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PAPER

Skeletal rearrangements resulting from reactions of 1,6:2,3- and 1,6:3,4-dianhydro-β-D-hexopyranoses with diethylaminosulphur trifluoride†

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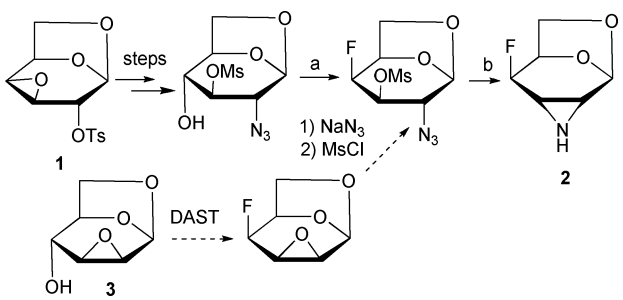
A complete series of eight 1,6:2,3- and 1,6:3,4-dianhydro-β-D-hexopyranoses were subjected to fluorination with DAST. The 1,6:3,4-dianhydropyranoses yielded solely products of skeletal rearrangement resulting from migration of the tetrahydropyran oxygen (educts of D-*altro* and D-*talo* configuration) or of the 1,6-anhydro bridge oxygen (D-*allo*, D-*galacto*). The major products yielded by the 1,6:2,3-dianhydropyranoses were compounds arising from nucleophilic substitution, with configuration at C4 either retained (D-*talo*, D-*gulo*) or inverted (D-*manno*), or from C6 migration (D-*allo*). The minor products in the 1,6:2,3-series resulted from migration of the tetrahydropyran oxygen (D-*gulo*) or the oxirane oxygen (D-*manno*), or from nucleophilic substitution with retention of configuration (D-*manno*). The structure of most of the rearranged products was verified by X-ray crystallography.

Introduction

Fluorinated sugars represent an important class of modified carbohydrates and considerable efforts have been expended on their synthesis.[1] The most attention has been devoted to deoxyfluoro carbohydrates, which arise formally from the replacement of a hydroxyl with a fluorine atom. The reasons for their synthesis are the similarity between the fluorine atom and the hydroxyl group in size, the ability of fluorine to participate in hydrogen bonding,[2] and significant changes in conformational, stereoelectronic and lipophilic properties induced by introduction of fluorine into a molecule.[3] For example, incorporation of fluorine into the carbohydrate moiety of nucleosides has a profound impact on their biological activity, which fact has been successfully employed in development of drugs.[4] Nucleophilic substitution is frequently utilized for regio- and stereoselective introduction of fluorine. This is usually achieved by treatment of sulphonates with a suitable source of fluoride anion,[5] by direct reaction of an unprotected hydroxyl group with diethylaminosulphur trifluoride (DAST),[6] or by nucleophilic cleavage of an epoxide.[7] Although the reaction with DAST has found widespread application, it often suffers from side reactions such as skeletal rearrangements (typically ring contractions in the case of pyranosides) and neighbouring group participation.[1c,8] On the other hand, DAST-induced one-pot rearrangement and fluorination can also be intentionally employed to prepare a variety of fluorinated products.[3g]

We have recently reported the synthesis of a full series of 4-fluoro-2,3-epimino derivatives of 1,6-anhydro-β-D-hexopyranoses.[9] The key synthetic step was a reaction between DAST and an azido tosylate possessing a free hydroxyl at C4 as illustrated in Scheme 1 for the synthesis of 1,6-anhydro-2,3,4-trideoxy-2,3-epimino-4-fluoro-β-D-gulopyranose (**2**) from tosylate **1**.[9] While the reaction with DAST proceeded smoothly with good stereoselectivity and moderate yields, and without rearrangements, the overall synthetic sequence required additional steps including introduction of a benzyloxy group and debenzylation. We hypothesised that such protecting group manipulation might be avoided if fluorine were introduced into the pyranose moiety by treatment of 1,6:2,3- or 1,6:3,4-dianhydro-β-D-hexopyranoses (also called epoxides) with DAST, as outlined in Scheme 1 for the synthesis of **2** from dianhydropyranose **3**. Because



Scheme 1 Synthesis of epimine **2** from **1** (ref. [9]) and suggested synthesis of **2** from dianhydroderivative **3**. *Reagent and conditions*: (a) DAST, CH_2Cl_2, –20 °C–rt, 71%; (b) $LiAlH_4$, THF, –15 °C–rt, 67%.

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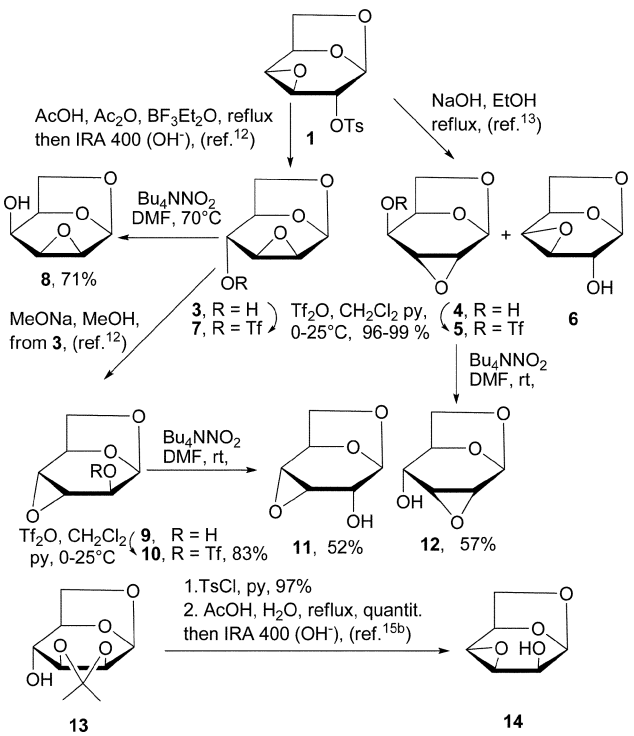
† Electronic supplementary information (ESI) available: Experimental details for compounds **8**, **11**, **12**, **31**, **36** and **37**, computational details, crystallographic data, copies of NMR spectra. CCDC reference numbers 832048–832066. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob06336g

dianhydrohexopyranoses possess just one free hydroxyl, the need for protection and deprotection steps is eliminated. Furthermore, the annulation of a three-membered ring to the 1,6-anhydrohexopyranose skeleton will probably induce higher rigidity of the tetrahydropyran ring along with deviation of its conformation from the chair conformation towards the envelope conformation.[10] We wished to find out whether these conformational changes could suppress rearrangements by moving the bonds that usually participate in a skeletal rearrangement out of the antiperiplanar arrangement. To this end we investigated the reactions of all possible configurational isomers of 1,6:2,3- and 1,6:3,4-dianhydro-β-D-hexopyranoses with DAST having the following results.

