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Synthesis of 2-Deoxy-2-fluoro-D-mannose Using Fluoride Ion

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Nucleophilic displacement reactions of the 3-*O*-acetyl, 3-*O*-methyl, and 3-*O*-benzyl derivatives (**5**, **11**, and **12**) of methyl 4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-β-D-glucopyranoside with tetraalkylammonium fluorides in acetonitrile proceeded smoothly to give, with inversion of configuration at C_2, the corresponding methyl 2-deoxy-2-fluoro-β-D-mannopyranosides in good yields. Similar treatment of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-α-D-glucopyranoside (**3**) or methyl 3,4,6-tri-*O*-acetyl-2-*O*-(trifluoromethanesulfonyl)-β-D-glucopyranoside (**8**) resulted in decreased yield of the fluoro-manno compound. Efficient conversion of these fluorinated intermediates into 2-deoxy-2-fluoro-D-mannose (**1**) was achieved by heating with acidic reagents. These synthetic sequences could be easily adapted for the preparation of the ^{18}F-labeled analog of 2-deoxy-2-fluoro-D-mannose (**1**).

Keywords——fluorination; nucleophilic displacement; tetraalkylammonium fluoride; methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-β-D-glucopyranoside; methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-β-D-glucopyranoside; 2-deoxy-2-fluoro-D-mannose

The increasing importance of fluorinated deoxy-hexoses, in the study of various aspects of carbohydrate transport and metabolism, has made it desirable to investigate new synthetic routes to this class of compounds.$^{1)}$ 2-Deoxy-2-fluoro-D-mannose (FDM) (**1**) has been used extensively for studies of glycoprotein biosynthesis and function,$^{2)}$ and more recently its ^{18}F-labeled analog (^{18}F, $T_{1/2}=110\,\text{min}$, β^+ decay) has been reported to be a promising radiopharmaceutical for cancer diagnosis in humans by positron emission tomography.$^{3)}$ Existing synthetic routes to FDM (**1**) involve the electrophilic addition either of F_2 or CF_3OF to 3,4,6-tri-*O*-acetyl-D-glucal followed by acid hydrolysis.$^{4,5)}$ The former method has also been adapted for the preparation of ^{18}F-labeled FDM.$^{6)}$ However, these methods have no practical synthetic utility for large amounts of FDM (**1**) or its ^{18}F-labeled analog since FDM (**1**) is produced as a by-product in these reactions. Therefore, there is a pressing need for an efficient preparative method for this substance and, moreover, one that is suitable for the radiopharmaceutical synthesis of ^{18}F-labeled FDM (*i.e.*, the reaction must be rapid and efficient in the use of radioactive ^{18}F available in the ionic form).

The introduction of fluorine at secondary positions of carbohydrates by nucleophilic displacement reactions of sulfonyloxy groups such as methanesulfonates and *p*-toluenesulfonates requires forcing and, frequently, destructive reaction conditions.$^{7)}$ The development of the trifluoromethanesulfonate (triflate) group with markedly improved leaving ability, however, has considerably increased the synthetic usefulness of the displacement reactions involving sulfonate esters in carbohydrate systems.$^{8)}$ Recent publications on the synthesis of 2-deoxy-2-fluoro-D-glucose$^{1b,9)}$ and 3-deoxy-3-fluoro-D-glucose$^{10)}$ include the successful nucleophilic substitution of methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-(trifluoromethanesulfonyl)-β-D-mannopyranoside and 1,2:5,6-di-*O*-isopropylidene-3-*O*-(trifluoromethanesulfonyl)-α-D-allofuranoside, respectively, with cesium fluoride in *N*,*N*-dimethylformamide (DMF). Ishido *et al.* have demonstrated that nucleophilic substitution of the S_N2 type is effectively induced at C_2 of methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-α-D-glucopyranoside by nucleophiles such as azide and benzoate ions, giving the methyl 2-deoxy-2-substituted α-D-mannopyranoside.[11] These literature precedents led us to investigate the reaction of fluoride ion with a protected glucopyranoside having triflate at C_2 as an alternative synthetic route to FDM (**1**). We report herein the synthesis of FDM (**1**) by the facile displacement of the C_2-triflate function of a suitably protected methyl β-D-glucopyranoside with tetraalkylammonium fluorides. This method can be easily adapted for the preparation of the ^{18}F-labeled analog of FDM (**1**) for medical imaging.

