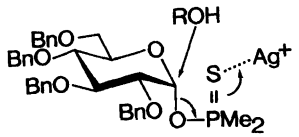


Fig. 3. Hypothesis of glycosidation using glycopyranosyl dimethylphosphinothioate.

and mercury acetate. This glucosidation was carried out with an equivalent amount of reagents in THF in the presence of molecular sieves 4A. We found that the corresponding glucoside was obtained in 63% yield, only when silver perchlorate was used. Other silver salts gave no glucoside. In the case of $Hg(OAc)_2$, only 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl acetate was obtained in 32% yield.

We then examined the effect of the reaction temperature in order to improve the stereoselectivities of glucosidation. The corresponding glucopyranoside was obtained in 18% yield at −5 °C, and the reaction at −30 °C gave no glucoside. We also found that the yield

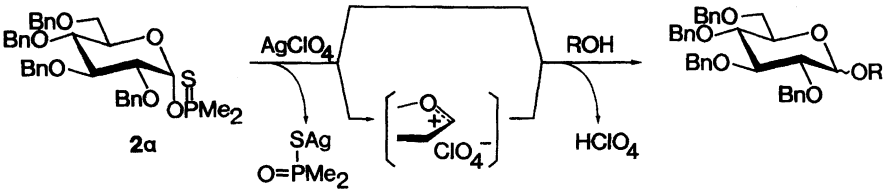


Fig. 4. Postulated mechanism of glycoside formation from **2α** with alcohol using $AgClO_4$.

was not improved at all even when the temperature was gradually raised from −5 °C to room temperature. This result suggested that the initial reaction temperature would be significant for this glucosidation reaction.

Further, we examined the solvent effect of this reaction using THF, diethyl ether, benzene, acetonitrile, and *N*,*N*-dimethylformamide (DMF). Acetonitrile and DMF did not give the glucoside at all. However, THF and diethyl ether gave the glucoside in 63 and 52% yields, respectively. In particular, the use of benzene increased the yield of glucoside up to 89%.

We also examined the effect of molecular seives. In the absence of molecular seives 4A, the yield decreased to 59%. We could not determine the apparent difference of the effect of various kinds of molecular seives, such as 3A, 4A, and 5A. While using molecular sieves to keep the reaction system drying, we assumed that the molecular seives would also act to capture $HClO_4$.

Under the above-described best reaction conditions, we examined glycosidation with several alcohols using compounds **2α** and **3**. Several α-glucosides were obtained predominantly in good yields (Fig. 4). The reaction of **2α** and methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (**10**) having a hindered hydroxyl group, gave the corresponding glucoside in only 48% yield. However, the yield increased up to 82% when **2α** and $AgClO_4$ were used in 2 equiv portions. We found that the reaction using *t*-butyl alcohol gave *t*-butyl glucoside in only 26% yield, and that the yield could not be improved, even under conditions using excess amounts of the reagents. These results are summarized in Table 3 (Fig. 5).

Table 3. Glycoside Formation from Dimethylphosphinothioates (**2α**, **3**) and Several Alcohols Using $AgClO_4$

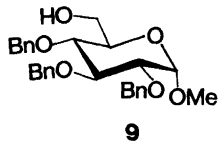
Donor	Acceptor	Yield/%	α/β Ratio[a]
2α	CH_3OH	90	69/31
2α	Cyclohexanol	91	75/25
2α	3β-Cholestanol	89	81/19
2α	Z-L-Ser-OMe[b]	89	69/31[c]
2α	**9**	86	70/30[c]
2α	**10**	82	90/10
2α	*t*-BuOH	26	N.D.[d]
3	Cyclohexanol	85	56/44
3	3β-Cholestanol	75	56/44[c]
3	**11**	60	64/36[c]

a) Determined by the isolated yield. b) Z = benzyloxycarbonyl. c) Determined by ^1H NMR spectra. d) N. D. = Not determined.

