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A FACILE FORMATION OF 2,5-ANHYDRO SUGARS BY RING CONTRACTION IN METHYL HEXOPYRANOSIDE 2-TRIFLATES UNDER CONDITIONS OF NUCLEOPHILIC DISPLACEMENT

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ABSTRACT

Reaction of methyl 3,4-*O*-isopropylidene-2-*O*-(trifluoromethylsulfonyl)-α-L-fucopyranoside and its β anomer with a variety of nucleophilic reagents under mild conditions led to displacement of the triflic ester group, with migration of the ring-oxygen atom to C-2 and entry of the nucleophile at C-1, to give good yields of 2,5-anhydro sugar derivatives. Reagents employed were hydrogen fluoride–triethylamine complex, methanol in the presence of sodium hydrogencarbonate, sodium benzoate, sodium azide, potassium thiocyanate, and sodium borohydride. The same type of substitutive ring-contraction also occurred in methyl 4-*O*-benzyl-3-*O*-(4-methoxybenzyl)-2-*O*-(trifluoromethylsulfonyl)-α-L-fucopyranoside and methyl 4,6-dideoxy-3-*O*-(4-methoxybenzyl)-2-*O*-(trifluoromethylsulfonyl)-α-L-*xylo*-hexopyranoside. The reaction is discussed in light of a literature survey of the chemical behavior of hexopyranoside 2-sulfonates in general, and 2-triflates in particular. Direct SN2 displacements, eliminations, and such different kinds of rearrangement as have previously been observed with structural analogs were not encountered in the present study. However, there is some precedent, in hexopyranoside 2-triflates, for the facile rearrangement that the four representatives here investigated have been found to undergo. The synthesis of these triflates from L-fucose is described.

INTRODUCTION

In the course of a project directed at the synthesis of certain aminofluoro sugars, to be used as glycons for structurally modified anthracycline antitumor agents[1–3], we considered possible preparative routes to hitherto unknown 3-amino-2,3,6-trideoxy-2-fluoro-L-talose (A), which was desired as such a glycon. In one of the approaches contemplated (see Scheme 1), the fluorine atom was to be introduced into an appropriately constituted glycoside (B) by SN2 displacement of a sulfonic ester function at C-2 while O-3 carried a nonparticipatory and selectively removable protecting-group; subsequent introduction of the amino function was

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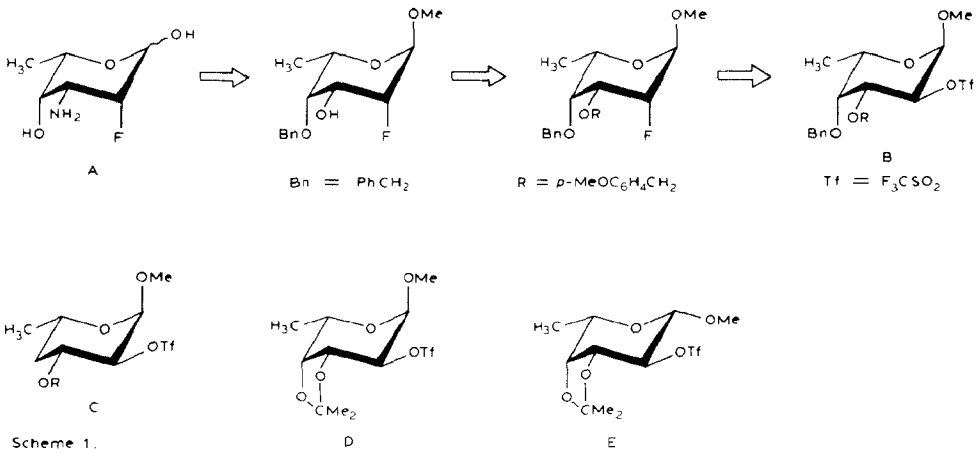


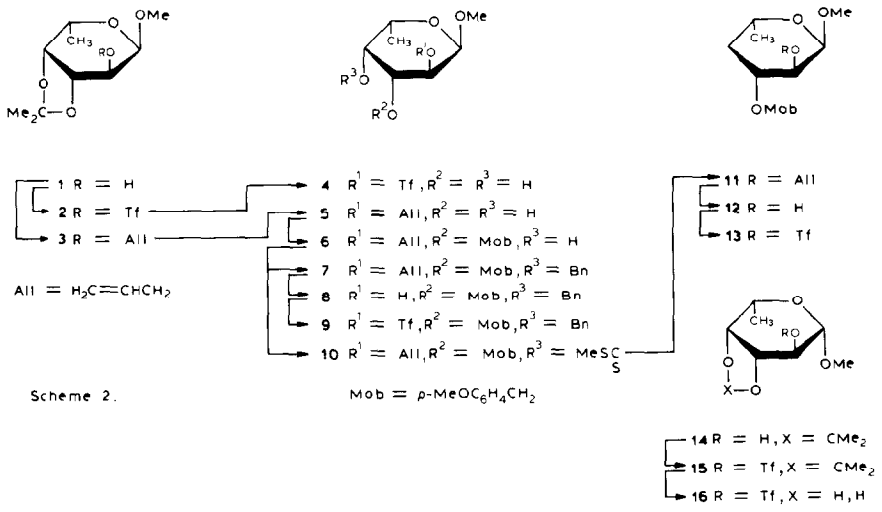
Scheme 1.

envisaged by way of deprotection and oxidation to the oxo stage at C-3, followed by oximation and reduction, or reductive amination. It was considered that compound B might be suitable as a starting point for such manipulations, because, whereas 2-tosylates and 2-mesylates of pyranosides are generally resistant to nucleophilic displacement, 2-triflates have in several instances been employed successfully in substitution reactions with various nucleophiles[4], including[5] fluoride ion (although, with fluoride, competing elimination and other undesired reactions have frustrated a number of attempts[3,5]). Should displacement in B prove achievable, then the stage would be set for selective cleavage of the *p*-methoxybenzyl ether and the subsequent operations referred to.

However, when B was synthesized and then treated with hydrogen fluoride–triethylamine complex, a reagent that has recently been shown highly effective for fluorination of carbohydrate triflates[6], displacement of the triflic ester group was accompanied by rearrangement of the pyranoid to a 2,5-anhydro ring. It was then discovered that such ring contraction also occurs with several other, nucleophilic reagents, including sodium azide, benzoate, borohydride, and methoxide, and potassium thiocyanate. Furthermore, it was not unique to the substrate B, but also took place in compounds D, C, and E (see Scheme 1).

RESULTS AND DISCUSSION

Preparation of the triflates that underwent ring contraction. — The triflates in which displacement reactions were investigated were compounds **2, 9, 13,** and **15**. They were procured as illustrated in Scheme 2. The known[7] methyl 3,4-*O*-isopropylidene-α- and -β-L-fucopyranosides (**1** and **14**) were triflated, to give the corresponding 2-triflates **2** and **15**. These were characterized by their ^{1}H-n.m.r. spectra, but they proved rather unstable in storage, tending to suffer loss of acetone with formation of the diols **4** and **16**, respectively; they were best prepared im-



Scheme 2.

mediately prior to the performance of the intended displacement reactions.

Allylation of **1** furnished the ether **3**, which was deacetalated by acetic acid to the 3,4-diol **5**. Regioselective (*p*-methoxybenzyl)ation of **5** by the stannylene procedure in the presence of tetrabutylammonium iodide[8] afforded the 2-*O*-allyl-3-*O*-(*p*-methoxybenzyl) derivative **6**, which was benzylated to give the fully protected glycoside **7**. Deallylation of **7** was accomplished by means of palladium-on-carbon in aqueous methanol in the presence of *p*-toluenesulfonic acid[9] (yield, 60%), or by the procedure of isomerization using a cationic iridium complex[10], followed by treatment[11] with mercuric chloride and mercuric oxide (yield, 77%) to give the alcohol **8**. Trityation of the latter provided **9**.

As our original intention was also to synthesize 2-fluoro derivatives of the 4,6-dideoxyhexose series, we branched off from the sequence just described, by converting the partially blocked glycoside **6** into the 4-*O*-[(methylthio)thiocarbonyl] derivative **10**, which was then cleaved[12] with tributylstannane to produce the 4-deoxy derivative **11**. Deallylation of **11** by the Pd and Ir methods was unsatisfactory in this instance, as the reactions were slow, and were accompanied by partial fission of the *p*-methoxybenzyl ether. However, the reaction proceeded well by isomerization with potassium *tert*-butoxide followed by mercuric chloride–mercuric oxide treatment[11]. The resulting alcohol **12** then gave the triflate **13**. The ^{1}H- and ^{13}C-n.m.r. data of the new compounds are listed in Tables I and II.

Nucleophilic displacements with ring contraction. — When the triflates **2** and **15** were treated with 5 mol. equiv. of hydrogen fluoride–triethylamine complex (3 HF·Et_3N) and added triethylamine (1.5 mol. equiv.) in acetonitrile solution for 16 h at room temperature (or for 3 h, followed by 2.5 h at 70°), they were, according to t.l.c., completely consumed, and what appeared to be the same product was seen to arise from both, giving essentially a single spot, except for some immobile products of decomposition. Isolated without delay by column chromatography, the

TABLE I

^{1}H-N.M.R. DATA AT 300 MHz FOR PYRANOSIDES **1–16** AND **31** IN CHLOROFORM-*d*

Compound	*Chemical shifts (δ)*										
	H-1	*H-2*	*H-3*	*H-4e*	*H-4a*	*H-5*	*H-6*[a]	*Me*-O[b]	*Me*-O[c]	Ar-CH_2[d]	*Others*[e]
1	4.70d	3.77m	4.17t	4.03dd		4.08dq	1.31	3.42			1.50, 1.34[f]
2	4.84d	4.72dd	4.36dd	4.1m		4.1m	1.35	3.42			1.51, 1.35[f]
3	4.70d	3.50dd	4.23m	4.22dd		4.06dq	1.33	3.38			1.41, 1.33[f,g]
4	← 4.90–4.86m →		4.11dd[h]	3.89dd[h]		4.01dq	1.29	3.42			
5	4.83d	3.63dd	3.95dd	3.81dd		3.93dq	1.29	3.40			[g]
6	4.76d	←	3.8–3.7m	→		3.89dq	1.26	3.38	3.79	4.69, 4.58	[g]
7	4.77d	3.93dd	3.83dd	3.57dd		3.8m	1.09	3.37	3.80	4.95, 4.62; 4.75, 4.61	[g]
8	4.79d	4.12ddd[i]	3.66dd	3.62dd		3.82dq	1.16	3.38	3.79	4.91, 4.63; 4.67, 4.61	
9	4.90d	5.22dd	3.97dd	3.60dd		3.84dq	1.11	3.39	3.80	4.92, 4.55; 4.67, 4.54	
10	4.81d	3.74dd	3.95dd	6.29dd		4.06dq	1.16	3.40	3.77	4.66, 4.46	2.57[j,g]
11	4.74d	3.36dd	~3.8m	2.00ddd	1.32dt	~3.8m	1.16	3.37	3.78	4.64, 4.55	[g]
12	4.75d	3.56dd	3.65td	2.04ddd	1.28dt	3.86dq	1.18	3.39	3.78	4.59, 4.53	
13	4.87d	4.66dd	3.93ddd	2.09ddd	1.40dt	3.88dq	1.17	3.39	3.79	4.56, 4.49	
14	4.04d	3.51dd	←	~4.0m	→	3.85dq	1.41	3.52			1.51, 1.34[f]
15	4.27d	4.57dd	4.22dd	4.07dd		3.89dq	1.42	3.53			1.51, 1.34[f]
16	4.35d	4.60dd	3.77dd	3.83dd		3.68dq	1.36	3.54			
31[k]	4.70d	3.51dd	4.39dd	4.1m		4.02~q	1.42	3.40			5.90[l,g]
31[m]	4.80d	3.66dd	4.55dd	4.02dd		4.06dq	1.36	3.42			6.12[l,g]

