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# Fluorination of 2-hydroxy-hexopyranosides by DAST: towards formyl C-glycofuranosides from *equatorial*-2-OH methyl hexopyranosides

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**Abstract**—Reaction of diversely configured and substituted, unbranched methyl D-hexopyranosides with the DAST in dichloromethane or acetonitrile led to normal substitution products and/or rearranged fluoro compounds (ring-contracted 2,5-anhydro-1-fluoro-1-*O*-methylhexitol derivatives, 2-methoxy-D-hexopyranosyl fluorides, and, for some 3-azido substrates, rearranged 2-azido-3-fluoro-D-hexopyranosides). When the reaction was performed in acetonitrile, the solvent participation as a nucleophile (Ritter reaction) was observed in one case. For a 2,4-unprotected 3-azido substrate, 2,3-dehydration and fluorination at C(4), the latter with epimerization, took place. $^{19}F/^{1}H$ and $^{19}F/^{13}C$ coupling constant values were systematically applied to discriminate between isomeric structures for fluorinated products, and for some, previously described, coming from five 3-branched-chain D- or L-hexopyranosides, thus discarding the previously reported structural assignment. From the synthetic point of view, the most outstanding result was the preparation of 2,5-anhydro-1-fluoro-1-*O*-methylhexitols, showing a latent formyl group functionality, a transformation, which was achieved in one case. A rationalization for the formation of the different types of product is also proposed.


## 1. Introduction

The role of organofluorine compounds, and in particular fluorocarbohydrates, in different branches of industry and medicine[1] has inspired great efforts to develop new, mild reagents[2,3] and methods[4] for regioselective fluorination, as well as to establish[5] the mechanistic features governing the corresponding or alternative reaction paths.

Among a large number of strategies to introduce fluorine into carbohydrates, diethylaminosulphur trifluoride (DAST) is known to be a useful reagent for the direct replacement of a hydroxyl group by fluorine.[6–9] However, unusual reactions caused by the action of DAST have also been described.[5,9–11] Over the last few years we have studied the reaction of 3-branched-chain hexopyranosides (and hexo-1-thiopyranosides) of the D- and L- series with DAST, and reported[12–15] three different kinds of rearrangement promoted by this fluorinating agent. These reactions take place with or without ring contraction, depending primarily on the substrate, and constitute a convenient route to branched-chain glycosyl fluorides and 2,5-anhydro-1-fluoro-1-*O*-methylhexitols, as well as conformationally constrained cyclic fluorinated glycos-β-amino acids.

We report herein our findings on the reactions of DAST with a series of unbranched methyl 2-hydroxy-hexopyranosides. The extension of the above methodology[12–15] to unbranched methyl 1,2-*trans*-diequatorial- and 1,2-*cis*-glycopyranosides allowed us to prepare a series of 2,5-anhydro-1-fluoro-1-*O*-methylhexitols (**A**) (Scheme 1), and to gain a better understanding of the structural requirements for each type of rearrangement path. Compounds of type **A** contain a masked aldehyde function, and the quantitative transformation into the corresponding formyl C-glycofuranoside **B** was achieved in one case. The mild conditions under which these ring-contraction reactions take place, highlight this kind of rearrangement promoted by DAST as a convenient method to generate a furanose-based anomeric C-formyl

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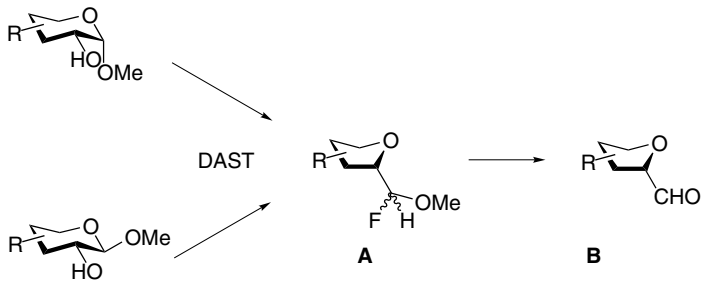
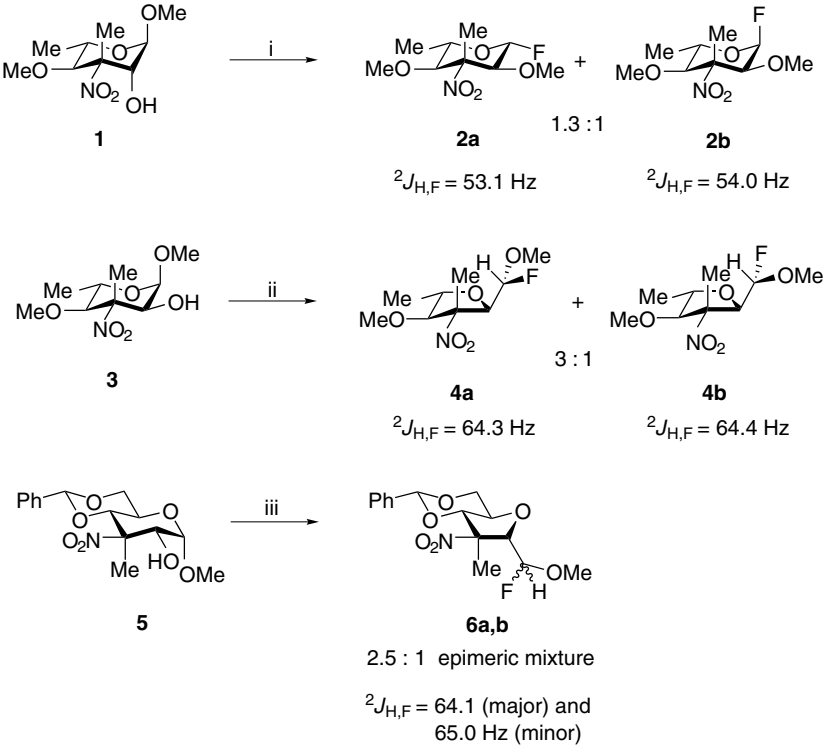



**Scheme 1.** General ring-contraction reaction of 2-*equatorial*-hydroxy 1,2-*cis* and 1,2-*trans* glycopyranosides, promoted by DAST, and transformation of the product into 2,5-anhydro-*aldehydo*-furanose ('formyl C-glycofuranoside'), as formulated for the D-series of sugars.

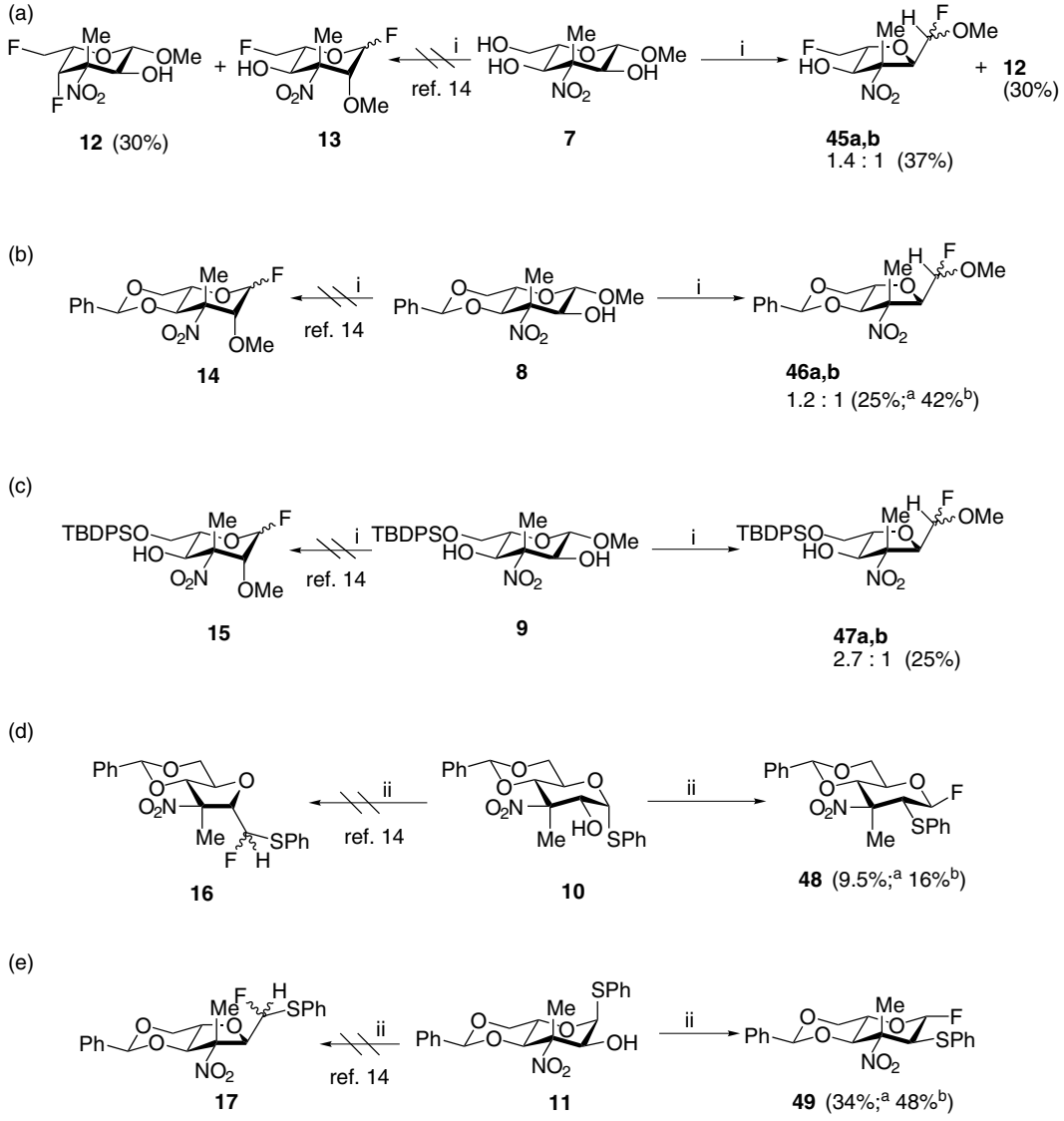
group. This provides a route to acid-stable C-glycofuranosides (C-oligosaccharides[16] and C-glycoconjugates[17,18]), using compounds of type **B** or their synthetic equivalents **A** as building blocks in standard coupling reactions with nucleophiles.

In a previous paper,[14] we demonstrated that the branched-chain 2-hydroxy-hexopyranoside **1**, whose anomeric substituent and the 2-hydroxyl group are in a *trans*-diaxial arrangement, when treated with DAST, affords a mixture of compounds **2a** and **2b** (Scheme 2), which are generated through a 1,2-migration with concomitant stereoselective fluorination at the anomeric position. When these substituents are *cis*, as is the case for **3** or **5**, the reaction leads to the ring-contracted products **4a** and **b** or **6a** and **b**, respectively. Other examples of similar ring contractions have been reported[9] by Dax et al. in a recent review, where those authors indicated that, for this kind of rearrangement, only an *equatorial* arrangement of the HO-2 group (activated by DAST), irrespective of the specific anomeric configuration, appears to be essential. The coupling constant $^2J_{1,F}$ values are spectroscopic data with a diagnostic value, useful for differentiating between ring-contracted products ($^2J_{1,F}$ 63–68 Hz) and 1,2-migration products ($^2J_{1,F}$ 48–54 Hz).[5]

We had found[14] that the reaction of the branched-chain 2-hydroxy-hexopyranosides **7**–**11** gives rise to products for which the structures **12**–**17** (Scheme 3) were initially assigned. However, the $^2J_{1,F}$ values observed for these compounds (except for **12**) were in conflict with the spectral data described above (see Scheme 2) and those deduced and later published[5] by Dax et al. All these facts prompted us to reconsider the structural assignment for the products obtained from **7**–**11**.




**Scheme 2.** Some antecedents[14] of reactions of 3-branched-chain substrates with DAST, showing two types of rearrangement depending upon the relative 1,2-configuration. (i) DAST, $CH_2Cl_2$, rt; 58% global yield. (ii) DAST, $CH_2Cl_2$, rt; 70% global yield. (iii) DAST, diglyme, rt; 95% from converted substrate.



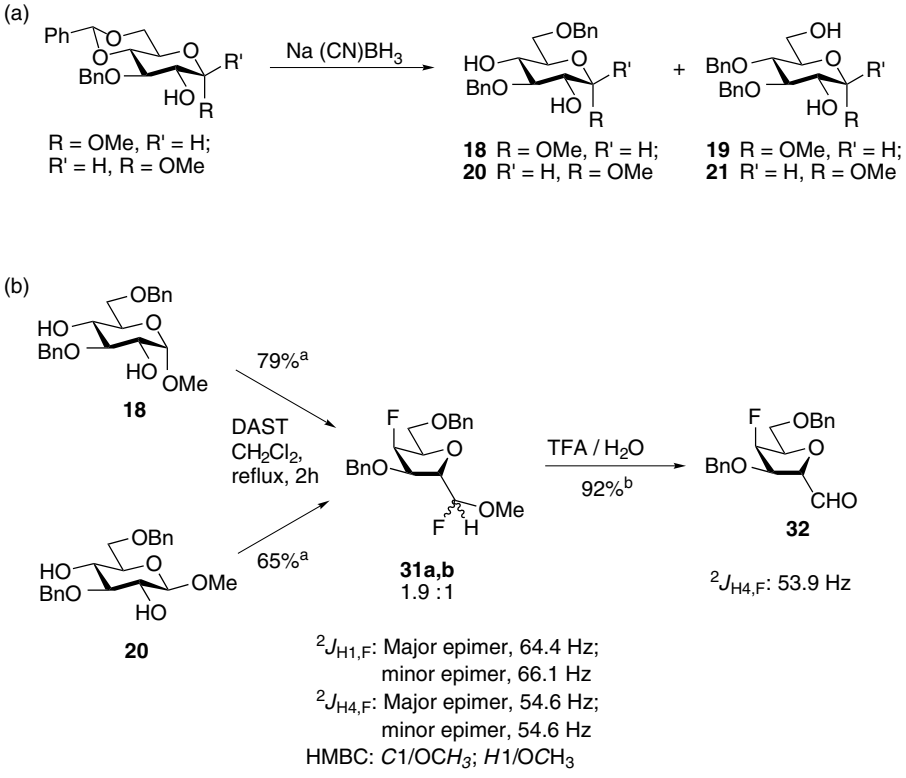

**Scheme 3.** Structural reassignment for the products obtained[14] in the fluorination of the five substrates **7**–**11**. (i) DAST (5 mol equiv), $CH_2Cl_2$; reflux (2 h). (ii) DAST (5 mol equiv), $CH_2Cl_2$, 0 °C (0.5 h) → reflux (1–3 h). [a]Isolated; [b]from converted substrate.

