The Use of Grignard Reagents in the Synthesis of Carbohydrates. III.[1] The One-way Anomerization of Methyl Glycofuranosides and the Opening of Their Furanose Rings

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The anomerization of methyl glycofuranoside derivatives with methylmagnesium iodide or *t*-butylmagnesium bromide occurred in a one-way manner. For example, methyl 5-*O*-benzyl-*β*-D-ribofuranoside (**3*β***) was converted into the corresponding α-anomer (**3*α***) in a 95% yield when a mixture of **3*β*** and *t*-butylmagnesium bromide in benzene–ether was heated at about 75 °C to remove the ether; the reverse reaction (from **3*α*** to **3*β***) did not proceed. The reaction of **3*β*** with methylmagnesium iodide gave open-chain products (33%), besides **3*α*** (30%). Twenty kinds of anomers were tested, and the mechanisms of the reactions were discussed. The cleavage of a benzyl- or trityl-protecting group with the Grignard reagent was also observed during the reaction.

Glycosidic linkages and furanose rings of methyl glycofuranosides are generally stable under neutral or mild alkaline reaction conditions, whereas, in the presence of an acid, these furanosides are hydrolyzed, anomerized, or converted into the corresponding pyranosides, depending upon the conditions used.[2] In this paper we would like to report the first example of the anomerization and furanose-ring opening of methyl glycofuranosides using Grignard reagents; two preliminary reports of this work have been published.[3]

Mallory *et al.*[4] have reported that the cyclic acetal protecting groups in steroids were cleaved by Grignard reagents. Recently, Fischer and Horton[5] and also two of the present authors have found similar reactions in the carbohydrate field. For example,[1a] when methyl 5,6-*O*-cyclohexylidene-3-deoxy-2-*C*-methyl-*β*-D-*arabino*-hexofuranoside (**1a-*β***) was treated with 4 molar equiv. of methylmagnesium iodide (MeMgI) in a benzene–ether solution under reflux for 3 h, the 5,6-*O*-cyclohexylidene ring of **1a-*β*** was cleaved and the methyl group was introduced to form the corresponding 6-*O*-(1-methylcyclohexyl) derivative (**2a-*β***) in a 73% yield (Fig. 1). We applied this reaction to the corresponding C-2 epimer (**1b-*β***) to obtain an expected 6-*O*-(1-methylcyclohexyl) derivative (**2b-*β***), besides two additional products which had relatively large values of the specific rotations with a positive sign. This suggested that these two compounds had α-D-glycoside structures. On the basis of a comparison of their spectroscopic data with those for authentic samples, the one was identified as methyl 5,6-*O*-cyclohexylidene-3-deoxy-2-*C*-methyl-α-D-*ribo*-hexofuranoside (**1*α***),[6] while the other was found to be the corresponding 6-*O*-(1-methylcyclohexyl) derivative (**2*α***).[1a] The latter could also be obtained by the treatment of **1*α*** with MeMgI. These results clearly indicated that the stereocontrolled anomerization occurred under strong conditions with the Grignard reagent.

In order to clarify the scope and mechanism of this new anomerization, simple sugar derivatives, methyl mono-, di-, or tri-*O*-benzylated α- and *β*-D-pentofuranosides, were subjected to similar Grignard anomerizations. The preparations of the starting materials will be described in the Experimental section. The anomeric configurations of pairs of the new methyl α- and *β*-D-pentofuranosides were determined by the comparison of their coupling constants[7] of anomeric protons (Table 2) and of their optical rotations[8] (Table 4).

Results

The results are summarized in Table 1.

The Reaction of Methyl D-*Ribofuranoside Derivatives.* When methyl 5-*O*-benzyl-*β*-D-ribofuranoside (**3*β***) was treated with 5 molar equiv. of MeMgI in a benzene–ether solution under forcing conditions,[1a] in which the ether was distilled out from the reaction mixture, an expected α-anomer (**3*α***) was obtained in a 30% yield, along with a 7:3 diastereomeric mixture of open-chain products (**4**) in a 33% yield (Fig. 2). As the reaction went on, undissolved materials were deposited in a solution rich in benzene, and the reaction mixture became heterogeneous. Under similar conditions, **3*α*** gave neither **3*β*** nor **4**. Therefore,

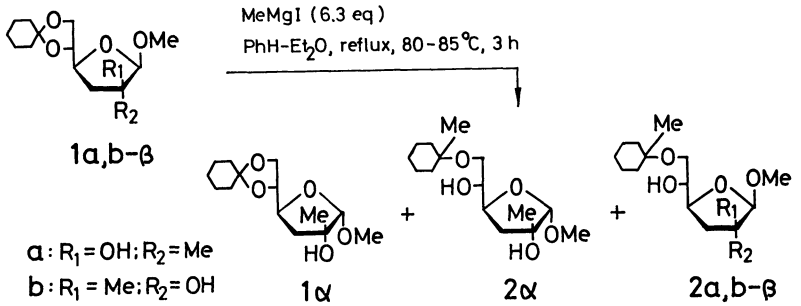
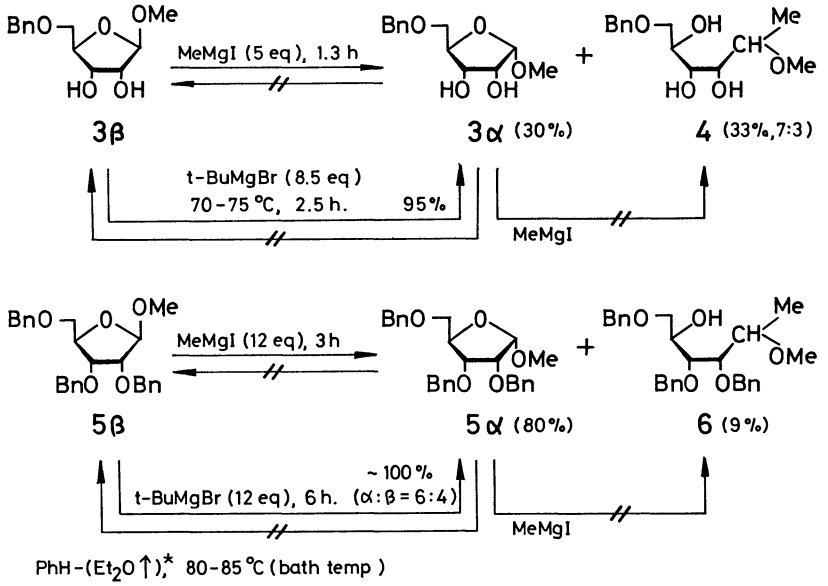


Fig. 1. The acetal ring-opening reaction and stereocontrolled anomerization of branched-chain deoxy sugars.



* The ether was allowed to evaporate.

Fig. 2. The reaction of methyl D-ribofuranoside derivatives with Grignard reagents.

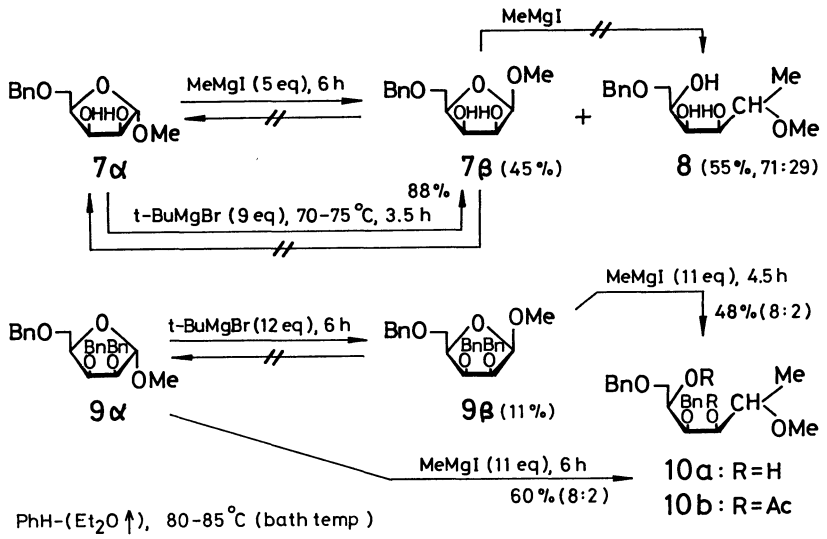


Fig. 3. The reaction of methyl D-lyxofuranoside derivatives with Griganrd reagents.

the anomerization took place in a one-way manner.

In order to obtain **3α** exclusively in the present reaction, we attempted to use *t*-butylmagnesium bromide (*t*-BuMgBr) instead of MeMgI, because the former reagent was sterically bulky, so that the formation of the open-chain products would be prevented. As expected, the reaction of **3β** with *t*-BuMgBr proceeded smoothly to give **3α** (95%) as the sole product, although it also contained a trace of the starting material, judging from TLC analyses and ^{1}H NMR spectroscopy.

Similarly, methyl 2,3,5-tri-*O*-benzyl-β-D-ribofuranoside (**5β**) reacted with MeMgI to give the corresponding α-anomer (**5α**, 80%) and open-chain products (**6**, 9%). The reverse reaction (from **5α** to **5β**) did not proceed. It should be noted here that, although the anomerization with MeMgI took place slower on the perbenzylated anomer (**5β**) than on the monobenzylated one (**3β**), the yield of **5α** was much better than that of **3α**. Some explanations for these phenomena will be presented later on. When *t*-BuMgBr was used in this reaction in place of MeMgI, the anomerization occurred very slowly and many precipitates were deposited during the reaction; after 6 h, we could not detect any anomers in the organic phase. The usual work-up gave a 6:4 mixture of **5α** and **5β**. Under the same reaction conditions, **5α** did not anomerize.

