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Synthesis and Structural Characteristics of all Mono- and Difluorinated 4,6-Dideoxy-D-*xylo*-hexopyranoses

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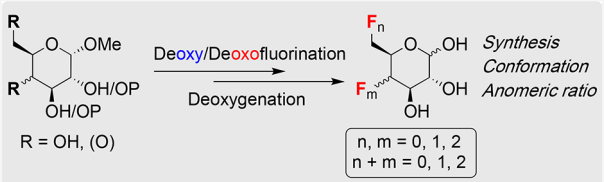
ABSTRACT: Protein−carbohydrate interactions are implicated in many biochemical/biological processes that are fundamental to life and to human health. Fluorinated carbohydrate analogues play an important role in the study of these interactions and find application as probes in chemical biology and as drugs/diagnostics in medicine. The availability and/or efficient synthesis of a wide variety of fluorinated carbohydrates is thus of great interest. Here, we report a detailed study on the synthesis of monosaccharides in which the hydroxy groups at their 4- and 6-positions are replaced by all possible mono- and difluorinated motifs. Minimization of protecting group use was a key aim. It was found that introducing electronegative substituents, either as protecting groups or as deoxygenation intermediates, was generally beneficial for increasing deoxyfluorination yields. A detailed structural study of this set of analogues demonstrated that dideoxygenation/fluorination at the 4,6-positions caused very little distortion both in the solid state and in aqueous solution. Unexpected trends in α/β anomeric ratios were identified. Increasing fluorine content always increased the α/β ratio, with very little difference between regio- or stereoisomers, except when 4,6-difluorinated.



All mono/difluoro 4,6-dideoxy-D-*xylo*-hexopyranoses

INTRODUCTION

Incorporation of fluorine into bioactive molecules is common in the drug discovery process due to the ability of fluorine to modulate various chemical and physical properties.[1−3] In the context of carbohydrates, fluorination enhances enzymatic and hydrolytic stabilities of glycosides by destabilizing the oxonium-type intermediates through which they typically degrade.[4,5] This has found application in, for example, the development of mechanism-based inhibitors.[6,7] Another important application of fluorine incorporation in carbohydrates is as a probe to study the interaction of individual hydroxyl groups with proteins,[8,9] and deoxyfluorination has also been shown to modulate other interactions, such as C−H···π.[10,11] Increasingly, the fluorine atom is introduced to serve as an NMR label to probe glycan−protein binding interactions[12] or to investigate sugar membrane transport.[13−16] The modulation in carbohydrate lipophilicity upon deoxofluorination reactions has also been reported.[17−20] Finally, the use of ^{18}F for PET imaging is another important application, with 2-deoxy-2-fluoroglucose being one of the most important PET radiopharmaceuticals, seeing use as a generic tumor tracer and to study glucose metabolism.[21,22] However, many other sugars have also been applied in this area.[21−23] Hence, the synthesis and investigation of fluorinated carbohydrates is of great interest.

There have been a number of vicinal difluorinated dideoxysugars reported. In a landmark study, the group of Withers reported that the affinity of 1,2-dideoxy-1,2-difluorinated glucoses analogues toward glycogen phosphorylase was higher than that of the respective monofluorinated derivatives.[9] The 1,2-dideoxy-1,2-difluorinated mannoses as well as 1,2-dideoxyglucose all have a much weaker binding affinity. The importance of the presence of fluorine substitution, and the stereochemistry of the C−F groups, points to effects such as hydrogen bonding or dipolar interactions. The difference between the monofluorinated and difluorinated motifs points to a hydrophobic desolvation effect, and the combination of these effects has aptly been coined "polar hydrophobicity".[15,24] Other examples include a 2,3,4-trideoxy-2,2,3,3,4,4-hexafluorinated hexose and 2,3,4-trideoxy-2,3,4-trifluorinated hexoses,[15,24] which have been shown to cross the erythrocyte membrane through GLUT-1 transporter protein. Our group has shown that 2,3-dideoxy-2,2,3,3-tetrafluorinated Gal*p*-UDP and Gal*f*-UDP derivatives have a higher affinity for galactose mutase than the parent galactose based derivatives.[25,26] Hence, the study of polyfluorinated sugars is of interest.

