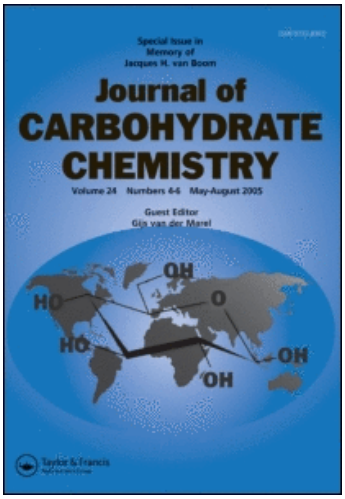

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Pavol Kováč[a]; Herman J. C. Yeh[a]; Grace L. Jung[a]; Cornelis P. J. Glaudemans[a]
[a] NIDDK, National Institutes of Health, Bethesda, Maryland, U.S.A.

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THE REACTION OF METHYL 3-O-BENZYL-4,6-O-BENZYLIDENE-α-D-MANNOPYRANOSIDE WITH DIETHYLAMINOSULFUR TRIFLUORIDE (DAST)

Pavol Kováč, Herman J. C. Yeh, Grace L. Jung and Cornelis P. J. Glaudemans

NIDDK, National Institutes of Health, Bldg. 8
Bethesda, Maryland 20892 (U.S.A.)

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ABSTRACT

Methyl 3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranoside (2), when treated in diglyme at 100° with DAST, undergoes a rapid reaction involving the participation of the axial methoxyl group at C-1 to give 3-O-benzyl-4,6-O-benzylidene-2-O-methyl-α- (4) and β-D-glucopyranosyl fluoride (3), isolated in a combined yield of 75-80%. In the presence of pyridine and at room temperature, the major product formed is methyl 3-O-benzyl-4,6-O-benzylidene-2-deoxy-α-D-erythro-hex-2-enopyranoside (11). The structures 3, 4 and 11 have been confirmed by analysis of their NMR spectral data, as well as by chemical transformations into compounds of established structure.

INTRODUCTION

This laboratory has used a large number of deoxyfluorosugars to map subsites in the combining area of monoclonal antigalactan antibodies and to investigate the possible role of hydrogen bonding in interactions between immunoglobulins and carbohydrates.[1-4] In connection with a similar study involving a dextran-specific

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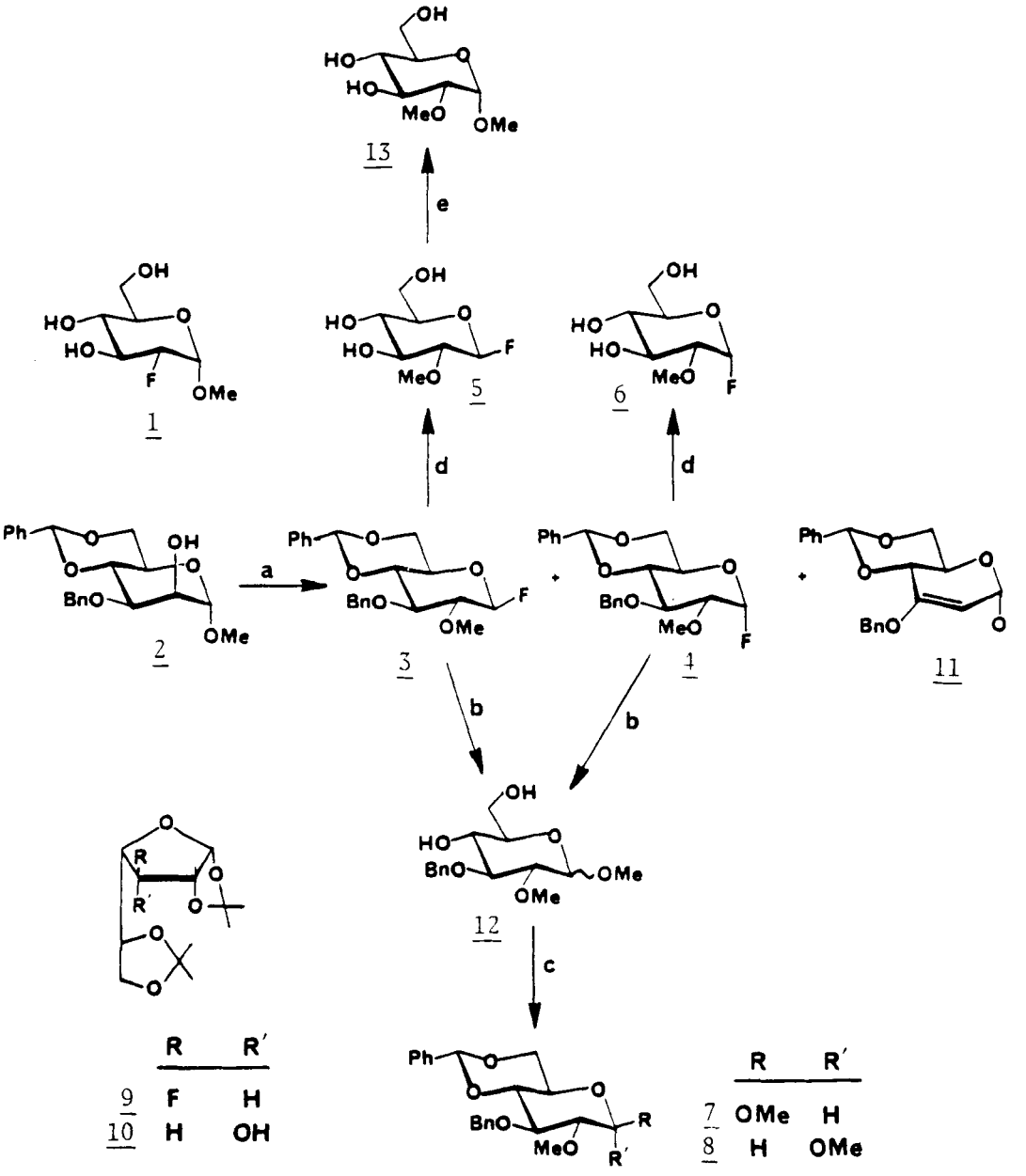
monoclonal antibody a need arose for methyl 2-deoxy-2-fluoro-α-D-glucopyranoside (1).