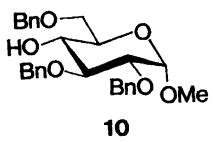
This glucosidation was not considered to be carried out by only the S_N2 reaction, as shown in Fig. 3. We have presently assumed that this glycosidation would proceed mainly by the S_N1 reaction, as shown in Fig. 4. Glycosyl perchlorate, which was known as an intermediate to give α-glucosides predominantly,[22] could be formed after leaving the Mpt group by the interaction of silver cation with the sulfur atom of the Mpt group.

We also attempted the glycosidation of **4** and **5** with 3β-cholestanol under the same reaction conditions. Compound **4** gave the corresponding α-glucoside predominantly in only 30% yield.[23] Although the glucoside was obtained in 51% yield by a reaction using **5**, the reproducibility of the stereoselectivity was poor.[23]

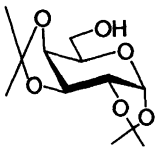
It is very important to develop a new class of activating reagents without using heavy metals. We thought that the iodonium cation would be effective for this glycosidation as well as the silver cation. We thus chose iodine as an iodonium cation source. Similarly, we attempted the reaction of compound **2α** and 3β-cholestanol with 1 equiv amount of iodine in the presence of molecular seives 4A. We postulated that these molecular seives could act not only as a drying reagent, but also as to capture HI. The corresponding glucoside was obtained in 47% yield. When 10 mol% amount of triphenylmethyl perchlorate ($TrtClO_4$)[24] was added to the above-mentioned reaction conditions, the yield increased remarkably up to 82%. On the other hand, the glucoside was obtained in 28% yield using only 10 mol% amount of $TrtClO_4$ in the absence of iodine. By



9



10



11

Fig. 5. Glycosyl acceptors.

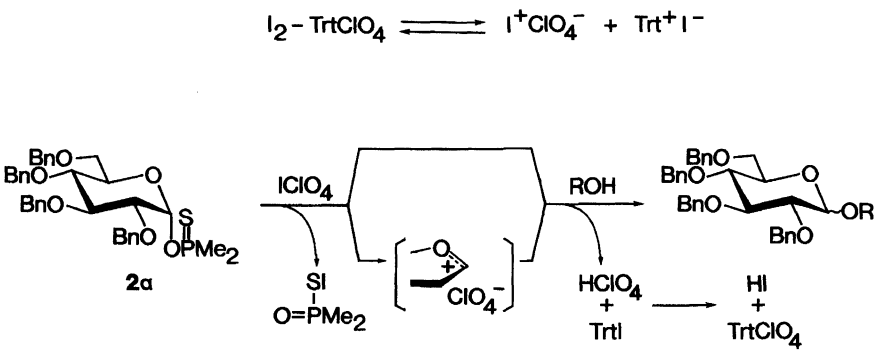


Fig. 6. Postulated mechanism of glycoside formation from **2α** and alcohol using iodine–10 mol% $TrtClO_4$.

Table 4. Glycoside Formation from Dimethylphosphinothioates (**2α**, **3**) and Several Alcohols Using Iodine–10 mol% $TrtClO_4$

Donor	Acceptor	Yield/%	α/β Ratio[a]
2α	3β-Cholestanol	82	72/28
2α	3β-Cholestanol	47[b]	N.D.[c]
2α	3β-Cholestanol	28[d]	N.D.[c]
2α	Cyclohexanol	67	62/38
2α	*t*-BuOH	84	68/32
2α	**11**	78	57/43[e]
2α	**9**	66	74/26[e]
3	Cyclohexanol	80	61/39

a) Determined by ^{1}H NMR spectra. b) Only 1 equiv amount of iodine was used as an activator. c) N. D. =Not determined. d) Only 10 mol% amount of $TrtClO_4$ was used as an activator. e) Determined by the isolated yield.

this activating system, the combined use of iodine and 10 mol% of $TrtClO_4$, several α-gluco- and α-fucopyranosides were predominantly obtained in good yields by the reaction of the corresponding dimethylphosphinothioate (**2α** and **3**) with a variety of alcohols. Interestingly, we found that the reaction of **2α** and *t*-butyl alcohol gave the corresponding glucoside in 84% yield with a selectivity of $\alpha/\beta=68/32$, which were different from glucosidation using $AgClO_4$. These results are summarized in Table 4.