## 2. Results

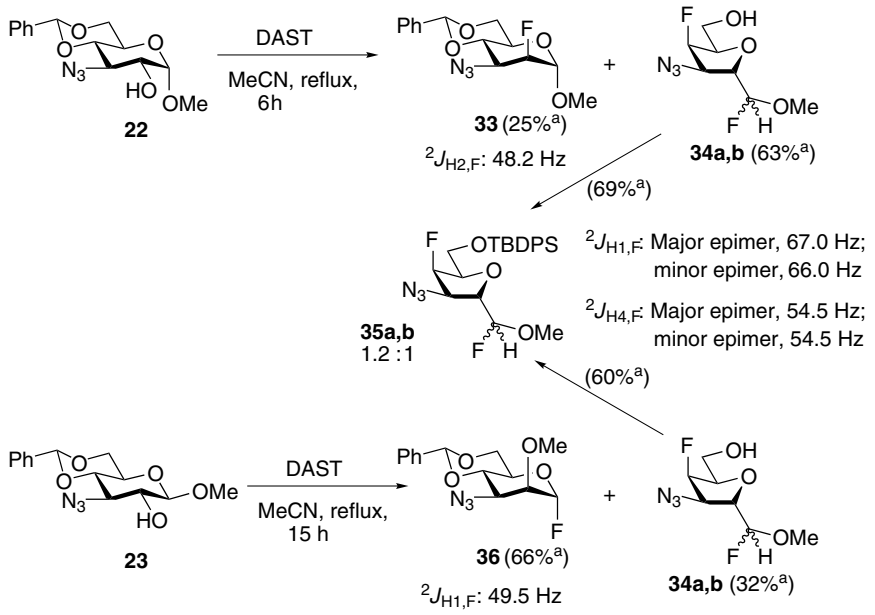
The opening of the 1,3-dioxane ring of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside or its β anomer[19] by treatment with sodium cyanoborohydride[20] led to compounds **18**[21,22] and **19**[19,21,23] (from the α anomer) or **20**[24] and **21** (from the β anomer), which were separated in each case by column chromatography. To our knowledge, compound **21** has not previously been described but is now completely characterized (see Experimental). The anomeric methyl 3-azido-4,6-*O*-benzylidene-D-glucopyranosides **22** and **23** were prepared as described in the literature,[25] as well as their respective, D-altro configured isomers **24**[26] and **25**.[27] By treatment of the 4,6-*O*-deprotected compound **26**,[28] derived from **24**, with *tert*-butyl-chloro-diphenylsilane, we prepared the substrate **27**. Similarly, deprotection of **25** afforded the methyl β-D-altropyranoside derivative **28**, which was characterized and transformed into its 6-*O*-*tert*-butyl-diphenylsilyl derivative **29**. Another substrate, the methyl 3,6-dideoxy-α-D-hexopyranoside **30**, was prepared according to a published procedure.[29] Branched-chain substrates **7**–**11** were obtained as previously described.[13,14,30]

Treatment of **18** or **20** with DAST (5 mol equiv) in dichloromethane at reflux for 1.5–2.0 h afforded the epimeric, ring-contracted difluoro products **31a** and **b**, in 40–41% overall yields (79% or 65% from converted substrate, starting from **1** or **3**, respectively). When this epimeric mixture was treated with aqueous trifluoroacetic acid, almost quantitative transformation into the 2,5-anhydro-4-fluoro-*aldehydo*-D-talose derivative **32** occurred (Scheme 4).

When the methyl 3-azido-4,6-*O*-benzylidene-D-glucopyranoside derivatives **22** and **23** were treated with DAST in dichloromethane for 6–8 h, no reaction was




**Scheme 4.** (a) Preparation of substrates **18** and **20**, and their respective regioisomers **19** and **21**; (b) fluorination of **18** and **20** by the DAST reagent, and hydrolysis of the product **31a**,**b** to the C-formyl derivative **32**. [a]Yield from converted substrate; [b]isolated yield.




**Scheme 5.** Fluorination of **22** and **23**, and transformation of product **34a**,**b** into the 6-*O*-protected derivative **35a**,**b**. [a]Yield from converted substrate.

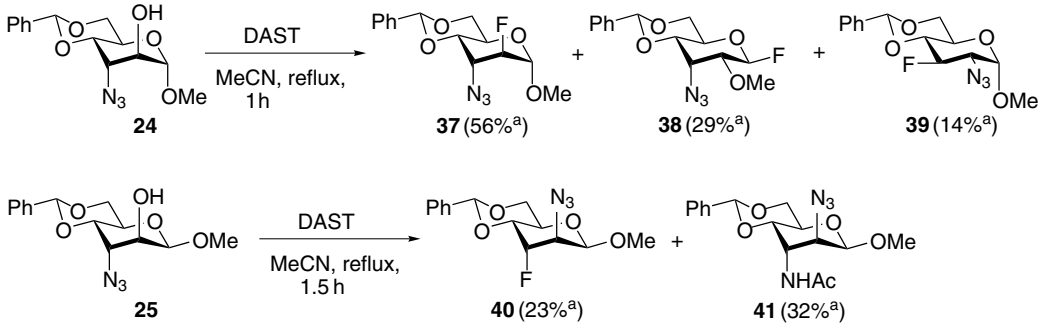
observed. When acetonitrile was used as the solvent at reflux for 6 h (Scheme 5), the α-D-glycoside **22** gave, after column chromatography, the 2-inverted fluoro compound **33** (23% yield, 25% from converted substrate) and the 1-epimeric mixture of 1,4-difluoro, ring-contracted products **34a** and **b** (57% overall yield; 63% from converted substrate), indicating an extensive loss of the benzylidene protecting group during the reaction. Characterization of **34a** and **b** was achieved by preparation of its 6-*O*-*tert*-butyl-diphenylsilyl derivative **35a** and **b**, also obtained as an epimeric mixture. In contrast with **22**, its β anomer **23**, under the same conditions,

except for heating for 15 h, was transformed into the 1,2-rearranged compound **36** (40%; 66% from converted substrate) and the same epimeric mixture of 4,6-*O*-deprotected compounds **34a** and **b** (20%; 32% from converted substrate).

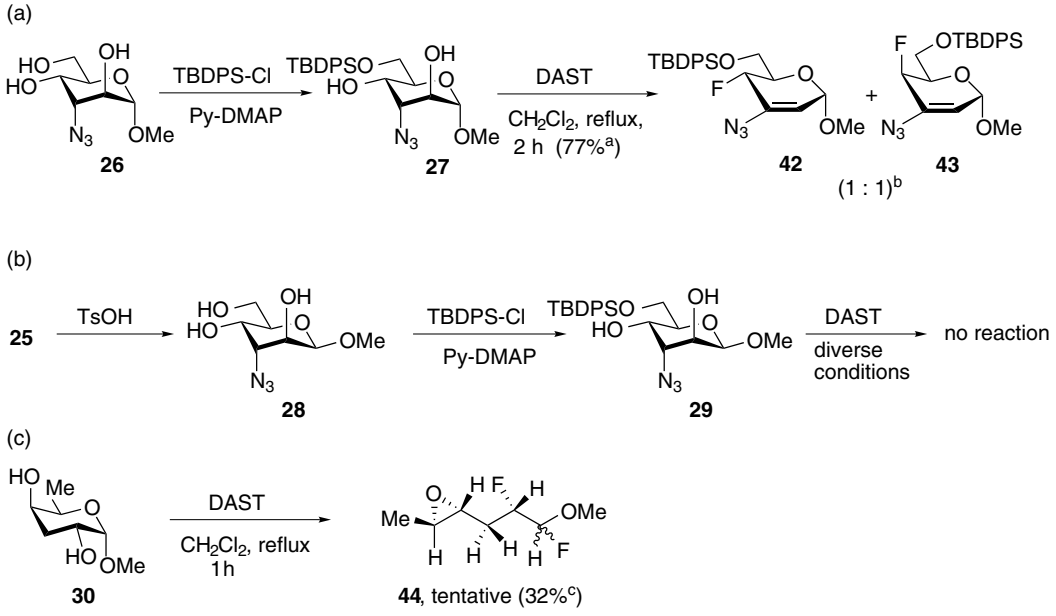
The 4,6-di-*O*-protected methyl 3-azido-α-D- and β-D-altropyranoside derivatives **24** and **25** behaved differently (Scheme 6) under fluorination conditions similar to those applied to **22** and **23** (DAST in refluxing acetonitrile, but for 1–1.5 h). Starting from **24**, three pyranosic, monofluorinated products were obtained (**37**, **38** and **39**, in 56%, 29% and 14% yields, respectively), two of them showing rearranged substitution patterns; from **25**, the 2,3-rearranged methyl β-D-altropyranoside derivative **40** and the non-fluorinated 2,3 rearranged product **41** (formed by solvent participation in a Ritter reaction) were obtained (31% and 42% yield from converted substrate, respectively). In an attempt to fluorinate the β-D-altropyranoside derivative **25** with DAST in dichloromethane at reflux for 2 h, no reaction occurred, as seen for **22** and **23**.

A different course of the reaction was observed when starting from the 4-*O*-deprotected compound **27**, derived from **24** through **26** [Scheme 7, (a)]. In this case, fluorination with DAST in dichloromethane at reflux for 2 h led to a 1:1 mixture (by $^1$H NMR) of the two 4-fluoro-2,3-dehydrated 4-epimers **42** and **43**, in 77% overall yield. Preparative TLC made possible the separation of the epimers, which could thus be characterized. It is noteworthy that the reaction of **27** with DAST in acetonitrile afforded a complex mixture of polar and non-fluorinated products.

The reactions of compounds **29** and **30** with DAST were also investigated. The former, the β anomer of **27**, did not react with DAST in dichloromethane at reflux and, when the solvent was acetonitrile, a complex mixture of non-fluorinated products was obtained [Scheme 7, (b)]. The latter, a methyl 3,6-dideoxy-2,4-unprotected-α-D-hexopyranoside, on treatment with DAST in dichloromethane at reflux for 1 h, afforded an unstable difluoro compound that could not be completely characterized, in low yield (up to 32%), for which we tentatively propose the structure **44** [Scheme 2, (c)].




**Scheme 6.** Fluorination of **24** and **25**. [a]Isolated yield.




**Scheme 7.** (a) Preparation of substrate **27** and its fluorination with DAST; (b) preparation of substrate **29** and its attempted fluorination with DAST, showing no reaction; (c) fluorination of substrate **30**. [a]Global yield; [b]separation of products was achieved by preparative TLC; [c]isolated yield.

A spectral reinvestigation of the products obtained from the branched-chain substrates **7**–**11** led us to conclude that a structural reassignment was necessary. Thus, the correct structures of the products are as follows (Scheme 3): (a) from **7**, the expected 4,6-difluoro-β-L-hexopyranoside **12** (correctly assigned before[14]) and the epimeric mixture of ring-contracted 1,6-difluoro-hexitol derivatives **45a** and **b**; (b) from **8**, the mixture of 4,6-di-*O*-protected 2,5-anhydro-1-fluoro-hexitol derivatives **46a** and **b**; (c) from **9**, the mixture of 6-*O*-protected 2,5-anhydro-1-fluoro-hexitol derivatives **47a** and **b**; (d) from **10**, the 2-phenylthio-β-D-glucopyranosyl fluoride derivative **48**; and (e) from **11** (enantiomer of **10**), **49** (the β-L-enantiomer of **48**).

## 3. Discussion

Structures for the foregoing new products **31**–**43** coming from unbranched hexopyranosides were assigned mainly on the basis of their high-resolution mass spectrometric data and $^{1}H$ and $^{13}C$ NMR spectra. In particular, the $^{19}F/^{1}H$ and $^{19}F/^{13}C$ coupling constant values were of diagnostic application. Compounds **31a** and **b** (Scheme 4) and **35a** and **b** (and their immediate precursor **34a** and **b**) (Scheme 5) contained one fluorine atom at the C(4) ring position ($^{2}J_{H4,F}$ 54.5–54.6 Hz) and a second fluorine atom at C(1), whose coupling constant with the *geminal* proton—$^{2}J_{H1,F}$ values of 64–67 Hz, in the range (63–68 Hz) observed[5] for analogous compounds—indicated an *exo*-cyclic position; consequently, these products must have a ring-contracted structure. For **31a** and **b**, heteronuclear multiple bond correlations (HMBC) were observed: On the one hand, between C(1) and the methyl protons and on the other, between C(1)H and the methyl carbon nucleus, thus corroborating the assignment. The structure of 2,5-anhydro-4-fluoro-*aldehydo*-D-talose derivative **32** was easily assigned to the hydrolysis product of **31a** and **b** from the $\delta$ value of the emerging C(1)H (doublet, 9.68 ppm) and carbonyl C(1) signals (singlet, 199.6 ppm) observed, as well as from the high-resolution, electron-impact mass spectrum (HRE-IMS).

Compound **33**, also obtained from **22** (Scheme 5), is a methyl 2-fluoro-α-D-hexopyranoside derivative, as deduced from the $^{2}J_{H2,F}$ and $^{1}J_{C2,F}$ values (48.2 and 180.0 Hz, respectively), whilst its isomer **36**, obtained as the major product from **23**, must be a 2-*O*-methyl-α-D-hexopyranosyl fluoride, since the highest $^{19}F/^{1}H$ and $^{19}F/^{13}C$ coupling constant values were found for the $^{1}H$ and $^{13}C$ nuclei at the 1-position ($^{2}J_{H1,F}$ 49.5 Hz; $^{1}J_{C1,F}$ 225.4 Hz). Both isomers **33** and **36** showed low proton/proton $^{3}J$ values between C(1)H, C(2)H, and C(3)H ($^{3}J_{1,2}$ 1.7 and 1.5 Hz; $^{3}J_{2,3}$ 2.3 and 3.3 Hz) and high ones between the remaining pairs of pyranosic vicinal protons ($^{3}J_{3,4}$ 10.6 and 9.9 Hz; $^{3}J_{4,5}$ 9.0 and 9.9 Hz), so that C(3)H must have the axial orientation, but C(2)H and C(1)H the equatorial one. For **33**, the absence of splitting of the C(4) signal is in agreement with a *gauche* C(4)/F relationship[31] (axial F), and not with an *anti* one (equatorial F), which should give rise[31] to a $^{3}J_{C4,F} \approx 8$ Hz; similarly, the low value of $^{3}J_{C3,F}$ (2.4 Hz) (for **36**) confirms the *gauche* C(3)/F relationship.

