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SYNTHESIS OF SOME MONODEOXYFLUORINATED METHYL AND 4-NITROPHENYL α-D-MANNOBIOSIDES AND A RELATED 4-NITROPHENYL α-D-MANNOTRIOSIDE*

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ABSTRACT

Treatment of methyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside with *N,N*-diethylaminosulfur trifluoride (Et_2NSF_3), followed by *O*-deacetylation and catalytic hydrogenolysis, afforded methyl 2-*O*-(6-deoxy-6-fluoro-α-D-mannopyranosyl)-α-D-mannopyranoside (**8**). Methyl 6-deoxy-6-fluoro-2-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (**11**) was similarly obtained from methyl 3-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-α-D-mannopyranoside. 1,2,3,4-Tetra-*O*-acetyl-6-deoxy-6-fluoro-β-D-mannopyranose (**13**), used for the synthesis of the 4-nitrophenyl analogs of **8** and **11**, as well as their 3-*O*-linked isomers, was obtained by treatment of 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose with Et_2NSF_3. Treatment of **13** with 4-nitrophenol in the presence of tin(IV) chloride, followed by sequential *O*-deacetylation, isopropylidenation, acetylation, and cleavage of the acetal group, afforded 4-nitrophenyl 4-*O*-acetyl-6-deoxy-6-fluoro-α-D-mannopyranoside (**18**). Treatment of **13** with HBr in glacial acetic acid furnished the 6-deoxy-6-fluoro bromide **19**. Glycosylation of diol **18** with **20** gave 4-nitrophenyl 4-*O*-acetyl-6-deoxy-6-fluoro-3-*O*- (**21**) and -2-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**23**) in the ratio of ~2:1, together with a small proportion of a branched trisaccharide. 4-Nitrophenyl 4,6-di-*O*-acetyl-α-D-mannopyranoside was similarly glycosylated with bromide **19** to give 4-nitrophenyl 4,6-di-*O*-acetyl-3-*O*- and -2-*O*-(2,3,4-tri-*O*-acetyl-6-deoxy-6-fluoro-α-D-mannopyranosyl)-α-D-mannopyranoside. The various di- and tri-saccharides were *O*-deacetylated by Zemplén transesterification.

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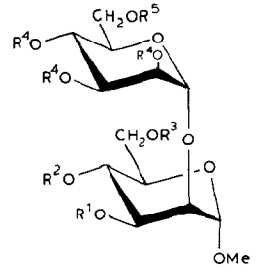
INTRODUCTION

D-Mannose 6-phosphate is now generally considered to be an essential part of a recognition marker involved in the targeting of the newly synthesized lysosomal enzymes to lysosomes[2]. Thus, in our study of lysosomal-enzyme targeting, we[3] explored the use of various D-mannobiosides as acceptor-substrate for GlcNAc-*P*-transferase. Of all the mannobiosides studied, methyl 2-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (**1**) was found to be the preferred acceptor for this enzyme. However, it was of interest to establish the site of phosphorylation in **1**. To this end, we employed two monodeoxyfluorinated analogs of **1**, and showed that phosphorylation occurs at the terminal D-mannopyranosyl groups[4]. In that communication, we briefly described the synthesis of the two disaccharides, methyl 2-*O*-(6-deoxy-6-fluoro-α-D-mannopyranosyl)-α-D-mannopyranoside (**8**) and methyl 6-deoxy-6-fluoro-2-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (**11**). We describe herein in more detail the synthesis of these two disaccharides and also that of their 4-nitrophenyl counterparts, their O-3-linked isomers, as well as a related 2,3-substituted trisaccharide.

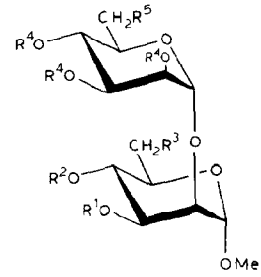
By analogy to recent studies on amyloglucosidase (EC. 3.2.1.3, AMP) inhibitors[5], it is possible that such compounds may also prove useful as inhibitors for the α-D-mannosidases that are involved in the processing of *N*-glycosyl-linked glycoproteins. The implication of this on studies related to the HIV-envelope glycoproteins cannot be overlooked[6].

RESULTS AND DISCUSSION

Treatment of methyl 3,4,6-tri-*O*-benzyl-2-*O*-α-D-mannopyranosyl-α-D-mannopyranoside[3] (**2**) with chlorotriphenylmethane, followed by acetylation and chromatography, afforded amorphous methyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-acetyl-6-*O*-triphenylmethyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**3**) in 82% yield, the ^{1}H-n.m.r. spectrum of which was consistent with the structure assigned. Hydrolysis of the triphenylmethyl group of **3** with hot, 80% aqueous acetic acid gave methyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**4**) in 66% yield. Treatment of **4** with *N,N*-diethylaminosulfur trifluoride (Et_2NSF_3) according to literature procedure[7], followed by purification of the crude product by chromatography, provided methyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-acetyl-6-deoxy-6-fluoro-α-D-mannopyranosyl)-α-D-mannopyranoside (**6**) in 67% yield. *O*-Deacetylation of **6** with 2:1:1 (v/v) methanol–triethylamine–water gave, in 93% yield, the benzylated disaccharide **7**, which was hydrogenolyzed to furnish the disaccharide methyl 2-*O*-(6-deoxy-6-fluoro-α-D-mannopyranosyl)-α-D-mannopyranoside (**8**). The ^{19}F-n.m.r. spectrum of **8** was consistent with the structure expected: doublets of triplets were observed at ϕ −233.5, with spacings of 47.3 and 26.7 Hz, attributable to the coupling of F-6 with H-6 and H-5, respectively.



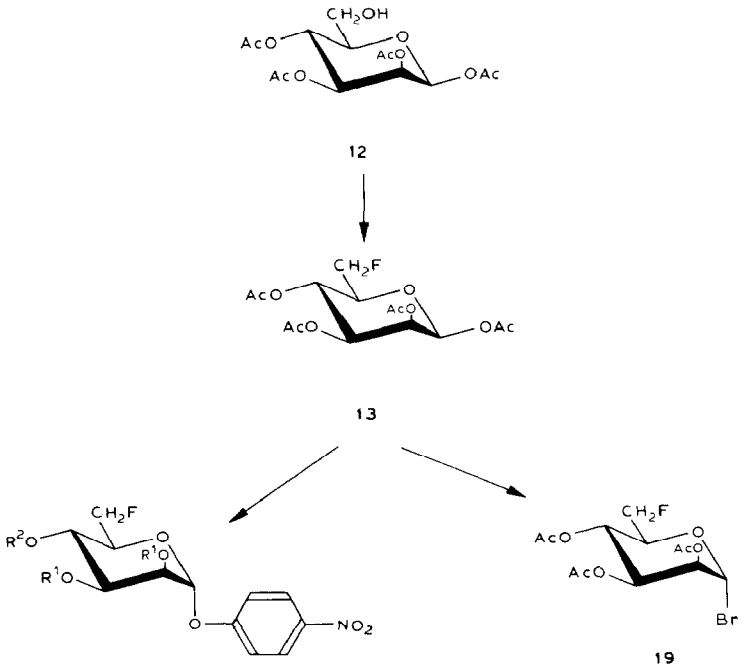
	R^1	R^2	R^3	R^4	R^5
1	H	H	H	H	H
2	Bn	Bn	Bn	H	H
3	Bn	Bn	Bn	Ac	Tr
4	Bn	Bn	Bn	Ac	H
5	Bn	H	H	Ac	Ac



