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Rearrangement reactions in the fluorination of 3-deoxy-3-*C*-methyl-3-nitro-hexopyranosides (and hexo-1-thiopyranosides) of the D- and L-series by the DAST reagent

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Abstract

Fluorination of diverse 3-deoxy-3-*C*-methyl-3-nitro-hexopyranosides and hexo-1-thiopyranosides of the D- and L-series by the DAST reagent was studied in order to establish, on this 3-branched-chain sugar domain, the influence of the stereochemical relationship of the substituents at positions 1 and 2, as well as the protection of the HO-4, on the kinds of rearrangement reaction promoted by this fluorinating agent. Three classes of pyranosidic substrate were employed: (*a*) 1,2-*trans* configured, irrespective of whether HO-4 is protected or not; (*b*) 4-*O*-protected 1,2-*cis* configured; and (*c*) 4-*O*-unprotected 1,2-*cis* configured. They were prepared starting from simple glycosides through routes involving a Baer reaction and subsequent transformations by known methodology. All the substrates of class *a* essayed underwent, on treatment with DAST at room or higher temperatures, a rearrangement involving a 1,2-shift to give both the anomeric 2-inverted pyranosyl fluorides (or, for the 1-thioglycosides, only the α fluoride). Substrates of class *b* led, through a mechanism similar to that proposed for transformations of related substrates, to ring-contracted 2,5-anhydro-1-fluoro-1-*O*-methyl- (or 1-deoxy-1-phenylthio-)hexitol derivatives (sometimes as 1-epimers), which are precursors of 2,5-anhydro-*aldehydo*-sugars. Substrates of class *c* led to 4,5-anhydro-1-fluoro-1-*O*-methylalditol derivatives in all cases, together with a ring-contracted 5-fluoro-hexofuranoside in only one case; a rationalisation for their formation is proposed.

1. Introduction

Of the known fluorinating agents of alcohols, diethylaminosulphur trifluoride (DAST) has become considered one of the most efficient and useful under very mild conditions. Thus, it compares favourably[1] with hydrogen fluoride, sulphur tetrafluoride, phenylsulphur trifluoride, selenium tetrafluoride, fluorophosphoranes, and others. The interest in fluoro sugars has

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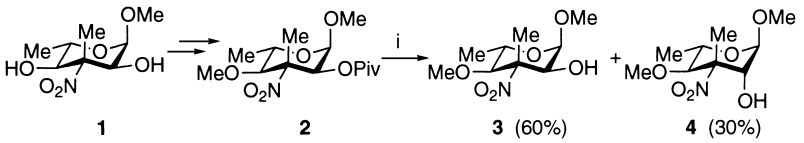
increased in the last two decades,[2–5] at least in part due to the observation that the presence of a fluorine atom at certain positions of the sugar moiety of glycosides[6] and nucleosides reinforces the glycosidic bond, consequently enhancing the therapeutic effect of pharmacologically active substrates.[7,8] Fluorination with DAST occurs with inversion of configuration (S_N2 mechanism); however, when the reaction is somewhat hindered, and an electron-rich group is at a *vicinal* position, the product with retained configuration and products showing migration of the neighbouring group may be obtained.[9,10] This kind of rearrangement requires the 1,2-*trans* relationship of the hydroxyl group and the neighbouring group, and it has been proposed[11,12] that it occurs through a cyclic onium ion intermediate. In a short communication,[13] we have reported on three different kinds of rearrangement reaction observed in the fluorination of methyl 6-deoxy-3-*C*-methyl-3-nitro-α-L-hexopyranosides by DAST under mild conditions: (i) for a 4-*O*-protected 1,2-*trans* configured substrate, the kind of rearrangement agreed with that cited above; (ii) when the 1,2-*cis* isomer was used as substrate, another kind of rearrangement—involving ring contraction—was observed, similar to those found for related substrates;[14–17] and (iii) finally, a 2,4-*O*-unprotected 1,2-*cis* substrate gave a mixture of a 5-fluoro-hexofuranoside and a 4,5-anhydro-1-fluoro-1-*O*-methylalditol. For the third type of rearrangement, we have also suggested[13] a possible bicyclic oxonium ion as intermediate, the attack of which by the fluoride at C-5 or at C-2 might account for the formation of the two products, respectively. Additional examples of the first type of rearrangement have also been encountered[18] in the fluorination of a 2,4,6-unprotected phenyl 3-*C*-methyl-3-nitro-1-thio-β-D-glucopyranoside and its β-L-enantiomer by DAST at low temperature (–35°C→rt); however, the same substrates underwent no rearrangement, but only fluorination at C-6, if the temperature was maintained below –20°C. A more detailed study on the influence of the substrate structure and fluorination conditions on the stereochemical course of the reaction and on the scope of each kind of rearrangement was undertaken, and we report here the results found for diverse 3-deoxy-3-*C*-methyl-3-nitro-hexopyranosides (and hexo-1-thiopyranosides) of the D- and L-series as substrates.

2. Results and discussion

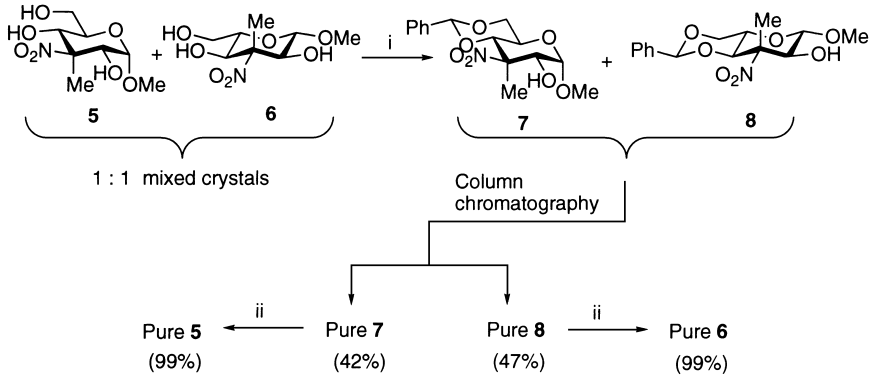
The 3-*C*-methyl-3-nitro-pyranosidic substrates can be classified in three groups according to their structural characteristics: (*a*) substrates having the relative 1,2-*trans* configuration, regardless of whether they are 4-*O*-protected or unprotected; (*b*) 4-*O*-protected 1,2-*cis* configured substrates; and (*c*) 4-*O*-unprotected 1,2-*cis* configured substrates.

We have prepared some of the substrates starting from methyl α-L-rhamnopyranoside by a route (Scheme 1) which involves a Baer reaction with nitroethane to give **1** (class *c*), selective 2-*O*-pivaloylation of which, followed by 4-*O*-methylation, afforded **2**;[19] finally, the crystalline epimers **3** (class *b*) and **4** (class *a*) were obtained as we had previously reported,[13] that is, by selective deprotection of the O-2 position of compound **2** following the method of Van Boeckel and Van Boom.[20]



Scheme 1. (i) (1) Bu_4N^+ HO^-/H_2O, N_2, rt; (2) IRA-120 (H^+) resin

Another route, also involving a dialdehyde–nitroethane cyclisation, but starting from methyl α-D-glucopyranoside, afforded a different set of substrates for our studies. From the crystalline 1:1 mixture of **5** and its diastereomer **6** obtained in this reaction,[18] diverse sugar derivatives of the D- and L-series became separately available. Benzylidenation of this mixture led to the 4,6-*O*-protected derivatives **7** (class *b*) and **8** (class *a*), which could be separated by column chromatography, thus opening access to pure **5** (α-D) (class *c*) and **6** (β-L) (class *a*) themselves by deprotection (Scheme 2).

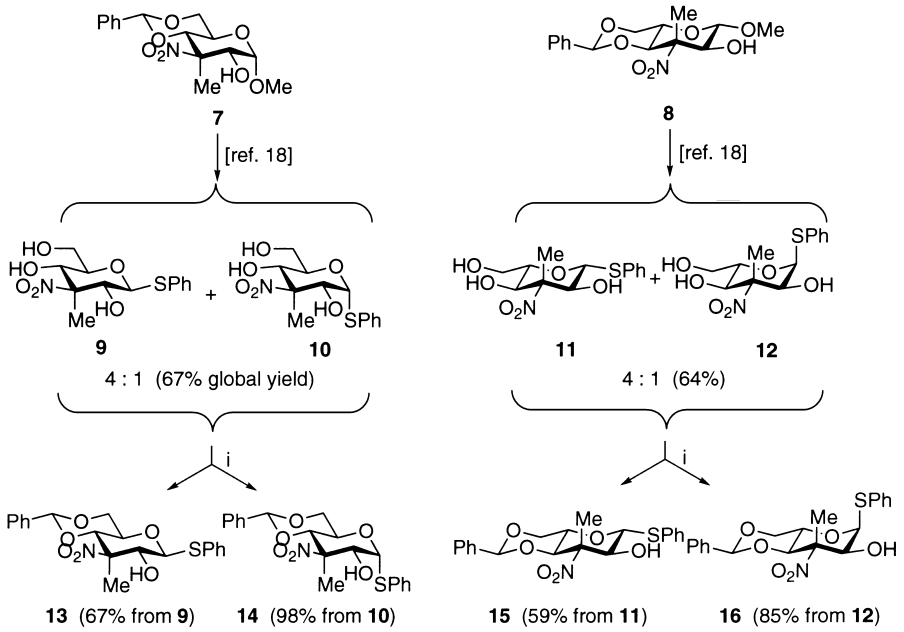


Scheme 2. (i) $PhCH(OMe)_2$/TsOH (DMF); (ii) TsOH/MeOH–dioxane

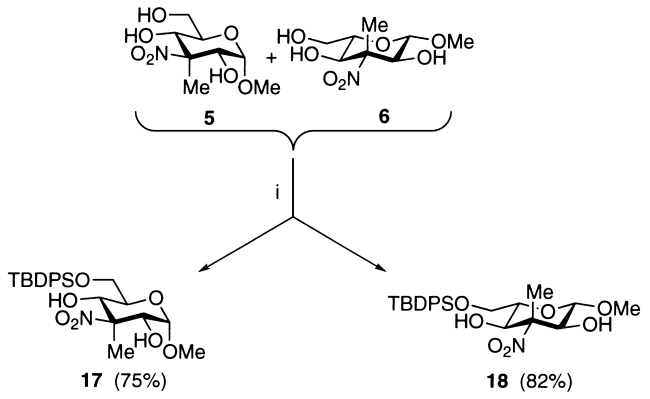
Furthermore, application of the method of Hanessian and Guindon[21] for preparing phenyl 1-thioglycosides to each of the pure compounds **7** and **8** led to 4:1 β:α anomeric mixtures of branched-chain phenyl 1-thioglycosides (**9**+**10**) and (**11**+**12**), respectively, the major components (**9** and **11**) being isolated as pure 2,4,6-*O*-unprotected 1-thioglucopyranosides by preparative column chromatography, as we had described.[18] Apart from that, each of the foregoing anomeric mixtures (**9**+**10**) and (**11**+**12**) was treated with benzaldehyde dimethylacetal to give the respective anomeric mixture of phenyl 4,6-*O*-benzylidene-1-thioglucopyranosides (**13**+**14**) and (**15**+**16**), separation of which, in each case, was performed by preparative thin-layer chromatography; thus, the pure β-anomers of the D-series **13** and L-series **15** (both of class *a*) were obtained in higher practical yields than their respective α-anomers **14** and **16** (both of class *b*), although the yield of formation was higher for the α-anomers (Scheme 3).