For compounds **37**, **38** and **39**, coming from **24** (Scheme 6), the highest $^{19}F/^{1}H$ and $^{19}F/^{13}C$ coupling constant values were measured on the signals of C(2)H and C(2) for **37**, C(1)H and C(1) for **38**, and C(3)H and C(3) for **39**, indicating the respective fluorination site. For **37**, the low $^{3}J_{3,4}$ value (2.9 Hz) suggests the equatorial arrangement of the C(3)H, since C(4)H is axial, while the absence of splitting of the C(4) signal ($^{3}J_{C4,F} \approx 0$ Hz) is again in agreement with the axial orientation of the F atom at C(2); this and the low values of $^{3}J_{1,2}$ and $^{3}J_{2,3}$ (1.0 and 2.8 Hz, respectively) agree with the equatorial arrangement of C(2)H and C(1)H. For **38**, the $^{3}J_{1,2}$ value (7.3 Hz) indicates a *trans*-diaxial relationship between these protons, and the $^{3}J_{2,3}$ and $^{3}J_{3,4}$ values (3.2 and 5.8 Hz) agree with an equatorial arrangement of C(3)H. For **39**, the high $^{3}J_{2,3}$, $^{3}J_{3,4}$ and $^{3}J_{4,5}$ values (9.0, 9.7 and 12.1 Hz, respectively) show the *trans*-diaxial relationship between the respective protons, while the low $^{3}J_{1,2}$ value (3.4 Hz) indicates the equatorial orientation of the anomeric proton. For both products **38** and **39**, the $^{3}J_{C,F}$ values (9.8 and 8.3 Hz) measured, respectively, in the C(3) and C(1) signals are indicative of the equatorial arrangement of the F atom, thus corroborating the foregoing assignments.

Of the two products obtained from **25**, only **40** contains one fluorine atom at C(3), as evidenced by the mass spectrum and the *J* values observed in the NMR spectra, the highest ones being observed in the C(3) signal ($^{1}J_{C3,F}$ 181.0 Hz) and in the C(3)H signal ($^{2}J_{H3,F}$ 49.7 Hz); the second product **41** has an acetamido group instead of the fluorine atom, as a consequence of solvent participation (Ritter reaction). For **40** and **41**, the substituent orientation pattern is the same—equatorial at C(1) and axial at C(2) and C(3)—in agreement with the vicinal coupling constant values observed in the respective proton signals: for **40**, $^{3}J_{1,2}$ 1.7, $^{3}J_{2,3}$ 3.7 and $^{3}J_{3,4}$ 1.7 Hz (and, to identify the signal correspondence, $^{4}J_{H1,F}$ 2.7, $^{3}J_{H2,F}$ 7.5 and $^{2}J_{H3,F}$ 49.7 Hz; $^{2}J_{C2,F}$ 26.4, $^{1}J_{C3,F}$ 181.0, $^{2}J_{C4,F}$ 16.3 and $^{3}J_{C5,F}$ 2.5 Hz); for **41**, $^{3}J_{1,2}$ 1.2, $^{3}J_{2,3}$ 3.0 and $^{3}J_{3,4}$ 4.5 Hz. For the latter product, the presence of an acetamido group is evidenced from the acetyl protons signal (singlet at $\delta$ 2.03 ppm), the amino proton signal (broad, $\delta$ 5.71 ppm), and the carbonyl $^{13}C$ signal ($\delta$ 171.5 ppm). The axial arrangement of the F atom at C(3) of **40** was confirmed by the absence of splitting of the C(1) signal.

The products **42** and **43** obtained from **27** [Scheme 7, (a)] are 4-epimeric 4-fluoro-α-D-hex-2-enopyranoside derivatives, as deduced from HRMS and NMR data. For **42**, the ethylenic proton signal (at $\delta$ 5.58 ppm) must be assigned to C(2)H, since it is split by the coupling with the anomeric proton ($^{3}J_{1,2}$ 3.5 Hz), and the $^{13}C$ signals at 134.0 and 114.4 ppm correspond to the two ethylenic carbon atoms C(3) and C(2), respectively, the former showing a two-bond coupling with fluorine ($^{2}J_{C3,F}$ 13.6 Hz). The position of the fluorine atom at C(4) is deduced from the *J* values found ($^{2}J_{H4,F}$ 51.5 and $^{1}J_{C4,F}$

173.6 Hz). Compound **43** gave rise to $^{1}H$ and $^{13}C$ spectra, respectively, similar to those of its isomer, the most outstanding difference being that observed between the $^{3}J_{4,5}$ values (8.8 and 2.0 Hz for **42** and **43**, respectively), indicating that the orientation of C(4)H must be axial for **42** and equatorial for **43**.

Structure **44** is tentatively assigned to the product obtained from **30**, since only the $^{1}H$ and $^{13}C$ NMR spectra could be registered. The presence of one fluorine atom at each position 1 and 2 was evidenced from the $\delta$ values observed for C(1)H, C(2)H, C(1), and C(2) (5.26, 4.44, 112.1 and 91.7 ppm, respectively), and, more significantly, from the $J_{H,F}$ and $J_{C,F}$ values: thus, the value of $^{2}J_{H1,F1}$ (65.5 Hz) is in the range (63–68 Hz) characteristic[5] of the presence of a fluorine atom and an alkoxy group at a terminal, *exo*-cyclic position, also in agreement with the long-range coupling $^{4}J_{F1,OMe}$ (1.5 Hz), while the $^{3}J_{H1,F2}$ and $^{3}J_{H2,F1}$ values (7.0 and 9.1 Hz, respectively) indicate a *vicinal* relationship between the two fluorine atoms in the molecule, corroborated by the high values of $J$ measured in the C(1) and C(2) signals ($^{1}J_{C1,F1}$ 219.6 Hz, $^{1}J_{C2,F2}$ 173.0 Hz, $^{2}J_{C1,F2}$ 28.3 Hz, $^{2}J_{C2,F1}$ 25.8 Hz), as well as in the C(3) signal ($^{2}J_{C3,F2}$ 20.4 Hz).

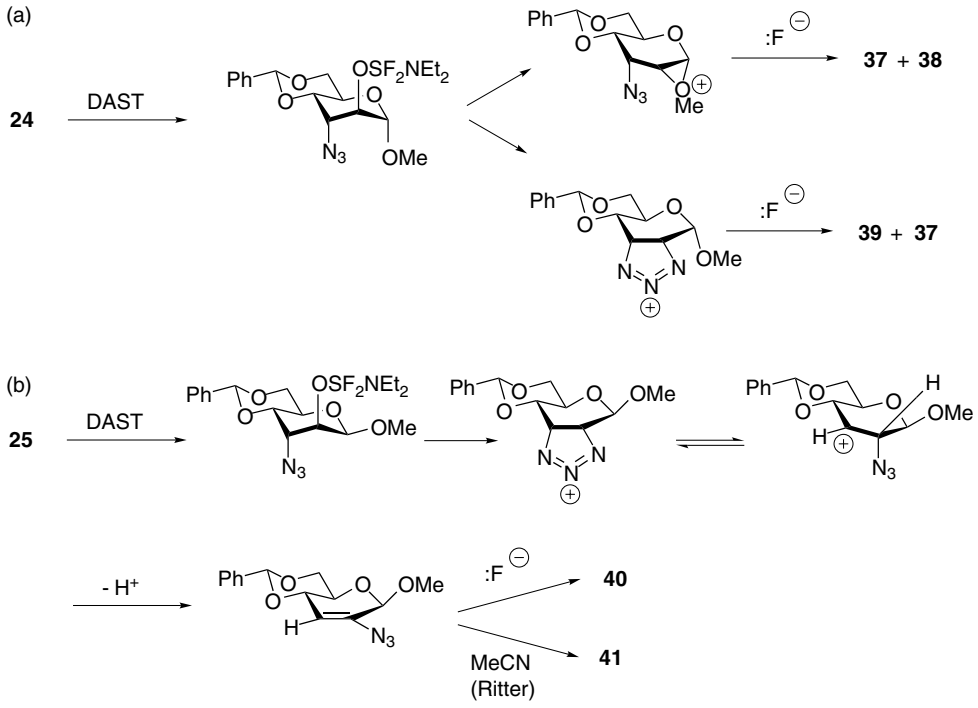
In the light of the foregoing structural study of the products obtained from unbranched methyl 2-hydroxyhexopyranosides, as well as of literature precedents[5,31] of assignments based on the $^{19}F/^{1}H$ and $^{19}F/^{13}C$ coupling constant values observed for related compounds, a structural reassignment for the products obtained from the 3-branched-chain substrates **7**–**11** (Scheme 3) was made. A common 2,5-anhydro-1-fluoro-1-*O*-methyl-L-mannitol derivative pattern was assigned to the 1-epimeric pairs **45a** and **b**, **46a** and **b**, and **47a** and **b** obtained from **7**, **8**, and **9**, respectively, since the $^{2}J_{H1,F}$ values measured (64.2, 64.0; 65.0, 64.0; 65.4, 64.0 Hz, respectively) are in agreement with the previous observations cited above, but very different from those found for glycosyl fluorides. Moreover, we found in our reinvestigation that all of these products showed $C(1)/OCH_3$ and C(1)*H*/O*C*H$_3$ heteronuclear multiple bond correlations (HMBC), indicating three bonds between the corresponding atoms and, therefore, that the fluorine atom and the methoxy group are substituents at C(1). Another feature of the $^{1}H$ NMR spectra of these compounds is the higher chemical shift value observed for the C(2)H signal of the 2,5-anhydro-hexitol structure ($\delta$ range: 4.62–4.82 ppm; for example,[14] **4a**, **4b** and **6a** and **b**) in comparison with a glycopyranosyl fluoride structure ($\delta$ range: 3.66–4.05 ppm; for instance,[14] **2a** and **2b**). It is noteworthy that the new structures **46a** and **b** assigned to the compounds obtained as a mixture from **8** correspond to the respective enantiomers of **6a** and **b** (Scheme 2), as corroborated by the respectively identical $^{1}H$ and $^{13}C$ NMR spectra,[14] in spite of the non-enantiomeric relationship between the respective substrates **8** (β-L-) and **5** (α-D-). Products **48** and **49**, being enantiomers (as obtained from the enantiomers **10** and **11**), showed identical $^{1}H$ and $^{13}C$ NMR spectra, respectively, in which the $^{2}J_{H1,F1}$ value (50.9 Hz) agreed with the reassigned glycosyl fluoride structure, confirmed in our reinvestigation by the observed HMBC *H*-2/(SPh)$C_{ipso}$; the anomeric β-configuration was easily assigned from the $^{3}J_{1,2}$ value (8.2 Hz), while the low C(2) $\delta$ value (59.6 ppm) was according to the presence of a phenylthio group at this position.

The findings described here for unbranched substrates led to the conclusion that a simplified correlation between structure and mechanistic pattern in the fluorination reaction, such as that described for branched-chain derivatives in our earlier article,[14] is no longer possible. Thus, the anomers **18** and **20**, both having the HO group at C(2) equatorially oriented, led (Scheme 4) to the same epimeric pair of ring-contracted products **31a** and **b**, in agreement with earlier observations[32] indicating that when the leaving group at C(2) is equatorial, the ring-contraction reaction takes place irrespective of the relative 1,2 configuration of the substrate.

The formation of **34a**,**b** occurs, after extensive 4,6-*O*-deprotection in the course of the reaction, through a mechanism involving ring-oxygen anchimeric assistance to the departure of the leaving group from C(2), similar to that proposed[9,12,14,32] for other ring-contractions, followed by difluorination.

The formation of **37** and **38** from **24** may be explained, as in similar cases,[11,14] by a scheme involving the anchimeric assistance of the axial methoxy group to the departure of the leaving group [Scheme 8, (a)], the attack of fluoride on C(2) leading to **37** with retained configuration, and on C(1) affording the rearranged β-D-hexopyranosyl fluoride **38**. The formation of the minor product **39** may be explained assuming the anchimeric assistance of the azido group, which might also lead to **37**. However, formation of **40** and **41**, both showing the azido group axially arranged at C(2) and the new substituent, F or NHAc, at C(3) with axial orientation again, seems to indicate [Scheme 8, (b)] a first mechanistic step of azido-assisted departure of the leaving group, a second step of equilibration of the intermediate cation to a carbocation at C(3), which might lose a proton from the vicinal C(2), and a third step, in which the conjugated addition of the nucleophile (fluoride or acetonitrile) on the less-hindered face of the double bond would lead to **40** or, through a Ritter-type reaction, to **41**; the *trans*-diaxial orientation of the C(2) and C(3) substituents for both compounds might also result from a dipole repulsion effect.

The formation of the unsaturated sugar derivatives **42** and **43** from **27** may be considered a normal β-elimination process, but the conditions used here are different (dichloromethane as the solvent) from those used in the foregoing examples (acetonitrile); this might be the reason why no nucleophilic addition to the α,β-unsaturated azide was observed, rather an allylic $S_N1$ reaction. That is, **27** might first undergo the departure of the leaving group from C(2)- assisted again by the methoxy or the azido group- followed by the loss of a proton from C(3) to form a β-elimination intermediate product, from which the departure of the leaving group from C(4) might become easier, since the remaining carbocation




**Scheme 8.** (a) Rationalization proposed for the formation of **37**, **38** and **39** from **24**; (b) proposal for the formation of **40** and **41** from **25**.

would be allylic; all of this is in agreement with the fact that two epimers, **42** and **43** are formed.

The product obtained from **30**, tentatively formulated as **44**, might have been formed like similar compounds[14] by ring-oxygen participation pushing out the leaving group from C(4), requiring in this case the adoption of the $^1C_4$ conformation by the pyranose ring, and the opening of the cyclic oxonium ion formed as intermediate by attack of the fluoride on C(1), followed by a standard $S_N2$ reaction of a second fluoride on C(2); since all this involves inversion of the configuration of C(4) and C(2), the D-*arabino* configuration was assigned.