We assumed that iodonium perchlorate would be generated by the reaction of iodine and $TrtClO_4$. This iodonium perchlorate would be effective as an activator for the leaving of the Mpt group, as shown in Fig. 6. Particularly, the perchlorate anion would be essential to produce glycosyl perchlorate as a key intermediate. $TrtClO_4$ could be regenerated in the reaction system.

Finally, we applied this method to the syntheses of complex carbohydrate. L-Fucose-containing glycoconjugates exist widely in nature and have interesting biological functions.[25] We tried to synthesize synthetic intermediates of H-disaccharide [α-L-Fuc-(1→2)-D-Gal][26] and the Lewis X antigen [α-L-Fuc-(1→3)[β-D-Gal-(1→4)]-D-GlcNAc].[27]

The condensation of **3** and 1,6-anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose (**12**)[28] using 1 equiv iodine and 10 mol% catalytic amount of $TrtClO_4$ in the presence of molecular seives 4A gave 1,6-anhydro-2-*O*-(2,3,4-tri-*O*-benzyl-L-fucopyranosyl)-3,4-*O*-isopropylidene-β-D-galactopyranose (**13**) in 79% yield with a selectivity of $\alpha/\beta=76/24$ (Fig. 7). The synthesis of H-disaccharide from **13** has been reported.[26]

Several syntheses of the Lewis X antigen have been reported.[27] We designed 4-*O*-allyl-1,6-anhydro-2-azido-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranose (**14**) as an intermediate for the synthesis of the Lewis X antigen.[29] Intermediate **14** was obtained in 60% yield with a selectivity of $\alpha/\beta=86/14$ by the reaction of **3** and 4-*O*-allyl-1,6-anhydro-2-azido-2-deoxy-β-D-glucopyranose (**15**) using $AgClO_4$ as an activator in benzene (Fig. 8).

Experimental

The melting points were determined with a Laboratory Devices MEL-TEMP apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on JEOL

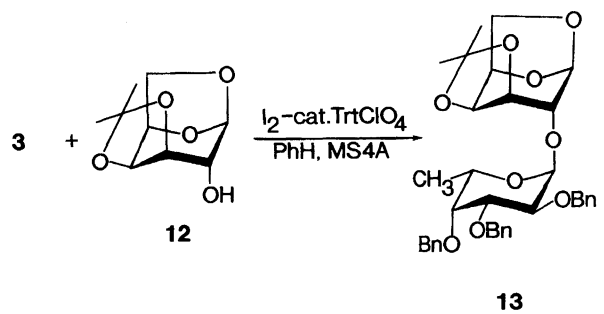


Fig. 7. Synthesis of the H-disaccharide derivative.

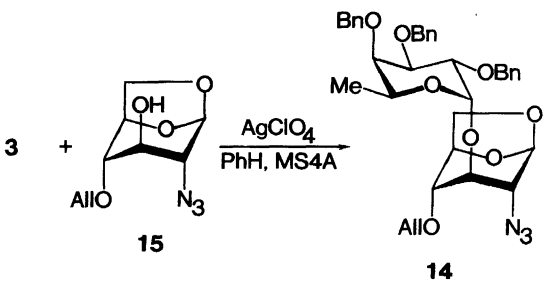


Fig. 8. Synthesis of the synthetic intermediate of Lewis X antigen (All=allyl).

PMX-60, FX-90A, and EX-400 spectrometers with tetramethylsilane used as an internal standard in $CDCl_3$. The optical rotations were recorded on a JASCO DIP-360 digital polarimeter.

General Synthesis of Glycopyranosyl Dimethylphosphinothioate. To a solution of glycose **1**,**6**,**7** or **8** (5 mmol) in dry THF (20 ml) at −30 °C was added a hexane solution of butyllithium (5.5 mmol) under an argon atmosphere and stirred for 30 min. Mpt-Cl (5.5 mmol) was added to the solution, and the mixture was stirred for 1 h at −30 °C; water was then added. The mixture was extracted with ether, and the organic layer was washed with water and a saturated NaCl solution. After being dried over sodium sulfate, the ether was evaporated under reduced pressure. The crude product was purified by silica-gel column chromatography or silica-gel thin-layer chromatography (hexane/ethyl acetate) to give the corresponding glycosyl dimethylphosphinothioates. The yields and physical data were given in Tables 1 and 2.