Results and discussion

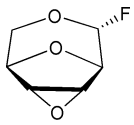
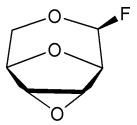
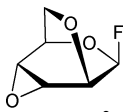
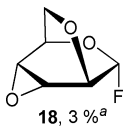
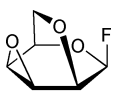
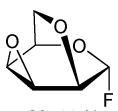
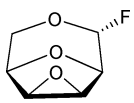
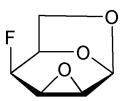
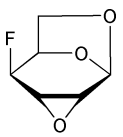
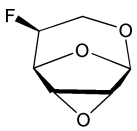
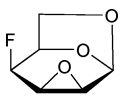
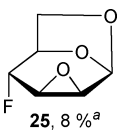
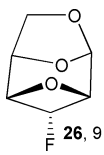
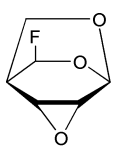
Preparation of the starting dianhydropyranoses is summarized in Scheme 2. We found it convenient to prepare most of the dianhydropyranoses from tosylate **1**.[11] First, published procedures were employed to synthesize **3**,[12] **4**,[13] **6**,[13] and **9**,[12] and then the dianhydrohexoses **8**, **11**, and **12** were obtained from their epimers **3**, **9**, and **4** by conversion into triflates **7**, **10**, and **5** followed by treatment with tetrabutylammonium nitrite in DMF.[14] Epoxide **14** was prepared from the readily available 2,3-isopropylidene-D-mannosan **13**.[15]



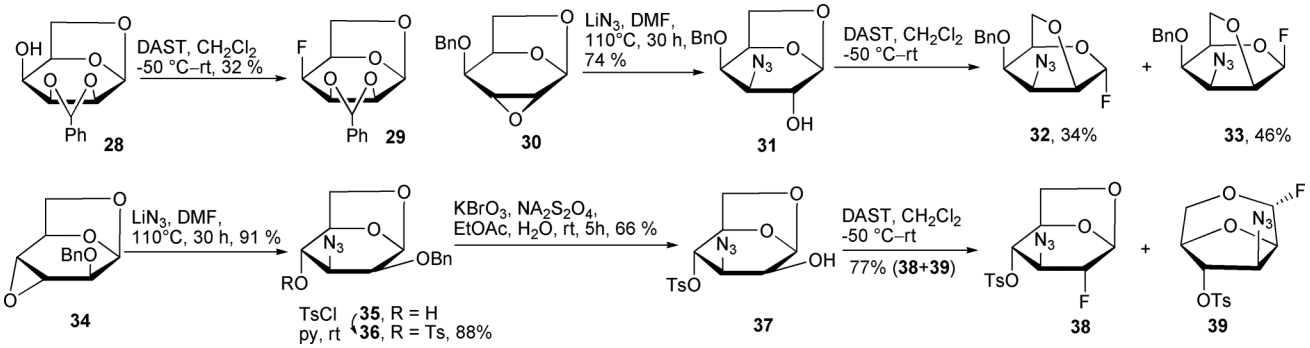
Scheme 2 Synthesis of dianhydrohexopyranoses.

With all the required dianhydropyranoses in hand, we subjected them to reaction with DAST. We used the reaction conditions that we had applied before for the reaction of epimino pyranoses with DAST.[9] The results are given in Table 1. The 1,6:3,4-dianhydropyranoses **9**, **11**, **6**, and **14** yielded exclusively the rearranged fluorinated products (see entries 1–4). Owing to rearrangement the products were glycosyl fluorides and were isolated mostly as anomeric pairs (entries 1–3). We were able to separate the anomeric pairs **15**/**16** and **19**/**20** by silicagel column chromatography. For **17**/**18** this was not possible, but a crystal suitable for X-ray structure determination of the major product **17** was obtained by crystallization. Product **21** was prepared as a

Table 1 Reactions of dianhydrohexopyranoses with DAST

Entry	Starting material	Product, isolated yield	
1	**9**	 **15**, 41 %	 **16**, 11 %
2	**11**	 **17**, 29 %[a]	 **18**, 3 %[a]
3	**6**	 **19**, 52 %	 **20**, 26 %
4	**14**	 **21**, 21 %	
5	**8**	 **22**, 55 %	
6	**4**	 **23**, 61 %	 **24**, 26 %
7	**3**	 **22**, 44 %[a]	 **25**, 8 %[a]  **26**, 9 %
8	**12**	 **27**, 17 %	

Reaction conditions: DAST, CH_2Cl_2, −50 °C–rt, 30–48 h. [a]pairs **17** and **18**, and **22** and **25**, are inseparable by column chromatography, the yields estimated by NMR from the combined yield after column chromatography purification.



Scheme 3 Reaction of **28**, **31** and **37** with DAST.

pure crystalline compound but it decomposed within a few weeks of storage in a refrigerator.

The prevalent reaction mode for 1,6:2,3-dianhydropyranoses **8**, **4**, and **3** was fluorination at C4 with retention (entries 5 and 6) or inversion (entry 7) of configuration with no rearrangement. However, fluorination of D-*allo*-epoxide **12** yielded only a rearranged product (**27**, entry 8).

Fluorination of **4** and **3** also provided rearranged compounds **24** (26%) and **26** (9%) respectively. The two epimeric substitution products **22** and **25** obtained on fluorination of the D-*manno*-epoxide **3** could not be separated either by column chromatography or by crystallization, and compound **25** could thus be characterized only by its ^{1}H, ^{13}C and ^{19}F NMR spectra. Despite the low isolated yield of **21** and **27** (entries 4 and 8), GC-MS analysis of the reaction after work-up did not indicate any other products, whereas TLC analysis of the reaction mixture showed an immobile component at the start. This may indicate extensive decomposition or polymerization. Generally, low yield of fluorinated products is encountered relatively often in reactions with DAST.[1c,8,16]

Because fluorination of **4** and **8** resulted in unexpected retention of configuration, structurally related 1,6-anhydro-2,3-di-*O*-benzylidene-β-D-talopyranose **28** was prepared[17] for comparison and subjected to DAST fluorination, which also furnished non-inverted 4-fluoro product **29** as the major product (Scheme 3). NMR performed after chromatographical purification showed another fluorine-containing product in about 5% yield, most probably a C4-epimer of **29**, which could not be separated by column chromatography. Pure **29** was obtained by crystallization in 32% yield.

Because reactions of 1,6:3,4-dianhydro-β-D-hexopyranoses with DAST failed to provide the desired 2-deoxy-2-fluorohexopyranose derivatives due to skeletal rearrangements, we attempted to introduce fluorine at C2 by DAST fluorination of known azido alcohol **31**.[18] This reaction, however, also resulted in rearrangement producing fluorides **32** and **33**. In another attempt at fluorination at C2 we employed azido tosylate **36**[18] (Scheme 3), which was oxidatively debenzylated[19] to **37** using the $KBrO_3/Na_2S_2O_4$ system and subjected to reaction with DAST to yield 2-fluoropyranose **38**, contaminated to the extent of about 20% by another product inseparable by column chromatography. An analytical sample of **38** was prepared by a semipreparative reverse phase HPLC, whereas the unknown minor product was obtained only as an enriched HPLC fraction. The minor product was tentatively assigned the structure of the glycosyl fluoride **39** on the basis of ^{1}H, ^{13}C and ^{19}F NMR spectra. Azido derivatives **31** and **35** were prepared by reaction of dianhydroderivatives **30** and **34** with lithium azide in DMF.[18]

Among rearranged tricyclic products, which we obtained *via* fluorination of dianhydropyranoses, compounds **15**, **16**, **17**, **18**, and **24** possess tricyclic ring systems already known in carbohydrate chemistry, though with a different substitution pattern: trianhydroallitol **40**,[20] methyl 2,6:3,4-dianhydro-α-D-altropyranoside **41**,[21] and 5-*O*-benzoyl-l,6:2,3-dianhydro-α-L-talofuranose **42**[22] (Fig. 1).