Lastly, treatment of the same 1:1 crystalline mixture of **5** and **6** with *tert*-butyl-diphenyl-chlorosilane afforded, after column chromatography, good yields of the 6-*O*-silylated-4-*O*-unprotected methyl α-D-glucopyranoside **17** (class *c*) and its β-L-isomer (**18**, class *a*) (Scheme 4).

Fluorination of substrates belonging to the class (*a* **4**, **6**, **8**, **9**, **11**, **13**, **15** and **18**) with DAST, under conditions allowing the temperature to rise at least to the ambient, led to rearranged pyranosyl fluorides **19**–**32** (Scheme 5); thus, the α-L-manno configured glycoside **4** gave rise[13] to the 1.3:1 mixture of the β-L- and α-L-gluco configured pyranosyl fluorides (**19** and **20**, global yield 58%). A β:α mixture (1.4:1) of the 6-fluoro-glycosyl fluorides **21** and **22** (global yield 37%) was obtained from **6**, now accompanied by a non-rearranged methyl 4,6-dideoxy-4,6-difluoro-pyranoside (**33**, 30%), but the 4,6-*O*-benzylidene derivative **8** afforded only the epimeric 1.2:1 α:β mixture **23**/**24** (42% from converted substrate). From each of the enantiomeric phenyl 1-thio-β-D- and β-L-glucopyranoside derivatives **9** and **11**, two rearranged α-manno-configured fluorides were obtained, as previously described,[18] the former having an additional fluorine atom at position 6



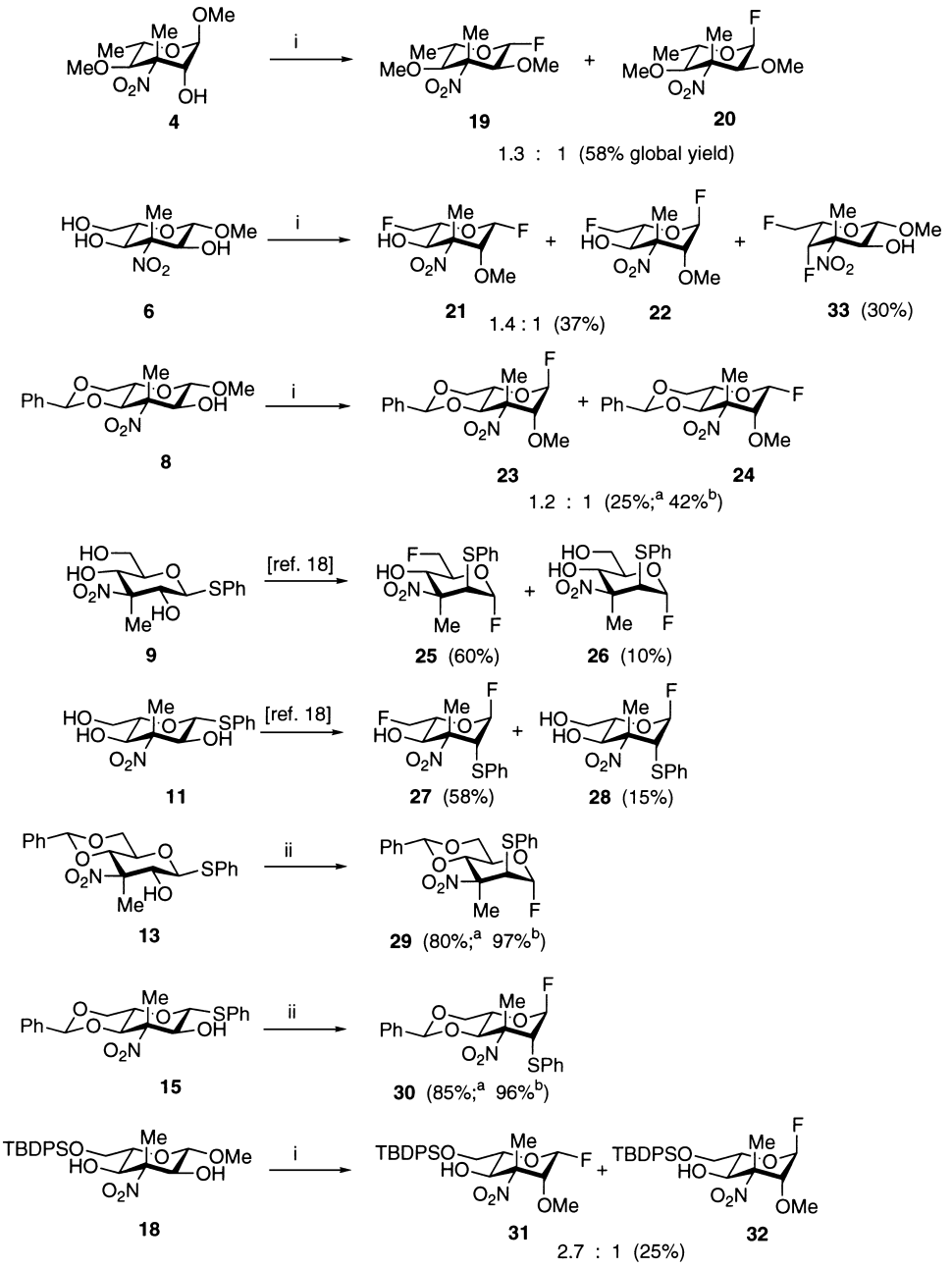
Scheme 3. (i) $PhCH(OMe)_2$/TsOH (DMF) and thin-layer chromatography



Scheme 4. (i) TBDPSCl/Py–DMAP and column chromatography

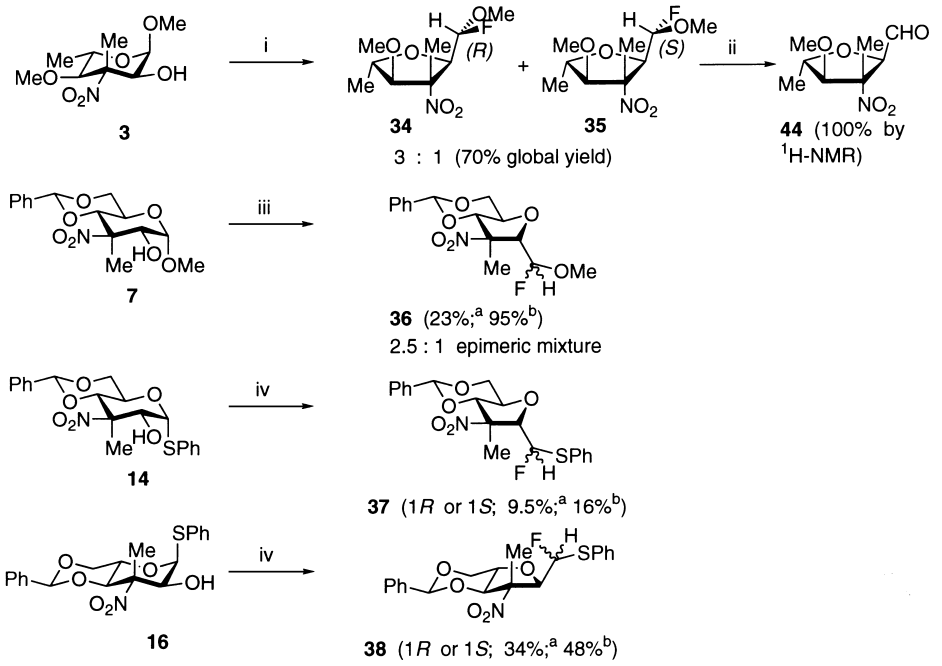
(**25** and **27**, in 60% and 58% yields, respectively) and the latter lacking it [**26** (10%) and **28** (15%)]; the corresponding 4,6-*O*-benzylidene derivatives **13** and **15**, having the expected behaviour, gave only the respective 2-phenylthio-α-D- and α-L-mannopyranosyl fluorides **29** and **30** in 97 and 96% yields, respectively, from converted substrate. Finally, a derivative of **6**, silylated at *O*-6 **18**, underwent partial *O*-desilylation as well as the same type of rearrangement without fluorination at position 4, to give only 25% of a 2.7:1 β:α mixture of L-manno-configured pyranosyl fluorides (**31** and **32**).

For the class *b* substrates (**3**, **7**, **14**, and **16**), the reaction, as carried out at room temperature or in boiling dichloromethane, afforded epimeric mixtures of 2,5-anhydro-1-fluoro-1-*O*-methyl- (or 1-deoxy-1-phenylthio-)hexitol derivatives [(**34**+**35**) from **3** (global yield 70%) and **36** from **7** (95% from converted substrate)] or only one of the epimers (**37** from **14**, **38** from **16**) (Scheme 6); it is



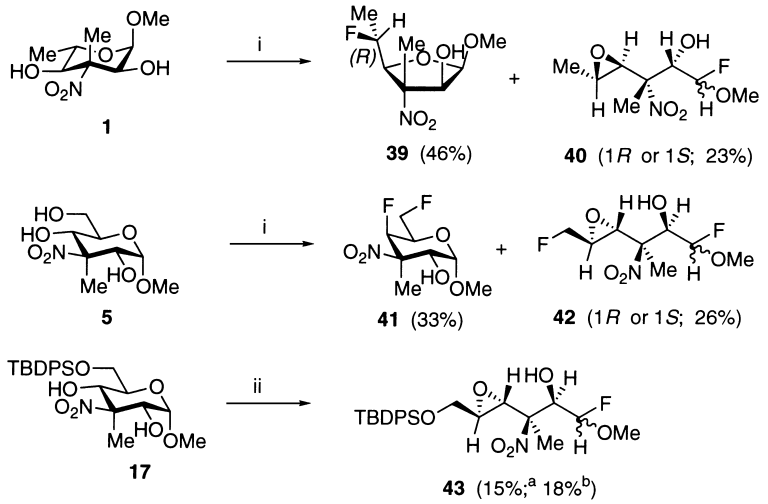
Scheme 5. (i) DAST (5 mol-equiv.)/CH_2Cl_2, reflux (2 h); (ii) DAST (5 mol-equiv.)/CH_2Cl_2, 0°C→rt (1 h). [a]Isolated; [b]from converted substrate

noteworthy that compound **36** slowly decomposed in chloroformic solution, whereas the enantiomeric 1-phenylthio derivatives **37** and **38** were obtained in low yields (16 and 48% from converted substrate, respectively) both facts indicate that the stability of these products is lower than that of the respective pyranosic isomers (**23**+**24**), **29**, and **30**, a feature also observed[14] for related pairs of compounds.