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In virtually all of the above examples, the fluorine atom(s) replaced one or more hydroxyl groups, but in principle, fluorination of deoxysugars at the position of the natural deoxygenation is also of interest. Deoxygenated sugars occur widely in nature and are an important class of sugars found in plants, fungi, and microorganisms.[27,28] Consequently, their synthesis and conformational analysis have received much attention,[27,29,30] and fluorination at the 6-position of common 6-deoxysugars such as L-fucose has been reported.[31−35]

Dideoxygenated sugars are less common, but 2,6-dideoxy- and 3,6-dideoxysugars are important constituents of bioactive compounds including macrolide antibiotics and cardiac glycosides (e.g., digitoxose), which without the sugar group have reduced or no bioactivity. Their synthesis[36−44] and conformational analysis[45] continue to be the subject of much study. Hexoses with dideoxygenation at the 4- and 6-positions are rarer sugars yet have been reported to play key roles in macrolide antibiotic pharmacokinetics, pharmacodynamics, and molecular target recognition.[46−49] Thorson et al. recently described an elegant approach for the synthesis of all eight possible 2,3-diastereomers of 4,6-dideoxyhexoses in enantiomerically pure form from a single natural product source.[50] The best known 4,6-dideoxysugar in nature is chalcose (Figure 1), which is an essential constituent of lankamycin and the

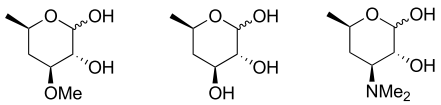

Figure 1. Naturally occurring 4,6-dideoxyhexoses.

chalcomycin macrolide antibiotics, which without chalcose do not show bioactivity.[51−53] The nonmethylated 4,6-dideoxy-D-*xylo*-hexopyranose has been found as part of the macrolide neutramycin. Finally, desosamine is an amino-4,6-dideoxy sugar also found as part of many macrolide antibiotics including erythromycin, oleandromycin, mycinamycin, methymycin/pikromycin, and megalomycin.[27,28,54−56] The biosynthesis of deoxysugars typically starts from common monosaccharides through deoxygenation reactions, which for dideoxygenated sugars is still subject to much research.[28,57]

As part of our interest in the synthesis and applications of fluorinated dideoxygenated carbohydrates, so far at the 2,3- and 3,4- positions, we report here the synthesis of a library of fluorinated 4,6-dideoxy-D-*xylo*-hexopyranoses comprising the three possible monofluorinated derivatives **1**−**3** (Figure 2), the two possible 4,6-difluorinated stereoisomers **4** and **5**, and the two possible geminal difluorides **6** and **7**. The emphasis was on efficient syntheses minimizing the use of protecting groups.

While most of these targets are novel or have not yet been described in the D-form, there is precedence for the introduction of many of these fluorination motifs. An overview is given in Schemes 1 and 2. Withers and co-workers synthesized **10** (Scheme 1a) from the 4-deoxyglucose **8** derivative by direct fluorination with diethylaminosulfur trifluoride (DAST), which gave yields below 20% after a tedious purification.[58] A three-step, one-pot protection strategy leading to the 2,3-*O*-acetylated derivative **11** allowed for a greater fluorination yield of 66%, but due to the protection/deprotection steps, overall a similar 22% yield for **11** from **8** was obtained. Compound **11** was then converted in a two-step

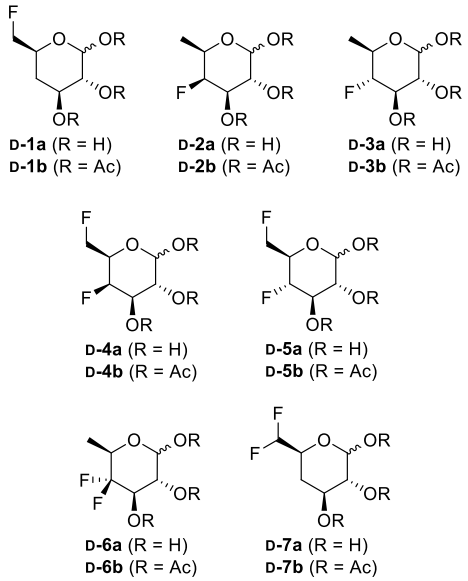

Figure 2. 4,6-Dideoxygenated target structures.