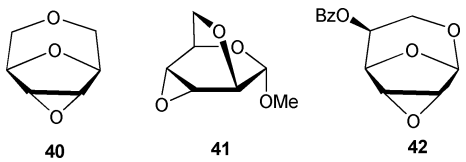
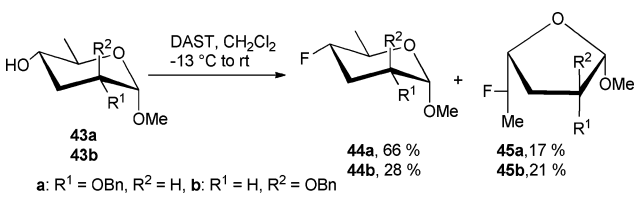


Fig. 1

Mechanistic considerations

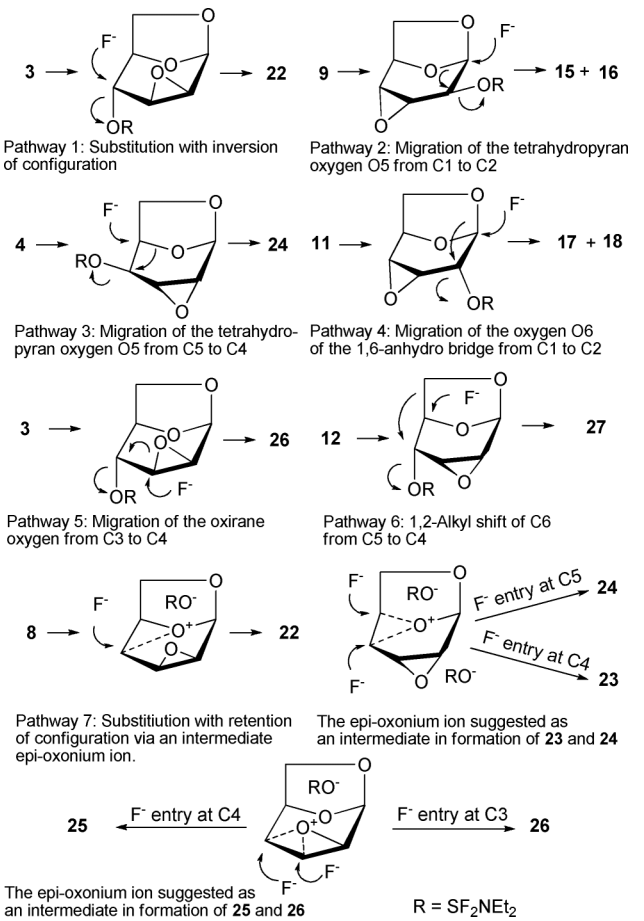
It is generally accepted that reaction of an alcohol with DAST converts the hydroxyl group into a good leaving group by formation of an unstable R-OSF_2NEt_2 intermediate.[8] This intermediate can undergo nucleophilic substitution with a fluoride anion, or with another external or intramolecular nucleophile, or it can react by elimination. The structure of the products which we obtained gives evidence of seven different reaction pathways with respect to the mechanism and the migrating atoms and bonds (see Scheme 5).



Scheme 4 Reaction of **43** with DAST.

1) S_N2 substitution with inversion of configuration. With our substrates this mechanism operates only in formation of 4-fluoro epoxide **22** from **3** and 2-fluoropyranose **38** from **37**.

2) Migration of the tetrahydropyran oxygen O5 from C1 to C2 with contraction of the tetrahydropyran ring and fluorine entry at C1. This mechanism was observed in fluorination of **9** and **14** (see Table 1 entries 1, 4). Both reagents have an equatorial C2 hydroxyl which is antiperiplanar to the migrating O5–C1



Scheme 5 Schematic representation of the mechanistic pathways and the postulated oxonium intermediate species discussed in the text.

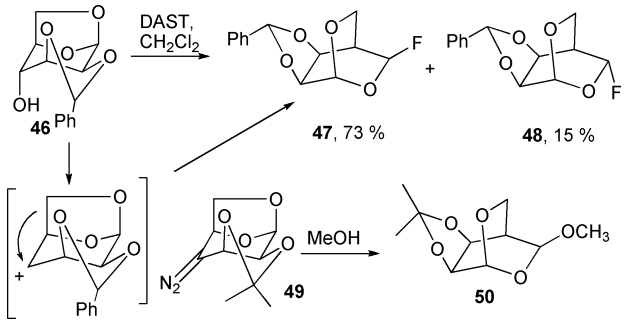
bond. These results confirm the strong migratory aptitude of the tetrahydropyran oxygen upon reaction of C2–OH with DAST as documented by Dax for other pyranoses.[8] Only substrates of β-D-*manno* configuration were reported to undergo fluorination at C2 by the S_N2 mechanism with configurational inversion as the preferred reaction mode.[8,23] The formation of **38** from the β-D-*manno* derivative **37** was in accordance with this finding.

3) Migration of the tetrahydropyran oxygen O5 from C5 to C4 with contraction of the tetrahydropyran ring and fluorine entry at C5. This pathway applies only for the formation of the minor product **24** from **4**. Parallel formation of **23** suggests that migration of the ring oxygen probably proceeds *via* an intermediate *epi*-oxonium ion comprising O5–C4–C5 (Scheme 5 and discussion under (7)). A published precedent from outside the 1,6-anhydrohexopyranose series is the formation of the furanoid by-products **45** during DAST fluorination of hexopyranosides **43** (Scheme 4).[24]

4) Migration of the oxygen O6 of the 1,6-anhydro bridge from C1 to C2 with an enlargement of the dioxolane ring and fluorine entry at C1. This reaction pathway applies to reaction of **6**, **11** and **31**. Migration of the 1,6-anhydro bridge oxygen from C1 to C2 is a reaction pattern sometimes observed[25] with 1,6-anhydrohexopyranoses possessing an axial leaving group at C2, and parallel results were obtained for DAST fluorination of 1,6-anhydro-3,4-di-*O*-isopropylidene-β-D-galactopyranose.[8] Even unprotected 1,6-anhydro-β-D-*gluco*- and galactopyranose were reported to give very low yields (of 10% and 6.5% respectively) of 2,6-anhydrohexopyranosyl fluorides.[16]

5) Migration of the oxirane oxygen from C3 to C4 with enlargement of the oxirane ring into oxetane and fluorine entry at C3. This pathway applies for the formation of the minor product **26**. Although produced in low yield, this compound is a rare example of a fluorinated oxetane (the few examples of isolated fluorooxetanes hitherto reported belong to δ-amino acids[26] and nucleosides[27]) and is unique in its incorporation of a fluorooxetane into a tricyclic ring system. Migration of the oxirane ring probably involves formation of a transient oxonium species and products **25** and **26** are most likely formed *via* the same species with fluorine entry at C4 or C3, respectively, (Scheme 5).

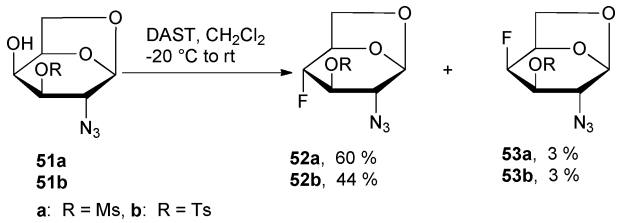
6) 1,2-Alkyl shift of C6 from C5 to C4 with enlargement of the dioxolane ring and fluorine entry at C5. This pathway applies to formation of **27** from **12**. We have also observed[9] this type of rearrangement upon reaction of 2,3-di-*O*-benzylidenemannosane **46** with DAST to afford **47** and **48** (Scheme 6). Since 1,2-alkyl shifts are typically displayed by carbocations, we assume that formation of **27**, **47**, and **48** may indicate a more carbocationic character of the intermediate species. This assumption is supported by a recently reported skeletal rearrangement of diazo compound **49** to **50** during methanolysis (Scheme 6) because diazo compounds are expected to decompose through generation of carbocations.[28]



Scheme 6 Rearrangements of **46** and **49**.