The reformulated (as ring-contracted) products **45a** and **b**, **47a** and **b**, coming from the 3-branched-chain, 1,2-*trans*-diequatorially substituted compounds **7**–**9**, were assumed to be formed by a mechanistic pathway similar to that proposed[9,12,14,32] for ring contractions. It is noteworthy that the 4,6-*O*-benzylidene substrate **8**, as well as **5**[14] (Scheme 2), led to ring-contracted products, thus refuting a generalization of the stated[9] principle, which establishes that 4,6-*O*-benzylidene hexopyranosides of the *trans*-decalin type containing an equatorial HO group at C(2) cannot undergo ring-contraction reactions.

For their part, the enantiomeric 4,6-*O*-benzylidene-1-thio-α-glucopyranoside derivatives **10** and **11** follow a pathway involving 1,2-migration of the phenylthio group with retention of configuration at C(2) but inversion at C(1). These results may be explained only if the departure of the leaving group occurs before the migration of the phenylthio group, which could lead to a cyclic sulphonium ion intermediate, a process that might be a consequence of the higher nucleophilicity of the sulphur of phenylthio group in comparison with the ring oxygen; later attack of fluoride at C(1) would open this ring, leading to the 1,2-diequatorial product.

## 4. Conclusion

The methyl 2-hydroxy-hexopyranosides that we have used as substrates for this study react with DAST showing the following general trends: (a) When the HO-2 is equatorial, a five-membered ring-contracted product—the synthetic equivalent of a 'formyl C-glycofuranoside'—is obtained, even when starting from 4,6-*O*-benzylidene derivatives. Nevertheless, for this rigidified *trans*-decalin-type system, when the 1,2 substituents have a *trans*-diequatorial arrangement, nucleophilic substitution by fluoride or 1,2-aglycon migration strongly competes with the ring-contraction process. (b) When the HO-2 is axial, nucleophilic substitution, elimination reaction, or 1,2-neighbouring group migration can take place; however, no ring-contracted product was detected by us in any case. As a consequence, a convenient and ready access to 'formyl C-glycofuranosides', starting from *equatorial*-2-OH methyl hexopyranosides, is established.

A different behaviour is observed for phenyl 1-thio-hexopyranosides, since a 2-phenylthio-glycopyranosyl fluoride is obtained, irrespective of the C(1)/C(2) configurational relationship, probably due to the higher nucleophilicity of sulphur.

The systematic use of $^{19}F/^{1}H$ and $^{19}F/^{13}C$ coupling constant values and heteronuclear multiple bond correlation (HMBC) technique led to a structural reassignment for the fluorinated products **45**–**49**, previously reported,[14] coming from five 3-branched-chain D- or L-hexopyranosides.

## 5. Experimental

### 5.1. General

Hexane and ether were distilled from sodium prior to use. TLC was performed on silica gel plates (DC-Alufolien $F_{254}$, E. Merck, or Alugram Sil G/$UV_{254}$, Macherey-Nagel), and preparative TLC on Kieselgel 60 $F_{254}$ DC-Platten 105715 HR; detection of compounds was accomplished with UV light (254 nm) and by charring with $H_2SO_4$ and an anisaldehyde reagent. Silica gel 60 (E. Merck, 230–400 mesh) was used for column chromatography. Solutions were concentrated under diminished pressure at <40 °C. Melting points were determined on a Gallenkamp MFB-595 apparatus and are uncorrected. A Perkin–Elmer 241 MC polarimeter was used for the measurement of optical rotations. IR spectra (neat or on a KBr disc) were obtained on a FTIR Bomem Michelson MB-120 spectrophotometer. $^{1}H$ NMR spectra (300 and 500 MHz) and $^{13}C$ NMR spectra (75.4 and 125.7 MHz) were recorded with a Bruker AMX-300 or an AMX-500 spectrometer; chemical shifts ($\delta$) are expressed in ppm from TMS; coupling constants ($J$), in Hz. Assignments were confirmed by decoupling, homonuclear 2D COSY correlated spectra, heteronuclear 2D correlated (HETCOR) spectra, heteronuclear 1D single quantum coherence (HSQC) spectra, differential NOE and 1D NOESY experiments. Heteronuclear multiple bond correlation (HMBC) experiments were acquired in the same conditions that HSQC corresponding experiments and optimized for long range coupling of 7 Hz. EI mass spectra (70 eV) were measured with a Kratos MS-80RFA instrument, with an ionizing current of 100 μA, an accelerating voltage of 4 kV, and a resolution of 10,000 (10% valley definition). Fast-atom bombardment mass spectrometry (FABMS) was performed on the same instrument; ions were produced by a beam of xenon atoms (6–7 keV) using a matrix consisting of *m*-nitrobenzyl alcohol or thioglycerol and NaI as salt. HREIMS (70 eV) and HRCIMS (150 eV) experiments were performed with a Micromass AutoSpecQ instrument with a resolution of 10,000 (5% valley definition). HRFABMS was performed on a VG AutoSpec spectrometer (Fisons Instruments) (30 keV).

### 5.2. Methyl 3,6-di-*O*-benzyl-α-D-glucopyranoside,[21,22] 18 and methyl 3,4-di-*O*-benzyl-α-D-glucopyranoside,[19,21,23] 19

To a solution of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[19] (0.298 g, 0.801 mmol) in dry tetrahydrofuran (11 mL) was added sodium cyanoborohydride (0.650 g, 10.3 mmol) and molecular sieve (3 Å). After 30 min stirring, HCl/$Et_2O$ was added until gas evolution stopped. The reaction mixture was kept for 5 min at room temperature and then diluted with dichloromethane. The organic layer was washed with water and saturated aqueous sodium hydrogen carbonate. After drying over $Na_2SO_4$, the organic layer was concentrated and the residue was subjected to column chromatography (1:1 → 5:1 gradient, ether/hexane) to give **18** (0.19 g, 62%) and **19** (0.11 g, 38%).

Compound **18** had $[\alpha]_D^{25} = +78.2$ (*c* 0.93, $CH_2Cl_2$) [lit.[21]: $[\alpha]_D^{25} = +79.2$ (*c* 3.50, $CHCl_3$)].

Compound **19** had $[\alpha]_D^{25} = +98.4$ (*c* 0.91, $CH_2Cl_2$) [lit.[21]: $[\alpha]_D^{25} = +101.3$ (*c* 0.545, $CHCl_3$)].

### 5.3. Methyl 3,6-di-*O*-benzyl-β-D-glucopyranoside,[24] 20, and methyl 3,4-di-*O*-benzyl-β-D-glucopyranoside, 21

To a solution of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside[19] (0.23 g, 0.62 mmol) in dry THF (8.7 mL) was added sodium cyanoborohydride (0.50 g, 7.97 mmol) and molecular sieve (3 Å). After 30 min of stirring, HCl/$Et_2O$ was added until gas evolution stopped. The reaction mixture was kept for 5 min at room temperature and then diluted with dichloromethane. The organic layer was washed with water and saturated aqueous sodium hydrogen carbonate. After drying over $Na_2SO_4$, the organic layer was concentrated and the residue subjected to column chromatography (1:1 → 5:1 gradient, ether/hexane) to give **20** (0.14 g, 61%) and **21** (0.04 g, 19%).

Compound **20** had $[\alpha]_D^{25} = -23.0$ (*c* 0.73, $CH_2Cl_2$) [lit.[24]: $[\alpha]_D^{24} = -29.5$ (*c* 0.76, $CHCl_3$)].

Compound **21**: Syrup; $R_f$ 0.47 (ether); $[\alpha]_D^{22} = -5.8$ (*c* 1.2, acetone); IR (film) $\nu_{max}$ 3306 (OH) and 1127, 1053 $cm^{-1}$ (C–O–C); $^{1}H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.40–7.12 (m, 10H, 2 Ph), 4.87 and 4.83 (2d, 2H, $J_{H,H'} = 11.3$, C$H_2$Ph), 4.83 and 4.62 (2d, 2H, $J_{H,H'} = 10.8$, C$H_2$Ph), 4.18 (d, 1H, $J_{1,2} = 7.5$, H-1), 3.84 (dd, 1H, $J_{6,6'} = 12.0$, $J_{5,6} = 2.3$, H-6), 3.69 (dd, 1H, $J_{5,6'} = 4.0$, H-6′), 3.56 (m, 2H, H-3 and H-4), 3.51 (3H, OMe), 3.45 (dd, 1H, $J_{2,3} = 8.0$, H-2), 3.35 (m, 1H, H-5), 2.44 (s, 1H, HO-2) and 1.98 (s, 1H, HO-6); $^{13}C$ NMR (127.5 MHz, $CDCl_3$) $\delta$ 138.4–127.8 (MHz, 2 Ph), 103.7 (C-1), 84.2 (C-3), 77.4 (C-4), 75.3, 75.1 and 75.0 (C-5 and 2 $C_2$ Ph), 74.6 (C-2), 61.8 (C-6) and 57.3 (O*Me*). HREIMS: $m/z$ 374.1722 (calcd for $C_{21}H_{26}O_6$: 374.1729).

### 5.4. Methyl 3-azido-6-*O*-*tert*-butyl-diphenylsilyl-3-deoxy-α-D-altropyranoside, 27

Dry pyridine (250 μL) and 4-(dimethylamino)pyridine (DMAP, 0.010 g) were added to a solution of methyl 3-azido-3-deoxy-α-D-altropyranoside[9] (**26**, 0.340 g, 1.56 mmol) in dry dichloromethane (2.5 mL) and the mixture then stirred under argon and cooled at 0 °C. *tert*-Butyl-chloro-diphenylsilane (550 μL, 2.43 mmol)

was then added to the mixture, which was allowed to warm to room temperature. After 72 h, the reaction was quenched by adding 1 M HCl until neutral pH (1 mL) and the mixture was shaken with dichloromethane (3×15 mL). The combined organic layers were dried over $Na_2SO_4$ and concentrated to a syrup, which was subjected to column chromatography (1:1 hexane/ethyl acetate) to give **27** (0.660 g, 92%); syrup; $R_f$ 0.42 (2:1 hexane/ethyl acetate); $[\alpha]_D^{25} = +35.7$ (*c* 0.9, acetone); IR (film) $\nu_{max}$ 3310 (OH), 2110 ($N_3$) and 702 $cm^{-1}$ (CSi); $^1H$ NMR (300 MHz, $CD_3COCD_3$) $\delta$ 7.79–7.38 (m, 10H, 2Ph), 4.65 (d, 1H, $J_{2,OH} = 5.1$, HO-2), 4.60 (d, 1H, $J_{1,2} = 2.4$, H-1), 4.27 (d, 1H, $J_{4,OH} = 6.1$, HO-4), 4.12 (ddd, 1H, $J_{4,5} = 7.9$, $J_{3,4} = 4.0$, H-4), 4.01–3.84 (m, 4H, H-2, H-5, H-6 and H-6′), 3.80 (dd, 1H, $J_{2,3} = 4.6$, H-3), 3.37 (s, 3H, OMe), and 1.05 (s, 9H, $CMe_3$); $^{13}C$ NMR (125.7 MHz, $CD_3COCD_3$) $\delta$ 136.5–128.3 (MHz, Ph), 102.9 (C-1), 72.5 (C-5), 70.2 (C-2), 66.4 (C-4), 65.1 (C-6), 64.6 (C-3), 55.3 (OMe), 27.2 (C*Me*$_3$), and 19.8 (*C*Me$_3$); HRFABMS: *m*/*z* 480.1933 (calcd for $C_{23}H_{31}N_3O_5Si$+Na: 480.1931).

### 5.5. Methyl 3-azido-3-deoxy-β-D-altropyranoside, 28

*p*-Toluenesulphonic acid (0.082 g, 0.434 mmol) was added to a solution of methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-altropyranoside[8] (1.33 g, 4.33 mmol) in 1:1 methanol/dioxane (44 mL). The mixture was heated at 85 °C for 2 h, neutralized with triethylamine and concentrated. The residue was subjected to column chromatography (1:4 hexane/ethyl acetate) to give **28** (0.920 g, 97%); syrup; $R_f$ 0.43 (ethyl acetate); $[\alpha]_D^{23} = -124.4$ (*c* 0.57, acetone); IR (film) $\nu_{max}$ 3313 (OH) and 2108 $cm^{-1}$ ($N_3$); $^1H$ NMR (300 MHz, $CD_3SOCD_3$, at 363 K) $\delta$ 4.88 (d, 1H, $J_{HO,4} = 4.0$, HO-4), 4.78 (d, 1H, $J_{1,2} = 2.0$, H-1), 4.37 (d, 1H, $J_{HO,2} = 5.5$, HO-2), 4.18 (dd, 1H, $J_{HO,6} = J_{HO,6'} = 5.7$, HO-6), 3.81–3.79 (m, 1H, H-4), 3.68–3.60 (m, 3H, H-3, H-5 and H-6), 3.59–3.56 (m, 1H, H-2), 3.51 (ddd, 1H, $J_{6',OH} = J_{6',5} = 5.5$, $J_{6,6'} = 11.0$, H-6′), and 3.42 (s, 3H, OMe); $^{13}C$ NMR (75.8 MHz, $CD_3SOCD_3$, at 363 K) 99.0 (C-1), 75.8 (C-5), 68.0 (C-4), 65.1 (C-2), 61.8 (C-3), 61.4 (C-6), and 55.5 (OMe); HRCIMS: *m*/*z* 220.0930 (calcd for $C_7H_{13}N_3O_5$+H: 220.0933).