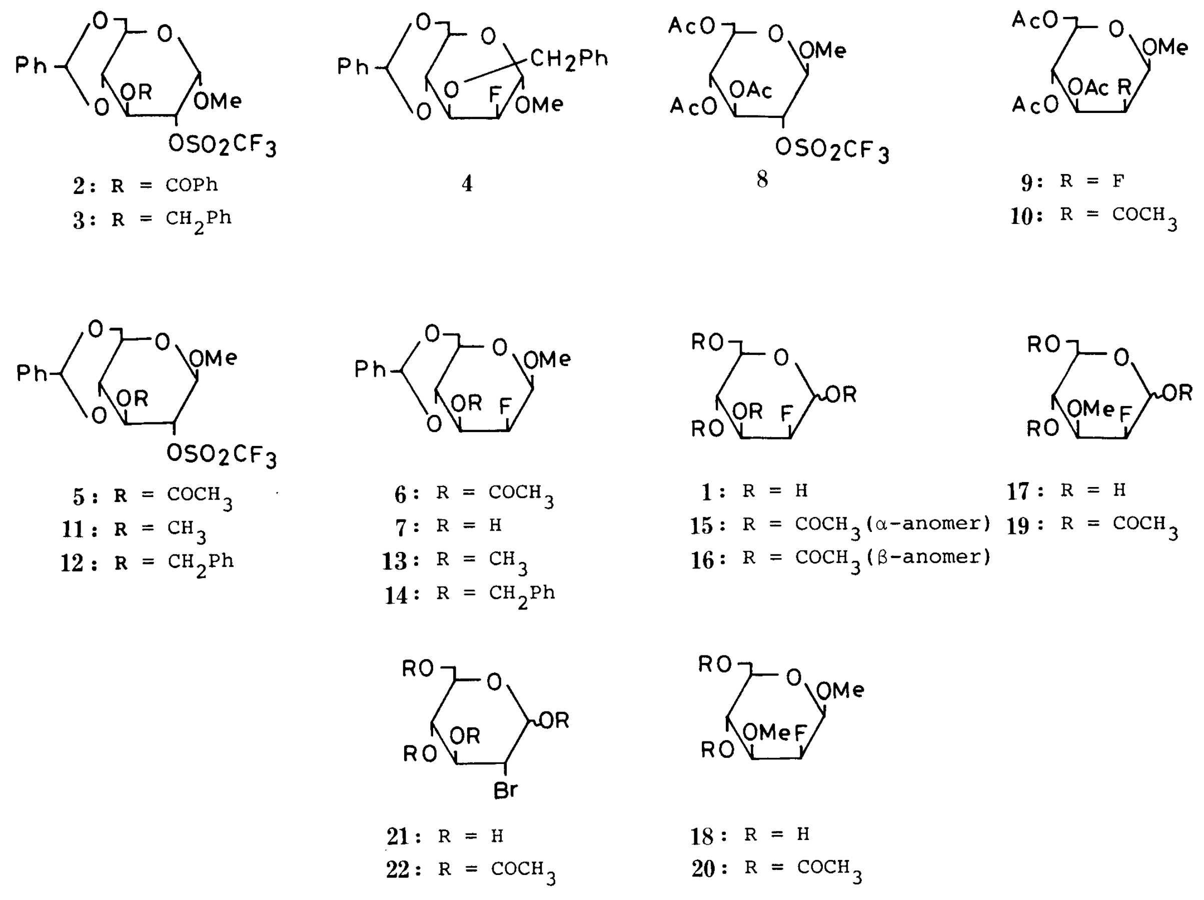
Results and Discussion

Methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-α-D-glucopyranoside (**2**), prepared according to the known procedure,[11] was initially used as a suitable triflate for a displacement reaction, and was treated with cesium fluoride, potassium fluoride or ammonium fluoride in DMF. In every case, thin layer chromatography (TLC) showed that the reaction product was a multicomponent mixture from which the desired fluoro compound could not be isolated. The reaction with tetraethylammonium fluoride (TEAF) in acetonitrile led to extensive decomposition of the triflate (**2**). On the other hand, the use of the triflate (**3**), protected as its benzyl ether, resulted in the isolation of the desired 2-fluoro-manno compound (**4**) in modest yield, on treatment with tetra-*n*-butylammonium fluoride (TBAF) in refluxing acetonitrile for 150 min.

In a further attempt to develop a facile displacement process in the fluorination step, the mechanistic requirements necessary for nucleophilic displacement of a sulfonyloxy group at C_2 in a hexopyranoside, as discussed by Richardson and Miljković *et al.*,[12] dictated the choice of a β-D-gluco-isomer. Thus, methyl 2-*O*-(trifluoromethanesulfonyl)-β-D-glucopyranosides in which the hydroxy functions were protected by acetyl groups at C_3, C_4 and C_6 (**8**) or by an acetyl (**5**), methyl (**11**) or benzyl (**12**) group at C_3 with a 4,6-benzylidene moiety were chosen for study. These triflates were prepared by sulfonylation of the corresponding protected methyl β-D-glucopyranosides with trifluoromethanesulfonic anhydride in pyridine.

The 3-*O*-acetyl triflate (**5**) reacted with tetramethylammonium fluoride (TMAF) or TEAF in refluxing acetonitrile to furnish, after 30 min, methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-fluoro-β-D-mannopyranoside (**6**) and methyl 4,6-*O*-benzylidene-2-deoxy-2-fluoro-β-D-mannopyranoside (**7**) in the yields listed in Table I. An experiment performed with TEAF at lower temperature gave a lower yield of **7** than of **6**. Furthermore, when **6** was boiled under reflux for 30 min with the same nucleophile in acetonitrile, the deacetylated compound (**7**) was produced in 70% yield. Therefore, the cleavage of the 3-*O*-acetyl bond in **6** might be a consequence of the fluoride ion's basic properties. The deacetylated compound (**7**) as a by-product was also considered to be one of the intermediates leading to FDM (**1**). Thus, fluorination of the triflate (**5**) afforded a high combined yield (81%) of the fluorinated mannopyranosides (**6** and **7**). Similar treatment of the 3,4,6-tri-*O*-acetyl triflate (**8**) with TBAF was unsatisfactory, giving a 31% yield of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-fluoro-β-D-mannopyranoside (**9**) in addition to **10** (8%) as the isolable products; side reactions, evident from TLC examination, were responsible for the low yield. The mechanism of formation of **10** during the reaction is not clear, and this was not further investigated.

In contrast to the sluggish displacement that occurred with **8**, fluorination of the triflates bearing 3-*O*-methyl and 3-*O*-benzyl groups (**11** and **12**) with tetraalkylammonium fluorides in acetonitrile proceeded smoothly, requiring only short heating for completion, to give exclusively the corresponding methyl 2-deoxy-2-fluoro-mannopyranosides (**13** and **14**) in



2: R = COPh
3: R = CH_2Ph

4

8

9: R = F
10: R = $COCH_3$

5: R = $COCH_3$
11: R = CH_3
12: R = CH_2Ph

6: R = $COCH_3$
7: R = H
13: R = CH_3
14: R = CH_2Ph

1: R = H
15: R = $COCH_3$ (α-anomer)
16: R = $COCH_3$ (β-anomer)

17: R = H
19: R = $COCH_3$

21: R = H
22: R = $COCH_3$

18: R = H
20: R = $COCH_3$

Chart 1

Table I. Fluorination of Protected Methyl 2-*O*-Trifluoromethanesulfonyl-D-glucopyranosides by Tetraalkylammonium Fluorides in Acetonitrile

Triflates	Fluorinating agents	Time (min)	Temp.	Products (% yield)	
3	$(Bu)_4NF$	150	Reflux	**4** (30)	
5	$(Et)_4NF$	30	47 °C	**6** (43)	**7** (20)
	$(Et)_4NF$	30	Reflux	**6** (10)	**7** (53)
	$(Me)_4NF$	30	Reflux	**6** (51)	**7** (30)
8	$(Bu)_4NF$	150	Reflux	**9** (31)	**10** (8)
11	$(Bu)_4NF$	40	Reflux	**13** (81)	
12	$(Bu)_4NF$	30	Reflux	**14** (77)	
	$(Me)_4NF$	80	Reflux	**14** (68)	
	$(Et)_4NF$	40	Reflux	**14** (73)	

good yields (see Table I). The best yield was achieved by the use of **11**. When cesium fluoride in DMF or acetamide was employed, **12** gave a complex mixture with little or no **14**, probably because of the formation of trifluoromethanesulfonic acid, leading to premature removal of the leaving group. The structures of the fluorinated intermediates (**6**, **7**, **9**, **13** and **14**) were determined from the elemental analyses, mass (MS) and proton nuclear magnetic resonance (^1H-NMR) spectra. In particular, the ^1H-NMR spectral analyses allowed definitive configurational assignments.