7) Unexpectedly, dianhydro derivatives **8** and **4** reacted with DAST to give the products **22** and **23** of nucleophilic substitution with retention of configuration. To retain configuration at C4 the fluoride anion must approach the molecule from the sterically more hindered β-face. The 1,6-anhydro-2,3-di-*O*-benzylidene-talopyranose **28** prepared for comparison was also found to provide mainly the non-inverted 4-fluoro product **29** of the D-*talo* configuration (Scheme 3). In contrast, we have found that D-*galacto*-azido sulphonates **51a**, **b** reacted with DAST chiefly to yield the 4-fluoro products **52a**, **b** with inversion of configuration at C4 (Scheme 7).[30]

To account for retention of configuration in fluorination of **8**, **4**, and **28** we assume the involvement of the pyranose oxygen O5 in the nucleophilic displacement, which proceeds by a transient *epi*-oxonium ion without actual ring rearrangement. Product **24** is most probably formed through the same *epi*-oxonium intermediate as product **23** with fluorine entry at C5 (Scheme 5). Although ring oxygen participation is commonly observed in reactions of hexopyranoses with DAST, it normally results in ring contraction.[8] Nevertheless, a bicyclic *epi*-oxonium ion



Scheme 7 Reaction of 51 with DAST.

has been suggested to explain retention of configuration during fluorination of 3,6-dideoxyhexopyranosides **43**[24] (Scheme 4), and an *epi*-oxonium ion comprising C1–C2–O5 has been suggested as an intermediate in the nitrous acid deamination of benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α- and β-D-glucopyranoside.[29] Participation of ring sulphur in thiofuranoid systems has also been postulated to account for retention of configuration during DAST fluorination.[30,31] An alternative explanation of configurational retention during fluorination of **8**, **4**, and **28** invokes internal fluorine substitution S_Ni in a fashion similar to chlorination of alcohols with $SOCl_2$. Interestingly, we did not observe formation of products arising from the ring enlargement *via* cleavage of the C–C bond of the oxirane ring. This reaction course during DAST-mediated fluorination has been documented for a number of vicinal bicyclic epoxy alcohols.[32]

Structure determination

All the starting epoxides were crystallized to produce single crystals suitable for X-ray crystallography and the ring puckering parameters[33] were calculated for these structures. The tetrahydropyran ring of 1,6:3,4-dianhydrohexopyranoses adopts a slightly deformed version of the envelope conformation E_O as evidenced by polar projection of the ring puckering parameters[10] (Fig. 2). The conformation of the tetrahydropyran ring of 1,6:2,3-dianhydrohexopyranoses reaches the border between the envelope conformation E_O and the half-chair conformation ^5H_O (Fig. 2).

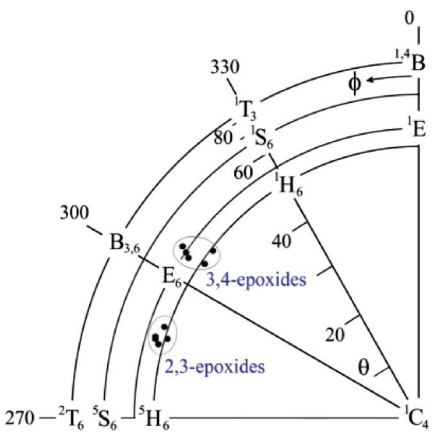


Fig. 2 The polar projection of the ring puckering parameters for the starting dianhydrohexopyranoses using pseudorotation itinerary for a general six-membered ring ($E_6 = E_O$).

The minimal variance of the ring puckering parameters within each group of epoxides documents conformational rigidity of the pyranose ring which is even higher than that of the corresponding epimines.[10] The absolute values of the torsion angles assumed by the bonds which participate in skeletal rearrangements (*i.e.* the migrating and leaving bond) are in the range of 161–172°. Thus the deviation from the ideal antiperiplanar arrangement is clearly negligible and cannot suppress the rearrangement. To present unequivocal evidence for the structure of the fluorinated products, we produced crystals suitable for X-ray crystallography for all compounds prepared by fluorination of dianhydrohexopyranoses except for **18** and **25**, which could not be isolated as pure compounds, and **24**, which did not crystallize. The structural analysis revealed four groups of products differing from each other in the molecule geometry of the carbohydrate skeleton (Fig. 3 – the oxirane ring and fluorine is omitted for clarity). The tetrahydropyran ring in unrearranged products **22** and **23** adopts a conformation on the border between half-chair and envelope (E_O–^5H_O) while the more flexible derivative **29** adopts a conformation somewhere between chair $^1C_4$ and envelope E_O. All three six-membered rings in products related to the bicyclo[2,2,2]octane skeleton (**17**, **19**, **20**, and **27**) adopt almost ideal boat conformations: $B_{2,5}$ and $^{2,5}B$ for **17**, **19**, and **20** (Fig. 3b), and $B_{1,4}$ and $^{1,4}B$ for **27**. The tetrahydrofuran ring in products related to bicyclo[3,2,1]octane skeleton (**15**, **16**, and **21**) adopts envelope conformation E_O and the 1,4-dioxane ring assumes chair conformation $^{O5}C_{O6}$. The products within each group differ only in the configuration at the fluorine-bearing carbon, and the configuration at the carbons of the oxirane ring, which remains unchanged during the reaction. The tetrahydropyran ring in **26** adopts the *boat* conformation $B_{3,O}$. The introduced fluorine atom plays an active role in molecular packing of the compounds studied as expected.[34] It attracts hydrogen atoms of the oxirane ring or another CH group proximate to the oxygen atom and forms a weak C–H···F attractive interaction. The distance varies from 2.40 to 2.75 Å in the structures studied. This kind of intermolecular interaction usually provides the main binding feature in one direction of the molecular packing (see Fig. 1 in ESI†).

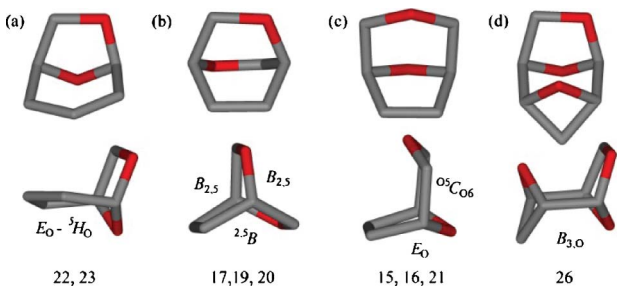


Fig. 3 Structural types of skeletons of fluorinated products and their conformation in solid state as determined by X-ray analysis. The oxirane ring, hydrogens and fluorine omitted.

The structures of the products were also characterized by multinuclear 1D (^{1}H, ^{13}C and ^{19}F) and 2D NMR spectroscopy (COSY, HSQC). The presence and position of the fluorine atom in the structure is demonstrated by strong geminal coupling ^2J (^{1}H, ^{19}F) ~ 60 Hz). Those rearranged products which are glycosyl fluorides (compounds **15–21**, **27**, **32**, **33**, and **39**) show the characteristic downfield shifted signal δ = 5.30–5.83 for the corresponding geminal proton (O–C*H*–F). For other fluorinated products the geminal proton resonates at δ = 4.69–5.03 except for **38** (δ = 4.17). In most cases the additional splitting due to

Table 2 Comparison of dihedral angles Φ H5–C5–C6–H6 [°][a] determined from X-ray analysis with measured and calculated coupling constants ^2J [Hz] for selected compounds

Parameter[a]	**15**	**16**	**17**	**19**	**20**	**27**	**21**	**22**	**23**	**26**
Φ H5-C5-C6-H6en	65.6	68.6	63.2	64.2	66.2	65.9	70.8	101.9	110.3	94.5
Φ H5-C5-C6-H6ex	−59.6	−54.5	−59.6	−58.0	−56.5	−55.3	−45.2	−24.5	−16.0	−29.6
^2J (H5, H-6en)	0.8	~0	0.9	1.2	<1	[b]	[b]	1.8	2.1	<1
^2J (H5, H-6ex)	2.4	2.4	2.3	2.4	2.8	2.2	[b]	6.3	7.6	4.0
^2J (H5, H-6en) calc	0.7	0.6	1.2	1.2	0.8	1.5	0.5	1.1	1.3	0.2
^2J (H5, H-6ex) calc	2.7	2.5	2.3	2.5	2.9	2.2	4.0	5.9	6.0	4.0

[a] Φ H4–C4–C6–H6en/ex and ^2J (H4, H6en/ex) applies for **27**. [b] The value could not be determined.