Scheme 6. (i) DAST (5 mol-equiv.)/CH_2Cl_2; reflux (2 h); (ii) NMR sample in $CDCl_3$: shaking with D_2O/conc. HCl (1 drop), rt (1 week); (iii) DAST (3.5 mol-equiv.)/diglyme, rt (16 h); (iv) DAST (5 mol-equiv.)/CH_2Cl_2, 0°C (0.5 h)→reflux (1–3 h)

Of the substrates of class *c* (**1**, **5**, and **17**) used for fluorination with DAST (Scheme 7) under conditions similar to those cited last, **1** gave rise,[13] after column chromatography, to a methyl 5-deoxy-5-fluoro-hexofuranoside (**39**, 46%) next to a 4,5-anhydro-1-fluoro-1-*O*-methylhexitol (**40**, 23%), both retaining the HO-2 free; substrate **5** afforded a non-rearranged methyl 4,6-



Scheme 7. (i) DAST (5 mol-equiv.)/CH_2Cl_2, reflux (2 h); (ii) DAST (3.5 mol-equiv.)/diglyme, rt (2 h). [a]Isolated; [b]from converted substrate

difluoro-hexopyranoside (**41**, 33%) next to a 4,5-anhydro-1,6-difluoro-1-*O*-methylhexitol (**42**, 26%) of the same kind as **40**; with substrate **17**, the reaction led to only one product **43** also having an oxirane ring involving C-4 and C-5, as well as a fluorine atom at C-1 of the hexitol chain—the poor yield (15%, corresponding to 18% from converted substrate) in this case was attributed to extensive 6-*O*-deprotection, as deduced from observations during the chromatographic control.

Structural assignment of the new products was made on the basis of analytical and spectral data (MS, IR, ^{1}H and ^{13}C NMR). For the pyranosic new compounds (every novel substrate—**3**, **4**, and **13**–**18**—as well as a number of fluoro derivatives—**19**–**24**, **29**–**33** and **41**), the configurational assignments were easier than for the remaining products. Thus, the 1,2-*cis* α-L-glycoside **3** was easily distinguished from the 1,2-*trans* epimer **4** by comparing, in their ^{1}H NMR spectra, the δ values for the H-2 [higher in compound **3** (H-2 *axial*) than in compound **4** (H-2 *equatorial*) as a consequence of the presence of the *equatorial* nitro group at the neighbouring position], and the H-1/H-2 coupling constant values (4.5 Hz for the *equatorial*/*axial*-relationship in **3** and 1.5 Hz for the *diequatorial* one in **4**). The β-configuration was assigned to both the enantiomeric phenyl 1-thioglucosides **13** and **15**, since they are 4,6-*O*-protected derivatives of β-configured described compounds,[18] and was confirmed by the high value of the coupling constant $J_{1,2}$ (9.9 Hz), indicative of the *trans*-diaxial relationship between H-1 and H-2; the $J_{1,2}$ value (6.4 Hz) for the respective isomers **14** and **16** is consistent with the α-configuration. Similarly, the coupling between protons of the same kind in compounds **17** and **18** gives rise to splitting values (4.5 Hz for **17** and 9.6 Hz for **18**) that are in agreement with the α- and β-configurations, respectively. With regard to the new fluoro pyranosic derivatives, the two components **19** and **20** of the mixture obtained from **4** showed separate signals in the ^{1}H and ^{13}C NMR spectra, in which the fluorine couplings, particularly with H-1 (53.1 and 54.0 Hz, respectively) and H-2 (12.7 and 25.6 Hz), and with C-1 (213.0 and 232.4 Hz) and C-2 (24.0 and 23.2 Hz), agreed with well-established antecedents[22] and revealed that the fluorine atom is at position 1, that is, a rearrangement had taken place; the β-configuration was assigned to **19** and the α one to **20** on the basis of the higher value of $^3J_{C\text{-}3,F}$ (11.4 Hz) for the former than for the latter (3.3 Hz), in agreement[22] with the *anti* and the *gauche* disposition of C-3 and F around the C-2/C-1 bond, respectively. This was confirmed by differential NOE experiments, which evidenced contacts between H-1 and the Me-3 protons in compound **19**, but not in compound **20**. In a similar manner, the presence of a fluorine atom at the anomeric position was evident from the deshielding effect on H-1 and C-1 and the fluorine couplings observed in the NMR spectra of compounds **21**–**32**; however, **33**—obtained together with **21** and **22** from **6**—lacks the fluorine atom at that position and bears it at position 4 instead, as indicated by the high values of δ for H-4 (4.96 ppm) and for C-4 (89.5 ppm), as well as by the coupling constants $^2J_{4,F}$ (47.7 Hz) and $^1J_{C\text{-}4,F}$ (189.2 Hz), while H-1 (δ 4.52 ppm) and C-1 (δ 102.2 ppm) are not deshielded, the H-1/H-2 constant coupling (7.9 Hz) is compatible with a 1,2-*trans*-diaxial relationship, $J_{H\text{-}1,F}$ has a very low value (1.4 Hz) indicative of a long-range coupling (five bonds), and the signal of C-1 appears as a singlet. The apparent absence of coupling between H-4 and H-5 in **33** agrees with an axial rather than an equatorial disposition of the fluorine atom, corroborated by the singlet appearance of the C-2 signal ($^3J_{C\text{-}2,F\text{-}4}\approx 0$ Hz), indicative of a *gauche* disposition around the C-2/C-3 bond.[23] Apart from that, these three compounds (**21**, **22**, and **33**) have another fluorine atom at the primary position 6, easily evidenced by the fluorine couplings observed in the two H-6 and the C-6 signals. Assignment of β-configuration to **21** was made on the basis of 1D NOESY experiments, which showed enhancement of the H-1 and H-5 signals on irradiating the Me-3 singlet; hence, compound **22** must be the α-isomer.

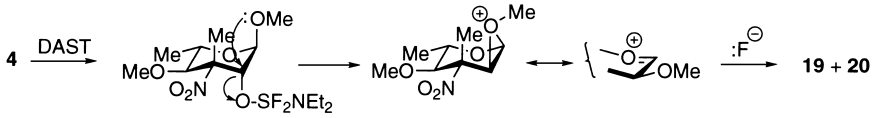
Similarly, the mixture obtained in the fluorination of **8** proved to consist of the rearranged 4,6-*O*-benzylidene glycosyl fluorides **23** and **24**, to which the respective α- and β-configurations were assigned again on the basis of the values observed for $^{3}J_{C\text{-}3,F}$ in the ^{13}C NMR spectra (0.9 and 2.8 Hz, respectively). The enantiomeric 2-deoxy-2-phenylthio-D- and L-mannopyranosyl fluorides **29** and **30** showed no apparent coupling between H-1 and H-2, incompatible with an H/H *trans*-diaxial relationship, and also no splitting of the C-3 signal, in agreement with a *gauche* disposition of this carbon atom and the fluorine atom around the C-1/C-2 bond. The β- and the α-configurations, respectively, were assigned to the anomeric rearranged glycosyl fluorides **31** and **32**, obtained from the methyl 6-*O*-*tert*-butyldiphenylsilyl-glycoside **18**, again by application of the same general rule ($^{3}J_{C\text{-}3,F}$ values: 6.4 and ≈0 Hz).

As previously reported,[13] the assignment of a structure of 2,5-anhydro-1-fluoro-1-*O*-methyl-alditol derivative for **34** and **35**, the components of the 3:1 mixture formed in the fluorination of **3** (class *b*), was based on the quantitative formation of a unique *aldehydo*-sugar (**44**; δ for C*H*O 9.65 ppm, $J_{1,2}$ 1.2 Hz) in the hydrolysis of the mixture in $CDCl_3$ with aqueous HCl, their respective 1*R* and 1*S* configurations at C-1 being tentatively assigned by considering the values of $J_{2,F}$ (6.8 and 10.4 Hz) and $J_{C\text{-}2,F}$ (30.6 and 24.9 Hz), in agreement with antecedents[14] for the H-2/F-1 *gauche* and *anti* and the F-1/ring O *anti* and *gauche* relationships observed in related compounds. Furthermore, **34** and **35** showed all the same NOE contacts (1D NOESY), except that shown by the latter between Me-3 and MeO-1, absent in the NOESY spectrum of the former. Spectral patterns similar to those shown by these compounds were found for the epimeric mixture **36**, and the enantiomeric compounds **37** and **38**; however, the values of the H-2/F-1 and C-2/F-1 coupling constants for these products were not conclusive for configurational assignments at C-1.

