Regioselectivity of Reductive Cleavage of Methyl 4,6-*O*-Benzylidene-3-deoxyhexopyranosides Containing Fluorine at the 2- or 3-Position with $LiAlH_4$–$AlCl_3$

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Reductive ring-opening reactions of the 4,6-*O*-benzylidene derivatives of methyl 3-deoxy-β-D-*arabino*-, 3-deoxy-α-D-*ribo*-, and 2-*O*-benzyl-3-deoxy-α-D-*ribo*-hexopyranosides with $LiAlH_4$ and $AlCl_3$ in the molar ratio of 4 : 4 gave the 4- and 6-*O*-benzyl derivatives in a ratio of 7 : 3. The product ratios for the reactions of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2-fluoro-α-D-*arabino*- and β-D-*ribo*-hexopyranosides and methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-3-fluoro-α-D-gluco- and β-D-allopyranosides were 3 : 2, 2 : 3, 1 : 1, and 3 : 7, respectively. When the molar ratio of the reagents was 2 : 4, however, the product ratios for the reactions of all the above-mentioned 4,6-*O*-benzylidene derivatives were approximately equal to 4 : 1. The influence of fluorine at C-2 or C-3, as well as that of the molar ratios of $LiAlH_4$ and $AlCl_3$, on the regioselectivity of the reductive cleavage of 4,6-*O*-benzylidenehexopyranosides are discussed.

The reductive ring-opening of the benzylidene derivatives using $LiAlH_4$–$AlCl_3$ has well been investigated in carbohydrate chemistry;[1] methyl 4,6-*O*-benzylidene-D-gluco- and D-mannopyranosides, having bulky substituents such as *O*-benzyl groups at C-3, open to form the 4-*O*-benzyl derivatives in high regioselectivity.[2] In contrast, the reduction of those compounds with $NaB(CN)H_3$–HCl favors 6-*O*-benzyl derivatives as products.[3] The reverse regioselectivity in the latter could be explained by the steric ease for the complex formation of O-4 with H^+, compared to that with $AlCl_3$.[3] An analogous report concerning the ring-opening of 4,6-*O*-benzylidene derivatives with $BH_3 \cdot Me_3N$–$AlCl_3$ shows that the 4-*O*-benzyl derivatives are obtained in toluene, whereas the 6-*O*-benzyl derivatives are obtained in tetrahydrofuran, which solvates the Lewis acid more strongly than does toluene.[4]

It was demonstrated that the ring-opening of cyclic acetals with $LiAlH_4$–$AlCl_3$ in diethyl ether preferably occurs at the closer position to the carbon atom, on which an electron-withdrawing substituent is attached.[5] However, studies concerning the hydrogenolysis of benzyl 4,6-*O*-benzylidene-β-D-glucopyranosides with various *O*-alkyl substituents at C-3 with $LiAlH_4$–$AlCl_3$ in diethyl ether–dichloromethane (2 : 1) have revealed that the larger is the substituent, the higher is the product ratio of the 4-*O*-benzyl derivative to the 6-*O*-benzyl isomer; the reaction of the 3-deoxy derivative showed the lowest ratio.[6] These results were interpreted in terms of the steric hindrance of substituents at C-3 to the complex formation of O-4 with Lewis acids. Therefore, in those ring-opening reactions, the electron-withdrawing effects of the *O*-alkyl groups at C-3 may be masked by their steric effects.

We now report on the influence of a fluorine at C-2 or C-3 of 4,6-*O*-benzylidene-3-deoxyhexopyranosides, which have no steric hindrance around C-3, upon the regiospecificity of the reductive cleavage with $LiAlH_4$–$AlCl_3$.

Results and Discussion

The $LiAlH_4$–$AlCl_3$ reduction of the 4,6-*O*-benzylidene derivatives of methyl 3-deoxy-β-D-*arabino*- (**1**),[7] 3-deoxy-α-D-*ribo*- (**2**),[8] 2-*O*-benzyl-3-deoxy-α-D-*ribo*- (**3**), 2,3-dideoxy-2-fluoro-α-D-*arabino*- (**4**), and 2,3-dideoxy-2-fluoro-β-D-*ribo*- (**5**)[9] hexopyranosides, methyl 3-*O*-benzyl-2-deoxy-2-fluoro-β- (**6**)[10] and 2-*O*-benzyl-3-deoxy-3-fluoro-α- (**7**) D-glucopyranosides, and methyl 2-*O*-benzyl-3-deoxy-3-fluoro-β-D-allopyranoside (**8**) were examined.