	R^1	R^2	R^3	R^4	R^5
6	Bn	Bn	OBn	Ac	F
7	Bn	Bn	OBn	H	F
8	H	H	OH	H	F
9	Bn	H	F	Ac	OAc
10	Bn	H	F	H	OH
11	H	H	F	H	OH

For the synthesis of methyl 6-deoxy-6-fluoro-2-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (**11**), methyl 3-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside[8] (**5**) was treated with Et_2NSF_3, as described for **4** (to give **6**), to afford after chromatography the 6-monodeoxyfluorinated derivative **9**, which was *O*-deacetylated to yield amorphous methyl 3-*O*-benzyl-6-deoxy-6-fluoro-2-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (**10**). Hydrogenolysis of the benzyl groups of **10** furnished the desired disaccharide **11**, the ^{19}F-n.m.r. spectrum of which was in accord with the structure proposed.

For the synthesis of the isomeric disaccharides **22** and **24**, or **29** and **31**, a diol system such as **18** or its nonfluorinated counterpart **27** can serve as a precursor, provided that the pairs of isomeric disaccharides are readily separable. This approach entailed the preparation of the glycosyl acceptor, 4-nitrophenyl 4-*O*-acetyl-6-deoxy-6-fluoro-α-D-mannopyranoside (**18**), and the glycosyl donor, 2,3,4-tri-*O*-acetyl-6-deoxy-6-fluoro-α-D-mannopyranosyl bromide (**19**). Both **18** and **19** were readily obtained from a common precursor, namely, 1,2,3,4-tetra-*O*-acetyl-6-deoxy-6-fluoro-β-D-mannopyranose[9] (**13**), obtained by treatment of the known[10] 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose (**12**) with *N*,*N*-diethylaminosulfur trifluoride (Et_2NSF_3) in Diglyme. Treatment of **13** with 4-nitrophenol in boiling dichloromethane in the presence of tin(IV) chloride afforded, in 60% yield, crystalline **14**. It was *O*-deacetylated with Amberlyst A-26 (OH^-) in methanol[11], and then converted into a 2,3-*O*-isopropylidene acetal **16** by reaction with 2,2-dimethoxypropane–acetone in the presence of 4-toluenesulfonic acid. Acetylation of **16**, followed by cleavage of the 2,3-*O*-acetal group with aqueous trifluoroacetic acid in chloroform, then gave the desired **18**. For the preparation of **19**, compound **13** was treated, in the cold, with 31% hydrobromic acid in glacial acetic acid in dichloromethane–acetic anhydride. Bromide **19** was obtained in 86% yield as an amorphous

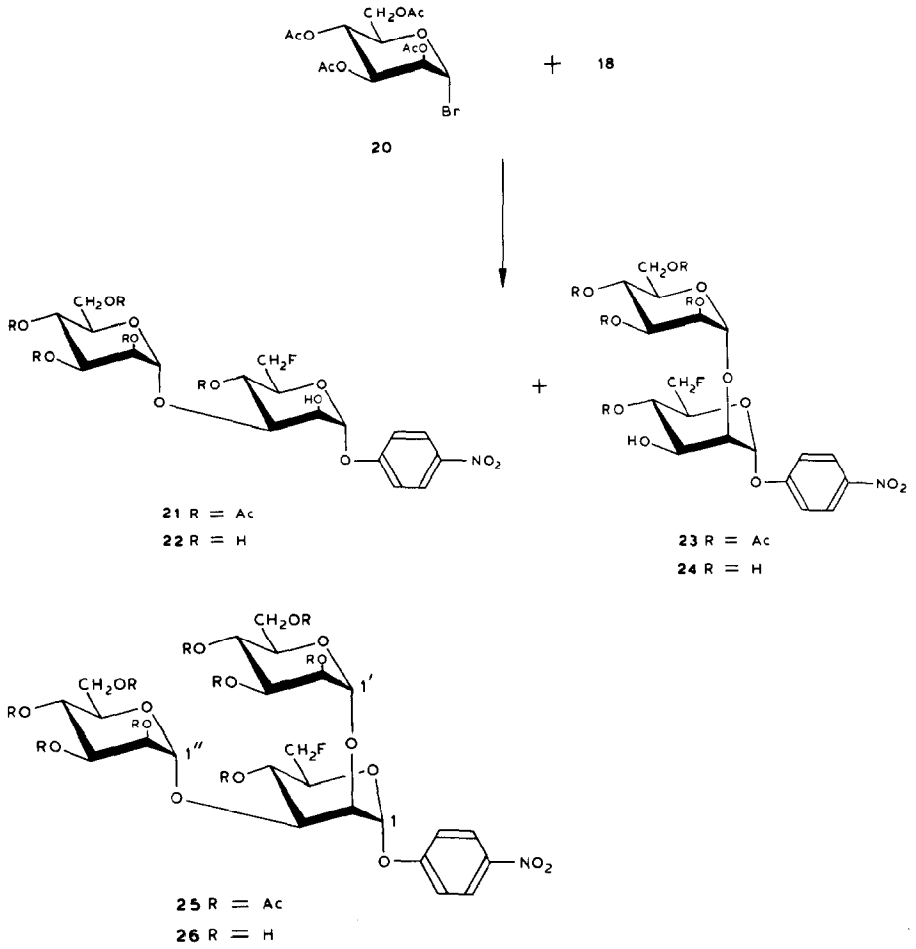


14 $R^1 = R^2 = R^3 = Ac$
15 $R^1 = R^2 = R^3 = H$
16 $R^1, R^2 = CMe_2$; $R^3 = H$
17 $R^1, R^2 = CMe_2$; $R^3 = Ac$
18 $R^1 = R^2 = H$; $R^3 = Ac$

solid. Its ^{1}H-n.m.r. spectrum exhibited a low-field (δ 6.33) one-proton doublet with a small (~1 Hz) spacing, suggesting that it existed almost exclusively as the α anomer. Its ^{19}F-n.m.r. spectrum contained doublets of triplet at ϕ −230 (J ~48.8 and 25.5 Hz), in agreement with the presence of a fluorine atom at C-6.