sequence to give D-**1b** as the pure β-anomer.[59] Synthesis of the 4-deoxy-4-fluorinated fucose derivatives proved to be low-yielding: a fluoride displacement on the mesylate derived from quinovose derivative **12** (Scheme 1b) led to **13** in 25% yield. The 4-deoxy-4-fluoro-D-fucoside D-**2b** was then obtained by two further protecting group manipulations.[60] DAST fluorination was attempted on the D-quinovose derivative **14** (Scheme 1c) but afforded none of the expected 4-deoxy-4-fluorofucoside **17**. Instead, a very low yield of the quinovose derivative **15** was obtained, with 5-fluoroaltrofuranoside **16** as the major product.[61] The retention and rearrangement were both explained by the displacement of the leaving group by the ring oxygen leading to a 4,5-epoxonium derivative (not shown), which was then opened by fluoride anion mainly at C-5, leading to **16**. Our group has reported that DAST treatment of unprotected methyl quinovoside **18** (Scheme 1d) did lead to the corresponding 4-deoxy-4-fluorofucose derivative **19**, albeit in a low yield.[62] In contrast, deoxyfluorination with DAST at the 4-position of L-fucose derivatives to give quinovose derivatives was more successful (Scheme 1e): **20**−**22** were converted to **23**−**25** with the desired inversion of configuration in reasonable to good yield.[63,64] It was reported that in the reaction of **21** a workup with NaOH resulted in the recovery of 42% of starting material, which was attributed to hydrolysis of unreacted aminosulfite intermediate (not shown).[64] Starting from **22**, the byproduct **26** was also isolated, the formation of which was explained by an elimination followed by glycal hydrofluorination.[59] Deprotection of **25** gave 4-deoxy-4-fluoro-L-quinovose (4,6-dideoxy-4-fluoro-L-glucose) L-**3a**.[59]

In general, the synthesis of the starting substrates mentioned in Scheme 1 requires several steps. While 4-deoxyglucose is commercially available, it is relatively expensive and its synthesis relies on the reduction of 2,3,6-protected 4-halo or 4-thiocarbonyl glucoside derivatives.[9,65,66] The synthesis of **12** was achieved *via* NBS-induced ring-opening of the 4,6-*O*-benzylidene-protected derivative of methyl-α-D-glucopyranoside, followed by THP ether protection and $LiAlH_4$ reduction of the resultant 6-bromo derivative. The quinovose derivative **14** was prepared by reduction of the corresponding 2,3-di-*O*-

