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A Highly Efficient and Shortcut Synthesis of Cyclitol Derivatives via Spiro Sugar Ortho Esters

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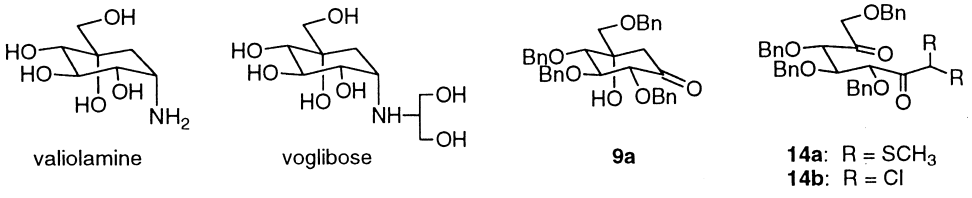
Abstract—Preparation of cyclitol derivatives from sugar lactones via spiro sugar ortho esters is described. The key steps are the novel enol ether formation from sugar ortho esters with $AlMe_3$ and the efficient intramolecular aldol cyclization of alkyl enol ethers with $ZnCl_2$ in THF/H_2O. Firstly, the spiro sugar ortho esters **3a**–**c** were prepared from the benzyl protected sugar lactones **1a**–**c** and 2,2-dimethylpropanediol (**2**). These ortho esters were efficiently converted into the enol ethers **5a**–**c** by the treatment of $AlMe_3$ in CH_2Cl_2. The initial step of this reaction was the pyran ring cleavage accompanied by the methyl anion insertion, and the second was the dioxane ring opening caused by the Lewis acidity of $AlMe_3$. The resulting alkyl enol ethers were treated with DMSO/Ac_2O, and the formed keto compounds were converted into the carbasugars **9a**–**c** by the $ZnCl_2$-catalyzed aldol cyclization in THF/H_2O. The overall yields of **9a**, **9b**, and **9c** based on the corresponding lactones **1a**–**c** were 64, 64, and 54%, respectively.

Introduction

Cyclitol and aminocyclitol derivatives have attracted much attention due to their activity as glycosidase inhibitors, whose potential use as therapeutic agents against HIV infection and metabolic disease such as diabetes was recently recognized.[1] Various methods for the synthesis of these molecules have been developed, and the use of carbohydrates as synthetic precursors for carbasugar derivatives has been widespread.[2,3]

One of the important target molecules in these studies is the natural product valiolamine (Scheme 1),[5] isolated from the fermentation broth of *Streptomyces hygroscopicus* subsp. *limoneus*, because of its high bioactivity as an enzyme inhibitor.[5] Many procedures for the preparation of the carbasugar molecules, which are structurally related to valiolamine or its dehydro derivative valienamine, have been developed based on the variety of strategies. Compared to the methods for the synthesis of valienamine,[7] only limited methods for valiolamine synthesis have been reported,[4a,6] which are the one starting from a Diels–Alder cycloadduct,[6a] the one from Quinic Acid,[6c] the one from D-glucose by Ferrier rearrangement,[6b] and the one from a gluconolactone derivative **1a**.[4a] The fourth method was developed by Fukase and Horii, researchers in Takeda Chemical Industries, Ltd. They prepared the inosose **9a**[4a] based on the intramolecular aldol condensation of the α,α-bis (methylthio)- or α,α-dichlorocarbonyl compound **14a**,**b** (Scheme 1), and synthesized various valiolamine derivatives[4b] including voglibose (Scheme 1)[4b,c] by the reductive amination from **9a**. Although their methods were efficient, final desulfurization or dechlorination step was necessary to accomplish the preparation of the compound **9a**.

Recently, we have also reported a novel procedure for the preparation of **9a** from **1a** via a spiro sugar ortho ester



Scheme 1.

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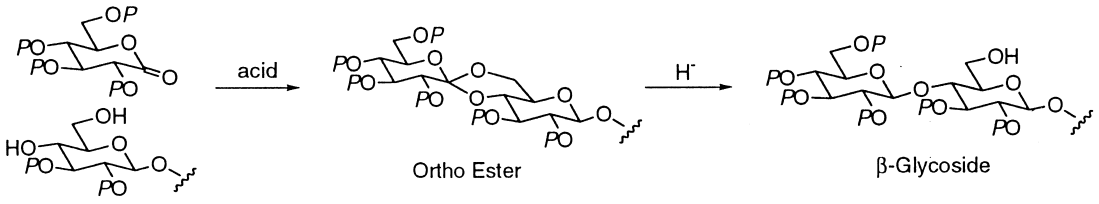


Scheme 2.

intermediate.[8] In our procedure, the alkyl enol ether compound, which was prepared from a sugar ortho ester by the novel methyl anion insertion and succeeding ring opening reaction caused by $AlMe_3$, was used as the precursor of the substrate for aldol cyclization. As this compound had no extra substituent on double bond moiety, the desired inosose could be obtained without further steps. In this paper, we report the details and the extension of this study including the results with the mannose and galactose type sugar derivatives.

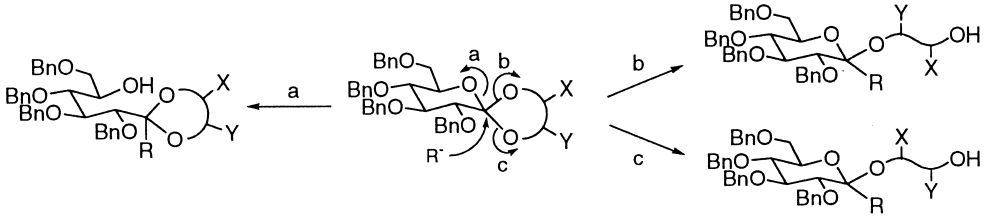
Results and Discussion

Enol ether formation from sugar ortho esters with $AlMe_3$

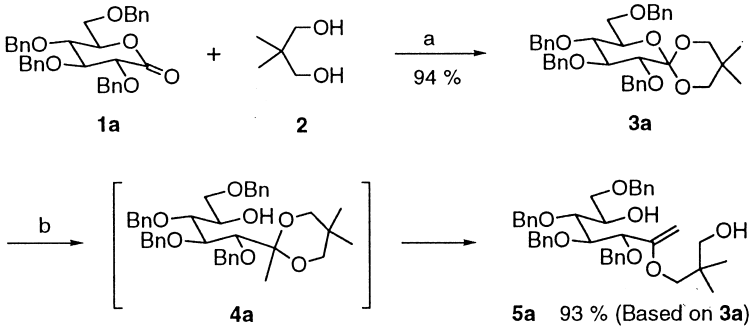
In these years, we have explored the reactivity of sugar ortho esters for the purpose of developing the reductive glycosilation methods.[9,10] In this procedure, the glycosyl linkages are formed as the results of the dioxane ring opening caused by the hydride anion attack to the spiro carbon atoms of the ortho ester molecules (Scheme 2). As the extension of this study, we next tried to investigate the reactivity of a methyl anion to the sugar ortho esters. In Scheme 3, three possible products of the reaction of ortho esters and an anion are shown. If one of the carbon–oxygen bonds of the dioxane ring is cleaved (route b or c) as the result of the anion insertion, the glycoside type product will be afforded. In the case that the C–O bond cleavage of the pyran ring occurs (route a), the ketal type product will be obtained. After several experiments, we found that sugar ortho esters were converted into the ketal type compounds selectively by using $AlMe_3$ as a methyl anion source.

As shown in Scheme 4, the ortho ester **3a** was treated with 5 equiv. of $AlMe_3$ (1.0 M *n*-hexane solution) in CH_2Cl_2 for 2 h at room temperature. The compound **3a** was finally converted into the enol ether **5a** in 93% yield via an intermediate (**4a**), whose process was monitored by the TLC analysis. By using less amount of aluminum reagent, this intermediate was isolated to be determined as the ketal type compound **4a**, which was easily converted into **5a** by the treatment of $AlMe_3$. It was reasonable that the first step of this reaction was the cleavage of a pyran ring of sugar moiety caused by the insertion of a methyl anion from $AlMe_3$ and the second was the cleavage of dioxane ring accompanied by the proton elimination.[11] The smooth first step ring opening which was caused by the two-faced character of $AlMe_3$ was presumed to be assisted by *n*-electrons of two oxygen atoms of a dioxane ring.[12]

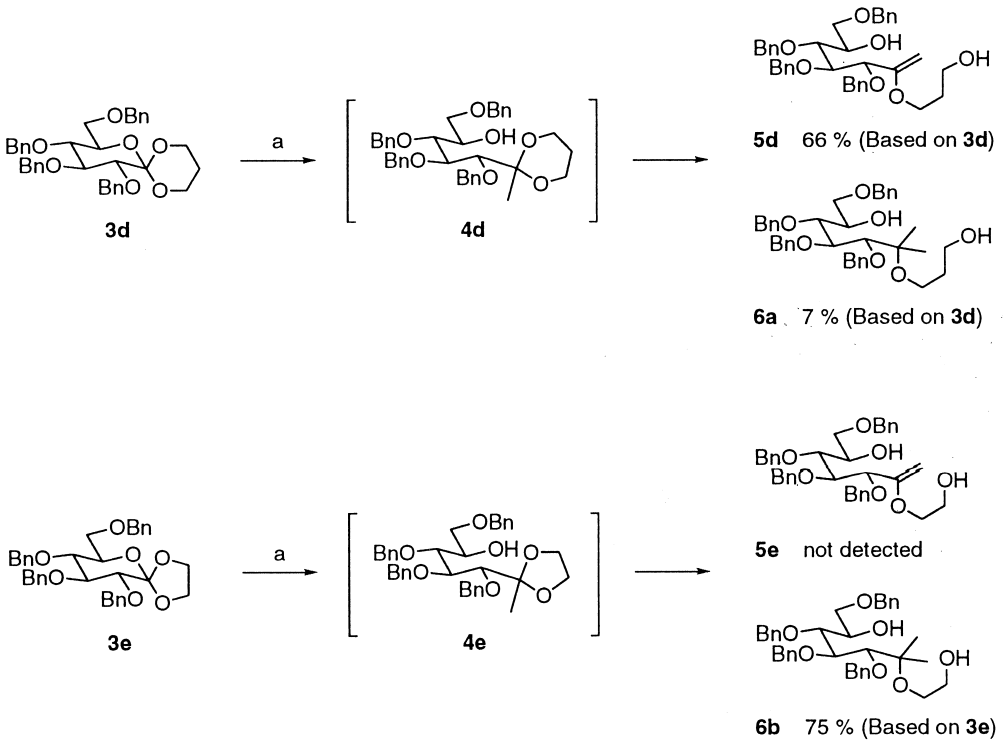
The starting material ortho ester was prepared from the lactone **1a**[13a,b] and 2,2-dimetylpropanediol (**2**) according to the method previously reported.[9a,c,14] The lactone **1a** was treated with **2** in the presence of an excess amount of TMSOMe and a catalytic amount of TMSOTf to be converted into **3a** in 94% yield (Scheme 4). It was necessary to remove the solvents under reduced pressure before



Scheme 3.



Scheme 4. *Reagents and conditions:* (a) TMSOMe, TMSOTf, toluene, rt; (b) $AlMe_3$, CH_2Cl_2, rt.



Scheme 5. *Reagents and conditions:* (a) $AlMe_3$, CH_2Cl_2, rt.

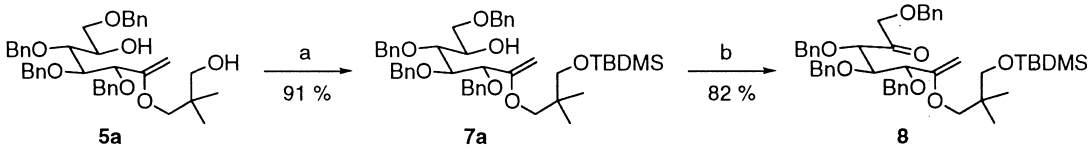
quenching the reaction to obtain the ortho ester in a satisfactory yield.