2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl Dimethylphosphinothioate (2α): Found: C, 67.97; H, 6.49; P, 4.96%. Calcd for $C_{36}H_{41}O_6PS$: C, 68.34; H, 6.53; P, 4.90%.

2,3,4-Tri-*O*-benzyl-α,β-L-fucopyranosyl Dimethylphosphinothioate (3): Found: C, 65.97; H, 6.82; P, 5.41%. Calcd for $C_{29}H_{35}O_5PS$: C, 66.14; H, 6.70; P, 5.88%.

Methyl 2,3,4-Tri-*O*-benzyl-1-*O*-dimethylphosphinothioyl-α,β-D-glucopyranuronate (4): Found: C, 63.00; H, 6.23%. Calcd for $C_{30}H_{35}O_7PS$: C, 63.14; H, 6.18%.

2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranosyl Dimethylphosphinothioate (5): Found: C, 61.41; H, 6.12; N, 7.34%. Calcd for $C_{29}H_{34}N_3O_5PS$: C, 61.36; H, 6.04; N, 7.40%.

General Glycosidation Procedure Using $AgClO_4$. To a benzene solution (2 ml) of glycosyl dimethylphosphinothioate (0.2 mmol) and alcohol (0.2 mmol) was added silver perchlorate (0.2 mmol) in the presence of molecular seives 4A (ca. 100 mg); the mixture was stirred overnight in a dark place. A 5% sodium sulfide solution and ethyl acetate was added into the reaction mixture. The insoluble materials were filtered off, and the filtrate was extracted with ethyl acetate. The organic layer was washed with a 5% sodium sulfide solution and a saturated NaCl solution, and then dried over anhydrous sodium sulfate. The extracts were filtered, and concentrated in vacuo to afford crude glycoside. The residue was purified by thin-layer chromatography on silica gel (hexane/ethyl acetate). The yields are given in Table 3.

General Glycosidation Procedure Using Iodine and 10 mol% Amount of $TrtClO_4$. A 0.1 M (1 M=1 mol dm^{-3}) benzene solution of iodine (2 ml, 0.2 mmol) was added to a benzene solution (1 ml) of glucopyranosyl dimethylphosphinothioate (0.2 mmol), alcohol (0.2 mmol) and triphenylmethyl perchlorate (0.02 mmol) in the presence of molecular seives 4A (ca. 100 mg); the resulting mixture was stirred overnight. The reaction was quenched by the addition a 5% sodium thiosulfate solution. The following procedure was carried out in the same manner as described concerning the method using $AgClO_4$. The yields are given in Table 4.

Cyclohexyl 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranoside: α Form: ^{13}C NMR δ=94.68 (C-1); $[\alpha]_D^{24}$ +48.2° (*c* 2.41, $CHCl_3$) (lit,[30] $[\alpha]_D^{20}$ +43° (*c* 1.0, $CHCl_3$)). β Form: ^{13}C NMR δ=101.94 (C-1); $[\alpha]_D^{24}$ +7.4° (*c* 1.36, $CHCl_3$); mp 98 °C (lit,[30] $[\alpha]_D^{20}$ +8° (*c* 1.0, $CHCl_3$); mp 104—105 °C).

3β-Cholestanyl 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranoside: α Form: ^{13}C NMR δ=94.72 (C-1); $[\alpha]_D^{24}$ + 72.9° (*c* 0.38, $CHCl_3$); mp 113—115 °C (lit,[31] $[\alpha]_D^{26}$ +65.1° (*c* 1.06, $CHCl_3$); mp 117.5—119.0 °C). β Form: ^{13}C NMR δ=101.89 (C-1); $[\alpha]_D^{24}$ +26.7° (*c* 0.21, $CHCl_3$); mp 90—92 °C (lit,[31] $[\alpha]_D^{20}$ +20.2° (*c* 1.04, $CHCl_3$); mp 93.5 °C).