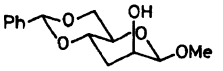
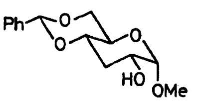
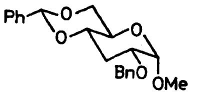
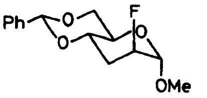
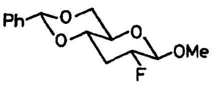
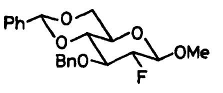
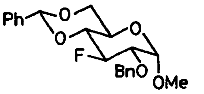
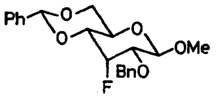
The benzylation of **2** using benzyl chloride and potassium hydroxide gave **3**, and the fluorination of **2** with diethylaminosulfur trifluoride (DAST), according to the preparation[9] of **5** from **1**, yielded **4**. Compound **7** was prepared from methyl 3-deoxy-3-fluoro-α-D-glucopyranoside[11] through benzylidenation and subsequent benzylation. The fluorination of methyl 4,6-*O*-benzylidene-β-D-glucopyranoside with DAST in dichloromethane containing pyridine gave the 3-deoxy-3-fluoro-β-D-allo derivative **24**, of which benzylation afforded **8**.

The choice of the anomeric configuration of the substrates depends on synthetic convenience, since it was mentioned[2] that the regioselectivity of the hydrogenolysis of 2,3-di-*O*-benzyl-4,6-*O*-benzylidede-D-gluco- and D-mannopyranosides was not influenced by the anomeric configuration, the configuration at C-2, and the bulkiness of the substituent at C-2.

The hydrogenolysis of the 4,6-*O*-benzylidene derivatives was performed by using 4 molar amounts of $LiAlH_4$–$AlCl_3$ (1 : 1) to each substrate in diethyl ether–dichloromethane (2 : 1) under refluxing. The results are summarized in Table 1.

The proportions of 4-*O*-benzyl derivatives **9**, **11**, and **13** formed in the hydrogenolysis of **1**, **2**, and **3**, respectively, were in the 72—75% range. This indicates that the absence of a bulky substituent at C-3 diminished the selective formation of 4-*O*-benzyl derivatives, and that the regioselectivity of the reactions of 3-deoxy deriva-

Table 1. Yields and Product Ratios for Hydrogenolysis with $LiAlH_4$–$AlCl_3$ (4 : 4)

4,6-*O*-Benzylidene derivative		Yield(%) of:		Product ratio
		4-*O*-Bn	6-*O*-Bn	4-*O*-Bn : 6-*O*-Bn
	(1)	64	25	72 : 28
	(2)	59	19	75 : 25
	(3)	64	25	72 : 28
	(4)	56	34	62 : 38
	(5)	34	55	38 : 62
	(6)	78	0	100 : 0
	(7)	43	39	52 : 48
	(8)	21	47	31 : 69

tives is also not affected by the anomeric configuration, or the configuration and substituent at C-2. However, the regioselectivity of the reaction of **4** is much different from that of **5**; in addition, the proportions of the 6-*O*-benzyl derivatives **16** and **18** (Chart 1) produced from **4** and **5** (38 and 62%), respectively, are higher than those of **1**—**3** (25—28%). The increased preference for the formation of the 6-*O*-benzyl derivative is in agreement with the interpretation[5] regarding the electron-withdrawing effect of the substituent on a reductive ring-opening of acetals with $LiAlH_4$–$AlCl_3$.

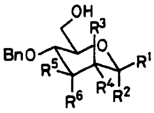
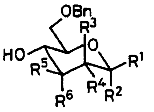
	R¹	R²	R³	R⁴	R⁵	R⁶	
9	OMe	H	OH	H	H	H	10
11	H	OMe	H	OH	H	H	12
13	H	OMe	H	OBn	H	H	14
15	H	OMe	F	H	H	H	16
17	OMe	H	H	F	H	H	18
19	OMe	H	H	F	OBn	H	
20	H	OMe	H	OBn	F	H	21
22	OMe	H	H	OBn	H	F	23

Chart 1.

The proposed intermediates and pathways for reductive ring-opening are illustrated in Fig. 1. The electron-withdrawing fluorine atom at C-2 may destabilize the intermediate ion IA, and, hence, another ion IB is favored to give a higher proportion of the 6-*O*-benzyl derivative. Furthermore, the presence of a W-conformation between F-2 and O-4 in **5** may cause a strong destabilizing effect of fluorine on IA generated from **5**, consequently leading to a higher proportion of the 6-*O*-benzyl isomer **18** compared to the proportion of **16**. Even the significant influence of the electronegativity of fluorine observed in **5** is still overshadowed by the steric effect of the *O*-benzyl group at C-3 in **6**, which exclusively afforded the 4-*O*-benzyl derivative **19** upon hydrogenolysis.