### 5.6. Methyl 3-azido-6-*O*-*tert*-butyl-diphenylsilyl-3-deoxy-β-D-altropyranoside, 29

Dry pyridine (145 μL), 4-(dimethylamino)pyridine (DMAP, 0.006 g), and *tert*-butyl-diphenyl-chlorosilane (360 μL, 1.38 mmol) were added at 0 °C, under argon, to a stirred solution of methyl 3-azido-3-deoxy-β-D-altropyranoside (**28**, 0.201 mg, 0.919 mmol) in dry $CH_2Cl_2$ (1.5 mL). The mixture was then allowed to warm to room temperature. After 72 h, the reaction was quenched by adding 1 M HCl until neutral pH (1 mL) after which the mixture was shaken with dichloromethane (3×15 mL). The combined organic layers were dried over $Na_2SO_4$ and concentrated to a syrup, which was subjected to column chromatography (1:1 hexane/ethyl acetate) to give **29** (0.382 g, 87%); syrup; $R_f$ 0.38 (2:1 hexane/ethyl acetate); $[\alpha]_D^{25} = -58.2$ (*c* 0.78, acetone); IR (film) $\nu_{max}$ 3308 (OH), 2110 ($N_3$) and 704 $cm^{-1}$ (CSi); $^1H$ NMR (300 MHz, $CD_3COCD_3$) $\delta$ 7.81–7.38 (m, 10H, 2Ph), 4.93 (d, 1H, $J_{1,2} = 1.6$, H-1), 4.44 (d, 1H, $J_{4,OH} = 3.7$, HO-4), 4.01 (dd, 1H, $J_{6,6'} = 10.7$, $J_{5,6} = 2.9$, H-6), 3.96–3.79 (m, 4H, H-3, H-4, H-5 and H-6′), 3.74 (dd, 1H, $J_{2,3} = 4.4$, H-2), 3.50 (s, 3H, OMe), and 1.05 (s, 9H, $CMe_3$); $^{13}C$ NMR (125.7 MHz, $CD_3COCD_3$) $\delta$ 136.5–128.5 (m, Ph), 100.7 (C-1), 76.4, 70.4 and 65.6 (C-3, C-4 and C-5), 65.0 (C-6), 63.4 (C-2), 56.7 (OMe), 27.1 (C*Me*$_3$), and 19.9 (*C*Me$_3$); HRFABMS: *m*/*z* 480.1932 (calcd for $C_{23}H_{31}N_3O_5Si$+Na: 480.1931).

### 5.7. (1*R* and 1*S*)-2,5-Anhydro-3,6-di-*O*-benzyl-4-deoxy-1,4-difluoro-1-*O*-methyl-D-talitols, 31a,b

(a) From **18**: DAST (177 μL, 1.33 mmol) was dropped into a solution of compound **18** (0.100 g, 0.267 mmol) in dry dichloromethane (5 mL) at 0 °C under argon. After a few minutes, the cooling bath was removed and the mixture heated to reflux for 1.5 h. After dilution with iced saturated aqueous sodium hydrogen carbonate (75 mL), the aqueous layer was extracted with dichloromethane (3×30 mL). The combined organic layers were washed with brine (60 mL), dried over $Na_2SO_4$, and concentrated to afford, after column chromatography (1:10 ether/hexane), unreacted starting material **18** (0.050 g, indicating 50% of conversion) and a 1.3:1.0 (by $^1H$ NMR) epimeric mixture **31a**,**b** (0.040 g, 40%, corresponding to 79% yield from converted substrate); syrup; $R_f$ 0.45 (1:1 ether/hexane); IR (film) $\nu_{max}$ 1127, 1053 (C–O–C) and 991 $cm^{-1}$ (CF); HRCIMS: *m*/*z* 379.1714 (calcd for $C_{21}H_{24}F_2O_4$+H: 379.1721).

Major epimer: $^1H$ NMR (500 MHz, $CD_3COCD_3$) $\delta$ 7.39–7.33 (m, 10H, 2 Ph), 5.33 (dd, 1H, $^2J_{1,F} = 66.1$, $J_{1,2} = 3.0$, H-1), 5.22 (ddd, 1H, $^2J_{4,F} = 54.6$, $J_{3,4} = 3.2$, $J_{4,5} = 2.3$, H-4), 4.72 and 4.63 (2d, 2H, $J_{H,H'} = 11.9$, C$H_2$Ph), 4.57 and 4.54 (2d, 2H, $J_{H,H'} = 12.0$, C$H_2$Ph), 4.38 (ddd, 1H, $^3J_{3,F} = 23.0$, $J_{2,3} = 7.3$, $J_{3,4} = 3.7$, H-3), 4.22 (dddd, 1H, $^3J_{5,F} = 29.8$, $J_{5,6} = J_{5,6'} = 6.2$, H-5), 4.00 (ddd, 1H, $^3J_{2,F} = 12.0$, H-2), 3.77 (dd; 1H, $J_{6,6'} = 9.9$, H-6), 3.62 (ddd, 1H, $^4J_{6',F} = 2.1$, H-6′), and 3.54 (d, 3H, $^4J_{OMe,F} = 1.2$, OMe); $^{13}C$ NMR (127.5 MHz, $CD_3COCD_3$) $\delta$ 139.5–128.5 (m, Ph), 113.4 (d, $^1J_{C1,F} = 220.0$, C-1), 91.0 (d, $^1J_{C4,F} = 189.8$, C-4), 81.0 (d, $^2J_{C2,F} = 24.5$, C-2), 80.6 (d, $^2J_{C5,F} = 17.6$, C-5), 79.5 (d, $^2J_{C3,F} = 16.2$, C-3), 73.8 and 72.7 (C$H_2$Ph), 68.3 (d, $^3J_{C6,F} = 10.3$, C-6), and 57.4 (s, OMe). HMBC correlations: *C*-1/OC$H_3$ and *H*-1/O*C*H$_3$.

Minor epimer: $^1H$ NMR (500 MHz, $CD_3COCD_3$) $\delta$ 7.39–7.33 (m, 10H, 2Ph); 5.30 (dd, 1H, $^2J_{1,F} = 64.4$, $J_{1,2} = 3.7$, H-1), 5.22 (ddd, 1H, $^2J_{4,F} = 54.6$, $J_{3,4} = 3.2$, $J_{4,5} = 2.3$, H-4), 4.72 and 4.63 (2d, 2H, $J_{H,H'} = 11.9$, C$H_2$Ph), 4.57 and 4.54 (2d, 2H, $J_{H,H'} = 12.0$, C$H_2$Ph), 4.37 (ddd, 1H, $^3J_{3,F} = 23.0$, $J_{2,3} = 7.3$, $J_{3,4} = 3.6$, H-3), 4.22 (dddd, 1H, $^3J_{5,F} = 29.8$, $J_{5,6} = J_{5,6'} = 6.2$, H-5), 4.00 (ddd, 1H, $^3J_{2,F} = 12.0$, H-2), 3.77 (dd, 1H, $J_{6,6'} = 9.9$, H-6), 3.62 (ddd, 1H, $^4J_{6',F} = 2.1$, H-6′), and 3.54 (d, 3H, $^4J_{OMe,F} = 1.2$, OMe); $^{13}C$ NMR (127.5 MHz, $CD_3COCD_3$) $\delta$ 139.5–128.5 (m, Ph), 112.8 (d,

$^1J_{C1,F} = 218.7$, C-1), 91.0 (d, $^1J_{C4,F} = 189.8$, $J_{C1,F}$, C-4), 80.9 (d, $^2J_{C2,F} = 26.9$, C-2), 80.4 (d, $^2J_{C5,F} = 17.6$, C-5), 79.6 (d, $^2J_{C3,F} = 16.2$, C-3), 73.8 and 72.7 ($CH_2$Ph), 68.3 (d, $^3J_{C6,F} = 10.3$, C-6), and 57.4 (s, OMe). HMBC correlations: *C*-1/OC$H_3$ and *H*-1/O*C*H$_3$.

(b) From **20**: DAST (165 μL, 1.24 mmol) was dropped to a solution of compound **20** (0.093 g, 0.249 mmol) in dry dichloromethane (4.8 mL) at 0 °C under argon. After a few minutes, the cooling bath was removed and the mixture heated to reflux for 2 h. After dilution with iced saturated aqueous sodium hydrogen carbonate (70 mL), the aqueous layer was extracted with dichloromethane (3×30 mL). The combined organic layers were washed with brine (70 mL), dried over $Na_2SO_4$, and concentrated, to afford, after column chromatography (1:8 ether/hexane), unreacted starting material (0.037 g, indicating 60% of conversion) and a 1.9:1.0 (by $^1$H NMR) epimeric mixture **31a** and **b** (0.039 g, 41%, corresponding to 65% yield from converted substrate).

### 5.8. 2,5-Anhydro-3,6-di-*O*-benzyl-4-deoxy-4-fluoro-*aldehydo*-D-talose, 32

A sample of (1*R* and 1*S*)-2,5-anhydro-3,6-di-*O*-benzyl-4-deoxy-1,4-difluoro-1-*O*-methyl-D-talitols **31a** and **b** (0.100 g, 265 mmol) was treated at room temperature with 9:1 trifluoroacetic acid/water (2 mL) for 1 h. The mixture was poured onto ice-water (100 mL) and extracted with dichloromethane (3×20 mL). The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate, dried over $Na_2SO_4$, and concentrated, to afford pure **32** (0.835 g, 92%) as a syrup. The analytical sample, obtained by column chromatography (3:1 ether/hexane), had $R_f$ 0.54 (ether); $[\alpha]_D^{22} = +29.6$ (*c* 1.02, acetone); IR (film) $\nu_{max}$ 1728 (CO), 1128, 1051 (C–O–C), and 988 cm$^{-1}$ (CF); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 9.68 (d, 1H, $J_{1,2} = 1.5$, C*H*O), 7.35–7.24 (m, 10H, 2 Ph), 4.99 (ddd, $^2J_{4,F} = 53.9$, $J_{3,4} = 3.4$, $J_{4,5} = 2.3$, H-4), 4.70 and 4.63 (2d, $J_{H,H'} = 11.8$, C$H_2$Ph), 4.59 and 4.53 (2d, $J_{H,H'} = 12.0$, C$H_2$Ph), 4.42 (ddd, $J_{2,3} = 8.4$, $^4J_{2,F} = J_{2,CHO} = 0.7$, H-2), 4.22 (dddd, $^3J_{5,F} = 28.9$, $J_{5,6} = J_{5,6'} = 6.3$, H-5), 4.10 (ddd, $^3J_{3,F} = 22.3$, H-3), 3.77 (dd, $J_{6,6'} = 9.9$, H-6), and 3.71 (ddd, $^4J_{6',F} = 2.2$, H-6′); NOE contacts (1D NOESY): H-5, H-4, H-3; $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 199.6 (*C*HO), 137.8–127.8 (Ph), 89.5 (d, $^1J_{C4,F} = 192.6$, C-4), 83.8 (C-2), 80.2 (d, $^2J_{C5,F} = 23.5$, C-5), 78.7 (d, $^2J_{C3,F} = 16.8$, C-3), 73.7 and 72.7 (C$H_2$Ph), and 67.1 (d, $^3J_{C6,F} = 10.8$, C-6); HREIMS: $m/z$ 344.1431 (calcd for $C_{20}H_{21}FO_4$: 344.1424).

### 5.9. Methyl 3-azido-4,6-*O*-benzylidene-2,3-dideoxy-2-fluoro-α-D-mannopyranoside, 33, and (1*R* and 1*S*)-2,5-anhydro-3-azido-6-*O*-*tert*-butyl-diphenylsilyl-3,4-dideoxy-1,4-difluoro-1-*O*-methyl-D-talitols, 35a and b

A solution of methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranoside[25] **22** (109 mg, 0.355 mmol) in dry acetonitrile (6.5 mL), cooled at 0 °C, was treated with DAST (236 μL, 1.79 mmol). After a few minutes, the cooling bath was removed and the mixture heated to reflux for 6 h. The solvent was then evaporated and the residue treated with dichloromethane and iced saturated aqueous sodium hydrogen carbonate. The aqueous layer was extracted with dichloromethane (3×30 mL). The combined organic layers were washed with brine, dried over $Na_2SO_4$ and concentrated to afford, after column chromatography (1:5 → 1:3 gradient, ether/hexane), the monofluoro compound **33** (0.025 g, 23%; corresponding to 25% from converted substrate) and a mixture of the unreacted starting material **22** and (1*R* and 1*S*)-2,5-anhydro-3-azido-3,4-dideoxy-1,4-difluoro-1-*O*-methyl-D-talitols **34a** and **b** (0.055 g, in the ratio 1:4.5 **22:34** by $^1$H NMR, indicating 91% of conversion and 63% yield of **34a** and **b** from converted substrate). In order to isolate and characterize the ring-contracted products, the above mixture **22** and **34**, dissolved in dichloromethane (330 μL) and dry pyridine (33 μL), was treated with DMAP (1.5 mg) and *tert*-butyl-chloro-diphenylsilane (75 μL) under the conditions indicated above to prepare compound **27**. Column chromatography (1:1 ether/hexane) of the resulting reaction mixture afforded a fraction containing only the epimers **35a** and **b** (0.050 g, 1.2:1 by $^1$H NMR) and a second fraction containing unreacted mixture **22** and **34** (0.020 g, 1:1 by $^1$H NMR).

Compound **33**: Solid; mp: 56–60 °C; $R_f$ 0.44 (1:3 ether/hexane); $[\alpha]_D^{22} = +60.8$ (*c* 0.53, acetone); IR (KBr) $\nu_{max}$ 2108 ($N_3$) and 980 cm$^{-1}$ (CF); $^1$H NMR (300 MHz, $CD_3COCD_3$) $\delta$ 7.49–7.36 (m, 5H; Ph), 5.81 (s, 1H, C*H*-Ph), 4.91 (dd, 1H, $^3J_{1,F} = 7.8$, $J_{1,2} = 1.7$, H-1), 4.78 (ddd, 1H, $^2J_{2,F} = 48.2$, $J_{2,3} = 2.3$, H-2), 4.27 (dd, 1H, $J_{6,6'} = 11.7$, $J_{5,6} = 1.7$, H-6), 4.12 (ddd, 1H, $J_{3,4} = 10.6$, $J_{4,5} = 9.0$, $^4J_{4,F} = 1.6$, H-4), 3.92 (ddd, $^3J_{3,F} = 29.0$, H-3), 3.89–3.83 (MHz, 2H, H-5 and H-6′), and 3.44 (s, 3H, OMe); $^{13}$C NMR (75.8 MHz, $CD_3COCD_3$) $\delta$ 138.8–127.2 (Ph), 102.5 (*C*H-Ph), 99.5 (d, $^2J_{C1,F} = 31.0$, C-1), 89.8 (d, $^1J_{C2,F} = 180.0$, C-2), 74.6 (C-4), 69.2 (C-6), 64.9 (C-5), 59.7 (d, $^2J_{C3,F} = 16.6$), and 55.7 (OMe); HRCIMS: $m/z$ 310.1207 (calcd for $C_{14}H_{16}FN_3O_4$+H: 310.1203).