When diol **18** was treated with 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide (**20**) in acetonitrile and in the presence of mercury(II) cyanide–mercury(II) bromide, substantial diglycosylation occurred; trisaccharide **25**, and disaccharides **21** and **23** were obtained in 19, 23, and 4.5% yields, respectively. However, when glycosylation of diol **18** was conducted in warm 1:1 benzene–nitromethane as solvent, the disaccharides **21** and **23** were obtained in a ratio of 2:1, and very little diglycosylation occurred. Crystalline **21**, as well as amorphous **23** and **25**, were all analytically pure, and had ^{1}H-n.m.r. spectra in support of their expected structures (see Experimental section). *O*-Deacetylation of **21, 23,** and **25** furnished the disaccharides **22, 24,** and trisaccharide **26**, in 68, 73, and 52% yield, respectively, the ^{13}C- and ^{19}F-n.m.r. spectra of which were consistent with the structures assigned.

Glycosylation of 4-nitrophenyl 4,6-di-*O*-acetyl-α-D-mannopyranoside[12] (**27**) with bromide **19** in warm 1:1 benzene–nitromethane in the presence of mercury(II)



cyanide–mercury(II) bromide afforded the (1→3)-linked disaccharide **28**, and the (1→2)-linked disaccharide **30** in 28.5 and 11.4% yield, respectively; very little diglycosylation occurred (t.l.c.). However, when acetonitrile was used as solvent, the overall yield of the isomeric disaccharides was substantially decreased. The ratio (5:1) of the two isomeric disaccharides **28** and **30** was similar to that observed for the products of the analogous reaction of **20** and **18** (to give **21** and **23**).

O-Deacetylation of **28** and **30** in a manner analogous to that described for **21** (to give **22**) then furnished the desired disaccharides, 4-nitrophenyl 3-*O*- (**29**) and 2-*O*-(6-deoxy-6-fluoro-α-D-mannopyranosyl)-α-D-mannopyranoside (**31**), in 68 and 58% yield, respectively. The ^{19}F- and ^{13}C-n.m.r. spectra of both compounds were consistent with the structures assigned (see Experimental section and Table I).

^{13}C-N.m.r. assignments. — The ^{13}C-n.m.r. resonances for the methyl α-D-mannobiosides **8** and **11** were assigned by comparing their spectra with each other and with that of methyl 2-*O*-α-D-mannopyranosyl-α-D-mannopyranoside[3] (**1**) (see

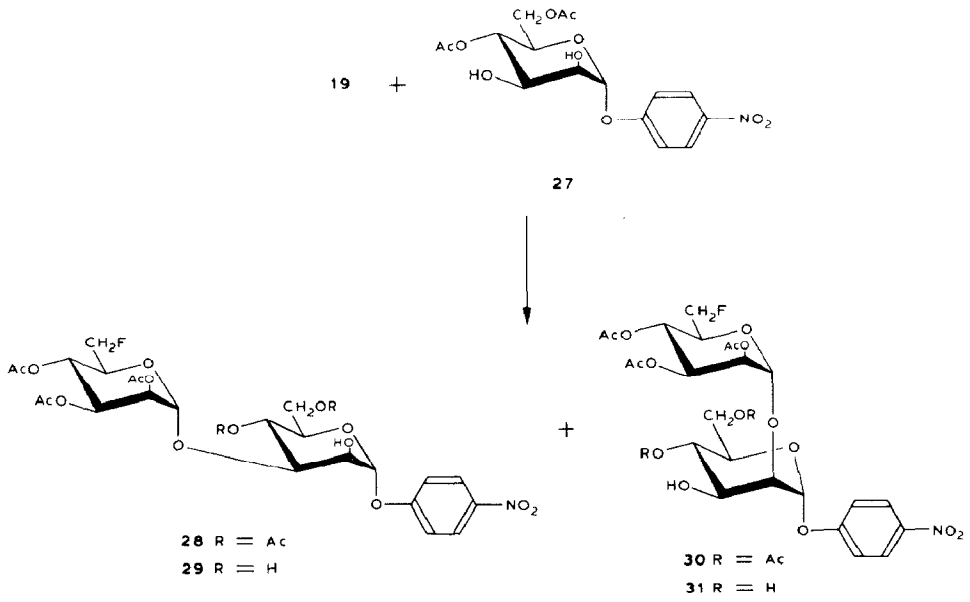


Table I). In the ^{13}C-n.m.r. spectrum of **8**, the signals for C-1 and C-1′ were observed at δ 100.80 and 103.73, whereas their counterparts in the spectrum of **11** occurred at δ 101.08 and 103.69, in agreement with α-D configurations at all of the anomeric centers. The signal for C-6′ in the ^{13}C-n.m.r. spectrum of **8**, and that for C-6 in the spectrum of **11** were observed at δ 83.97 and 83.72, respectively, thereby showing noticeable downfield shifts by comparison to their counterparts in the spectrum of the parent disaccharide **1**. Both signals resonated as doublets (J ~167.5 Hz) because of substitution with fluorine atoms. The resonances for C-4′ (δ 66.93) and C-5′ (δ 73.21) in the ^{13}C-n.m.r. spectrum of **8**, and for C-4 (δ 66.98) and C-5 (δ 72.65) in the spectrum of **11** were all shifted slightly upfield (0.75–0.89 p.p.m.), and resonated as doublets with spacings of 7.2–17.4 Hz, also because of the presence of fluorine atoms at C-6 and C-6′.

In the case of the disaccharides **22, 24, 29,** and **31,** and the trisaccharide **26**, the ^{13}C-n.m.r. assignments were made by comparing their spectra with each other and with those of 4-nitrophenyl 6-deoxy-6-fluoro-α-D-mannopyranoside (**15**) (see Table I) and the parent disaccharides 4-nitrophenyl 2-*O*- and 3-*O*-α-D-mannopyranosyl-α-D-mannopyranoside[13]. Similar trends were observed for the effect of substitution on the chemical shifts of the various carbon resonances. Thus, in the ^{13}C-n.m.r. spectra of **22, 24, 26, 29,** and **31**, the resonances for C-1 were in the range of δ 96.42–98.38, in agreement with an α-D configuration for C-1 bearing a 4-nitrophenyl group. The resonances for C-1′ of **22, 24, 26, 29,** and **31**, and for C-1″ of **26** were all in the range of δ 102.22–102.80, in agreement with an α-D configuration at the interglycosidic linkages. The occurrence at low field of the signals attributable to C-3 (δ 77.40) of **22**, C-2 (δ 77.50) of **24**, C-2 and C-3 (δ 76.33 and

TABLE I

PROPOSED ^{13}C-N.M.R. CHEMICAL SHIFTS (δ)[a] AND C-F COUPLING CONSTANTS[b]