In the hydrogenolysis of 3-deoxy-3-fluoro compounds **7** and **8**, the steric effect of fluorine on the complexation of O-4 would be almost negligible, because a fluorine atom is only slightly larger in size than a hydrogen atom. Consequently, the regioselectivity of the ring-opening reactions of **7** and **8** is thought to be mainly controlled by the electron-withdrawing property of fluorine.

Indeed, the proportions of the 6-*O*-benzyl derivatives **21** and **23** produced from **7** and **8** (48 and 69%), respectively, are obviously high, though a considerable difference in the product ratio between **7** and **8** is observed. This can be rationalized in terms of the difference in the strength of the influence of electronegative fluorine to O-4 through three bonds, based on an analogy of electron intercourse through F–H coupling pathways in equivalent situations.

In ^1H NMR spectroscopy of a six-membered ring system, the vicinal coupling constants between axial fluorine (F_{ax}) and equatorial proton (H_{eq}) (*cis-gauche*) are usually larger than those between equatorial fluorine (F_{eq}) and H_{eq} (*trans-gauche*). For instance, the F_{ax}–H_{eq} coupling constants for methyl 2-*O*-benzyl-3,4,6-trideoxy-4-fluoro-α-D-*xylo*- and α-D-*lyxo*-hexopyranosides[12] are 11.1 and 12.3, respectively, and those for both **15** and **16** are 11.2; the F_{eq}–H_{eq} coupling constants for methyl 2-*O*-benzyl-3,4,6-trideoxy-4-fluoro-α-D-*ribo*- and α-D-*arabino*-hexopyranosides,[12] **17**, and **18**, however, are 5.2, 4.8, 5.4, and 5.6, respectively. This indicates that the intercourse of electons in the F_{ax}–H_{eq} coupling pathway surpasses that in the F_{eq}–H_{eq} pathway; this tendency can be applied to interpreting the difference in the product ratio of hydrogenolysis between **7** and **8**.

Table 2 shows the results of the hydrogenolysis with 2 molar amounts of $LiAlH_4$ and 4 molar amounts of $AlCl_3$ to the substrate. Surprisingly, the product ratios of the reactions of all substrates, except for **6**, are in a quite narrow range between 77 : 23 and 81 : 19. The following discussion is given in order to provide an understanding of why such a difference between both results shown in Tables 1 and 2 was observed.

The presumed species[13] generated from $LiAlH_4$ and

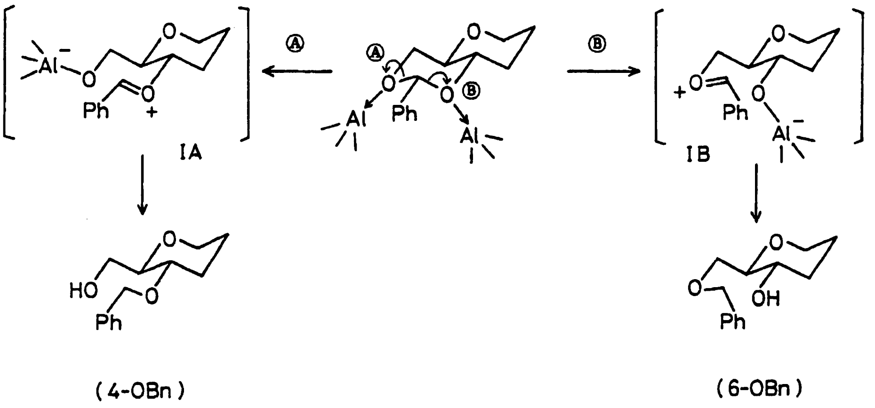
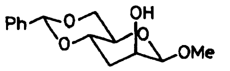
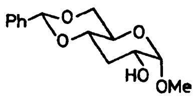
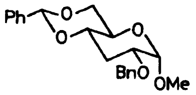
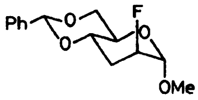
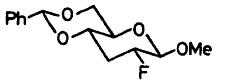
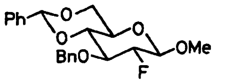
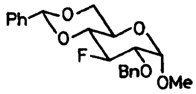
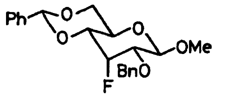


Fig. 1. Pathways for the reductive ring-opening of 4,6-*O*-benzylidene derivatives.