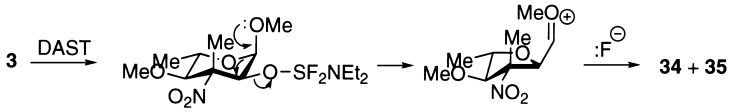
One of the products obtained from each substrate (**1**, **5**, and **17**) of class *c* had a structure of 4,5-anhydro-1-fluoro-1-*O*-methyl-alditol derivative (**40**, **42**, and the sole product **43**, respectively), as deduced from the shielding effect observed over H-4 (δ 3.28–3.61 ppm) and H-5 (δ 3.06–3.46 ppm), as atoms bonded to an oxirane ring, and from the low value of $J_{4,5}$ (2.0–2.1 Hz), indicative of a *trans* relationship with respect to the ring plane. Moreover, the presence of a preferential conformer around the C-3/C-4 bond in the chloroformic solution of **40**, as has been formulated, was established from the Me-3/H-5 contact observed in its 1D NOESY spectrum. The other product obtained from **1** was a methyl 5-fluoro-β-D-altrofuranoside (**39**), as evidenced by the downfield shift of the H-5 signal exerted by the fluorine atom at C-5, the *R* configuration being assigned to this centre on the basis of: (i) the high value of $J_{4,5}$ (9.3 Hz), which shows the *anti* arrangement of these protons; (ii) the value of $J_{4,F}$ (5.9 Hz), indicative of a *gauche* orientation between H-4 and F; and (iii) the value of $J_{C\text{-}4,F}$ (30.1 Hz), which suggests[14] the *anti* disposition of the fluorine and the ring oxygen. In the fluorination of **5**, the oxirane derivative **42** obtained was accompanied by the non-rearranged 4,6-difluoro-glycopyranoside **41**, NMR of which showed downshifting of the signals of H-4, H-6, and H-6′ (δ 4.99, 4.55, and 4.52 ppm, respectively), as well as C-4 and C-6 (δ 89.9 and 80.4 ppm); the apparent lack of H-4/H-5 coupling is incompatible with a *trans*-diaxial disposition of these protons, thus evidencing the inverted configuration at C-4, as expected.

The formation of the hexopyranosyl fluorides **19**–**32** is considered an additional case of the 1,2-shift cited above[9,10] and can be explained in terms of a classical neighbouring group effect involving a cyclic onium ion intermediate, similarly to those proposed for related compounds,[12,13] here formulated as applied to the formation of (**19**+**20**) (Scheme 8). The ring contraction that occurs in the formation of the 2,5-anhydro-1-fluoroalditols **34**–**38** is explained similarly to those described for other ring contractions undergone by hexopyranosides,[14–17] application of which to the

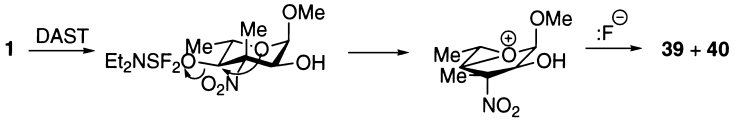
formation of (**34+35**) being represented in Scheme 9. A possible rationalisation for the formation of the 5-fluorofuranoside **39** and the 4,5-anhydro-1-fluoroalditol **40** is a ring-oxygen participation in pushing out the leaving group from C-4 to form a cyclic oxonium ion as intermediate, which subsequently may be opened by attack of the fluoride on either C-5 or C-1 (Scheme 10). The absence of products similar to **39** when starting from **5** and **17** may be attributed, for **5**, to the presence of the free HO group at C-6, thus allowing the normal fluorination at the positions 4 and 6 to give **41**, or the preferred opening of the cyclic oxonium ion by attack of the fluoride on C-1 rather than on C-5 (having a fluoromethyl substituent) to give **42**, whereas for **17**, the bulky group at O-6 may hinder the attack, not only on C-4 of the first intermediate, but also on C-5 of the cyclic cation, the formation of **43** apparently being the only possibility. The steric hindrance of the fluoromethyl substituent at C-5 of the cyclic oxonium ion formed from **5** could alternatively explain the difficulty in attacking this position.



Scheme 8.



Scheme 9.



Scheme 10.

3. Conclusion

The foregoing results can be summarised as follows: each class of glycoside used as substrate (*a*, *b*, *c*, as defined above) fits into one of the three types of rearrangement mechanism previously cited,[13] corroborating that the course of the reaction depends on the 1,2-stereochemical pattern of the substrate and, in the case of the 1,2-*cis* relationship of the substituents, on whether the HO group at C-4 is protected or not, in the terms expressed above. The new glycosyl fluorides **19**–**32** should behave as good glycosyl donors[5] in the synthesis of glycosides, oligosaccharides and nucleosides having 3-*C*-methyl-3-nitro-hexopyranosyl units; moreover, a good stereocontrol in the formation of the glycosidic bond is to be expected for the 2-phenylthio derivatives **25**–**30** in a route that, for analogues,[10] leads to 2-deoxy-glycosidic products. The presence of a fluorine atom at C-5 in compound **39** and at C-6 in some of the foregoing glycosyl fluorides is expected to enhance the therapeutic activity of glycosides and nucleosides derived from them, as a

consequence of the reinforcing of the glycosidic bond. An *aldehydo*-sugar latent functionality is present in the 2,5- (**34**–**38**) and 4,5-anhydro-1-fluoro-1-*O*-methylalditols (**40**, **42**, **43**) obtained, thus giving synthetic interest also to the last two types of rearrangement reaction described herein.

4. Experimental

4.1. General

Hexane and ether were distilled from sodium prior to use. A commercial 40% aq. solution of tetrabutylammonium hydroxide (Fluka) was used. 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. Silica gel 60 (E. Merck, 230–400 mesh) was used for column chromatography. Solutions were concentrated under diminished pressure at $<40^{\circ}C$. Melting points were determined on a Gallenkamp MFB-595 apparatus and are uncorrected. A Perkin–Elmer 241 MC polarimeter was used for measurement of optical rotations. IR spectra (neat or on a KBr disc) were obtained on an FTIR Bomem Michelson MB-120 spectrophotometer. ^1H 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 (δ) are expressed in ppm from TMS; coupling constants (J), in hertz. 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. EI mass spectra (70 eV) were measured with a Kratos MS-80RFA instrument, with an ionising 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).

4.2. *Methyl 3,6-dideoxy-3*-C-*methyl-4*-O-*methyl-3-nitro-α-L-glucopyranoside* **3** *and methyl 3,6-dideoxy-3*-C-*methyl-4*-O-*methyl-3-nitro-α-L-mannopyranoside* **4**

A magnetically stirred solution of methyl 3,6-dideoxy-4-*O*-methyl-3-*C*-methyl-3-nitro-2-*O*-pivaloyl-α-L-glucopyranoside **2**[19] (1.07 g, 3.37 mmol) in dioxane (20 mL) was treated with tetrabutylammonium hydroxide (1.31 g, 5.05 mmol) in water (20 mL) under nitrogen. The mixture was stirred at room temperature until TLC (30:1 dichloromethane:acetone) indicated that all starting material had disappeared (1 h). After neutralisation with IRA-120 (H^+) resin, the mixture was concentrated. Column chromatography (60:1 dichloromethane:acetone) of the residue afforded pure **3** (0.48 g, 60%, R_f 0.45) and **4** (0.24 g, 30%, R_f 0.33). Compound **3**: colourless crystals; mp 99–101°C; $[\alpha]_D^{24}=-17$ (*c* 1.0, CH_2Cl_2); IR (KBr) ν_{max} 3428 (OH), 1541, and 1372 cm^{-1} (NO_2); ^1H NMR (500 MHz, $CDCl_3$): δ 4.75 (d, 1H, $J_{1,2}=4.5$, H-1), 4.36 (dd, 1H, $J_{2,OH}=11.0$, H-2), 3.68 (d, 1H, $J_{4,5}=9.7$, H-4), 3.64 (dq, 1H, H-5), 3.43 (s, 3H, MeO-4), 3.37 (s, 3H, MeO-1), 2.37 (d, 1H,

HO-2), 1.67 (s, 3H, Me-3), and 1.34 (d, 3H, $J_{5,6}=5.9$, Me-5); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 98.5 (C-1), 95.1 (C-3), 84.8 (C-4), 72.3 (C-2), 65.6 (C-5), 61.0 (MeO-1), 55.2 (MeO-4), 17.6 (Me-5), and 11.2 (Me-3). Anal. calcd for $C_9H_{17}NO_6$: C, 45.95; H, 7.23; N, 5.96. Found: C, 45.81; H, 7.34; N, 5.97. Compound **4**: colourless crystals; mp 101–103°C; $[\alpha]_D^{24}=-22$ (*c* 1.0, CH_2Cl_2); IR (KBr) ν_{max} 3409 (OH), 1545 and 1348 cm^{-1} (NO_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.67 (d, 1H, $J_{1,2}=1.5$, H-1), 4.10 (dd, 1H $J_{2,OH}=8.1$, H-2), 3.94 (d, 1H, $J_{4,5}=9.7$, H-4), 3.67 (dq, 1H, $J_{5,6}=6.3$, H-5), 3.62 (s, 3H, MeO-4), 3.39 (s, 3H, MeO-1), 2.43 (d, 1H, HO-2), 1.71 (s, 3H, Me-3), and 1.41 (d, 3H, Me-5); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 101.1 (C-1), 92.9 (C-3), 79.5 (C-4), 73.5 (C-2), 66.2 (C-5), 60.9 (MeO-4), 55.1 (MeO-1), 18.0 (Me-5), and 17.0 (Me-3). Anal. calcd for $C_9H_{17}NO_6$: C, 45.95; H, 7.23; N, 5.96. Found: C, 45.91; H, 7.34; N, 5.97.

*4.3. Phenyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-1-thio-β-D-glucopyranoside **13** and phenyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-1-thio-α-D-glucopyranoside **14***

Benzaldehyde dimethylacetal (46 μL, 0.309 mmol) and catalytic amounts of *p*-toluenesulphonic acid were added to a solution of the 4:1 mixture of phenyl 3-deoxy-3-*C*-methyl-3-nitro-1-thio-β-D-glucopyranoside **9** and phenyl 3-deoxy-3-*C*-methyl-3-nitro-1-thio-α-D-glucopyranoside **10**[18] (0.065 g, 0.206 mmol) in *N*,*N*-dimethylformamide (0.5 mL). The solution was kept at room temperature (TLC monitoring, 20:1 dichloromethane:methanol) and the methanol evolved was from time to time evaporated under diminished pressure. It was necessary to replace the benzaldehyde dimethylacetal partially evaporated during the process. After neutralisation with saturated aqueous sodium hydrogen carbonate, the reaction mixture was concentrated, the residue was diluted with dichloromethane, and the insoluble salts were filtered off. The filtrate was then concentrated to a syrup, preparative TLC (3:2 hexane:ether) of which afforded pure **13** (0.044 g, 67% from **9**) and **14** (0.016 g, 98% from **10**). Compound **13**: $[\alpha]_D^{24}=-43.8$ (*c* 1.0, $CHCl_3$); HREIMS: *m*/*z* 403.1111 (calcd for $C_{20}H_{21}NO_6S$: 403.1090); 294.0945 (calcd for $C_{20}H_{21}NO_6S$–SPh: 294.0978); this product showed IR and NMR spectra identical to those of its enantiomer **15**. Compound **14**: $[\alpha]_D^{22}$+211 (*c* 1.0, $CHCl_3$); HREIMS: *m*/*z* 403.1079 (calcd for $C_{20}H_{21}NO_6S$: 403.1090); 294.0985 (calcd for $C_{20}H_{21}NO_6S$–SPh: 294.0978); this compound showed IR and NMR spectra identical to those of its enantiomer **16**.