	Coupling constants (Hz)								
	$J_{1,2}$	$J_{2,3}$	$J_{3,4e}$	$J_{3,4a}$	$J_{4e,4a}$	$J_{4e,5}$	$J_{4a,5}$	$J_{5,Me}$	*Others*
1	3.9	6.3	6.3			2.2		6.6	
2	3.5	7.9	5.2			2		6.5	
3	3.6	7.9	5.5			2.6		6.6	[n]
4	3.7	10	4			1.5		6.7	
5	3.5	10.0	3.2			1.3		6.6	[n]
6	3.4					~1.5		6.7	[n]
7	3.6	10.2	2.7			1.2		6.5	[n]
8	3.9	9.8	2.7			1.1		6.6	
9	3.5	10.2	3.0			~1		6.5	
10	3.7	10.2	3.4			1.0		6.6	[n]
11	3.6	9.3	5.1	~12	12.8	2.3	~12	6.3	[n]
12	3.7	9.3	4.5	10.8	12.9	2.3	~12	6.3	
13	3.7	9.5	5.3	~11.5	13.2	2.2	~11.5	6.3	
14	8.3	6.9				2.2		6.6	
15	8.3	7.5	5.25			2.1		6.6	
16	7.8	9.4	3.5			0.5		6.5	
31[k]	3.6	7.6	5.9			~1.5		6.6	[n]
31[m]	3.7	8.0	5.2			2.2		6.7	[n]

[a]Three-proton doublets. [b]Anomeric; 3-proton singlets. [c]Aromatic; 3-proton singlets. [d]Benzylic and (or) *p*-methoxybenzylic; midpoints of the A and B parts of AB-quartets (J_{gem} 11.0–11.7 Hz) are given. [e]All compounds bearing aromatic substituents showed the requisite, aromatic-proton signals in the δ-7 region. All compounds having free hydroxyl groups showed doublets or broad singlets (exhangeable) in the δ 2.0–2.5 region. [f]Isopropylidenic 3-proton singlets. [g]Resonances for the allyl group: a 16-line multiplet for H-2 near δ 5.9; two ddt for H-3 and H-3′, close together but clearly separated in the δ-5.3–5.1 region; and an AB-quartet of triplets for magnetically non-equivalent H-1 and H-1′ in the δ-4.3–4.1 region. [h]After D_2O exchange. [i]Collapsing to dd on D_2O exchange; $J_{2,OH}$ 7.1 Hz. [j]Me-SCS. [k]*R*-isomer. [l]*Ph*-CHO_2. [m]*S*-isomer. [n]Couplings in the allyl group: $J_{2,3(trans)}$ 17.2, $J_{2,3(cis)}$ 10.3, $J_{1,2}$ 6.3, $J_{1',2}$ 5.5, $J_{1,1'}$ 12.8, $J_{1,3} \approx J_{1,3'} \approx J_{3,3'} \approx 1.35$ Hz.

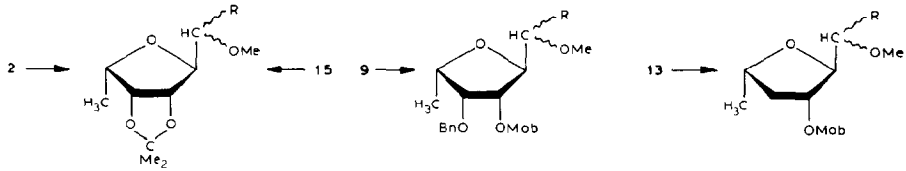
TABLE II

^{13}C-N.M.R. DATA AT 75.43 MHz FOR PYRANOSIDES

Compound[a]	*Chemical shifts (p.p.m.)*[b]							
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*OMe*	*Others*[c]
2	97.2	85.2	76.8, 72.8		63.2	16.0	55.9	118.4d[d]; 109.9[e]; 27.9, 26.3[f]
3	98.3	←76.4, 76.2, 76.0→			62.9	16.4	55.4	108.7[e]; 28.4, 26.5[f]
5	97.5	76.2	←71.6, 69.4→		65.3	16.2	55.3	
6	98.5	←77.4, 75.3→		70.4	65.0	16.2	55.2, 55.3	
7	98.8	←79.0, 77.9, 76.2→			66.1	16.7	55.25[g]	
8	99.6	68.7	←79.6, 76.7→		66.5	16.7	55.25[g]	
9	97.3	83.5	←77.6, 75.8→		66.4	16.2	55.2, 55.6	118.5d[d]
10	99.1	←80.4, 76.0, 75.5→			65.1	16.4	55.5, 55.25	19.1[h]
11	99.0	←80.6, 74.9→		39.4	63.5	21.0	55.0, 55.25	
12	99.9	←75.7, 73.7→		38.1	63.9	21.0	55.1, 55.3	
13	97.5	86.4	71.5	39.2	63.6	20.6	55.4, 55.3	118.5d[d]
15	99.8	86.6	←77.2, 76.3→		69.3	16.4	57.1	118.4[d]; 110.8[e]; 27.8, 26.3[f]
31[i]	98.5	←78.7, 76.8, 75.7→			62.8	16.3	55.5	103.6[j]
31[k]	98.2	←77.3, 76.1, 73.5→			62.9	16.5	55.5	102.45[j]

[a]In chloroform-*d*. [b]With reference to the tetramethylsilane signal. [c]Compounds containing an allyl group gave signals at 134.7 ±0.3 (C-2), 117.6 ±0.5 (C-3), and 71.8 ±0.7 (C-1) p.p.m. Compounds containing a *p*-methoxybenzyl group gave signals at 159.2 ±0.3, 130.3 ±0.7, 129.3 ±0.3, and 113.8 for aromatic, and 72.5 ±0.5 p.p.m. for benzylic carbon, and those containing a benzyl group gave the corresponding signals at 138.5 ±0.6, 128.7 ±0.4, 128.2 ±0.2, 126.9 ±0.8, and 74.85 ±0.15 p.p.m. [d]CF_3-SO_3; $J_{C,F}$ 319 Hz. [e]Me_2CO_2. [f]Me_2CO_2. [g]Coinciding signals for 2 methoxyl groups. [h]Me-*S*; a thiocarbonyl carbon signal was not discernible. [i]*R* isomer. [j]*Ph*-CHO_2. [k]*S* isomer.

product was obtained as a colorless syrup (55% yield in each case), and found to have lost the triflyl group but to have retained the methoxyl and *O*-isopropylidene groups; a newly introduced fluorine atom was present (mass and n.m.r. spectroscopy). However, the product did not display the characteristics expected of a stable 2-deoxy-2-fluoro glycoside but, instead, was very unstable. Although the syrup could be stored for a day or two at −40° with little change, it tended to decompose rapidly at higher temperatures, turning into a tar having an acidic reaction (indicator paper). This instability may have been a cause of the relatively low yield obtained, after processing, from what appeared by t.l.c. to be a fairly clean reaction. Spectroscopic analysis established the structure as that of 2,5-anhydro-6-deoxy-1-fluoro-3,4-*O*-isopropylidene-1-*O*-methyl-L-talitol* (**17**). When prepared from **2**, compound **17** was obtained as a levorotatory, 1:3 mixture of 1-epimers (provisionally designated as epimers I and II). Interestingly, the product obtained under identical conditions from **15** was dextrorotatory and consisted almost exclusively of epimer I, accompanied by only a minute proportion of epimer II.



17 R = F
18 R = OMe
19 R = OBz
20 R = N_3
21 R = −N=C=S
22 R = H

23 R = F
24 R = OMe
25 R = OBz
26 R = N_3

27 R = OMe
28 R = OBz
29 R = N_3

The ^{1}H-n.m.r. spectrum of epimer I showed the substituent resonances for *C*-CH_3 and the isopropylidene group as required by formula **17**. The 3-proton resonance due to the *O*-CH_3 group was not the usual singlet, but showed a small (1.2 Hz) splitting from long-range coupling with the fluorine atom. The H-1 atom gave a low-field (δ 5.16) doublet of doublets indicating vicinal and geminal coupling ($J_{1,2}$ 2.7, $J_{1,F}$ 63.7 Hz), and H-2 resonated at δ 4.07 as a triple doublet reflecting three vicinal couplings ($J_{2,3}$ 1, $J_{1,2}$ 2.7, and $J_{2,F}$ 8 Hz). The ^{19}F-n.m.r. spectrum confirmed these data. In the proton-decoupled ^{13}C-n.m.r. spectrum, C-1 resonated as a doublet due to coupling with the fluorine atom (δ 111.8, $J_{C,F}$ 221.5 Hz), as did C-2 (δ 83.4, $J_{C,F}$ 30 Hz). The spectra of **17** obtained from **2** exhibited the same set of signals but additionally contained a second set, with approximately threefold intensity, attributable to epimer II. Therein, the H-1 doublet of doublets ($J_{1,2}$ 2.3,

*According to carbohydrate nomenclature rules pertaining to alphabetic precedence, the equivalent designation 2,5-anhydro-1-deoxy-6-fluoro-3,4-*O*-isopropylidene-6-*O*-methyl-L-altritol should be used. However, in view of the need to designate several close analogs in this paper as L-talose derivatives, we prefer the L-talitol name, which facilitates comparative discussion and tabulation of data where positional indicators are cited.