Table 2. Yields and Product Ratios for Hydrogenolysis with $LiAlH_4$–$AlCl_3$ (2 : 4)

4,6-*O*-Benzylidene derivative		Yield(%) of: 4-*O*-Bn	6-*O*-Bn	Product ratio 4-*O*-Bn : 6-*O*-Bn
	(1)	69	19	78 : 22
	(2)	74	18	80 : 20
	(3)	76	22	78 : 22
	(4)	70	18	80 : 20
	(5)	54	13	81 : 19
	(6)	90	0	100 : 0
	(7)	52	16	77 : 23
	(8)	43	13	77 : 23

$AlCl_3$ of some different molar ratios are listed in Table 3 along with the yields and product ratios for the reactions of **4** using such reagents. When the reagents' ratio is 1 : 1 (2 : 2 and 4 : 4), the higher is the concentration of the reagents, the lower is the influence of fluorine. The excess $AlCl_3$ existing in the reactions using the reagents of 2 : 3 and 2 : 4 may predominantly coordinate with O-4 or O-6, since $AlCl_3$ is a more acidic Lewis acid than is AlH_2Cl. However, $AlCl_3$ requires greater space for complex formation compared to that for AlH_2Cl. Therefore, the product ratios are thought to represent the relative coordinating abilities of $AlCl_3$ with O-6 and O-4 under each condition, even in such a 3-deoxy structure as **4**, which would have no steric hindrance at C-3 for coordinating AlH_2Cl. This is well supported by the fact that the product ratios are independent on the presence of fluorine at C-2 or C-3 in the hydrogenolysis when the molar ratio of $LiAlH_4$ to $AlCl_3$ is 2 : 4.

Experimental

The melting points were determined with a Yanagimoto MP-500D melting-point apparatus and are uncorrected. The optical rotations were measured with a Horiba SEPA-200 polarimeter at 20 °C. NMR spectra were recorded with a Varian VXR-300 spectrometer at 300 MHz for ^{1}H NMR and at 75.4 MHz for ^{13}C NMR in $CDCl_3$. Assignment of all proton and carbon signals was performed based on H–H and C–H COSY measurements. The chemical shifts of the protons were calculated from that of the satellite peak of $CDCl_3$ at δ=7.26, and those of the carbons are relative to the central peak of $CDCl_3$ at δ=77.0. The ^{1}H and ^{13}C NMR spectral data for the following compounds are summarized in Tables 4, 5, and 6. Silica gel (Wakogel C-300) was used for column chromatography.

Methyl 2-*O*-Benzyl-4,6-*O*-benzylidene-3-deoxy-α-D-*ribo*-hexopyranoside (3). A mixture of **2** (444 mg, 1.67 mmol), benzyl chloride (9.0 ml), and powdered potassium hydroxide (374 mg, 6.68 mmol) was stirred at 110 °C for 3 h. Insoluble matter was filtered off through Celite; the filtrate was evaporated and purified by column chromatography using a gradient mixed-solvent system of toluene–ethyl acetate (50 : 1 → 3 : 1) to afford crystalline **3** (504 mg, 85%). Recrystallization from diisopropyl ether gave fine needles; mp 98.5—99.0 °C; $[\alpha]_D$ +21.2° (*c* 1, $CHCl_3$).

Found: C, 70.80; H, 6.69%. Calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79%.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-2-fluoro-α-D-*arabino*-hexopyranoside (4). To a solution of **2** (1.14 g, 4.31 mmol) in benzene (57 ml) and pyridine (7 ml), DAST (1.17 ml, 12.9 mmol) was added dropwise at 5 °C; the resulting solution was kept at the same temperature for 30 min and then heated at 65 °C for 3 h. After cooling, the solution was poured into iced aqueous sodium hydrogencarbonate under efficient stirring, which continued for 30 min. The mixture was extracted with benzene; the organic layer was dried over sodium sulfate and evaporated to give a

Table 3. Influence of Molar Ratio of $LiAlH_4$ and $AlCl_3$ on Hydrogenolysis of **4**

$LiAlH_4$: $AlCl_3$ mol : mol	Species generated from the reagents	%Yield **15**	%Yield **16**	Product ratio 4-*O*-Bn : 6-*O*-Bn
2 : 2	$2LiCl + 4AlH_2Cl$	48	45	52 : 48
2 : 3	$2LiCl + 4AlH_2Cl + AlCl_3$	60	39	61 : 39
2 : 4	$2LiCl + 4AlH_2Cl + 2AlCl_3$	70	18	80 : 20
4 : 4	$4LiCl + 8AlH_2Cl$	56	34	62 : 38

Table 4. ^1H NMR Spectral Data for the 4,6-*O*-Benzylidene Derivatives **3**, **4**, **7**, **8**, and **24**[a)]