Interestingly, the dimethylated compound **6a** was detected as the minor product of the reaction of the propanediol ortho ester **3d** with $AlMe_3$ under above conditions, and only **6b** was afforded in the case of the ethylene glycol ortho ester **3e**[10a] (Scheme 5). It was revealed by the isolation of the intermediates that the initial step in each of these reactions was also the ketal (**4d** or **4e**) formation which was followed by the dioxane or dioxolane ring cleavage. The difference in the types of secondary ring cleavage among ortho esters might be explained by the difference in steric hindrance.

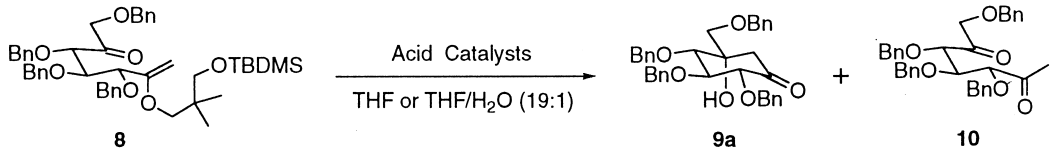
Intramolecular aldol condensation with $ZnCl_2$ in THF/H_2O

As the resulting enol ether compounds seemed to be a suitable precursor for the preparation of cyclitols based on the intramolecular aldol condensation, we planed to develop a new method for the synthesis of these molecules. The conversion of **5a** to an appropriate 5-oxo compound was firstly required, and the 5-keto enol ether **8** was prepared according to the conditions shown in Scheme 6. Treatment of **5a** with TBDMSCl (2 equiv.), Et_3N (5 equiv.), and DIMAP (0.2 equiv.) in DMF provided the silyl protected compound **7a** in 91% yield,[15] which was converted into the keto derivative **8** by exposure to excess Ac_2O/DMSO. The yield of **8** was increased by changing the ratio between Ac_2O and DMSO to 1:4 from usual 1:1, however, the keto product **8** was partially decomposed during column chromatography, which reduced the yield to 82%.

While the aldol condensation with silyl enol ethers has been well developed,[16] there have been few reports on the



Scheme 6. *Reagents and conditions:* (a) TBDMSCl, Et_3N, DIMAP, DMF, rt; (b) DMSO/Ac_2O (4:1), rt.



Scheme 7.

Table 1. Intramolecular aldol condensation of **8** with acid catalysts

Entry	Reagent	Reagent/**8**	Additive	Conditions	*t* (H)	Yield (%)[a]		
						9a	**10**	**8**[b]
1[c]	PPTS	1.0	–	rt	18	28	51	n.d.[d]
2[c]	$BF_3{\cdot}Et_2O$	1.0	–	rt	0.5	69	1	n.d.
3[c]	$ZnCl_2$	1.0	–	rt	18	68	n.d.	n.d.
4[e]	$ZnCl_2$	1.0	H_2O	rt	18	28	n.d.	67
5[e]	$ZnCl_2$	2.0	H_2O	rt	18	43	n.d.	50
6[e]	$ZnCl_2$	2.0	H_2O	Reflux	4	90	n.d.	n.d.
7[e]	HCl	2.0	H_2O	rt	0.5	4	62	n.d.
8[e]	$La(OTf)_3$	1.0	H_2O	rt	18	9	n.d.	84
9[e]	$YbCl_3{\cdot}6H_2O$	1.0	H_2O	rt	24	Trace[f]	n.d.	91

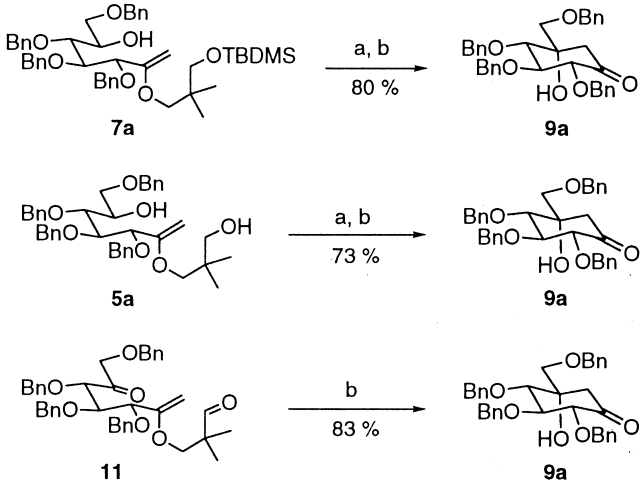
[a] Isolated yields based on **8**.
[b] Recovered yields.
[c] Reactions were carried out in THF.
[d] Not detected.
[e] Reactions were carried out in THF/H_2O (19:1).
[f] <0.5%.

reaction with alkyl enol ethers recently.[17] Thus, the conditions for the cyclization of **8** were next investigated (Scheme 7). These results are summarized in Table 1. As shown in entry 1, the hydrolysis product **10** was mainly afforded instead of the desired compound **9a** when PPTS was used as an acid catalyst. In the case with $ZnCl_2$ or $BF_3{\cdot}Et_2O$ in non-aqueous solvent (entry 2 or 3), the formation of **10** was suppressed, however, the yield of **9a** did not rise up to 70% because of the undesired side reaction and of the product decomposition. Remarkably, it was revealed that the addition of water to the reaction mixture improved the product selectivity in the $ZnCl_2$-catalyzed cyclization of **8** (entry 4, 5). Although the rate of the reaction was reduced by the addition of water (entry 4 vs. 3), the reaction with 2 equiv. of the catalyst under the reflux conditions proceeded selectively and efficiently to afford **9a** in 90% yield (entry 6). The structural and stereochemical confirmation of **9a** has been done by the comparison with that of the literature.[4a]

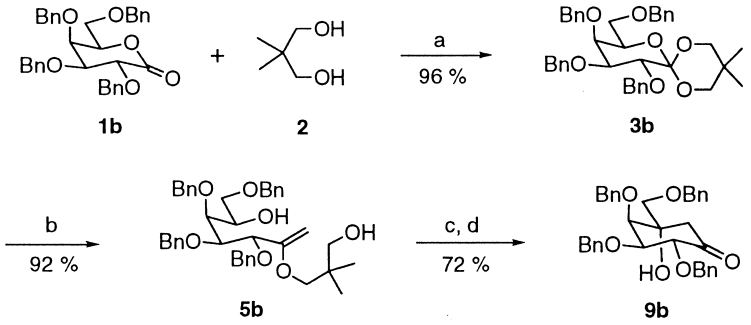
As shown in entry 7, the hydrolysis product **10** was mainly produced in the presence of HCl. The products distribution in the reaction with HCl was far different from that in the case with $ZnCl_2$ (entry 7 vs. 5). It seemed rational that zinc complex catalyzed the reaction instead of proton also in aqueous solvent. Water might change the reactivity of $ZnCl_2$ by the coordination to metal center or might assist the reaction by providing excess amount of hydroxy units.

Recently, aldol condensation of silyl enol ethers with various metal catalysts including lanthanide salts or complexes in aqueous THF was reported.[18] However, La $(OTf)_3$ or $YbCl_3{\cdot}6H_2O$ which was an efficient catalyst for the reaction with silyl enol ethers was not so effective as $ZnCl_2$ for this cyclization (entry 8, 9 vs. 4). These results might be explained by considering steric hindrance of large lanthanide complexes.

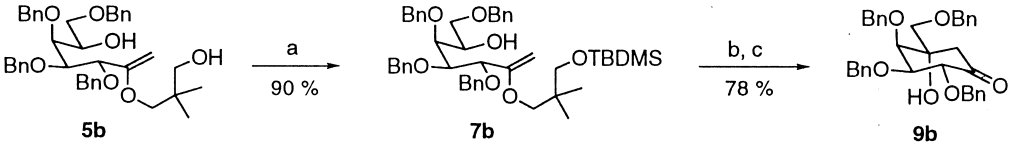
As describe above, the 5-keto enol ether **8** was not stable in silicagel column, however, it was revealed that the column purification of **8** was not necessary for the efficient cyclization under above conditions. After usual work up (washing with H_2O), crude **8** was treated with $ZnCl_2$ in THF/H_2O to be converted into **9a** in 80% yield based on **7a** (Scheme 8). More practically, oxidation of **5a** and succeeding cyclization of crude oxidation products afforded **9a** in 73% yield



Scheme 8. *Reagents and conditions:* (a) DMSO/Ac_2O (4:1), rt; (b) $ZnCl_2$, THF/H_2O (19:1), reflux.



Scheme 9. *Reagents and conditions:* (a) TMSOMe, TMSOTf, toluene, rt; (b) $AlMe_3$, CH_2Cl_2, reflux; (c) $DMSO/Ac_2O$ (4:1), rt; (d) $ZnCl_2$, THF/H_2O (19:1), reflux.



Scheme 10. *Reagents and conditions:* (a) TBDMSCl, Et_3N, DIMAP, DMF, rt; (b) $DMSO/Ac_2O$ (4:1), rt; (c) $ZnCl_2$, THF/H_2O (19:1), reflux.

based on **5a** (Scheme 8). The main product of the oxidation of **5a** was the dioxo compound **11**, which was generated by the oxidation of both of 1°- and 2°-alcohols. In this oxidation, the 5-keto compound containing sulfur, which was derived from DMSO was also detected. Fortunately, the enol ether moiety of **11** selectively reacted with ketone in the sugar part instead of terminal aldehyde under above conditions to afford **9a** in 83% yield (Scheme 8), thus the desired product could be obtained directly from **5a** in good yield without the protection of 1°-alcohol. In this case, **9a** was obtained in 64% total yield based on **1**.

Preparation of carbasugar from a galactonolactone derivative

To prepare another stereoisomer of **9a**, we next applied this procedure to the conversion of perbenzylgalactonolactone (**1b**)[13c] to the analogous inosose compound. Firstly, the spiro sugar ortho ester **3b** was prepared from the lactone **1b** and the diol **2** in 96% yield according to the same procedure described above for the preparation of the glucose type ortho ester (Scheme 9). The ortho ester **3b** was subsequently treated with excess amount of $AlMe_3$ in CH_2Cl_2 at room temperature for 15 h to be converted into the enol ether **5b** in 92% yield. This ring opening reaction required longer time for completion than the reaction with the glucose derivative, however, it was possible to shorten the time to 4 h without the decrease in product yield by a gentle heating of the reaction mixture until at the boiling point of methylene chloride.

The resulting enol ether **5b** was directly used as the substrate for the next step oxidation with $DMSO/Ac_2O$, and the crude oxidation products were treated with $ZnCl_2$ in THF/H_2O under reflux conditions. As shown in Scheme 9, **5b** was efficiently converted into the inosose **9b** in 72% yield. The cyclization was finished during 2 h, and the resulting product **9b** was afforded as a structurally single isomer like in the case of the glucose type inosose **9a**. When the silyl protected compound **7b** was use as the substrate, **9b** was obtained in 78% yield (based on **7b**) also as a single isomer (Scheme 10).

The configuration of the newly formed chiral center in **9b** was determined by X-ray single crystallographic analysis. The compound **9b** was a well crystalline compound, and the analytical sample was obtained as colorless needles from ether–hexane. The X-ray single crystallographic structure of **9b** was represented in Fig. 1 by ball and stick model. From the spatial relationship of the substituents, the configuration of the tertiary carbon atom of **9b** was determined to be *S* like in the case of **9a**.