In view of the recent literature on the difficulty of removing water from tetraalkylammonium fluorides and their thermal instability, the successful fluorination described here might involve either hydrated fluoride ion or bifluoride ion,[13] although their presence in the fluorinating agents was not checked after conventional drying procedure in a vacuum desiccator. The three quaternary ammonium fluorides (TBAF, TEAF and TMAF) used as fluorinating agents showed no major differences, but TBAF and TEAF were preferred for the fluorination of the triflate (**12**) in terms of the efficiency and rate of the reaction.

The next stage in the synthesis was removal of the protecting groups in a single reaction step to give the required FDM (**1**). Hydrolysis of **9** and of a mixture of **6** and **7** with 5 N HCl under reflux for 30 min gave, in 87 and 82% yields, respectively, crystalline FDM (**1**), which showed mp, optical rotation, ^{1}H- and carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectral properties consistent with those reported.[5,14,15] The product FDM (**1**) was further characterized by conversion into an anomeric mixture of the tetraacetate, **15** and **16**, which were separable by column chromatography. On the other hand, attempts to convert methyl 4,6-*O*-benzylidene-2-deoxy-2-fluoro-3-*O*-methyl-β-D-mannopyranoside (**13**) in a single reaction step into FDM (**1**) with acidic reagents such as 50% methanesulfonic acid, $B(OCOCF_3)_3$–CF_3COOH, and Nafion-H resulted in incomplete reactions: all of these reagents removed the benzylidene substituent from **13**, but the cleavage of the methyl ether bond at C_3 and the glycosidic methyl bond proceeded poorly, and 2-deoxy-2-fluoro-3-*O*-methyl-D-mannose (**17**) or methyl 2-deoxy-2-fluoro-3-*O*-methyl-β-D-mannopyranoside (**18**) was obtained as the only isolable product (Table II). The structural proof of **17** and **18** was provided by their acetylation with acetic anhydride in pyridine. A similar difficulty due to the electronegative effect of the fluorine atom at C_2 has been reported for acidic hydrolysis of methyl 4,6-*O*-benzylidene-2-deoxy-2-fluoro-3-*O*-methyl-β-D-glucopyranoside.[9] Treatment of **13** with boron tribromide in methylene chloride was again disappointing, resulting in defluorination of the product to give 2-bromo-2-deoxy-D-glucose (**21**) as the major product, as determined by elemental analysis, MS and ^{1}H-NMR spectral analyses of its tetraacetate (**22**). Therefore, this synthetic approach to FDM (**1**) *via* the triflate (**11**), which gave an excellent yield of the fluorinated intermediate (**13**), was made ineffective by the failure in removing the protecting groups in **13**.

Defluorination by the action of boron tribromide also occurred with **4**. However, short heating of **4** with 50% methanesulfonic acid gave the required FDM (**1**), which was identical with that obtained by the reaction of **9** with 5 N HCl. Furthermore, excellent conversion of **14** into FDM (**1**) was accomplished by heating with 30 or 50% methanesulfonic acid in the yields shown in Table II.

TABLE II. Removal of the Protecting Groups from Methyl 2-Deoxy-2-fluoro-D-mannopyranoside Derivatives

Compounds	Acidic reagents	Time (min)	Temp.	Products (% yield)
4	50% CH_3SO_3H	20	Reflux	**1** (67)
	BBr_3	50	r.t.	**21** (65)
6+**7**	5 N HCl	30	Reflux	**1** (82)
9	5 N HCl	25	Reflux	**1** (87)
13	50% CH_3SO_3H	40	Reflux	**17** (93)
	Nafion-H	20	Reflux	**18** (95)
	$B(OCOCF_3)_3$	60	r.t.	**18** (86)
	BBr_3	50	r.t.	**21** (73)
14	50% CH_3SO_3H	20	Reflux	**1** (81)
	30% CH_3SO_3H	20	Reflux	**1** (88)

r.t.: room temperature.

In conclusion, our synthetic routes based on fluoride ion displacement in the triflates, followed by hydrolysis, provided more ready access to FDM (**1**) than previously available methods. With respect to the isolated yield, the ease of deblocking and the rapidity of the reaction, the synthetic sequences **5**→**6**+**7**→FDM (**1**) and **12**→**14**→FDM (**1**) proved to be more efficient (the overall yields of FDM (**1**) were 66 and 65% based on **5** and **12**, respectively). Another important feature of the present method lies in the apparent applicability of the techniques to the preparation of the ^{18}F-labeled analog of FDM (**1**), which is currently under investigation.

Experimental

All melting points are uncorrected. ^{1}H-NMR spectra were recorded on a JNM PS-100 or a JEOL FX-100 spectrometer, with tetramethylsilane (in $CDCl_3$) or sodium 4,4-dimethyl-4-silapentane-1-sulfonate (DSS) (in D_2O) as an internal reference. ^{13}C-NMR spectra were recorded on a JEOL FX-100 spectrometer in D_2O with DSS as an internal reference. Infrared (IR) spectra were recorded on a JASCO IRA-1 spectrometer. Optical rotations were determined with a JASCO DIP-SL automatic polarimeter at ambient temperature. Elemental analyses were performed by the staff of the microanalytical section of Kyushu University. Column chromatography was carried out on silica gel (Kiesel gel-60, 70—230 mesh, Merck). TLC on Kiesel gel 60-F (Merck) was used to monitor the reactions and to ascertain the purity of reaction products. The spots were visualized by spraying with aqueous sulfuric acid followed by heating. Organic extracts were dried over anhydrous sodium sulfate. Solvents were removed under reduced pressure on a rotary evaporator. Commercially available tetraalkylammonium fluorides were used for the fluorinations immediately after the following procedures. Tetramethylammonium fluoride tetrahydrate was dissolved in dry acetonitrile and the solution was evaporated to dryness at 70 °C. This procedure was repeated twice, and the resultant solid was kept under reduced pressure for 30 min at room temperature. Tetraethylammonium fluoride dihydrate was kept under reduced pressure for 5 d at room temperature. Tetra-*n*-butylammonium fluoride trihydrate was dissolved in dry benzene and the solution was evaporated to dryness at 30 °C. This procedure was repeated twice, and the resultant solid was kept under reduced pressure for 3 d at room temperature. Alternatively, this fluorinating agent was kept under reduced pressure for 7 d at room temperature.

Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-α-D-glucopyranoside (3)——Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[16] (240 mg, 0.65 mmol) was dissolved in dry pyridine (2.8 ml), then trifluoromethanesulfonic anhydride (0.3 ml, 1.78 mmol) was slowly added at −10 °C. The mixture was stirred for 80 min at 0 °C, and poured into ice-water. The resultant precipitate was filtered off, washed with water, and dissolved in chloroform. The chloroform solution was dried and evaporated at 40 °C. The resultant solid was chromatographed on silica gel using chloroform as the eluent to give **3** (298 mg, 92%) as needles, after recrystallization from ether–petroleum ether, mp 83—85 °C. $[\alpha]_D$ +35.7° ($c=2.0$, chloroform). IR (Nujol): 1150 (SO_2) cm^{-1}. MS *m/e*: 504 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 3.44 (3H, s, OCH_3), 3.56—4.36 (5H, m, H-3, 4, 5, 6), 4.70 (1H, dd, $J_{1,2}=4$ Hz, $J_{2,3}=10$ Hz, H-2), 4.72 and 4.86 (2H, 2d, $J_{gem}=12$ Hz, $PhCH_2O$), 4.95 (1H, d, H-1), 5.54 (1H, s, PhCH), 7.26—7.48 (10H, m, aromatic). *Anal.* Calcd for $C_{22}H_{23}F_3O_8S$: C, 52.37; H, 4.60. Found: C, 52.46; H, 4.64.

Methyl 3-*O*-Acetyl-4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-β-D-glucopyranoside (5)——Methyl 3-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside[17] (2.33 g, 7.2 mmol) was dissolved in dry pyridine (30 ml), and trifluoromethanesulfonic anhydride (2.66 ml, 15.8 mmol) was slowly added at −10 °C. The mixture was stirred for 1 h at 0 °C. The reaction mixture was worked up as described above. Column chromatography on silica gel with benzene gave **5** (2.5 g, 78%) as colorless needles, after recrystallization from ether, mp 112—114 °C. $[\alpha]_D$ −52° ($c=1.37$, chloroform). IR (Nujol): 1150 (SO_2) and 1760 (C=O) cm^{-1}. MS *m/e*: 456 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 2.12 (3H, s, $OCOCH_3$), 3.60 (3H, s, OCH_3), 3.48—3.88 (3H, m, H-5, 6), 4.39 (1H, dd, $J_{3,4}=8$ Hz, $J_{4,5}=6$ Hz, H-4), 4.55 (1H, d, $J_{1,2}=8$ Hz, H-1), 4.66 (1H, t, $J_{2,3}=8$ Hz, H-2), 5.48 (1H, t, H-3), 5.48 (1H, s, PhCH), 7.28—7.48 (5H, m, aromatic). *Anal.* Calcd for $C_{17}H_{19}F_3O_9S$: C, 44.74; H, 4.20. Found: C, 44.87; H, 4.24.

Methyl 3,4,6-Tri-*O*-acetyl-2-*O*-(trifluoromethanesulfonyl)-β-D-glucopyranoside (8)——Methyl 3,4,6-tri-*O*-acetyl-β-D-glucopyranoside[18] (575 mg, 1.8 mmol) was dissolved in dry pyridine (7 ml), and trifluoromethanesulfonic anhydride (0.8 ml, 4.7 mmol) was slowly added at −10 °C. The mixture was stirred for 50 min at 0 °C. After work-up as described above, the resulting solid was chromatographed on silica gel with chloroform to give **8** (500 mg, 62%) as colorless needles, after recrystallization from *n*-hexane–ether, mp 93 °C. MS *m/e*: 421 (M^+-OCH_3). ^{1}H-NMR ($CDCl_3$) δ: 2.04, 2.08, 2.10 (3H, s, $OCOCH_3$), 3.60 (3H, s, OCH_3), 3.64—3.82 (1H, m, H-5), 4.04—4.37 (2H, m, H-6), 4.51 (1H, d, $J_{1,2}=9$ Hz, H-1), 4.68 (1H, t, $J_{2,3}=9$ Hz, H-2), 5.08 (1H, t, $J_{3,4}=9$ Hz, H-3), 5.37 (1H, t, $J_{4,5}=9$ Hz, H-4). *Anal.* Calcd for $C_{14}H_{19}F_3O_{11}S$: C, 37.17; H, 4.23. Found: C, 37.12; H, 4.27.

Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-(trifluoromethanesulfonyl)-β-D-glucopyranoside (11)——Methyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranoside[19] (650 mg, 2.2 mmol) was dissolved in dry pyridine (10 ml), and trifluoromethanesulfonic anhydride (0.83 ml, 4.9 mmol) was slowly added at −10 °C. The mixture was stirred for 2 h at 0 °C, then poured into ice-water. The resultant precipitate was extracted with chloroform. The combined extracts were dried and evaporated at 40 °C. The resulting solid was chromatographed on silica gel with benzene to give **11** (744 mg, 79%) as needles, after recrystallization from ether–petroleum ether, mp 78—80 °C. $[\alpha]_D$ −41.9° (c = 1.5, chloroform). IR (Nujol): 1150 (SO_2) cm^{-1}. MS *m/e*: 428 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 3.56, 3.60 (3H, s, OCH_3), 3.30—3.68 (3H, m, H-5, 6), 3.78 (1H, t, $J_{2,3} = J_{3,4} = 10$ Hz, H-3), 4.38 (1H, dd, $J_{4,5} = 5$ Hz, H-4), 4.42—4.60 (2H, m, H-1, 2), 5.54 (1H, s, PhCH), 7.30—7.48 (5H, m, aromatic). *Anal.* Calcd for $C_{16}H_{19}F_3O_8S$: C, 44.86; H, 4.47. Found: C, 44.77; H, 4.51.

Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-*β*-D-glucopyranoside (12)——Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside[20] (300 mg, 0.8 mmol) was dissolved in dry pyridine (3 ml), and trifluoromethanesulfonic anhydride (0.3 ml, 1.78 mmol) was slowly added at −10 °C. The mixture was stirred for 2 h at 0 °C. After work-up as described for the preparation of **3**, the resulting solid was chromatographed on silica gel with benzene to give **12** (334 mg, 82%) as needles, after recrystallization from ether–petroleum ether, mp 110—111 °C. $[\alpha]_D$ −39.7° (c = 0.6, chloroform). IR (Nujol): 1150 (SO_2) cm^{-1}. MS *m/e*: 504 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 3.56 (1H, s, OCH_3), 3.32—3.96 (4H, m, H-3, 5, 6), 4.38 (1H, dd, $J_{3,4} = 10$ Hz, $J_{4,5} = 5$ Hz, H-4), 4.50 (1H, d, $J_{1,2} = 9$ Hz, H-1), 4.62 (1H, t, $J_{2,3} = 9$ Hz, H-2), 4.76 and 4.92 (2H, 2d, $J_{gem} = 11$ Hz, $PhCH_2O$), 5.56 (1H, s, PhCH), 7.26—7.50 (10H, m, aromatic). *Anal.* Calcd for $C_{22}H_{23}F_3O_8S$: C, 52.37; H, 4.60. Found: C, 52.34; H, 4.55.