One way of introducing a fluorine atom into a carbohydrate involves a nucleophilic displacement of an activated hydroxyl function (e.g. a corresponding sulfonate) by a fluoride ion. For this approach, methyl 3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranoside (2) appears to be an easily accessible precursor for the synthesis of 1, but previous attempts at effecting nucleophilic displacement of 2-sulfonates in the α-manno series have met with little success. For example, methyl 4,6-O-benzylidene-2-O-methanesulfonyl-3-O-methyl-α-D-mannopyranoside was found[5] to be largely unreactive towards displacement with benzoate anion. In another study, both methyl 4,6-O-benzylidene-3-O-methyl- or 3-O-acetyl-2-O-trifluoromethanesulfonyl-α-D-mannopyranoside gave[6] only unwanted products when treated with a number of fluoride ion sources. However, it has been shown that in cases where fluorinations of carbohydrates using common fluoride ion sources have proven problematic, better results were usually obtained by treating the nonactivated (i.e. containing free hydroxyl) carbohydrate directly with diethylaminosulfur trifluoride (DAST).

We have previously reported[7] the isolation of 3-deoxy-3-fluoro-1,2:5,6-di-O-isopropylidene-α-D-galactofuranose (9) from the reaction of the D-gulo derivative 10 with DAST in 90% yield. In contrast, when 3-sulfonates of 10 were treated[7,8] with various F-nucleophiles, a large amount of the starting materials underwent an elimination reaction and the yields of the desired products due to S_N2 displacement were only 40-50%. The effectiveness of DAST in the introduction of fluorine into carbohydrates is also evident in the comparison of two recent syntheses of 2-deoxy-2-fluoro-D-glucose from derivatives of alkyl β-D-mannopyranosides. When the 2-trifluoromethanesulfonates of a number of derivatized methyl β-D-mannopyranosides were treated[6] with a number of fluoride ion sources, the conversions were invariably accompanied by side reactions and the yields of the desired 2-deoxy-2-fluoro-D-glucose derivatives ranged from 17-



[a] Et_2NSF_3 [b] H^+, MeOH [c] $(MeO)_2CHPh$ [d] H_2, Pd/C [e] NaOM

Scheme I

64%. Dessinges et al.[9] treated benzyl 3,4,6-tri-O-benzyl-2-O-trifluoromethanesulfonyl-β-D-mannopyranoside with tetra-n-butylammonium fluoride or CsF_2 and obtained the corresponding 2-deoxy-2-fluoro-β-D-gluco derivative in yields of 45-50%. On the other hand, when benzyl-3,4,6-tri-O-benzyl-β-D-mannopyranoside was treated[9] with DAST, the reported yield of benzyl 3,4,6-tri-O-benzyl-2-deoxy-2-fluoro-β-D-glucopyranoside was 80%.