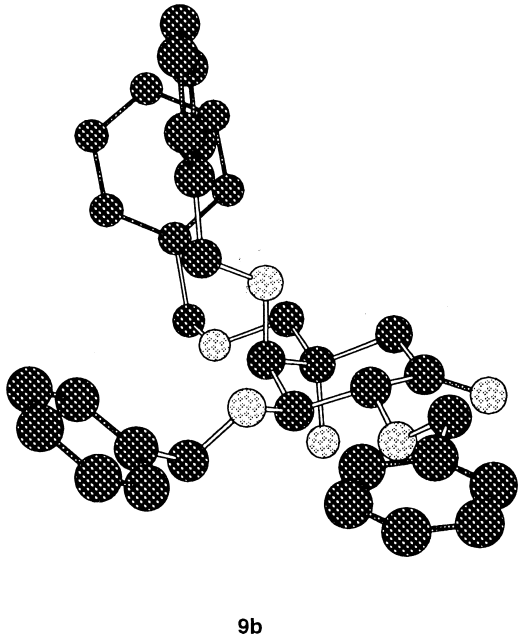
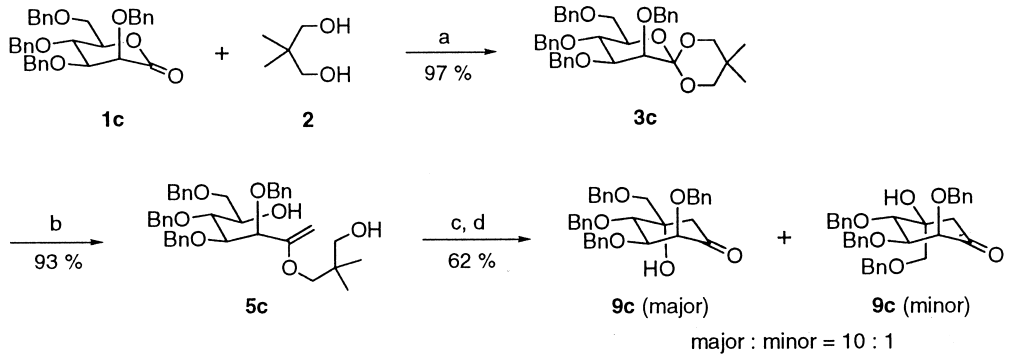
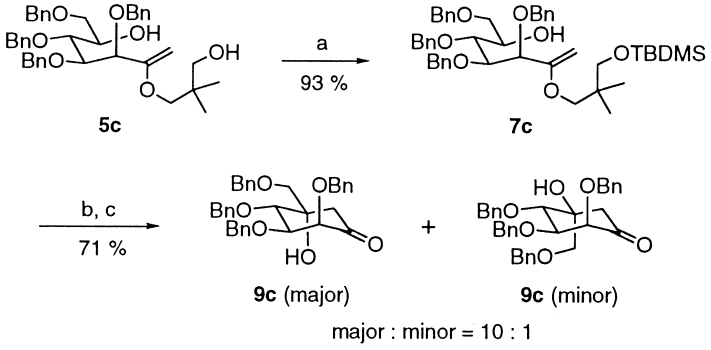


Figure 1. The X-ray single-crystal structure of the inosose **9b**. Hydrogen atoms were omitted.



Scheme 11. *Reagents and conditions:* (a) TMSOMe, TMSOTf, toluene, rt; (b) $AlMe_3$, CH_2Cl_2, rt; (c) DMSO/Ac_2O (4:1), rt; (d) $ZnCl_2$, THF/H_2O (19:1), reflux.



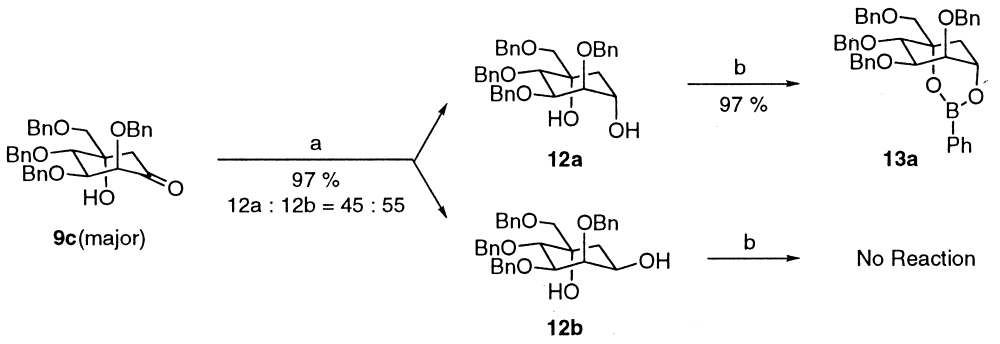
Scheme 12. *Reagents and conditions:* (a) TBDMSCl, Et_3N, DIMAP, DMF, rt; (b) DMSO/Ac_2O (4:1), rt; (c) $ZnCl_2$, THF/H_2O (19:1), reflux.

Preparation of carbasugar from a mannonolactone derivative

Presented method was also applied for the preparation of the mannose type analogous compound.[6c] As shown in Scheme 11, the ortho ester **3c** was prepared from perbenzylmannonolactone (**1c**)[13c] and the diol **2**, and then was treated with excess amount of $AlMe_3$ in CH_2Cl_2 at room temperature for 3 h. These reactions proceeded efficiently, and the enol ether compound **5c** was obtained in 90% yield based on **3c**.

Both of **5c** and its silyl protected compound **7c** were used as the substrate for next oxidation/cyclization step (Schemes 11 and 12). In these cases, intramolecular aldol cyclization proceeded slowly compared to the case with glucose or galactose type enol ether. Moreover, the cyclized product **9c** was not afforded as a structurally single isomer, but a mixture of the major and the minor products. However, one of the isomers was obtained highly selectively (major: minor=10:1), and the ratios between them were the same both in the cases with **5c** and **7c**. The yields of **9c** from **5c** and **7c** were 62 and 71%, respectively.

The separated major isomer of **9c** was reduced by $NaBH_4$ in THF/MeOH (1:4)[4a] to afford the diols **12a,b** in 97% yield (**12a**:**12b**=45:55). Each of the diols **12a,b** was treated with phenylboronic acid in the presence of a catalytic amount of *p*-toluenesulfonic acid under heated conditions (Scheme 13). Although phenylboronate ester[4a] was obtained in the case with **12a**, the starting diol was remained intact in the case with **12b**. These results indicated that two hydroxy groups of **12a** were in the same side of the cyclohexane ring. Considering the ^1H NMR spectrum splitting pattern,



Scheme 13. *Reagents and conditions:* (a) $NaBH_4$, MeOH/THF (4:1), −10°C; (b) $PhB(OH)_2$, $TsOH·H_2O$, 110°C.

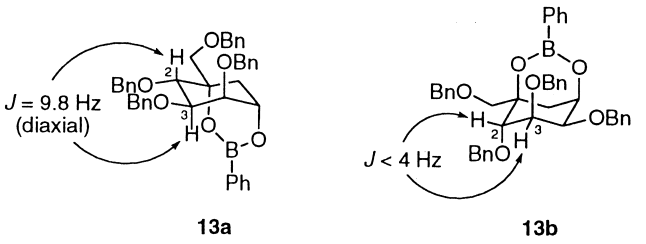


Figure 2.

especially the coupling constant (J=9.8 Hz) between H-2 and H-3 signals, the structure of resulting phenylboronate ester was assigned as **13a** rather than **13b** shown in Fig. 2. Thus, the configuration of the tertiary carbon atom of **9c** (major) was determined to be *S*.

Conclusion

Carbasugars were prepared from sugar lactones via spiro sugar ortho esters. The key steps of this procedure were the enol ether formation from sugar ortho esters with $AlMe_3$ and the intramolecular aldol cyclization of alkyl enol ethers with $ZnCl_2$ in THF/H_2O. With these reactions, glucose, galactose, and mannose type carbasugar derivatives **9a**–**c** were prepared from the corresponding perbenzylated sugar lactones **1a**–**c** in high overall yields (64, 64, and 56%, respectively). The presented process would be a facile and efficient method for the synthesis of valiolamine derivatives, and might be a new practical entry for the preparation of cyclitols. Extension of this study is now under investigation in this laboratory.

Experimental

General

Melting points are uncorrected. Infrared (IR) spectra were measured on a Jasco FT/IR-8000 Fourier-transform infrared spectrometer. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a JEOL JNM-GSX400 (400 MHz) pulse Fourier-transform NMR spectrometer in $CDCl_3$ solution with tetramethylsilane as an internal standard. Low resolution mass spectra (MS) and high resolution (HR) mass spectra were obtained with a JEOL JMS-SX102A mass spectrometer. Optical rotations were determined using a Jasco DIP-370 digital polarimeter. 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).

Materials

Solvents were freshly distilled prior to use. All the reagents and the starting substrates were commercially available, and were used as received or were purified, if necessary. 2,3,4,6-Tetra-*O*-benzyl-D-glucono-1,5-lactone (**1a**),[13a,b] 2,3,4,6-tetra-*O*-benzyl-D-galactono-1,5-lactone (**1b**),[13c] 2,3,4,6-tetra-*O*-benzyl-D-mannono-1,5-lactone (**1c**),[13c] 2,3,4,6-tetra-*O*-benzylspiro[1,5-anhydro-D-glucitol-1,2′-[1,3]dioxolane] (**3e**)[10a] were prepared according to the established methods.

Preparation of the ortho esters 3a–d from the sugar lactones 1a–c and propanediols

To a solution of lactone **1a** (2.7 g, 5.0 mmol) and 2,2-dimethylpropanediol **2** (780 mg, 7.5 mmol) in toluene (50 ml) was added TMSOMe (3.4 ml, 25 mmol) and TMSOTf (45 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 dissolved in CH_2Cl_2 containing 5% of Et_3N. The resulting mixture was evaporated, and the residue was applied to a silica gel column chromatography (ether–hexane 1:3 then 1:2) to afford **3a** as colorless needles (2.9 g, 94%). According to the same procedure, other sugar ortho esters (**3b**–**d**) were prepared. In the case of ortho ester **3c**, 2 equiv. of **2** was used, and in the case of orthoester **3d**, propanediol was used instead of **2**.

2,3,4,6-Tetra-*O*-benzyl-5′,5′-dimethylspiro[1,5-anhydro-D-glucitol-1,2′-[1,3]dioxane] (3a). Colorless needle; mp 103.0–104.0°C; $[\alpha]_D^{28}$+47.7° (C=1.0, $CHCl_3$); IR (KBr, cm^{-1}) 3032, 2957, 2915, 2876, 1497, 1455, 1404, 1366, 1352; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76 (3H, s, Me), 1.30 (3H, s, Me), 3.38 (1H, dd, J=10.2, 2.4 Hz, dioxaneH), 3.40 (1H, dd, J=10.2, 2.4 Hz, dioxaneH), 3.53–3.76 (6H, m, H-2, H-4, H-5, H-6, H-6, dioxaneH), 3.87 (1H, t, J=9.2 Hz, H-3), 4.06 (1H, d, J=10.7 Hz, dioxaneH), 4.51 (1H, d, J=11.0 Hz, $PhCH_2$), 4.55 (1H, d, J=12.2 Hz, $PhCH_2$), 4.63 (1H, d, J=12.2 Hz, $PhCH_2$), 4.74 (1H, d, J=11.0 Hz, $PhCH_2$), 4.76 (1H, d, J=11.3 Hz, $PhCH_2$), 4.83 (1H, d, J=11.0 Hz, $PhCH_2$), 4.95 (1H, d, J=11.0 Hz, $PhCH_2$), 5.02 (1H, d, J=11.3 Hz, $PhCH_2$), 7.14–7.40 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.9, 22.9, 29.4, 68.7, 68.9, 70.3, 72.3, 73.3, 74.9, 75.2, 75.9, 78.1, 82.4, 83.1, 109.8, 127.5, 127.5, 127.6, 127.7, 127.9, 128.2, 128.2, 128.3, 128.3, 128.3, 128.6, 138.2, 138.3, 138.3, 138.8; MS (EI) *m/z* 624 (M), 533 (M−Bn); Anal. Calcd for $C_{39}H_{44}O_7$: C, 74.98; H, 7.10. Found: C, 74.62; H, 7.11.