***t*-Butyl 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranoside:** ^{13}C NMR δ=97.79 (C-1β), 91.43 (C-1α); ^{1}H NMR δ=1.325 (s, $CH_3\beta$), 1.262 (s, $CH_3\alpha$) (lit,[32] ^{1}H NMR δ=1.24 (s, $CH_3\beta$), 1.20 (s, $CH_3\alpha$)).

***N*-Benzyloxylcarbonyl-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl)-L-serine Methyl Ester:** ^{13}C NMR δ=103.86 (C-1β), 98.68 (C-1α); ^{1}H NMR δ=6.06 (d, *J*=9.4 Hz, NHα), 5.76 (d, *J*=8 Hz, NHβ), (lit,[33] ^{13}C NMR 103.85 (C-1β), 98.67 (C-1α); ^{1}H NMR δ=5.97 (d, *J*=9 Hz, NHα)).

Methyl 6-*O*-(2,3,4,6-Tetra-*O*-benzyl-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside: ^{13}C NMR δ=103.70 (C-1′β), 97.94 (C-1β), 97.85 (C-1α), 97.15 (C-1′α); ^{1}H NMR δ=3.350 (s, OMeα), 3.327 (s, OMeβ) (lit,[34] ^{1}H NMR δ=3.348 (s, OMeβ), 3.323 (s, OMeα)).

Methyl 4-*O*-(2,3,4,6-Tetra-*O*-benzyl-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside: α Form: ^{13}C NMR δ=97.77 (C-1), 96.63 (C-1′); $[\alpha]_D^{25}$ +51.0° (*c* 1, $CHCl_3$) (lit,[2b] $[\alpha]_D^{20}$ +45.4° (*c* 0.82, $CHCl_3$)). β Form: ^{13}C NMR δ=102.49 (C-1′), 98.43 (C-1).

6-*O*-(2,3,4,6-Tetra-*O*-benzyl-D-glucopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside: ^{13}C NMR δ=104.30 (C-1′β), 96.97 (C-1′α), 96.31 (C-1β), 96.24 (C-1α); ^{1}H NMR δ=5.57 (d, *J*=4.9 Hz, H-1β), 5.52 (d, *J*=5.3 Hz, H-1α), (lit,[35] ^{13}C NMR δ=103.2 (C-1′β), 97.0 (C-1′α)).

Cyclohexyl 2,3,4-Tri-*O*-benzyl-L-fucopyranoside: MS(FAB) 516 (M^+). α Form: ^{13}C NMR δ=95.34 (C-1), $[\alpha]_D^{24}$ −56.8° (*c* 1.29, $CHCl_3$). β Form: ^{13}C NMR δ=101.71 (C-1), $[\alpha]_D^{24}$ −0.4° (*c* 2.27, $CHCl_3$).

3β-Cholestanyl 2,3,4-Tri-*O*-benzyl-L-fucopyranoside: ^{13}C NMR δ=102.07 (C-1β), 95.34 (C-1α).

6-*O*-(2,3,4-Tri-*O*-benzyl-L-fucopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside: ^{13}C NMR δ=104.12 (C-1′β), 97.21 (C-1′α), 96.22 (C-1β), 96.14 (C-1α), 16.78 (Fuc-$CH_3\beta$), 16.54 (Fuc-$CH_3\alpha$); ^{1}H NMR δ=5.52 (d, *J*=5.4 Hz, H-1β), 5.50 (d, *J*=5.4 Hz, H-1α), 1.15 (d, *J*=6.4 Hz, H-6′α), 1.11 (d, *J*=6.8 Hz, H-6′β). Found: C, 69.00; H, 7.48%. Calcd for $C_{39}H_{48}O_{10}$: C, 69.21; H, 7.15%.