The above-cited studies indicate that under the reaction conditions employing DAST, elimination and other competing reactions might proceed to a lesser extent than in S_N2 displacement reactions using common fluoride ion sources. Moreover, the use of DAST bypasses the necessity of isolating the intermediate sulfonates, thereby shortening the preparation of fluorosugars by one synthetic operation. We therefore set out to explore the reaction of the readily available[10] 2 with DAST.

RESULTS AND DISCUSSION

In initial experiments compound 2 was treated with DAST for up to 48 h in dichloromethane or toluene at temperatures ranging from 20-70°. After conventional processing, involving treatment with aqueous sodium hydrogen carbonate, TLC showed that a large amount of starting material remained and that, essentially, two products were formed in low yield. The reaction rate could be increased in the presence of an organic base, such as pyridine, but the major product, 11, formed under these conditions was the product of an elimination rather than substitution process. The structure of 11, analogous to that of a compound isolated[6] in 87% yield from the reaction of methyl 4,6-O-benzylidene-2-O-methanesulfonyl-3-O-methyl-α-D-mannopyranoside with tetra-n-butylammonium fluoride, was deduced from analysis of its IR and NMR spectral data (cf. Experimental Section and Tables I-III).

At 100° and in diglyme, the reaction of 2 with DAST gave the two above-mentioned products in a combined yield of ~75-80%. The

peaks at m/z 392 (M^++18) and 355 (M^++1) in their ammonia CI MS spectra suggested the presence of a fluorine atom in both molecules. Brief inspection of the NMR spectra of these fluorine-containing compounds showed, however, that the spectral characteristics of both materials were inconsistent with the anticipated structure 17. Most informative in this respect were the ^{13}C NMR spectra. For example, for structure 17 one would expect[11] the ^{13}C NMR spectrum to show a doublet at ∿90 ppm with a J_{FC} ∿180 Hz for C-2 and a doublet for each of C-1 and C-3 to exhibit a J_{FC} ∿20 Hz. On the contrary, the doublet for C-1 in the spectra of both compounds isolated showed a splitting of ∿220 Hz. Also, the spectra showed only one doublet with a J_{FC} consistent with a carbon vicinal to a C-F functionality. This ruled out the possibility that the two compounds were products of simple fluorine substitution at C-2 of 2 (either with[12] or without inversion of configuration at that asymmetic center). That these products were anomeric glycosyl fluorides 3 and 4 became evident from complete analysis of their NMR spectral data, and from chemical transformations.

Fluorination at C-1 in 3 and 4 is evident[11] from the large $^1J_{F,C-1}$ (∿220 Hz) and the large geminal coupling constant ($^2J_{F,H-1}$ 52 Hz) observed for the anomeric carbon and hydrogen, respectively, as well as the large deshielding effect on C-1 (δ_C 109) by the fluorine. The ^{19}F chemical shifts of compounds 3 and 4, δ 26.68 and 14.25, respectively, are also well within the expected region for fluorine substituion at C-1[12-14] but not at C-2[12,13] in a number of fluorinated carbohydrates.

The stereochemistry at the anomeric position of 3 and 4 was determined from the vicinal couplings, $^3J_{H-1,H-2}$ and $^3J_{F,H-2}$, which are dependent on the dihedral angle between the coupled nuclei. The large $^3J_{F,H-2}$ (23.9 Hz) and small $^3J_{H-1,H-2}$ (2.8 Hz) exhibited by 4, indicative of a trans diaxial relationship between the H-2 and fluorine atom, and a gauche relationship between the H-1 and $H\text{-}2_{ax}$, respectively, are consistent with the α stereochemistry of the fluorine at C-1. On the other hand, the β geometry of the fluorine in 3 is evidenced by $^3J_{F,H-2}$ 12.1 Hz and $^3J_{H-1,H-2}$ 6.1 Hz, which

are typical for the F_{eq}-H-2_{ax} and H-1_{ax}-H-2_{ax} relationships. Finally, the chemical shift data of the anomeric hydrogen and fluorine support the stereochemical assignments. In accordance with literature precedent,[13] the chemical shift of H-1_{eq} (and F_{eq}) was found to be more deshielded than that of the H-1_{ax} (and F_{ax}), respectively (see NMR spectral data for 3 and 4 in Tables I and III).