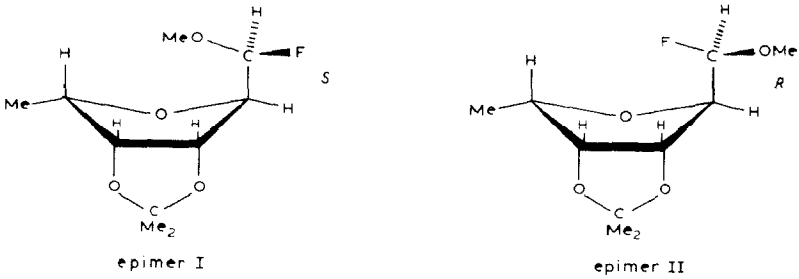


Fig. 1. Favored rotamers of epimeric components of **17**.

$J_{1,F}$ 63.4 Hz) occurred at δ 5.20, and H-2 at δ 4.00 showed similar, small vicinal proton couplings ($J_{1,2}$ 2.3, $J_{2,3}$ ~1 Hz), but a larger vicinal fluorine coupling ($J_{2,F}$ 25 Hz), which was also revealed in the ^{19}F-n.m.r. spectrum of the epimeric mixture. The proton-decoupled ^{13}C-n.m.r. spectrum of the mixture contained, for epimer II, doublets assignable to C-1 (δ 113.3, $J_{C,F}$ 221.5 Hz) and C-2 (δ 83.9, $J_{C,F}$ 21.4 Hz). The configuration at C-2 was revealed, for both epimers, by the small value of ~1 Hz for $J_{H\text{-}2,H\text{-}3}$, which indicated a dihedral angle near 90° between H-2 and H-3, requiring these protons to be *trans* related on the five-membered anhydro sugar ring in the E_0 conformation (see Fig. 1).

Some of the n.m.r. data just mentioned are relevant also to the C-1 stereochemistry of **17**. Thus, the small $J_{H\text{-}1,H\text{-}2}$ values indicate, for both epimers, a favored rotameric disposition comprising a *gauche* H-1,H-2 arrangement. The vicinal F–H coupling of 8 Hz for epimer I suggests a *gauche* orientation also between F and H-2, whereas the value of 25 Hz for epimer II suggests an *anti* orientation of these nuclei[13]. The $^2J_{F,C\text{-}2}$ values for the epimers I (30 Hz) and II (21.4 Hz) accord[13] with *anti* and *gauche* relationships, respectively, of the fluorine atom with respect to the electronegative substituent (the ring-oxygen atom) on C-2. These features, depicted in Fig. 1, support a tentative attribution of 1*R* and 1*S* configuration as indicated.

The aforementioned instability of **17**, *i.e.*, its ready decomposition with loss of hydrogen fluoride, was chemical evidence in support of the α-fluoro ether structure. A sample stored in moist chloroform was partially converted into the dimethyl acetal **18**, which was isolated chromatographically, and identified by its ^{1}H-n.m.r. spectrum. Evidently, methanol liberated by hydrolysis had reacted with surviving **17**.

In one experiment, **15** was allowed to react with tetrabutylammonium fluoride in acetonitrile instead of the hydrogen fluoride–triethylamine reagent. Completion of the reaction appeared to occur faster (after 3 h at 0°), but the product was the same (namely, **17**), according to t.l.c. No further studies with fluoride-containing nucleophilic reagents were undertaken. Instead, a range of other nucleophiles were examined in reactions with both **2** and **15**, and ring contraction was observed in every case, leading to the products **18–22** (see Table III). Except, of

TABLE III

FORMATION OF 2,5-ANHYDRO SUGARS **17–29**

Starting compound	*Reagent (mol. equiv.)*	*Solvent*	*Reaction temperature (°C)*	*Reaction time (h)*	*Product*	*Isolated yield (%)*[a]
2	3 HF·Et_3N (5)[b]	MeCN	25	16	**17**	55
15	3 HF·Et_3N (5)[b]	MeCN	25	16	**17**	55
2	$NaHCO_3$ (1.2)	MeOH	50	3	**18**	68
15	$NaHCO_3$ (1.2)	MeOH	65	22	**18**	82
2	NaOBz (2)	DMF	25	26	**19**	55
15	NaOBz (2)	DMF	25	6	**19**	59
2	NaN_3	DMF	25	6	**20**	68
15	NaN_3	DMF	25	22	**20**	72
2	KSCN (2)	DMF	25	18	**21**	54
15	KSCN	DMF	25	18	**21**	69
2	$NaBH_4$ (3)	MeCN	70	16	**22**	40[c]
15	$NaBH_4$ (3)	MeCN	70	16	**22**	37[c]
9	3 HF·Et_3N (5)[b]	MeCN	25	18	**23**	45[d]
	$NaHCO_3$ (3)	MeOH	65	48	**24**	98[d]
	NaOBz (2)	DMF	110	3	**25**	85[d]
	NaN_3	DMF	110	1.75	**26**	84[d]
13	$NaHCO_3$ (3)	MeOH	65	24	**27**	66
	NaOBz (2)	DMF	60	24	**28**	70
	NaN_3	DMF	60	24	**29**	51

[a]Based on starting hydroxy compound before triflation, unless otherwise indicated. [b]Plus Et_3N (1.5). [c]See Experimental section. [d]Based on crystalline triflate **9**.

TABLE IV

^{1}H-N.M.R. DATA AT 300 MHz FOR 2,5-ANHYDRO SUGARS **17–29** IN CHLOROFORM-*d*

Compound	*Chemical shifts (δ)*[a]						
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*Me-O*[b]	Ar-CH_2[c]
17[d]	5.16dd	4.09ddd	4.92dd	4.57dd	4.16dq	3.53d	
17[e]	5.20dd	4.00ddd	4.92dd	4.58dd	~4.1m	3.54d	
18	4.26d	4.02dd	4.84dd	4.55dd	4.14dq	3.42, 3.41	
19[f]	6.04d	4.23dd	4.94dd	4.65dd	4.13dq	3.50	
19[g]	6.00d	4.23dd	5.00dd	4.60dd	4.13dq	3.49	
20[h]	4.30d	4.14dd	4.75dd	4.60dd	4.28dq	3.49	
20[i]	4.45d	4.04dd	4.80dd	4.57dd	4.15dq	3.50	
21[f]	4.81d	4.05dd	4.89dd	4.57dd	4.19dq	3.48	
21[g]	4.79d	4.09dd	4.83dd	4.62dd	4.29dq	3.50	
22	3.43dd	4.12m	4.71dd	4.57dd	4.12m	3.33	
23[f]	5.11dd	← 4.2–4.1m →		3.84t	~4.15m	3.54d	4.72, 4.56; 4.51s (2 H)
24	4.22d	4.14dd	4.02t	3.82t	~4.15m	3.40, 3.38	4.69, 4.54; 4.51s (2 H)
25[f]	6.02d	4.28dd	4.15t	3.88t	4.16dq	3.46	4.71, 4.57; 4.51, 4.44
25[g]	6.01d	4.28dd	4.17t	3.90t	4.19dq	3.51	4.73, 4.59; 4.54s (2 H)
26[f]	← 4.2m →		4.02dd	3.85dd	~4.2m	3.51	4.70, 4.59; 4.53, 4.44
26[g]	4.29d	~4.2m	4.015dd	3.84dd	~4.2m	3.44	4.71, 4.57; 4.53, 4.44
27	4.21d	← 4.2–4.1m →		2.25dt, 1.64sp	4.2–4.1m	3.41 (6 H)	4.46, 4.40
28[f]	6.00d	← 4.3–4.15m →		2.32dt, 1.69sp	4.3–4.15m	3.51	4.41, 4.37
28[g]	5.97d	← 4.3–4.2m →		2.33dt, 1.67sp	4.3–4.2m	3.49	4.48, 4.43
29[f]	← 4.2–4.1m →			2.29dt, 1.68m	4.24m	3.51	4.43s (2 H)
29[g]	4.31d	← 4.2–4.1m →		~2.29dt, 1.68m	4.24m	3.50	4.42s (2 H)

	Coupling constants (Hz)					
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	*Others*
17[d]	2.7	1.1	6.1	4.0	6.4	$^2J_{F,1}$ 63.3; $^3J_{F,2}$ 8.0; $^4J_{F,MeO}$ 1.3
17[e]	2.3	1	6.1	3.6	6.3	$^2J_{F,1}$ 67.2; $^3J_{F,2}$ 25; $^4J_{F,MeO}$ 1.2
18	4.15	1.15	6.1	4.9	6.4	
19[f]	4.2	1.4	6.15	4.0	6.4	
19[g]	3.2	0.9	6.15	3.7	6.4	
20[h]	3.5	1.4	6.1	3.9	6.4	
20[i]	4.3	1.35	6.1	3.9	6.4	
21[f]	3.6	1.2	6.1	3.9	6.4	
21[g]	3.7	1.6	6.1	3.9	6.4	
22	4.65	1.1	6.15	3.9	6.4	$J_{1',2}$ 0.9; $J_{1,1'}$ 0
23[f]	2.2		4.3	4.3	6.5	$^2J_{F,1}$ 64.4; $^3J_{F,2}$ 10; $^4J_{F,OMe}$ 1.2
24	4.4	5.4	4.9	4.8	6.5	
25[f]	3.9	5.9	4.45	4.45	6.4	
25[g]	3.3	5.8	4.6	4.6	6.5	
26[f]		6.5	4.3	4.3	6.4	
26[g]	3.5	6.5	4.3	4.3	6.5	
27	5.0		6.7	6.7	6.7	$J_{3,4'}$ 5.1; $J_{4',5}$ 7.4; $J_{4,4'}$ 12.5
28[f]	6.6		6.35	6.35	6.2	$J_{3,4'}$ 5.0; $J_{4',5}$ 7.7; $J_{4,4'}$ 12.7
28[g]	5.4		6.8	6.8	6.2	$J_{3,4'}$ 5.0; $J_{4',5}$ 7.7; $J_{4,4'}$ 12.7
29[f]			6	6	6.15	$J_{3,4'}$ 5; $J_{4',5}$ 7; $J_{4,4'}$ 12
29[g]	4.2		6	6	6.2	$J_{3,4'}$ 5; $J_{4',5}$ 7; $J_{4,4'}$ 12

[a]The following, almost invariant signals were recorded in addition to those tabulated: For all compounds, δ 1.28 ±0.02 (d, 3 H, Me–*CH*); two 3-proton singlets (Me_2C) at δ 1.48 and 1.33 ±0.01 for all *O*-isopropylidene derivatives, except **19**, which gave these signals at δ 1.50 and 1.35 (major epimer), and 1.54 and 1.48 (minor epimer); and for **23**–**29**, δ 3.78 ±0.01 (s, 3 H, MeO–*Ar*). [b]Singlet, 3 H, unless otherwise indicated. [c]Double values refer to midpoints of the A and B parts of AB quartets (J_{gem} 11.5 ±0.5 Hz). [d]Epimer I. [e]Epimer II. [f]Major epimer. [g]Minor epimer. [h]Major epimer from **15** (= minor epimer from **2**). [i]Major epimer from **2** (= minor epimer from **15**).