Table 3 ^{1}H and ^{19}F NMR chemical shifts (ppm) and signal multiplicity of fluorine-containing compounds in $CDCl_3$

Compound	H-1	H-2	H-3	H-4	H-5	H-6en	H-6ex	Other protons	^{19}F
15	5.30 bd	4.19 bd	3.75 dd	3.72 d	4.20 bs	3.58 d	4.27 dt		−136.4 bd
16	5.46 dd	4.17 bt	3.73 d	3.84 dd	4.11 dd	3.95 d	4.05 dd		−213.6 bd
21	5.40 bd	4.30 m	4.30 m	4.30 m	4.30 m	3.84 dd	4.30 m		−117.0bddd
39	5.32 bd	4.31 bs	4.31 bs	5.01 bd	4.31 bs	3.60 bd	4.23 bd	Ts 2.48 s (3H), 7.41 m (2H), 7.85 m (2H)	−145.6 bd
17	5.67 dt	4.29ddd	3.76 ddd	3.46 ddd	4.44 bs	3.72 bdd	4.25 bdd		−124.4 bd
18	5.66 ddd	4.27[a]	3.68 m	3.49 dt	4.50 bt	3.65 dd	3.95 dd		−122.2 bdd
19	5.68 bd	4.24 bt	3.50 dd	3.75 t	4.41 ddd	4.10 bs	4.11 bs		−130.4 bd
20	5.81 dd	4.27 ddd	3.56bddd	3.74 t	4.56 bt	4.03 dd	3.66 ddd		−120.1 bdd
32	5.83 dd	4.15 m	3.78 bd	4.15 m	4.08 t	4.15 m	3.85 ddd	Bn 4.61 d, 4.87 d, 7.37–7.39 m (5H)	−119.8 dd
33	5.55 dd	4.18 bt	3.21 bd	4.00 ddd	4.01 m	4.29 ddd	4.29 ddd	Bn 4.63 d, 4.96 d, 7.38–7.39 m (5H)	−123.7 dd
22	5.66 dd	3.64 ddd	3.41 ddd	5.03 ddd	4.54 dt	4.09 dt	3.67 dddd		−185.7 dt
23	5.61 bd	3.01 bdt	3.22 ddd	4.93 bdd	4.56 bddd	4.13 dt	3.86 dd		−199.8 bdd
25	5.74 d	3.52 bt	3.29 bt	4.69 d	4.60 dddd	3.74 m	3.74 m		−189.6 dddd
29	5.43 bdd	4.26 dd	4.66 bt	4.99 bdt	4.63 bt	4.45 bd	3.82 bdd	CH 5.87 s, Ph 7.41–7.70 m (5H)	−204.0 ddd
24	5.24 d	3.69 d	3.93 dd	4.51 d	4.89 dddd	3.91 m	4.05 dd		−194.7 ddd
26	5.64 bd	4.50 ddd	5.02 dt	4.62 ddd	4.83 t	4.39 bd	3.81 dd		−168.4 d
27	5.44 d	3.53 ddd	3.67 m	2.73 bs	5.92 dt	3.67 m	4.21 dd		−127.7 dp
38	5.50 bd	4.17 dd	3.77 dt	4.19 bd	4.73 bd	3.90 bd	3.71 bdd	Ts 2.48 s (3H), 7.39 m (2H), 7.84 m (2H)	−185.7 ddd

[a] Overlap with signal of 17.

Table 4 Coupling constants ^nJ (H-*n*, H-*m*, Hz) of protons of fluorine-containing compounds in $CDCl_3$

Compound	1,2	2,3	3,4	4,5	5,6en	5,6ex	6en,6ex	1,3	2,4	3,5	4,6ex	4,6en	1,6en	1,5	1,6ex	Other couplings
15	<1	~0	3.1	~0	<1	2.4	11.7	~0	~0	~0	~0	~0	~0	~0	<1	
16	2.3	~0	3.2	~0	~0	2.4	11.7	~0	~0	~0	~0	~0	~0	~0	~0	
21	[a]	[a]	[a]	[a]	[a]	[a]	10.4	[a]	[a]	[a]	[a]	[a]	[a]	[a]	[a]	
39	~0	[a]	2.2	~0	~0	~0.6	11.6	~0	~0	~0	~0	~0	~0	~0	~0	
17	1.6	4.6	4.6	2.9	~1	2.3	9.9	<0.5	~0	<0.5	~0	<1	~1	~0	~0	
18	2.6	[a]	4.5	2.8	<1	2.6	9.7	2.0	[a]	[a]	[a]	[a]	[a]	[a]	[a]	
19	1.6	3.0	4.5	4.4	1.2	2.4	8.8	~0	~0	0	<0.5	<0.5	<1	~0	<0.5	
20	3.1	3.0	4.3	4.2	<1	2.8	8.7	~0	~0	~0	<1	<1	~0	~0	~0	
32	3.3	1.8	8.7	3.1	~0	3.0	9.8	~0	[a]	~0	[a]	[a]	~0	~0	[a]	CH_2 J_{gem} 11.6
33	1.7	1.6	8.4	4.5	1.6[b]	1.6[b]	10.0	0	0	1.7	1.4[b]	1.4[b]	0.6[b]	0	0.6[b]	CH_2 J_{gem} 11.8
22	2.8	4.2	3.1	6.1	1.8	6.3	7.5	~0	~0	1.1	~0	~0	<1	~0	<1	
23	1.1	3.7	~0	5.5	2.1	7.6	8.5	<0.5	1.0	2.0	1.0	<1	<1	~0	~0	
25	3.1	3.3	<0.5	~0	0.6	6.7	[a,b]	~0	<1	0.6	~0	~0	~0	~0	~0	
29	2.9	5.9	5.1	5.2	<1	5.4	7.7	<1	~0	~0	~0	~0	~0	~0	~0	
24	~0	2.9	~0	4.7	9.1	6.8	11.1	~0	<0.5	~0	<1	~0	~0	~0	~0	1,4 <0.5
26	2.4	4.5	4.5	3.2	<1	4.0	6.1	~0	5.0	~0	~0	~0	<1	<1	~0	
27	2.3	4.4	[a]	2.2	2.1	~0	9.0	[a]	~0	[a]	2.2	[a]	~0	~0	<1	
38	<1	4.6	5.3	1.0	<1	5.2	8.0	~0	~0	~0	~0	~0	<1	~0	~0	

[a] Not determined value, [b] Signals of protons H-6ex and H-6en are overlapped.