The Reaction of Methyl D-*Lyxofuranosides.* The behavior of MeMgI upon methyl 5-*O*-benzyl-α- and β-D-lyxofuranosides (**7α** and **7β**) was almost the same as that on the corresponding ribose derivatives (Fig. 3). Thus, **7α** was converted into **7β** by the use of MeMgI (yield, 45%) and *t*-BuMgBr (yield, 88%); the reaction with the former reagent also gave open-chain products (**8**, 55%). On the other hand, **7β**

did not react with these reagents under conditions similar to those used for the conversion of **7α**. However, the reaction of methyl 2,3,5-tri-*O*-benzyl-α-D-lyxofuranoside (**9α**) with MeMgI provided a 8:2 diastereomeric mixture of open-chain products (**10a**, 60%) as the main products; here the benzyloxy group originally attached to the C-2 position of **9α** was lacking. Starting from **9β**, we also obtained **10a** (48%) in the same diastereomeric ratio as that from **9α**.

When *t*-BuMgBr was used instead of MeMgI, only an 11% conversion of **9α** to **9β** was accomplished; many precipitates were deposited during this reaction, and no anomers survived in the organic phase after 6 h. The reverse reaction (from **9β** to **9α**) did not proceed under the same reaction conditions.

The Reaction of Methyl D-*Xylofuranosides.* The anomerization of methyl 5-*O*-benzyl-β-D-xylofuranoside (**11β**) with MeMgI occurred in a one-way manner to give an inseparable mixture of the anomers (**11α** and **11β**, *ca.* 19%, 1:1) and open-chain products (**12a**), which were isolated as their acetates (**12b**, 37%) (Fig. 4). With *t*-BuMgBr, only a small percentage of the **11β** was converted into **11α**.

When a 3,5-di-*O*-benzylated derivative (**13β**) was treated with MeMgI, the reaction smoothly proceeded in a one-way manner to provide the corresponding α-anomer (**13α**, 16%) and open-chain products (**14**, 38%). Similarly, *t*-BuMgBr was effective for the conversion of **13β** to **13α** (37%). However, in this case, we also obtained an unexpected crystalline ketone (**15a**) in a 52% yield. This compound was further converted into its acetate (**15b**). The structures of both compounds were tentatively assigned as depicted in Fig. 4.

The behavior of MeMgI or *t*-BuMgBr upon methyl-perbenzylated xylofuranosides (**16α** and **16β**) was somewhat different from that for **11** and **13** (Fig. 5). Thus, **16β** reacted with MeMgI to afford a 6:4 diastereomeric mixture of open-chain products (**17**, 19%), but 63% of the starting β-anomer was recovered. On the other hand, **16α** was easily converted into the corresponding β-anomer (**16β**, 32%), along with **17** (54%, 83:17), the main diastereomer being identical with that from **16β**. Both anomers reacted with *t*-BuMgBr to afford an anomeric mixture.

The Reaction of Methyl D-*Arabinofuranosides.* Only

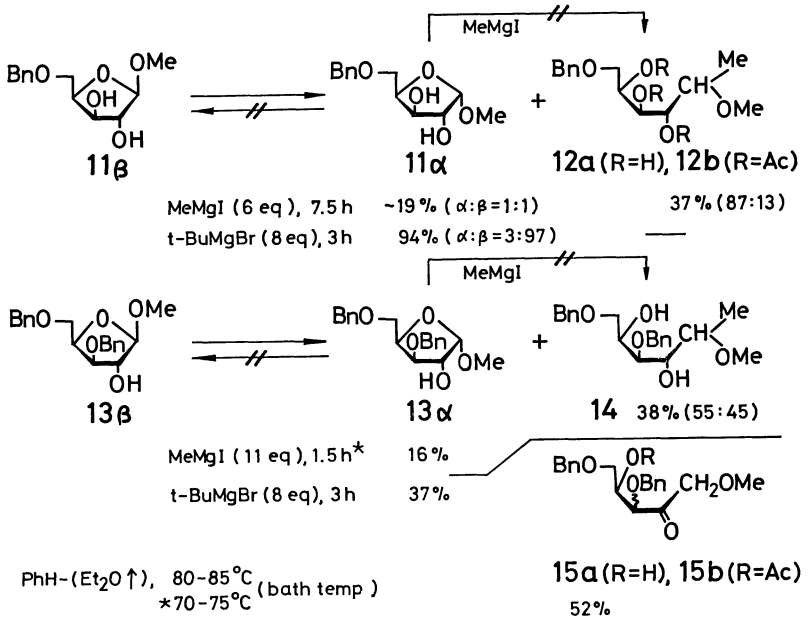


Fig. 4. The reaction of methyl D-xylofuranoside derivatives with Grignard reagents.

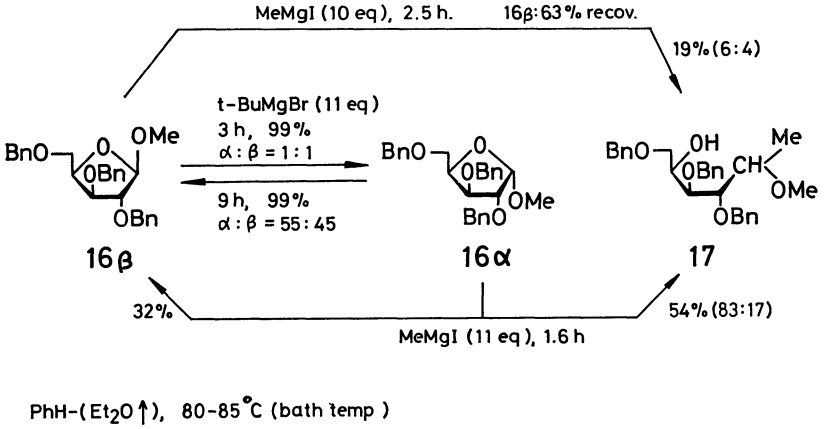


Fig. 5. The reaction of methyl 2,3,5-tri-*O*-benzyl-D-xylofuranosides with Grignard reagents.

perbenzylated anomers, methyl 2,3,5-tri-*O*-benzyl-α- and β-D-arabinofuranosides (**18α** and **18β**), were examined (Fig. 6). Upon treatment with MeMgI, both anomers were converted into a diastereomeric mixture of open-chain products (**19a** and **19b**), which were subsequently separated by silica-gel column chromatography. The selectivity of these reactions was higher on **18β** than on **18α**. The anomerization was also observed by means of TLC analyses, but neither anomer accumulated because of its consumption in the ring-opening reaction. Both anomers were anomerized with *t*-BuMgBr to give an anomeric mixture, the results being similar to those for the anomerization of **16**.

The Reaction of Other Methyl D-*Ribofuranosides.* Methyl 5-*O*-trityl-β-D-ribofuranoside (**20a-β**) also reacted with *t*-BuMgBr to produce the corresponding α-anomer (**20a-α**) in a 57% yield (Fig. 7). Since the trityl group was labile under the present Grignard reaction conditions, some of this group was removed from the α-anomer which had been formed during the reaction.

Similarly, methyl 5-deoxy-β-D-ribofuranoside (**20b-β**) was found to be converted into the corresponding α-anomer (**20b-α**) in a 59% yield; this yield was improved to 94% when a small amount of *t*-butyl alcohol was added to a Grignard solution prior to the addition of **20b-β**.[9]

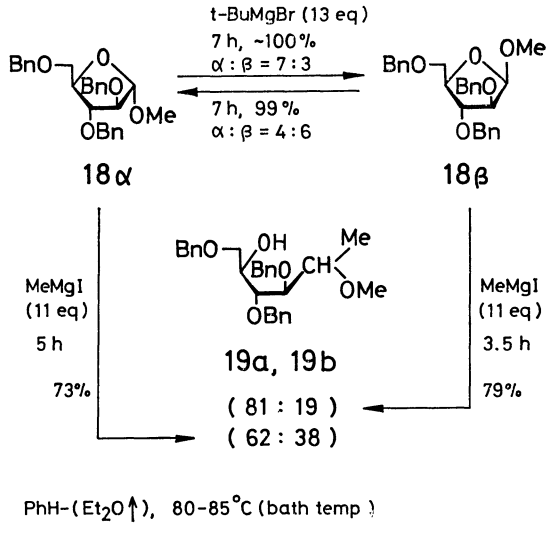


Fig. 6. The reaction of methyl 2,3,5-tri-*O*-benzyl-D-arabinofuranosides with Grignard reagents.

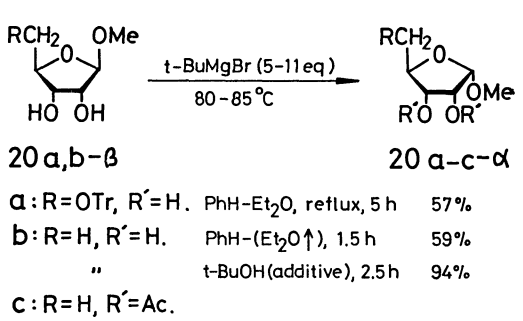


Fig. 7. The reaction of methyl 5-*O*-trityl- and 5-deoxy-β-D-ribofuranosides with *t*-BuMgBr.