TABLE V

^{13}C-N.M.R. DATA AT 75.43 MHz FOR 2,5-ANHYDRO SUGARS **17–29**

Compound[a]	*Chemical shifts (p.p.m.)*[b,c]						
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*O-Me*
17[d]	111.8d[e]	83.4d[f]	81.35	82.3	78.4	14.4	57.3d[g]
17[h]	111.8d[e]	83.9d[i]	81.45d[j]	82.3	78.45	14.4	57.15
18	105.0	83.6	82.5, 82.3		78.0	14.5	56.1, 55.1
19[k]	97.8	84.2	82.4, 82.3		78.5	14.6	57.5
19[l]	98.2	84.1	82.5, 82.2		78.3	14.4	57.45
20[m]	93.2	85.6	82.7, 82.5		79.1	14.6	57.4
20[n]	93.2	85.2	82.4, 82.1		78.4	14.45	57.5
21[k]	89.9	85.3	82.4, 81.9		79.0	14.5	57.6
21[l]	90.1	84.9	82.35, 82.3		79.0	14.7	57.6
22	73.4	83.3, 82.4, 82.35			77.5	14.3	59.2
23[k]	112.2d[e]	80.8d[o]	78.6, 78.1		76.8	15.4	57.1
24	104.8	80.8	79.2, 78.9		76.5	15.7	55.8, 54.8
25[k]	98.3	80.75	79.0, 78.4		76.95	15.6	57.4
25[l]	98.3	80.8	79.1, 78.8		76.95	15.6	57.8
26[k]	92.7	82.0	79.8, 78.3		77.15	15.6	57.7
26[l]	93.1	81.95	79.2, 78.5		77.1	15.5	57.3
27	104.7	83.2	80.4	40.2	75.4	21.6	55.7, 54.4
28[k]	98.3	83.5	80.0	40.1	75.8	21.65	57.4
28[l]	98.4	83.7	80.0	40.4	75.8	21.6	57.7
29[k]	93.0	84.8	80.2	40.0	75.8	21.6	57.6
29[l]	93.6	84.6	80.2	40.15	76.0	21.7	57.3

[a]In chloroform-*d*. [b]With reference to the tetramethylsilane signal. [c]The *p*-methoxybenzylic and benzylic CH_2 signals for **23–29** occurred at 71.7 ±0.6 and 73.0 ±0.1 p.p.m., respectively, and the aromatic-ring carbons resonated in the ranges given in Table II, footnote *c*; the *p*-MeO group resonated at 55.3 p.p.m. in every instance. The benzoates **19, 25,** and **28** exhibited a carbonyl signal at 166.0 ±0.1 and four ring-carbon signals in the range 133.5–128.4 p.p.m. for the ester group. The isopropylidene derivatives **17–22** showed signals at 112.3 ±0.5 for the acetal carbon, and at 26.45 ±0.05 and 25.2 ±0.1 for CMe_2. [d]Epimer I. [e]$^1J_{C,F}$ 221.5 Hz. [f]$^2J_{C,F}$ 29.2 Hz. [g]$^3J_{C,F}$ 2 Hz. [h]Epimer II. [i]$^2J_{C,F}$ 21.4 Hz. [j]$^3J_{C,F}$ 3.3 Hz. [k]Major epimer. [l]Minor epimer. [m]Major epimer from **15** (= minor epimer from **2**). [n]Major epimer from **2** (= minor epimer from **15**). [o]$^2J_{C,F}$ 25 Hz.

course, for the dimethyl acetal **18** (obtained with methanol in the presence of sodium hydrogencarbonate) and the alcohol **22** (produced by sodium borohydride), the products were mixtures of 1-epimers present in various ratios. All the products were isolated (without separation of epimers), and characterized analytically and spectroscopically. For the ^{1}H- and ^{13}C-n.m.r. parameters, see Tables IV and V.

Displacement studies with the 2-triflate **9** led to entirely analogous results. Reaction with hydrogen fluoride–triethylamine gave a ring-contracted, highly unstable 1-fluoro-1-*O*-methyl derivative (**23**), identified on the basis of its ^{1}H- and ^{19}F-n.m.r. spectra. With methanol, sodium benzoate, and sodium azide, respectively, the stable analogs **24–26** were produced. Similarly, the 4-deoxy-2-triflate **13** furnished the analogs **27–29** by reaction with the three last-named nucleophiles. Reaction conditions and yields are listed in Table III. Only the benzoates **25** and

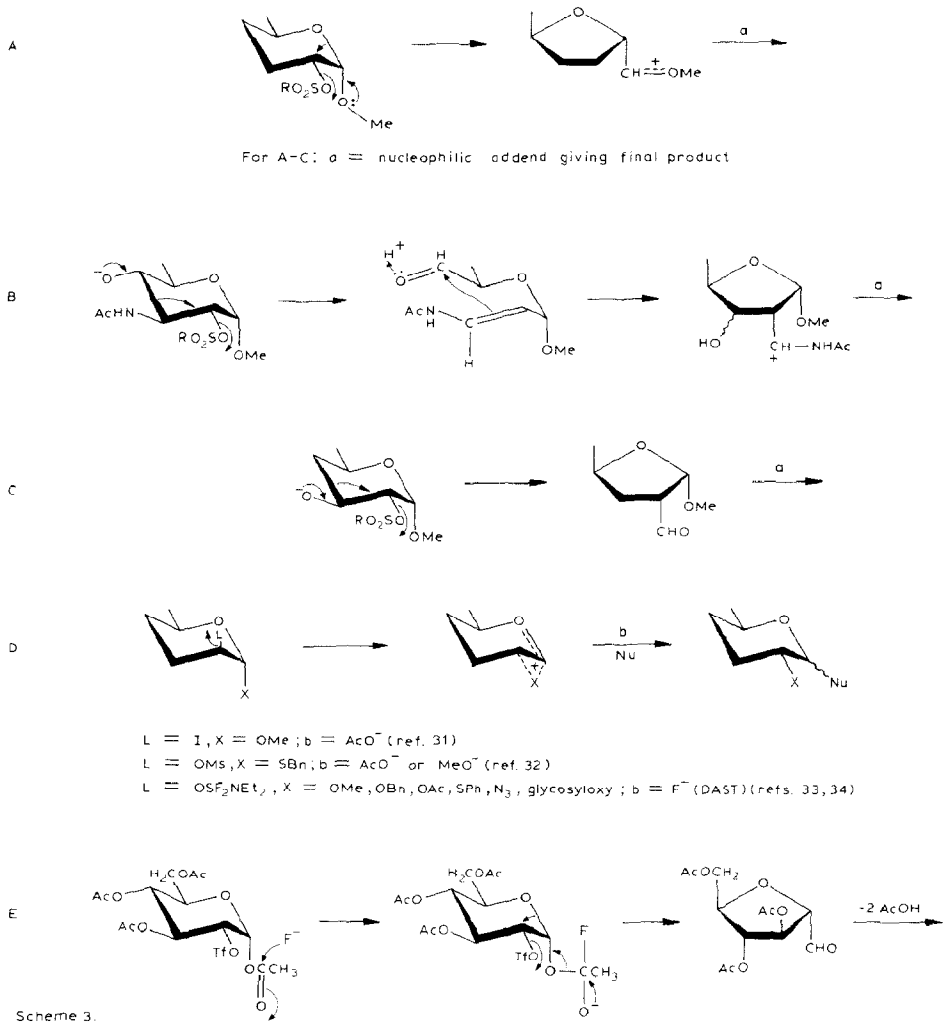
28 could be partially resolved into pure 1-epimers. Fluoride displacement in **13** was not investigated.

Discussion. — Rearrangement of the hexopyranoside to the 2,5-anhydro-*aldehydo*-hexose structure as here encountered is not uncommon. It has been observed in nitrous acid deamination of 2-amino-2-deoxy-D-glucose derivatives[14], in brominolysis of a 2-deoxy-2-iodo-D-glucoside[15], in the action of lead tetrafluoride upon a hex-2-enopyranoside[16], in solvolysis of a 2-*O*-(*p*-nitrophenylsulfonyl)-D-glucopyranoside[17], and, most recently, during attempted SN2 displacements (with tetrabutylammonium azide and benzoate) in certain D-galactopyranoside 2-(*N*-imidazolylsulfonates)[18]. In 2-sulfonates with less-nucleofugal leaving-groups, ring contraction is rare*. Mechanistically, these reactions all have in common the development of positive charge on C-2 in concert with the departure of the leaving group, and migration of the ring-oxygen bond from the anomeric center to C-2, with formation of a (more-stable) C-1 oxocarbonium ion that is then attacked by a basic species from the medium[24] (see Scheme 3,A). Intermediacy of a resonance-stabilized C-1 oxocarbonium ion in the rearrangements here reported is in accord with the fact that **2** (and **15**) gave, with potassium thiocyanate, the *iso*thiocyanato derivatives **21**, rather than the isomeric thiocyanato derivatives. The ambident thiocyanate ion is known to react predominantly at sulfur in SN2 reactions, but, in reactions with carbocations, its reactivity is shifted more and more to nitrogen as the cation stability increases[25a]. (The isothiocyanate structure of **21** was deduced from spectroscopic data**.)

Notwithstanding the rearrangements found in some other, highly reactive 2-sulfonates[17,18], the behavior of the triflates **2, 9, 13,** and **15** under conditions of nucleophilic displacement would have been difficult to predict at the outset of our investigation, as the following survey will indicate. As already mentioned in the Introduction, several 2-triflates of hexopyranosides had proved amenable to direct SN2 displacement by various nucleophiles[4], including fluoride ion[5], although 2-mesylates and 2-tosylates are extremely unreactive in that regard[26]. Impressive examples are the high-yielding displacements achieved, with sodium benzoate and

*We found no examples for its occurrence in 2-tosylates. The methyl 3,4-*O*-isopropylidene-5-thio-α- and -β-D-ribopyranoside 2-mesylates gave 2,5-dideoxy-2,5-epithio-3,4-*O*-isopropylidene-D-arabinose dimethyl acetal with methanol and sodium hydrogencarbonate[19]. Rearrangement of pyranoside 4-sulfonates to furanosides by migration of the ring-oxygen atom is more-common[20]; an analogous sulfur migration occurred in a 5-thio-D-ribopyranose 4-mesylate[19]. The pyranoside moiety of 4′-triflated daunorubicin rearranged differently, namely, by way of a 4,5-hydride shift, to form a 4-deoxy-5-keto structure[21]. In solvolyses of hexopyranoside 3-(*p*-nitrobenzenesulfonates)[17] and 3-triflates[22], and in a reductive desulfonyloxylation of a 3-triflate[23], C-3 branched furanosides arose by migration of the C-4–5 bond.