1,6-Anhydro-3,4-*O*-isopropylidene-2-*O*-(2,3,4-tri-*O*-benzyl-L-fucopyranosyl)-β-D-galactopyranose (13): ^{13}C NMR δ=108.46 (acetal-Cα), 108.18 (acetal-Cβ), 104.41 (C-1′β), 100.35 (C-1α), 99.71 (C-1β), 99.13 (C-1′α), 16.69 (Fuc-$CH_3\beta$), 16.56 (Fuc-$CH_3\alpha$); ^{1}H NMR δ=5.458 (s, H-1β), 5.424 (s, H-1α) (lit,[26] ^{13}C NMR δ=108.46 (acetal-Cα), 108.26 (acetal-Cβ), 104.53 (C-1′β), 100.41 (C-1α), 99.87 (C-1′β), 99.13 (C-1′α), 16.76 (Fuc-$CH_3\beta$), 16.59 (Fuc-$CH_3\alpha$)).

4-*O*-Allyl-1,6-anhydro-2-azido-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-L-fucopyranosyl)-β-D-galactopyranose (14): MS (FAB) 644 (M^+). α Form: ^{13}C NMR δ=97.3 (C-1′); ^{1}H NMR δ=4.94 (1H, d, *J*=3.9 Hz, H-1′); $[\alpha]_D^{24}$ −8° (*c* 0.3, $CHCl_3$). β Form: ^{13}C NMR δ=103.6 (C-1′); ^{1}H NMR

δ=4.31 (1H, d, J=7.3 Hz, H-1′).

We would like to thank Professor Teruaki Mukaiyama, Science University of Tokyo, for his helpful discussions, and Professor Yoshirou Yoshihiro and Mr. Akihiko Murota, Meiji University, for their kind help in measuring the MS spectra. A part of this study was performed through Special Coordination Funds of the Science and Technology Agency of the Japanese Government.

References

1) a) A. F. Bochkov and G. E. Zaikov, "Chemistry of the *O*-Glycosidic Bond," Pergamon Press, Oxford (1979); b) H. Paulsen, *Angew. Chem., Int. Ed. Engl.*, **21**, 155 (1982); c) R. R. Schmidt, *Angew. Chem., Int. Ed. Engl.*, **25**, 212 (1986); d) H. Kunz, *Angew. Chem., Int. Ed. Engl.*, **26**, 294 (1987); e) K. Suzuki and T. Nagasawa, *Yuki Gosei Kagaku Kyokai Shi*, **50**, 378 (1992).

2) a) T. Mukaiyama, Y. Murai, and S. Shoda, *Chem. Lett.*, **1981**, 431; b) S. Hashimoto, M. Hayashi, and R. Noyori, *Tetrahedron Lett.*, **25**, 1379 (1984); c) T. Matsumoto, H. Maeta, K. Suzuki, and G. Tsuchihashi, *Tetrahedron Lett.*, **29**, 3567 (1988).

3) R. R. Schmidt and J. Michel, *Angew. Chem., Int. Ed. Engl.*, **19**, 731 (1980).

4) B. Fraser-Reid, P. Konradsson, D. R. Mootoo, and U. Udodong, *J. Chem. Soc., Chem. Commun.*, **1988**, 823.

5) P. Sinaÿ, *Pure Appl. Chem.*, **63**, 519 (1991), references cited therein.

6) a) H. Bielawska and M. Michalska, *J. Carbohydr. Chem.*, **5**, 445 (1986); b) H. Bielawska and M. Michalska, *J. Carbohydr. Chem.*, **10**, 107 (1991).

7) S. Hashimoto, T. Honda, and S. Ikegami, *J. Chem. Soc., Chem. Commun.*, **1989**, 685.

8) a) S. Hashimoto, T. Honda, and S. Ikegami, *Tetrahedron Lett.*, **31**, 4769 (1990); b) S. Hashimoto, T. Honda, and S. Ikegami, *Heterocycles*, **30**, 775 (1990); c) S. Hashimoto, Y. Yanagiya, T. Honda, H. Harada, and S. Ikegami, *Tetrahedron Lett.*, **33**, 3523 (1992); d) L. Laupichler, H. Sajus, and J. Thiem, *Synthesis*, **1992**, 1133; e) T. J. Martin and R. R. Schmidt, *Tetrahedron Lett.*, **33**, 6123 (1992).