Residue or group	*Compd.*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
α-D-Man*p*OMe	**1**	100.1	79.3	70.8	67.8	73.4	61.9
α-D-Man*p*-(1→2)		103.0	71.7	71.7	67.8	74.1	61.8
α-D-Man*p*OMe	**8**	100.80	79.97	71.53	68.24	74.01	62.22
6-F-α-D-Man*p*-(1→2)		103.73	71.53	71.17	66.93	73.21	83.97
					(7.2)	(17.4)	(167.4)
6-F-α-D-Man*p*OMe	**11**	101.08	79.58	71.32	66.98	72.65	83.72
					(7.5)	(17.4)	(167.5)
α-D-Man*p*-(1→2)		103.69	71.46	71.67	68.14	74.65	62.36
6-F-α-D-Man*p*$OC_6H_4NO_2$-4	**15**	98.49	70.39	69.57	75.17	73.40	82.41
					(6.8)	(17.3)	(169.8)
6-F-α-D-Man*p*$OC_6H_4NO_2$-4	**22**	98.38	68.70	77.40	64.03	73.35	82.08
					(6.9)	(17.5)	(169.3)
α-D-Man*p*-(1→3)		102.22	70.20	70.73	67.12	73.88	61.15
6-F-α-D-Man*p*$OC_6H_4NO_2$-4	**24**	96.59	77.50	69.51	65.17	73.04	82.10
					(6.2)	(17.2)	(170.0)
α-D-Man*p*-(1→2)		102.80	70.67	69.98	67.11	74.48	61.42
6-F-α-D-Man*p*$OC_6H_4NO_2$-4	**26**	96.42	76.33	77.54	64.51	73.15	82.04
					(7.6)	(17.5)	(170.6)
α-D-Man*p*-(1→2)		102.75	70.36	70.89	67.12	74.57	61.39
α-D-Man*p*-(1→3)		102.56	70.81	70.20	67.12	74.76	61.56
α-D-Man*p*$OC_6H_4NO_2$-4	**29**	98.59	70.49	77.83	65.40	75.52	60.67
6-F-α-D-Man*p*-(1→3)		103.46	70.06	70.06	65.61	71.91	82.89
					(5.0)	(17.4)	(169.0)
α-D-Man*p*-$OC_6H_4NO_2$-4	**31**	97.13	76.83	69.83	66.66	75.45	60.84
6-F-α-D-Man*p*-(1→2)		102.33	70.48	69.83	65.52	72.24	83.21
					(6.1)	(15.8)	(169.2)

[a]At 100.6 MHz for solutions in ($^2H_3$)Me_2SO with Me_4Si as the internal standard; except for compounds **1**, **8**, and **11**, which were recorded at 25.2 MHz and the solvent was D_2O with Me_4Si as the external standard. All spectra were recorded at ~25°, and the aromatic and OMe resonances are not shown. [b]In hertz in parentheses.

77.54, respectively) of **26**, C-3 (δ 77.83) of **29**, and C-2 (δ 76.83) of **31** was a clear indication that these carbon atoms were sites of glycosylation. In the ^{13}C-n.m.r. spectra of **22**, **24**, and **26**, the resonance for C-6 was observed at low field (δ 82) with spacings of ~170 Hz because of substitution with a fluorine atom at this position. A similar situation was also observed for C-6′ of **29** and **31**. Similarly, the signals for both C-5 and C-4 of **22**, **24**, and **26** occurred as doublets with spacings of 17.2–17.5 Hz for the former, and 6.2–7.6 Hz for the latter, and an exactly analogous picture was also observed for C-5′ and C-4′ of **29** and **31**.

EXPERIMENTAL

General methods. — Melting points were determined with a Fisher–Johns apparatus and are uncorrected. Optical rotations were measured at ~25° with a Perkin–Elmer 241 polarimeter. N.m.r. spectra were recorded at ~250°; ^{1}H-n.m.r.

spectra with a Varian EM-390 instrument operating at 90 MHz; ^{19}F-n.m.r. spectra either with a Varian EM 390, or with a Varian XL-100, or a Bruker AM-400 instrument, at 84.7, 94.1, and 376.4 MHz, respectively; and ^{13}C-n.m.r. spectra with a Varian XL-100 or a Bruker AM-400 instrument at 25.2 and 100.6 MHz, respectively. The chemical shifts (δ and ϕ) are reported downfield from those of Me_4Si and $CFCl_3$, respectively.

T.l.c. was conducted on aluminum sheets, precoated with 0.2-mm layers of Silica Gel 60F-25 (E. Merck, Darmstadt, Germany); the components were located either by exposure to u.v. light or by spraying with 5% H_2SO_4 in ethanol (or both) and heating. Preparative t.l.c. was conducted on 20 × 20 cm glass sheets, precoated with 1-mm layers of silica gel (Analtech, New York, U.S.A.), and applying u.v. detection. Silica gel used for column chromatography was Baker Analyzed (60–200 mesh). All proportions of solvents are v/v. Unless otherwise indicated, the following solvent systems were used for chromatography: (*A*) 13:6:1 chloroform–methanol–water, (*B*) 9:1 chloroform–methanol, and (*C*) 4:1 chloroform–acetone. Solutions in organic solvents were dried with anhydrous Na_2SO_4. Pyridine and benzene were dried over KOH and Na, respectively. Dichloromethane was dried over 4A molecular sieves. Nitromethane and acetonitrile were distilled from P_2O_5 immediately before use. Elemental analyses were performed by Robertson Laboratory, 29 Samson Ave., Madison, New Jersey 07940.

*Methyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-acetyl-6-*O*-triphenylmethyl-α-*D*-mannopyranosyl)-α-*D*-mannopyranoside* (**3**). — A mixture of methyl 3,4,6-tri-*O*-benzyl-2-*O*-α-D-mannopyranosyl-α-D-mannopyranoside[3] (**2**; 3 g) and chlorotriphenylmethane (6 g) in pyridine (100 mL) was stirred overnight at 60°. Acetic anhydride (25 mL) was then added and the stirring was continued for 2 h at the same temperature. The mixture was cooled to room temperature and poured, with stirring, into ice–water. The solid that separated was filtered off, thoroughly washed with cold water, dried, and chromatographed (2:1 hexane–ethyl acetate) to give **3** (4.3 g, 82%), amorphous powder, $[\alpha]_D^{25}$ +43° (*c* 0.6, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.03–7.45 (m, 30 H, arom.), 3.24 (s, 3 H, OMe), 2.09, 1.84, and 1.60 (s, 3 H each, 3 OAc).

Anal. Calc. for $C_{59}H_{62}O_{14}$: C, 71.20; H, 6.29. Found: C, 70.98; H, 6.05.

*Methyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-*D*-mannopyranosyl)-α-*D*-mannopyranoside* (**4**). — A suspension of **3** (3.8 g) in 80% aqueous acetic acid (150 mL) was heated for 1 h at 80°. After conventional processing, the crude product was chromatographed (1:49 acetone–chloroform) to give **4** (1.9 g, 66%), a syrup, $[\alpha]_D^{25}$ +40.5° (*c* 1.0, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.03–7.33 (m, 15 H, arom.), 3.27 (s, 3 H, OMe), 2.06 (s, 3 H, OAc), and 1.87 (s, 6 H, 2 OAc).

Anal. Calc. for $C_{40}H_{48}O_{14}$: C, 63.81; H, 6.44. Found: C, 63.67; H, 6.35.

*Methyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-acetyl-6-deoxy-6-fluoro-α-*D*-mannopyranosyl)-α-*D*-mannopyranoside* (**6**). — A solution of **4** (1.5 g, 2 mmol) in dry Diglyme (25 mL) was added with stirring, in small portions, to a cold (−20°, bath) solution of *N,N*-diethylaminosulfur trifluoride (Et_2NSF_3; 1.0 mL, 8.2 mmol) in

Diglyme (20 mL), and stirring was continued for 20 min at −20°. The mixture was allowed to warm to room temperature, and stirring was continued for additional 5 h. After the usual processing, the crude product was purified by chromatography (chloroform) to afford syrupy **6** (1 g, 66.5%), $[\alpha]_D^{25}$ +43° (*c* 0.5, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.09–7.33 (m, 15 H, arom.), 3.33 (s, 3 H, OMe), 2.09 (s, 3 H, OAc), and 1.99 (s, 6 H, 2 OAc).

Anal. Calc. for $C_{40}H_{47}FO_{13}$: C, 63.64; H, 6.29. Found: C, 63.60; H, 5.95.

*Methyl 3,4,6-tri-*O*-benzyl-2-*O*-(6-deoxy-6-fluoro-α-*D*-mannopyranosyl)-α-*D*-mannopyranoside* (**7**). — Compound **6** (0.9 g) was stirred overnight at room temperature in 2:1:1 (v/v) methanol–triethylamine–water (120 mL). The mixture was concentrated with coevaporation of toluene and the residue was chromatographed. Elution with 1:49 methanol–chloroform afforded **7** (0.7 g, 93%), amorphous, $[\alpha]_D^{26}$ +48.5° (*c* 1.0, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.06–7.36 (m, 15 H, arom.) and 3.33 (s, 3 H, OMe).

Anal. Calc. for $C_{34}H_{41}FO_{10}\cdot 0.5H_2O$: C, 64.02; H, 6.65. Found: C, 63.88; H, 6.60.

*Methyl 2-*O*-(6-deoxy-6-fluoro-α-*D*-mannopyranosyl)-α-*D*-mannopyranoside* (**8**). — A mixture of compound **7** (0.4 g) and 10% Pd–C (0.4 g) in glacial acetic acid (30 mL) was shaken under H_2 at ~345 kPa for 2 days at room temperature. The suspension was processed conventionally and the crude product was chromatographed. Elution with solvent *A* furnished amorphous **8** (0.2 g, 91%), $[\alpha]_D^{26}$ +51° (*c* 1.3, water; ^{19}F-n.m.r. (D_2O): φ −233.47 (dt, $J_{F\text{-}6',H\text{-}6a',6b'}$ 47.30, $J_{F\text{-}6',H\text{-}5'}$ 26.70 Hz, F-6′); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{13}H_{23}FO_{10}$: C, 43.79; H, 6.46. Found: C, 43.37; H, 6.46.

*Methyl 3-*O*-benzyl-6-deoxy-6-fluoro-2-*O*-(2,3,4,6-tetra-*O*-acetyl-α-*D*-mannopyranosyl)-α-*D*-mannopyranoside* (**9**). — Compound **5** (ref. 8; 5.4 g, 8.8 mmol) was allowed to react with Et_2NSF_3 (2.4 mL, 19.65 mmol), as described for **4** (to give **6**), to give after chromatography (7:3 hexane–ethyl acetate) amorphous **9** (2.5 g, 48%), $[\alpha]_D^{25}$ +48° (*c* 1.4, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.10–7.29 (m, 5 H, arom.), 3.36 (s, 3 H, OMe), and 2.10–1.79 (cluster of s, 12 H, 4 OAc).

Anal. Calc. for $C_{28}H_{37}FO_{14}\cdot H_2O$: C, 52.98; H, 6.20. Found: C, 52.94; H, 5.95.

*Methyl 3-*O*-benzyl-6-deoxy-6-fluoro-2-*O*-α-*D*-mannopyranosyl-α-*D*-mannopyranoside* (**10**). — Compound **9** (1.9 g) was *O*-deacetylated as described for **6** (to give **7**) to give after chromatography (solvent *B*) **10** (1.2 g, 87%), amorphous, $[\alpha]_D^{26}$ +36° (*c* 0.9, chloroform).

Anal. Calc. for $C_{20}H_{29}FO_{10}$: C, 53.56; H, 6.53. Found: C, 53.47; H, 6.77.

*Methyl 6-deoxy-6-fluoro-2-*O*-α-*D*-mannopyranosyl-α-*D*-mannopyranoside* (**11**). — Compound **10** (0.6 g) was hydrogenolyzed in 4:1 (v/v) ethanol–glacial acetic acid (30 mL), as decribed for **7** (to give **8**), to give after chromatography (solvent *A*) **11** (0.45 g, 90%), amorphous, $[\alpha]_D^{25}$ +55° (*c* 1.5, water); ^{19}F-n.m.r. (D_2O): φ −234.06 (ddt, $J_{F\text{-}6,H\text{-}6a,6b}$ 47.50, $J_{F\text{-}6,H\text{-}5}$ 30.50, $J_{F\text{-}6,H\text{-}4}$ 3.0 Hz, F-6); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{13}H_{23}FO_{10}$: C, 43.79; H, 6.46. Found: C, 43.38; H, 6.20.

*1,2,3,4-Tetra-O-acetyl-6-deoxy-6-fluoro-β-*D*-mannopyranose* (**13**). — A solution of 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose[10] (**12**; 6 g, 17.23 mmol) in dry Diglyme (50 mL) was slowly introduced with stirring into a cold (−10°, bath) solution of Et_2NSF_3 (8.6 mL, 70.43 mmol) in Diglyme (50 mL). After 1 h at −10°, the mixture was allowed to warm to room temperature, and stirring was continued for an additional 5 h. It was then poured into ice–water and extracted with chloroform (~300 mL). The chloroform solution was repeatedly washed with water, dried, and concentrated to a yellowish syrup, which showed (t.l.c., solvent *C*) the presence of a major product migrating faster than **12**, a trace of **12**, as well as some slower-migrating contaminants. The crude product was chromatographed (1:1 chloroform–hexane→chloroform) to afford **13** (2.5 g, 42%), m.p. 114–116° (chloroform–ether), $[\alpha]_D^{24}$ −13.5° (*c* 1.1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 5.90 (s, 1 H, H-1), 4.47 (dd, 2 H, $J_{H\text{-}6a,6b,F\text{-}6}$ ~46.5, $J_{H\text{-}6a,6b,H\text{-}5}$ ~4 Hz, H-6a,6b), 2.27, 2.17, 2.13, and 1.97 (s, 3 H each, 4 OAc); ^{19}F-n.m.r. ($CDCl_3$): φ +229.35 (dt, $J_{F\text{-}6,H\text{-}6a,6b}$ ~47.60, $J_{F\text{-}6,H\text{-}5}$ ~21.60 Hz, F-6).

Anal. Calc. for $C_{14}H_{19}FO_9$: C, 48.00; H, 5.47; Found: C, 48.19; H, 5.37.