Compound **21 showed in the i.r. spectrum a very strong, *broad band* at 2100–2000 cm^{-1} characteristic for isothiocyanates, as opposed to a very *sharp peak* expected near 2150 cm^{-1} for a thiocyanate[25b], and a ^{13}C-n.m.r. signal for –NCS at[25b] δ 131.2. Although the presence of a minor proportion of thiocyanate cannot be precluded on the basis of these data, as the broad i.r. band may have obscured an adjacent, less-intense peak for –SCN and a low-intensity, ^{13}C signal for that group expected near δ 112 may have coincided with an acetal carbon signal, the well-resolved ^1H-n.m.r. spectrum indicated the presence of only two isomers (1.5:1 ratio), and these are believed to be 1-epimers.



Scheme 3.

azide, in the α-D-*gluco* moiety of certain 4,6;4′,6′-bis(benzyliden)ated, trehalose-type disaccharides (68–90% yields after 1–21 h in DMF at 80–110°)[4f], contrasting with a 3% yield of benzoate-displacement product obtained[26b] from methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-(methylsulfonyl)-α-D-glucopyranoside (after 120 h in refluxig DMF). In the realm of fluorine substitution, hexopyranoside 2-triflates successfully subjected to displacement include 4,6-acetalated derivatives having the α-D-*gluco*[5b,g,k], β-D-*gluco*[5b,g,m], β-D-*manno*[5a–c,i,m], α-D-*ido*[5l], and β-D-*ido*[5k] configurations; a 3,4-acetalated β-D-taloside[5f]; nonacetalated β-D-mannosides[5c,g,i,m], and a β-D-glucoside[5d]; and 1,6-anhydro-β-D-mannopyranose derivatives[4g,5h]. However, competing elimination of triflic acid was a significant side-reaction in a few of these

instances[5i,j], and it was the predominant or exclusive occurrence in 4,6-acetalated pyranosides having the α-D-*manno*[5i], β-D-*talo*[5f], and α-D-*altro*[3] configuration, as well as in a (nonacetalated) α-D-mannoside[5m], a 4,6-dideoxy-α-L-*lyxo*-hexopyranoside[3], and, reportedly, for a β-L-fucopyranoside[5k] (no data disclosed). As far as we know, there was but a single, reported instance[4c] of ring contraction, and this involved a pentopyranoside. Methyl 3-azido-3,4-dideoxy-2-*O*-triflyl-α-DL-*threo*-pentopyranoside gave, with sodium benzoate, a 62% yield of a 2,5-anhydro product (analogous to **28**). Its β anomer underwent normal displacement[4c]. However, contemporary with our studies, another, closely related precedent was published by Fleet and Seymour[27], who reported azide displacements for the 6-*tert*-butyldiphenyloxy analogs of **2** and **15**, as well as for the corresponding α-D-*altro* isomer, giving products structurally analogous to **20**.

These results[27], and our own, clearly establish 2,5-anhydro sugar formation from pyranoid 2-triflates as an important alternative to simple displacement or elimination, but it is difficult at present to identify structural factors that are conducive to its occurrence. It may be significant that the reaction appears to be prevalent in the *galacto* series (see also, ref. 18) and was, moreover, observed in at least one[27] altroside. However, the notion[18] that rearrangement in galactosides might occur, as a diversion, because normal, SN2 approach of the nucleophile to C-2 is disfavored owing to 1,3-diaxial interaction with O-4, must be discounted in view of the reactions of **13** and of the aforementioned[4c] deoxypentoside, which lack a C-4 substituent. An ancillary suggestion[18], namely, that the lone electron pair on the ring-oxygen atom might similarly discourage such an approach, is untenable in view of the many successful SN2 displacements achieved in glucopyranoside 2-triflates (see the preceeding). Perhaps the question of rearrangement *versus* simple displacement is one of product development control, that is, the furanoid ring generated from *galacto* and *altro* pyranosides (and, of course, from **13**) bears no oxygen substituent *cis* to the developing C-1 oxocarbonium group, whereas *cis* oxygen would be present, at C-3 and (or) C-4, for all other hexose configurations, and this might translate into energy differences sufficient to direct the course of reaction*.

The general problem of chemical behavior of sulfonates is complicated by the fact that rearrangements other than the one involving ring-oxygen migration as just discussed have also been known to occur in certain pyranoside 2-sulfonates and related compounds, and it may be asked why our compounds (**2, 9, 13,** and **15**) and the analogs cited[4c,18,27] did not undergo such alternative rearrangements.

Thus, ring contractions by migration of C-4 to C-2, producing C-2 branched furanosides, are well documented. Cases in point are the reaction of methyl 3-acetamido-3,6-dideoxy-2-*O*-(methylsulfonyl)-α-L-glucopyranoside with methanolic methoxide[28], the reaction of methyl 6-deoxy-6-(*p*-toluenesulfonamido)-2-*O*-(trifluoromethylsulfonyl)-α-D-glucopyranoside with sodium in liquid ammonia[29], and the reactions of methyl 6-deoxy-2-*O*-(*p*-tolylsulfonyl)-α-D-gluco- and -α-D- (and L)-

*To test this hypothesis, allopyranoside and gulopyranoside 2-triflates ought to be studied, to see whether they incur simple displacement like their *gluco, ido, manno,* and *talo* counterparts referred to[4,5].

galactopyranosides with lithium triethylborohydride[30]. However, these substrates all differ from the fully blocked sulfonic esters of the present study in that they contain a suitably positioned, free hydroxyl group essential to the contraction mechanisms that are presented in Scheme 3,B,C*.

Another transformation to which at least the 1,2-*trans* glycoside **15**, its 6-silyloxy analog[27], and the aforementioned[4c] α-D-*threo* deoxypentoside might have been thought susceptible is 1,2-migration of the anomeric methoxyl group (see Scheme 3,D). Lemieux and Fraser-Reid[31] first demonstrated such a shift when they observed 2-*O*-methyl-D-glucose tetraacetate as a product of brominolysis of methyl 2-deoxy-2-iodo-α-D-mannopyranoside triacetate. Subsequently, a similar shift of the anomeric benzylthio group in benzyl 2-*O*-mesyl-1-thio-α-D-arabinoside was achieved[32], and, recently, migration of methoxyl[33,34], benzyloxy[5k,34], and other anomeric substituents[34] was reported to take place when 1,2-*trans* glycosyl derivatives bearing an unprotected OH-2 group are treated with *N*,*N*-diethylaminosulfur trifluoride (DAST)**. However, we detected no product of methoxyl migration from reactions performed with **15**.

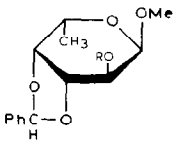
Finally, it is worth noting that 2-*O*-triflyl-α-D-glucopyranose tetraacetate was converted into 5-(acetoxymethyl)-2-formylfuran by action of tetrabutylammonium fluoride[35]. Although constituting a ring contraction formally analogous to the present topic, this reaction probably differed mechanistically, with attack by fluoride ion on the anomeric ester carbonyl group being suggested as the initiating event[35] (see Scheme 3,E). The stereoisomeric β-D-*manno* compound partly underwent SN2 displacement, and, partly, elimination of triflic acid, under the same conditions[35].

In summary, the facile rearrangement of **2, 9, 13**, and **15** and their analogs[4c,27] by action of nucleophilic reagents, although having precedents in other carbohydrate systems, appears unique with respect to the general behavior of pyranoside 2-triflates. A full understanding of the factors governing its occurrence in preference to more-commonly observed displacements and eliminations requires further study.

Addendum. — We record additionally the preparation, from known[36] methyl 3,4-*O*-benzylidene-α-L-fucopyranoside (**30**), of the allyl ether **31** (obtained as *R* and *S* isomers), which was used initially as a precursor for **5**. Triflation of **31** gave an unstable triflate (**32**) that tended to lose benzaldehyde during processing, forming the diol **4**. Preliminary displacement trials with **32** and tetrabutylammonium fluoride were inconclusive.

*For the rearrangement by sodium in liquid ammonia, the authors[29] suggested a radical mechanism involving a ring-opened, triradical intermediate. A process such as that in Scheme 3,C would appear more plausible.

**Reference 5k appears to be at variance with Scheme 3,D, as it reports a migration in a 1,2-*cis* glycoside.



30 R = H
31 R = All
32 R = Tf

EXPERIMENTAL

General methods. — Column chromatography was performed on silica gel Merck 7734 (100–200 mesh), and thin-layer chromatography on plates precoated with silica gel. Unless otherwise stated, the following solvent combinations (v/v) were used: (*A*) 1:1, (*B*) 1:2, (*C*) 1:4, (*D*) 1:6, (*E*) 1:8, and (*F*) 1:10 ethyl acetate–hexane; (*G*) 2:1, (*H*) 1:1, (*I*) 1:2, (*J*) 1:3, (*K*) 1:4, (*L*) 1:5, (*M*) 1:6, (*N*) 1:8, and (*O*) 1:10 ether–hexane. Optical rotations were determined at ~25° with a Perkin–Elmer 241 polarimeter and refer to chloroform solutions, *c* 1, unless otherwise specified. Infrared data (ν_{max}) were recorded from Nujol mulls for solids, and from thin films for syrups. Mass-spectral data (*m/z*) were obtained by the chemical ionization mode, using ether.

*Methyl 3,4-O-isopropylidene-α- and -β-*L*-fucopyranoside* (**1** *and* **14**). — Methyl α-L-fucopyranoside[37] was isopropylidenated with 2,2-dimethoxypropane as described[38] for the analogous benzyl glycoside, but with a reaction time of 18 h. The product (**1**), obtained in 91% yield after chromatographic purification (solvent *C*), showed $[\alpha]_D$ −168° (*c* 1, water) [lit.[7a] −160°], and ^{1}H-n.m.r. data as reported[7c].

The mother liquor from the preparation of methyl α-L-fucopyranoside was treated with potassium acetate in ethanolic solution to give the crystalline, molecular complex of methyl β-L-fucopyranoside[37a]. Liberated by treament of an aqueous solution with Amberlite IR-120 (H^+) resin, the pure β-glycoside, m.p. 121–122°, was isopropylidenated like its anomer, affording, after chromatography, a 70% yield of **14**, $[\alpha]_D$ −23.7° [lit.[7c] −23°]. The ^{1}H-n.m.r. data agreed with those reported[7b,c].