9) T. Inazu, H. Hosokawa, and Y. Satoh, *Chem. Lett.*, **1985**, 297.

10) T. Inazu and T. Yamonoi, *Chem. Lett.*, **1989**, 69.

11) T. Yamanoi and T. Inazu, *Chem. Lett.*, **1990**, 849.

12) T. Yamanoi, K. Nakamura, H. Takeyama, K. Yanagihara, and T. Inazu, *Chem. Lett.*, **1993**, 343.

13) a) M. Ueki, T. Inazu, and S. Ikeda, *Bull. Chem. Soc. Jpn.*, **52**, 2424 (1979); b) Mpt-Cl can be synthesized easily in laboratory. Also it is available from Tokyo Kasei and Alfa Products.

14) T. Inazu, H. Hosokawa, and M. Amemiya, *Bull. Chem. Soc. Jpn.*, **61**, 4467 (1988).

15) M. Ueki and T. Inazu, *Chem. Lett.*, **1982**, 45.

16) R. L. Whistler and J. N. BeMiller, *Methods Carbohydr. Chem.*, **6**, 373 (1972).

17) P. E. Pfeffer, E. S. Rothman, and G. G. Moore, *J. Org. Chem.*, **41**, 2925 (1976).

18) a) A. Granata and A. S. Perlin, *Carbohydr. Res.*, **94**, 165 (1981); b) M. Inage, H. Chaki, S. Kusumoto, and T. Shiba, *Chem. Lett.*, **1982**, 1281.

19) M. Dejter-Juszynski and H. M. Flowers, *Carbohydr. Res.*, **18**, 219 (1971).

20) a) P. Kovac, J. Alfoldi, and M. Kosiki, *Chem. Zresti*, **28**, 820 (1974); b) R. R. Schmidt and E. Rücker, *Tetrahedron Lett.*, **21**, 1421 (1980).

21) a) W. Kinzy and R. R. Schmidt, *Liebigs Ann. Chem.*, **1985**, 1537; b) A. Marra, F. Gauffeny, and P. Sinaÿ, *Tetrahedron*, **47**, 5149 (1991).

22) K. Igarashi, J. Irisawa, and T. Honma, *Carbohydr. Res.*, **39**, 213 (1975).

23) The details of these glycosidation will be reported elsewhere.

24) T. Mukaiyama, S. Kobayashi, and S. Shoda, *Chem. Lett.*, **1984**, 907.

25) J. F. Kennedy and C. A. White, "Bioactive Carbohydrates: In Chemistry, Biochemistry, and Biology," John Wiley & Sons, New York (1983).

26) B. Wegmann and R. R. Schmidt, *Carbohydr. Res.*, **184**, 254 (1988).

27) a) S.-I. Nishimura, S. Murayama, K. Kurita, and H. Kuzuhara, *Chem. Lett.*, **1992**, 141; b) K. C. Nicolaou, T. J. Caulfield, H. Kataoka, and N. A. Styliannides, *J. Am. Chem. Soc.*, **112**, 3693 (1990).

28) R. W. Jeanloz and P. J. Stoffyn, *Methods Carbohydr. Chem.*, **1**, 221 (1962).

29) This strategy of the synthesis of Lewis X antigen will be reported elsewhere.

30) S. Koto, N. Morishima, and S. Zen, *Bull. Chem. Soc. Jpn.*, **52**, 784 (1979).

31) T. Mukaiyama, T. Murai, and S. Shoda, *Chem. Lett.*, **1979**, 487.

32) H. B. Mereyala and G. V. Reddy, *Tetrahedron*, **47**, 6435 (1991).

33) J. M. Lacombe, A. A. Pavia, and J. M. Rocheville, *Can. J. Chem.*, **59**, 473 (1981).

34) Y. Ito and T. Ogawa, *Carbohydr. Res.*, **202**, 165 (1990).

35) H. Kunz, P. Werning, and M. Schultz, *Synlett*, **1990**, 631.