Discussion

The formation of the 7:3 diastereomeric open-chain products, **4**, from **3β** suggested that the anomerization of this anomer proceeded through the opening of the furanose ring. A possible mechanism of the reactions for the ribose series is illustrated in Fig. 8. The magnesium atom of the Grignard reagnet is coordinated with the ring oxygen of the furanoside (**A** or **B**),[1a,10] resulting in a weakening of the C_1–O bond of the furan ring. Furthermore, either the oxygen at C-5 or the methoxyl one may participate in this coordination.[1a] When a large amount of the ether is distilled out from the reaction mixture, the complexation of the sugar with the Grignard reagent comes to be more favorable.[4] The cleavage of the C_1–O bond is thus accelerated to form an open-chain intermediate (**C**), which reacts with a methyl anion of MeMgI to yield the diastereomeric products (**D**). When the sterically bulky *t*-BuMgBr is used, the Grignard addition to **C** is prevented, presumably because for a steric reason. It is not clear whether or not there is another pathway to form **D** by the direct attack of MeMgI on the anomeric carbon of **A** or **B**.

The ring closure of **C** gives either the α- or β-anomer, although the presence of a **C**→**A** or **B** path has not been proved in this case. However, once the α-anomer (**E**) is produced, it may attain a high stability, probably by the appropriate coordination of the oxygens of the sugar to the Grignard reagent. At the end of the anomerization reaction, we observed many undissolved materials in the reaction mixture; the Grignard complex of the α-anomer precipitated out more easily than that of the respective β-anomer. The α-anomers, **3α** and **5α**, did not react with either MeMgI or *t*-BuMgBr, but were recovered. Therefore, the anomerization of **3β** and **5β** occurs in a one-way manner, the *trans*-1,2-anomers being preferably transformed into the respective *cis*-1,2-anomers. In a preliminary report,[3a] the selective ring closure of **C** to **E** has been proposed, but the present mechanism, based on these experimental results, dose not necessarily involve this selectivity. Recently, a catalytic anomerization of alkyl per-*O*-benzyl-β-D-glucopyranosides with titanium tetrachloride has been found by Morishima *et al.*,[11] who have also proposed a ring-opening, reclosure mechanism for the anomerization.

The perbenzylated anomer (**5β**) gave a better yield for the anomerization with MeMgI than the monobenzylated one (**3β**). This finding can be explained as follows. We have postulated the presence of a complex (**C'** in Fig. 8) as an intermediate for the reaction of **5β** with MeMgI. Ohrui *et al.*[12] have reported the base-catalyzed epimerization of *C*-glycosides (Fig. 9); for example, 2,3,-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosylacetonitrile is epimerized to the corresponding α-*C*-glycoside via an open-chain intermediate (**F**), the latter epimer being thermodynamically more stable than the former one. They have also pointed out that the presence of one five-membered ring such as an isopropylidene group in **F** strongly favors the formation of a second, fused five-membered

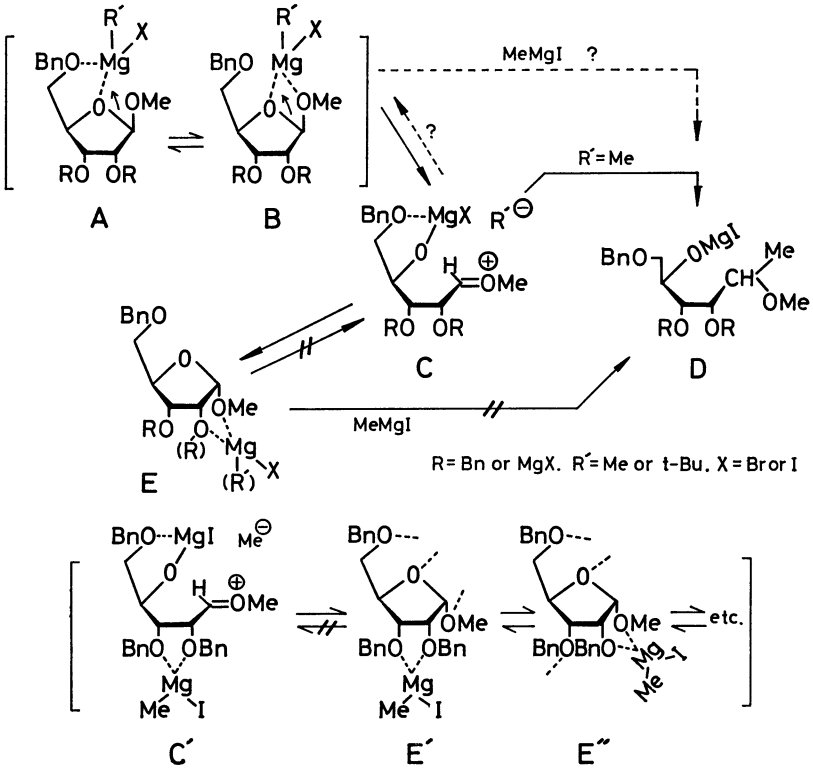


Fig. 8. The possible mechanisms of the one-way anomerization and of the formation of open-chain products.

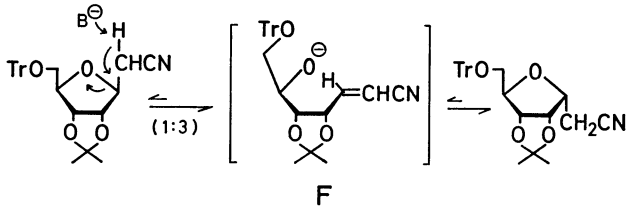


Fig. 9. The base-catalyzed epimerization of a *C*-glycoside reported by Ohrui *et al.*

ring.[12a] The two intermediates, **C'** and **F**, are quite similar in shape. Therefore, it seems likely that the structure of **C'** also fits a cyclization, resulting in the preferred formation of complexes (**E'**, **E''**,..*etc.*). On the other hand, it is rather difficult for **3β** to form an intermediate similar to **C'**.

The equilibrium between **3α** and **3β** in a boiling methanolic solution in the presence of an acid was found to be largely on the side of **3β** in a ratio of 20:80. Similarly, in the case of **5**, the ratio of **5α** to **5β** was 15:85. Therefore, the present one-way anomerization is a "contrathermodynamic" interconversion[13] of more stable isomers into less stable ones.

The reaction of all the lyxose and xylose derivatives except **16** resulted in the one-way anomerization and/or the formation of the open-chain products according to a mechanism similar to that for the ribose series. However, the extent of the one-way anomerization depended on the structure of the starting furanoside and on the reagent. For example, the reactions of **5β**, **9α**, and **11β** with *t*-BuMgBr proceeded very slowly and were incomplete; many precipitates appeared during these reactions.

The perbenzylated xylose derivative (**16α**), which had a *cis*-1,2 relationship, was predominantly transformed, with MeMgI, into the *trans*-1,2-anomer (**16β**), while it was apparent that the latter anomer did not anomerize. The direction of this transformation is in contrast with that for the other furanosides, but this phenomenon can be explained in terms of the difference in reaction rates. The reaction of **16α** with MeMgI is much faster than that of **16β**. In this reaction, **16β** may also anomerize to **16α** (we could observe the presence of a trace of **16α** on a TLC plate), but the latter anomer is consumed rapidly to form the former one and **17**. Both anomers, **16** and **18**, could be anomerized with *t*-BuMgBr. However, before the equilibrium of the anomerization was reached, these anomers had been precipitated out from the reaction mixture.

When the one-way anomerization did not occur, no, or only a small amount of, precipitates were observed at the early stage of the reaction, except that the reaction of **16α** with *t*-BuMgBr gave many precipitates like gels after a few minutes. There may be a relationship between the reactivity and the solubility of the Grignard complex of the sugar.

The newly formed chiral centers in the open-chain products have not been determined in the present work. In the case of the formation of the open-chain products from **16** and **18**, the *cis*-1,2-anomers showed a higher selectivity than did the *trans*-1,2-anomers; the reaction rates for the former anomers were also faster than those for the latter. These results suggest that the reactions involve the pathways of the direct attack of MeMgI on the anomeric carbons of **16α**