Reaction of Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-*α*-D-glucopyranoside (3) with TBAF——A solution of **3** (2.03 g, 4 mmol) and TBAF (10 g) in freshly distilled acetonitrile (20 ml) was heated under reflux. The reaction was monitored by TLC (*n*-hexane–acetone, 5 : 1) and was continued until all the starting material had disappeared. After 2.5 h, the solvent was evaporated off and the residue was dissolved in chloroform. The chloroform solution was washed with water and dried. After removal of the solvent, the resulting solid was chromatographed on silica gel with *n*-hexane–acetone (5 : 1) to give methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-fluoro-*α*-D-mannopyranoside (**4**) (450 mg, 30%) as syrup. IR (neat): 1110 (C–O–C) cm^{-1}. MS *m/e*: 374 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 3.38 (3H, s, OCH_3), 3.72—4.36 (5H, m, H-3, 4, 5, 6), 4.74 (1H, dt, $J_{1,2} = J_{2,3} = 2$ Hz, $J_{2,F} = 48$ Hz, H-2), 4.86 (1H, dd, $J_{1,F} = 7$ Hz, H-1), 4.76 and 4.96 (2H, 2d, $J_{gem} = 12$ Hz, $PhCH_2O$), 5.64 (1H, s, PhCH), 7.30—7.58 (10H, m, aromatic). *Anal.* Calcd for $C_{21}H_{23}FO_5$: C, 67.37; H, 6.19. Found: C, 67.39; H, 6.26.

Reaction of Methyl 3-*O*-Acetyl-4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-*β*-D-glucopyranoside (5) with Tetraalkylammonium Fluorides——A) A solution of **5** (400 mg, 0.88 mmol) and TMAF (245 mg) in freshly distilled acetonitrile (3 ml) was refluxed for 30 min. After removal of the solvent, the residue was chromatographed on silica gel. Elution with benzene gave methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-fluoro-*β*-D-mannopyranoside (**6**) (148 mg, 51%) as colorless needles, after recrystallization from ether, mp 169 °C. $[\alpha]_D$ −80° (c = 1.15, chloroform). IR (Nujol): 1750 (C=O) cm^{-1}. MS *m/e*: 326 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 2.14 (3H, s, $OCOCH_3$), 3.60 (3H, s, OCH_3), 3.38—4.18 (3H, m, H-5, 6), 4.39 (1H, dd, $J_{3,4} = 10.3$ Hz, $J_{4,5} = 4.9$ Hz, H-4), 4.57 (1H, d, $J_{1,2} < 1$ Hz, $J_{1,F} = 20$ Hz, H-1), 4.92 (1H, dd, $J_{2,3} = 2.7$ Hz, $J_{2,F} = 50$ Hz, H-2), 5.07 (1H, ddd, $J_{3,F} = 25.8$ Hz, H-3), 5.57 (1H, s, PhCH), 7.30—7.52 (5H, m, aromatic). *Anal.* Calcd for $C_{16}H_{19}FO_6$: C, 58.89; H, 5.87. Found: C, 58.94; H, 5.72.

Further elution with benzene–acetone (10 : 1) gave methyl 4,6-*O*-benzylidene-2-deoxy-2-fluoro-*β*-D-mannopyranoside (**7**) (76 mg, 30%) as colorless needles, after recrystallization from *n*-hexane–acetone, mp 194 °C. $[\alpha]_D$ −71.5° (c = 0.9, chloroform). IR (Nujol): 3200 (OH) cm^{-1}. MS *m/e*: 284 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 2.68 (1H, s, OH), 3.58 (3H, s, OCH_3), 3.24—4.0 (4H, m, H-3, 5, 6), 4.36 (1H, dd, $J_{3,4} = 10$ Hz, $J_{4,5} = 6$ Hz, H-4), 4.42 (1H, d, $J_{1,2} < 1$ Hz, $J_{1,F} = 20$ Hz, H-1), 4.78 (1H, dd, $J_{2,3} = 3$ Hz, $J_{2,F} = 50$ Hz, H-2), 5.56 (1H, s, PhCH), 7.28—7.56 (5H, m, aromatic). *Anal.* Calcd for $C_{14}H_{17}FO_5$: C, 59.15; H, 6.03. Found: C, 59.18; H, 5.76.

B) The reaction of **5** (1.0 g) in acetonitrile (8 ml) with TEAF (1.6 g) was carried out for 30 min at 47 °C by the same procedure as described in part A; the yields of the products are shown in Table I.

C) The reaction of **5** (400 mg) in acetonitrile (3 ml) with TEAF (650 mg) was carried out for 30 min at reflux by the same procedure as described in part A; the yields of the products are shown in Table I.

Reaction of Methyl 3-*O*-Acetyl-4,6-*O*-benzylidene-2-deoxy-2-fluoro-*β*-D-mannopyranoside (6) with TEAF——A solution of **6** (100 mg) and TEAF (206 mg) in freshly distilled acetonitrile (2 ml) was stirred for 30 min at 50 °C. Afrer removal of the solvent, the residue was chromatographed on silica gel with benzene–acetone (10 : 1) to give **7** (63.6 mg, 73%) as colorless needles.

Reaction of Methyl 3,4,6-Tri-*O*-acetyl-2-*O*-(trifluoromethanesulfonyl)-*β*-D-glucopyranoside (8) with TBAF——TBAF (564 mg) was added to a solution of **8** (205 mg, 0.45 mmol) in freshly distilled acetonitrile (3 ml), and the mixture was refluxed until the starting material disappeared (TLC; chloroform–ethyl acetate, 20 : 1). After 2.5 h, the solvent was evaporated off and a chloroform solution of the residue was washed with water, dried, and evaporated. The residue was chromatographed on silica gel. Elution with benzene–ethyl acetate (10 : 1) gave methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-fluoro-*β*-D-mannopyranoside (**9**) (46 mg, 31.5%) as colorless plates, after recrystallization from *n*-hexane–acetone, mp 147.5—148.5 °C. $[\alpha]_D$ −48.5° (c = 9.7, chloroform). IR (chloroform): 1750 (C=O) cm^{-1}. MS *m/e*: 291 ($M^+ - OCH_3$). ^{1}H-NMR ($CDCl_3$) δ: 2.05, 2.10, 2.11 (3H, s, $OCOCH_3$), 3.60 (3H, s, OCH_3), 3.54—3.76 (1H, m, H-5), 4.06—4.32 (2H, m, H-6), 4.52 (1H, d, $J_{1,2} < 1$ Hz, $J_{1,F} = 17.6$ Hz, H-1), 4.82 (1H, dd, $J_{2,3} = 2.5$ Hz, $J_{2,F} = 51$ Hz, H-2), 4.99 (1H, ddd, $J_{3,4} = 9.9$ Hz, $J_{3,F} = 27$ Hz, H-3), 5.36 (1H, t, $J_{4,5} = 9.9$ Hz, H-4). *Anal.* Calcd for $C_{13}H_{19}FO_8$: C, 48.45; H, 5.94. Found: C, 48.35; H, 5.97.