Further support for the proposed structures 3 and 4 was provided by the conversion of these substances into independently synthesized compounds of known structures, under conditions known not to cause migration of methoxyl groups (Scheme I). The transformation of 3 and 4 into the corresponding methyl glycosides 7 and 8 using sodium methoxide was initially attempted since the latter two compounds were previously prepared by independent means.[15] However, compounds 3 and 4 were found to be unreactive under such conditions (see Experimental Section). Micheel and Klemer[16] obtained methyl 2-O-methyl-α-D-glucopyranoside by treatment of 2-O-methyl-β-D-glucopyranosyl fluoride with sodium methoxide. Therefore, compound 3 was hydrogenolyzed to give 5, the physical constants of which agreed well with those reported.[16] The α-fluoride 6 was obtained in the same manner and its structure, as well as that of 5, was fully confirmed by NMR spectral data (Tables I-III). Subsequent treatment of 5 with sodium methoxide in accordance with the procedure reported by Micheel and Klemer,[16] afforded a compound which exhibited a ^{13}C NMR spectrum consistent with the expected structure 13.[17,18]

Glycosyl fluorides have also been previously converted into methyl glycosides by methanolysis.[1] When compounds 3 and 4 were each treated with methanolic hydrogen chloride, the NMR spectra of the products showed that the same mixture of α- and β-glycosides (12) was formed regardless of the anomeric configuration of the starting material. Unfortunately, the compounds could not be separated by column chromatography, but when the mixture 12 was treated with benzaldehyde dimethyl acetal, the resulting derivatives 7 and 8 were readily separated by chromatography[15] and found to be identical with the previously described compounds.[15]

TABLE I: ^{1}H NMR Spectral Data[a] (300 MHz) for 3-6 and 11

Compound	^{1}H Chemical Shifts (δ, ppm)[b] and First-Order Coupling Constants (Hz)[c]									
	H-1 ($J_{1,2}$)	H-2 ($J_{2,3}$)	H-3 ($J_{3,4}$)	H-4 ($J_{4,5}$)	H-5 ($J_{5,6}$)	H-6 ($J_{5,6a}$)	H-6a ($J_{6,6a}$)	OH	CH_2 (^2J)	CH_3
3[d]	5.27 dd (6.1)	3.36 oddd (7.3)	3.70 odd (8.7)	3.83 odd (9.8)	3.54-3.58 m (4.9)	4.37 dd (9.8)	3.54-3.58 m (10.5)	5.57 s	4.89 d 4.79 d (11.4)	3.56 s
4[d,h]	5.70 dd (2.8)	3.38 ddd (9.0)	3.99 odd (9.4)	3.68 odd (9.7)	3.99 oddd (4.9)	4.34 dd (10.3)	3.73 odd (10.2)	5.57 s	4.81 d 4.92 d (11.2)	3.61 s
5[e]	5.12 dd (7.1)	2.93-3.03 m (8.7)	3.29-3.41 m f	3.29-3.41 m f	3.29-3.41 m (0)	3.85 d (2.0)	3.68 dd (12.0)	--	--	3.56 s
6[e]	5.74 dd (2.6)	3.13 ddd (9.7)	3.66 odd (9.3)	3.41 odd (9.3)	3.65 ddd (1.8)	3.81 dd (4.8)	3.70 dd (11.6)	--	--	3.52 s
11[d,g]	5.02 d (3.1)	4.75 dd --	--	4.27 d (8.9)	4.12 ddd (4.6)	4.31 dd (10.2)	3.84 odd (10.2)	5.60 s	4.81 d 4.95 d (12.1)	3.43 s

[a] spectral assignments verified by homonuclear decoupling or HOMCOR 2-D experiments
[b] downfield from Me_4Si [c] peak multiplicities: s, singlet; d, doublet; m, multiplet; o, overlapping
[d] in $CDCl_3$ [e] in CD_3OD [f] not measured due to complexity of overlapping signals [g] $J_{2,4}$ 1.6 Hz, $J_{1,4}$ 0.8 Hz