Table 1. The reactions of the sugar derivatives with the Grignard reagents

Starting material (mg, mmol)	Reagent (mmol)	[RMgX]/[Sugar]	Solvent PhH-Et_2O[a] ml	Reaction Temp[b]	Reaction Time/h	Products[c] or recovered material (mg)	Yield/%	Chromatography[d]
1b-β (170, 0.63)	MeMgI (4)	6	5—5	H[e]	3	**1b-α** (10) 6; **2b-α** (68) 38; **2b-β** (32) 18		A (9:1)
2b-β (41, 0.14)	MeMgI (4)	29	14—5	H[e]	6	**2b-α** (13)	33	A (7:3)
3α (207, 0.81)	MeMgI (8)	10	15—10	H	2	**3α** (187)	90	D
3α (211, 0.83)	*t*-BuMgBr (8)	10	15—10	L	2.5	**3α** (200)	95	D
3β (250, 0.98)	MeMgI (5)	5	15—10	H	1.3	**3α** (74) 30; **4** (65) 33 (7:3)		A (1:1)
3β (238, 0.94)	*t*-BuMgBr (8)	9	15—10	L	2.5	**3α** (225)	95[f]	D
5α (150, 0.34)	MeMgI (6)	18	15—10	H	6	**5α** (150)	100[g]	D
5α (215, 0.49)	*t*-BuMgBr (6)	12	15—10	H	6	**5α** (208)	97[g]	D
5β (226, 0.52)	MeMgI (6)	12	15—10	H	3	**5α** (180) 80; **6** (20) 9[h]		A (7:3)
5β (215, 0.49)	*t*-BuMgBr (6)	12	15—10	H	6	**5α**+**5β** (214) (6:4)	99.5	D
7α (254, 1.0)	MeMgI (5)	5	15—10	H	6	**7β** (115) 45; **8** (105) 55[i] (71:29)		B (99:1)
7α (220, 0.87)	*t*-BuMgBr (8)	9	15—10	L	3.5	**7β** (194)	88	D
7β (120, 0.47)	MeMgI (2.5)	5	7—5	H	6	**7β** (118)	98	D
7β (123, 0.48)	*t*-BuMgBr (5.5)	11	7—7	L	3.5	**7β** (123)	100	D
9α (240, 0.55)	MeMgI (6)	11	15—10	H	6	**10a** (120) (8:2)[j]	60	A (6:4)
9α (220, 0.51)	*t*-BuMgBr (6)	12	15—10	H	6	**9α** (194) 88; **9β** (25) 11		A (95:5)
9β (250, 0.57)	MeMgI (6)	11	15—10	H	4.5	**10a** (100) (8:2)[j]	48	A (7:3)
9β (220, 0.51)	*t*-BuMgBr (6)	12	15—10	H	6	**9β** (213)	97	D
11α (230, 0.91)	MeMgI (6)	7	18—10	H	6.5	**11α** (222)	97	D
11α (240, 0.94)	*t*-BuMgBr (8)	8	15—10	H	3	**11α** (233)	97	D
11β (470, 1.85)	MeMgI (12)	6	25—20	H	7.5	**11α**+**11β**+**12a** (387)[k] (α:β=1:1)		D
11β (250, 0.98)	*t*-BuMgBr (8)	8	15—10	H	3	**11α**+**11β** (234)[g] **11β** (3:97)	94	D
13α (180, 0.52)	MeMgI (6)	12	15—10	L	3	**13α** (104)	58[i]	A (9:1)
13α (220, 0.64)	*t*-BuMgBr (5)	8	12—8	H	3	**13α** (225)	102	D
13β (195, 0.57)	MeMgI (6)	11	15—10	L	1.5	**13α** (32) 16; **14** (77) 38 (55:45)		A (95:5)
13β (515, 1.5)	*t*-BuMgBr (12)	8	25—20	H	3	**13α** (188) 37; **15a** (270) 52		A (7:3)
16α (245, 0.56)	MeMgI (6)	11	15—10	H	1.6	**16β** (78) 32; **17** (138) 54 (83:17)[m]		C (1:1)
16α (250, 0.57)	*t*-BuMgBr (6)	11	15—10	H	9	**16α**+**16β** (248) (55:45)	99	D
16β (260, 0.6)	MeMgI (6)	10	15—10	H	2.5	**16β** (163) 63; **17** (50) 19 (6:4)[m]		C (6:4)
16β (250, 0.57)	*t*-BuMgBr (6)	11	15—10	H	3	**16α**+**16β** (248) (1:1)	99	D
18α (240, 0.55)	MeMgI (6)	11	15—10	H	5	**19a** (112) 45; **19b** (70) 28		C (7:3)
18α (210, 0.48)	*t*-BuMgBr (6)	13	15—10	H	7	**18α**+**18β** (213) (7:3)	101	D
18β (230, 0.53)	MeMgI (6)	11	15—10	H	3.5	**19a** (153) 64; **19b** (35) 15		C (1:1)

TABLE 1. (Continued)

Starting material (mg, mmol)	Reagent (mmol)	[RMgX]/[Sugar]	Solvent PhH-Et_2O[a] ml	Reaction Temp[b]	Reaction Time h	Products[c] or recovered material (mg)	Yield/%	Chromatography[d]
18β (220, 0.51)	*t*-BuMgBr (6)	12	15—10	H	7	**18α**+**18β** (217) (4:6)	99	D
20a-β (325, 0.8)	*t*-BuMgBr (6.4)	8	10—10	H[e]	5	**20a-α** (185)	57[n]	B (99:1)
20b-β (170, 1.1)	*t*-BuMgBr (6)	5	15—10	H	1.5	**20b-α** (100)	59[o]	B (99:1)
20b-β (170, 1.1)[p]	*t*-BuMgBr (12)	11	20—20	H	2.5	**20b-α** (160)	94	B (99:1)

a) During the reaction, the ether was allowed to evaporate from the reaction mixture. b) H: 80—85 °C (bath temperature). L: 70—75 °C (bath temperature). c) The ratios of the diastereomers or anomers were estimated by ^1H NMR spectroscopy and TLC analyses. d) Each product was isolated by chromatography on a silica-gel column with the following solvent systems: A, benzene-ethyl acetate; B, chloroform-methanol; C, hexane-ether. D: The crude products were identified by ^1H NMR spectroscopy and TLC analyses. e) A reaction mixture was refluxed in a flask equipped with a condenser. f) Contained a trace amount of **3β**. g) Contained a small amount of by-products. h) Diastereomerically almost pure. i) A main diastereomer was crystallized. j) The ^1H NMR spectrum of the **10a** prepared from **9α** was identical with that prepared from **9β**. This product (**10a**) was characterized as its acetate (**10b**). k) **11α,β**:**12a**=4:6. The product (**12a**) was isolated as its diastereomeric acetate (**12b**, 87:13); see Experimental. l) A large amount of the starting material was decomposed under these conditions. m) The ^1H NMR spectrum of the main isomer obtained from **16α** was identical with that of the major isomer prepared from **16β**. n) Some of the trityl groups in **20a-α** were deblocked. o) An unknown by-product (10 mg) was isolated; see Ref. 9. p) Before the addition of **20b-β**, a solution of *t*-butyl alcohol (170 mg, 2.3 mmol) in dry benzene (1 ml) was added to a Grignard solution.

and **18β**, besides the pathways via common intermediates similar to **C** in Fig. 8. It seems likely that the *cis*-1,2 structure is desirable for the direct attack, presumably because of steric reasons, thus giving a high selectivity.

The crystalline ketone, **15a**, was the only open-chain product produced by the use of *t*-BuMgBr. The formation of this product results from the elimination of a proton on the carbon adjacent to the C–OMe group of an intermediate similar to **C** in Fig. 8, followed by the ketonization of the resulting enol in the work-up step. Although the configuration of the benzyloxy group next to the keto function of **15a** had not been determined, this compound was proved to be diastereomerically pure, judging from ^1H NMR spectroscopy and TLC analyses.

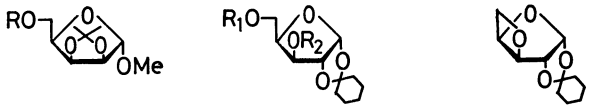
The present anomerization reaction was found to be applicable to 5-*O*-trityl- and 5-deoxy-ribose derivatives (**20a-β** and **20b-β**). Under the Grignard reaction conditions, however, some of the trityl groups of **20a-α** were removed. Debenzylation was also observed during the formation of **10a**. These findings suggest the posibility that the trityl and benzyl protecting groups in sugars may be selectively deblocked under appropriate reaction conditions with the Grignard reagents.

Experimental

The melting points were determined with a Yamato capillary-melting point apparatus and are uncorrected. The IR spectra were recorded on a Shimadzu IR-27 instrument. The ^1H NMR spectra were recorded on a Varian HA-100D apparatus, with tetramethylsilane as the internal standard. The optical rotations were measured on a Perkin-Elmer Model 241MC polarimeter.

Merck silica gel GF_{254} was used for the TLC, and the compounds were detected by heating after spraying them with a methanol–sulfuric acid–*p*-methoxybenzaldehyde (85:15:5, v/v) mixture. Merck silica gel 60 (0.063—0.29 mm) was utilized for the column chromatography. The elemental analyses were performed by this Institute.

The ^1H NMR spectral data of the compounds are listed in Tables 2 and 3, while their physical properties and the results of their elemental analyses are summarized in Table 4.



21: R = H
22: R = Bn

23: R_1 = Ts : R_2 = H
25: R_1 = Bn; R_2 = H
26: R_1, R_2 = Bn

24

Materials. In order to obtain new methyl pentofuranosides, the following sugar derivatives were prepared by the conventional methods. The oxidation of methyl 2,3-*O*-isopropylidene-α-D-mannofuranoside[14] with sodium metaperiodate, followed by reduction with sodium borohydride, gave methyl 2,3-*O*-isopropylidene-α-D-lyxofuranoside (**21**), which was then treated with sodium hydride-benzyl chloride to yield methyl 5-*O*-benzyl-2,3-*O*-isopropylidene-α-D-lyxofuranoside (**22**). The deprotection of **22** with an acid afforded **7α**. Starting from 1,2-*O*-cyclohexylidene-α-D-xylofuranose,[15] the corresponding 5-*O*-tosyl (**23**) and 3,5-di-*O*-benzyl (**26**) derivatives were prepared. An anhydro compound (**24**) was synthesized by the reaction of **23** with sodium methoxide. The treatment of **24** with sodium benzylate yielded 5-*O*-benzyl-1,2-*O*-cyclohexylidene-α-D-xylofuranose (**25**), which was then converted into an anomeric mixture of **11** by methanolysis. Similarly, an anomeric mixture of **13** was obtained from **26**.