Further elution with the same solvent system gave methyl 2,3,4,6-tetra-*O*-acetyl-*β*-D-mannopyranoside (**10**) (13.5 mg, 8.2%) as needles, after recrystallization from ethanol, mp 161—162 °C (lit.[21] 161 °C). IR (chloroform): 1760 (C=O) cm^{-1}. MS *m/e*: 362 (M$^+$). ^{1}H-NMR ($CDCl_3$) δ: 2.0, 2.05, 2.10, 2.19 (3H, s, $OCOCH_3$), 3.53 (3H, s, OCH_3), 3.59—3.76 (1H, m, H-5), 4.07—4.43 (2H, m, H-6), 4.56 (1H, d, $J_{1,2}=1.2$ Hz, H-1), 5.05 (1H, dd, $J_{2,3}=3.2$ Hz, $J_{3,4}=10$ Hz, H-3), 5.28 (1H, t, $J_{4,5}=10$ Hz, H-4), 5.48 (1H, dd, H-2). *Anal.* Calcd for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12. Found: C, 49.73; H, 6.09.

Reaction of Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-(trifluoromethanesulfonyl)-*β*-D-glucopyranoside (11) with TBAF——TBAF (1.17 g) was added to a solution of **11** (0.453 g, 1.05 mmol) in freshly distilled acetonitrile (5 ml), and the mixture was refluxed until the starting material disappeared (TLC; *n*-hexane–acetone, 5 : 1). After 40 min, the solvent was evaporated off and the residue was dissolved in chloroform. The chloroform solution was washed with water, dried, and evaporated. The residue was chromatographed on silica gel. Elution with *n*-hexane–acetone (5 : 1) gave methyl 4,6-*O*-benzylidene-2-deoxy-2-fluoro-3-*O*-methyl-*β*-D-mannopyranoside (**13**) (0.256 g, 81%) as needles, after recrystallization from chloroform–petroleum ether, mp 180—182 °C. $[\alpha]_D$ $-32°$ ($c=0.3$, chloroform). IR (Nujol): 1110 (C–O–C) cm^{-1}. MS *m/e*: 298 (M$^+$). ^{1}H-NMR ($CDCl_3$) δ: 3.58, 3.59 (3H, s, OCH_3), 3.30—4.44 (5H, m, H-3, 4, 5, 6), 4.48 (1H, d, $J_{1,2}<1$ Hz, $J_{1,F}=19$ Hz, H-1), 4.90 (1H, dd, $J_{2,3}=4$ Hz, $J_{2,F}=50$ Hz, H-2), 5.60 (1H, s, PhCH), 7.30—7.54 (5H, m, aromatic). *Anal.* Calcd for $C_{15}H_{19}FO_5$: C, 60.40; H, 6.42. Found: C, 60.22; H, 6.42.

Reaction of Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-*O*-(trifluoromethanesulfonyl)-*β*-D-glucopyranoside (12) with Tetraalkylammonium Fluorides——A) **12** (500 mg, 0.99 mmol) was added to a solution of TMAF (280 mg) in freshly distilled acetonitrile (10 ml), and the mixture was refluxed until the starting material disappeared (TLC; *n*-hexane–acetone, 5 : 1). After 80 min, the solvent was evaporated off and the residue was chromatographed on silica gel. Elution with *n*-hexane–acetone (5 : 1) gave methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-fluoro-*β*-D-mannopyranoside (**14**) (224 mg, 68%) as needles, after recrystallization from chloroform–petroleum ether, mp 169—171 °C. $[\alpha]_D$ $-1.1°$ ($c=0.9$, chloroform). IR (Nujol): 1090 (C–O–C) cm^{-1}. MS *m/e*: 374 (M$^+$). ^{1}H-NMR ($CDCl_3$) δ: 3.24—3.60 (1H, m, H-5), 3.56 (3H, s, OCH_3), 3.72—4.44 (4H, m, H-3, 4, 6), 4.40 (1H, d, $J_{1,2}<1$ Hz, $J_{1,F}=19$ Hz, H-1), 4.78 (1H, dd, $J_{2,3}=3$ Hz, $J_{2,F}=51$ Hz, H-2), 4.78 and 4.90 (2H, 2d, $J_{gem}=13$ Hz, $PhCH_2O$), 5.62 (1H, s, PhCH), 7.30—7.56 (10H, m, aromatic). *Anal.* Calcd for $C_{21}H_{23}FO_5$: C, 67.37; H, 6.19. Found: C, 67.12; H, 6.05.

B) A solution of **12** (383 mg) and TEAF (340 mg) in freshly distilled acetonitrile (10 ml) was heated under reflux for 40 min. The same work-up and purification as described in part A gave crystalline **14** (184 mg, 73%).

C) A solution of **12** (312 mg) and TBAF (480 mg) in acetonitrile (10 ml) was refluxed for 30 min. The same work-up and purification as described in part A gave crystalline **14** (78 mg, 77%).

Hydrolysis of Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-2-fluoro-*α*-D-mannopyranoside (4) with 50% (v/v) Methanesulfonic Acid——A mixture of **4** (66 mg, 0.176 mmol) and water (0.5 ml) containing methanesulfonic acid (0.5 ml) was refluxed for 20 min. The mixture was neutralized with ion exchange resin (AG 11A8, Bio Rad Lab.) or powdered silver carbonate. After filtration through Celite, the filtrate was evaporated to a syrup. The syrup was purified by dry-column chromatography on silica gel. Elution with ethyl acetate gave pure FDM (**1**) (21.3 mg, 67%) as a solid. Recrystallization from methanol–ethyl acetate had mp 127.5—128.5 °C (lit.[5] mp 131—132 °C). $[\alpha]_D$ $+23.4°$ ($c=1.1$, water) (lit.[5] $[\alpha]_D$ $+19°$). ^{1}H-NMR (D_2O)[14] δ: 3.29—3.84 (m, H-3, 4, 5, 6), 4.95 (d, $J_{1,2}<1$ Hz, $J_{1,F}=20.3$ Hz, H-1, *β*-anomer), 5.32 (dd, $J_{1,2}=2.0$ Hz, $J_{1,F}=7.5$ Hz, H-1, *α*-anomer). ^{13}C-NMR (D_2O)[15] *α*-anomer δ: 63.2 (s, C_6), 69.4 (s, C_4), 72.05 (d, $J_{3,F}=18$ Hz, C_3), 74.9 (s, C_5), 93.0 (d, $J_{2,F}=172$ Hz, C_2), 93.9 (d, $J_{1,F}=29$ Hz, C_1). *β*-anomer δ: 63.4 (s, C_6), 69.3 (s, C_4), 74.5 (d, $J_{3,F}=21$ Hz, C_3), 78.7 (s, C_5), 93.9 (d, $J_{2,F}=179$ Hz, C_2), 94.9 (d, $J_{1,F}=19$ Hz, C_1). *Anal.* Calcd for $C_6H_{11}FO_5$: C, 39.57; H, 6.09. Found: C, 39.56; H, 6.13.