*Methyl 2-O-allyl-3,4-O-isopropylidene-α-*L*-fucopyranoside* (**3**). — A solution of **1** (8.7 g) in dry *N,N*-dimethylformamide (50 mL) was stirred at 0° in the presence of NaH (3.65 g). Allyl bromide (8.35 mL) was added, and the mixture was kept for 30 min at 25°. A faster-moving product was formed (t.l.c., solvent *A*). Methanol was carefully added to decompose the excess of NaH, and the mixture was evaporated *in vacuo* with several additions of toluene. A solution of the residue in chloroform was washed well with water, dried, and evaporated, to afford syrupy **3** (9.6 g, 93%); $[\alpha]_D$ −147.6°; i.r.: no OH band; *m/z* 227 ($M^+ + 1 - OCH_3$).

Anal. Calc. for $C_{13}H_{22}O_5$ (258.3): C, 60.45; H, 8.59. Found: C, 60.24; H, 8.34.

Methyl 2-O-allyl-α-L-fucopyranoside (**5**). — A solution of the acetal **3** (9.5 g) in aqueous, 60% acetic acid (30 mL) was heated for 90 min at 60°, after which time a single, slow-moving product was observed (t.l.c., solvent *A*). Coevaporation with added toluene gave **5** as a syrup which, after drying over KOH (desiccator) was purified chromatographically (solvent *A*). The pure **5** was obtained crystalline (7.11 g, 88.6%); m.p. 69–72°, $[\alpha]_D$ −172°; ν_{max} 3400 cm^{-1} (OH); *m/z* 219 ($M^+ + 1$) and 187 (M^+ − MeOH).

Anal. Calc. for $C_{10}H_{18}O_5$ (218.2): C, 55.03; H, 8.31. Found: C, 55.20; H, 8.23.

Methyl 2-O-allyl-3-O-(4-methoxybenzyl)-α-L-fucopyranoside (**6**). — A mixture of **5** (7.0 g) and dibutyltin oxide (8 g) in dry benzene (300 mL) was boiled overnight under reflux, with azeotropic removal of water[8]. The solution was concentrated to about one-half its volume and, after addition of tetrabutylammonium iodide (17.5 g) and 4-methoxybenzyl chloride (8.65 mL), the boiling was continued for 5 h. Evaporation of the mixture to dryness gave a residue which was processed by column chromatography (solvent *F*), to give **6** (10.0 g, 92%) as a syrup; $[\alpha]_D$ −72.5°; ν_{max} 3460 cm^{-1} (OH); *m/z* 338 (M^+) and 306 (M^+ − MeOH).

Anal. Calc. for $C_{18}H_{26}O_6$ (338.4): C, 63.88; H, 7.75. Found: C, 63.86; H, 7.62.

Methyl 2-O-allyl-4-O-benzyl-3-O-(4-methoxybenzyl)-α-L-fucopyranoside (**7**). — A solution of **6** (1.6 g) in dry *N,N*-dimethylformamide (10 mL) was treated with NaH (0.23 g). Benzyl bromide (0.84 mL) was added after 5 min, and the mixture was then kept for 2 h at 25°. After decomposition of the excess of NaH by moist methanol, and evaporation of the mixture *in vacuo*, the residue was dissolved in chloroform, and the solution was washed exhaustively with water, dried, and evaporated. The crude material was purified by column chromatography (solvent *G*), giving **7** (1.45 g, 72%) as a colorless syrup; $[\alpha]_D$ −45.6°; i.r.: no OH band; *m/z* 429 ($M^+ + 1$), 428, 427 ($M^+ - 1$), and 397 ($M^+ - OCH_3$).

Anal. Calc. for $C_{25}H_{32}O_5$ (428.5): C, 70.01; H, 7.53. Found: C, 70.22; H, 7.35.

Methyl 4-O-benzyl-3-O-(4-methoxybenzyl)-α-L-fucopyranoside (**8**). — *Procedure*[9] *A*. A solution of **7** (60 mg) in methanol (4 mL) and water (1 mL) was stirred and boiled under reflux in the presence of 10% Pd–C (10 mg) and *p*-toluenesulfonic acid (5 mg). Monitoring by t.l.c. (solvent *A*) indicated completion of the reaction after 30 min. The suspension was filtered, and the filtrate was diluted with brine and ice, and extracted three times with dichloromethane. The extracts were combined, dried, and evaporated. The syrup obtained was passed through a column of silica gel with solvent *I*, to give **8** (33 mg, 60%) as a syrup, identical with **8** (i.r., n.m.r.) prepared by procedure B.

Procedure[10] *B*. A solution of **7** (428 mg) and 1 mg of 1,5-cyclooctadiene–bis-(methyldiphenylphosphine)iridium hexafluorophosphate (Alfa Products) in peroxide-free oxolane (20 mL, distilled from $LiAlH_4$) was agitated for 3 min at room temperature in an ultrasonic bath, placed under an atmosphere of dry,

oxygen-free N_2, and sonicated for 5 min. The N_2 atmosphere was replaced by H_2 under a slight, positive pressure, and the solution agitated for 5 min, during which operation, the reddish suspension became colorless. The atmosphere was now changed to pure N_2, and sonication was continued for 1 h. Monitoring by t.l.c. (solvent *I*) indicated formation of the faster-moving, isomerized, 1-propenyl ether. The solution was evaporated, the oily residue dissolved in chloroform, and the solution successively washed with aqueous $NaHCO_3$ (10 mL) and water (10 mL), dried, and evaporated.

The syrupy 1-propenyl ether so obtained was dissolved in 10:1 acetone–water (20 mL), yellow HgO (280 mg) was added, and a solution of $HgCl_2$ in 10:1 acetone–water was introduced dropwise, with magnetic stirring. Rapid cleavage of the enol ether was indicated by t.l.c. (solvent *H*). Filtration of the mixture through a bed of Celite, and evaporation of the filtrate gave a residue whose solution in ether was washed successively with saturated, aqueous KI solution and water, dried, and evaporated. Part of the product (**8**) crystallized directly from ether–hexane, and processing of the mother liquor by chromatography (solvent *C*) gave an additional crop, for a total of 298 mg (77%); m.p. 121–123° (from ethyl acetate–hexane), $[\alpha]_D$ −112° (*c* 0.5); ν_{max} 3400 cm^{-1} (OH); *m/z* 267 ($M^+ + 1 - MeOC_6H_4CH_2O$).

Anal. Calc. for $C_{22}H_{28}O_6$ (388.4): C, 68.02; H, 7.26. Found: C, 67.89; H, 7.09.

Methyl 2-O-allyl-3-O-(4-methoxybenzyl)-4-O-[(methylthio)thiocarbonyl]-α-L-fucopyranoside (**10**). — A solution of **6** (4.0 g, 11.8 mmol) in dry ether (25 mL) was boiled under reflux in the presence of NaH (1.4 g, 58 mmol). After 1.5 h, carbon disulfide (3.6 mL, 58 mmol) was added, followed after 1 h by methyl iodide (3.6 mL, 58 mmol), and refluxing was continued for 2 h. The formation of fast-moving **10** was monitored by t.l.c. (solvent *A*). Water was then carefully added to decompose the excess of NaH, and the ethereal phase was successively washed with dilute HCl, aqueous $NaHCO_3$ solution, and water, dried, and evaporated, to give **10** as a yellow syrup that was purified by column chromatography (solvent *J*). The yield of pure **10** was 4.50 g (88.8%); $[\alpha]_D$ −123°; i.r.: no OH band; *m/z* 429 ($M^+ + 1$) and 381 ($M^+ - MeS$).

Anal. Calc. for $C_{20}H_{28}O_6S_2$ (428.6): C, 56.05; H, 6.58; S, 14.96. Found: C, 56.34; H, 5.45; S, 15.14.

Methyl 2-O-allyl-4,6-dideoxy-3-O-(4-methoxybenzyl)-α-L-xylo-hexopyranoside (**11**). — A solution of **10** (4.18 g), tributylstannane (7.9 mL), and azodiisobutanonitrile (1.6 g) in benzene (50 mL) was boiled under reflux for 20 min and then stored for 2 h at room temperature. Removal of the solvent, and column chromatography (solvent *N*) of the residue, gave **11** (2.34 g, 73%) as a syrup; $[\alpha]_D$ −68°; *m/z* 323 ($M^+ + 1$) and 291 ($M^+ - CH_3O$).

Anal. Calc. for $C_{18}H_{26}O_5$ (322.4): C, 67.05; H, 8.13. Found: C, 66.97; H, 8.20.

Methyl 4,6-dideoxy-3-O-(4-methoxybenzyl)-α-L-xylo-hexopyranoside (**12**). — A solution of **11** (1.65 g) and potassium *tert*-butoxide (1.7 g) in dimethyl sulfoxide

(20 mL, freshly distilled from NaOH) was heated for 15 min in an oil bath (100°). Formation of the faster-moving, isomerized 1-propenyl ether was noted (t.l.c., solvent *H*). The solution was cooled, diluted with water (30 mL), and exhaustively extracted with ether. The extract was dried, and evaporated, and the residue chromatographed on silica gel (solvent *J*), to give 1.26 g (76.4%) of syrupy *methyl 4,6-dideoxy-3-*O*-(4-methoxybenzyl)-2-*O*-(1-propenyl)-α-*L*-xylo-hexopyranoside;* ^{1}H-n.m.r. (300 MHz, $CDCl_3$): δ 7.25, 6.84 (2 d, 2 H each, arom.), 6.11 (m, $^3J_{cis}$ 6.2, $^4J_{H,Me}$ 1.7 Hz, *O*–CH=*CH*–*Me*), 4.75 (d, $J_{1,2}$ 3.6 Hz, H-1), 4.63, 4.50 (2 d, J_{gem} 11 Hz, *Ar*–CH_2), 4.42 (dq, *J* 6.2 and 6.8 Hz, *O*–*CH*=CH–*Me*), 3.85 (m, 2 H, H-3,5), 3.78 (s, 3 H, *Ar*–OMe), 3.57 (dd, $J_{1,2}$ 3.6, $J_{2,3}$ 9.5 Hz, H-2), 3.39 (s, 3 H, OMe), 2.02 (ddd, H-4e), 1.64 (dd, 3 H, ^4J 1.7, ^3J 6.8 Hz, *O*–*CH*=*CH*–Me), 1.34 (dt, H-4e), and 1.16 (d, 3 H, $J_{5,Me}$ 6.3 Hz, Me–*C*-5).

The 1-propenyl ether was then cleaved with $HgCl_2$ and HgO (840 mg of each) in aqueous acetone as described for the preparation of **8** (procedure B). The crude **12** was purified by chromatography using initially 1:10 ether–hexane, the proportion being gradually changed to 1:1. Pure **12** (800 mg; 55.4% based on **11**) crystallized from the column eluate; m.p. 60–62°, $[\alpha]_D$ −136°; ν_{max}^{KBr} 3453 cm^{-1} (OH); *m/z* 283 (M^+ + 1) and 251 (M^+ − OMe).