2,3,4,6-Tetra-*O*-benzyl-5′,5′-dimethylspiro[1,5-anhydro-D-galactitol-1,2′-[1,3]dioxane] (3b). Colorless syrup; $[\alpha]_D^{21}$+30.1° (C=1.1, $CHCl_3$); IR (KBr, cm^{-1}) 2955, 2920, 2874, 1455, 1364; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.73 (3H, s, Me), 1.29 (3H, s, Me), 3.36 (1H, dd, J=10.7, 2.4 Hz, dioxaneH), 3.36 (1H, dd, J=11.0, 2.4 Hz, dioxaneH), 3.53 (1H, dd, J=9.7, 6.2 Hz, H-6), 3.62 (1H, dd, J=9.7, 6.2 Hz, H-6), 3.72 (1H, d, J=11.0 Hz, dioxaneH), 3.75 (1H, bt, J=6.2 Hz, H-5), 3.80 (1H, dd, J=9.8, 2.6 Hz, H-3), 3.86 (1H, bd, J=2.6 Hz, H-4), 3.97 (1H, d, J=9.8 Hz, H-2), 4.04 (1H, d, J=10.7 Hz, dioxaneH), 4.44 (1H, d, J=11.6 Hz, $PhCH_2$), 4.49 (1H, d, J=11.6 Hz, $PhCH_2$), 4.59 (1H, d, J=11.6 Hz, $PhCH_2$), 4.67 (1H, d, J=11.6 Hz, $PhCH_2$), 4.78 (1H, d, J=11.3 Hz, $PhCH_2$), 4.84 (1H, d, J=11.6 Hz, $PhCH_2$), 4.93 (1H, d, J=11.6 Hz, $PhCH_2$), 4.99 (1H, d, J=11.3 Hz, $PhCH_2$), 7.21–7.41 (20H, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.9, 22.9, 29.4, 69.0, 69.4, 70.2, 71.7, 73.5, 73.9, 74.5, 74.7, 75.6, 79.8, 80.8, 110.3, 127.4, 127.5, 127.6, 127.7, 128.1, 128.1, 128.3,

128.4, 128.5, 128.5, 128.6, 138.2, 138.6 (2C), 138.9; MS (EI) *m*/*z* 624 (M), 533 (M−Bn); HRMS (EI) calcd for $C_{39}H_{44}O_7$ 624.3087, found 624.3102.

2,3,4,6-Tetra-*O*-benzyl-5′,5′-dimethylspiro[1,5-anhydro-D-mannitol-1,2′-[1,3]dioxane] (3c). Colorless syrup; $[\alpha]_D^{23}$ −17.9° (*C*=1.1, $CHCl_3$); IR (KBr, cm^{-1}) 2957, 2917, 2874, 1455, 1364; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74 (3H, s, Me), 1.19 (3H, s, Me), 3.19 (1H, dd, *J*=10.7, 2.4 Hz, dioxaneH), 3.39 (1H, dd, *J*=11.0, 2.4 Hz, dioxaneH), 3.64 (1H, ddd, *J*=9.4, 6.3, 1.8 Hz, H-5), 3.69 (1H, d, *J*=10.7 Hz, dioxaneH), 3.73 (1H, dd, *J*=10.7, 6.3 Hz, H-6), 3.82 (1H, dd, *J*=10.7, 1.8 Hz, H-6), 3.84 (1H, d, *J*=3.2 Hz, H-2), 3.88 (1H, t, *J*=9.4 Hz, H-4), 3.93 (1H, dd, *J*=9.4, 3.2 Hz, H-3), 4.07 (1H, d, *J*=10.7 Hz, dioxaneH), 4.47 (2H, s, $PhCH_2$), 4.52 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.58 (1H, d, *J*=11.9 Hz, $PhCH_2$), 4.65 (1H, d, *J*=11.9 Hz, $PhCH_2$), 4.80 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.90 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.97 (1H, d, *J*=12.2 Hz, $PhCH_2$), 7.15–7.45 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 22.0, 22.8, 29.5, 68.7, 69.7, 70.2, 71.7, 73.3, 73.3, 74.4, 74.8, 75.0, 75.6, 81.2, 109.6, 127.3, 127.3, 127.3, 127.4, 127.5, 128.0, 128.2, 128.2, 128.3, 128.3, 138.4, 138.6, 138.7, 138.7; MS (EI) *m*/*z* 624 (M), 533 (M−Bn); HRMS (EI) calcd for $C_{39}H_{44}O_7$ 624.3087, found 624.3091.

2,3,4,6-Tetra-*O*-benzylspiro[1,5-anhydro-D-glucitol-1,2′-[1,3]dioxane] (3d). Colorless needle; mp 43.5–45.0°C; $[\alpha]_D^{24}$ +51.6° (*C*=1.0, $CHCl_3$); IR (KBr, cm^{-1}) 3063, 3031, 2917, 2892, 1497, 1455, 1360; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (1H, bd, *J*=12.8 Hz, $-CH_2CH_2CH_2-$), 2.22 (1H, m, $-CH_2CH_2CH_2-$), 3.49 (1H, d, *J*=9.8 Hz, H-2), 3.56–3.76 (4H, m), 3.83–3.90 (3H, m), 4.03 (1H, bdt, *J*=12.5, 2.1 Hz, $-OCH_2CH_2-$), 4.37 (1H, bdt, *J*=12.8, 2.4 Hz, $-OCH_2CH_2-$), 4.50 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.56 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.63 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.73 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.76 (1H, d, *J*=11.3 Hz, $PhCH_2$), 4.82 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.93 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.98 (1H, d, *J*=11.3 Hz, $PhCH_2$), 7.14–7.40 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 24.4, 58.7, 60.2, 68.9, 72.4, 73.4, 74.9 (2C), 75.8, 78.1, 82.7, 82.9, 110.4, 127.5, 127.5, 127.5, 127.6, 127.6, 127.9, 127.9, 128.2, 128.3, 128.3, 128.5, 138.2, 138.3, 138.5, 138.8; MS (EI) *m*/*z* 596 (M), 505 (M−Bn); HRMS (EI) calcd for $C_{37}H_{40}O_7$ 596.2774, found 596.2784; Anal. Calcd for $C_{39}H_{44}O_7$: C, 74.47; H, 6.76. Found: C, 74.34; H, 6.81.

Preparation of the enol ethers 5a–c from the sugar ortho esters 3a–c

To a solution of ortho ester **3a** (2.77 g, 4.4 mmol) in CH_2Cl_2 (44 ml) was added a 1.0 M solution of $AlMe_3$ in *n*-hexane (22 ml, 22 mmol) at room temperature under Ar. After 2 h of stirring, small amount of water was added to the solution cautiously until the generation of foams was ceased. After pouring an additional amount of water (44 ml) and ether (88 ml), the mixture was stirred for 10 min, and then moved to a separatory funnel. The organic layer was separated, and the water layer was extracted twice with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and then evaporated. The residue was applied to a silica gel column chromatography (ether–hexane 1:1 then 2:1) to afford **5a** as colorless syrup (2.64 g, 93%). According to above procedure, enol ethers (**5b,c**) were also prepared in excellent yields. It should be noted that the reaction mixture was heated until at the boiling point of CH_2Cl_2 to shorten the time in the case with enol ether **5b**.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-2-*O*-(3-hydroxy-2,2-dimethylpropyl)-D-*gluco*-hept-1-enitol (5a). Colorless syrup; $[\alpha]_D^{28}$ +44.1° (*C*=1.1, $CHCl_3$); IR (neat, cm^{-1}) 3445, 3031, 2921, 2870, 1628, 1497, 1455, 1397, 1360; ^{1}H NMR (400 MHz, $CDCl_3$) δ0.91 (3H, s, Me), 0.94 (3H, s, Me), 2.45 (1H, bs, OH), 2.76 (1H, bd, *J*=4.1 Hz, OH), 3.27 (1H, bd, *J*=10.7 Hz, $HOCH_2C(Me)_2-$), 3.39 (1H, d, *J*=9.3 Hz, $-OCH_2C(Me)_2-$), 3.49 (1H, bd, *J*=10.7 Hz, $HOCH_2C(Me)_2-$), 3.53 (1H, dd, *J*=9.8, 6.1 Hz, H-7), 3.54 (1H, d, *J*=9.3 Hz, $-OCH_2C(Me)_2-$), 3.56 (1H, dd, *J*=7.6, 2.4 Hz, H-5), 3.60 (1H, dd, *J*=9.8, 3.4 Hz, H-7), 3.97 (1H, m, H-6), 4.10 (1H, dd, *J*=7.6, 2.4 Hz, H-4), 4.13 (1H, d, *J*=2.0 Hz, H-1), 4.20 (1H, d, *J*=2.0 Hz, H-1), 4.23 (1H, d, *J*=7.6 Hz, H-3), 4.45 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.46 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.50 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.50 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.53 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.66 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.73 (1H, d, *J*=11.3 Hz, $PhCH_2$), 4.91 (1H, d, *J*=11.3 Hz, $PhCH_2$), 7.18–7.36 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.8, 22.0, 36.0, 68.9, 70.4, 70.8, 71.3, 73.3, 73.5, 73.6, 74.9, 78.4, 78.9, 82.4, 86.9, 127.4, 127.4, 127.6, 127.7, 127.8, 127.9, 128.2, 128.3, 128.4, 128.6, 138.0, 138.4, 138.5, 138.6, 158.4; MS (EI) *m*/*z* 640 (M), 625 (M−Me), 549 (M−Bn); HRMS (EI) calcd for $C_{40}H_{48}O_7$ 640.3400, found 640.3401.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-2-*O*-(3-hydroxy-2,2-dimethylpropyl)-D-*galacto*-hept-1-enitol (5b). Colorless syrup; $[\alpha]_D^{24}$ −14.4° (*C*=1.0, $CHCl_3$); IR (neat, cm^{-1}) 3465, 3031, 2921, 2870, 1630, 1497, 1455, 1397, 1364; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (3H, s, Me), 0.95 (3H, s, Me), 2.15 (1H, t, *J*=5.8 Hz, OH), 3.39–3.51 (7H, m, $-OCH_2C(Me)_2-$, $HOCH_2C(Me)_2-$, H-7, H-7, OH), 3.66 (1H, dd, *J*=4.4, 1.6 Hz, H-5), 4.00 (1H, d, *J*=6.4 Hz, H-3), 4.08 (1H, dd, *J*=4.4, 6.4 Hz, H-4), 4.07–4.12 (1H, m, H-6), 4.20 (1H, d, *J*=2.1 Hz, H-1), 4.31 (1H, d, *J*=2.1 Hz, H-1), 4.33 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.38 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.38 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.44 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.47 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.68 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.71 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.81 (1H, d, *J*=11.0 Hz, $PhCH_2$), 7.20–7.35 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.7, 21.8, 36.0, 69.5, 70.2, 70.9, 71.0, 72.6, 73.1, 74.1, 75.5, 76.7, 81.0 (2C), 85.7, 127.5, 127.6, 127.7, 127.8, 127.9, 128.2, 128.2, 128.3, 138.0, 138.1, 138.1, 138.2, 158.4; MS (EI) *m*/*z* 640 (M), 625 (M−Me), 549 (M−Bn); HRMS (EI) calcd for $C_{40}H_{48}O_7$ 640.3400, found 640.3397.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-2-*O*-(3-hydroxy-2,2-dimethylpropyl)-D-*manno*-hept-1-enitol (5c). Colorless syrup; $[\alpha]_D^{21}$ −0.9° (*C*=1.2, $CHCl_3$); IR (neat, cm^{-1}) 3449, 3031, 2926, 2870, 1455; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (3H, s, Me), 1.01 (3H, s, Me), 2.02 (1H, t, *J*=5.8 Hz, OH), 2.49 (1H, bd, *J*=6.4 Hz, OH), 3.40 (1H, d, *J*=12.2 Hz, $-OCH_2C(Me)_2-$), 3.44 (1H, d, *J*=12.2 Hz, $-OCH_2C(Me)_2-$), 3.51 (1H, d, *J*=10.9 Hz, $-OCH_2C(Me)_2-$), 3.53 (1H, dd, *J*=9.7, 5.0 Hz, H-7), 3.54 (1H, d, *J*=9.9 Hz, $-OCH_2C(Me)_2-$), 3.62 (1H, dd, *J*=9.7, 3.2 Hz, H-7),