TABLE II: ^{13}C NMR Spectral Data[a] (75 MHz) for 3-6 and 11

Compound	^{13}C Chemical Shifts (δ, ppm)[b] and ^{19}F-^{13}C Coupling Constants (Hz)								
	C-1 ($J_{F,C-1}$)	C-2 ($J_{F,C-2}$)	C-3 ($J_{F,C-3}$)	C-4	C-5 ($J_{F,C-5}$)	C-6	CH	CH_2	CH_3
3[c]	109.26 (217.3)	83.10 (24.7)	79.42 (8.5)	80.45	65.40 (4.9)	68.60	101.28	74.39	60.23
4[c]	105.34 (228.5)	81.28 (23.9)	77.97 (~0)	81.03	64.49 (4.1)	68.58	101.44	75.15	59.91
5[d]	111.39 (212.2)	84.80 (20.5)	76.59 (12.5)	70.82	78.04 (6.8)	62.37	--	--	60.66
6[d]	106.20 (225.2)	82.35 (24.6)	75.91 (3.32)	70.57	73.72 --	62.05	--	--	59.09
11[e]	98.20 --	97.20 --	155.27 --	75.71	64.81 --	69.54	102.71	69.99	55.46

[a] spectral assignments verified by HETCOR 2-D experiments [b] downfield from Me_4Si [c] in $CDCl_3$ [d] in CD_3OD
[e] in $(CD_3)_2CO$

TABLE III: ^{19}F NMR Spectral Data (282 MHz) for 3-6

Compound	Chemical Shifts (ppm)	Coupling Constants (Hz) $^{2}J_{F,H-1}$	$^{3}J_{F,H-2}$
3[b]	26.68	53.2	12.1
4[b]	14.25	52.8	26.4
5[c]	23.93	55.1	12.9
6[c]	14.92	53.6	25.5

[a] downfield from C_6F_6 [b] in $CDCl_3$ [c] in CD_3OD

A plausible mechanistic sequence which accounts for the formation of 3, 4 and 11 from 2 is illustrated in Scheme II. In accordance with the mechanism discussed in detail by Middleton[19] for the reaction of DAST with alcohols, the initial step, upon treatment of 2 with DAST, involves the formation of the sulfoxo derivative 14, from which the desired 2-fluoro-glucopyranoside 17 could arise from S_N2 displacement of the sulfoxyl moiety at C-2. However, it is clear from the examination of a model of the intermediate 14 that a potentially severe steric interaction between the C-1 methoxy group and a fluorine ion or fluorinated nucleophile incoming from the α-plane could preclude formation of the anticipated 17. The shielding provided by the C-1 methoxyl group against nucleophilic attack from the α-plane apparently allows other processes to occur. One pathway (a), which is enhanced when the reaction is conducted in the presence of a base (e.g. pyridine), involves the abstraction of H-3 followed by the elimination of the axial sulfoxyl moiety to yield the benzyl enol ether 11. Alternatively, by pathway (b) the C-2 sulfoxyl group is displaced via participation of the axial C-1

methoxyl to give a 1,2-methoxonium species 15,* from which the β-glucosyl fluoride 3 could arise. The strained methyloxonium ion 15 could conceivably rearrange in favour of a glucosyloxonium intermediate 16, the presence of which could lead to the formation of both α- and β-glucosyl fluorides 3 and 4. This constitutes a rare example** of 1,2-methoxy group migration in carbohydrate chemistry, the first of which was reported by Lemieux and Fraser-Reid.[22] The described reaction, which did not allow the introduction of a fluorine atom into C-2 of the substrate 2, may be of preparative interest when applied to related α-manno compounds bearing C-1 substituents other than methoxy (e.g. benzyloxy, cf. ref. 12).

EXPERIMENTAL

Melting points were determined with a Büchi melting point apparatus. Optical rotations were recorded at 25° using a Perkin-Elmer automatic polarimeter, Model 241 MC. Thin-layer chromatography (TLC) on glass slides coated with Silica Gel 60 and preparative chromatography on Silica Gel (Merck, Cat. No. 9385) was performed with mixtures of appropriately adjusted polarity consisting of A. toluene-ethyl acetate, and B. dichloromethane-methanol. Detection was effected by charring with sulfuric acid in ethanol (5%, v/v) and, when applicable, with UV light.

Ammonia CI spectra were recorded with a Finnigan 10151 D spectrometer at a source pressure and temperature of 133 Pa and 100°, respectively.