Table 5 Coupling constants ^{n}J (F, H-n, Hz) in $CDCl_3$

Compound	H-1	H-2	H-3	H-4	H-5	H-6en	H-6ex
15	53.2	3.1	1.2	~0	~0	~0	2.4
16	54.6	1.8	~0	1.2	5.3	~0	~0
21	59.4	[a]	[a]	[a]	[a]	[a]	[a]
39	52.2	[a]	[a]	~0	[a]	~0	~1.5
17	66.1	2.3	4.9	4.9	1.1	~1	~0
18	66.8	[a]	[a]	2.4	[a]	6.2	[a]
19	64.4	1.5	~0	~0	~0	~0	~0
20	66.4	2.0	2.6	~0	1.2	5.8	1.4
32	66.4	6.3	~0	[a]	~0	[a]	[a]
33	62.3	~0	~0	~0	~0	0.8[b]	0.8[b]
22	5.6	4.2	~0	46.9	~0	~0	~0
23	3.5	~0	12.9	47.2	~0	~0	<1
25	~0	~0	5.5	46.9	15.1	~0	2.8
29	5.7	~0	~0	44.5	~0	1.2	~0
24	5.7	~0	1.3	~0	49.5	14.9	~0
26	~0	~0	59.5	~0	~0	~0	~0
27	~0	3.9	7.2	~0	68.7	3.4	~0
38	6.9	48.1	21.0	~0	~0	~0	~0

[a] Not determined value. [b] Signals of H-6ex and H-6en are overlapped.

the presence of the ^{19}F nucleus in combination with a strong signal overlap prevented structure elucidation *via* analysis of the proton coupling constants. The splitting in ^{13}C spectra provided a complementary assignment tool for structure elucidation in cases where X-ray structure analysis was not available. The magnitude of ^{n}J (^{13}C, ^{19}F) corresponds to the distance from the fluorine centre in the molecule and allows one to determine the position of oxygen and skeleton bond branching (see Table 6). In order to obtain correct values of proton coupling constants we applied DFT calculations using the XYZ coordinates from X-ray crystallography as the starting point of the geometrical optimization.[35] The calculated values of the coupling constants were then compared with the experimental values and the final values of all proton-proton and proton-fluorine coupling constants reported in Tables 4 and 5 were obtained by fitting to the experimental spectra.[36] The type of annulation of the oxirane ring in the rearranged products is reflected in the values of the coupling constants of the oxirane protons: $^{3}J = 4.3–4.6$ Hz if the oxirane is annulated to a tetrahydropyran ring (compounds **17–20**, **27**), or $^{3}J = 2.9–3.2$ Hz if the oxirane is annulated to a tetrahydrofuran ring (compounds **15**, **16**, and **24**). Coxon has observed[21] a noticeable difference in the coupling constants $^{3}J_{H5,H6}$ and $^{3}J_{H5,H6'}$ in methyl 2,6:3,4-dianhydro-α-D-altropyranoside, despite the almost identical magnitude of the respective dihedral angles (~|60|°). We encountered an analogous situation in products **17**, **19**, **20**, and **27**, which possess a closely related skeleton (derived from bicyclo[2,2,2]octane), and also in products **15** and **16** (see Table 2 for comparison of dihedral angles with the measured and calculated coupling constants of selected products). The assignment of H-6en and H-6ex was therefore made by comparison of H-6 chemical shifts and vicinal $^{3}J_{H5,H6en/ex}$ coupling constants (or, in the case of **27**, $^{3}J_{H4,H6}$) with values provided by DFT calculation (Table 2).

Conclusions

We have investigated reactions of all possible 1,6:2,3- and 1,6:3,4-dianhydrohexopytanoses with DAST. The 1,6:3,4-dianhydrohexopyranoses reacted exclusively through skeletal rearrangement in which the oxygen antiperiplanar to the C2-OH bond migrates from C1 to C2. The 1,6:2,3-dianhydrohexopyranoses

Table 6 ^{13}C NMR chemical shifts (ppm) and coupling constants ^{n}J (^{19}F,^{13}C, Hz) in $CDCl_3$

Compound	C-1	C-2	C-3	C-4	C-5	C-6
	($^{1}J_{F,C}$)	($^{2}J_{F,C}$)	($^{3}J_{F,C}$)	($^{4}J_{F,C}$)	($^{4}J_{F,C}$)	($^{3}J_{F,C}$)
15	101.78 (231)	72.44 (24)	50.36 (10)	49.49 (~0)	71.66 (1)	61.41 (1)
16	103.16 (215)	71.64 (25)	50.20 (~0)	48.82 (~0)	70.99 (2)	66.42 (3)
21	101.86 (220)	74.62 (25)	62.81 (9)	73.20 (~0)	62.93 (2)	63.84 (1)
39	101.95 (226)	75.93 (25)	67.05 (6)	85.53 (2)	79.96 (2)	64.24 (~0)
	($^{1}J_{F,C}$)	($^{2}J_{F,C}$)	($^{3}J_{F,C}$)	($^{4}J_{F,C}$)	($^{3}J_{F,C}$)	($^{4}J_{F,C}$)
17	106.24 (223)	68.20 (21)	47.03 (7)	46.25 (5)	66.37 (1)	63.60 (~0)
18	106.71 (232)	66.99 (20)	48.34 (4)	47.26 (1)	66.87 (~0)	62.68 (~0)
19	105.56 (228)	65.71 (20)	51.27 (12)	51.29 (~0)	70.37 (1)	67.16 (~0)
20	104.33 (224)	63.68 (24)	49.20 (4)	48.95 (~0)	70.25 (2)	66.31 (~0)
32	105.48 (226)	68.16 (24)	54.29 (4)	71.06 (~0)	68.39 (2)	61.62 (~0)
33	106.13 (230)	71.03 (20)	55.17 (8)	70.88 (8)	68.33 (2)	63.45 (~0)
	($^{4}J_{F,C}$)	($^{3}J_{F,C}$)	($^{2}J_{F,C}$)	($^{1}J_{F,C}$)	($^{2}J_{F,C}$)	($^{3}J_{F,C}$)
22	96.89 (2)	58.62 (2)	47.37 (19)	85.54 (185)	68.35 (27)	63.24 (1)
23	97.07 (1)	48.21 (~0)	49.71 (39)	81.67 (181)	70.91 (26)	63.28 (2)
25	97.44 (~0)	54.56 (~0)	46.46 (42)	85.76 (176)	71.56 (21)	64.52 (9)
29	99.02 (2)	75.88 (1)	73.99 (14)	84.56 (193)	70.79 (14)	63.80 (1)
	($^{4}J_{F,C}$)	($^{4}J_{F,C}$)	($^{3}J_{F,C}$)	($^{2}J_{F,C}$)	($^{1}J_{F,C}$)	($^{2}J_{F,C}$)
24	95.24 (~0)	48.74 (~0)	49.01 (~0)	71.15 (23)	81.04 (182)	62.34 (30)
	($^{3}J_{F,C}$)	($^{2}J_{F,C}$)	($^{1}J_{F,C}$)	($^{2}J_{F,C}$)	($^{3}J_{F,C}$)	($^{4}J_{F,C}$)
26	99.74 (5)	88.44 (17)	73.75 (254)	86.79 (16)	75.07 (3)	67.33 (~0)
	($^{3}J_{F,C}$)	($^{4}J_{F,C}$)	($^{3}J_{F,C}$)	($^{2}J_{F,C}$)	($^{1}J_{F,C}$)	($^{3}J_{F,C}$)
27	91.89 (2)	47.96 (3)	45.48 (10)	33.58 (21)	105.30 (221)	56.53 (6)
	($^{2}J_{F,C}$)	($^{1}J_{F,C}$)	($^{2}J_{F,C}$)	($^{3}J_{F,C}$)	($^{4}J_{F,C}$)	($^{4}J_{F,C}$)
38	99.46 (32)	88.95 (187)	60.24 (28)	75.38 (~0)	77.12 (32)	66.67 (~0)
Other carbons						
29	CH 106.31 Ph 135.73 129.81 128.31(2) 127.61 (2)					
32	Bn 73.39 136.92 128.61(2) 128.21 127.80(2)					
33	Bn 73.92 137.00 128.60(2) 128.19 127.79(2)					
38	Ts 21.73 145.81 130.27 130.27(2) 127.96(2)					

reacted predominantly by nucleophilic displacement to nonrearranged products except for 2,3-alloepoxide **12** which rearranges *via* migration of the C5–C6 bond. Atypical oxirane oxygen participation was observed for 2,3-mannoepoxide **3** and an unusual retention of configuration was observed in displacement of the C4 equatorial hydroxyl in **4**, **8**, and **28**. In most cases the structures of rearranged products were determined by X-ray crystallography. DFT calculations and spectra fitting were employed to obtain the refined values of the proton-proton and proton-fluorine coupling constants. In most cases the rearranged products are glycosyl fluorides which are very useful glycosyl donors.[37] Nonrearranged 4-fluorohexopyranoses **22** and **23** have potential for further functionalization through oxirane-ring opening.