*4.4. Phenyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-1-thio-β-L-glucopyranoside **15** and phenyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-1-thio-α-L-glucopyranoside **16***

Benzaldehyde dimethylacetal (175 μL, 1.17 mmol) and catalytic amounts of *p*-toluenesulphonic acid were added to a solution of the 4:1 mixture of phenyl 3-deoxy-3-*C*-methyl-3-nitro-1-thio-β-L-glucopyranoside **11** and phenyl 3-deoxy-3-*C*-methyl-3-nitro-1-thio-α-L-glucopyranoside **12**[18] (0.245 g, 0.778 mmol) in *N*,*N*-dimethylformamide (1.5 mL). The solution was kept at room temperature (TLC monitoring, 20:1 dichloromethane: methanol) and the methanol evolved was from time to time evaporated under diminished pressure. It was necessary to replace the benzaldehyde dimethylacetal partially evaporated during the process. After neutralisation with saturated aqueous sodium hydrogen carbonate, the reaction mixture was concentrated, the residue was diluted with dichloromethane and the insoluble salts were filtered off. The filtrate was then concentrated to a syrup, column chromatography (4:1 hexane:ether) of which, followed by preparative TLC of mixed fractions, afforded pure **15** (0.147 g, 59% from **11**) and **16** (0.053 g, 85% from **12**). Compound **15**: syrup; R_f 0.45 (1:1 ether:hexane); $[\alpha]_D^{23}=+63$ (*c* 1.0, $CHCl_3$); IR

(film) ν_{max} 3460 (OH), 1551 and 1395 cm^{-1} (NO_2); ^1H NMR (300 MHz, $CDCl_3$): δ 7.57–7.34 (m, 10H, 2Ph), 5.53 (s, 1H, C*H*-Ph), 4.65 (d, 1H, $J_{1,2}=9.9$, H-1), 4.44 (dd, 1H, $J_{5,6}=4.9$, $J_{6,6'}=10.5$, H-6), 4.26 (d, 1H, $J_{4,5}=9.5$, H-4), 4.17 (dd, 1H, $J_{2,OH}=2.6$, H-2), 3.82 (dd, 1H, $J_{5,6'}=10.4$, H-6′), 3.66 (ddd, 1H, H-5), 2.63 (d, 1H, HO), and 1.78 (s, 3H, Me); ^{13}C NMR (75.6 MHz, $CDCl_3$): δ 136.2–125.9 (2Ph), 101.4 (*C*H-Ph), 92.4 (C-3), 88.0 (C-1), 80.1 (C-4), 72.3 (C-2), 68.9 (C-5), 68.7 (C-6), and 9.7 (Me); HREIMS: *m*/*z* 403.1085 (calcd for $C_{20}H_{21}NO_6S$: 403.1090); 294.0953 (calcd for $C_{20}H_{21}NO_6S$–SPh: 294.0978). Anal. calcd for $C_{20}H_{21}NO_6S$: C, 59.54; H, 5.24; N, 3.47. Found: C, 59.88; H, 5.24; N, 3.44. Compound **16**: syrup; R_f 0.40 (1:1 ether:hexane); $[\alpha]_D^{22}=-227$ (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3468 (OH), 1545 and 1395 (NO_2), and 650 cm^{-1} (CS); ^1H NMR (300 MHz, $CDCl_3$): δ 7.52–7.35 (m, 10H, 2Ph), 5.61 (d, 1H, $J_{1,2}=6.4$, H-1), 5.57 (s, 1H, C*H*-Ph), 4.78 (brdd, 1H, $J_{2,OH}=8.6$, H-2), 4.43 (dd, 1H, $J_{5,6}=5.0$, $J_{6,6'}=10.5$, H-6), 4.41 (d, 1H, $J_{4,5}=9.8$, H-4), 4.22 (ddd, 1H, $J_{5,6'}=9.8$, H-5), 3.86 (dd, 1H, H-6′), 2.70 (brd, 1H, HO), and 1.85 (s, 3H, Me); ^{13}C NMR (75.6 MHz, $CDCl_3$): δ 132.1–126.0 (2Ph), 101.4 (*C*H-Ph), 93.0 (C-3), 91.4 (C-1), 79.7 (C-4), 72.1 (C-2), 68.7 (C-5), 62.3 (C-6), and 11.4 (Me); HREIMS: *m*/*z* 403.1073 (calcd for $C_{20}H_{21}NO_6S$: 403.1090); 294.0965 (calcd for $C_{20}H_{21}NO_6S$–SPh: 294.0978). Anal. calcd for $C_{20}H_{21}NO_6S$: C, 59.54; H, 5.24; N, 3.47. Found: C, 60.02; H, 5.38; N, 3.34.

4.5. *Methyl 6*-O-tert-*butyl-diphenylsilyl-3-deoxy-3*-C-*methyl-3-nitro-α-D-glucopyranoside* **17** *and methyl 6*-O-tert-*butyl-diphenylsilyl-3-deoxy-3*-C-*methyl-3-nitro-β-L-glucopyranoside* **18**

Dry pyridine (0.4 mL) and 4-(dimethylamino)pyridine (DMAP, 0.017 g) were added to a suspension of 1:1 mixed crystals of methyl 3-deoxy-3-*C*-methyl-3-nitro-α-D-glucopyranoside **5** and methyl 3-deoxy-3-*C*-methyl-3-nitro-β-L-glucopyranoside **6**[18,24] (0.600 g, 2.53 mmol) in dry dichloromethane (4 mL), and the mixture was stirred under argon. *tert*-Butyl-diphenylchlorosilane (1.00 mL, 3.80 mmol) was added at 0°C to the mixture, which was then allowed to warm to room temperature for 48 h (TLC monitoring, 12:1 dichloromethane:methanol, or two elutions with ether). The reaction was quenched by adding 1 M HCl until neutral pH (2 mL) and the mixture was shaken with dichloromethane (3×5 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to a syrup, which was subjected to column chromatography (1:4 ether:hexane) to give, separately, **17** (0.451 g, 75%) and **18** (0.496 g, 82%). Compound **17**: syrup; R_f 0.22 (1:2 ether:hexane); $[\alpha]_D^{27}=+54.3$ (*c* 1.0, CH_2Cl_2); IR (film) ν_{max} 3477 (OH), 1547 and 1391 (NO_2), and 704 cm^{-1} (CSi); ^1H NMR (500 MHz, $CDCl_3$): δ 7.7–7.4 (m, 10H, 2Ph), 4.78 (d, 1H, $J_{1,2}=4.5$, H-1), 4.37 (d, 1H, $J_{4,5}=9.9$, H-4), 4.33 (d, 1H, H-2), 3.95 (dd, 1H, $J_{5,6}=4.7$, $J_{6,6'}=11.1$, H-6), 3.92 (dd, 1H, $J_{5,6'}=4.2$, H-6′), 3.54 (m, 1H, H-5), 3.36 (s, 3H, MeO), 2.77 (br s, 1H, HO-4 or 2), 2.45 (br s, 1H, HO-2 or 4), 1.70 (s, 3H, Me-3), and 1.08 (d, 9H, C*Me*$_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 135.6–127.8 (2Ph), 98.8 (C-1), 95.5 (C-3), 71.7 (C-4), 71.5 (C-2), 68.8 (C-5), 64.4 (C-6), 55.8 (MeO), 26.8 (C*Me*$_3$), 19.2 (*C*Me$_3$), and 11.6 (Me-3); FABMS: *m*/*z* 498 (37, $[M+Na]^+$); HRCIMS: *m*/*z* 476.2098 (calcd for $C_{24}H_{33}NO_7Si$+H: 476.2104). Anal. calcd for $C_{24}H_{33}NO_7Si{\cdot}0.5H_2O$: C, 59.48; H, 7.07; N, 2.89. Found: C, 59.36; H, 6.68; N, 2.75. Compound **18**: colourless crystals; mp 128–132°C; R_f 0.29 (1:2 ether:hexane); $[\alpha]_D^{27}=+24.1$ (*c* 0.8, CH_2Cl_2); IR (film) ν_{max} 3468 (OH), 1545 and 1394 (NO_2), and 703 cm^{-1} (CSi); ^1H NMR (500 MHz, $CDCl_3$): δ 7.70–7.38 (m, 10H, 2Ph), 4.41 (dd, 1H, $J_{4,5}=9.6$, $J_{4,OH}=2.0$, H-4), 4.24 (d, 1H, $J_{1,2}=7.9$, H-1), 4.08 (d, 1H, H-2), 3.95 (dd, 1H, $J_{5,6}=4.5$, $J_{6,6'}=10.8$, H-6), 3.92 (dd, 1H, $J_{5,6'}=5.5$, H-6′), 3.50 (s, 3H, MeO), 3.46 (ddd, 1H, H-5), 3.04 (d, 1H, HO-4), 2.39 (br s, 1H, HO-2), 1.68 (s, 3H, Me-3), and 1.06 (s, 9H, C*Me*$_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 135.6–127.8 (2Ph), 101.9 (C-1), 94.3 (C-3), 73.4 (C-5), 73.3 (C-2), 73.0 (C-4), 65.0 (C-6), 57.1 (MeO), 26.8 (C*Me*$_3$), 19.2 (*C*Me$_3$), and 10.2 (Me-3);

FABMS: *m/z* 498 (100, $[M+Na]^+$); HRCIMS: *m/z* 476.2086 (calcd for $C_{24}H_{33}NO_7Si+H$: 476.2104). Anal. calcd for $C_{24}H_{33}NO_7Si$: C, 60.61; H, 6.99; N, 2.94. Found: C, 60.37; H, 6.89; N, 2.89.