Compd	δ: H-1		H-2		H-3$_{ax}$		H-3$_{eq}$		H-4		H-5		H-6$_{ax}$		H-6$_{eq}$	OH	OMe	C<u>H</u>Ph
J/Hz		1,2		2,3$_{ax}$		3$_{ax}$,3$_{eq}$		3$_{ax}$,4		4,5		5,6$_{ax}$		6$_{ax}$,6$_{eq}$		OH,H		
				2,3$_{eq}$				3$_{eq}$,4				5,6$_{eq}$						
	(1,F)		(2,F)		(3$_{ax}$,F)		(3$_{eq}$,F)		(4,F)		(5,F)		(6$_{ax}$,F)		(6$_{eq}$,F)			
3	4.69		3.61		2.06		2.28		3.49		3.78		3.67		4.25		3.46	5.50
		3.5		11.7		11.3		11.8		9.0		9.9		9.9				
				4.5				4.3				4.2						
4	4.73		4.71		2.07		2.35		3.96		3.85		3.80		4.26		3.43	5.58
		1.2		2.4		13.8		11.5		9.8		9.5		9.0				
				3.0				4.5				3.7						
	(8.5)		(46.3)		(44.5)		(11.4)											
7	4.65		3.64		4.96				3.69		3.83		3.73		4.29		3.40	5.53
		3.7		8.7				9.1		9.2		9.6		9.8				
												4.1						
	(3.0)		(12.0)		(55.4)				(12.2)		(0.5)				(2.0)			
8	4.78		3.33				5.01		3.50		3.96		3.73		4.42		3.61	5.49
		7.8								9.4		10.1		10.4				
				2.1				1.6				5.0						
	(0.6)		(27.3)				(53.7)		(27.6)		(1.3)		(1.5)					
24	4.64		3.57				5.13		3.63		3.97		3.77		4.43	2.46	3.60	5.55
		7.8								9.4		10.0		10.2		5.5		
				2.2				1.8				4.9						
	(1.2)		(27.0)				(53.9)		(28.0)		(1.4)		(1.7)					

a) Data for protons of benzyl and phenyl groups are not shown.

syrup. Column chromatograpy using a gradient mixed-solvent system of hexane–ethyl acetate (30 : 1 → 2 : 1) provided **4** (424 mg, 37%) as the major product; mp 78.9—79.5 °C; $[\alpha]_D$ +106.8° (*c* 0.9, $CHCl_3$).

Found: C, 62.64; H, 6.38%. Calcd for $C_{14}H_{17}FO_4$: C, 62.68; H, 6.39%.

Methyl 2-*O*-Benzyl-4,6-*O*-benzylidene-3-deoxy-3-fluoro-α-D-glucopyranoside (7). A mixture of methyl 3-deoxy-3-fluoro-α-D-glucopyranoside (612 mg, 3.12 mmol), *N*,*N*-dimethylformamide (22 ml), benzaldehyde dimethyl acetal (0.52 ml, 3.43 mmol), and *p*-toluenesulfonic acid monohydrate (6.0 mg) was stirred at 80 °C for 15 min. Neutralization with triethylamine, followed by evaporation, left a syrup which was purified through a short column of silica gel to give a crystalline product (740 mg). This was dissolved in *N*,*N*-dimethylformamide (7.4 ml); benzyl bromide (0.48 ml, 3.91 mmol) and sodium hydride (60% dispersion in oil, 135 mg, 3.39 mmol) were added to the solution at 0 °C, and the resulting mixture was stirred at 0 °C for 2 h. After dilution with chloroform and successive filtration through Celite, the solution was evaporated to a syrup which was chromatographed using a mixed solvent of toluene and ethyl acetate (8 : 1). Crystallization from diisopropyl ether gave **7** (852 mg, 73%); mp 110.9—111.6 °C; $[\alpha]_D$ +5.9° (*c* 0.8, $CHCl_3$).

Found: C, 67.31; H, 6.19%. Calcd for $C_{21}H_{23}FO_5$: C, 67.37; H, 6.19%.

Methyl 2-*O*-Benzyl-4,6-*O*-benzylidene-3-deoxy-3-fluoro-β-D-allopyranoside (8). A mixture of methy 4,6-*O*-benzylidene-β-D-glucopyranoside (600 mg, 2.13 mmol), dichloromethane (12 ml), and pyridine (0.34 ml, 4.22 mmol) was cooled to −45 °C, at which temperature DAST (1.27 ml, 9.59 mmol) was added dropwise. After being kept at that temperature for 30 min, the mixture was stirred at room temperature for 16 h. Methanol (2 ml) was added dropwise to the mixture at −10 °C. Evaporation followed by chromatographic separation provided methyl 4,6-*O*-benzylidene-3-deoxy-3-fluoro-β-D-allopyranoside (**24**, 276 mg, 46%) as crystals, mp 182.5—183.5 °C; $[\alpha]_D$ −53.0° (*c* 0.8, $CHCl_3$).

Found: C, 59.06; H, 6.03%. Calcd for $C_{14}H_{17}FO_5$: C, 59.15; H, 6.03%.