Experimental

General methods

^{1}H, ^{13}C, COSY and gHSQC NMR spectra were measured in $CDCl_3$ solution at 499.9 MHz for ^{1}H and at 125.7 MHz for ^{13}C measurements. The ^{1}H and ^{13}C NMR spectra were referenced to the line of the solvent ($CDCl_3$, $\delta = 7.26$ ppm and $\delta = 76.99$ ppm respectively). The ^{19}F NMR spectra were recorded at 282.2 MHz and referenced to $CFCl_3$. The NMR data are given in Tables 3–6 (compounds in tables are grouped according to structural type – see Table 6). LRMS were recorded using EI ionization at 70 eV, $[\alpha]_D^{25}$ values are given in 10^{-1} deg cm^2 g^{-1}. TLC was carried out with Merck DC Alufolien with Kiesegel F254 and spots were detected with an anisaldehyde solution in H_2SO_4. UV detection at 254 nm was also used where appropriate. Column chromatography was performed with silica gel 60 (70–230 mesh, Merck). The solvents systems which were most commonly used are denoted as S1 = ethyl acetate, S2 = ethyl acetate-light petroleum 1 : 1, S3 = ethyl acetate-light petroleum 1 : 2, S4 = ethyl acetate-light petroleum 1 : 5. The term light petroleum refers to petroleum fractions boiling 40–65 °C. The solutions were concentrated using a vacuum rotary evaporator at less than 45 °C. Anhydrous sodium sulfate was used to dry solutions during workup. Tetrahydrofuran was dried by distillation from $LiAlH_4$, dichloromethane was dried by distillation from CaH_2. All other chemicals were of reagent grade and were used without purification. Synthesis of compounds **8**, **11**, **12**, **31**, **36** and **37** is described in Supplementary Information.

General procedure for reaction of dianhydro hexopyranoses with DAST. Neat DAST was added to a stirred suspension of the starting dianhydro hexopyranose in CH_2Cl_2 (3 mL, c(DAST) = 1.26–1.64 mmol mL^{-1}, c(dianhydropyranose) = 0.35–0.46 mmol mL^{-1}) in a teflon flask under cooling (−50 °C). The cooling bath was removed after 30 min and the stirring continued for 30 h or 48 h (reaction of **3**) at rt. The reaction mixture was then diluted with CH_2Cl_2, cooled to −15 °C and methanol (0.5 mL) was added to quench the reaction. After 30 min was the reaction mixture washed with 1% aqueous HCl, the water phase was saturated with NaCl and extracted with CH_2Cl_2 (3 × 20 mL). Combined organic layers were dried, concentrated and the residue was chromatographed. Because the products are fairly volatile, prolonged drying on a rotary vacuum pump should be avoided.

Reaction of 1,6:3,4-dianhydro-β-D-altropyranose (9)

The reaction was carried out using **9** (155 mg, 1.08 mmol) and DAST (0.6 mL, 4.54 mmol). Chromatography in S3 afforded 2,5:3,4-dianhydro-β-D-alloseptanosyl fluoride (**16**, 17 mg, 11%); mp 85–87 °C (from ethyl acetate–light petroleum); found: C, 49.3; H, 4.8. Calc. for $C_6H_7O_3F$: C, 49.3; H, 4.8%; *m/z* (EI) 70 (100%), 71 (83), 69 (79), 146 (M$^+$, 59), 97 (50). Further elution gave first a mixture of **15** and **16** (9 mg, 6%) in 2 : 3 ratio (NMR) and then 2,5:3,4-dianhydro-α-D-alloseptanosyl fluoride (**15**, 65 mg, 41%); mp 115–116 °C; $[\alpha]_D^{25}$ +12 (*c* 0.23 in $CHCl_3$); found: C, 49.3; H, 4.8. Calc. for $C_6H_7O_3F$: C, 49.3; H, 4.8%; *m/z* (EI) 70 (100%), 71 (85), 69 (82), 146 (M$^+$, 54), 97 (53).

Reaction of 1,6:3,4-dianhydro-β-D-allopyranose (11)

The reaction was carried out using **11** (150 mg, 1.04 mmol) and DAST (0.6 mL, 4.54 mmol). Chromatography in S1 afforded an anomeric mixture of 2,6:3,4-dianhydro-D-altropyranosyl fluorides **17** and **18** (49 mg, 32%) as a crystalline substance that could not be resolved either by column chromatography or by crystallization from EtOH. The ratio of β-anomer **17** and α-anomer **16** was 91 : 9 according to ^{1}H NMR. X-Ray analysis of a crystal taken from crystalline material obtained from EtOH allowed to determine the structure of the major anomer **17**, mp 81–84 °C (ethanol); *m/z* (EI) 69 (100%), 59 (84), 97 (45), 115 (31), 146 (M$^+$, 4).

Reaction of 1,6:3,4-dianhydro-β-D-galactopyranose (6)

The reaction was carried out using **6** (200 mg, 1.39 mmol) and DAST (0.65 mL, 4.92 mmol). Chromatography in ethyl acetate-light petroleum 1 : 3 afforded first 2,6:3,4-dianhydro-α-D-talopyranosyl fluoride (**20**) with trace of an unidentified (GC-MS). Further recrystallization from ethanol at −20 °C gave pure **20** (52 mg, 26%); mp 95–101 °C (from ethanol); $[\alpha]_D^{25}$ +38 (*c* 0.36 in $CHCl_3$); found: C, 49.2; H, 4.8. Calc. for $C_6H_7O_3F$: C, 49.3; H, 4.8%; *m/z* (EI) 69 (100%), 71 (82), 97 (69), 75 (33), 146 (M$^+$, 0.1). Further elution gave 2,6:3,4-dianhydro-β-D-talopyranosyl fluoride (**19**, 155 mg, 52%); mp 99–100 °C; $[\alpha]_D^{25}$ +43 (*c* 0.17 in $CHCl_3$); found: C, 49.3; H, 4.8. Calc. for $C_6H_7O_3F$: C, 49.3; H, 4.8%; *m/z* (EI) 69 (100%), 71 (80), 97 (64), 41 (60), 146 (M$^+$, 0.2).

Reaction of 1,6:3,4-dianhydro-β-D-talopyranose (14)

The reaction was carried out using **14** (200 mg, 1.39 mmol) and DAST (0.65 mL, 4.92 mmol). Since an initial experiment showed that the product is sensitive to chromatography, the crude product obtained after work-up was purified by crystallization from ethanol to afford 2,5:3,4-dianhydro-α-D-mannoseptanosyl fluoride (**21**, 43 mg, 21%); mp 113–115 °C (from ethanol); $[\alpha]_D^{25}$ +26 (*c* 0.1 in $CHCl_3$); found: C, 49.2; H, 4.8. Calc. for $C_6H_7O_3F$: C, 49.3; H, 4.8%; *m/z* (EI) 68 (100%), 69 (42), 71 (33), 87 (26), 97 (17), 146 (M$^+$, 2).