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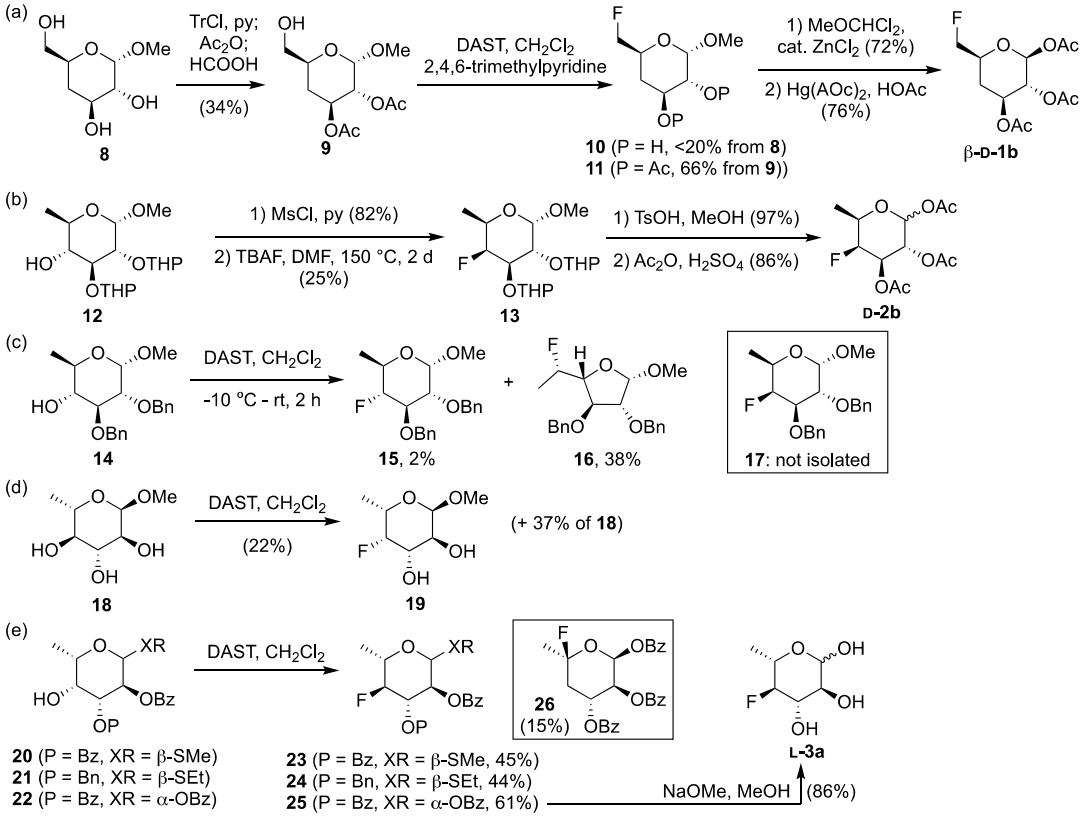
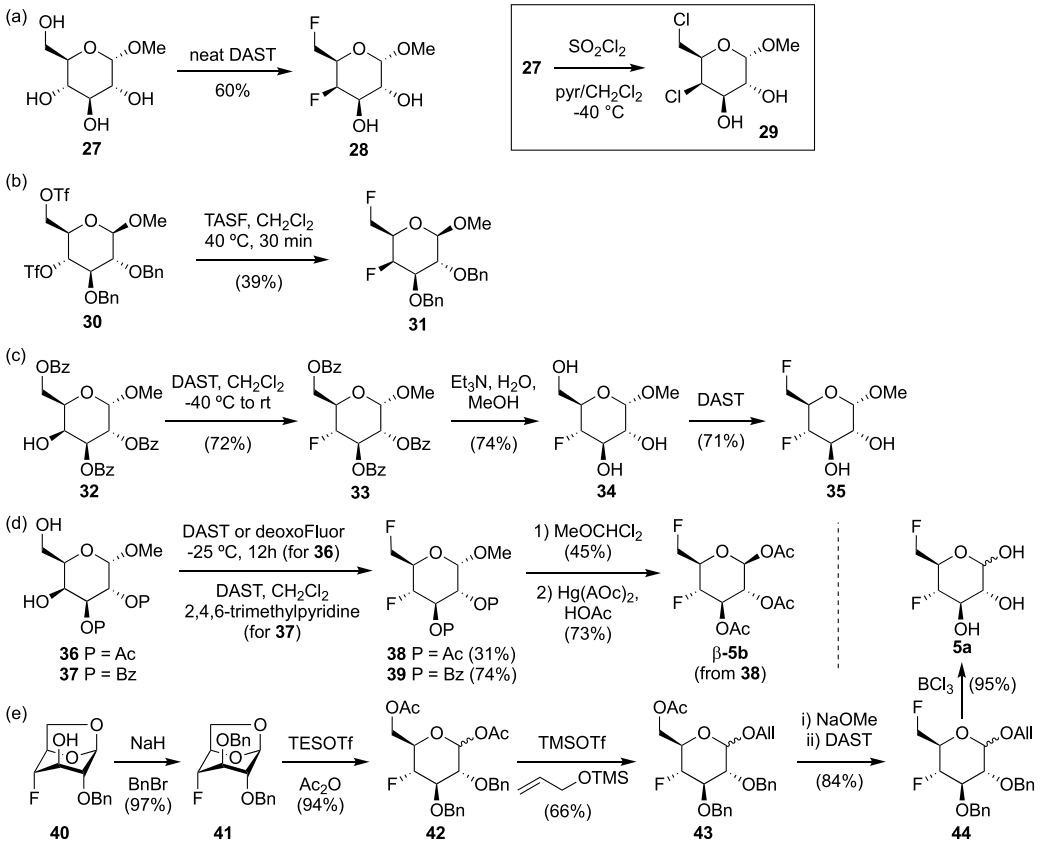
Scheme 1. Overview of Previous Syntheses of Monofluorinated 4,6-Dideoxyhexose Sugars