To a solution of **24** (228 mg, 0.803 mmol) in *N*,*N*-dimethylformamide (2.3 ml), benzyl bromide (0.14 ml, 1.20 mmol) and sodium hydride (60% dispersion in oil, 39 mg, 0.964 mmol) were added at 0 °C; the resulting mixture was stirred at 0 °C for 1 h. Toluene (5 ml) and acetic acid (0.2 ml) were successively added to the mixture. Evaporation left a turbid syrup which was purified by column chromatography using a mixed solvent of toluene and ethyl acetate (8 : 1) to afford **8** (300 mg, 99%). Recrystallization from diisopropyl ether gave needles, mp 138.9—139.6 °C; $[\alpha]_D$ −54.2° (*c* 1, $CHCl_3$).

Found: C, 67.14; H, 6.09%. Calcd for $C_{21}H_{23}FO_5$: C, 67.37; H, 6.19%.

Table 5. ^{1}H NMR Spectral Data for the 4-*O*- and 6-*O*-Benzyl Derivatives **9**—**23** [a]

Compd	δ: H-1		H-2		H-3$_{ax}$		H-3$_{eq}$		H-4		H-5		H-6$_{a}$		H-6$_{b}$	OH-2	OH-4	OH-6	OMe
J/Hz	(1,F)	1,2 1,3$_{eq}$	(2,F)	2,3$_{ax}$ 2,3$_{eq}$	(3$_{ax}$,F)	3$_{ax}$,3$_{eq}$	(3$_{eq}$,F)	3$_{ax}$,4 3$_{eq}$,4	(4,F)	4,5	(5,F)	5,6$_{a}$ 5,6$_{b}$		6$_{a}$,6$_{b}$		2,OH	4,OH	6a,OH 6$_{b}$,OH	
9	4.47		3.93		1.60		2.49		3.82		3.47		3.77		3.90	2.32		2.18	3.55
		1.1		3.1		13.4		10.6		8.9		5.0		11.6		2.0		6.8	
				4.6				4.5				3.6						5.7	
10	4.40		3.88		1.57		2.32		3.98		3.47		3.73		3.78	2.31	2.81		3.52
		1.1		3.0		13.5		10.9		9.0		6.1		9.5		2.5	– [b]		
				3.7				4.7				5.1							
11	4.64		3.65		1.68		2.38		3.46		3.59		3.74		3.83	1.98		1.91	3.44
		3.5		11.6		11.2		11.0		9.8		4.2		11.6		11.1		7.0	
				4.8				4.3				3.5						5.7	
12	4.63		3.68		1.66		2.21		3.68		3.61		3.62		3.74	1.95	2.60		3.44
		3.4		11.5		11.3		11.0		9.8		8.8		9.1		10.8	3.0		
				4.7				4.3				4.1							
13	4.65		3.46		1.88		2.34		3.43		3.63		3.69 ——		—— 3.83			1.84	3.41
		3.3		11.5		11.3		12.0		9.2		4.0		– [b]				– [b]	
				4.0				4.5				3.3						– [b]	
14	4.64		3.51		1.84		2.20		3.59		——		——		—— 3.73		2.46		3.41
		3.3		12.0		11.4		11.7		– [c]		– [c]		– [c]			– [b]		
				4.5				4.0				– [c]							
15	4.70		4.59		1.87		2.44		3.94		3.71		3.77		3.86			2.03	3.40
		1.2		2.2		13.5		10.7		8.7		4.5		11.3				5.1	
		1.0		3.0				4.4				2.7						7.0	
	(6.0)		(49.0)		(46.8)		(11.2)												
16	4.68		4.60		1.83		2.30		3.94		3.72		3.71		3.78		2.81		3.40
		1.5		2.2		13.8		11.1		8.4		6.0		11.4			– [b]		
		1.0		3.3				4.6				7.1							
	(8.2)		(48.2)		(46.7)		(11.2)												
17	4.42		4.23		1.72		2.68		3.56		3.45		3.75		3.90			1.93	3.57
		7.5		11.4		11.8		10.8		9.3		4.5		11.8				7.6	
				5.3				4.6				3.0						5.8	
	(2.9)		(48.6)		(11.6)		(5.4)		(1.0)										
18	4.37		4.27		1.72		2.52		3.72		3.48		3.67		3.79		3.00		3.54
		7.3		11.3		12.0		11.0		8.9		6.5		9.6			– [b]		
				5.2				5.0				4.9							
	(3.8)		(48.0)		(11.5)		(5.6)		(– [b])										
19	4.44		4.30		3.80				3.61		3.39		3.72		3.88			1.85	3.58
		7.8		8.4				9.0		9.7		4.3		12.0				7.7	
												2.8						5.8	
	(3.6)		(50.0)		(15.0)														
20	4.63		3.55		4.99				3.64		3.63		3.72		3.79			1.63	3.34
		3.8		9.1				7.9		9.5		3.0		10.0				5.8	
												2.6						7.0	
	(3.5)		(12.2)		(53.5)				(10.0)										
21	4.64		3.56		4.76				3.82		3.68		3.71		3.72		2.54		3.36
		3.8		9.2				8.9		8.7		1.7		9.0			3.0		
												7.0							
	(3.5)		(12.0)		(54.0)				(14.0)										
22	4.73		3.18				4.98		3.48		3.82		3.76		3.91			1.84	3.57
		7.9								9.0		3.6		11.8				8.2	
				2.2				1.9				2.7						5.0	
	(1.2)		(28.2)				(52.6)		(27.7)		(0.8)								
23	4.67		3.29				4.89		3.62		3.80		3.73		3.76		2.59		3.56
		7.9								8.5		2.0		11.0			7.2		
				2.3				1.9				4.9							
	(1.2)		(28.7)				(52.6)		(27.3)										