Hydrolysis of Methyl 3-*O*-Acetyl-4,6-*O*-benzylidene-2-deoxy-2-fluoro-*β*-D-mannopyranoside (6) and Methyl 4,6-*O*-Benzylidene-2-deoxy-2-fluoro-*β*-D-mannopyranoside (7) with 5 N Hydrochloric Acid——A mixture of **6** (110 mg, 0.34 mmol) and **7** (92 mg, 0.33 mmol) was refluxed with 5 N hydrochloric acid (3 ml) for 30 min. The cooled solution was neutralized with 1 N sodium hydroxide and evaporated to dryness. The residue was chromatographed on dry silica gel. Elution with ethyl acetate gave FDM (**1**) (98 mg, 82%) as a solid, which was identical with that obtained by the reaction of **4** with 50% methanesulfonic acid.

Hydrolysis of Methyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-fluoro-*β*-D-mannopyranoside (9) with 5 N Hydrochloric Acid——The tri-*O*-acetyl mannopyranoside (**9**) (494 mg, 1.53 mmol) was refluxed with 5 N hydrochloric acid (5 ml) for 25 min. The cooled solution was neutralized with 1 N sodium hydroxide and evaporated to dryness. The residue was chromatographed on dry silica gel. Elution with ethyl acetate gave FDM (**1**) (242 mg, 87%), which was identical with that obtained by the hydrolysis of **4**.

Hydrolysis of Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-2-fluoro-*β*-D-mannopyranoside (14) with Methanesulfonic Acid——A) A mixture of **14** (102 mg, 0.2 mmol) and water (0.77 ml) containing methanesulfonic acid (0.77 ml) was heated under reflux for 20 min. The hydrolyzate was worked up as described in the case of hydrolysis of **4**. Purification by dry-column chromatography on silica gel using chloroform–methanol (5 : 1) as the eluent gave FDM (**1**) (40 mg, 81%), which was identical with that obtained by the reaction of **4** with 50% methanesulfonic acid.

B) Hydrolysis of **14** (100 mg) with 30% (v/v) methanesulfonic acid (1.56 ml) under reflux and subsequently the same procedure as described in part A gave FDM (**1**) (43 mg, 88%), which was identical with that obtained by the reaction of **4** with 50% methanesulfonic acid.

Acetylation of FDM (1)——The obtained FDM (**1**) (56 mg) was acetylated with a large excess of acetic anhydride in pyridine for 24 h at room temperature. The usual work-up afforded an α- and β-anomeric mixture (3.5 : 1) of the tetraacetate as determined from the ^{1}H-NMR spectrum, and the components were separated by chromatography on silica gel. Elution with petroleum ether–ether (5 : 3) gave 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-fluoro-α-D-mannopyranose (**15**) (55 mg) as syrup. IR (chloroform): 1760 ($C=O$) cm^{-1}. MS *m/e*: 291 ($M^+-OCOCH_3$). ^{1}H-NMR ($CDCl_3$) δ: 2.06, 2.09, 2.12, 2.18 (3H, s, $OCOCH_3$), 3.97—4.39 (3H, m, H-5, 6), 4.76 (1H, dt, $J_{1,2}=J_{2,3}=2.2$ Hz, $J_{2,F}=48.7$ Hz, H-2), 5.25 (1H, ddd, $J_{3,4}=10.2$ Hz, $J_{3,F}=25.8$ Hz, H-3), 5.42 (1H, t, $J_{4,5}=10.2$ Hz, H-4), 6.28 (1H, dd, $J_{1,F}=6.6$ Hz, H-1). *Anal.* Calcd for $C_{14}H_{19}FO_9$: C, 48.0; H, 5.47. Found: C, 48.24; H, 5.38.

Further elution with the same solvent system gave 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-fluoro-β-D-mannopyranose (**16**) (15 mg) as colorless needles, after recrystallization from ether–petroleum ether, mp 110 °C (lit.[5] mp 107—108 °C). IR (chloroform): 1765 ($C=O$) cm^{-1}. MS *m/e*: 291 ($M^+-OCOCH_3$). ^{1}H-NMR ($CDCl_3$) δ: 2.06, 2.09, 2.12, 2.19 (3H, s, $OCOCH_3$), 3.71—4.41 (3H, m, H-5, 6), 4.87 (1H, dd, $J_{1,2}<1$ Hz, $J_{2,3}=2.4$ Hz, $J_{2,F}=51.7$ Hz, H-2), 5.05 (1H, ddd, $J_{3,4}=10$ Hz, $J_{3,F}=26.5$ Hz, H-3), 5.38 (1H, t, $J_{4,5}=10$ Hz, H-4), 5.80 (1H, d, $J_{1,F}=18.9$ Hz, H-1). *Anal.* Calcd for $C_{14}H_{19}FO_9$: C, 48.0; H, 5.47. Found: C, 48.07; H, 5.54.

Reaction of Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-deoxy-2-fluoro-β- and α-D-Mannopyranoside (13 and 4) with Boron Tribromide——A) A mixture of **13** (122 mg, 0.41 mmol) and boron tribromide in dichloromethane solution (1.4 ml of 2 M solution) was allowed to stand at room temperature. After 50 min, the mixture was quenched *via* addition of crushed ice and the solution was then evaporated. The residue was dissolved in water, and neutralized with powdered silver carbonate. The resulting suspension was filtered through Celite and evaporated. The residue was chromatographed on dry silica gel. Elution with chloroform–methanol (5 : 1) gave 2-bromo-2-deoxy-D-glucopyranose (**21**) (72 mg, 73%) as a syrup.