Scheme 2. Overview of the Syntheses of Difluorinated 4,6-Dideoxyhexose Sugars



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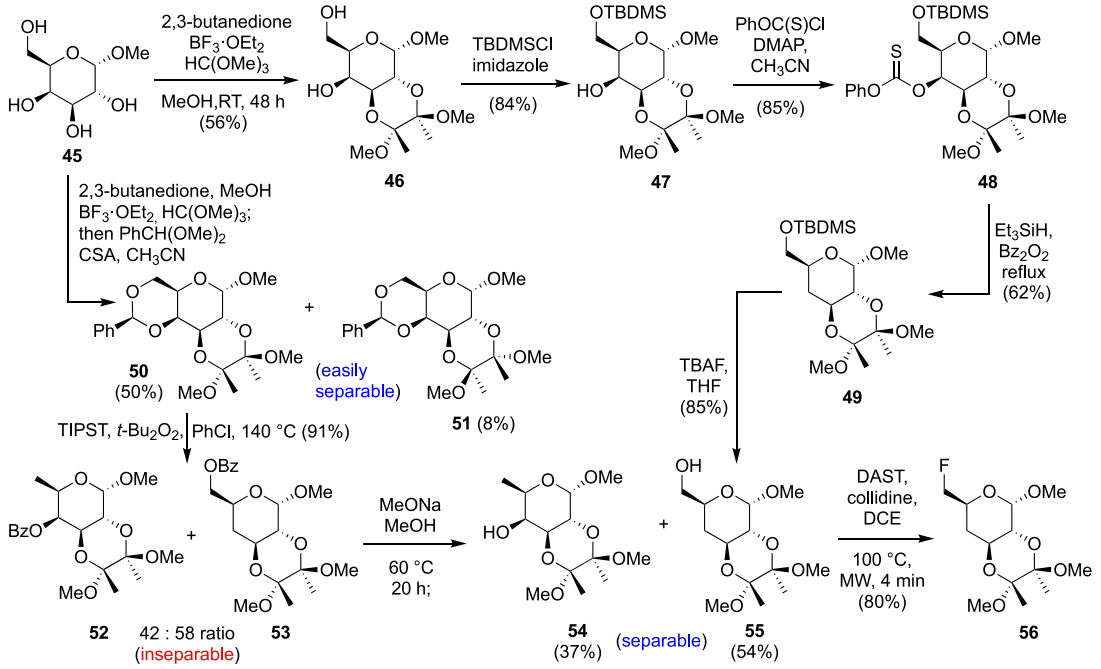
Scheme 3. Routes toward 4- and 6-Deoxygalactoside Derivatives Using the BDA Protecting Group[a]



[a]TIPST = triisopropylsilanethiol.

benzyl 6-*O*-tosyl precursor,[67] ultimately derived from the same benzylidene-protected glucoside as **12** (not shown). Conversely, **20**−**22** were efficiently obtained from either methyl or ethyl thiofucoside or fucose itself. However, given D-fucose is much more expensive, access to D-**2**/**3** is less straightforward.