a) Data for protons of benzyl and phenyl groups are not shown. b) Not determined because of broadening of signals. c) Not determined because of overlapping of signals.

Methyl 4-*O*-Benzyl-3-deoxy- and Methyl 6-*O*-Benzyl-3-deoxy-β-D-*arabino*-hexopyranosides (9 and 10). To a mixture of **1** (100 mg, 0.376 mmol), diethyl ether (1.5 ml), dichloromethane (1.5 ml), and $LiAlH_4$ (57.2 mg, 1.50 mmol), a solution of $AlCl_3$ (199 mg, 1.50 mmol) in diethyl ether (1.5 ml) was added at 42 °C. After stirring at that temperature for 40 min, ethyl acetate was added dropwise to decompose excess $LiAlH_4$. The mixture was diluted with diethyl ether (45 ml) and washed with 10% aqueous potassium sodium tartarate (15 ml). After the aqueous layer was

Table 6. ^{13}C NMR Spectral Data for the Fluorinated 4,6-*O*-Benzylidene Derivatives **4**, **7**, **8**, and **24** [a)]

Compd	δ ($J_{C,F}$/Hz)								
	C-1	C-2	C-3	C-4	C-5	C-6	OMe	$\underline{C}$HPh	$\underline{C}H_2Ph$
4	97.8 (32.3)	88.0 (171.3)	30.3 (19.7)	73.4	66.2	64.8	55.0	102.1	
7	99.4 (10.2)	79.7 (17.1)	91.2 (186.9)	77.3 (16.3)	61. 5 (7.6)	68.9	55.5	101.7	73.5
8	102.5	76.2 (16.6)	88.3 (183.8)	77.3 (17.3)	62.9 (3.4)	69.1	57.6	102.1	72.9
24	102.3	71.0 (17.1)	89.0 (182.6)	77.4 (17.0)	63.5 (3.2)	69.0	57.6	102.2	

a) Data for carbons of phenyl groups are not shown.

extracted with diethyl ether (3×25 ml), the ether layers were combined, dried over sodium sulfate, and evaporated. Chromatographic separation using a gradient mixed-solvent system of cloroform–methanol (50 : 1 → 10 : 1) provided **9** (64.6 mg, 64%) and **10** (25.0 mg, 25%).

9: $[\alpha]_D$ −5.0° (*c* 1.1, $CHCl_3$).

Found: C, 62.37; H, 7.52%. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51%.

10: $[\alpha]_D$ −70.3° (*c* 1.2, $CHCl_3$).

Found: C, 61.87; H, 7.52%. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51%.

Compound **1** (449 mg, 1.69 mmol) was hydrogenolyzed with $LiAlH_4$ (129 mg, 3.39 mmol) and $AlCl_3$ (900 mg, 6.75 mmol) in the same manner as described above. Column chromatography provided **9** (316 mg, 69%) and **10** (87 mg, 19%).

Methyl 4-*O*-Benzyl-3-deoxy- and Methyl 6-*O*-Benzyl-3-deoxy-α-D-*ribo*-hexopyranosides (11 and 12). Compound **2** was hydrogenolyzed according to the procedure described for the reaction of **1**. The reaction mixture was worked-up and chromatographed as described for isolating **9** and **10**. The yields of **11** and **12** are given in Tables 1 and 2.

11: mp 126.1—127.5 °C, $[\alpha]_D$ +191.4° (*c* 1, $CHCl_3$) (lit,[14] mp 124 °C, $[\alpha]_D$ +194.2° (*c* 1, $CHCl_3$)).

Found: C, 62.88; H, 7.43%. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51%.

12: $[\alpha]_D$ +84.6° (*c* 1, $CHCl_3$).

Found: C, 62.42; H, 7.75%. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51%.

Methyl 2,4-Di-*O*-benzyl-3-deoxy- and Methyl 2,6-Di-*O*-benzyl-3-deoxy-α-D-*ribo*-hexopyranosides (13 and 14). Compound **3** was hydrogenolyzed according to the procedure described for **1**. Chromatographic separation using a gradient mixed-solvent system of dichloromethane–ethyl acetate (30 : 1 → 3 : 1) afforded **13** and **14**. The yields are given in Tables 1 and 2.