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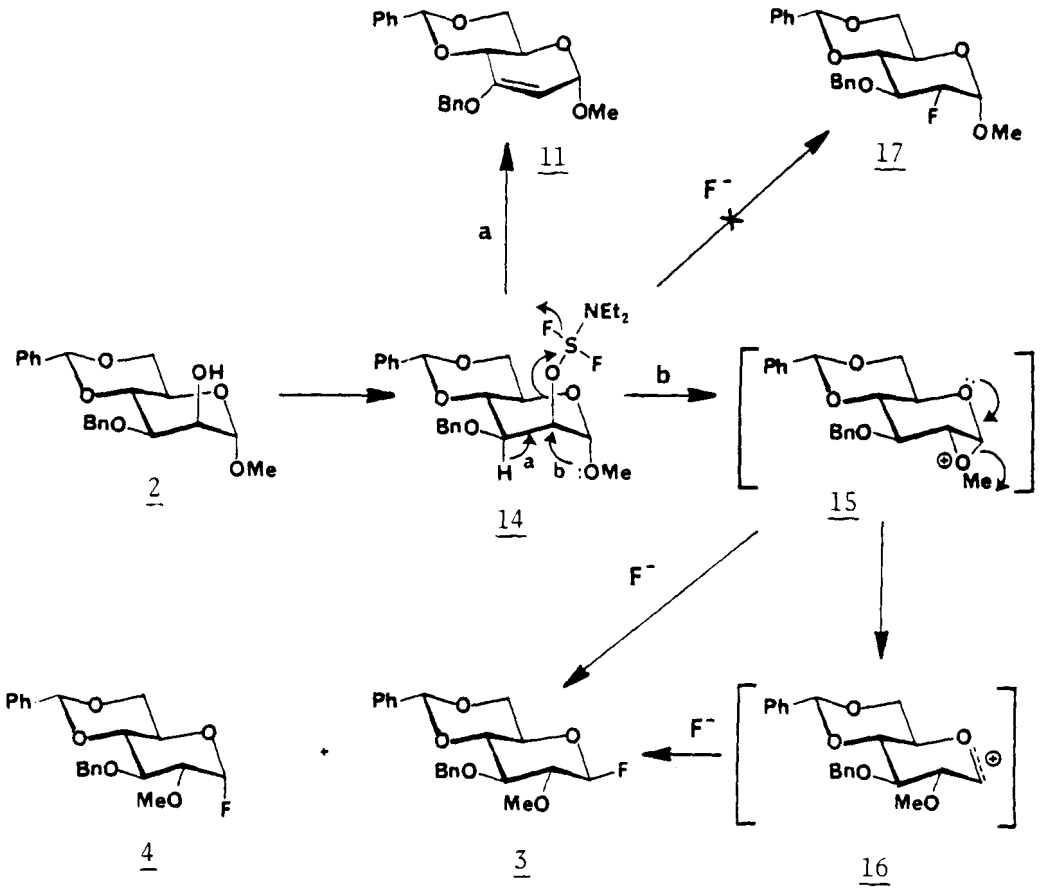
*Although unusual, methoxyl group participation is not without precedent, and a number of cases have been documented for carbohydrates.[20-26]

**After this paper was submitted for publication, reports of such 1,2-migrations appeared in the literature. Hasegawa et al.[20] observed the migration of methoxyl and benzyloxyl groups from C-1 to C-2, with concomitant introduction of fluorine at C-1 of talofuranosides. Similar 1,2-migration of not only O-, but S- and N-containing substitutents with concomitant C-1 fluorination in a variety of glycopyranosyl systems, has been noted by Nicolaou et al.[21]



Scheme II

^{1}H, ^{13}C and ^{19}F NMR spectra were taken at 21° using a Varian XL-300 spectrometer equipped with an advanced data system.

DAST was purchased from Aldrich Chemical Co. and distilled. 5% Palladium-on-charcoal catalyst was a product of Engelhardt Industries.

3-O-Benzyl-4,6-O-benzylidene-2-O-methyl-α- (4) and β-D-glucopyranosyl fluoride (3). To a solution of methyl 3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranoside[10] (2) (5.3 g, 14.2 mmol) in diglyme (45 mL) was added DAST (5.2 mL, 47.7 mmol) and the mixture was stirred at 100-110° (bath) for 30 min. TLC (solvent A) showed

that essentially two products, both with higher R_f values than that of the starting material, were formed. The dark solution was concentrated under reduced pressure (60°/133 Pa) and the residue was partitioned between aqueous sodium hydrogen carbonate solution and dichloromethane. The organic phase was concentrated and the residue was chromatographed to give first the β-halide 3 (3.2 g, 60%). Crystallization from 2-propanol gave pure 3, mp 107-107.5°, $[\alpha]_D$ -48° (c 0.6, chloroform).