Epimeric mixture **35a** and **b** (69% from converted substrate **34a** and **b**): Syrup; $R_f$ 0.49 (1:9 ether/hexane); IR (film) $\nu_{max}$ 2110 ($N_3$), 990 (CF) and 704 cm$^{-1}$ (CSi); HRCIMS: $m/z$ 462.2030 (calcd for $C_{23}H_{29}F_2N_3O_3Si$+H: 462.2024).

Major epimer: $^1$H NMR (500 MHz, $CD_3COCD_3$) $\delta$ 7.72–7.43 (m, 10H, 2 Ph), 5.44 (dd, 1H, $^2J_{1,F} = 67.0$, $J_{1,2} = 3.5$, H-1), 5.17 (ddd, 1H, $^2J_{4,F} = 54.5$, $J_{3,4} = J_{4,5} = 4.5$, H-4), 4.51 (ddd, 1H, $^3J_{3,F} = 22.0$, $J_{2,3} = 6.0$, H-3), 4.24 (ddd, 1H, $^3J_{5,F} = 19.5$, $J_{5,6} = J_{5,6'} = 4.5$, H-5), 4.00 (ddd, 1H, $^3J_{2,F} = 15.5$, H-2), 3.84 (dd, 2H, $J_{6\text{ and }6',F} = 3.0$, H-6 and H-6′), 3.61 (d, 3H, $^4J_{OMe,F} = 1.5$, OMe), and 1.05 (s, 9H, $CMe_3$); $^{13}$C NMR(127.5 MHz, $CD_3COCD_3$) $\delta$ 136.3–128.7 (m, 2Ph), 112.0 (d, $^1J_{C1,F} = 220.3$, C-1), 97.3 (d, $^1J_{C4,F} = 186.0$, C-4), 83.2 (d, $^2J_{C5,F} = 24.7$, C-5), 82.7 (d, $^2J_{C2,F} = 20.5$, C-2), 66.2 (d, $^2J_{C3,F} = 25.3$, C-3), 63.7 (d, $^3J_{C6,F} = 4.9$, C-6), 57.6 (O*Me*), 27.1 (C*Me*$_3$), and 19.7 (*C*Me$_3$).

Minor epimer: $^1$H NMR (500 MHz, $CD_3COCD_3$) $\delta$ 7.72–7.43 (m, 10H, 2 Ph), 5.38 (dd, 1H, $^2J_{1,F} = 66.0$, $J_{1,2} = 5.5$, H-1), 5.16 (ddd, 1H, $^2J_{4,F} = 54.5$, $J_{3,4} = J_{4,5} = 4.5$, H-4), 4.51 (ddd, 1H, $^3J_{3,F} = 22.0$, $J_{2,3} = 6.0$, H-3), 4.24 (ddd, 1H, $^3J_{5,F} = 19.5$, $J_{5,6} = J_{5,6'} = 4.5$, H-5), 4.00 (ddd, 1H, $^3J_{2,F} = 15.5$, H-2), 3.84 (dd, 2H, $J_{6 \text{ and } 6',F} = 3.0$, H-6 and H-6′), 3.62 (d, 3H, $^4J_{OMe,F} = 1.5$, OMe), and 1.05 (s, 9H, $CMe_3$); $^{13}$C NMR (127.5 MHz, $CD_3COCD_3$) $\delta$ 136.3–128.7 (m, 2Ph), 112.6 (d, $^1J_{C1,F} = 219.3$, C-1), 97.4 (d, $^1J_{C4,F} = 185.4$, C-4), 83.0 (d, $^2J_{C5,F} = 24.7$, C-5), 82.6 (d, $^2J_{C2,F} = 20.9$, C-2), 66.7 (d, $^2J_{C3,F} = 21.2$, C-3), 63.9 (d, $^3J_{C6,F} = 5.4$, C-6), 57.7 (O*Me*), 27.1 (C*Me*$_3$), and 19.7 (*C*Me$_3$).

### 5.10. 3-Azido-4,6-*O*-benzylidene-3-deoxy-2-*O*-methyl-α-D-mannopyranosyl fluoride, 36, and (1*R* and 1*S*)-2,5-anhydro-3-azido-6-*O*-*tert*-butyl-diphenylsilyl-3,4-dideoxy-1,4-difluoro-1-*O*-methyl-D-talitols, 35a and b

DAST (197 μL, 1.490 mmol) was added to a cooled solution of 3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside **23**[25] (91.6 mg, 0.298 mmol) in dry acetonitrile (5.4 mL); after a few minutes, the cooling bath was removed and the mixture heated to reflux for 15 h. After removing the solvent, the mixture was treated with dichloromethane and iced saturated aqueous sodium hydrogen carbonate and the aqueous layer extracted with dichloromethane (3 × 30 mL). The combined organic layers were washed with brine, dried over $Na_2SO_4$ and concentrated to afford, after column chromatography (1:4 → 1:2 gradient, ether/hexane), compound **36** (0.037 g, 40%; corresponding to 66% from converted substrate) and a mixture of unreacted starting material **23** and (1*R* and 1*S*)-2,5-anhydro-3-azido-3,4-dideoxy-1,4-difluoro-1-*O*-methyl-D-talitols **34a** and **b** (0.048 g, in the ratio 2.7:1 **23**:**34** by $^1$H NMR, indicating 61% of conversion and 32% yield of **34** from converted substrate). In order to isolate the ring-contracted products, the above mixture **23** and **34**, dissolved in dichloromethane (330 μL) and dry pyridine (33 μL) was treated with DMAP (1.5 mg) and *tert*-butyl-chloro-diphenylsilane (75 μL) under the conditions indicated above to prepare compound **27**. Column chromatography (1:1 ether/hexane) of the resulting reaction mixture afforded a fraction containing only the epimers **35a** and **b** (0.010 g, 60% from converted substrate **34a** and **b**, epimeric ratio 1.1:1.0 by $^1$H NMR) and a second fraction containing unreacted mixture **23** and **34** (0.040 g, 7:1 by $^1$H NMR).

Compound **36**: Amorphous material; $R_f$ 0.46 (1:2 ether/hexane); $[\alpha]_D^{25} = -23.4$ (*c* 0.82, acetone); IR (film) $\nu_{max}$ 2108 ($N_3$) and 978 cm$^{-1}$ (CF); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.48–7.33 (m, 5H, Ph), 5.65 (s, C*H*-Ph), 5.60 (d, 1H, $^2J_{1,F} = 49.5$, $J_{1,2} = 1.5$, H-1), 4.34 (dd, 1H, $J_{6,6'} = 10.1$, $J_{6,5} = 4.6$, H-6), 4.17 (dd, 1H, $J_{3,4} = J_{4,5} = 9.9$, H-4), 3.98 (ddd, 1H, $J_{5,6'} = 9.7$, H-5), 3.84 (ddd, 1H, $^5J_{6',F} = 1.1$, H-6′), 3.83 (ddd, 1H, $J_{2,3} = 3.3$, $^4J_{3,F} = 1.6$, H-3), 3.69 (ddd, 1H, $J_{2,F} = 1.0$, H-2), and 3.59 (s, 3H, O*Me*); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 136.7–125.9 (m, Ph), 105.1 (d, $^1J_{C1,F} = 225.4$, C-1), 101.7 (*C*H-Ph), 78.2 (d, $^2J_{C2,F} = 35.8$, C-2), 75.9 (C-4), 68.3 (C-6), 66.0 (d, $^3J_{C5,F} = 2.4$, C-5), 60.2 (O*Me*), and 58.5 (d, $^3J_{C3,F} = 2.4$, C-3); HRCIMS: *m*/*z* 310.1191 (calcd for $C_{14}H_{16}FN_3O_4$+H: 310.1203). Epimeric mixture **35a** and **b** had identical properties, respectively, to those of the product obtained from **22**.

### 5.11. Methyl 3-azido-4,6-*O*-benzylidene-2,3-dideoxy-2-fluoro-α-D-altropyranoside, 37, 3-azido-4,6-*O*-benzylidene-3-deoxy-2-*O*-methyl-β-D-allopyranosyl fluoride, 38, and methyl 2-azido-4,6-*O*-benzylidene-2,3-dideoxy-3-fluoro-α-D-glucopyranoside, 39

DAST (223 μL, 1.69 mmol) was added to a solution of methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranoside[26] **24** (0.104 g, 0.337 mmol) in dry acetonitrile (6.2 mL), and the mixture refluxed for 1 h. The solvent was evaporated and the residue treated with dichloromethane and iced saturated aqueous sodium hydrogen carbonate (75 mL); the organic layer was washed with brine, dried and $Na_2SO_4$, and concentrated to afford a crude product. After column chromatography (4:1 hexane/ethyl acetate), three products were isolated: **37** (0.0585 g, 56%), **38** (0.0304 g, 29%), and **39** (0.0149 g, 14%).

Compound **37**: Solid; mp: 112–116 °C; $R_f$ 0.45 (4:1 hexane/ethyl acetate); $[\alpha]_D^{22} = +40.8$ (*c*1, acetone); IR (KBr) $\nu_{max}$ 2106 ($N_3$) and 1053 cm$^{-1}$ (CF); $^1$H NMR (500 MHz, $CD_3COCD_3$) $\delta$ 7.51–7.36 (m, 5H, Ph), 5.76 (s, 1H, C*H*-Ph), 4.78 (br d, 1H, $^3J_{1,F} = 11.6$, H-1), 4.68 (ddd, 1H, $^2J_{2,F} = 43.1$, $J_{2,3} = 2.8$, $J_{2,1} = 1.0$, H-2), 4.40 (ddd, 1H, $^3J_{3,F} = 9.6$, $J_{3,4} = 2.9$, H-3), 4.28 (dd, 1H, $J_{6,6'} = 9.6$, $J_{5,6} = 4.5$, H-6), 4.16–4.11 (m, 2H, H-4 and H-5), 3.80 (dd, 1H, $J_{6',5} = 9.6$, H-6′), and 3.40 (s, 3H, O*Me*); $^{13}$C NMR (125.7 MHz, $CD_3COCD_3$) $\delta$ 138.8–127.2 (m, Ph), 102.7 (*C*H-Ph), 99.1 (d, $^2J_{1,F} = 33.9$, C-1), 88.5 (d, $^1J_{1,F} = 172.2$, C-2), 76.2 (C-4), 69.4 (C-6), 59.7 (C-5), 58.2 (d, $^2J_{2,F} = 28.9$, C-3), and 55.7 (OMe); HRCIMS: *m*/*z* 310.1196 (calcd for $C_{14}H_{16}FN_3O_4$+H: 310.1203).

Compound **38**: Amorphous material; $R_f$ 0.39 (4:1 hexane/ethyl acetate); $[\alpha]_D^{23} = -83.5$ (*c* 0.9, acetone); IR (film) $\nu_{max}$ 2103 ($N_3$) and 993 cm$^{-1}$ (CF); $^1$H NMR (300 MHz, $CD_3COCD_3$) $\delta$ 7.50–7.36 (m, 5H, Ph), 5.67 (s, 1H, C*H*-Ph), 5.40 (dd, 1H, $^2J_{1,F} = 53.4$, $J_{1,2} = 7.3$, H-1), 4.68 (dd, 1H, $J_{3,4} = 5.8$, $J_{2,3} = 3.2$, H-3), 4.30 (dd, 1H, $J_{6,6'} = 10.0$, $J_{5,6} = 4.8$, H-6), 3.94–3.84 (m, 2H, H-4 and H-5), 3.78 (dd, 1H, $J_{5,6'} = 10.0$, H-6′), 3.53 (d, 3H, $^5J_{Me,F} = 0.7$, OMe), and 3.52 (ddd, 1H, $^3J_{2,F} = 12.7$, H-2); $^{13}$C NMR (75.8 MHz, $CD_3COCD_3$) $\delta$ 138.5–127.1 (m, Ph), 109.1 (d, $^1J_{1,F} = 214.5$, C-1), 102.4 (*C*H-Ph), 80.0 (d, $^2J_{2,F} = 21.2$, C-2), 77.3 (C-4), 69.0 (C-6), 64.9 (d, $^3J_{5,F} = 5.3$, C-5), 61.2 (d, $^3J_{3,F} = 9.8$, C-3), and 58.4 (OMe); HRCIMS: *m*/*z* 310.1194 (calcd for $C_{14}H_{16}FN_3O_4$+H: 310.1203).

Compound **39**: Amorphous material; $R_f$ 0.34 (4:1 hexane/ethyl acetate); $[\alpha]_D^{23} = +63.2$ (*c* 0.94, acetone); IR (film) $\nu_{max}$ 2106 ($N_3$) and 991 cm$^{-1}$ (CF); $^1$H NMR (300 MHz, $CD_3COCD_3$) $\delta$ 7.48–7.36 (m, 5H, Ph), 5.70 (s, 1H, C*H*-Ph), 4.99 (dd, 1H, $^4J_{1,F} = J_{1,2} = 3.4$, H-1),

4.85 (ddd, 1H, $^2J_{3,F} = 54.9$, $J_{3,4} = 9.7$, $J_{2,3} = 9.0$, H-3), 4.27 (ddd, 1H, $J_{6,6'} = 9.0$, $J_{5,6} = 3.7$, $^5J_{6,F} = 2.1$, H-6), 3.92 (ddd, 1H, $^3J_{4,F} = 20.0$, $J_{4,5} = 12.1$, H-4), 3.85–3.80 (m, 2H, H-5 and H-6′), 3.73 (ddd, 1H, $^3J_{2,F} = 11.3$, H-2), and 3.45 (s, 3H, OMe); $^{13}$C NMR (75.8 MHz, $CD_3COCD_3$) $\delta$ 138.5–127.1 (m, Ph), 102.2 (*C*H-Ph), 100.5 (d, $^3J_{1,F} = 8.3$, C-1), 89.9 (d, $^1J_{3,F} = 187.2$, C-3), 80.1 (d, $^2J_{4,F} = 17.4$, C-4), 69.1 (C-6), 63.0 (d, $^3J_{5,F} = 7.6$, C-5), 62.7 (d, $^2J_{2,F} = 17.4$, C-2), and 55.7 (OMe); HRCIMS: $m/z$ 310.1190 (calcd for $C_{14}H_{16}FN_3O_4$+H: 310.1203).