The synthesis of methyl 4,6-difluorogalacto and -glucosides is well described (Scheme 2). Direct diaminosulfur trifluoride (DAST) treatment of methyl α-D-glucopyranoside **27** leads to the 4,6-dideoxy-4,6-difluorogalactoside **28** in relatively high yield (Scheme 2a).[68,69] The corresponding sulfuryl chloride mediated chlorination leading to the dichlorogalactoside **29** has also been reported, obtained in 45% yield from **27**.[70,71] In both cases, all alcohols are thought to be activated for nucleophilic attack by fluoride or chloride, but the axial anomeric substituent repels the approach of the nucleophile at the 3-position, and the presence of the more electron-withdrawing anomeric acetal group slows down attack at the 2-position. The primary 6-position reacts first, then the 4-position, and once the axial fluoride/chloride is installed at the 4-position, it then additionally hinders S_N2 reaction at the 2-position.[68,72] As an alternative to the DAST-mediated deoxyfluorination, Szarek and co-workers effected the double displacement of bis-triflate **30** (Scheme 2b) with tris-(dimethylamino)sulfonium difluorotrimethylsilicate (TASF), accessing benzyl-protected methyl 4,6-dideoxy-4,6-difluoro-β-D-galactoside **31** in 39% yield.[73] However, routes toward the gluco-configured analogue are more circuitous. 4,6-Dideoxy-4,6-difluoroglucoside **35** (Scheme 2c) is prepared by a sequential fluorination from 2,3-protected galactoside: starting from the 2,3,6-tribenzoate **32**, accessible in one step from methyl α-D-galactopyranoside,[74] fluorination at the 4-position of **32** gives the glucose derivative **33** in excellent yield.[75,76] Benzoate hydrolysis then gives methyl 4-deoxy-4-fluoro α-D-glucopyranoside **34**,[77] which can then be selectively fluorinated at the primary 6-OH, again in excellent yield to give **35**.[77] Direct dideoxydifluorination has been widely applied. From the 2,3-diacetate **36** (Scheme 2d) a moderate yield of **38** was reported,[58] but on the equivalent dibenzoate **37**, an high yield of **39** was obtained.[75] Two-step anomeric acetylation of **38** then gave the triacetate **5b** as the β-anomer. More recently, Giguère and co-workers reported a 1,6-anhydrosugar-based route toward **5a** (Scheme 2e).[20] This approach begins from known fluorinated levoglucosan derivative **40**, itself prepared in five steps from levoglucosan.[78]

Benzylation of the free hydroxyl to obtain **41** preceeds Lewis acid catalyzed ring-opening and concomitant acetolysis, affording an anomeric mixture of **42**. In order to access the 6-OH selectively, the anomeric acetate was first transformed into allyl glycoside **43**, allowing selective Zemplén deprotection and deoxyfluorination of the 6 position, furnishing **44**. Global deprotection using BCl_3 unmasks 4,6-dideoxy-4,6-difluoroglucose **5a** in 48% overall yield from **40**.

Finally, it is relevant to mention that 4,6-dideoxygenated 6,6,6-trifluorinated sugars have been synthesized by the group of Qing, based on a de novo synthesis using Sharpless dihydroxylation chemistry (not shown).[79]

RESULTS AND DISCUSSION

Introduction of 4,6-Dideoxy-6-fluoro Substitution. To avoid the use of 4-deoxyglucose as starting material (cf. Scheme 1), it was decided to devise a new synthesis of 4,6-dideoxy-6-fluoro-D-*xylo*-hexopyranoside sugars. Our initial approach was based on the selective protection of the equatorial 2- and 3-OH groups of methyl α-D-galactopyranoside **45** (Scheme 3) to give the most stable butanediacetal ring appendage (BDA).[80,81] In the first instance, a mixture of 2,3-protected BDA isomers is obtained;[82] however, the use of BF_3·OEt_2 with prolonged reaction times—followed by meticulous chromatography—led to the BDA-protected galactoside **46**.[82−84] This was followed by selective protection of the 6-position as silyl ether **47**. Tin-free reductive deoxygenation of the corresponding thiocarbonate **48** using triethylsilane and