Anal. Calcd for $C_{21}H_{23}FO_5$: C, 67.36; H, 6.19; F, 5.07. Found: 67.52; H, 6.07; F, 5.10.

Continued elution gave the α-halide 4 (0.85 g, 16%). When recrystallized from acetone-ether, compound 4 had mp 150-150.5° and showed $[\alpha]_D$ -22° (c, 0.8, chloroform).

Anal Calcd for $C_{21}H_{23}FO_5$: C, 67.36; H, 6.19; F, 5.07. Found: C, 67.41; H, 6.24; F, 4.90.

Under acidic conditions, compound 3 rearranged slowly forming 4, as shown by ^1H NMR spectroscopy.

Methyl 3-O-benzyl-4,6-O-benzylidene-2-deoxy-α-D-erythro-hex-2-enopyranoside (11). Pyridine (0.5 mL) followed by DAST (0.21 mL, 1.7 mmol) was added to a solution of 2 (0.32 g, 0.86 mmol) in diglyme (2 mL), and the mixture was kept at room temperature for 3 days. TLC (solvent A) then showed that only traces of the starting material were present, and that essentially three products were formed. Besides small amounts of 3 and 4 (and some base-line material), a third compound, which appeared to be the major component of the mixture, was present. This material exhibited a R_f value only slightly lower than that of 4 and immediately decolourized a dilute acetone solution of potassium permanganate.[27] After processing as described above, TLC showed the presence of a large amount of starting material, liberated obviously from a reactive intermediate[28,29] as a result of aqueous treatment. The major product 11, isolated in poor yield* (~20%) exhibited a strong IR absorption

*Compound 11 is very sensitive to traces of acid, such as those present in common chloroform, and partially decomposes during chromatography on silica gel.

band at 1660 cm^{-1} (C=C) and a mp 120-121°, $[\alpha]_D$ +59° (c 0.6, chloroform).

Anal. Calcd for $C_{21}H_{22}O_5$: C, 71.16; H, 6.25. Found: C, 71.06; H, 6.26.

2-O-Methyl-α-D-glucopyranosyl fluoride (6). A solution of 4 (100 mg) in 2-methoxyethanol (5 mL) was stirred at room temperature under an atmosphere of hydrogen in the presence of 5% palladium-on-charcoal catalyst (100 mg) until hydrogen uptake ceased (∿30 min). TLC (solvent B) showed that one product was formed. After filtration and concentration, the product (50 mg, 96%) was crystallized from acetone (twice), to give pure 6, mp 125-127°, $[\alpha]_D$ +104° (c 1, water).

Anal. Calcd for $C_7H_{13}FO_5$: C, 42.85; H, 6.67; F, 9.68. Found: C, 43.11; H, 6.92; F, 9.33.

2-O-Methyl-β-D-glucopyranosyl fluoride (5). A solution of 3 (100 mg) in 2-methoxyethanol (5 mL) was treated as described for the preparation of 6. The product 5 (46 mg, 88%), when crystallized from ethanol-ether melted unsharply with concomitant decomposition ∿115° and had $[\alpha]_D$ +28° (c 0.6, water); lit.[15] mp 108-112° (dec.), $[\alpha]_D$ +25° (c 1, water).

Anal. Calcd for $C_7H_{13}FO_5$: C, 42.85; H, 6.67; F, 9.68. Found: C, 43.11; H, 6.92; F, 9.68.

Methyl 3-O-benzyl-4,6-O-benzylidene-2-O-methyl-α- (8) and β-D-glucopyranoside (7). To a solution of compound 3 (175 mg) in benzene-methanol (3:1, 4 mL) was added acetyl chloride (0.5 mL) and the resulting solution was refluxed for 8 h. After cooling, the solution was neutralized with Amberlite IR-45 (carbonate form) resin and concentrated. While TLC (solvent B) showed that the product(s) formed migrated as a single spot, ^1H and ^{13}C NMR spectroscopy indicated that a ∿3:1 mixture of the methyl α- and β-pyranosides of 3-O-benzyl-2-O-methyl-D-glucose (100 mg, ∿100%) was formed. Diagnostically important signals in the ^1H NMR spectrum (220 MHz, $CDCl_3$) were at δ: 4.91 (d, 0.75 H, ^2J 11 Hz, benzylic-α), 4.89 (d, 0.25 H, ^2J 11 Hz, benzylic-β), 4.82 (d, 0.75 H, $J_{1,2}$ 3.5 Hz, H-1-α), 4.72 (d, 0.25 H, ^2J 11 Hz, benzylic-β), 4.69 (d, 0.75 H, ^2J 11 Hz,