### 5.12. Methyl 2-azido-4,6-*O*-benzylidene-2,3-dideoxy-3-fluoro-β-D-altropyranoside, 40, and methyl 3-acetamido-2-azido-4,6-*O*-benzylidene-2,3-dideoxy-β-D-altropyranoside, 41

DAST (235 μL, 1.69 mmol) was added to a cold solution of methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-altropyranoside[27] **25** (0.109 g, 0.355 mmol) in dry acetonitrile (6.5 mL) and the mixture refluxed for 1.5 h. The solvent was then evaporated and the residue treated with dichloromethane and iced saturated aqueous sodium hydrogen carbonate; the organic layer was washed with brine, dried over $Na_2SO_4$, and concentrated to afford a crude product. Column chromatography (10:1 hexane/ethyl acetate) led to the separation of the unreacted starting material **25** (0.026 g, indicating 76% of conversion), the fluoro compound **40** (0.025 g, 23%, corresponding to 31% yield from converted substrate), and the Ritter reaction product **41** (0.039 g, 32%, corresponding to 42% from converted substrate).

Compound **40**: Amorphous material; $R_f$ 0.56 (4:1 hexane/ethyl acetate); $[\alpha]_D^{22} = -107.3$ (*c* 1.14, acetone); IR (film) $\nu_{max}$ 2112 ($N_3$) and 986 cm$^{-1}$ (CF); $^1$H NMR (500 MHz, $CD_3COCD_3$) $\delta$ 7.49–7.34 (m, 5H, Ph), 5.71 (s, 1H, C*H*-Ph), 4.98 (dd, 1H, $^4J_{1,F} = 2.7$, $J_{1,2} = 1.7$, H-1), 4.91 (ddd, 1H, $^2J_{3,F} = 49.7$, $J_{2,3} = 3.7$, $J_{3,4} = 1.7$, H-3), 4.31 (dd, 1H, $J_{6,6'} = 9.8$, $J_{6,5} = 4.4$, H-6), 4.21 (ddd, 1H, $^3J_{2,F} = 7.5$, H-2), 3.89–3.78 (m, 3H, H-4, H-5 and H-6′), and 3.55 (s, 3H, OMe); $^{13}$C NMR (125.7 MHz, $CD_3COCD_3$) $\delta$ 138.7–127.2 (m, Ph), 102.8 (*C*H-Ph), 100.9 (C-1), 88.6 (d, $^1J_{3,F} = 181.0$, C-3), 75.6 (d, $^2J_{4,F} = 16.3$, C-4), 69.3 (C-6), 64.5 (d, $^3J_{5,F} = 2.5$, C-5), 61.6 (d, $^2J_{2,F} = 26.4$, C-2), and 57.4 (OMe); HRCIMS: $m/z$ 310.1191 (calcd for $C_{14}H_{16}FN_3O_4$+H: 310.1203).

Compound **41**: Syrup; $R_f$ 0.37 (1:1 hexane/ethyl acetate); $[\alpha]_D^{24} = -54.6$ (*c* 0.80, acetone); IR (film) $\nu_{max}$ 3304 (NH), 2106 ($N_3$), 1695 (CO) and 1353 cm$^{-1}$ (NCO); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.50–7.37 (m, 5H, Ph), 5.71 (br, 1H, N*H*), 5.62 (s, 1H, C*H*-Ph), 4.75 (d, 1H, $J_{1,2} = 1.2$, H-1), 4.44 (dd, 1H, $J_{2,3} = 3.0$, H-2), 4.39 (dd, 1H, $J_{5,6} = 4.9$, $J_{6,6'} = 10.3$, H-6), 4.20 (m, 1H, H-3), 4.05 (dd, 1H, $J_{4,5} = 9.9$, $J_{3,4} = 4.5$, H-4), 3.88 (dd, 1H, $J_{5,6'} = 10.0$, H-6′), 3.69 (ddd, 1H, H-5), 3.56 (s, 3H, OMe), and 2.03 (s, 3H, COMe); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 171.5 (CO), 129.1–127.7 (m, Ph), 101.8 (*C*H-Ph), 100.1 (C-1), 73.3 (C-4), 68.9 (C-6), 65.0 (C-5), 59.7 (C-2), 57.2 (OMe), 51.4 (C-3), and 23.7 (CO*Me*); HRCIMS: $m/z$ 349.1509 (calcd for $C_{16}H_{20}N_4O_5$+H: 349.1512).

### 5.13. Methyl 3-azido-6-*O*-*tert*-butyl-diphenylsilyl-2,3,4-trideoxy-4-fluoro-α-D-*erythro*-hex-2-enopyranoside, 42, and methyl 3-azido-6-*O*-*tert*-butyl-diphenylsilyl-2,3,4-trideoxy-4-fluoro-α-D-*threo*-hex-2-enopyranoside, 43

DAST (137 μL, 1.04 mmol) was added to an ice-cooled solution of methyl 3-azido-6-*O*-*tert*-butyl-diphenylsilyl-3-deoxy-α-D-altropyranoside **27** (0.094 g, 0.207 mmol) in dry dichloromethane (3.8 mL). After a few minutes, the cooling bath was removed and the mixture refluxed for 2 h. After dilution with iced saturated aqueous sodium hydrogen carbonate (70 mL), the aqueous layer was extracted with dichloromethane (3 × 30 mL). The combined organic layers were washed with brine (70 mL), dried over $Na_2SO_4$, and concentrated to afford, after column chromatography (10:1 hexane/ethyl acetate), a 1:1 mixture (by $^1$H NMR) of **42** and **43** (0.070 g, 77%), which could be separated by TLC (40:1 hexane/ethyl acetate, 4 runs).

Compound **42**: Syrup; $R_f$ 0.45 (10:1 hexane/ethyl acetate); $[\alpha]_D^{25} = -1.8$ (*c* 0.67, acetone); IR (film) $\nu_{max}$ 2114 ($N_3$), 978 (CF), and 702 cm$^{-1}$ (CSi); $^1$H NMR (300 MHz, $CD_3COCD_3$) $\delta$ 7.76–7.43 (m, 10H, 2 Ph), 5.58 (d, 1H, $J_{1,2} = 3.5$, H-2), 5.29 (dd, 1H, $^2J_{4,F} = 51.5$, $J_{4,5} = 8.8$, H-4), 5.11 (d, 1H, H-1), 4.14 (ddd, 1H, $J_{5,6 \text{ and } 6'} = 4.0$, $^3J_{5,F} = 13.4$, H-5), 3.96 (dd, 2H, $^4J_{6 \text{ and } 6',F} = 1.4$, H-6 and H-6′), 3.41 (s, 3H, OMe), and 1.06 (s, 9H, $CMe_3$); $^{13}$C NMR (75.8 MHz, $CD_3COCD_3$) $\delta$ 136.4–128.6 (m, Ph), 134.0 (d, $^2J_{3,F} = 13.6$, C-3), 114.4 (C-2), 96.5 (C-1), 83.5 (d, $^1J_{4,F} = 173.6$, C-4), 70.9 (d, $^2J_{5,F} = 24.3$, C-5), 63.8 (C-6), 55.9 (OMe), 27.1 ($CMe_3$), and 19.8 (*C*Me$_3$); HRCIMS: $m/z$ 442.1968 (calcd for $C_{23}H_{28}FN_3O_3Si$+H: 442.1962).

Compound **43**: Syrup; $R_f$ 0.43 (10:1 hexane/ethyl acetate); $[\alpha]_D^{25} = -4.4$ (*c* 0.60, acetone); IR (film) $\nu_{max}$ 2110 ($N_3$), 1055 (CF) and 702 cm$^{-1}$ (CSi); $^1$H NMR (500 MHz, $CD_3COCD_3$) $\delta$ 7.76–7.44 (m, 10 H, 2 Ph), 5.71 (dd, 1H, $J_{1,2} = {}^4J_{2,F} = 3.3$, H-2), 5.12 (dd, 1H, $^5J_{1,F} = 3.5$, H-1), 4.91 (dd, 1H, $^2J_{4,F} = 49.9$, $J_{4,5} = 2.0$, H-4), 4.29 (dddd, 1H, $^3J_{5,F} = 30.3$, $J_{5,6} = J_{5,6'} = 6.5$, H-5), 4.00 (dd, 1H, $J_{6,6'} = 10.3$, H-6), 3.88 (ddd, 1H, $^4J_{6',F} = 1.7$, H-6′), 3.37 (s, 3H, OMe) and 1.06 (s, 9H, $CMe_3$); $^{13}$C NMR (125.7 MHz, $CD_3COCD_3$) $\delta$ 136.7 (d, $^2J_{3,F} = 15.1$, C-3), 136.3–128.7 (m, 2Ph), 116.0 (d, $^3J_{2,F} = 7.5$, C-2), 96.2 (C-1), 82.2 (d, $^1J_{4,F} = 178.5$, C-4), 71.1 (d, $^2J_{5,F} = 17.6$, C-5), 62.9 (d, $^3J_{6,F} = 7.5$, C-6), 55.7 (OMe), 27.1 ($CMe_3$), and 19.7 (*C*Me$_3$); HRCIMS: $m/z$ 442.1972 (calcd for $C_{23}H_{28}FN_3O_3Si$+H: 442.1962).

### 5.14. Reaction of methyl 3,6-dideoxy-α-D-*xylo*-hexopyranoside, 30, with DAST

DAST (410 μL, 3.09 mmol) was added to a solution of methyl 3,6-dideoxy-α-D-*xylo*-hexopyranoside[29] **30** (0.100 g, 0.617 mmol) in dry dichloromethane (4.4 mL) cooled at 0 °C, under argon. After 15 min, the cooling

bath was removed and the mixture refluxed for 1 h. The solvent was evaporated and the residue treated with dichloromethane and iced saturated aqueous sodium hydrogen carbonate (75 mL); the organic layer was washed with brine, dried over $Na_2SO_4$, and concentrated to afford a crude product. After column chromatography (3:1 to 1:1 gradient hexane/ether), an almost pure product was isolated to which the tentative structure of (**1*R*** or **1*S***)-4,5-anhydro-2,3,6-trideoxy-1,2-difluoro-1-*O*-methyl-D-arabino-hexitol, **44** (0.0328 g, 32%) was assigned. Syrup; $^1$H NMR (500 MHz, $CD_3COCD_3$) $\delta$ 5.26 (ddd, 1H, $J_{1,2} = 4.7$, $^2J_{1,F1} = 65.5$, $^3J_{1,F2} = 7.0$, H-1), 4.44 (ddddd, 1H, $^2J_{2,F2} = 48.5$, $^3J_{2,F1} = J_{2,3a} = 9.1$, $J_{2,3b} = 4.0$, H-2), 3.57 (d, 3H, $^4J_{OMe,F1} = 65.5$, OMe), 2.66–2.63 (m, 1H, H-4), 2.11–2.08 (m, 1H, H-5), 2.00–1.86 (m, 2H, H-3a and H-3b), and 1.34 (d, 3H, $J_{5,6} = 7.0$, Me-6); $^{13}$C NMR (125.7 MHz, $CD_3COCD_3$) $\delta$ 112.4 (dd, $^1J_{1,F1} = 219.6$, $^2J_{,F2} = 28.3$, C-1), 91.7 (dd, $^1J_{2,F2} = 173.0$, $^2J_{2,F1} = 25.8$, C-2), 57.5 (OMe), 24.2 (d, $^2J_{3,F2} = 20.4$, C-3), 38.2 (d, $^3J_{4,F2} = 3.5$, C-4), 30.3 (overlapped with the acetone signal, C-5), and 14.3 (C-6).

### 5.15. Reaction of DAST with the 3-*C*-methyl-3-nitro sugar derivatives 7–11. General procedure[14]

DAST (660 μL, 5 mmol; or 462 μL, 3.5 mmol, as indicated in each case) was added to a solution of the respective sugar derivative (1 mmol) in the solvent indicated in each case, cooled at 0 °C, under argon. After 15 min, the cooling bath was removed and the mixture allowed to warm to room temperature or heated to reflux, under stirring, until either complete transformation of the substrate or until no further progress of the reaction was observed (TLC monitoring, 2:1 or 1:1 ether/hexane). The mixture was poured onto iced saturated aqueous sodium hydrogen carbonate (50 mL) and the aqueous layer extracted with dichloromethane (2×25 mL). The combined organic layers were washed with brine (25 mL), dried over $MgSO_4$ and concentrated. Separation and purification of the new products were achieved by column chromatography or preparative TLC as indicated below for each substrate.

(a) From methyl 3-deoxy-3-*C*-methyl-3-nitro-β-L-glucopyranoside[13,30] **7** (0.237 g); DAST: 660 μL; solvent: dry dichloromethane (10 mL); temperature: reflux for 2 h. The reaction afforded, after column chromatography (1:4, ethyl acetate/hexane), two fractions; the first one consisted of a 1.4:1 (by $^1$H NMR) syrupy mixture (0.089 g, 37%) of the two epimeric compounds **45a** (major) and **45b**; IR (film) $\nu_{max}$ 3485 (OH), 1551 and 1354 ($NO_2$), and 980 cm$^{-1}$ (CF); HRCIMS: *m*/*z* 222.0781 (calcd for $C_8H_{13}F_2NO_5$–F: 222.0778), 210.0580 (calcd for $C_8H_{13}F_2NO_5$–$OCH_3$: 210.0578); the other fraction was pure methyl glycoside **12** (0.071 g, 30%).

**5.15.1. (1*R* and 1*S*)-2,5-Anhydro-3,6-dideoxy-1,6-difluoro-3-*C*-methyl-1-*O*-methyl-3-nitro-L-mannitols, 45a and b.** Major isomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.26 (dd, 1H, $J_{1,2} = 4.5$, $^2J_{1,F} = 64.2$, H-1), 4.91 (d, 1H, $J_{4,5} = 7.0$, H-4), 4.78 (dd, 1H, $^3J_{2,F} = 9.1$, H-2), 4.61 (ddd, 1H, $^2J_{6,F} = 47.6$, $J_{5,6} = 2.7$, $J_{6,6'} = 10.7$, H-6), 4.51 (ddd, 1H, $^2J_{6',F} = 46.6$, $J_{5,6'} = 3.7$, H-6′), 4.00 (dddd, 1H, $^3J_{5,F} = 25.4$, H-5), 3.59 (s, 3H, MeO), and 1.70 (d, 3H, $^5J_{Me,F} = 1.6$, Me-3); NOE contacts (1D NOESY): Me-3, H-1, H-5; $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 110.9 (d, $^1J_{1,F} = 226.3$, C-1), 94.9 (C-3), 82.4 (d, $^2J_{5,F} = 20.1$, C-5), 81.6 (d, $^1J_{6,F} = 174.7$, C-6), 81.4 (d, $^2J_{2,F} = 25.1$, C-2), 76.2 (d, $^3J_{4,F} = 6.3$, C-4), 57.5 (MeO), and 13.8 (Me-3); HMBC correlations: *H*-1/O*C*H$_3$ and *C*-1/OC*H*$_3$.