*4.6. Reaction of DAST with the 3-C-methyl-3-nitro sugar derivatives **1**, **3–8**, and **13–18**. General procedure*

DAST (660 μL, 5 mmol; or 462 μL, 3.5 mmol, as indicated in each case) was dropped into 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 was allowed to warm to room temperature or heated to reflux, under stirring, until almost complete transformation of the substrate (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 was extracted with dichloromethane (2×25 mL). The combined organic layers were washed with brine (25 mL), dried ($MgSO_4$), 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 3,6-dideoxy-3-*C*-methyl-4-*O*-methyl-3-nitro-α-L-mannopyranoside (**4**, 0.235 g); DAST: 660 μL; solvent: dry dichloromethane (10 mL); temperature: reflux for 2 h. After column chromatography (1:2 dichloromethane:hexane), a 1.3:1 (by ^1H NMR) syrupy mixture of the two anomeric glycosyl fluorides **19** (β) and **20** (α) (global yield, 0.137 g, 58%) was obtained; IR (film): 1553 and 1348 cm^{-1} (NO_2); HRMS: *m/z* 218.1035 (calcd for $C_9H_{16}FNO_5$–F: 218.1028), 191.1079 (calcd for $C_9H_{16}FNO_5$–NO_2: 191.1083).

*4.6.1. 3,6-Dideoxy-3-C-methyl-2,4-di-O-methyl-3-nitro-β-L-glucopyranosyl fluoride **19***

^1H NMR (500 MHz, $CDCl_3$): δ 5.14 (dd, 1H, $J_{1,2}=7.2$, $^2J_{1,F}=53.1$, H-1), 3.92 (dd, 1H, $^3J_{2,F}=12.7$, H-2), 3.67 (d, 1H, $J_{4,5}=9.6$, H-4), 3.55 (dqd, 1H, $J_{5,6}=6.1$, $^4J_{5,F}=0.5$, H-5), 3.46 (d, 3H, $^5J_{OMe,F}=1.3$, MeO-2), 3.35 (s, 3H, MeO-4), 1.58 (s, 3H, Me-3), and 1.40 (d, 3H, Me-5); NOE contacts (differential NOE): Me-3, H-1, H-5; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 118.7 (d, $^1J_{1,F}=213.0$, C-1), 93.1 (d, $^3J_{3,F}=11.4$, C-3), 85.1 (C-4), 82.4 (d, $^2J_{2,F}=24.0$, C-2), 71.1 (d, $^3J_{5,F}=5.2$, C-5), 60.7 (MeO-4), 60.6 (d, $^4J_{OMe,F}=2.1$, MeO-2), 18.0 (Me-5), and 10.4 (Me-3).

*4.6.2. 3,6-Dideoxy-3-C-methyl-2,4-di-O-methyl-3-nitro-α-L-glucopyranosyl fluoride **20***

^1H NMR (500 MHz, $CDCl_3$): δ 5.76 (dd, 1H, $J_{1,2}=3.2$, $^2J_{1,F}=54.0$, H-1), 4.05 (dd, 1H, $^3J_{2,F}=25.6$, H-2), 3.84 (brdq, 1H, $J_{4,5}=10.2$, $J_{5,6}=6.2$, H-5), 3.65 (d, 1H, H-4), 3.42 (br s, 3H, MeO-2), 3.36 (s, 3H, MeO-4), 1.69 (d, 3H, $^5J_{Me,F}=1.3$, Me-3), and 1.36 (d, 3H, Me-5); NOE contacts (differential NOE): Me-3, H-5; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 103.2 (d, $^1J_{1,F}=232.4$, C-1), 93.3 (d, $^3J_{3,F}=3.3$, C-3), 84.8 (C-4), 80.3 (d, $^2J_{2,F}=23.2$, C-2), 68.1 (d, $^3J_{5,F}=1.4$, C-5), 60.8 (MeO-4), 58.8 (MeO-2), 17.6 (Me-5), and 11.3 (d,$^4J_{Me,F}=6.5$, Me-3).

(b) From methyl 3-deoxy-3-*C*-methyl-3-nitro-β-L-glucopyranoside (**6**, 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 ^1H NMR) syrupy mixture (0.089 g, 37%) of the two anomeric glycosyl fluorides **21** (β) and **22** (α); IR (film): 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 **33** (0.071 g, 30%).

*4.6.3. 3,6-Dideoxy-6-fluoro-3-*C*-methyl-2-*O*-methyl-3-nitro-β-L-mannopyranosyl fluoride* ***21***

^{1}H NMR (500 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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).

*4.6.4. 3,6-Dideoxy-6-fluoro-3-*C*-methyl-2-*O*-methyl-3-nitro-α-L-mannopyranosyl fluoride* ***22***

^{1}H NMR (500 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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).

*4.6.5. Methyl 3,4,6-trideoxy-4,6-difluoro-3-*C*-methyl-3-nitro-β-L-galactopyranoside* ***33***

Syrup; R_f 0.25 (1:2 ethyl acetate:hexane); $[\alpha]_D^{23}=+4.7$ (*c* 0.75, $CHCl_3$); IR (film) ν_{max} 3480 (OH), 1556 and 1352 (NO_2), and 1058 cm^{-1} (CF); ^{1}H NMR (500 MHz, $CDCl_3$): δ 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, $CDCl_3$) δ 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); HRCIMS: *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).

(c) From methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-β-L-glucopyranoside (**8**,[18] 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), 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 anomeric glycosyl fluorides **23** (α) and **24** (β); IR (film): 1561 and 1379 cm^{-1} (NO_2).

*4.6.6. 4,6-*O*-Benzylidene-3-deoxy-3-*C*-methyl-2-*O*-methyl-3-nitro-α-L-mannopyranosyl fluoride* ***23***

^{1}H NMR (500 MHz, $CDCl_3$): δ 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, $^5J_{MeO,F}=1.3$, MeO), and 1.84 (d, 3H, $^5J_{Me,F}=0.7$, Me-3); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 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, $^3J_{5,F}=2.8$, C-5), 71.1 (C-6), 57.3 (MeO), and 14.1 (d,$^4J_{Me,F}=1.5$, Me-3).

*4.6.7. 4,6-*O*-Benzylidene-3-deoxy-3-*C*-methyl-2-*O*-methyl-3-nitro-β-L-mannopyranosyl fluoride* ***24***

^{1}H NMR (500 MHz, $CDCl_3$): δ 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, $^5J_{MeO,F}=1.3$, MeO), and 1.89 (d, 3H, $^5J_{Me,F}=1.3$, Me-3); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 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, $^3J_{5,F}=2.8$, C-5), 71.1 (C-6), 57.5 (MeO), and 14.3 (d,$^4J_{Me,F}=2.6$, Me-3).

(d) From phenyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-1-thio-β-D-glucopyranoside (**13**, 0.403 g); DAST: 660 μL; solvent: dry dichloromethane (10 mL); temperature: 0°C (1 h) to ambient (1 h). The reaction afforded, after preparative TLC (1:2 ether:hexane), unreacted starting material (0.074 g, indicating 82% of conversion) and pure compound **29** (0.324 g, 80%, corresponding to 97% yield from converted substrate).

*4.6.8. 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-methyl-3-nitro-2-phenylthio-α-D-mannopyranosyl fluoride **29***

Compound **29** showed physical and spectroscopic properties identical, respectively, to those of **30** [see (e), next paragraph], except for the rotatory power: $[\alpha]_D^{25}=-3.5$ (*c* 1.1, $CHCl_3$).

(e) From phenyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-1-thio-β-L-glucopyranoside (**15**, 0.403 g); DAST: 660 μL; solvent: dry dichloromethane (10 mL); temperature: 0°C (1 h) to ambient (1 h). The reaction afforded, after column chromatography (gradient 1:12 to 1:10 ether:hexane), unreacted starting material (0.048 g, indicating 88% of conversion) and pure compound **30** (0.343 g, 85%, corresponding to 96% yield from converted substrate).

*4.6.9. 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-methyl-3-nitro-2-phenylthio-α-L-mannopyranosyl fluoride **30***

Syrup; R_f 0.41 (1:3 ether:hexane); $[\alpha]_D^{22}=+1.3$ (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 1555 and 1375 (NO_2), and 1007 cm^{-1} (CF); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48–7.37 (m, 10H, 2Ph), 5.95 (d, 1H, $^2J_{1,F}=52.3$, H-1), 5.79 (s, 1H, C*H*-Ph), 4.59 (d, 1H, $J_{4,5}=9.7$, H-4), 4.43 (dd, 1H, $^2J_{6,6'}=10.3$, $J_{5,6}=4.5$, H-6), 4.09 (ddd, 1H, $J_{5,6'}=9.9$, H-5), 3.93 (dd, 1H, H-6′), 3.66 (d, 1H, $^3J_{2,F}=3.7$, H-2), and 2.00 (s, 3H, Me); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 136.4–125.9 (2Ph), 108.4 (d, $^1J_{1,F}=234.8$, C-1), 101.7 (*C*H-Ph), 88.5 (C-3), 75.5 (C-4), 68.5 (C-6), 63.9 (C-5), 57.0 (d, $^2J_{2,F}=25.5$, C-2), and 19.6 (d, $^4J_{Me,F}=6.2$, Me); HRMS: *m*/*z* 405.1051 (calcd for $C_{20}H_{20}FNO_5S$: 405.1046), 249.0925 (calcd for $C_{20}H_{20}FNO_5S$–NO_2–SPh–H: 249.0927). Anal. calcd for $C_{20}H_{20}FNO_5S$: C, 59.25; H, 4.97; N, 3.45. Found: C, 59.32; H, 5.12; N, 3.41.

(f) From methyl 6-*O*-*tert*-butyldiphenylsilyl-3-deoxy-3-*C*-methyl-3-nitro-β-L-glucopyranoside (**18**, 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 anomeric glycosyl fluorides **31** (β) and **32** (α); IR (film): 3452 (OH), 1553 and 1363 (NO_2), 1085 (CF), and 703 cm^{-1} (CSi); FABMS: *m*/*z* 500 (20, $[M+Na]^+$); HRFABMS: *m*/*z* 500.1879 (calcd for $C_{24}H_{32}FNO_6Si$+Na: 500.1881).

*4.6.10. 6-*O*-tert-Butyldiphenylsilyl-3-deoxy-3-*C*-methyl-2-*O*-methyl-3-nitro-β-L-mannopyranosyl fluoride **31***

^{1}H NMR (500 MHz, $CDCl_3$): δ 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, $^5J_{MeO,F}=1.1$, 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, $CDCl_3$): δ 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).

4.6.11. 6-O-tert-*Butyldiphenylsilyl-3-deoxy-3*-C-*methyl-2*-O-*methyl-3-nitro-α-*L*-mannopyranosyl fluoride* ***32***

^{1}H NMR (500 MHz, CDCl$_3$): δ 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, $^5J_{MeO,F}=1.3$, 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$_3$): δ 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).