benzylic-α), 4.20 (d, 0.25 H, $J_{1,2}$ 8 Hz, H-1-β). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 104.60 (C-1-β), 97.49 (C-1-α), 84.10, 83.71 (C-2-β, C-3-β), 81.91, 81.43 (C-2-α, C-3-α), 61.81 (C-6-β), 61.64 (C-6-α), 60.37 (2-OMe-β), 58.73 (2-OMe-α), 57.08 (1-OMe-β), 55.12 (1-OMe-α).

To the foregoing mixture dissolved in DMF (1 mL), was added benzaldehyde dimethyl acetal (3 mL), followed by anhydrous p-toluenesulfonic acid (5 mg). The mixture was stirred at 65-70°/2 kPa in a round bottom flask fitted with an air condenser which was connected to a water aspirator. After 2 h, the mixture was diluted with dichloromethane, neutralized with solid sodium hydrogen carbonate, and concentrated. TLC (solvent A) showed the presence of two major components. Chromatography gave first the faster moving β-anomer 7 (32.5 mg, 18%), mp 130-130.5°, $[\alpha]_D$ -78° (c 0.5, $CHCl_3$); lit.[15] mp 127.5-129°, $[\alpha]_D$ -80° (c 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.32 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 3.10-3.21 (m, 1 H, H-2), 3.61-3.69 (m, 2 H, H-3, H-4), 3.32-3.46 (m, 1 H, H-5), 3.77 (t, 1 H, $J_{6,6a}$ 10.5 Hz, $J_{5,6}$ 10.1 Hz, H-6), 4.35 (dd, 1 H, $J_{5,6a}$ 5.2 Hz, H-6a), 4.90, 4.79 (d, d, 1 H each, ^2J 11.8 Hz, benzylic CH_2), 3.56, 3.61 (s, s, 3 H each, OMe).

Continued elution gave the α-anomer 8 (112 mg, 62%), mp 113-114°C, $[\alpha]_D$ +29° (c 1.2, $CHCl_3$); lit.[15] mp 112-113°, $[\alpha]_D$ +31° (c 1.03, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.86 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 3.38 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-2), 3.98 (t, 1 H, $J_{3,4}$ 9.3 Hz, H-3), 3.62 (dd, 1 H, $J_{4,5}$ 9.3 Hz, H-4), 3.83 (dt, 1 H, $J_{5,6}$ 4.3 Hz, H-5), 4.29 (dd, 1 H, $J_{6,6a}$ 9.7 Hz, H-6), 3.76 (dd, 1 H, $J_{5,6a}$ 9.4 Hz, H-6a), 4.80, 4.88 (d, d, 1 H each, ^2J 11.5 Hz, benzylic CH_2), 3.44, 3.58 (s, s, 3 H each, OMe).

When compound 4 was treated with methanolic HCl as described above for 3, the ^{1}H NMR spectrum of the crude product showed that it was identical with that formed from 3.

Treatment of glycosyl fluorides 3-6 with sodium methoxide in methanol. a) Compound 5 (20 mg) was treated with sodium methoxide in methanol as described.[16] After 7 days TLC (solvent A) indicated the presence of a small amount of the starting material and one slower moving product.

b) A solution of 5 (20 mg) in 2 M methanolic sodium methoxide (3 mL) was refluxed overnight. TLC (solvent A) showed the absence of starting material and the presence of one product, indistinguishable (TLC) from the one formed as described above in a). The solution was neutralized with Amberlite IR-120 (H^+-form) resin, concentrated and eluted from a small column of silica gel, to remove some coloured material. Concentration of the eluant gave methyl 2-O-methyl-α-D-glucopyranoside 13; ^{13}C NMR (25 MHz, $CDCl_3$) δ: 97.2 (C-1), 81.0 (C-2), 73.0 (C-3), 71.1 (C-5), 70.1 (C-4), 61.7 (C-6), 58.4 (OMe-2), 55.3 (OMe-1).

c) Compounds 4-6, when treated as described in b), remained unchanged (TLC).

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