*4-Nitrophenyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-fluoro-α-*D*-mannopyranoside* (**14**). — A mixture of **13** (3.5 g, 10 mmol), 4-nitrophenol (1.39 g, 10 mmol) and $SnCl_4$ (2.4 mL, 20.51 mmol) in dichloromethane (10 mL) was boiled for 4 h in an atmosphere of N_2. After cooling to room temperature, the mixture was diluted with dichloromethane (100 mL), and successively washed with water, saturated aqueous $NaHCO_3$, water, dried, and concentrated. The crude product was chromatographed (3:1 chloroform–hexane→chloroform) to give **14** (2.59 g, 60%), m.p. 171–173° (from 2-propanol), $[\alpha]_D^{24}$ +120.5° (*c* 1.0, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 8.20 and 7.16 (d, 2 H each, *J* ~9 Hz, arom.), 5.60 (s, 1 H, H-1), 4.40 (dd, 2 H, $J_{H\text{-}6a,6b,F\text{-}6}$ ~48, $J_{H\text{-}6a,6b,H\text{-}5}$ ~4 Hz, H-6a,6b), 2.16 (s, 3 H, OAc), and 2.03 (s, 6 H, 2 OAc).

Anal. Calc. for $C_{18}H_{20}FNO_{10}$: C, 50.35; H, 4.69; N, 3.26. Found: C, 50.12; H, 4.58; N, 3.16.

*4-Nitrophenyl 6-deoxy-6-fluoro-α-*D*-mannopyranoside* (**15**). — A mixture of **14** (2.56 g) and Amberlyst A-26 (OH^-) anion-exchange resin (0.35 g) in methanol (60 mL) was stirred overnight at room temperature. T.l.c. (solvent *B*) then showed that the reaction was complete. The resin was filtered off and thoroughly washed with methanol, and the combined filtrates were concentrated to give a solid. Crystallization from ethanol afforded **15** (1.7 g, 92%), m.p. 161–162°, $[\alpha]_D^{24}$ +155° (*c* 1.1, methanol); ^{1}H-n.m.r. [($^2H_3$)Me_2SO]: δ 8.17 and 7.24 (d, 2 H each, *J* ~9 Hz, arom.) and 5.60 (d, 1 H, *J* ~1 Hz, H-1); ^{19}F-n.m.r. [($^2H_3$)Me_2SO]: φ −230.81 (dt, $J_{F\text{-}6,H\text{-}6a,6b}$ 47.9, $J_{F\text{-}6,H\text{-}5}$ 25.7 Hz, F-6).

Anal. Calc. for $C_{12}H_{14}FNO_7$: C, 47.53; H, 4.65; N, 4.62. Found: C, 47.50; H, 4.50; N, 4.49.

*4-Nitrophenyl 6-deoxy-6-fluoro-2,3-*O*-isopropylidene-α-*D*-mannopyranoside* (**16**). — A mixture of **15** (1.58 g) and 4-toluenesulfonic acid monohydrate (0.3 g) in

acetone (25 mL) and 2,2-dimethoxypropane (25 mL) was stirred overnight at room temperature. T.l.c. (solvent *C*) showed the presence of a major product, faster-migrating than **15**, together with small proportions of faster- and slower-migrating contaminants. The acid was neutralized with a few drops of triethylamine, the mixture was concentrated, the residue was partitioned between chloroform and water, dried, and concentrated to give a solid, which crystallized from dichloromethane–ether–hexane to afford **16** (1.49 g, 83%), m.p. 103–104°, $[\alpha]_D^{24}$ +123° (*c* 1.2, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 8.20 and 7.13 (d, 2 H each, *J* 9 Hz, arom.), 5.83 (s, 1 H, H-1), and 1.53 and 1.37 (s,. 3 H each, CMe_2).

Anal. Calc. for $C_{15}H_{18}FNO_7$: C, 52.48; H, 5.28; N, 4.08. Found: C, 52.24; H, 5.11; N, 4.07.

4-Nitrophenyl 4-O-acetyl-6-deoxy-6-fluoro-2,3-O-isopropylidene-α-D-mannopyranoside (**17**). — A solution of **16** (1 g) in 1:2 acetic anhydride–pyridine (15 mL) was stirred overnight at room temperature. It was then concentrated with co-evaporation of toluene. Crystallization from dichloromethane–ether furnished **17** (1.1 g, 98%), m.p. 152–154°, $[\alpha]_D^{24}$ +96° (*c* 1.0, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 8.19 and 7.15 (d, 2 H each, *J* ~9 Hz, arom.), 5.84 (s, 1 H, H-1), 2.09 (s, 3 H, OAc), and 1.57 and 1.39 (s, 3 H each, CMe_2).

Anal. Calc. for $C_{17}H_{20}FNO_8$: C, 52.98; H, 5.23; N, 3.64. Found: C, 52.74; H, 4.95; N, 3.57.

4-Nitrophenyl 4-O-acetyl-6-deoxy-6-fluoro-α-D-mannopyranoside (**18**). — A solution of **17** (1.11 g) in trifluoroacetic acid (4 mL), water (0.2 mL), and chloroform (30 mL) was stirred for 2 h at room temperature. It was then concentrated with coevaporation of toluene. The residue crystallized from ethyl acetate–ether–hexane to afford **18** (0.93, 94%), m.p. 155–157°, $[\alpha]_D^{24}$ +164° (*c* 1.3, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 8.15 and 7.12 (d, 2 H each, *J* 9 Hz, arom.), 5.65 (d, 1 H, *J* ~1 Hz, H-1), and 2.08 (s, 3 H, OAc).

Anal. Calc. for $C_{14}H_{16}FNO_8$: C, 48.69; H, 4.67; N, 4.06. Found: C, 48.91; H, 4.54; N, 3.95.

2,3,4-Tri-O-acetyl-6-deoxy-6-fluoro-α-D-mannopyranosyl bromide (**19**). — A cold (0°, bath) stirred solution of **13** (3 g) in dichloromethane (10 mL) and acetic anhydride (1.2 mL) was treated with a 31% solution of HBr in glacial acetic acid (14.4 mL) for 30 min. It was then allowed to warm to room temperature, and the stirring was continued for an additional 3.5 h. The mixture was cooled, diluted with chloroform (~150 mL), and shaken with ice–water. The chloroform solution was successively washed with ice-cold water, cold saturated $NaHCO_3$, and cold water, dried, and concentrated (30°, bath) to give a yellowish syrup, which was dissolved in a small volume of ether. Addition of hexane caused the precipitation of **19** (2.73, 86%), amorphous, $[\alpha]_D^{25}$ +145° (*c* 2.7, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 6.33 (d, 1 H, *J* ~1 Hz, H-1), 4.53 (dd, 2 H, $J_{H\text{-}6a,6b,F\text{-}6}$ ~48, $J_{H\text{-}6a,6b,H\text{-}5}$ ~4 Hz, H-6a,6b), and 2.20, 2.13, and 2.03 (s, 3 H each, 3 OAc); ^{19}F-n.m.r. ($CDCl_3$): φ −229.93 (dt, $J_{F\text{-}6,H\text{-}6a,6b}$ ~48.80, $J_{F\text{-}6,H\text{-}5}$ ~25.50 Hz, F-6).