3.87 (1H, dd, J=8.1, 2.1 Hz, H-5), 3.98 (1H, m, H-6), 4.07 (1H, dd, J=8.5, 2.1 Hz, H-4), 4.10 (1H, d, J=8.5 Hz, H-3), 4.23 (1H, d, J=11.6 Hz, $PhCH_2$), 4.32 (1H, d, J=1.8 Hz, H-1), 4.41 (1H, d, J=1.8 Hz, H-1), 4.43 (1H, d, J=11.6 Hz, $PhCH_2$), 4.43 (1H, d, J=11.6 Hz, $PhCH_2$), 4.47 (1H, d, J=11.6 Hz, $PhCH_2$), 4.50 (1H, d, J=11.6 Hz, $PhCH_2$), 4.56 (1H, d, J=11.0 Hz, $PhCH_2$), 4.57 (1H, d, J=11.6 Hz, $PhCH_2$), 4.59 (1H, d, J=11.0 Hz, $PhCH_2$), 7.15–7.35 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.8, 21.9, 36.1, 70.0, 70.1, 70.1, 71.3, 73.2, 73.9, 74.3, 74.4, 78.4, 78.5, 79.7, 87.8, 127.4, 127.5, 127.5, 127.7, 127.8, 127.9, 127.9, 128.2, 128.2, 128.3, 128.4, 138.0, 138.1, 138.6, 138.6, 158.4; MS (EI) m/z 640 (M), 625 (M−Me), 549 (M−Bn); HRMS (EI) calcd for $C_{40}H_{48}O_7$ 640.3400, found 640.3392.

Reaction of the sugar ortho esters 3d, e with $AlMe_3$

To a solution of ortho ester **3d** (48 mg, 80 μmol) in CH_2Cl_2 (1.6 ml) was added a 1.0 M solution of $AlMe_3$ in *n*-hexane (0.56 ml, 0.56 mmol) at room temperature under Ar. After 3 h of stirring, small amount of water was added to the solution cautiously until the generation of foams was ceased. The products were extracted with ether and CH_2Cl_2 according to the same procedure for the extraction of enol ether **5a**–**c**, and were applied on a silica gel column chromatography (ether–hexane 1:1 then 2:1). The mixture of the dimethylated compound **6a** and the enol ether **5d** was obtained as a colorless syrup (35 mg, 73%), and the ratio between **6a** and **5d** was determined by comparing the intensity of ^{1}H NMR spectrum (**5d**:**6a**=66:7). The analytical samples of **6a** and **5d** were isolated from the resulting mixture of a lager scale reaction. The reaction of **3e** with 6 equiv. of $AlMe_3$ was also performed according to the above procedure to afford the dimethylated compound **6b** as colorless syrup in 75% yield.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-2-*O*-(3-hydroxypropyl)-D-*gluco*-hept-1-enitol (5d). Colorless syrup; $[\alpha]_D^{22}$+50.7° (C=1.0, $CHCl_3$); IR (neat, cm^{-1}) 3434, 3031, 2928, 2870, 1630, 1455; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.88 (2H, dt, J=11.3, 5.8 Hz, $-CH_2CH_2CH_2-$), 2.21 (1H, bs, OH), 2.76 (1H, bs, OH), 3.54–3.88 (7H, m, H-5, H-7, $-CH_2CH_2OH$, $-OCH_2CH_2-$), 3.99 (1H, m, H-6), 4.10 (1H, dd, J=7.6, 2.6 Hz, H-4), 4.16 (1H, d, J=2.1 Hz, H-1), 4.22 (1H, d, J=2.1 Hz, H-1), 4.23 (1H, d, J=7.6 Hz, H-3), 4.46 (1H, d, J=11.6 Hz, $PhCH_2$), 4.46 (1H, d, J=11.6 Hz, $PhCH_2$), 4.50 (1H, d, J=11.6 Hz, $PhCH_2$), 4.51 (2H, s, $PhCH_2$), 4.68 (1H, d, J=11.6 Hz, $PhCH_2$), 4.71 (1H, d, J=11.3 Hz, $PhCH_2$), 4.92 (1H, d, J=11.3 Hz, $PhCH_2$), 7.17–7.36 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 31.1, 59.6, 64.8, 70.4, 71.0, 71.3, 73.3, 73.5, 75.0, 78.3, 79.3, 82.2, 86.9, 127.4, 127.5, 127.5, 127.7, 127.8, 128.0, 128.2, 128.3, 128.3, 128.4, 128.5, 138.0, 138.1, 138.5, 138.6, 158.4; MS (EI) m/z 612 (M), 597 (M−Me), 536 (M−$HOCH_2CH_2CH_2OH$), 521 (M−Bn); HRMS (EI) calcd for $C_{38}H_{44}O_7$ 612.3087, found 612.3091.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-2-*O*-(3-hydroxypropyl)-2-*C*-methyl-D-*gluco*-heptitol (6a). Colorless syrup; $[\alpha]_D^{23}$−15.5° (C=0.9, $CHCl_3$); IR (neat, cm^{-1}) 3422, 3031, 2928, 2870, 1497, 1455, 1397, 1362; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (3H, s, Me), 1.21 (3H, s, Me), 1.67 (2H, dt, J=11.6, 5.8 Hz, $-CH_2CH_2CH_2-$), 2.21 (1H, bs, OH), 2.98 (1H, bs, OH), 3.38 (1H, d, J=6.7 Hz, H-3), 3.42–3.51 (2H, m), 3.57–3.72 (5H, m), 4.03 (1H, dd, J=6.7, 2.1 Hz, H-4), 4.04–4.09 (1H, m, H-6), 4.43 (1H, d, J=11.6 Hz, $PhCH_2$), 4.46 (1H, d, J=11.0 Hz, $PhCH_2$), 4.54 (2H, s, $PhCH_2$), 4.55 (1H, d, J=11.6 Hz, $PhCH_2$), 4.74 (1H, d, J=11.6 Hz, $PhCH_2$), 4.78 (1H, d, J=11.0 Hz, $PhCH_2$), 4.92 (1H, d, J=11.6 Hz, $PhCH_2$), 7.22–7.36 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 19.8, 23.6, 32.7, 59.6, 61.3, 70.5, 71.7, 73.5, 73.5, 74.4, 74.5, 77.4, 77.9, 79.4, 82.3, 127.1, 127.6, 127.7, 127.8, 127.8, 128.0, 128.1, 128.2, 128.3, 128.4, 128.6, 128.8, 138.0, 138.2, 138.5, 139.3; MS (FAB) m/z 667 $(M+K)^+$, 651 $(M+Na)^+$, 576 $(M-Bn+K)^+$, 560 $(M-Bn+Na)^+$; HRMS (FAB) calcd for $C_{39}H_{48}O_7Na$ 651.3298, found 651.3306.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-2-*O*-(2-hydroxyethyl)-2-*C*-methyl-D-*gluco*-heptitol (6b). Colorless syrup; $[\alpha]_D^{27}$−19.2° (C=1.0, $CHCl_3$); IR (neat, cm^{-1}) 3420, 3031, 2928, 2869, 2361, 1456, 1385, 1362; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (3H, s, Me), 1.23 (3H, s, Me), 1.61 (1H, bs, OH), 2.89 (1H, bs, OH), 3.31 (1H, d, J=7.0 Hz, H-3), 3.31–3.34 (1H, m, CH_2CH_2OH), 3.42 (1H, ddd, J=9.5, 6.4, 3.3 Hz, CH_2CH_2OH), 3.54–3.56 (2H, m, CH_2CH_2OH), 3.63 (2H, d, J=10.4 Hz, H-7), 3.66 (2H, d, J=10.4 Hz, H-7), 3.80 (1H, dd, J=7.0, 2.1 Hz, H-5), 4.03 (1H, dd, J=7.0, 2.1 Hz, H-4), 4.05–4.09 (1H, m, H-6), 4.38 (1H, d, J=11.6 Hz, $PhCH_2$), 4.42 (1H, d, J=11.0 Hz, $PhCH_2$), 4.52 (1H, d, J=11.6 Hz, $PhCH_2$), 4.53 (2H, s, $PhCH_2$), 4.74 (1H, d, J=11.6 Hz, $PhCH_2$), 4.79 (1H, d, J=11.0 Hz, $PhCH_2$), 4.92 (1H, d, J=11.6 Hz, $PhCH_2$), 7.22–7.35 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 19.1, 24.0, 62.2, 62.5, 70.1, 71.6, 73.5, 73.5, 74.4, 74.5, 77.2, 77.8, 79.5, 82.6, 127.2, 127.6, 127.7, 127.8, 128.0, 128.2, 128.3, 128.4, 128.4, 128.6, 128.9, 137.8, 138.2, 138.4, 139.1; MS (EI) m/z 614 (M), 552 (M−$HOCH_2CH_2OH$), 523 (M−Bn); HRMS (EI) calcd for $C_{38}H_{46}O_7$ 614.3244, found 614.3237.

Isolation of the intermediate acetals 4a, d, e

To a solution of ortho ester **3e** (58 mg, 0.1 mmol) in CH_2Cl_2 (1 ml) was added a 1.0 M solution of $AlMe_3$ in *n*-hexane (0.1 ml, 0.1 mmol) at room temperature under Ar. After 1 h of stirring, the reaction mixture was dealt with according to the procedure described above for the isolation of enol ethers **5a**–**c**. The acetal **4e** was obtained as colorless syrup in 20% yield by the purification with a silica gel column chromatography (ether–hexane 1:3 then 1:2). Two other intermediate acetals **4a,d** were also isolated by using appropriate amounts of $AlMe_3$.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-D-*gluco*-2-heptulose 2,2-dimethylpropane-1,3-diyl acetal (4a). Colorless syrup; $[\alpha]_D^{23}$−30.6° (C=1.0, $CHCl_3$); IR (neat, cm^{-1}) 3484, 3031, 2953, 2869, 1455, 1397, 1364; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80 (3H, s, Me), 1.04 (3H, s, Me), 1.42 (3H, s, Me), 3.03 (1H, d, J=5.2 Hz, OH), 3.31 (1H, dd, J=11.2, 2.0 Hz, dioxaneH), 3.43 (1H, dd, J=11.2, 2.0 Hz, dioxaneH), 3.56 (1H, dd, J=9.9, 5.5 Hz, H-7), 3.62 (1H, dd, J=9.9, 4.6 Hz, H-7), 3.62 (2H, d, J=11.2 Hz, dioxaneH), 3.75 (1H, dd, J=6.7, 3.4 Hz, H-5), 3.78 (1H, d, J=5.0 Hz, H-3), 4.05 (1H, m, H-6), 4.30 (1H, dd, J=5.0, 3.4 Hz, H-4), 4.49 (1H, d, J=11.9 Hz, $PhCH_2$), 4.53 (1H, d, J=11.9 Hz,