General Procedure for the Anomerization and Ring-opening Reactions. Some of the reaction conditions and the results are summarized in Table 1. A solution of a Grignard reagent in ether was prepared from magnesium and an alkyl halide in a three-necked flask, and was then diluted with dry benzene. A solution of a sugar derivative (*ca.* 0.7 mmol) in dry benzene (2—3 ml) was added to the stirred Grignard

Table 2. The ^{1}H NMR spectral data of the sugar derivatives in $CDCl_3$

Compound	Anomeric proton δ	Other protons δ
2b-β[a)]	4.37 (1H, s)	1.0—2.0 (12H, m, CH_2 of cyclohexane ring and H-3,3′), 1.06 and 1.19 (6H, s, C-CH_3×2), 3.1—3.5 (3H, m), 3.32 (3H, s, OCH_3), 4.09 (1H, m, H-4), 4.32 (1H, d, J=5.3 Hz, OH), 4.72 (1H, s, OH).
3α	4.93 (1H, d, J=4.1 Hz)	3.47 (3H, s, CH_3), 3.59 (2H, d, J=4.0 Hz, H-5,5′), 3.80—4.24 (3H, m), 4.55 (2H, s, CH_2Ph), 7.29 (5H, s, phenyl protons).
3β	4.80 (1H, s)	3.30 (3H, s, CH_3), 3.59 (2H, d, J=4.6 Hz, H-5,5′), 3.90—4.26 (3H, m), 4.57 (2H, s, CH_2Ph), 7.30 (5H, s, phenyl protons).
5α	4.86 (1H, br d, J=4 Hz)	3.38 (2H, m, H-5,5′), 3.44 (3H, s, CH_3), 3.70—3.96 (2H, m), 4.16—4.36 (1H, m), 4.44 (2H, s, CH_2Ph), 4.60 (4H, m, CH_2Ph×2), 7.0—7.6 (15H, m, phenyl protons).
5β	4.89 (1H, s)	3.28 (3H, s, CH_3), 3.5 (2H, m, H-5,5′), 3.8, 4.0, and 4.3 (3H, m), 4.48 (2H, d, J=3.2 Hz, CH_2Ph), 4.54 and 4.62 (4H, s, CH_2Ph×2), 7.1—7.4 (15H, m, phenyl protons).
7α	4.79 (1H, s)	2.97 (1H, d, J=9.2 Hz, OH), 3.32 (3H, s, CH_3), 3.59—4.01 (3H, m, 4.2 (1H, m), 4.5 (1H, m), 4.59 (2H, s, CH_2Ph), 7.29 (5H, s, phenyl protons).
7β	4.79 (1H, d, J=4.4 Hz)	2.92 (1H, br d, J=8 Hz, OH), 3.07 (1H, br d, J=10 Hz, OH), 3.37 (3H, s, CH_3), 3.54—3.90 (2H, m, H-5,5′), 3.90—4.30 (3H, m), 4.57 (2H, s, CH_2Ph), 4.29 (5H, s, phenyl protons).
9α	5.00 (1H, d, J=2.4 Hz)	3.35 (3H, s, CH_3), 3.75 (2H, m, H-5,5′), 3.88 (1H, m), 4.11—4.47 (2H, m), 4.47—4.77 (6H, m, CH_2Ph×3), 7.23 and 7.26 (15H, s, phenyl protons).
9β	4.81 (1H, d, J=4.8 Hz)	3.41 (3H, s, CH_3), 3.57—3.89 (3H, m), 3.98—4.29 (2H, m), 4.48—4.89 (6H, m, CH_2Ph×3), 7.26 and 7.28 (15H, s, phenyl protons).
11α	4.94 (1H, d, J=4.6 Hz)	3.44 (3H, s, CH_3), 3.74 (2H, m, H-5,5′), 3.96—4.40 (3H, m), 4.55 (2H, s, CH_2Ph), 7.27 (5H, s, phenyl protons).
11β	4.81 (1H, s)	3.33 (3H, s, CH_3), 3.51—3.93 (2H, m, H-5,5′), 3.93—4.20 (2H, m), 4.35—4.57 (1H, m), 4.58 (2H, s, CH_2Ph), 7.29 (5H, s, phenyl protons).
13α	4.95 (1H, d, J=4.6 Hz)	2.74 (1H, d, J=7.2 Hz, OH), 3.44 (3H, s, CH_3), 3.65 (2H, m, H-5,5′), 3.98 (1H, m), 4.14—4.48 (2H, m), 4.50—4.79 (4H, m, CH_2Ph×2), 7.1—7.5 (10H, m, phenyl protons).
13β	4.76 (1H, d, J=2.0 Hz)	2.36 (1H, d, J=5.0 Hz, OH), 3.36 (3H, s, CH_3), 3.7 (2H, m, H-5,5′), 3.9 (1H, m), 4.2 (1H, m), 4.4 (1H, m), 4.54 (4H, m, CH_2Ph×2), 7.1—7.4 (10H, m, phenyl protons).
16α	4.72 (1H, d, J=4.0 Hz)	3.38 (3H, s, CH_3), 3.44—3.82 (2H, m, H-5,5′), 4.0 (1H, m), 4.20—4.46 (2H, m), 4.46—4.72 (6H, m, CH_2Ph×3), 7.1—7.4 (15H, m, phenyl protons).
16β	4.89 (1H, d, J=1.3 Hz)	3.38 (3H, s, CH_3), 3.68—3.82 (2H, m, H-5,5′), 3.92—4.12 (2H, m), 4.34—4.46 (1H, m), 4.46—4.70 (6H, m, CH_2Ph×3), 7.1—7.5 (15H, m, phenyl protons).
18α	4.93 (1H, br s)	3.37 (3H, s, CH_3), 3.60 (2H, d, J=4.7 Hz, H-5,5′), 3.80—4.08 (2H, m), 4.08—4.33 (1H, m), 4.33—4.65 (6H, m, CH_2Ph×3), 7.22 and 7.26 (15H, s, phenyl protons).
18β	4.72 (1H, br d, J=4 Hz)	3.30 (3H, s, CH_3), 3.44—3.66 (2H, m, H-5,5′), 3.96—4.26 (3H, m), 4.53 (2H, s, CH_2Ph), 4.60 (4H, s, CH_2Ph×2), 7.24, 7.26, and 7.28 (15H, s, phenyl protons).
20a-α	4.97 (1H, d, J=4.0 Hz)	2.53 (1H, d, J=8.0 Hz, OH), 2.88 (1H, d, J=9.4 Hz, OH), 3.03—3.43 (2H, q, H-5,5′), 3.46 (3H, s, CH_3), 3.83—4.37 (3H, m), 7.1—7.5 (15H, m, phenyl protons).

TABLE 2. (Continued)

Compound	Anomeric proton δ	Other protons δ
20a-β	4.82 (1H, s)	2.31 (1H, br d, J=6 Hz, OH), 2.60 (1H, br d, J=4 Hz, OH), 3.28 (2H, m, H-5,5'), 3.30 (3H, s, CH_3), 3.9—4.32 (3H, m). 7.1—7.6 (15H, m, phenyl protons).
20b-α	4.88 (1H, d, J=4.4 Hz)	1.28 (3H, d, J=6.4 Hz, C-CH_3), 3.13 (1H, br d, J=8 Hz, OH), 3.32 (1H, br d, J=9 Hz, OH), 3.44 (3H, s, OCH_3), 3.5—3.7 (1H, m), 3.9—4.2 (2H, m).
20b-β	4.78 (1H, s)	1.35 (3H, d, J=6.0 Hz, C-CH_3), 3.36 (3H, s, OCH_3), 3.7 (2H, br s, OH×2), 3.9—4.1 (3H, m).
20c-α	4.75—5.10[b]	1.36 (3H, d, J=6.6 Hz, C-CH_3), 2.10 (6H, s, acetyl protons), 3.41 (3H, s, OCH_3), 4.16 (1H, dd, J=6.6, 4.3 Hz, H-4), 4.75—5.10 (3H, m, H-1,2, and 3).
21	4.91 (1H, s, H-1)	1.30 and 1.45 (6H, s, isopropylidene protons), 2.65 (1H, t, J=6.6 Hz, OH), 3.32 (3H, s, OCH_3), 3.8—4.2 (3H, m), 4.56 (1H, d, J=6.4 Hz, H-2), 4.76 (1H, dd, J=6.4, 3.6 Hz, H-3).
22	4.90 (1H, s, H-1)	1.29 and 1.42 (6H, s, isopropylidene protons), 3.32 (3H, s, OCH_3), 3.58—3.94 (2H, m), 4.04—4.26 (1H, m), 4.44—4.78 (4H, m), 7.2—7.4 (5H, m, phenyl protons).
23	5.84 (1H, d, J=3.6 Hz)	1.2—2.0 (10H, cyclohexylidene protons), 2.42 (3H, s, CH_3), 2.54 (1H, d, J=5.6 Hz, OH), 4.1—4.4 (4H, m), 4.46 (1H, d, J=3.6 Hz, H-2), 7.75 and 7.31 (4H, ABq, J=8.8 Hz, phenyl protons).
24	6.26 (1H, d, J=3.6 Hz)	1.2—1.9 (10H, m, cyclohexylidene protons), 4.24 (1H, dd, J=7.4, 2.0 Hz, H-5), 4.72 (1H, dd, J=7.4, 4.4 Hz, H-5'), 4.72 (1H, d, J=3.6 Hz, H-2), 5.08 (1H, dt, J=4.0, 2.0 Hz, H-4), 5.20 (1H, d, J=4.4 Hz, H-3).
25	5.96 (1H, d, J=3.8 Hz)	1.2—1.8 (10H, m, cyclohexylidene protons), 3.45 (1H, d, J=3.4 Hz, OH), 3.91 (2H, d, J=4.0 Hz, H-5,5'), 4.10—4.40 (2H, m), 4.49 (1H, d, J=3.8 Hz, H-2), 4.60 (2H, d, J=2 Hz, CH_2Ph), 7.29 (5H, s, phenyl protons).
26	5.91 (1H, d, J=4.0 Hz)	1.2—1.8 (10H, m, cyclohexylidene protons), 3.75 (2H, d, J=6.0 Hz, H-5,5'), 3.97 (1H, d, J=3.2 Hz), 4.3—4.7 (6H, m), 7.24 and 7.26 (10H, s, phenyl protons).

a) Measured in DMSO-d_6. b) Did not resolve.

solution in the flask without a refluxing condenser[3b] at room temperature under an atmosphere of dry nitrogen, and the mixture was heated at a given temperature for a given period to remove the ether. After cooling, aqueous ammonium chloride was added; the mixture was then extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated. The crude products were purified by silica gel column chromatography with a given solvent system.