4-Nitrophenyl 4-O-acetyl-6-deoxy-6-fluoro-3-O- (**21**) *and -2-O-(2,3,4,6-tetra-*

O-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**23**), *and 4-nitrophenyl 4-O-acetyl-6-deoxy-6-fluoro-2,3-di-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside* (**25**). — (*a*) *In 1:1 benzene–nitromethane as solvent.* A mixture of **18** (0,86 g, 2.5 mmol), powdered $Hg(CN)_2$ (0.33 g, 1.31 mmol), $HgBr_2$ (0.5 g, 1.39 mmol), and powdered 4A molecular sieves (1 g) in 1:1 benzene–nitromethane (70 mL) was boiled until ~20 mL of the solvent had distilled off. After cooling to room temperature, a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide (**20**; 1.2 g, 2.9 mmol) in 1:1 benzene–nitromethane (6 mL) was added, and the stirring was continued for 21 h at 45–48°. T.l.c. (solvent *C*) then showed the presence of two major products, both faster-migrating than **18**; a small portion of **18**, as well as some slower and some faster-migrating compounds, were also present. More portions of **20** (0.6 g, 1.25 mmol) in 1:1 benzene–nitromethane (4 mL), $Hg(CN)_2$ (0.17 g, 0.67 mmol), and $HgBr_2$ (0.25 g, 0.69 mmol) were added, and stirring was continued for an additional 20 h at the same temperature. The mixture was cooled and filtered (Celite), the solids were thoroughly washed with benzene, and the filtrate and washings were combined and diluted with benzene to a total volume of ~250 mL. The solution was successively washed with water, M KI solution, saturated aqueous $NaHCO_3$, and water, dried, and concentrated. The crude product was chromatographed [1:3 → 1:1 ethyl acetate–petroleum ether (b.p. 40–60°)] to give first (0.12 g) a mixture of **21** (see below) and a faster-migrating product having identical chromatographic mobility with **25** (see below), but which was neither separated nor characterized at this stage. On concentration, the fraction eluted next gave a residue which was dissolved in a small volume of dichloromethane. Addition of ether–hexane caused the crystallization of **21** (0.35 g, 21%), m.p. 170–173°, $[\alpha]_D^{23}$ +74° (*c* 0.52, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 8.13 and 7.10 (d, 2 H each, *J* ~9 Hz, arom.), 5.66 (br. s, 1 H, H-1), 2.13 and 2.06 (s, 6 H each, 4 OAc), and 1.96 (s, 3 H, OAc).

Anal. Calc. for $C_{28}H_{34}FNO_{17}$: C, 49.70; H, 5.07; N, 2.07. Found: C, 49.77; H, 5.10; N, 2.11.

Continued elution gave a mixture (0.1 g) of **21** and **23**. The last fractions contained chromatographically homogeneous, amorphous **23** (0.16 g, 9.5%), $[\alpha]_D^{23}$ +53° (*c* 0.43, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 8.20 and 7.19 (d, 2 H each, *J* ~9 Hz, arom.), 5.90 (s, 1 H, H-1), 2.15 (s, 6 H, 2 OAc), and 2.07, 1.99, and 1.95 (s, 3 H each, 3 OAc).

Anal. Calc. for $C_{28}H_{34}FNO_{17}$: C, 49.70; H, 5.07; N, 2.07. Found: C, 49.65; H, 5.20; N, 2.15.

(*b*) *In acetonitrile as solvent.* A mixture of **18** (0.86 g, 2.5 mmol), bromide **20** (1.2 g, 2.9 mmol), powdered $Hg(CN)_2$ (0.33 g, 1.3 mmol), and $HgBr_2$ (0.5 g, 1.39 mmol) in dry acetonitrile (20 mL) was stirred for 5 h at room temperature. The solvent was evaporated under diminished pressure, the residue was suspended in chloroform, and the suspension was filtered (Celite). The combined filtrate and washings were processed as described above. After concentration, the residue was chromatographed (chloroform → 1:49 acetone–chloroform) to give first amorphous

25 (0.48 g, 10%), $[\alpha]_D^{25}$ +62° (*c* 0.43, chloroform); t.l.c. (solvent *C*): R_F 0.47 (identical with that of the faster-migrating compound just described); ^{1}H-n.m.r. ($CDCl_3$): δ 8.18 and 7.16 (d, 2 H each, *J* ~9 Hz, arom.), 5.83 (s, 1 H, H-1), and 2.15–1.93 (cluster of s, 27 H, 9 OAc).

Anal. Calc. for $C_{42}H_{52}FNO_{26}$: C, 50.15; H, 5.21; N, 1.39. Found: C, 49.93; H, 4.93; N, 1.31.

Eluted next was chromatographically pure **21** (0.35 g). The last fraction (0.17 g) contained a mixture of **21** and **23**. Preparative thin-layer chromatography of the latter compound (solvent *C*) gave **21** (0.04 g, combined yield, 23%) and **23** (0.075 g, 4.5%).

*4-Nitrophenyl 6-deoxy-6-fluoro-3-*O*-α-*D*-mannopyranosyl-α-*D*-mannopyranoside* (**22**). — Compound **21** (0.3 g) in 0.02M methanolic sodium methoxide (40 mL) was stirred overnight at room temperature. T.l.c. (solvent *A*) showed the disappearance of **21** and the presence of a slower-migrating product; some slower-migrating contaminants (undetectable in u.v. light) were also present. The base was neutralized with a few drops of glacial acetic acid, the mixture concentrated to dryness, and the residue was redissolved in methanol. After treatment with Amberlite 1R-120 (H^+) resin and filtration (Celite), the combined filtrate and washings were concentrated to a small volume. Addition of ether–hexane caused the precipitation of amorphous **22** (0.14 g, 68%), $[\alpha]_D^{24}$ +155.5° (*c* 0.8, methanol); ^{19}F-n.m.r. [($^2H_3$)Me_2SO]: φ −231.37 (dt, $J_{F\text{-}6,H\text{-}6a,6b}$ 47.70, $J_{F\text{-}6,H\text{-}5}$ 25.2 Hz, F-6); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{18}H_{24}FNO_{12}$: C, 46.45; H, 5.19; N, 3.01. Found: C, 46.44; H, 5.10; N, 2.92.

*4-Nitrophenyl 6-deoxy-6-fluoro-2-*O*-α-*D*-mannopyranosyl-α-*D*-mannopyranoside* (**24**). — Compound **23** (0.07 g) was subjected to Zemplén transesterification, as described for **21** (to give **22**) to furnish **24** (0.035 g, 73%), amorphous, $[\alpha]_D^{25}$ +81° (*c* 0.6, methanol); ^{19}F-n.m.r. [($^2H_3$)Me_2SO]: φ −231.30 (dt, $J_{F\text{-}6,H\text{-}6a,6b}$ 47.75, $J_{F\text{-}6,H\text{-}5}$ 26.47 Hz, F-6); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{18}H_{24}FNO_{12}$: C, 46.45; H, 5.19; N, 3.01. Found: C, 46.52; H, 5.22; N, 2.99.