$PhCH_2$), 4.54 (1H, d, J=11.6 Hz, $PhCH_2$), 4.61 (1H, d, J=11.3 Hz, $PhCH_2$), 4.63 (1H, d, J=11.3 Hz, $PhCH_2$), 4.68 (1H, d, J=11.6 Hz, $PhCH_2$), 4.77 (1H, d, J=11.3 Hz, $PhCH_2$), 4.80 (1H, d, J=11.3 Hz, $PhCH_2$), 7.21–7.36 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 15.9, 22.5, 23.4, 30.0, 69.8, 70.3, 71.1, 71.7, 73.3, 73.4, 73.8, 74.3, 76.6, 78.8, 80.2, 100.4, 127.4, 127.5, 127.6, 127.7, 128.1, 128.2, 128.3, 128.3, 128.3, 128.5, 128.8, 138.4 (2C), 138.4, 138.6; MS (EI) *m/z* 640 (M), 625 (M−Me), 549 (M−Bn), 536 (M−$HOCH_2C(Me)_2CH_2OH$); HRMS (EI) calcd for $C_{40}H_{48}O_7$ 640.3400, found 640.3399.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-D-*gluco*-2-heptulose propane-1,3-diyl acetal (4d). Colorless syrup; $[\alpha]_D^{25}$−25.5° (C=1.2, $CHCl_3$); IR (neat, cm^{-1}) 3432, 2923, 2870, 1588, 1455, 1385; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (1H, m, $-CH_2CH_2CH_2-$), 1.46 (3H, s, Me), 1.85 (1H, m, $-CH_2CH_2CH_2-$), 3.10 (1H, d, J=5.2 Hz, OH), 3.54–3.61 (2H, m), 3.69–3.76 (3H, m), 3.84–3.98 (3H, m), 4.06 (1H, m, H-6), 4.27 (1H, dd, J=5.2, 3.4 Hz, H-4), 4.49 (1H, d, J=12.2 Hz, $PhCH_2$), 4.53 (1H, d, J=12.2 Hz, $PhCH_2$), 4.55 (1H, d, J=11.3 Hz, $PhCH_2$), 4.59 (1H, d, J=11.3 Hz, $PhCH_2$), 4.65 (1H, d, J=11.3 Hz, $PhCH_2$), 4.65 (1H, d, J=11.6 Hz, $PhCH_2$), 4.78 (1H, d, J=11.3 Hz, $PhCH_2$), 4.80 (1H, d, J=11.6 Hz, $PhCH_2$), 7.20–7.35 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 16.3, 25.7, 59.2, 59.7, 71.0, 71.8, 73.3, 73.3, 73.8, 74.2, 76.6, 79.0, 80.7, 100.3, 127.3, 127.5, 127.7, 128.0, 128.2, 128.3, 128.5, 128.7, 138.3, 138.4 (2C), 138.6; MS (EI) *m/z* 612 (M), 597 (M−Me), 536 (M−$HOCH_2CH_2CH_2OH$), 521 (M−Bn); HRMS (EI) calcd for $C_{38}H_{44}O_7$ 612.3087, found 612.3076.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-D-*gluco*-2-heptulose ethane-1,2-diyl acetal (4e). Colorless syrup; $[\alpha]_D^{27}$3.7° (C=1.1, $CHCl_3$); IR (neat, cm^{-1}) 3484, 3031, 2880, 1497, 1455, 1397, 1360; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (3H, s, Me), 3.01 (1H, d, J=4.3 Hz, OH), 3.60–3.64 (3H, m), 3.74–3.99 (7H, m), 4.50 (1H, d, J=11.9 Hz, $PhCH_2$), 4.55 (1H, d, J=11.0 Hz, $PhCH_2$), 4.55 (1H, d, J=11.0 Hz, $PhCH_2$), 4.59 (1H, d, J=11.9 Hz, $PhCH_2$), 4.62 (1H, d, J=11.3 Hz, $PhCH_2$), 4.70 (1H, d, J=11.3 Hz, $PhCH_2$), 4.72 (1H, d, J=11.3 Hz, $PhCH_2$), 4.80 (1H, d, J=11.3 Hz, $PhCH_2$), 7.22–7.36 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.1, 64.4, 64.8, 71.0, 71.4, 73.3, 73.4, 73.9, 74.0, 77.8, 77.8, 79.7, 110.9, 127.4, 127.6, 127.6, 127.8, 128.1, 128.2, 128.2, 128.3, 128.3, 128.4, 138.2, 138.3, 138.3, 138.5; MS (EI) *m/z* 598 (M), 583 (M−Me), 537 (M−OCH_2CH_2OH), 507 (M−Bn); HRMS (EI) calcd for $C_{37}H_{42}O_7$ 598.2931, found 598.2949.

Protection of 1°-alcohols of the enol ethers 5a–c

To a solution of **5a** (2.57 g, 4.0 mmol) in DMF (40 ml) was added Et_3N (2.8 ml, 20 mmol), 4- (dimethylamino)pyridine (48 mg, 0.40 mmol), and TBDMSCl (1.21 g, 8.0 mmol) successively. The mixture was stirred at room temperature under Ar for 2 h, and then poured into a mixture of ether (300 ml) and diluted water (300 ml). The organic layer was washed twice with diluted water (300 ml×2), dried over Na_2SO_4, and then evaporated. The residue was applied to a silica gel column chromatography (ether–hexane 1:4) to afford **7a** as colorless syrup (2.74 g, 91%). Compounds **7b** and **7c** were also prepared with this procedure in 90 and 93% yields, respectively.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-2-*O*-(3-*tert*-butyldimethylsilyloxy-2,2-dimethylpropyl)-D-*gluco*-hept-1-enitol (7a). Colorless syrup; $[\alpha]_D^{28}$+30.4° (C=1.1, $CHCl_3$); IR (neat, cm^{-1}) 3486, 3032, 2955, 2930, 2859, 1624, 1497, 1455, 1397, 1362; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.00 (3H, s, MeSi), 0.01 (3H, s, MeSi), 0.87 (3H, s, Me), 0.88 (9H, s, *t*-BuSi), 0.89 (3H, s, Me), 2.87 (1H, d, J=4.9 Hz, OH), 3.33 (1H, d, J=9.8 Hz, $-OCH_2C(Me)_2-$), 3.35 (1H, d, J=9.8 Hz, $-OCH_2C(Me)_2-$), 3.39 (1H, d, J=9.2 Hz, $-OCH_2C(Me)_2-$), 3.46 (1H, d, J=9.2 Hz, $-OCH_2C(Me)_2-$), 3.56 (1H, dd, J=10.0, 5.7 Hz, H-7), 3.60 (1H, dd, J=10.0, 3.6 Hz, H-7), 3.65 (1H, dd, J=6.7, 3.4 Hz, H-5), 3.94–3.99 (1H, m, H-6), 4.03 (1H, dd, J=5.9, 3.4 Hz, H-4), 4.19 (1H, d, J=2.0 Hz, H-1), 4.19 (1H, d, J=5.9 Hz, H-3), 4.22 (1H, d, J=2.0 Hz, H-1), 4.41 (1H, d, J=11.3 Hz, $PhCH_2$), 4.47 (1H, d, J=11.9 Hz, $PhCH_2$), 4.50 (1H, d, J=11.6 Hz, $PhCH_2$), 4.51 (1H, d, J=11.9 Hz, $PhCH_2$), 4.53 (1H, d, J=11.6 Hz, $PhCH_2$), 4.66 (1H, d, J=11.3 Hz, $PhCH_2$), 4.66 (1H, d, J=11.3 Hz, $PhCH_2$), 4.83 (1H, d, J=11.3 Hz, $PhCH_2$), 7.18–7.36 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ −5.5, −5.5, 18.3, 21.7 (2C), 25.8 (3C), 36.5, 68.7, 70.8, 71.0, 71.3, 72.8, 73.3, 73.4, 74.7, 78.2, 79.2, 81.0, 85.2, 127.4, 127.4, 127.5, 127.6, 127.7, 127.8, 128.0, 128.0, 128.1, 128.2, 128.2, 128.2, 128.3, 128.3, 128.5, 138.2, 138.3, 138.5, 138.5, 158.8; MS (EI) *m/z* 754 (M), 663 (M−Bn), 536 (M−TBDMSO$CH_2C(Me)_2CH_2OH$); HRMS (EI) calcd for $C_{46}H_{62}O_7Si$ 754.4265, found 754.4269.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-2-*O*-(3-*tert*-butyldimethylsilyloxy-2,2-dimethylpropyl)-D-*galacto*-hept-1-enitol (7b). Colorless syrup; $[\alpha]_D^{24}$−13.0° (C=1.1, $CHCl_3$); IR (neat, cm^{-1}) 3503, 3032, 2955, 2930, 2859, 1456; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (3H, s, MeSi), 0.01 (3H, s, MeSi), 0.88 (9H, s, *t*-BuSi), 0.91 (3H, s, Me), 0.92 (3H, s, Me), 3.17 (1H, d, J=4.9 Hz, OH), 3.35 (1H, d, J=9.5, $-OCH_2C(Me)_2-$), 3.38 (1H, d, J=9.5, $-OCH_2C(Me)_2-$), 3.40 (1H, d, J=9.2, $-OCH_2C(Me)_2-$), 3.46 (1H, dd, J=9.5, 6.1, H-7), 3.51 (1H, d, J=9.2, $-OCH_2C(Me)_2-$), 3.52 (1H, dd, J=9.5, 5.9, H-7), 3.69 (1H, dd, J=5.4, 1.5, H-5), 4.02 (1H, d, J=5.4, H-3), 4.06 (1H, t, J=5.4, H-4), 4.10–4.14 (1H, m, H-6), 4.22 (1H, d, J=2.1, H-1), 4.32 (1H, d, J=11.6, $PhCH_2$), 4.34 (1H, d, J=11.9, $PhCH_2$), 4.35 (1H, d, J=2.1, H-1), 4.37 (1H, d, J=11.6, $PhCH_2$), 4.39 (1H, d, J=11.9, $PhCH_2$), 4.49 (1H, d, J=11.9, $PhCH_2$), 4.66 (1H, d, J=11.0, $PhCH_2$), 4.72 (1H, d, J=11.9, $PhCH_2$), 4.76 (1H, d, J=11.0, $PhCH_2$), 7.18–7.35 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ −5.5, −5.5, 18.3, 21.8 (2C), 25.9 (3C), 36.5, 68.7, 70.0, 70.9, 71.4, 72.8 (2C), 73.1, 75.5, 76.8, 80.2, 80.2, 84.7, 127.5, 127.5, 127.6, 127.6, 127.7, 128.0, 128.2, 128.3, 128.3, 128.3, 128.3, 138.2, 138.2, 138.3, 138.3, 158.6; MS (EI) *m/z* 754 (M), 663 (M−Bn), 536 (M−Bn−TBDMSO$CH_2C(Me)_2CH_2OH$); HRMS (EI) calcd for $C_{46}H_{62}O_7Si$ 754.4265, found 754.4257.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-2-*O*-(3-*tert*-butyldimethylsilyloxy-2,2-dimethylpropyl)-D-*manno*-hept-1-enitol (7c). Colorless syrup; $[\alpha]_D^{23}$+3.9° (C=1.3, $CHCl_3$); IR (neat, cm^{-1}) 3459, 3032, 2955, 2930, 2859, 1624, 1497, 1455,

1391, 1362; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.00 (3H, s, MeSi), 0.01 (3H, s, MeSi), 0.87 (9H, s, *t*-BuSi), 0.96 (3H, s, Me), 0.98 (3H, s, Me), 2.49 (1H, d, *J*=6.1 Hz, OH), 3.43 (2H, s, $-OCH_2C(Me)_2-$), 3.53 (2H, s, $-OCH_2C(Me)_2-$), 3.55 (1H, dd, *J*=9.5, 5.5 Hz, H-7), 3.63 (1H, dd, *J*=9.5, 3.1 Hz, H-7), 3.94 (1H, dd, *J*=7.9, 1.8 Hz, H-5), 4.01–4.04 (1H, m, H-6), 4.11 (1H, d, *J*=8.7 Hz, H-3), 4.14 (1H, dd, *J*=8.7, 1.8 Hz, H-4), 4.23 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.33 (1H, d, *J*=1.5 Hz, H-1), 4.39 (1H, d, *J*=1.5 Hz, H-1), 4.44 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.46 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.48 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.53 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.56 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.58 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.59 (1H, d, *J*=11.6 Hz, $PhCH_2$), 7.17–7.35 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ −5.5 (2C), 18.2, 21.8, 21.8, 25.8 (3C), 36.6, 68.8, 69.7, 70.0, 71.4, 72.7, 73.2, 74.0, 74.4, 78.5, 78.6, 79.8, 87.7, 127.3, 127.4, 127.7, 127.8, 127.8, 127.9, 127.9, 128.1, 128.1, 128.2, 128.2, 128.4, 138.0, 138.3, 138.6, 138.7, 158.6; MS (EI) *m/z* 754 (M), 663 (M−Bn), 536 (M−$OCH_2C(Me)_2CH_2OTBDMS$); HRMS (EI) calcd for $C_{46}H_{62}O_7Si$ 754.4265, found 754.4271.