(g) From methyl 3,6-dideoxy-3-*C*-methyl-4-*O*-methyl-3-nitro-α-L-glucopyranoside (**3**, 0.235 g); DAST: 660 μL; solvent: dry dichloromethane (10 mL); temperature: reflux for 2 h. After column chromatography (1:1 dichloromethane:hexane), a 3:1 mixture of **34** and **35** (by ^{1}H NMR) was obtained as a syrup (global yield, 0.166 g, 70%) IR (film): 1545 and 1345 cm^{-1} (NO$_2$); HRMS: *m*/*z* 218.1025 (calcd for $C_9H_{16}FNO_5$–F: 218.1028), 206.0839 (calcd for $C_9H_{16}FNO_5$–OCH$_3$: 206.0828), 191.1082 (calcd for $C_9H_{16}FNO_5$–NO$_2$: 191.1083).

*4.6.12. (1*R*)-2,5-Anhydro-3,6-dideoxy-1-fluoro-3*-C-*methyl-1,4-di*-O-*methyl-3-nitro-L-mannitol* ***34***

^{1}H NMR (500 MHz, CDCl$_3$): δ 5.20 (dd, 1H, $J_{1,2}=5.9$, $^2J_{1,F}=64.3$, H-1), 4.65 (dd, 1H, $^3J_{2,F}=6.8$, H-2), 4.21 (d, 1H, $J_{4,5}=7.7$, H-4), 3.92 (dq, 1H, $J_{5,6}=6.3$, H-5), 3.58 (d, 3H, $^4J_{OMe,F}=1.4$, MeO-1), 3.37 (s, 3H, MeO-4), 1.71 (d, 3H, $^5J_{Me,F}=1.4$, Me-3), and 1.42 (d, 3H, Me-6); NOE contacts (1D NOESY): Me-6, H-4, H-2; Me-3, H-5, H-1; MeO-4, H-1; ^{13}C NMR (125.7 MHz, CDCl$_3$): δ 110.5 (d, $^1J_{1,F}=218.7$, C-1), 93.1 (C-3), 92.2 (C-4), 81.3 (d, $^2J_{2,F}=30.6$, C-2), 77.7 (C-5), 58.9 (MeO-4), 57.2 (MeO-1), 19.3 (C-6), and 12.4 (d, $^4J_{Me,F}=2.2$, Me-3).

*4.6.13. (1*S*)-2,5-Anhydro-3,6-dideoxy-1-fluoro-3*-C-*methyl-1,4-di*-O-*methyl-3-nitro-L-mannitol* ***35***

^{1}H NMR (500 MHz, CDCl$_3$): δ 5.14 (dd, 1H, $J_{1,2}=6.3$, $^2J_{1,F}=64.4$, H-1), 4.62 (dd, 1H, $^3J_{2,F}=10.4$, H-2), 4.22 (d, 1H, $J_{4,5}=7.6$, H-4), 3.93 (dq, 1H, $J_{5,6}=6.2$, H-5), 3.53 (d, 3H, $^4J_{OMe,F}=1.2$, MeO-1), 3.36 (s, 3H, MeO-4), 1.63 (s, 3H, Me-3), and 1.43 (d, 3H, Me-6); NOE contacts (1D NOESY): Me-6, H-4, H-2; Me-3, H-5, H-1, MeO-1; MeO-4, H-1; ^{13}C NMR (125.7 MHz, CDCl$_3$): δ 110.8 (d, $^1J_{1,F}=222.7$, C-1), 93.0 (d, $^3J_{3,F}=6.1$, C-3), 92.2 (C-4), 81.6 (d, $^2J_{2,F}=24.9$, C-2), 77.8 (C-5), 58.9 (MeO-4), 57.0 (MeO-1), 19.4 (C-6), and 12.1 (Me-3).

A few drops of D$_2$O and one drop of concentrated hydrochloric acid were added to the same solution of the 3:1 mixture of **34** and **35** in CDCl$_3$ used for NMR spectroscopy. After a week at room temperature, the ^{1}H NMR spectrum of this reaction mixture showed the quantitative transformation into 2,5-anhydro-3,6-dideoxy-4-*O*-methyl-3-*C*-methyl-3-nitro-aldehydo-L-mannose **44**: ^{1}H NMR (300 MHz, CDCl$_3$): δ 9.65 (dd, 1H, $J_{1,2}=1.2$, CHO), 5.00 (m, 1H, H-2), 4.16 (d, 1H, $J_{4,5}=6.2$, H-4), 4.11 (ddq, 1H, $J_{5,Me\text{-}6}=6.2$, $^5J_{2,5}=0.5$, H-5), 3.46 (s, 3H, MeO), 1.65 (s, 3H, Me-3), and 1.41 (d, 3H, Me-6); ^{13}C NMR (75.8 MHz, CDCl$_3$): δ 198.4 (C-1), 93.1 (C-3), 92.8 (C-4), 85.3 (C-2), 79.3 (C-5), 59.1 (MeO), 19.1 (C-6), and 11.5 (Me-3).

(h) From methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-α-D-glucopyranoside (**7**[18], 0.325 g); DAST: 470 μL; solvent: dry diglyme (7.9 mL); temperature: ambient (16 h). The reaction afforded, after preparative TLC (two elutions with 1:2 ether:hexane), unreacted starting material (0.247 g, indicating 24% of conversion) and a 2.5:1 (by ^{1}H NMR) mixture of epimers **36**

(0.074 g, 23%, corresponding to 95% yield from converted substrate). Syrup; R_f 0.54 (1:2 ether:hexane); IR (film) ν_{max} 1548 and 1379 (NO_2), and 1028 cm^{-1} (CF); HRMS: m/z 327.1124 (calcd for $C_{15}H_{18}FNO_6$: 327.1118).

*4.6.14. (1*R *and 1*S*)-2,5-Anhydro-4,6-*O*-benzylidene-3-deoxy-1-fluoro-3-*C*-methyl-1-*O*-methyl-3-nitro-D-mannitol* ***36***

Major isomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50–7.36 (m, 5H, Ph), 5.61 (s, 1H, C*H*-Ph), 5.37 (dd, 1H, $^2J_{1,F}=64.1$, $J_{1,2}=4.3$, H-1), 4.72 (dd, 1H, $^3J_{2,F}=12.4$, H-2), 4.60 (dd, 1H, $^2J_{6,6'}=9.5$, $J_{5,6}=4.2$, H-6), 4.49 (d, 1H, $J_{4,5}=9.7$, H-4), 3.98 (dd, $J_{5,6'}=9.7$, H-6′), 3.91 (ddd, 1H, H-5), 3.64 (d, 3H, $^4J_{MeO,F}=1.3$, MeO), and 1.90 (d, 3H, $^5J_{Me,F}=1.4$, Me-3); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 132.3–126.1 (Ph), 111.0 (d, $^1J_{1,F}=219.6$, C-1), 110.1 (*C*H-Ph), 94.2 (C-3), 83.0 (C-4), 81.1 (d, $^2J_{2,F}=28.8$, C-2), 65.5 (C-5), 61.5 (C-6), 57.4 (MeO), and 13.7 (d, $^4J_{Me,F}=10.5$, Me-3).

Minor isomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50–7.36 (m, 5H, Ph), 5.62 (s, 1H, C*H*-Ph), 5.33 (dd, 1H, $^2J_{1,F}=65.0$, $J_{1,2}=5.0$, H-1), 4.67 (dd, 1H, $^3J_{2,F}=12.6$, H-2), 4.50 (d, 1H, $J_{4,5}=9.9$, H-4), 3.99 (dd, $^2J_{6,6'}=9.8$, $J_{5,6'}=9.8$, H-6′), 3.63 (d, 3H, $^4J_{MeO,F}=1.2$, MeO), and 1.59 (s, 3H, Me-3).

(i) From phenyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-1-thio-α-D-glucopyranoside (**14**, 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), unreacted starting material (0.169 g, indicating 58% of conversion), compound **37** (0.038 g, 9.5%, corresponding to 16% yield from converted substrate), and a more polar product ($R_f \approx 0$) which was not studied.

*4.6.15. (1*R *or 1*S*)-2,5-Anhydro-4,6-*O*-benzylidene-1,3-dideoxy-1-fluoro-3-*C*-methyl-3-nitro-1-phenylthio-D-mannitol* ***37***

Compound **37** showed physical and spectroscopic properties identical, respectively, to those of **38** [see (j), next paragraph], except for the rotatory power: $[\alpha]_D^{26}=-92.3$ (*c* 0.65, acetone).

(j) From phenyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-nitro-1-thio-α-L-glucopyranoside (**16**, 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), compound **38** (0.139 g, 34%, corresponding to 48% yield from converted substrate), and a more polar product (0.118 g, $R_f \approx 0$) which was not studied.

*4.6.16. (1*R *or 1*S*)-2,5-Anhydro-4,6-*O*-benzylidene-1,3-dideoxy-1-fluoro-3-*C*-methyl-3-nitro-1-phenylthio-L-mannitol* ***38***

Syrup; R_f 0.54 (1:1 ether:hexane); $[\alpha]_D^{23}=+84.5$ (*c* 0.84, acetone); IR (film) ν_{max} 1557 and 1391 (NO_2), and 1107 cm^{-1} (CF); ^{1}H NMR (500 MHz, CD_3COCD_3): δ 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, 1H, $^2J_{6,6'}=9.1$, $J_{5,6}=4.0$, 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); ^{13}C NMR (125.7 MHz, CD_3COCD_3): δ 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, $^4J_{5,F}=5.0$, C-5), 59.6 (d, $^2J_{2,F}=25.1$, C-2), and 12.8 (Me); HRMS: m/z 405.1046 (calcd for $C_{20}H_{20}FNO_5S$: 405.1046).

(k) From methyl 3,6-dideoxy-3-*C*-methyl-3-nitro-α-L-glucopyranoside (**1**[19], 0.221 g); DAST: 660 μL; solvent: dry dichloromethane (10 mL); temperature: reflux for 2 h. After column chromatography (1:3 ether:hexane), the pure products **39** (0.102 g, 46%) and **40** (0.051 g, 23%) were obtained.