Reaction of 1,6:2,3-dianhydro-β-D-talopyranose (8)

The reaction was carried out using **8** (150 mg, 1.04 mmol) and DAST (0.5 mL, 3.78 mmol). Chromatography in S3 afforded 1,6:2,3-dianhydro-4-deoxy-4-fluoro-β-D-talopyranose (**22**, 84 mg, 55%); mp 96–97 °C (from ether-light petroleum); $[\alpha]_D^{25}$ −63 (*c* 0.19

in $CHCl_3$); found: C, 49.3; H, 4.7. Calc. for $C_6H_7O_3F$: C, 49.3; H, 4.8%; *m/z* (EI) 99 (100%), 59 (18), 72 (15), 75 (12), 146 (M^+, 0.1).

Reaction of 1,6:2,3-dianhydro-β-D-gulopyranose (4)

The reaction was carried out using **4** (200 mg, 1.39 mmol) and DAST (0.6 mL, 4.54 mmol). Chromatography in ethyl acetate - light petroleum 1 : 7 afforded 1,6:2,3-dianhydro-4-deoxy-4- fluoro-β-D-gulopyranose (**23**, 125 mg, 61%); mp 73–75 °C (from ethanol); $[\alpha]_D^{25}$ +42 (*c* 0.1 in $CHCl_3$); found: C, 49.4; H, 4.8. Calc. for $C_6H_7O_3F$: C, 49.3; H, 4.8%; *m/z* (EI) 99 (100%), 59 (19), 72 (14), 75 (11), 146 (M^+, 0.2). Further elution gave first a mixture of **23** and **24** (29 mg, 15%) in ratio 1 : 17 by GC-MS, then syrupy 1,6:2,3-dianhydro-5-deoxy-5-fluoro-α-L-talofuranose (**24**) (52 mg, 26%), found: C, 49.5; H, 4.9. Calc. for $C_6H_7O_3F$: C, 49.3; H, 4.8%; *m/z* (EI) 88 (100%), 71 (46), 59 (45), 99 (27), 146 (M^+, 0.4).

Reaction of 1,6:2,3-dianhydro-β-D-mannopyranose (3)

The reaction was carried out using **3** (200 mg, 1.39 mmol) and DAST (0.6 mL, 4.54 mmol). Chromatography in S3 gave first an inseparable mixture of 1,6:2,3-dianhydro-4-deoxy-4-fluoro-β-D-talopyranose and 1,6:2,3-dianhydro-4-deoxy-4-fluoro-β-D-mannopyranose (**22** and **25**, 107 mg, 52%), the ratio of **22** and **25** was 21 : 4 according to ^{1}H NMR, the NMR spectrum of the major product **22** was identical with that of the product prepared from **8**. The epimers **22** and **25** were also inseparable by GC-MS. Further elution gave 1,6:2,4-dianhydro-3-deoxy-3-fluoro-β-D-idopyranose (**26**, 24 mg, 12%) contaminated with impurities (GC-MS), recrystallization from ethyl acetate-light petroleum gave pure **26** (19 mg, 9%) mp 110 °C, found: C, 49.4; H, 4.85. Calc. for $C_6H_7O_3F$: C, 49.3; H, 4.8%; *m/z* (EI) 72 (100%), 59 (75), 116 (15), 40 (6).

Reaction of 1,6:2,3-dianhydro-β-D-allopyranose (12)

The reaction was carried out using **12** (200 mg, 1.39 mmol) and DAST (0.6 mL, 4.54 mmol). Chromatography in S3 gave (5*R*)-1,4^1:2,3-dianhydro-4-deoxy-4-*C*-hydroxymethyl-D-*lyxo*-pentodialdo-1,5-pyranosid-5-yl fluoride (**27**, 34 mg, 17%), mp 83–92 °C, found: C, 49.3; H, 4.8. Calc. for $C_6H_7O_3F$: C, 49.3; H, 4.8%; *m/z* (EI) 69 (100%), 87 (46), 100 (42), 115 (3). Further elution gave the starting dianhydro derivative **12** (10 mg, 5%).

Reaction of 37 with DAST. The reaction was carried out using **37** (150 mg, 0.44 mmol) and DAST (0.5 mL, 3.78 mmol). Chromatography in ethyl acetate-light petroleum 1 : 7 afforded 116 mg (77%) of a mixture of 1,6-anhydro-3-azido-2,3-dideoxy-2-fluoro-4-*O*-tosyl-β-D-glucopyranose (**38**) and 2,5-dianhydro-3-azido-3-deoxy-4-*O*-tosyl-α-D-altroseptanosyl fluoride (**39**). The ratio of **38** and **39** was estimated to be 6 : 1 (NMR). Semipreparative reverse phase HPLC of a sample of the mixture (7 mg) in acetonitrile-water 1 : 1 afforded pure syrupy **38** (4 mg), ν_{max}(film)/cm^{-1} 2098(N_3), HREIMS: *m/z* 366.05295 calcd. for $C_{13}H_{14}O_5FN_3SNa$: 366.05304. Compound **39** was obtained only as an enriched HPLC fraction (in cca 73% purity)

Reaction of 28 with DAST. A solution of **28**[17] (166 mg, 0.66 mmol) in dichloromethane (2.0 mL) was added to a solution of DAST (0.35 mL, 2.65 mmol) in dichloromethane (2.0 mL) under cooling (–50 °C) and stirring. The cooling bath was removed after 20 min and the stirring continued for 48 h at rt. TLC in S2 indicated absence of the starting **28**. The reaction mixture was worked-up as described in general procedure for reaction with DAST except that water was used instead of 1% aqueous HCl. Chromatography in S3 afforded first crystalline 1,6-anhydro-2,3-di-*O*-benzylidene-4-deoxy-4-fluoro-β-D-talopyranose (**29**, 89 mg) which contained 9% of an unknown fluorine-containing product according to NMR. Recrystallization from ethanol gave pure **29** (53 mg, 32%), mp 109–112 °C, $[\alpha]_D^{25}$ –56 (*c* 0.20 in $CHCl_3$); found: C, 61.8; H, 5.2. Calc. for $C_{13}H_{13}O_4F$: C, 61.9; H, 5.2%. Further elution afforded the unreacted **28** (9 mg, 5%).

Reaction of 31 with DAST. A solution of **31** (200 mg, 0.72 mmol) in dichloromethane (1.5 mL) was added to a solution of DAST (0.35 mL, 2.65 mmol) in dichloromethane (2.0 mL) under cooling (–50 °C) and stirring. The cooling bath was removed after 20 min and the stirring continued for 24 h at rt. TLC in S2 indicated absence of the starting **31**. The reaction mixture was worked-up as described in general procedure for reaction with DAST. Chromatography in. S4 afforded first syrupy 2,6-anhydro-3-azido-3-deoxy-4-*O*-benzyl-α-D-talopyranosyl fluoride (**32**, 69 mg, 34%), $[\alpha]_D^{25}$ –135 (*c* 0.44 in $CHCl_3$); found: C, 56.05; H, 5.1; N, 14.7. Calc. for $C_{13}H_{14}O_3N_3$: C, 55.9; H, 5.05; N, 15.05%. Further elution afforded syrupy 2,6-anhydro-3-azido-3-deoxy-4-*O*-benzyl-β-D-talopyranosyl fluoride (**33**, 92 mg, 46%), $[\alpha]_D^{25}$ –108 (*c* 0.27 in $CHCl_3$); found: C, 56.2; H, 5.1; N, 14.5. Calc. for $C_{13}H_{14}O_3N_3$: C, 55.9; H, 5.05; N, 15.05%.

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