13: $[\alpha]_D$ +90.8° (*c* 1, $CHCl_3$).

Found: C, 69.76; H, 7.25%. Calcd for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31%.

14: $[\alpha]_D$ +46.6° (*c* 0.8, $CHCl_3$).

Found: C, 69.80; H, 7.32%. Calcd for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31%.

Methyl 4-*O*-Benzyl-2,3-dideoxy-2-fluoro- and Methyl 6-*O*-Benzyl-2,3-dideoxy-2-fluoro-α-D-*arabino*-hexopyranosides (15 and 16). Compound **4** was hydrogenolyzed according to the procedure described for **1**. Chromatographic separation using a gradient mixed-solvent system of toluene–2-butanone (50 : 1 → 5 : 1) gave **15** and **16**. The yields are given in Tables 1, 2, and 3.

15: $[\alpha]_D$ +146.2° (*c* 0.7, $CHCl_3$).

Found: C, 62.00; H, 7.14%. Calcd for $C_{14}H_{19}FO_4$: C, 62.21; H, 7.09%.

16: $[\alpha]_D$ +83.6° (*c* 1, $CHCl_3$).

Found: C, 61.74; H, 7.08%. Calcd for $C_{14}H_{19}FO_4$: C, 62.21; H, 7.09%.

Methyl 4-*O*-Benzyl-2,3-dideoxy-2-fluoro- and Methyl 6-*O*-Benzyl-2,3-dideoxy-2-fluoro-β-D-*ribo*-hexopyranosides (17 and 18). Compound **5** was hydrogenolyzed according to the procedure described for **1**. Chromatographic separation using a gradient mixed-solvent system of toluene–ethyl acetate (30 : 1 → 3 : 1) gave **17** and **18**. The yields are given in Tables 1 and 2.

17: $[\alpha]_D$ +13.8° (*c* 1.7, $CHCl_3$).

Found: C, 61.72; H, 7.00%. Calcd for $C_{14}H_{19}FO_4$: C, 62.21; H, 7.09%.

18: $[\alpha]_D$ −68.5° (*c* 1, $CHCl_3$).

Found: C, 61.65; H, 7.15%. Calcd for $C_{14}H_{19}FO_4$: C, 62.21; H, 7.09%.

Methyl 3,4-Di-*O*-benzyl-2-deoxy-2-fluoro-β-D-glucopyranoside (19). Compound **6** was hydrogenolyzed according to the procedure described for **1**. Column chromatography using a mixed solvent of toluene and ethyl acetate afforded **19**; mp 83.0—83.5 °C; $[\alpha]_D$ −16.6° (*c* 0.9, $CHCl_3$).

Found: C, 67.11; H, 6.66%. Calcd for $C_{21}H_{25}FO_5$: C, 67.00; H, 6.69%.

Methyl 2,4-Di-*O*-benzyl-3-deoxy-3-fluoro- and Methyl 2,6-Di-*O*-benzyl-3-deoxy-3-fluoro-α-D-glucopyranosides (20 and 21). Compound **7** was hydrogenolyzed according to the procedure described for **1**. Chromatographic separation using a gradient mixed-solvent system of toluene–ethyl acetate (40 : 1 → 5 : 1) gave **20** and **21**. The yields are given in Tables 1 and 2.

20: $[\alpha]_D$ +66.2° (*c* 1, $CHCl_3$).

Found: C, 66.75; H, 6.71%. Calcd for $C_{21}H_{25}FO_5$: C, 67.01; H, 6.69%.

21: $[\alpha]_D$ +36.7° (*c* 1, $CHCl_3$).

Found: C, 67.28; H, 6.84%. Calcd for $C_{21}H_{25}FO_5$: C, 67.01; H, 6.69%.

Methyl 2,4-Di-*O*-benzyl-3-deoxy-3-fluoro- and Methyl 2,6-Di-*O*-benzyl-3-deoxy-3-fluoro-β-D-allopyranosides (22 and 23). Compound **8** was hydrogenolyzed according to the procedure described for **1**. Chromatographic separation using a gradient mixed-solvent system of toluene–ethyl acetate (40 : 1 → 5 : 1) gave **22** and **23**. The yields are given in Tables 1 and 2.

22: $[\alpha]_D$ +13.6° (*c* 1, $CHCl_3$).

Found: C, 67.19; H, 6.83%. Calcd for $C_{21}H_{25}FO_5$: C, 67.01; H, 6.69%.

23: mp 58.7—60.1 °C; $[\alpha]_D$ −23.7° (*c* 1.1, $CHCl_3$).

Found: C, 67.45; H, 6.84%. Calcd for $C_{21}H_{25}FO_5$: C, 67.01: H, 6.69%.

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