*4-Nitrophenyl 6-deoxy-6-fluoro-2,3-di-*O*-α-*D*-mannopyranosyl-α-*D*-mannopyranoside* (**26**). — Compound **25** (0.4 g) in methanol (40 mL) was treated with M sodium methoxide in methanol (1 mL) overnight at room temperature. T.l.c. (5:4:1 chloroform–methanol–water) then showed the disappearance of **25** and the presence of a slower-migrating product; some slower- and some faster-migrating contaminants were also present. After processing, as described for **21** (to give **22**), the crude product was chromatographed. Elution with solvent *A* and lyophilization gave amorphous **26** (0.13 g, 52%), $[\alpha]_D^{25}$ +106° (*c* 0.8, water); ^{19}F-n.m.r. [($^2H_3$)Me_2SO]: φ +231.73 (dt, $J_{F\text{-}6,H\text{-}6a,6b}$ 47.63, $J_{F\text{-}6,H\text{-}5}$ 25.72 Hz, F-6); ^{13}C-n.m.r.; see Table I.

Anal. Calc. for $C_{24}H_{34}FNO_{17} \cdot 1.5H_2O$: C, 44.04; H, 5.70; N, 2.14. Found: C, 44.00; H, 5.47; N, 2.06.

4-Nitrophenyl 4,6-di-O-acetyl-3-O- (**28**) *and -2-O-(2,3,4-tri-O-acetyl-6-deoxy-6-fluoro-α-D-mannopyranosyl)-α-D-mannopyranoside* (**30**). — (*a*) *In 1:1 benzene–nitromethane as solvent.* A stirred mixture of 4-nitrophenyl 4,6-di-*O*-acetyl-α-D-mannopyranoside[12] (**27**; 0.2 g, 0.52 mmol), powdered $Hg(CN)_2$ (0.07 g, 0.27 mmol), and $HgBr_2$ (0.11 g, 0.3 mmol) in 1:1 benzene–nitromethane (40 mL) was boiled until ~20 mL of the solvent had distilled off. After cooling to room temperature, a solution of bromide **19** (0.24 g, 0.65 mmol) in 1:1 benzene–nitromethane (2 mL) was added, and the stirring was continued for 25 h at 40–45°. T.l.c. (solvent *C*) showed the presence of two major products, both faster-migrating than **27**; a small proportion of **27**, as well as some faster- and some slower-migrating compounds were also present. More of **19** [0.12 g, 0.33 mmol, in 1:1 benzene–nitromethane (2 mL)], powdered $Hg(CN)_2$ (0.03 g, 0.14 mmol), and $HgBr_2$ (0.05 g, 0.15 mmol) were added, and stirring was continued for an additional 8 h at 40–45°. After processing, the crude product was chromatographed (1:3 → 1:1 ethyl acetate–petroleum ether) to give first a mixture (~0.05 g) of **28** and a faster-migrating compound (detectable under u.v. light; which was neither separated nor further characterized). Eluted next was **28** (0.1 g, 28.5%), m.p. 149–151° (dichloromethane–ether), $[\alpha]_D^{23}$ +96° (*c* 0.7, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 8.19 and 7.17 (d, 2 H each, *J* ~9 Hz, arom.), 5.67 (s, 1 H, H-1), and 2.15–1.95 (cluster of s, 15 H, 5 OAc).

Anal. Calc. for $C_{28}H_{34}FNO_{17}$: C, 49.78; H, 5.07; N, 2.07. Found: C, 49.79; H, 5.00; N, 2.07.

Continued elution gave a mixture (0.04 g) of **28** and **30**, followed by chromatographically homogeneous (solvent *C*) **30** (0.09 g, 11%), obtained as an amorphous solid by addition of ether into its solution in dichloromethane, $[\alpha]_D^{25}$ +69° (*c* 0.6, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 8.17 and 7.10 (d, 2 H each, *J* ~9 Hz, arom.), 5.95 (s, 1 H, H-1), and 2.12–1.97 (cluster of s, 15 H, 4 OAc).

Anal. Calc. for $C_{28}H_{34}FNO_{17}$: C, 49.78; H, 5.07; N, 2.07. Found: C, 49.52; H, 5.33; N, 2.02.

(*b*). *In acetonitrile as solvent.* A mixture of **27** (1 g, 2.6 mmol), bromide **19** (1.12 g, 3.0 mmol), powdered $Hg(CN)_2$ (0.34 g, 1.35 mmol), $HgBr_2$ (0.53 g, 1.46 mmol), and powdered 4A molecular sieves (2 g) in dry acetonitrile (20 mL) was stirred for 15 h at room temperature. After processing as described earlier, the crude product was chromatographed (chloroform → 1:24 acetone–chloroform) to give pure (t.l.c., solvent *C*) **28** (0.24 g, 14%), followed by a mixture of **28** and **30** (~0.12 g). This fraction was subjected to p.t.l.c. with 9:1 chloroform–acetone (double irrigation) to furnish **28** (0.025 g; combined yield 15%) and **30** (0.055 g, 3%).

4-Nitrophenyl 3-O-(6-deoxy-6-fluoro-α-D-mannopyranosyl)-α-D-mannopyranoside (**29**). — Compound **28** (0.15 g) was *O*-deactylated with 0.03M methanolic sodium methoxide (20 mL), as described for **21** (to give **22**), to afford **29** (0.07 g, 68%), m.p. 232–234° (95% ethanol–ethyl acetate–hexane), $[\alpha]_D^{24}$ +167° (*c* 0.56, methanol); ^{19}F-n.m.r. [($^2H_3$)Me_2SO]: ϕ −230.52 (dt, $J_{F\text{-}6',H\text{-}6a',6b'}$ 47.98, $J_{F\text{-}6',H\text{-}5'}$ 26.77 Hz, F-6′); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{18}H_{24}FNO_{12} \cdot 0.5H_2O$: C, 45.57; H, 5.31; N, 2.95. Found: C, 45.85; H, 4.92; N, 2.80.

4-Nitrophenyl 2-O-(6-deoxy-6-fluoro-α-D-mannopyranosyl)-α-D-mannopyranoside (**31**). — Compound **30** (0.1 g) in methanol (20 mL) was treated with M methanolic sodium methoxide (0.4 mL) under stirring overnight at room temperature. The mixture was then processed as described for **21** (to give **22**), and the crude product was chromatographed (solvent $B \rightarrow$ 6:2:1 ethyl acetate–2-propanol–water) to furnish amorphous **31** (0.04 g, 58%), $[\alpha]_D^{24}$ +100° (*c* 0.5, methanol); ^{19}F-n.m.r. [($^2H_3$)Me_2SO]: ϕ −229.45 (dt, $J_{F\text{-}6',H\text{-}6a',6b'}$ 47.45, $J_{F\text{-}6',H\text{-}5'}$ 24.57 Hz, F-6′); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{18}H_{24}FNO_{12} \cdot H_2O$: C, 44.72; H, 5.42; N, 2.90. Found: C, 44.36; H, 5.05; N, 2.94.

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