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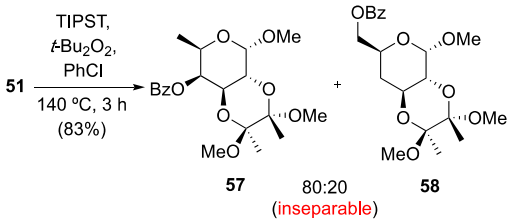
benzoyl peroxide led to **49**, and TBDMS removal finally gave the 4-deoxy-D-*xylo*-hexopyranoside derivative **55**. This substrate was also obtained by an alternative route based on a deoxygenation protocol developed by Dang and co-workers of sugar-based 2-phenyl-1,3-dioxolane rings under radical conditions.[85] They reported that radical chain redox rearrangement of methyl 4,6-*O*-benzylidene-α-D-galactopyranoside with the (commercially available) triisopropylsilanethiol (TIPST) reagent, using only 5 mol % of TIPST and 0.5 equiv of di-*tert*-butyl peroxide, gives a 40:60 mixture of 4-*O*-benzoyl-6-deoxy- and 6-*O*-benzoyl-4-deoxy- derivatives, regardless of the nature of the alcohol protecting groups at the 2- and 3-position (acetyl or methyl). The required 4,6-benzylidene substrate **50** was synthesized from **45** as reported.[82] The BDA diastereomers were now easily separated. From **50**, application of the Dang methodology afforded **52** and **53** in 91% combined yield on a 7 g scale, and it was shown to occur with the expected regioselectivity (ratio **52** (6-deoxy):**53** (4-deoxy) = 42:58). The inseparable mixture was treated with sodium methoxide to offer the now separable 6-deoxy and 4-deoxy galactosides **54** and **55** in 37% and 54% yield, respectively. Finally, deoxofluorination of **55** using a modified procedure by Wagner et al. that employed DAST and 2,4,6-collidine under microwave irradiation[86] successfully afforded the desired **56** in excellent yield.

As a curiosity, the reduction of the benzylidene acetal of the 2,3-butane diacetal diastereomer **51** (Scheme 4) proceeded with the opposite regioselectivity. The 6-deoxygenated product **57** was now obtained as the major isomer in an 80:20 ratio. The origin for this reversal in reduction regiochemistry is unclear but will be related to the different butanediacetal ring conformation of **50** and **51**.

Scheme 4. Reduction of the Benzylidene Acetal of the 2,3-Protected BDA Minor Diastereomer 51



While this process was easily conducted on scale, a shorter, protecting group free route was also developed (Scheme 5), inspired by a successful deoxychlorination example at the 4-position of *N*-Cbz-protected methyl 6-aminoglucoside[70,71] with SO_2Cl_2.[87] Hence, it was envisioned to introduce the 4-Cl group directly on a 6-deoxy-6-fluoroglucose derivative. Starting from methyl D-glucoside **27**, selective monofluorination at the most reactive 6-position was achieved by Card's method[76] to give the 6-fluoro derivative **59** in excellent yield. In our hands, the number of equivalents of DAST could be reduced from 6 to 3 without observing any decrease in yield.

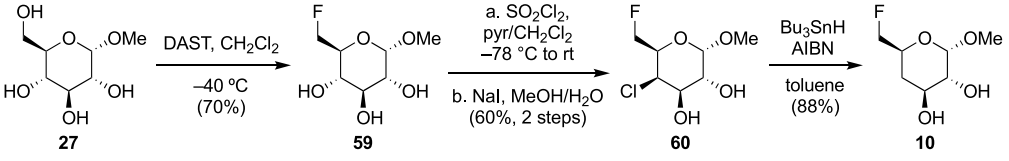
Pleasingly, applying the deoxychlorination reaction using conditions developed by Minnaard et al.[88] followed the expected regioselectivity as observed for the 4,6-dideoxydifluorination (cf. Scheme 2) to give the 4-chloro-6-fluorogalactose derivative **60** in 60% yield. The *galacto* stereochemistry was confirmed by ^{1}H NMR analysis, in which H4 was found to appear as a doublet of doublets, with $^3J_{H4-H3}$ 3.7 Hz and $^3J_{H4-H5}$ 1.2 Hz, indicative of two ax−eq couplings. Finally, reduction of the chloride with tributyltin hydride initiated by AIBN in refluxing toluene smoothly afforded the desired 4,6-dideoxy-6-fluoro derivative **10** in 88% yield. Therefore, the 4,6-dideoxy-6-fluoro motif could be introduced via a new three-step operation in 37% overall yield, without the use of protecting groups.