Anal. Calc. for $C_{15}H_{22}O_5$ (282.3): C, 63.81; H, 7.85. Found: C, 63.86; H, 8.04.

Preparation of triflates. — A. General procedure. For triflation of **1, 8, 12,** and **14** the procedure of Kloosterman *et al.*[4i] was employed, except that the molar ratios of sugar:trifluoromethanesulfonic anhydride:pyridine were 1:2:5. The method is illustrated by the following example. Triflic anhydride (0.22 mL, 1.31 mmol) in dry[4i] 1,2-dichloroethane (3 mL) was added to a solution of pyridine (0.26 mL, 3.19 mmol) in 1,2-dichloroethane (5 mL), stirred under pure N_2 at −20°. After 10 min, a solution of the alcohol **8** (250 mg, 0.64 mmol) in 1,2-dichloroethane (5 mL) was added, and stirring was continued for 30 min, the temperature being allowed to rise gradually to 0°. (The reaction, monitored by t.l.c. with solvent *A*, appeared essentially complete after 10 min.) Dichloromethane (25 mL) and aqueous $NaHCO_3$ solution were added, the phases were shaken and then separated, and the aqueous phase was extracted with dichloromethane. The combined organic phase was washed with water, dried, and evaporated with addition of toluene (2 × 20 mL), to give crude triflate **9**. Triflation of **14** required 1 h.

B. *Methyl 3,4-*O*-isopropylidene-2-*O*-(trifluoromethylsulfonyl)-α-*L*-fucopyranoside* (**2**) *and methyl 2-*O*-(trifluoromethylsulfonyl)-α-*L*-fucopyranoside* (**4**). The crude triflate (**2**) obtained from **1** was used for the intended reactions without purification because of its instability. However, an analytical sample was purified by rapid passage through a short column of silica gel by means of solvent *M*, and was thereby obtained crystalline; m.p. 68–70°, $[\alpha]_D$ −131.3°; *m/z* 351 (M^+ + 1), 319 (M^+ − OMe), and 201 (M^+ + 1 − TfOH). The n.m.r. spectra of the purified **2** were recorded without delay.

On storage, neat or in solution, compound **2** suffered loss of the acetal group, to give the diol **4**, as revealed by the appearance of a slow-moving spot in t.l.c. (solvent *B*). Isolated by column chromatography, **4** was an amorphous solid; *m/z* 311 ($M^+ + 1$), 279 ($M^+ - OMe$), 261 ($M^+ - H_2O - OMe$), and 161 ($M^+ + 1 -$ TfOH).

Anal. Calc. for $C_8H_{13}F_3O_7S$ (310.2): C, 30.97; H, 4.22; S, 10.33. Found: C, 31.15, H, 4.37; S, 10.46.

C. *Methyl 4-O-benzyl-3-O-(4-methoxybenzyl)-2-O-(trifluoromethylsulfonyl)-α-*L*-fucopyranoside* (**9**). The crude **9** (see section A) was purified by column chromatography (solvent *K*), giving pure **9** (319 mg, 95%) that crystallized from the eluate; m.p. 89–91° (dec.), $[\alpha]_D$ −64.8° (*c* 0.7); i.r.: no OH band; *m/z* 429 ($M^+ - C_7H_7$), 399 ($M^+ - MeOC_6H_4CH_2$), and 370 ($M^+ -$ TfOH).

Anal. Calc. for $C_{23}H_{27}F_3O_8S$ (520.5): C, 53.07; H, 5.23; S, 6.16. Found: C, 53.12; H, 5.24; S, 6.39.

D. *Methyl 4,6-dideoxy-3-O-(4-methoxybenzyl)-2-O-(trifluoromethylsulfonyl)-α-*L*-xylo-hexopyranoside* (**13**). Triflation of **12** (95 mg) followed by chromatography of the crude product using solvent *K* furnished **13** (130 mg, 93%) as a syrup; $[\alpha]_D$ −73°; i.r.: no OH band; *m/z* 415 ($M^+ + 1$), 414 (M^+), and 264 ($M^+ -$ TfOH).

Anal. Calc. for $C_{16}H_{21}F_3O_7S$ (414.4): C, 46.37; H, 5.11; S, 7.74. Found: C, 46.53; H, 5.17; S, 7.59.

Although **13** was evidently stable at room temperature for at least the time needed to obtain an (external) elemental analysis, the product from a parallel experiment incurred partial decomposition overnight, probably catalyzed by some impurity. A slow-moving product was separated from unchanged **13** by chromatography, and it proved to be *methyl 4,6-dideoxy-2-O-(trifluoromethylsulfonyl)-α-*L*-xylo-hexopyranoside*, resulting from loss of the *p*-methoxybenzyl group; ^{1}H-n.m.r. data (300 MHz, $CDCl_3$): δ 4.89 (d, $J_{1,2}$ 3.6 Hz, H-1), 4.55 (dd, $J_{2,3}$ 9.3 Hz, H-2), 4.21 (ddd, $J_{3,4e}$ 5.3, $J_{3,4a}$ 11.4 Hz, H-3), 3.95 (sxd, $J_{4e,5}$ 2.2, $J_{5,Me}$ 6.2, $J_{4a,5}$ ~12 Hz, H-5), 3.40 (s, 3 H, OMe), 2.12 (ddd, J_{vic} 2.2 and 5.3, J_{gem} 13.2 Hz, H-4e), 1.50 (m, splittings ~11–13 Hz, H-4a), and 1.21 (d, 3 H, *C*-Me).

E. *Methyl 3,4-O-isopropylidene-2-O-(trifluoromethylsulfonyl)-β-*L*-fucopyranoside* (**15**) *and methyl 2-O-(trifluoromethylsulfonyl)-β-*L*-fucopyranoside* (**16**). The crude triflate **15** obtained from **14** was a yellow solid that was used directly for the intended experiments. For characterization, a sample was chromatographed as described for **2** and so obtained crystalline; m.p. 78–79° (dec.), $[\alpha]_D$ −19°, $[\alpha]_{436}$ −39.1°, $[\alpha]_{365}$ −61.3°; *m/z* 351 ($M^+ + 1$), 319 ($M^+ - OMe$), and 201 ($M^+ + 1 -$ TfOH).

Storage of **15** was attended by loss of the acetal group, as revealed by the appearance of a slow-moving spot in t.l.c. (solvent *A*). Isolated by column chromatography, the diol **16** was a syrup; *m/z* 311 ($M^+ + 1$), 279 ($M^+ - OMe$), 261 ($M^+ - H_2O - OMe$), and 161 ($M^+ + 1 -$ TfOH).

Nucleophilic displacements with ring contraction in **2, 9, 13,** *and* **15**. — *A. General procedure.* All experiments were performed starting with 75–100 mg of the

corresponding alcohols (**1, 8, 12,** and **14**). The rather unstable triflates **2** and **15** were used crude, immediately following their preparation; the triflates **9** and **13** were chromatographically purified. The triflates and reagents were dissolved in 5 mL of carefully dried and distilled solvent (see Table III). Reactions were monitored by t.l.c. For processing, the solvent was evaporated *in vacuo* (with coevaporation of added toluene in the case of use of *N,N*-dimethylformamide). The crude products were dissolved in chloroform, and the solutions washed with cold, saturated $NaHCO_3$ solution followed by water (in the case of fluoride displacements), or with water alone (in all other cases), dried ($MgSO_4$), and evaporated. The resulting syrups were chromatographed on columns, giving the yields of isolated, pure products listed in Table III. The solvents used for t.l.c. and column chromatography (c.c.) are given in the individual sections. Infrared spectra of all products were in accord with the structures assigned. The n.m.r.-spectral data are listed in Tables IV and V.

B. *Individual 2,5-anhydro sugar derivatives.*

*2,5-Anhydro-6-deoxy-1-fluoro-3,4-*O*-isopropylidene-1-*O*-methyl-*L*-talitol* (**17**) was isolated by c.c. with solvent *I*. Prepared from **2**, it was a syrupy, ~1:3 mixture of epimers I and II; $[\alpha]_D$ −18.5°. From **15**, syrupy epimer I containing only a trace of epimer II (n.m.r.) was obtained, $[\alpha]_D$ +27.3°. The i.r. and mass spectra of both preparations showed only insignificant differences; *m/z* 221 ($M^+ + 1$), 215, and 201 ($M^+ - F$). Isolated **17** decomposed rapidly at room temperature; it also deteriorated noticeably during overnight storage at 0°, but could be stored for 1–2 days at −40°.

*2,5-Anhydro-6-deoxy-3,4-*O*-isopropylidene-*aldehydo-*L-talose dimethyl acetal* (**18**), isolated by c.c. (solvent *D* or *M*), had R_F 0.6 (t.l.c., solvent *A*); $[\alpha]_D$ −2.5°, $[\alpha]_{546}$ −2.2°; *m/z* 233 ($M^+ + 1$), 216, and 201 ($M^+ - OMe$); volatile in oil-pump vacuum. The products prepared from **2** and **15** were identical according to ^{1}H-n.m.r. and mass spectra.

Anal. Calc. for $C_{11}H_{20}O_5$ (232.3): C, 56.88; H, 8.68. Found: C, 56.99; H, 8.75.

*2,5-Anhydro-6-deoxy-3,4-*O*-isopropylidene-*aldehydo-*L-talose methyl hemiacetal 1-benzoate* (**19**) was isolated (c.c. with solvent *L* or *M*) in the form of syrupy mixtures of 1-epimers, not separated in t.l.c. (R_F 0.65, solvent *A*; 0.3, solvent *C*). The preparations from **2** and **15** had $[\alpha]_D$ −3° and −7°, respectively, and gave identical mass spectra: *m/z* 323 ($M^+ + 1$), 247, and 201 ($M^+ + 1 - BzOH$). The ^{1}H-n.m.r. spectra indicated epimer ratios of 1.5–2:1 (from **2**) and 5–6:1 (from **15**).

Anal. Calc. for $C_{17}H_{22}O_6$ (322.4): C, 63.34; H, 6.88. Found: C, 63.10; H, 6.93.

*2,5-Anhydro-1-azido-6-deoxy-3,4-*O*-isopropylidene-1-*O*-methyl-*L*-talitol* (**20**) was isolated (c.c. with solvent *A*) in the form of syrupy mixtures of 1-epimers showing $[\alpha]_D$ −23.4° (from **2**) and −76.4° (from **15**), and nearly identical i.r. spectra; ν_{max} 2100 cm^{-1} (N_3); *m/z* 215 ($M^+ + 1 - N_2$) and 201 ($M^+ - N_3$). Epimer proportions were estimated (^{1}H-n.m.r.) as 3:2 (from **2**) and 1:3 (from **15**).