*4.6.17. Methyl 3,5,6-trideoxy-5-fluoro-3-*C*-methyl-3-nitro-β-D-altrofuranoside* ***39***

Syrup; R_f 0.4 (3:1 ether:hexane); $[\alpha]_D^{22} = -104$ (*c* 1.2, CH_2Cl_2); IR (film) ν_{max} 3540 (OH), 1549, and 1352 cm^{-1} (NO_2); ^1H NMR (500 MHz, $CDCl_3$): δ 4.99 (dd, 1H, $J_{1,2} = 5.2$, $^5J_{1,F} = 2.9$, H-1), 4.89 (dd, 1H, $J_{2,OH} = 9.7$, H-2), 4.62 (ddq, 1H, $J_{4,5} = 9.3$, $J_{5,6} = 6.1$, $J_{5,F} = 47.4$, H-5), 4.48 (dd, 1H, $^3J_{4,F} = 5.9$, H-4), 3.47 (s, 3H, MeO), 2.73 (d, 1H, HO), 1.76 (d, 3H, $^5J_{Me,F} = 1.65$, Me-3), 1.45 (dd, 3H, $^3J_{6,F}$ 25.2, Me-6); NOE contacts (1D NOESY): Me-3, H-5; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 101.7 (C-1), 94.4 (C-3), 87.9 (d, $^1J_{5,F} = 168.9$, C-5), 84.3 (d, $^2J_{4,F} = 30.1$, C-4), 78.2 (C-2), 56.1 (MeO), 18.3 (d, $^2J_{Me,F} = 21.2$, C-6), and 13.2 (d, $^4J_{Me,F} = 3.8$, Me-3); FABMS: *m*/*z* 246 (100, $[M+Na]^+$); HRMS: *m*/*z* 192.0671 (calcd for $C_8H_{14}FNO_5$–OCH_3: 192.0672).

*4.6.18. (1*R *or 1*S*)-4,5-Anhydro-3,6-dideoxy-1-fluoro-3-*C*-methyl-1-*O*-methyl-3-nitro-L-galactitol* ***40***

Syrup; R_f 0.6 (3:1 ether:hexane); $[\alpha]_D^{22} = -28.4$ (*c* 0.90, CH_2Cl_2); IR (film) ν_{max} 3532 (OH), 1547, and 1350 cm^{-1} (NO_2); ^1H NMR (500 MHz, $CDCl_3$): δ 5.31 (dd, 1H, $J_{1,2} = 4.1$, $^2J_{1,F} = 64.7$, H-1), 4.38 (dd, 1H, $^3J_{2,F} = 9.0$, H-2), 3.61 (d, 3H, $^4J_{MeO,F} = 1.4$ Hz, MeO), 3.28 (dd, 1H, $J_{4,5} = 2.1$, $^5J_{4,F} = 3.3$, H-4), 3.06 (dq, 1H, $J_{5,6} = 5.2$, H-5), 2.76 (br s, 1H, HO), 1.42 (d, 3H, $^5J_{Me,F} = 1.0$, Me-3), and 1.32 (d, 3H, Me-6); NOE contacts (1D NOESY): Me-3, H-5; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 110.1 (d, $^1J_{1,F} = 221.4$, C-1), 90.9 (d, $^3J_{3,F} = 3.0$, C-3), 75.2 (d, $^2J_{2,F} = 27.8$, C-2), 58.7 (d, $^4J_{4,F} = 2.0$, C-4), 57.4 (MeO), 51.4 (C-5), 16.7 (C-6), and 12.9 (d, $^4J_{Me,F} = 1.0$, Me-3); FABMS *m*/*z* 246 (100, $[M+Na]^+$); HRMS: *m*/*z* 192.0674 (calcd for $C_8H_{14}FNO_5$–OCH_3: 192.0672).

(l) From methyl 3-deoxy-3-*C*-methyl-3-nitro-α-D-glucopyranoside (**5**, 0.236 g); DAST: 660 μL; solvent: dry dichloromethane (10 mL); temperature: reflux for 2 h. After column chromatography (1:3 ether:hexane), the pure products **41** (0.080 g, 33%) and **42** (0.062 g, 26%) were obtained.

*4.6.19. Methyl 3,4,6-trideoxy-4,6-difluoro-3-*C*-methyl-3-nitro-α-D-galactopyranoside* ***41***

Syrup; R_f 0.26 (1:1 ether:hexane); $[\alpha]_D^{19} = +92.4$ (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3460 (OH), 1555 and 1358 (NO_2), and 1064 cm^{-1} (CF); ^1H NMR (500 MHz, $CDCl_3$): δ 4.99 (d, 1H, $^2J_{4,F} = 47.8$, $J_{4,5} = 0$, H-4), 4.91 (d, 1H, $J_{1,2} = 4.5$, H-1), 4.73 (d, 1H, H-2), 4.55 (ddd, 1H, $^2J_{6,F} = 46.1$, $J_{6,6'} = 9.5$, $J_{5,6} = 6.4$, H-6), 4.52 (dddd, 1H, $^2J_{6',F} = 46.4$, $^4J_{6',F} = 1.3$, $J_{5,6'} = 6.3$, H-6′), 4.13 (dddd, 1H, $^3J_{5,F} = 29.0$, $^3J_{5,F} = 11.4$, H-5), 3.42 (s, 3H, MeO), and 1.75 (d, 3H, $^4J_{Me,F} = 1.3$, Me-3); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 99.0 (C-1), 90.2 (d, $^2J_{3,F} = 17.3$, C-3), 89.9 (dd, $^1J_{4,F} = 187.5$, $^3J_{4,F} = 5.4$, C-4), 80.4 (dd, $^1J_{6,F} = 170.8$, $^3J_{6,F} = 6.4$, C-6), 66.1 (C-2), 65.8 (d, $^2J_{5,F} = 24.8$, $^2J_{5,F} = 18.1$, C-5), 56.4 (MeO), and 17.7 (Me-3); HRCIMS: *m*/*z* 242.0840 (calcd for $C_8H_{13}F_2NO_5$+H: 242.0840), 210.0582 (calcd for $C_8H_{13}F_2NO_5$–OCH_3: 210.0578).

*4.6.20. (1*R *or 1*S*)-4,5-Anhydro-3,6-dideoxy-1,6-difluoro-3-*C*-methyl-1-*O*-methyl-3-nitro-D-galactitol* ***42***

Syrup; R_f 0.31 (1:1 ether:hexane); $[\alpha]_D^{25} = -19.0$ (*c* 0.85, acetone); IR (film) ν_{max} 3515 (OH), 1553 and 1355 (NO_2), 1220 (oxirane), and 1093 cm^{-1} (CF); ^1H NMR (500 MHz, CD_3COCD_3): δ 5.35 (dd, 1H, $J_{1,2} = 5.0$, $^2J_{1,F} = 64.2$, H-1), 5.27 (s, HO), 4.74 (ddd, 1H, $J_{5,6} = 2.0$, $J_{6,6'} = 11.2$, $^2J_{6,F} = 47.8$, H-6), 4.41 (dd, 1H, $^3J_{2,F} = 11.2$, H-2), 4.36 (ddd, 1H, $J_{5,6'} = 5.7$, $^2J_{6',F} = 47.2$, H-6′), 3.57 (d, 3H, $^4J_{MeO,F} = 1.5$, MeO), 3.55 (dd, 1H, $J_{4,5} = 2.0$, $^4J_{4,F} = 3.5$, H-4), 3.46 (dddd, 1H, $^3J_{5,F} = 13.7$, H-5), and 1.52 (d, 3H, $^5J_{Me,F} = 0.7$, Me-3); ^{13}C NMR (125.7 MHz, CD_3COCD_3, at –25°C): δ 112.2 (d, $^1J_{1,F} = 226.3$, C-1), 92.3 (C-3), 83.1 (d, $^1J_{6,F} = 176.0$, C-6), 75.1 (d, $^2J_{2,F} = 27.7$, C-2), 57.4 (MeO), 55.1 (dd, $^3J_{4,F} = 8.8$, $^4J_{4,F} = 5.0$, C-4), 53.1 (d, $^2J_{5,F} = 22.6$, C-5), and 12.6 (Me-3); CIMS: *m*/*z* 242 (10, $[M+1]^+$); HRCIMS: *m*/*z* 242.0841 (calcd for $C_8H_{13}F_2NO_5$+H: 242.0840).

(m) From methyl 6-*O*-*tert*-butyldiphenylsilyl-3-deoxy-3-*C*-methyl-3-nitro-α-D-glucopyranoside (**17**, 0.475 g); DAST: 462 μL; solvent: diglyme (7.6 mL); temperature: ambient for 2 h. After quenching the reaction by adding methanol (20 mL), the general workup was followed. Column chromatography (1:4 ether:hexane) afforded unreacted starting material (0.076 g, indicative of 85% of conversion) and pure product **43** (0.076 g, 15%, corresponding to 18% yield from converted substrate).

*4.6.21. (1*R *or 1*S*)-4,5-Anhydro-6-*O-tert-*butyldiphenylsilyl-3-deoxy-1-fluoro-3-*C*-methyl-1-*O*-methyl-3-nitro-D-galactitol **43***

Syrup; R_f 0.35 (1:1 ether:hexane); $[\alpha]_D^{21} = +17.4$ (*c* 0.86, acetone); IR (film) ν_{max} 3436 (OH), 1545 and 1386 (NO_2), 973 (CF), 820 (oxirane), and 703 cm^{-1} (CSi); ^1H NMR (500 MHz, CD_3COCD_3): δ 7.70–7.43 (m, 10H, 2Ph), 5.35 (dd, 1H, $J_{1,2} = 4.9$, $^2J_{1,F} = 64.2$, H-1), 4.46 (m, 1H, $^3J_{2,F} = 5.7$, H-2), 3.93 (dd, 1H, $J_{5,6} = 2.7$, $J_{6,6'} = 12.0$, H-6), 3.76 (dd, 1H, $J_{5,6'} = 4.4$, H-6′), 3.61 (dd, 1H, $J_{4,5} = 2.0$, $^5J_{4,F} = 1.8$, H-4), 3.57 (s, 3H, MeO), 3.32 (ddd, 1H, H-5), 1.52 (s, 3H, Me-3), and 1.03 (s, 9H, *t*-Bu); ^{13}C NMR (125.7 MHz, CD_3COCD_3): δ 136.5–128.5 (2Ph), 112.6 (d, $^1J_{1,F} = 226.3$, C-1), 93.0 (C-3), 75.9 (d, $^2J_{2,F} = 25.1$, C-2), 63.9 (C-6), 57.7 (C-4), 55.8 (C-5), 56.1 (MeO), 27.1 (CMe_3), 19.8 (CMe_3), and 13.6 (Me-3); FABMS: *m*/*z* 500 (45, $[M+Na]^+$); HRCIMS *m*/*z* 478.2036 (calcd for $C_{24}H_{32}FNO_6Si$+H: 478.2061).

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