*Methyl 5-O-Benzyl-α-D-ribofuranoside (**3α**) and Its β-Anomer (**3β**).* The method of Tener and Khorana[16] was modified. To a solution of methyl 5-*O*-benzyl-2,3-*O*-isopropylidene-β-D-ribofuranoside[16] (970 mg, 3.3 mmol) in methanol (20 ml) and water (4 ml), we added concd sulfuric acid (0.2 ml) after which the mixture was heated at 75—80 °C (bath temperature) for 1.5 h with stirring. After cooling, the acid was neutralized with calcium hydroxide (500 mg). The undissolved materials were filtered through a Celite pad and washed with methanol. The combined filtrate and washings were concentrated. The residue was chromatographed on a silica-gel column with chloroform–methanol (98:2) to give **3α** (160 mg, 19%) and **3β** (550 mg, 66%).

*Methyl 2,3,5-Tri-O-benzyl-α-D-ribofuranoside (**5α**) and Its β-Anomer (**5β**).*[17] To a stirred solution of **3α** (350 mg, 1.4 mmol) in dry benzene (5 ml) and *N,N*-dimethylformamide (2 ml) we added sodium hydride (*ca.* 60% in oil, 300 mg) at room temperature under an atmosphere of dry nitrogen. After 5 min, benzyl chloride (0.6 ml) was added, and the mixture was heated at 75—80 °C (bath temperature) for 30 min. After cooling, methanol was carefully added to decompose the excess sodium hydride. The mixture was then extracted with ether, and the extract was washed with water, dried ($MgSO_4$), and concentrated. The residue was chromatographed on a silica-gel column with benzene–ethyl acetate (95:5) to give **5α** (510 mg, 85%).

A solution of **3β** (460 mg, 1.8 mmol) in dry benzene (25 ml) and *N,N*-dimethylformamide (5 ml) was treated with sodium hydride (*ca.* 60% in oil, 850 mg) and benzyl chloride (0.8 ml) under conditions similar to those described above to give, after chromatography, **5β** in a quantitative yield.

*Methyl 5-O-Benzyl-α-D-lyxofuranoside (**7α**).* The method of Shunk *et al.*[18] was slightly modified. To a solution of **22** (4.0 g, 13.6 mmol) in methanol (75 ml), we added a solution of concd sulfuric acid (0.35 ml) in water (30 ml). The mixture was refluxed at 85—90 °C (bath temperature) for 5 h. After cooling, calcium hydroxide (2 g) was added.

Table 3. The ^{1}H NMR spectral data of the open-chain products

Compound[a]	δ (in $CDCl_3$)
4	1.21 and 1.24 (3H, d, J=6.0 Hz, 7:3, C-CH_3), 3.35 (3H, s, OCH_3), 3.4—4.0 (6H, m), 4.55 (2H, s, CH_2Ph), 7.30 (5H, s, phenyl protons).
6	1.19 (3H, br d, J=5.8 Hz, C-CH_3), 3.15 (1H, br d, J=3 Hz, OH), 3.32 (3H, s, OCH_3), 3.5—3.8 (5H, m), 4.04 (1H, br s), 4.50 (2H, s, CH_2Ph), 4.59 (2H, d, J=2 Hz, CH_2Ph), 4.65 (2H, s, CH_2Ph), 7.23 and 7.26 (15H, s, phenyl protons).
8[b]	1.19 (3H, d, J=6.4 Hz, C-CH_3), 3.00, 3.15, and 3.22 (3H, d, J=4.7, 5.6, 5.2 Hz, OH×3), 3.32 (3H, s, OCH_3), 3.38—3.88 (5H, m), 4.10 (1H, m), 4.54 (2H, s, CH_2Ph), 7.28 (5H, s, phenyl protons).
10a	1.13 and 1.16 (3H, d, J=6.4 Hz, 8:2, C-CH_3), 2.7—3.2 (2H, br m, OH×2), 3.25 (3H, s, OCH_3), 3.3—3.7 (4H, m), 3.9 (1H, m), 4.1 (1H, m), 4.35—4.70 (4H, m, CH_2Ph×2), 3.22 and 3.24 (10H, s, phenyl protons).
10b[c]	1.09 (3H, d, J=6.4 Hz, C-CH_3), 2.00, 2.02, and 2.06 (6H, s, acetyl protons), 3.30 (3H, s, OCH_3), 3.46—3.80 (3H, m, -CH(OMe)- and CH_2OBn), 2.89 and 4.17 (1H, dd, J=7.5, 3.8 Hz, J=9.8, 2 Hz, 75:25, -CH(OBn)-), 4.46 and 4.48 (2H, s, 25:75, CH_2Ph), 4.60 (2H, s, CH_2Ph), 4.96—5.38 (2H, m, -CH(OAc)-×2), 7.24 (10H, s, phenyl protons).
12b[d]	1.11 (3H, d, J=6.0 Hz, C-CH_3), 2.03, 2.04, and 2.06 (9H, s, acetyl protons), 3.26 (3H, s, OCH_3), 3.40 (2H, m), 3.55 (2H, d, J=5.0 Hz, CH_2Ph), 4.50 (2H, s, CH_2Ph), 5.04—5.26 (2H, m), 5.57 (1H, m), 7.28 (5H, s, phenyl protons).
14	1.10 and 1.20 (3H, d, J=6.0 Hz, 45:55, C-CH_3), 2.9 (2H, br m, OH×2), 3.26 and 3.32 (3H, s, 45:55, OCH_3), 3.3—3.7 (4H, m), 3.8—4.2 (2H, m), 4.49 (2H, d, J=2.0 Hz, CH_2Ph), 4.65 (2H, s, CH_2Ph), 7.26 (10H, s, phenyl protons).
15a	3.0 (1H, br s, OH), 3.33 (3H, s, OCH_3), 3.4—3.6 (2H, m, CH_2OBn), 4.0—4.2 (2H, m), 4.26 (2H, d, J=2.0 Hz, CH_2Ph), 4.46 and 4.61 (2H, ABq, J=12.0 Hz, $COCH_2$), 4.47 (2H, s, CH_2Ph), 7.26 (10H, s, phenyl protons).
15b	2.01 (3H, s, acetyl protons), 3.32 (3H, s, OCH_3), 3.63 (2H, d, J=6.4 Hz, CH_2OBn), 4.17 (2H, d, J=2.0 Hz, CH_2Ph), 4.34 (1H, d, J=4.0 Hz, -CH(OBn)-), 4.48 (2H, s, CH_2Ph), 4.3—4.9 (2H, m, $COCH_2$), 5.40 (1H, dt, J=6.4, 4.0 Hz, -CH(OAc)-), 7.26 and 7.27 (10H, s, phenyl protons).
17[e]	1.16 and 1.26 (3H, d, J=6.0 Hz, 83:17, C-CH_3), 2.89 (1H, d, J=6.0 Hz, OH), 3.30 (3H, s, OCH_3), 3.40—3.70 (4H, m), 3.76—4.08 (2H, m), 4.42—4.82 (6H, m, CH_2Ph×3), 7.22, 7.24, and 7.25 (15H, s, phenyl protons).
19a	1.10 (3H, d, J=6.0 Hz, C-CH_3), 3.22 (1H, br m, OH), 3.32 (3H, s, OCH_3), 3.44—3.86 (5H, m), 4.0 (1H, br s), 4.53 (4H, s, CH_2Ph×2), 4.67 (2H, s, CH_2Ph), 7.22, 7.26, and 7.28 (15H, s, phenyl protons).
19b	1.25 (3H, d, J=6.0 Hz, C-CH_3), 2.73 (1H, br d, J=6 Hz, OH), 3.24 (3H, s, OCH_3), 3.44—4.10 (6H, m), 4.48 (2H, s, CH_2Ph), 4.55 (2H, d, J=2 Hz, CH_2Ph), 4.67 (2H, s, CH_2Ph), 7.22, 7.25, and 7.26 (15H, s, phenyl protons).

a) The values of the diastereomeric ratios for the open-chain products refer to Table 1. b) A crystalline isomer. c) Decoupling experiments showed that one proton (δ 5.26) on the carbon bearing an acetoxyl group coupled with a proton (δ 3.75) on the carbon bearing the methyl and methoxyl groups. d) The major isomer. e) A diastereomeric mixture from **16α**.

The undissolved materials were filtered through a Celite pad and washed with methanol. The combined filtrate and washings were concentrated to dryness. The residue was dissolved in methanol (100 ml), and concd sulfuric acid (0.7 ml) was added. The mixture was then refluxed at 80 °C (bath temperature) for 1 h. The acid was neutralized with calcium hydroxide (3 g). The work-up gave a syrupy product, which was chromatographed on a silica-gel column with benzene–ethyl acetate (7:3) to provide **7α** (2.1 g, 61%).

*Methyl 5-O-Benzyl-β-D-lyxofuranoside (**7β**).* A solution of **7α** (220 mg, 0.78 mmol) in dry benzene (2 ml) was added to a solution of *t*-BuMgBr (7.9 mmol) in dry benzene (15 ml) and ether (10 ml) at room temperature with stirring under an atmosphere of dry nitrogen. The mixture was heated at 70—75 °C for 3.5 h to remove the ether. The usual work-up gave a crystalline product (**7β**, 194 mg, 88%). Its TLC and ^{1}H NMR spectral analyses showed that the product was almost pure. Recrystallization from benzene–hexane afforded an analytically pure sample.