Acetylation of **21** (70 mg) with acetic anhydride–pyridine for 24 h at room temperature and subsequent chromatography on silica gel with chloroform gave 1,3,4,6-tetra-*O*-acetyl-2-bromo-2-deoxy-D-glucopyranose (**22**) (69 mg) as colorless needles, after recrystallization from chloroform–petroleum ether, mp 73—75 °C. The ^{1}H-NMR spectrum showed it to be a mixture of the anomers with a ratio of $\alpha:\beta=3:8$. IR (Nujol): 1740 and 1765 ($C=O$) cm^{-1}. MS *m/e*: 353 ($M^++2-OCOCH_3$), 351 ($M^+-OCOCH_3$). ^{1}H-NMR ($CDCl_3$) δ: 2.0—2.21 (m, $OCOCH_3$), 3.78—4.40 (m, H-2, 5, 6), 5.01 (t, $J_{2,3}=J_{3,4}=9$ Hz, H-3, β-anomer), 5.08 (t, $J_{2,3}=J_{3,4}=9$ Hz, H-3, α-anomer), 5.34 (dd, $J_{4,5}=11$ Hz, H-4, β-anomer), 5.52 (dd, $J_{4,5}=11.5$ Hz, H-4, α-anomer), 5.82 (d, $J_{1,2}=10$ Hz, H-1, β-anomer), 6.34 (d, $J_{1,2}=3.5$ Hz, H-1, α-anomer). *Anal.* Calcd for $C_{14}H_{19}BrO_9$: C, 40.89; H, 4.66. Found: C, 40.84; H, 4.65.

B) A mixture of **4** (112 mg, 0.41 mmol) and boron tribromide in dichloromethane solution (0.95 ml of 2 M solution) was allowed to stand for 50 min at room temperature. The same work-up as described in part A gave **21** (47 mg, 65%) as a syrup.

Hydrolysis of 13 with 50% (v/v) Methanesulfonic Acid——A mixture of **13** (100 mg, 0.34 mmol) and water (0.77 ml) containing methanesulfonic acid (0.77 ml) was refluxed for 40 min. The cooled solution was stirred with ion exchange resin (AG 11A8) and then the resin was removed by filtration. The filtrate was evaporated to dryness. The residue was chromatographed on dry silica gel. Elution with chloroform–methanol (5 : 1) gave 2-deoxy-2-fluoro-3-*O*-methyl-D-mannopyranose (**17**) (61 mg, 93%) as a syrup.

Acetylation of **17** (53 mg) with acetic anhydride–pyridine in the usual manner and subsequent chromatography on silica gel with benzene–ethyl acetate (6 : 1) gave 1,4,6-tri-*O*-acetyl-2-deoxy-2-fluoro-3-*O*-methyl-D-mannopyranose (**19**) (45 mg) as colorless needles, after recrystallization from *n*-hexane–ether, mp 79.5—80.5 °C. The ^{1}H-NMR spectrum showed the product to be a mixture of the anomers with a ratio of $\alpha:\beta=7:1$. IR (chloroform): 1750 ($C=O$) cm^{-1}. MS *m/e*: 263 ($M^+-OCOCH_3$). ^{1}H-NMR ($CDCl_3$) δ: 2.06—2.19 (m, $OCOCH_3$), 3.4—4.34 (m, H-3, 5, 6), 4.80 (dt, $J_{1,2}=J_{2,3}=2$ Hz, $J_{2,F}=49$ Hz, H-2, α-anomer), 4.93 (dd, $J_{1,2}<1$ Hz, $J_{2,3}=2$ Hz, $J_{2,F}=52$ Hz, H-2, β-anomer), 5.26 (t, $J_{3,4}=J_{4,5}=10$ Hz, H-4, β-anomer), 5.32 (t, $J_{3,4}=J_{4,5}=10$ Hz, H-4, α-anomer), 5.74 (d, $J_{1,F}=19$ Hz, H-1, β-anomer), 6.28 (dd, $J_{1,F}=7$ Hz, α-anomer). *Anal.* Calcd for $C_{13}H_{19}FO_8$: C, 48.45; H, 5.94. Found: C, 48.43; H, 5.90.

Hydrolysis of 13 with Nafion-H——A mixture of **13** (102 mg, 0.34 mmol) and Nafion-H (100 mg) (supplied by Mitsui Fluoro Chemical Co., Ltd., Japan) in water (50 ml) was refluxed for 20 min. The solution was neutralized with powdered silver carbonate. The mixture was filtered through Celite and the filtrate was evaporated. Dry-column chromatography of the residue on silica gel with chloroform–methanol (5 : 1) gave methyl 2-deoxy-2-fluoro-3-*O*-methyl-β-D-mannopyranoside (**18**) (68 mg, 95%) as a solid, mp 123 °C.

Acetylation of **18** (68 mg) with acetic anhydride in pyridine in the usual manner followed by chromatography on silica gel with *n*-hexane–acetone (4 : 1) gave methyl 4,6-di-*O*-acetyl-2-deoxy-2-fluoro-3-*O*-methyl-β-D-mannopyranoside (**20**) (81 mg) as colorless needles, after recrystallization from chloroform–petroleum ether, mp 91—92 °C. IR (Nujol): 1750 ($C=O$) cm^{-1}. MS *m/e*: 263 (M^+-OCH_3). ^{1}H-NMR ($CDCl_3$) δ: 3.19—3.68 (2H, m, H-3, 5), 3.44, 3.58 (3H, s, OCH_3), 4.06—4.36 (2H, m, H-6), 4.44 (1H, d, $J_{1,2}<1$ Hz, $J_{1,F}=18$ Hz, H-1), 4.90 (1H, dd, $J_{2,3}=2$ Hz, $J_{2,F}=52$ Hz, H-2), 5.24 (1H, t, $J_{3,4}=J_{4,5}=10$ Hz, H-4). *Anal.* Calcd for $C_{12}H_{19}FO_7$: C, 48.98; H, 6.50. Found: C, 48.96; H, 6.47.

Hydrolysis of 13 with Boron Tris(trifluoroacetate)——**13** (100 mg, 0.33 mmol) was slowly added to a solution of tris(trifluoroacetate) in trifluoroacetic acid (2 mmol), prepared as described in the literature.[22] The mixture was allowed to stand for 60 min at room temperature and then evaporated. The residue was dissolved in water. Powdered silver carbonate was then added to the solution to neutralize it, the mixture was filtered through Celite, and the filtrate was evaporated. The residue was chromatographed on dry silica gel. Elution with chloroform–methanol (5 : 1) gave **18** (61 mg, 86%) as a solid, mp 123 °C, which was further characterized as the acetate **20**.

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References and Notes

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