Oxidation of alcohols of the enol ethers 5a and 7a

The solution of **7a** (453 mg, 0.60 mmol) in DMSO/Ac_2O (4:1) (6 ml) was stirred at room temperature for 18 h. The resulting mixture was extracted with Et_2O and the organic layer was washed several times with distilled water. The ethereal solution was dried over Na_2SO_4 and then evaporated. The residue was applied to a silica gel column chromatography (ether–hexane 1:5 then 1:4) to afford **8** as colorless syrup (370 mg, 82%). In the case of the oxidation of **5a** with DMSO/Ac_2O (4:1), dioxo compound **11** was mainly afforded.

1,3,4,5-Tetra-*O*-benzyl-7-deoxy-6-*O*-(3-*tert*-butyldimethylsilyloxy-2,2-dimethylpropyl)-L-*xylo*-hept-6-en-2-ulose (8). Colorless syrup; $[\alpha]_D^{22}$+16.1° (*C*=1.0, $CHCl_3$); IR (neat, cm^{-1}) 3032, 2955, 2930, 2859, 1732, 1626, 1497, 1456, 1397; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.00 (3H, s, MeSi), 0.01 (3H, s, MeSi), 0.86 (9H, s, *t*-BuSi), 0.91 (3H, s, Me), 0.92 (3H, s, Me), 3.36 (1H, d, *J*=9.5, $-OCH_2C(Me)_2-$), 3.39 (1H, d, *J*=9.5, $-OCH_2C(Me)_2-$), 3.39 (1H, d, *J*=9.2, $-OCH_2C(Me)_2-$), 3.45 (1H, d, *J*=9.2, $-OCH_2C(Me)_2-$), 3.96 (1H, d, *J*=3.1, H-3), 4.11–4.20 (5H, m, H-4, H-1, H-1, H-7, H-7), 4.27 (1H, d, *J*=6.4, H-5), 4.29 (1H, d, *J*=11.6, $PhCH_2$), 4.34 (1H, d, *J*=11.6, $PhCH_2$), 4.37 (1H, d, *J*=11.6, $PhCH_2$), 4.39 (1H, d, *J*=11.6, $PhCH_2$), 4.40 (1H, d, *J*=11.3, $PhCH_2$), 4.43 (1H, d, *J*=11.0, $PhCH_2$), 4.56 (1H, d, *J*=11.3, $PhCH_2$), 4.79 (1H, d, *J*=11.0, $PhCH_2$), 7.17–7.32 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ −5.5, −5.5, 18.3, 21.7, 21.8, 25.9 (3C), 36.6, 68.6, 71.1, 72.8, 73.2, 74.2, 74.5, 75.4, 81.1,, 81.4, 83.5, 85.9, 127.4, 127.6, 127.7, 127.9, 128.0, 128.0, 128.1, 128.2, 128.3, 128.4, 137.1, 137.6, 138.2, 138.3, 158.3, 207.6; MS (EI) *m/z* 752 (M), 734 (M−H_2O), 661 (M−Bn); HRMS (EI) calcd for $C_{46}H_{60}O_7Si$ 752.4108, found 752.4110.

1,3,4,5-Tetra-*O*-benzyl-7-deoxy-6-*O*-(2,2-dimethyl-3-oxopropyl)-L-*xylo*-hept-6-en-2-ulose (11). Colorless syrup; $[\alpha]_D^{24}$+17.2° (*C*=1.1, $CHCl_3$); IR (neat, cm^{-1}) 3032, 2924, 2870, 1732, 1632, 1497, 1455, 1399; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (3H, s, Me), 1.15 (3H, s, Me), 3.62 (1H, d, *J*=9.4 Hz, $-OCH_2C(Me)_2-$), 3.67 (1H, d, *J*=9.4 Hz, $-OCH_2C(Me)_2-$), 3.99 (1H, d, *J*=3.4 Hz, H-3), 4.05 (1H, dd, *J*=6.4, 3.4 Hz, H-4), 4.14 (1H, d, *J*=6.4 Hz, H-5), 4.19–4.23 (4H, m, H-1, H-1, H-7, H-7), 4.32 (1H, d, *J*=11.3 Hz, $PhCH_2$), 4.36 (1H, d, *J*=11.9 Hz, $PhCH_2$), 4.38 (1H, d, *J*=11.3 Hz, $PhCH_2$), 4.40 (1H, d, *J*=11.9 Hz, $PhCH_2$), 4.47 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.50 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.54 (1H, d, *J*=11.3 Hz, $PhCH_2$), 4.75 (1H, d, *J*=11.3 Hz, $PhCH_2$), 7.18–7.33 (20H, m, PhH), 9.51 (1H, s, CHO); ^{13}C NMR (400 MHz, $CDCl_3$) δ 19.2 (2C), 46.4, 71.3, 71.7, 73.2, 74.0, 74.3, 75.1, 80.5, 80.8, 82.9, 86.6, 127.5, 127.6, 127.7, 127.9, 128.0, 128.0, 128.1, 128.2, 128.2, 128.3, 128.4, 137.1, 137.5, 138.0, 138.1, 158.0, 204.1, 207.3; MS (EI) *m/z* 636 (M), 545 (M−Bn); HRMS (EI) calcd for $C_{40}H_{44}O_7$ 636.3087, found 636.3087.

Survey of the catalysts for the intramolecular aldol cyclization of the enol ether 8

To a solution of **8** (0.5 M) in THF or THF/H_2O (19:1) was added 1–2 equiv. of each acid catalyst. The solution was stirred under Ar at room temperature or under reflux conditions for appropriate time shown in Table 1. In the cases of the reaction in dry THF, the reaction mixtures were quenched with several drops of H_2O and poured into mixtures of Et_2O and H_2O, while the resulting mixtures of the reaction in THF/H_2O were directly poured into mixtures of Et_2O and H_2O. After the organic layer of each mixture was separated, aqueous layer was again extracted with Et_2O. The combined organic layer was washed with saturated $NaHCO_3$ (aq) solution and H_2O, dried over Na_2SO_4, and then concentrated. Silica gel column chromatography (ether–hexane 1:2 then 1:1) of the residue afforded **9a**[4a] as colorless needles and (in some cases) **10** as colorless syrup.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-D-*xylo*-hepto-2,6-diulose (10). Colorless syrup; $[\alpha]_D^{22}$+2.4° (*C*=1.0, $CHCl_3$); IR (neat, cm^{-1}) 3063, 3032, 2870, 1730, 1497, 1455, 1399, 1352; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.12 (3H, s, H-7), 4.06 (1H, d, *J*=4.2 Hz, H-3), 4.10 (1H, t, *J*=4.2 Hz, H-4), 4.22 (1H, d, *J*=4.2 Hz, H-5), 4.22 (2H, s, H-1, H-1), 4.40 (2H, s, $PhCH_2$), 4.47 (1H, d, *J*=11.3 Hz, $PhCH_2$), 4.47 (1H, d, *J*=11.3 Hz, $PhCH_2$), 4.49 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.52 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.52 (1H, d, *J*=11.3 Hz, $PhCH_2$), 4.57 (1H, d, *J*=11.3 Hz, $PhCH_2$), 7.14–7.37 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 27.9, 73.2, 73.6, 73.8, 74.3, 74.3, 80.9, 81.1, 82.5, 127.8, 127.9, 128.1, 128.1, 128.4, 128.4, 128.4, 128.4, 128.5, 136.8, 136.9, 137.0, 137.4, 206.7, 208.8; MS (EI) *m/z* 552 (M), 509 (M−Ac), 461 (M−Bn); HRMS (EI) calcd for $C_{35}H_{36}O_6$ 552.2512, found 552.2512.

Preparation of the carbasugar derivatives 9a–c from the enol ethers 5a–c or 7a–c without purification of the intermediate ketones

The solution of **5a** (1.15 g, 1.8 mmol) in DMSO/Ac_2O (4:1) (9 ml) was stirred at room temperature for 24 h. The resulting mixture was extracted with Et_2O and the organic layer was washed three times with distilled water. The ethereal solution was dried over Na_2SO_4, filtered, and then concentrated. The residue was dissolved in THF/H_2O (19:1, 36 ml), and $ZnCl_2$ (490 mg, 3.6 mmol) was added to this solution. The mixture was stirred under reflux conditions for 4 h, and

then was poured into a mixture of Et_2O and H_2O. After the organic layer was separated, aqueous layer was again extracted with Et_2O. The combined organic layer was washed with saturated $NaHCO_3$ (aq) solution and H_2O, dried over Na_2SO_4, and then concentrated. The residue was applied to a silica gel column chromatography (ether–hexane 1:2 then 1:1) to afford **9a**[4a] (720 mg, 73%) as colorless needles. According to above procedure, **9a** was prepared also from **7a** in 80% yield, and **9b,c** were prepared from the corresponding enol ethers in the yields shown in the text. In the case with **5b** or **7b**, the refluxing time for aldol cyclization was shorter than the case with **5a** or **7a**, while it was longer in the case with **5c** or **7c**. The resulting inosose from **5c** or **7c** was afforded as the mixture of two stereoisomers (major:minor=10:1).

2D-(2,5/3,4)-2,3,4-Tri-*O*-benzyl-5-*C*-benzyloxymethyl-2,3,4,5-tetrahydroxycyclohexanone (9b). Colorless needle; mp 109.5–110.5°C; $[\alpha]_D^{24}$+42.3° (*C*=1.0, $CHCl_3$); IR (neat, cm^{-1}) 3438, 3031, 2911, 2845, 1719, 1497, 1455, 1410, 1360; ^1H NMR (400 MHz, $CDCl_3$) δ 2.32 (1H, dd, *J*=14.0, 1.2 Hz, H-6), 2.67 (1H, bs, OH), 2.69 (1H, bd, *J*=14.0, 1.8 Hz, H-6), 3.25 (1H, d, *J*=8.9 Hz, BnOC*H*$_2$), 3.57 (1H, d, *J*=8.9 Hz, BnOC*H*$_2$), 3.99 (1H, bs, H-4), 4.18 (1H, dd, *J*=9.9, 2.6 Hz, H-3), 4.45 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.50 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.52 (1H, bd, *J*=9.9 Hz, H-2), 4.54 (1H, d, *J*=11.0 Hz, $PhCH_2$), 4.59 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.72 (1H, d, *J*=11.9 Hz, $PhCH_2$), 4.93 (1H, d, *J*=11.9 Hz, $PhCH_2$), 4.94 (1H, d, *J*=11.6 Hz, $PhCH_2$), 5.04 (1H, d, *J*=11.0 Hz, $PhCH_2$), 7.19–7.43 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 44.8, 72.8, 73.5, 73.6, 74.1, 74.5, 75.1, 78.4, 81.6, 84.4, 127.5, 127.5, 127.7, 127.9, 127.9, 128.0, 128.1, 128.2, 128.3, 128.3, 128.3, 128.5, 137.3, 138.2, 138.3, 138.7, 204.8; MS (EI) *m*/*z* 552 (M), 534 (M−H_2O), 461 (M−Bn); HRMS (EI) calcd for $C_{35}H_{36}O_6$ 552.2512, found 552.2527; Anal. Calcd for $C_{35}H_{36}O_6$: C, 76.06; H, 6.57. Found: C, 76.09; H, 6.65.