*Methyl 2,3,5-Tri-O-benzyl-α-D-lyxofuranoside (**9α**) and Its β-Anomer (**9β**).* To a stirred solution of **7α** (590 mg, 2.3 mmol) in dry benzene (10 ml) and *N,N*-dimethylformamide (4 ml) we added sodium hydride (*ca.* 60% in oil, 600 mg) at 0—5 °C (bath temperature) under an atmosphere of dry nitrogen, after which the mixture was stirred at room temperature for 30 min. Benzyl chloride (0.8 ml) was then added, and the mixture was heated at 75—80 °C (bath

temperature) for 30 min. A work-up similar to that used for the synthesis of **5α** gave a syrup, which was chromatographed on a silica-gel column with benzene–ethyl acetate (95:5) to afford **9α** in a quantitative yield.

The sugar derivative (**7β**, 280 mg, 1.1 mmol) was treated in a manner similar to that described above to yield **9β** (365 mg, 76%).

*Acetylation of the Open-chain Products (**10α**).* Acetic anhydride (0.4 ml) was added to a cold (0—5 °C) solution of **10a** (116 mg, 0.32 mmol) in dry pyridine (2 ml), after which the mixture was allowed to stand at room temperature overnight. The usual work-up gave a syrup, which was chromatographed on a silica-gel column with benzene–ethyl acetate (96:4) to afford **10b** (130 mg, 91%). IR (neat): 1735 (C=O) cm^{-1}. The ^1H NMR spectrum of **10b** showed that it consisted of a 75:25 diastereomeric mixture.

*Methyl 5-O-Benzyl-α-D-xylofuranoside (**11α**) and Its β-Anomer (**11β**).* A mixture of **25** (1.5 g, 4.7 mmol) and concd sulfuric acid (0.2 ml) in methanol (40 ml) was heated at 65 °C (bath temperature) for 3 h with stirring. After cooling, calcium hydroxide (2 g) was added and the mixture was vigorously stirred. The undissolved material were filtered through a Celite pad and washed with methanol. The combined filtrate and washings were concentrated, and the residue was chromatographed on a silica-gel column with chloroform–methanol (99:1) to give **11α** (350 mg, 29%) and **11β** (580 mg, 49%).

*Acetylation of the Open-chain Products (**12α**).* The sugar derivative (**11β**, 470 mg, 1.85 mmol) was treated with MeMgI according to the conditions described in Table 1 and according to the general procedure for the anomerization to yield a syrupy mixture, which consisted mainly of **11α**, **11β**, and **12a** in a ratio of 1:1:8, judging from the ^1H NMR spectroscopy. This mixture (340 mg) was dissolved in dry pyridine (5 ml). To this solution we then added acetic anhydride (2 ml) at 0—5 °C (bath temperature), after which the mixture was allowed to stand at room temperature overnight. The excess acetic anhydride was decomposed by iced water, and the mixture was extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated. The pyridine was removed by co-evaporation with xylene. The residue was chromatographed on a silica-gel column with hexane–ether (6:4) to give an anomeric mixture of methyl 2,3-di-*O*-acetyl-5-*O*-benzyl-D-xylofuranoside (120 mg, 19% based on the starting material), and **12b** (239 mg, 37% based on the starting material). IR (neat): 1735 (C=O) cm^{-1}.

*Methyl 3,5-Di-O-benzyl-α-D-xylofuranoside (**13α**) and Its β-Anomer (**13β**).* To a stirred suspension of **26** (2.3 g, 5.6 mmol) in methanol (80 ml) we added concd sulfuric acid (0.25 ml), after which the mixture was heated at 60—65 °C (bath temperature) for 6 h. After cooling, calcium hydroxide (2.5 g) was added. After the mixture had been vigorously stirred, the undissolved materials were filtered through a Celite pad and washed with methanol. The combined filtrate and washings were concentrated, and the residue was chromatographed on a silica-gel column with benzene–ethyl acetate (9:1) to give **13α** (930 mg, 48%) and **13β** (1.0 g, 52%).

*Acetylation of the Open-chain Product (**15α**).* A mixture of **15a** (200 mg, 0.58 mmol) and acetic anhydride (0.8 ml) in dry pyridine (3 ml) was stirred at room temperature for 4 h. The usual work-up gave a syrup, which was chromatographed on a silica-gel column with benzene–ethyl acetate (8:2) to give **15b** (188 mg, 84%). IR (neat): 1735 (C=O) cm^{-1}.

*Methyl 2,3,5-Tri-O-benzyl-α-D-xylofuranoside (**16α**) and Its β-Anomer (**16β**).* *From Methyl D-Xylofuranoside*: Sodium hydride (*ca.* 60% in oil, 3.0 g) was added to a stirred solution of methyl D-xylofuranoside[19] (3.2 g, 19.5 mmol) in dry benzene (60 ml) and *N,N*-dimethylformamide (35 ml) at 0—5 °C (bath temperature) under an atmosphere of dry nitrogen, after which the mixture was stirred for 10 min. Benzyl chloride (10 ml) was added, and the mixture was then heated at 75—80 °C (bath temperature) for 2 h. A work-up similar to that described in the synthesis of **5α** gave a syrup, which was chromatographed on a silica-gel column with hexane–ether (7:3) to afford **16β** (2.8 g, 33%) and **16α** (2.3 g, 27%).

*From **13α***: A solution of **13α** (80 mg, 0.23 mmol) in dry benzene (1 ml) and *N,N*-dimethylformamide (0.4 ml) was treated with sodium hydride (*ca.* 60% in oil, 60 mg) and benzyl chloride (0.1 ml), in a manner similar to that described for the synthesis of **16α** from methyl D-xylofuranoside, to give pure **16α** (55 mg, 54%) after chromatography. The physical properties of this product was identical with those of the sample prepared from methyl D-xylofuranoside.

*Methyl 2,3,5-Tri-O-benzyl-α-D-arabinofuranoside (**18α**) and Its β-Anomer (**18β**).* To a stirred solution of methyl D-arabinofuranoside[19] (1.6 g, 0.01 mol) in dry benzene (40 ml) and *N,N*-dimethylformamide (20 ml) we added sodium hydride (*ca.* 60% in oil, 1.8 g) at 0—5 °C (bath temperature) under an atmosphere of dry nitrogen. After the mixture had been stirred at this temperature for 5 min, benzyl chloride (5 ml) was added. The mixture was stirred at room temperature for 30 min and then heated at 75—80 °C for 1 h. After cooling, the mixture was treated in a manner similar to that described for the synthesis of **5α** to give a syrup, which was subsequently chromatographed on a silica-gel column with hexane–ether (8:2) to afford **18α** (1.8 g, 42%) and **18β** (1.1 g, 26%).

*Methyl 5-O-Trityl-α-D-ribofuranoside (**20a-α**) and Its β-Anomer (**20a-β**).* The method of Leonard *et al.*[20] was modified. To a cold (0—5 °C) solution of methyl D-ribofuranoside[21] (5.5 g, 34 mmol) in dry pyridine (70 ml) we added trityl chloride (15 g, 54 mmol), after which the mixture was stirred at room temperature for 2 d. After cooling, iced water was added and the mixture was extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated. The pyridine was removed by co-evaporation with xylene. The residue was chromatographed on a silica-gel column with chloroform–methanol (99:1) to give **20a-α** (1.8 g, 13%) and **20a-β** (9.4 g, 69%).

*Methyl 5-Deoxy-α-D-ribofuranoside (**20b-α**) and Its β-Anomer (**20b-β**).* The method of Shunk *et al.*[18,22] was modified. A solution of methyl 5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside[23] (1.7 g, 9 mmol) in a mixture of methanol (10 ml) and aqueous sulfuric acid (0.2 mol dm^{-3}, 4 ml) was refluxed at 85—90 °C (bath temperature) for 85 min. After cooling, the acid was neutralized with calcium hydroxide. The undissolved materials were filtered through a Celite pad and washed with methanol. The combined filtrate and washings were concentrated to give a syrup, which was subsequently chromatographed on a silica-gel column with chloroform–methanol (95:5) to afford **20b-α** (240 mg, 18%) and **20b-β** (780 mg, 58%).

*Methyl 2,3-Di-O-acetyl-5-deoxy-α-D-ribofuranoside (**20c-α**).* To a solution of **20b-α** (60 mg, 0.41 mmol) in dry pyridine (2 ml) we added acetic anhydride (0.4 ml), after which the mixture was allowed to stand at room temperature overnight. The usual work-up gave a syrup, which was chromatographed on a silica-gel column with benzene–ethyl acetate (85:15) to give **20c-α** (85 mg, 90%). IR (neat): 1740 (C=O) cm^{-1}.