Minor isomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.28 (dd, 1H, $J_{1,2} = 4.6$, $^2J_{1,F} = 64.0$, H-1), 4.92 (d, 1H, $J_{4,5} = 7.8$, H-4), 4.76 (dd, 1H, $^3J_{2,F} = 9.2$, H-2), ≈4.61 (overlapped, H-6), ≈4.51 (overlapped, H-6′), 3.97 (m, 1H, H-5), 3.58 (s, 3H, MeO), and 1.74 (d, 3H, $^5J_{Me,F} = 0.9$, Me-3); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 110.8 (d, $^1J_{1,F} = 213.7$, C-1), 94.0 (C-3), 82.2 (d, $^2J_{5,F} = 22.6$, C-5), 81.4 (d, $^1J_{6,F} = 174.7$, C-6), 81.3 (d, $^2J_{2,F} = 21.4$, C-2), 76.2 (d, $^3J_{4,F} = 6.3$, C-4), 57.4 (MeO), and 13.5 (Me-3); HMBC correlations: *H*-1/O*C*H$_3$ and *C*-1/OC*H*$_3$.

**5.15.2. Methyl 3,4,6-trideoxy-4,6-difluoro-3-*C*-methyl-3-nitro-β-L-galactopyranoside, 12.** Syrup; $R_f$ 0.25 (1:2 ethyl acetate/hexane); $[\alpha]_D^{23} = +4.7$ (*c* 0.75, $CHCl_3$); IR (film) $\nu_{max}$ 3480 (OH), 1556 and 1352 ($NO_2$), and 1058 cm$^{-1}$ (CF); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.96 (d, 1H, $^2J_{4,F} = 47.7$, H-4), 4.60 (2ddd, 2H, $^2J_{6,F} = 46.1$, H-6 and H-6′), 4.52 (dd, 1H, $J_{1,2} = 7.9$, $^5J_{1,F} = 1.4$, H-1), 4.35 (dd, 1H, $^4J_{2,F} = 1.0$, H-2), 4.00 (m, 1H, $^3J_{5,F} = 27.2$, $^3J_{5,F} = 10.0$, H-5), 3.61 (s, 3H, MeO), and 1.72 (d, 3H, $^4J_{Me,F} = 1.3$, Me-3); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 102.2 (C-1), 90.4 (d, $^2J_{3,F} = 17.7$, C-3), 89.5 (dd, $^1J_{4,F} = 189.2$, $^3J_{4,F} = 4.9$, C-4), 79.9 (dd, $^1J_{6,F} = 170.9$, $^3J_{6,F} = 6.3$, C-6), 72.8 (C-2), 70.3 (dd, $^2J_{5,F} = 25.0$, $^2J_{5,F} = 18.4$, C-5), 57.4 (MeO), and 10.9 (Me-3); HRC-IMS *m*/*z* 242.0842 (calcd for $C_8H_{13}F_2NO_5$+H: 242.0840), 210.0575 (calcd for $C_8H_{13}F_2NO_5$-$OCH_3$: 210.0578).

(b) From methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-β-L-glucopyranoside[13] **8** (0.326 g); DAST: 660 μL; solvent: dry dichloromethane (10 mL); temperature: reflux for 2 h. The reaction afforded, after preparative TLC (1:1 ether/hexane), the unreacted starting material (0.148 g, indicating 59% of conversion) and a 1.2:1 (by $^1$H NMR) syrupy mixture (0.081 g, 25%, corresponding to 42% yield from converted substrate) of the two epimeric compounds **46a** and **b**; IR (film) 1556 and 1352 cm$^{-1}$ ($NO_2$), and 1058 cm$^{-1}$ (CF); HREIMS: *m*/*z* 327.1118 (calcd for $C_{15}H_{18}FNO_6$–F: 327.1124).

**5.15.3. (1*R* and 1*S*)-4,6-*O*-Benzylidene-2,5-anhydro-3-deoxy-1-fluoro-3-*C*-methyl-1-*O*-methyl-3-nitro-L-mannitols, 46a and b.** Major isomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.48–7.36 (m, 5H, Ph), 5.60 (s, 1H, C*H*-Ph), 5.31 (dd, 1H, $J_{1,2} = 5.0$, $^2J_{1,F} = 65.0$, H-1), 4.66 (dd, 1H, $^3J_{2,F} = 12.5$, H-2), 4.59 (dd, 1H, $J_{5,6} = 4.2$, $J_{6,6'} = 9.8$, H-6), 4.49 (d, 1H, $J_{4,5} = 9.9$, H-4), 3.98 (dd, 1H, $J_{5,6'} = 9.8$, H-6′), 3.90 (ddd, 1H, H-5), 3.63 (d, 3H, $^4J_{MeO,F} = 1.3$, MeO), and 1.84 (d, 3H, $^5J_{Me,F} = 0.7$, Me-3); $^{13}$C NMR

(125.7 MHz, $CDCl_3$) $\delta$ 136.1–126.3 (Ph), 110.1 (d, $^1J_{1,F} = 222.5$, C-1), 102.2 (*C*H-Ph), 91.7 (d, $^3J_{3,F} = 0.9$, C-3), 84.6 (C-4), 83.0 (d, $^2J_{2,F} = 23.4$, C-2), 72.1 (d, $^4J_{5,F} = 2.8$, C-5), 71.1 (C-6), 57.3 (MeO), and 14.1 (d,$^4J_{Me,F} = 1.5$, Me-3); HMBC correlations: *H*-1/O*C*H$_3$ and *C*-1/OC*H*$_3$.

Minor isomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.48–7.36 (m, 5H, Ph), 5.60 (s, 1H, C*H*-Ph), 5.35 (dd, 1H,$J_{1,2} = 4.3$, $^2J_{1,F} = 64.0$, H-1), 4.70 (dd, 1H, $^3J_{2,F} = 12.4$, H-2), 4.59 (dd, 1H, $J_{5,6} = 4.4$, $J_{6,6'} = 9.8$, H-6), 4.48 (d, 1H, $J_{4,5} = 9.7$, H-4), 3.96 (dd, 1H, $J_{5,6'} = 9.9$, H-6′), 3.88 (ddd, 1H, H-5), 3.63 (d, 3H, $^4J_{MeO,F} = 1.3$, MeO), and 1.89 (d, 3H, $^5J_{Me,F} = 1.3$, Me-3); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 136.1–126.3 (Ph), 110.6 (d, $^1J_{1,F} = 222.5$, C-1), 102.2 (*C*H-Ph), 91.5 (d, $^3J_{3,F} = 2.8$, C-3), 84.5 (C-4), 82.8 (d, $^2J_{2,F} = 26.5$, C-2), 72.1 (d, $^4J_{5,F} = 2.8$, C-5), 71.1 (C-6), 57.5 (MeO), and 14.3 (d,$^4J_{Me,F} = 2.6$, Me-3); HMBC correlations: *H*-1/O*C*H$_3$ and *C*-1/OC*H*$_3$.

(c) From methyl 6-*O*-*tert*-butyldiphenylsilyl-3-deoxy-3-*C*-methyl-3-nitro-β-L-glucopyranoside[13] **9** (0.476 g); DAST: 660 μL; solvent: dry dichloromethane (10 mL); temperature: reflux for 2 h. The reaction afforded, after preparative TLC (1:1 ether/hexane), a 2.7:1 (by $^1$H NMR) syrupy mixture (0.119 g, 25%) of the two epimeric compounds **47a** and **b**; IR (film) $\nu_{max}$ 3452 (OH), 1553 and 1363 ($NO_2$), 1085 (CF), and 703 (CSi) cm$^{-1}$; FABMS: *m*/*z* 500 (20, [M+Na]$^+$); HRFABMS: *m*/*z* 500.1879 (calcd for $C_{24}H_{32}FNO_6Si$+Na: 500.1881).

**5.15.4. (1*R* and 1*S*)-6-*O*-*tert*-Butyldiphenylsilyl-2,5-anhydro-3-deoxy-1-fluoro-3-*C*-methyl-1-*O*-methyl-3-nitro-L-mannitols, 47a and b.** Major isomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.70–7.38 (m, 10H, 2Ph), 5.21 (dd, 1H, $J_{1,2} = 5.4$, $^2J_{1,F} = 65.4$, H-1), 5.12 (d, 1H, $J_{4,5} = 7.2$, H-4), 4.82 (dd, 1H, $^3J_{2,F} = 9.8$, H-2), 3.90 (dd, 1H, $J_{5,6} = 3.8$, $J_{6,6'} = 11.2$, H-6), 3.84 (m, 1H, H-5), 3.79 (dd, 1H, $J_{5,6'} = 2.9$, H-6′), 3.57 (d, 3H, $^4J_{MeO,F} = 1.1$, MeO), 3.48 (br s, 1H, HO), 1.68 (d, 3H, $^5J_{Me,F} = 0.4$, Me-3), and 1.09 (s, 9H, *t*-Bu); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 135.6–127.7 (2Ph), 111.2 (d, $^1J_{1,F} = 223.8$, C-1), 93.9 (d, $^3J_{3,F} = 6.4$, C-3), 83.0 (C-5), 81.6 (d, $^2J_{2,F} = 25.6$, C-2), 77.4 (C-4), 63.1 (C-6), 57.2 (MeO), 26.7 (C*Me*$_3$), 19.1 (*C*Me$_3$), and 12.6 (Me-3); HMBC correlations: *H*-1/O*C*H$_3$ and *C*-1/OC*H*$_3$.

Minor isomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.70–7.38 (m, 10H, 2Ph), 5.26 (dd, 1H, $J_{1,2} = 5.2$, $^2J_{1,F} = 64.0$, H-1), 5.09 (d, 1H, $J_{4,5} = 7.9$, H-4), 4.80 (dd, 1H, $^3J_{2,F} = 7.6$, H-2), 3.93 (dd, 1H, $J_{5,6} = 3.7$, $J_{6,6'} = 11.3$, H-6), 3.84 (m, 1H, H-5), 3.81 (dd, 1H, $J_{5,6'} = 2.8$, H-6′), 3.60 (d, 3H, $^4J_{MeO,F} = 1.3$, MeO), 3.37 (br s, 1H, HO), 1.73 (d, 3H, $^5J_{Me,F} = 0.9$, Me-3), and 1.09 (s, 9H, *t*-Bu); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 135.6–127.7 (2Ph), 110.8 (d, $^1J_{1,F} = 218.7$, C-1), 93.5 (C-3), 82.4 (C-5), 81.2 (d, $^2J_{2,F} = 29.7$, C-2), 77.4 (C-4), 63.0 (C-6), 57.3 (MeO), 26.7 (C*Me*$_3$), 19.1 (*C*Me$_3$), and 12.7 (Me-3); HMBC correlations: *H*-1/O*C*H$_3$ and *C*-1/OC*H*$_3$.

(d) From phenyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-1-thio-α-D-glucopyranoside[14] **10** (0.403 g); DAST: 660 μL; solvent: dry dichloromethane (10 mL); temperature: 0 °C (0.5 h) to reflux (3 h). The reaction afforded, after preparative TLC (1:1.5 ether/hexane), the unreacted starting material (0.169 g, indicating 58% of conversion) and compound **48** (0.038 g, 9.5%, corresponding to 16% yield from converted substrate).

**5.15.5. 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-methyl-3-nitro-2-phenylthio-β-D-glucopyranosyl fluoride, 48.** Compound **48** showed physical and spectroscopic properties identical, respectively, to those of **49** [see (e), next paragraph], except for the rotatory power: $[\alpha]_D^{26} = -92.3$ (*C* 0.65, acetone).

(e) From phenyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-1-thio-α-L-glucopyranoside[14] **11** (0.403 g); DAST: 660 μL; solvent: dry dichloromethane (10 mL); temperature: 0 °C (0.5 h) to reflux (1 h). The reaction afforded, after preparative TLC (1:1.5, ether/hexane), unreacted starting material (0.118 g, indicative of 71% of conversion) and the glycosyl fluoride **49** (0.139 g, 34%, corresponding to 48% yield from converted substrate) containing trace amounts of its α-anomer.

**5.15.6. 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-methyl-3-nitro-2-phenylthio-β-L-glucopyranosyl fluoride, 49.** Syrup; $R_f$ 0.54 (1:1 ether/hexane); $[\alpha]_D^{23} = +84.5$ (*c* 0.84, acetone); IR (film) $\nu_{max}$ 1557 and 1391 ($NO_2$), and 1107 cm$^{-1}$ (CF); $^1$H NMR (500 MHz, $CD_3COCD_3$) $\delta$ 7.58–7.33 (m, 10H, 2Ph), 5.76 (s, 1H, C*H*-Ph), 5.75 (dd, 1H, $^2J_{1,F} = 50.9$, $J_{1,2} = 8.2$, H-1), 4.48 (d, 1H, $J_{4,5} = 9.2$, H-4), 4.39 (dd, H, $^2J_{6,6'} = 9.1$, $J_{5,6} = 4.0$, H-6), 4.00–3.95 (m, 2H, H-5 and H-6′), 3.91 (dd, 1H, $^3J_{2,F} = 21$, H-2), and 1.87 (s, 3H, Me); NOE contacts: H-1/Me-3, H-1/H-5 and H-2/H-4; $^{13}$C NMR (125.7 MHz, $CD_3COCD_3$) $\delta$ 134.0–127.1 (2Ph), 110.2 (d, $^1J_{1,F} = 212.4$, C-1), 102.4 (*C* H-Ph), 92.5 (d, $^3J_{3,F} = 7.6$, C-3), 81.8 (C-4), 69.0 (C-6), 66.3 (d, $^3J_{5,F} = 5.0$, C-5), 59.6 (d, $^2J_{2,F} = 25.1$, C-2), and 12.8 (Me); HREIMS *m*/*z* 405.1046 (calcd for $C_{20}H_{20}FNO_5S$: 405.1046); HMBC correlation: *H*-2/(SPh)*C*$_{ipso}$.

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