2L-(2,3/4,5)-2,3,4-Tri-*O*-benzyl-5-*C*-benzyloxymethyl-2,3,4,5-tetrahydroxycyclohexanone (9c (major)). Colorless syrup; $[\alpha]_D^{22}$−6.4° (*C*=1.0, $CHCl_3$); IR (neat, cm^{-1}) 3447, 3031, 2923, 2867, 1732, 1497, 1455, 1364; ^1H NMR (400 MHz, $CDCl_3$) δ 2.37 (1H, dd, *J*=14.3, 0.9 Hz, H-6), 2.61 (1H, d, *J*=1.8 Hz, OH), 3.16 (1H, dd, *J*=14.3, 1.8 Hz, H-6), 3.23 (1H, d, *J*=8.9 Hz, BnOC*H*$_2$), 3.49 (1H, d, *J*=8.9 Hz, BnOC*H*$_2$), 3.92 (1H, dd, *J*=7.6, 3.0 Hz, H-3), 4.11 (1H, dd, *J*=3.0, 0.9 Hz, H-2), 4.30 (1H, d, *J*=7.6 Hz, H-4), 4.43 (1H, d, *J*=11.9 Hz, $PhCH_2$), 4.45 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.50 (1H, d, *J*=11.9 Hz, $PhCH_2$), 4.53 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.53 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.59 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.71 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.86 (1H, d, *J*=11.6 Hz, $PhCH_2$), 7.16–7.37 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 44.8, 72.1, 72.5, 73.3, 73.4, 74.1, 75.1, 77.4, 79.5, 81.1, 127.7, 127.7, 127.8, 127.9, 127.9, 128.0, 128.2, 128.3, 128.4, 137.2, 137.8, 137.9 (2C), 206.5; MS (EI) *m*/*z* 552 (M), 534 (M−H_2O), 461 (M−Bn); HRMS (EI) calcd for $C_{35}H_{36}O_6$ 552.2512, found 552.2515.

2L-(2,3,5/4)-2,3,4-Tri-*O*-benzyl-5-*C*-benzyloxymethyl-2,3,4,5-tetrahydroxycyclohexanone (9c (minor)). Colorless syrup; $[\alpha]_D^{21}$−67.1° (*C*=0.8, $CHCl_3$); IR (neat, cm^{-1}) 3470, 3031, 2923, 2869, 1734, 1497, 1455, 1364; ^1H NMR (400 MHz, $CDCl_3$) δ 2.47 (1H, dd, *J*=13.7, 1.7 Hz, H-6), 2.62 (1H, bd, *J*=13.7 Hz, H-6), 3.32 (1H, d, *J*=9.8 Hz, BnOC*H*$_2$), 3.62 (1H, dd, *J*=9.9, 1.8 Hz, BnOC*H*$_2$), 3.96 (1H, dd, *J*=4.0, 1.7 Hz, H-4), 4.19 (1H, t, *J*=4.0 Hz, H-3), 4.31 (1H, d, *J*=1.8 Hz, OH), 4.40 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.45 (1H, d, *J*=11.3 Hz, $PhCH_2$), 4.45 (1H, d, *J*=4.0 Hz, H-2), 4.54 (1H, d, *J*=11.3 Hz, $PhCH_2$), 4.54 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.57 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.67 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.83 (1H, d, *J*=12.2 Hz, $PhCH_2$), 4.87 (1H, d, *J*=12.2 Hz, $PhCH_2$), 7.05–7.08 (2H, m, PhH), 7.22–7.37 (18H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 47.5, 72.5, 73.6 (2C), 73.8, 74.4, 76.1, 79.5, 81.2, 81.3, 127.6, 127.8, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 128.5, 136.8, 137.4, 137.8, 138.1, 204.8; MS (EI) *m*/*z* 552 (M), 534 (M−H_2O), 461 (M−Bn); HRMS (EI) calcd for $C_{35}H_{36}O_6$ 552.2512, found 552.2510.

Reduction of the inosose 9c (major) with $NaBH_4$

To a solution of **9c** (major) (57 mg, 0.10 mmol) in MeOH/THF (4:1) (2 ml) was added $NaBH_4$ (5.7 mg, 0.15 mmol) at −10°C under Ar. The reaction mixture was stirred at −10°C for 30 min. The resulting mixture was concentrated and then extracted with Et_2O. The organic layer was washed with 1N HCl, saturated $NaHCO_3$ (aq) solution, dried over Na_2SO_4, filtered, and then concentrated. The residue was applied to a silica gel column chromatography. The less polar compound **12a** was eluded with ether–hexane 1:1 to 2:1, and more polar **12b** was eluded with ether–hexane 3:1. Both of **12a** and **12b** were afforded as colorless syrup in 44 and 53% yield, respectively.

1L-(1,2,5/3,4)-2,3,4-Tri-*O*-benzyl-1-*C*-benzyloxymethyl-1,2,3,4,5-cyclohexanepentol (12a). Colorless syrup; $[\alpha]_D^{17}$−11.6° (*C*=1.1, $CHCl_3$); IR (neat, cm^{-1}) 3395, 3063, 3031, 2923, 2861, 1497, 1455, 1364; ^1H NMR (400 MHz, $CDCl_3$) δ 1.86 (1H, bd, *J*=14.8, H-6), 2.26 (1H, bd, *J*=14.8, H-6), 2.87 (1H, d, *J*=2.1 Hz, OH), 3.24 (1H, d, *J*=8.9 Hz, BnOC*H*$_2$), 3.42 (1H, d, *J*=8.9 Hz, BnOC*H*$_2$), 3.81 (1H, bd, *J*=7.9 Hz, OH), 3.95–4.01 (2H, m, H-4, H-5), 4.08 (2H, s, H-2, H-3), 4.45 (1H, d, *J*=12.0, $PhCH_2$), 4.53 (1H, d, *J*=12.0, $PhCH_2$), 4.53 (1H, d, *J*=10.7, $PhCH_2$), 4.63 (1H, d, *J*=12.0, $PhCH_2$), 4.64 (1H, d, *J*=12.0, $PhCH_2$), 4.67 (1H, d, *J*=12.0, $PhCH_2$), 4.80 (1H, d, *J*=12.0, $PhCH_2$), 4.94 (1H, d, *J*=10.7, $PhCH_2$), 7.18–7.37 (20H, m, PhH) (not chair form); ^{13}C NMR (400 MHz, $CDCl_3$) δ 32.8, 68.7, 72.5, 72.8, 73.3, 73.9, 75.6, 77.0, 77.9, 78.1, 78.4, 127.5, 127.5, 127.6, 127.7, 127.7, 128.1, 128.3, 128.3, 128.4, 138.0, 138.4, 138.6, 138.8; MS (EI) *m*/*z* 554 (M), 463 (M−Bn); HRMS (EI) calcd for $C_{35}H_{38}O_6$ 554.2668, found 554.2666.

1L-(1,2/3,4,5)-2,3,4-Tri-*O*-benzyl-1-*C*-benzyloxymethyl-1,2,3,4,5-cyclohexanepentol (12b). Colorless syrup; $[\alpha]_D^{18}$−4.0° (*C*=1.3, $CHCl_3$); IR (neat, cm^{-1}) 3447, 3063, 3031, 2928, 2863, 1497, 1455, 1362; ^1H NMR (400 MHz, $CDCl_3$) δ 1.85 (1H, ddd, *J*=13.5, 4.0, 0.9 Hz, H-6), 1.96 (1H, d, *J*=10.7 Hz, OH), 2.06 (1H, ddd, *J*=13.5, 11.6, 2.1 Hz, H-6), 2.38 (1H, d, *J*=2.1 Hz, OH), 3.22 (1H, d, *J*=8.7 Hz, BnOC*H*$_2$), 3.41 (1H, d, *J*=8.7 Hz, BnOC*H*$_2$), 3.82 (1H, dd, *J*=9.8, 2.4 Hz, H-3), 3.88–3.96 (1H, m, H-5), 4.05 (1H, bs, H-4), 4.06 (1H, d, *J*=9.8 Hz, H-2),

4.44 (1H, d, J=12.0 Hz, $PhCH_2$), 4.52 (1H, d, J=12.0 Hz, $PhCH_2$), 4.54 (1H, d, J=11.0 Hz, $PhCH_2$), 4.65 (1H, d, J=11.6 Hz, $PhCH_2$), 4.71 (1H, d, J=11.6 Hz, $PhCH_2$), 4.75 (1H, d, J=11.6 Hz, $PhCH_2$), 4.91 (1H, d, J=11.0 Hz, $PhCH_2$), 5.16 (1H, d, J=11.6 Hz, $PhCH_2$), 7.19–7.37 (20H, m, PhH); ^{13}C NMR (400 MHz, $CDCl_3$) δ 36.6, 66.8, 72.99, 73.3, 73.4, 74.3, 74.3, 75.6, 78.1, 79.1, 81.4, 127.5, 127.6, 127.6, 127.6, 127.7, 128.1, 128.3, 128.4, 128.4, 138.1, 138.4, 138.5, 139.1; MS (FAB) m/z 593 $(M+K)^+$, 577 $(M+Na)^+$, 486 $(M-91+Na)^+$; HRMS (FAB) calcd for $C_{35}H_{38}O_6Na$ 577.2566, found 577.2537.

Preparation of the cyclic phenylboronate ester of the cyclohexanepentol 12a

A mixture of **12a** (20 mg, 0.04 mmol), phenylboric acid (10 mg, 0.08 mmol), and *p*-toluenesulfonic acid monohydrate (1 mg, 15 mol%) in toluene (1 ml) was stirred at 110°C under Ar for 30 min. The resulting mixture was extracted with CH_2Cl_2, and the organic layer was washed with saturated $NaHCO_3$ (aq) solution, dried over Na_2SO_4, filtered, and then concentrated. The residue was applied to a silica gel column chromatography (ether–hexane 1:2, 1:1, then 2:1) to afford **13a** (22 mg, 95%) as colorless syrup.

1L-(1,2,5/3,4)-2,3,4-Tri-*O*-benzyl-1-*C*-benzyloxymethyl-1,2,3,4,5-cyclohexanepentol 1,5-phenylboronate (13a). Colorless syrup; $[\alpha]_D^{16}$ −17.4° (C=1.2, $CHCl_3$); IR (neat, cm^{-1}) 3063, 3031, 2924, 2863, 1497, 1455, 1393, 1360, 1323; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.80 (1H, ddd, J=14.0, 3.4, 1.2 Hz, H-6), 2.52 (1H, dd, J=14.0, 1.7 Hz, H-6), 3.39 (1H, d, J=8.9 Hz, $BnOCH_2$), 3.83 (1H, dd, J=9.8, 3.4 Hz, H-3), 3.89 (1H, d, J=8.9 Hz, $BnOCH_2$), 4.04 (1H, dt, J=3.4 Hz, 1.2 H-4), 4.07 (1H, d, J=9.8 Hz, H-2), 4.35–4.39 (1H, m, H-5), 4.49 (1H, d, J=12.2 Hz, $PhCH_2$), 4.52 (1H, d, J=12.2 Hz, $PhCH_2$), 4.56 (1H, d, J=11.6 Hz, $PhCH_2$), 4.62 (1H, d, J=11.6 Hz, $PhCH_2$), 4.66 (1H, d, J=11.3 Hz, $PhCH_2$), 4.67 (1H, d, J=12.2 Hz, $PhCH_2$), 4.85 (1H, d, J=12.2 Hz, $PhCH_2$), 4.94 (1H, d, J=11.3 Hz, $PhCH_2$), 7.18–7.44 (23H, m, PhH), 7.78 (2H, dd, J=7.9, 1.5); ^{13}C NMR (400 MHz, $CDCl_3$) δ 31.3, 68.7, 73.0, 73.31, 73.4 (2C), 75.3, 76.2, 76.4, 79.6, 79.7, 127.3, 127.5, 127.5, 127.6, 127.6, 127.7, 127.8, 128.2, 128.3, 128.3, 128.4, 130.9, 134.1 (2C), 138.2, 138.4, 138.5, 139.1; MS (FAB) m/z 679 $(M+K)^+$, 663 $(M+Na)^+$; HRMS (FAB) calcd for $C_{41}H_{41}BO_6Na$ 663.2894, found 663.2897.

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