Table 4. The physical properties and elemental analyses of the sugar derivatiyes and open-chain products

Compound[a]	Mp/°C	$[\alpha]_D$ (c, $CHCl_3$)	Temp/°C	Formula	Found (%) C	Found (%) H	Calcd (%) C	Calcd (%) H
2b-β	syrup	−75.4° (0.7)	22	$C_{15}H_{28}O_5$	62.39	9.82	62.47	9.79
3α	syrup	+96.5° (0.9)	21	$C_{13}H_{18}O_5$	61.43	7.16	61.40	7.14
3β	syrup	−49.6° (1.5)	21	$C_{13}H_{18}O_5$	61.23	7.10	61.40	7.14
4[b]	syrup	+15.4° (1.4)	23	$C_{14}H_{22}O_5$	62.28	8.15	62.20	8.20
5α	syrup	+77.6° (1.4)	24	$C_{27}H_{30}O_5$	74.45	6.92	74.63	6.96
5β[c]	syrup	+25.8° (1.2)	21	$C_{27}H_{30}O_5$	74.74	6.96	74.63	6.96
6	syrup	+23.6° (0.8)	22	$C_{28}H_{34}O_5$	74.83	7.64	74.64	7.61
7α	syrup	+110° (1.2)	18	$C_{13}H_{18}O_5$	61.32	7.15	61.40	7.14
7β	103—104	−78.0° (1.0)	18	$C_{13}H_{18}O_5$	61.43	7.13	61.40	7.14
8	70.0—71.5[d]	−3.8° (1.0)	22	$C_{14}H_{22}O_5$	62.30	8.20	62.20	8.20
9α	syrup	+17.0° (1.5)	24	$C_{27}H_{30}O_5$	74.39	6.90	74.63	6.96
9β	syrup	−49.1° (1.2)	26	$C_{27}H_{30}O_5$	74.38	6.92	74.63	6.96
10b	syrup	+15.3° (1.4)	28	$C_{25}H_{32}O_7$	67.70	7.28	67.55	7.26
11α	64—65[e]	+118° (1.1)	22	$C_{13}H_{18}O_5$	61.23	7.19	61.40	7.14
11β	syrup	−60.5° (1.1)	20	$C_{13}H_{18}O_5$	61.23	7.06	61.40	7.14
12b[b]	syrup	−26.3° (1.1)	25	$C_{20}H_{28}O_8$	60.61	7.01	60.59	7.12
13α	syrup	+69.8° (1.4)	22	$C_{20}H_{24}O_5$	69.55	7.03	69.75	7.02
13β	syrup	−43.2° (1.3)	23	$C_{20}H_{24}O_5$	69.58	7.07	69.75	7.02
15a[f]	79—80[d]	−41.6° (1.0)	20	$C_{20}H_{24}O_5$	69.74	6.87	69.75	7.02
15b	syrup	−5.0° (1.1)	23	$C_{22}H_{26}O_6$	68.36	6.63	68.38	6.78
16α	syrup	+63.8° (1.3)	23	$C_{27}H_{30}O_5$	74.53	6.91	74.63	6.96
16β	syrup	−22.7° (1.4)	24	$C_{27}H_{30}O_5$	74.64	6.96	74.63	6.96
17[g]	syrup	−22.7° (1.0)	27	$C_{28}H_{34}O_5$	74.62	7.70	74.64	7.61
18α	syrup	+46.0° (1.4)	24	$C_{27}H_{30}O_5$	74.63	6.95	74.63	6.96
18β	syrup	−43.6° (1.0)	20	$C_{27}H_{30}O_5$	74.37	7.02	74.63	6.96
19a	syrup	+21.9° (1.0)	25	$C_{28}H_{34}O_5$	74.46	7.63	74.64	7.61
19b	syrup	+19.8° (1.0)	26	$C_{28}H_{34}O_5$	74.54	7.62	74.64	7.61
20a-α	104—105[d]	+82.7° (1.0)	21	$C_{25}H_{26}O_5$	73.98	6.45	73.86	6.45
20a-β[h]	glass	−26.1° (1.2)	19	$C_{25}H_{26}O_5$	74.03	6.25	73.86	6.45
20b-α	syrup	+150° (0.1)	22	$C_6H_{12}O_4$	48.26[i]	7.92	48.64	8.16
20b-β[j]	40—42[k]	−93.6° (0.9)	26	$C_6H_{12}O_6$	48.65	8.18	48.64	8.16
20c-α	syrup	+142° (0.6)	21	$C_{10}H_{16}O_6$	51.72	6.80	51.72	6.94
21	syrup	+72.3° (1.1)	18	$C_9H_{16}O_5$	52.66	7.68	52.93	7.90
22	syrup	+31.5° (1.0)	18	$C_{16}H_{22}O_5$	65.11	7.28	65.29	7.53
23	118—119	−8.6° (1.1)	24	$C_{18}H_{24}O_7S$[l]	56.19	6.24	56.23	6.29
24	syrup	+17.2° (1.2)	26	$C_{11}H_{16}O_4$	62.10	7.53	62.25	7.60
25	76—77	+6.9° (1.0)	22	$C_{18}H_{24}O_5$	67.56	7.53	67.48	7.55
26	90—91	−39.6° (1.0)	21	$C_{25}H_{30}O_5$	73.36	7.39	73.14	7.37

a) The values of the diastereomeric ratios for the open-chain products refer to Table 1. b) The major isomer. c) See Ref. 17. d) Recrystallized from benzene-hexane. e) Crystallized on standing. f) IR (KBr): 3510 (OH), 1728 (C=O) cm^{-1}. g) A 83:17 diastereomeric mixture from **16α**. h) See Ref. 20. i) The experimental error was 0.38%. This compound, which was volatile and hygroscopic, was further characterized as its acetate (**20c-α**). j) See Refs. 18 and 22. k) Crystallized on standing; hygroscopic. l) S: Found; 8.33%. Calcd; 8.34%.

Methyl 2,3-O-Isopropylidene-α-D-lyxofuranoside (21). A solution of sodium metaperiodate (20 g) in water (150 ml) was stirred into a solution of methyl 2,3-*O*-isopropylidene-α-D-mannofuranoside[14] (10 g, 43 mmol) in dioxane (250 ml) and water (20 ml) at room temperature. After the mixture had been stirred for 2 h, it was extracted with ether (750 ml) and the extract was washed with water. Sodium borohydride (3 g) was added to the extract. The mixture was stirred at room temperature for 1.5 h; then it was washed with water and dried ($MgSO_4$). The evaporation of the solvent gave a syrup, which was chromatographed on a silica-gel column with benzene–ethyl acetate (8:2) to afford **21** (3.6 g, 41%).

Methyl 5-O-Benzyl-2,3-O-isopropylidene-α-D-lyxofuranoside (22). To a solution of **21** (3 g, 15 mmol) in dry benzene (50 ml) and *N,N*-dimethylformamide (8 ml) we added sodium hydride (*ca.* 60% in oil, 900 mg) at room temperature under an atmosphere of dry nitrogen, after which the mixture was stirred for 1 h. Benzyl chloride (2.6 ml) was added, and the mixture was stirred at room temperature overnight. A work-up similar to that described for the synthesis of **5α** gave a syrup, which was chromatographed on a silica-gel column with benzene–ethyl acetate (95:5) to provide **22** (4.0 g, 93%).

1,2-O-Cyclohexylidene-5-O-tosyl-α-D-xylofuranose (23). Tosyl chloride (1.42 g, 5.1 mmol) was added to a stirred solution of 1,2-*O*-cyclohexylidene-α-D-xylofuranose[15] (1.15 g, 5 mmol) in dry pyridine (9 ml) at 0—5 °C (bath temperature). The mixture was stirred at this temperature for 1 h and then at room temperature for another 1.5 h. The

usual work-up gave a solid, which was chromatographed on a silica-gel column with benzene–ethyl acetate (9:1) to afford crystalline **23** (1.59 g, 83%). An analytically pure sample was obtained by recrystallization from ether–hexane. IR (KBr): 3440 (OH), 1365 (S=O), 1176 (S=O) cm^{-1}.

*3,5-Anhydro-1,2-O-cyclohexylidene-α-D-xylofuranose (**24**).* This compound was prepared according to the method used for the synthesis of the corresponding isopropylidene derivative reported by Levene *et al.*[24] To a solution of sodium methoxide (65 mmol) in methanol (50 ml) we added **23** (5.0 g, 13 mmol) at 0—5 °C (bath temperature), after which the mixture was stirred at room temperature for 17 h. After cooling, iced water was added, and the mixture was extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated to give a syrup, which was subsequently chromatographed on a silica-gel column with benzene–ethyl acetate (95:5) to afford **24** (2.6 g, 94%).

*5-O-Benzyl-1,2-O-cyclohexylidene-α-D-xylofuranose (**25**).* The method of Kuzuhara and Emoto[25] was modified. A mixture of sodium (2 g) and benzyl alcohol (30 ml) was stirred at room temperature until the exothermic reaction had finished; the mixture was then heated at 120—125 °C (bath temperature) for 4 h. After the mixture had been cooled to room temperature, **24** (2.5 g, 12 mmol) was added. The mixture was heated at 120—125 °C (bath temperature) for 3 h. After cooling, iced water was added, and the mixture was extracted with ether, dried ($MgSO_4$), and concentrated. The benzyl alcohol was removed by co-evaporation with xylene. The resulting syrup was chromatographed on a silica-gel column with benzene–ethyl acetate (95:5) to give **25** (3.1 g, 82%).

*3,5-Di-O-benzyl-1,2-O-cyclohexylidene-α-D-xylofuranose (**26**).* To a stirred solution of 1,2-*O*-cyclohexylidene-α-D-xylofuranose[15] (2.3 g, 0.01 mol) in dry benzene (40 ml) and *N,N*-dimethylformamide (5 ml) we added sodium hydride (*ca.* 60% in oil, 1.1 g) at 0—5 °C (bath temperature) under an atmosphere of dry nitrogen, after which the stirring was continued for 30 min. Benzyl chloride (3.2 ml) was then added, and the mixture was heated at 70 °C (bath temperature) for 4 h and subsequently treated in a manner similar to that described for the synthesis of **5α** to give **26** as a syrup, which was then crystallized from benzene–hexane: 3.7 g (90%).

*Anomerization of **3β** and **5β** with an Acid.* A mixture of **3β** (75 mg) and concd sulfuric acid (30 mg) in methanol (5 ml) was refluxed at 80—85 °C (bath temperature) for 6 h. Aliquots were analyzed by ^1H NMR spectroscopy after the usual work-up. An equilibrium was reached within 3 h, the ratio of **3α** to **3β** being 20:80.

In a similar way, a mixture of **5β** (99 mg) and concd sulfuric acid (30 mg) in methanol (4 ml) was treated for 24 h. An equilibrium was reached within 6 h (**5α**:**5β**= 15:85).

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