Anal. Calc. for $C_{10}H_{17}N_3O_4$ (243.3): C, 49.37; H, 7.05; N, 17.27. Found: C, 49.16; H, 6.94; N, 17.06.

*2,5-Anhydro-6-deoxy-3,4-O-isopropylidene-1-isothiocyanato-1-O-methyl-*L*-talitol* (**21**) was isolated (c.c. with solvent *M*) as almost identical, 1.5:1 mixtures of syrupy isomers, $[\alpha]_D$ +10.5° (from **2**) and +11° (from **15**), not separated in t.l.c. by solvent *B* (R_F 0.6); ν_{max} ~2000 cm^{-1} (broad, very strong; –N=C=S); *m/z* 260 ($M^+ + 1$), 228 ($M^+ - OMe$), and 201 ($M^+ - NCS$).

Anal. Calc. for $C_{11}H_{17}NO_4S$ (259.3): C, 50.95; H, 6.61; N, 5.40; S, 12.36. Found: C, 51.08; H, 6.53; N, 5.39; S, 12.13.

*2,5-Anhydro-6-deoxy-3,4-O-isopropylidene-1-O-methyl-*L*-talitol* (**22**), prepared from both **2** and **15**, was isolated (c.c. with solvent *M*) as an oil. It was remarkably volatile, and losses occurred during solvent evaporation and drying under diminished pressure, accounting for low isolated yields for reactions that appeared to be quantitative. Prior to processing, t.l.c. of the reaction mixtures indicated complete consumption of **2** (or **15**) and showed a single spot for **22** (R_F 0.5, double irrigation with solvent *I*). Compound **22** had $[\alpha]_D$ ~0°, $[\alpha]_{436}$ +3°, $[\alpha]_{365}$ +10.7°; *m/z* 203 ($M^+ + 1$), 187 ($M^+ - Me$), 171 ($M^+ - OMe$), 157 ($M^+ - MeOCH_2$), and 145 ($M^+ + 1 - Me_2CO$).

Anal. Calc. for $C_{10}H_{18}O_4$ (202.3): C, 59.38; H, 8.97. Found: C, 59.35; H, 9.08.

There was no n.m.r.-spectroscopic evidence for any pyranosidic product resulting from direct reductive displacement, such as has been observed[39] in reactions of other carbohydrate triflates with $NaBH_4$.

*2,5-Anhydro-4-O-benzyl-6-deoxy-1-fluoro-3-O-(4-methoxybenzyl)-1-O-methyl-*L*-talitol* (**23**), R_F 0.3, was seen to arise as a single, major product (accompanied by a trace of faster-moving impurity) from **9** (R_F 0.45) which was completely consumed in the reaction (t.l.c., double irrigation with solvent *I*). Isolated by c.c. (solvent *K*) in 45% yield, the syrupy **23** proved very unstable at room temperature, but, when analyzed without delay, gave good n.m.r. spectra. These showed two 1-epimers, with one moderately preponderating; *m/z* 389 ($M^+ - 1$), 339 ($M^+ - F - MeOH$), 299 ($M^+ - C_7H_7$), and 269 ($M^+ - MeOC_7H_6$).

*2,5-Anhydro-4-O-benzyl-6-deoxy-3-O-(4-methoxybenzyl)-*aldehydo-L*-talose dimethyl acetal* (**24**) was, after purification by c.c. (solvent *E*), a syrup showing $[\alpha]_D$ and $[\alpha]_{546}$ –4°, $[\alpha]_{436}$ –3°; *m/z* 403 ($M^+ + 1$), 371 ($M^+ - OMe$), and 339 ($M^+ + 1 - 2\ MeOH$).

Anal. Calc. for $C_{23}H_{30}O_6$ (402.5): C, 68.63; H, 7.51. Found: C, 68.49; H, 7.57.

*2,5-Anhydro-4-O-benzyl-6-deoxy-3-O-(4-methoxybenzyl)-*aldehydo-L*-talose methyl hemiacetal 1-benzoate* (**25**) was obtained from **9** (75 mg) as a syrup showing 2 distinct spots, R_F 0.30 and 0.25, in t.l.c. (solvent *I*, double irrigation). Column chromatography (solvent *L*) gave 3 fractions, A (9 mg, $[\alpha]_D$ –5.3°, R_F 0.3), B (43 mg, $[\alpha]_D$ –16.6°, mixture), and C (8 mg, $[\alpha]_D$ –22.2°, R_F 0.25). Fractions A and C were pure 1-epimers, and B contained these in an ~1:1.5 ratio, according to

^{1}H-n.m.r. spectra. Neither epimer was crystalline; *m/z* 370 ($M^+ - BzOH$) and 339 ($M^+ + 1 - BzOH - MeOH$).

Anal. Calc. for $C_{29}H_{32}O_7$ (492.6): C, 70.71; H, 6.55. Found: C, 70.56; H, 6.71.

2,5-Anhydro-1-azido-4-O-benzyl-3-O-(4-methoxybenzyl)-1-O-methyl-L-*talitol* (**26**) was isolated by c.c. (solvent *K*) as a colorless syrup that gave a single spot, R_F 0.35 in t.l.c. (solvent *I*, double irrigation), but consisted of 1-epimers in a ratio of ~1.5:1 (n.m.r.); $[\alpha]_D$ −31.1°; ν_{max} 2100 cm^{-1} (N_3); *m/z* 386 ($M^+ + 1 - N_2$) and 371 ($M^+ - N_3$).

Anal. Calc. for $C_{22}H_{27}N_3O_5$ (413.4): C, 63.91; H, 6.58; N, 10.16. Found: C, 63.66; H, 6.35; N, 9.82.

2,5-Anhydro-4,6-dideoxy-3-O-(4-methoxybenzyl)-aldehydo-L-lyxo-*hexose dimethyl acetal* (**27**) was obtained as a syrup purified by c.c. (solvent *K*); $[\alpha]_D$ −9.3°, $[\alpha]_{546}$ −10.2°, $[\alpha]_{436}$ −13°; *m/z* 295 ($M^+ - 1$), 265 ($M^+ - OMe$), and 233 ($M^+ + 1 - 2\,MeOH$).

Anal. Calc. for $C_{16}H_{24}O_5$ (296.4): C, 64.84; H, 8.16. Found: C, 64.89; H, 8.10.

2,5-Anhydro-4,6-dideoxy-3-O-(4-methoxybenzyl)-aldehydo-L-lyxo-*hexose methyl hemiacetal 1-benzoate* (**28**), prepared from **13** (130 mg), showed 2 barely separated spots, R_F 0.28 and 0.25, in t.l.c. (solvent *M*, double irrigation), corresponding to two epimers. Column chromatography using ether–hexane (1:50, gradually changed to 1:25) gave 3 fractions, A (2 mg, R_F 0.28), B (78 mg, mixture), and C (4 mg, R_F 0.25), for which ^{1}H-n.m.r. spectra were recorded. The mixture B was composed of A and C in a ratio of ~1:1.5; *m/z* 265 ($M^+ - BzO$) and 233 ($M^+ - BzO - MeOH$). Partial resolution by p.t.l.c. (triple irrigation with solvent *L*) gave pure epimers in amounts sufficient for measuring optical rotations: For A, $[\alpha]_D$ +3.4°, $[\alpha]_{546}$ +5.0°, $[\alpha]_{436}$ +12.2°, $[\alpha]_{365}$ +27.2°; for C, $[\alpha]_D$ −38.2°, $[\alpha]_{546}$ −45.2°, $[\alpha]_{436}$ −73.4°, $[\alpha]_{365}$ −107.8°.

Anal. Calc. for $C_{22}H_{26}O_6$ (386.5): C, 68.38; H, 6.78. Found for B: C, 68.23; H, 6.77.

2,5-Anhydro-1-azido-4,6-dideoxy-3-O-(4-methoxybenzyl)-1-O-methyl-L-lyxo-*hexitol* (**29**) was isolated by c.c. (solvent *O*) as a colorless, chromatographically homogeneous syrup that contained 1-epimers in a ratio of ~2:1 (by n.m.r.); $[\alpha]_D$ −20.3°; ν_{max} 2100 cm^{-1} (N_3); *m/z* 280 ($M^+ + 1 - N_2$), 265 ($M^+ - N_3$), and 233 ($M^+ - N_3 - MeOH$).

Anal. Calc. for $C_{15}H_{21}N_3O_4$ (307.3): C, 58.62; H, 6.89; N, 13.67. Found: C, 58.43; H, 6.88; N, 13.58.

*Methyl 2-O-allyl-3,4-O-[(R,S)-benzylidene]-α-*L-*fucopyranoside* (**31**). — Methyl 3,4-*O*-[(*R,S*)-benzylidene]-α-L-fucopyranoside was prepared[36] from methyl α-L-fucopyranoside by the acetal-exchange method, which in our hands gave the isomers in the ratio *R:S* = 1.2:1; their ^{1}H-n.m.r. parameters agreed with those reported[36]. To a solution of the mixed acetal (**30**, 2.0 g) and NaH (720 mg) in dry *N,N*-dimethylformamide (10 mL) was added allyl bromide (1.62 mL) at room

temperature. After 1 h, the conversion of **30** into faster-moving **31** was complete (t.l.c., solvent *B*). Methanol, followed by some water, was added to the mixture, which was then evaporated, and a solution of the residue in chloroform (50 mL) was washed twice with water, dried, and evaporated to give crude **31**. Purification by c.c. (solvent *C*) gave pure **31** (2.04 g, 89%), with slight preponderance of the *R* isomer (R_F 0.45) over the *S* isomer (R_F 0.50, t.l.c. with solvent *B*). Partial separation of a sample by c.c. (solvent *E*) furnished pure *S* isomer as crystals; m.p. 62–65°, $[\alpha]_D$ −108.2°, and syrupy *R* isomer, $[\alpha]_D$ −104.5° (*c* 0.6). The *R,S* mixture showed *m/z* 307 ($M^+ + 1$), 275 ($M^+ - OMe$), 229 ($M^+ - Ph$), and 201 ($M^+ + 1 -$ PhCHO).

Anal. Calc. for $C_{17}H_{22}O_5$ (306.4): C, 66.65; H, 7.24. Found: C, 66.89; H, 7.13.

Triflation of **31** by the general method previously detailed for **8** gave a syrupy product showing two faster-moving spots in t.l.c., presumably representing the triflates **32**. During chromatographic processing, however, a slow-moving compound was formed and isolated, which proved identical to the diol **4**, according to its ^{1}H-n.m.r. spectrum.

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