Introduction of 4,6-Dideoxy-4-fluoro Substitution (4-Deoxy-4-fluoro Fucose Stereochemistry). As shown in Scheme 1, attempted deoxyfluorination on the D-quinovose derivative **14** did not lead to the expected 4-deoxy-4-fluorofucoside product **17**,[61] but when the 2 and 3-positions were unprotected, a low 22% yield was obtained.[62] We presumed that the nonreacting alcohol groups at the 2- and 3-positions are converted to the strongly electron-withdrawing aminodifluorosulfite intermediates by the DAST reagent, which may have minimized rearrangement reactions. Hence, introduction of an electron-withdrawing group at the 6-position was proposed to further enhance the deoxyfluorination yield (Scheme 6). Selective primary tosylation of α-D-glucopyranoside **27** was achieved at low temperature, as position 2 was found to slowly react at room temperature.

Pleasingly, deoxyfluorination of 6-*O*-tosylated **61** resulted in a markedly improved 49% yield of the corresponding 4-fluoro-6-tosyl product **62**. However, the subsequent reduction of tosylate **62** proved capricious; the reaction did not progress at 0 °C, and carrying out the reaction with $LiAlH_4$ at reflux resulted in the isolation of D-**19** in only 4% yield. Without a 4-OH group, reduction via an oxetane intermediate is not possible, which could be the reason for the reaction failure. These harsh conditions also lead to the formation of an anhydro byproduct **63**, isolated in 16% yield. This outcome can be rationalized by deprotonation of the 3-OH proton and subsequent displacement of the 6-OTs upon ring inversion to the $^1C_4$ chair form.[89] Replacement of $LiAlH_4$ with $LiBEt_3H$ at 0 °C resulted in a much improved 67% yield of **63**, at the expense of complete suppression of the desired reduction to D-**19**.

Hence, to achieve 4-deoxyfluorination with an electron-withdrawing group at the 6-position, we applied the deoxychlorination/reduction strategy previously employed for the 4,6-dideoxy-6-fluoro derivative **10** (cf. Scheme 5). Initially, Appel conditions[90] accessed methyl 6-chloro-6-deoxy-D-glucopyranoside **64** in 64% yield; however, we were drawn to a little-used procedure published by Long in 1969, which

Scheme 5. Introduction of the 4,6-Dideoxy-6-fluoro Substitution



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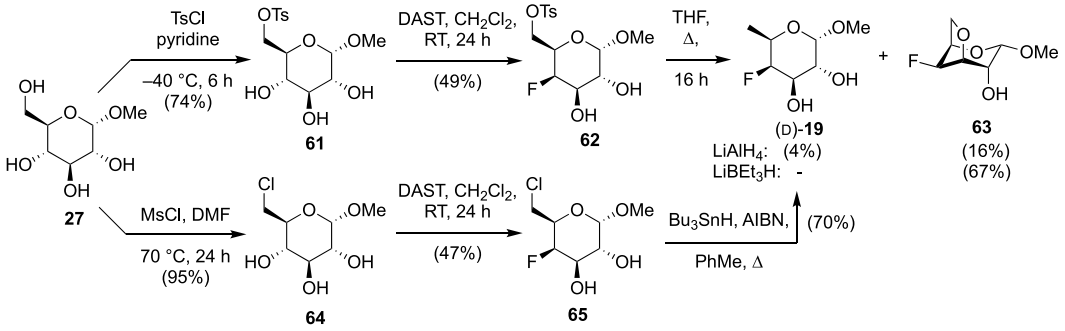
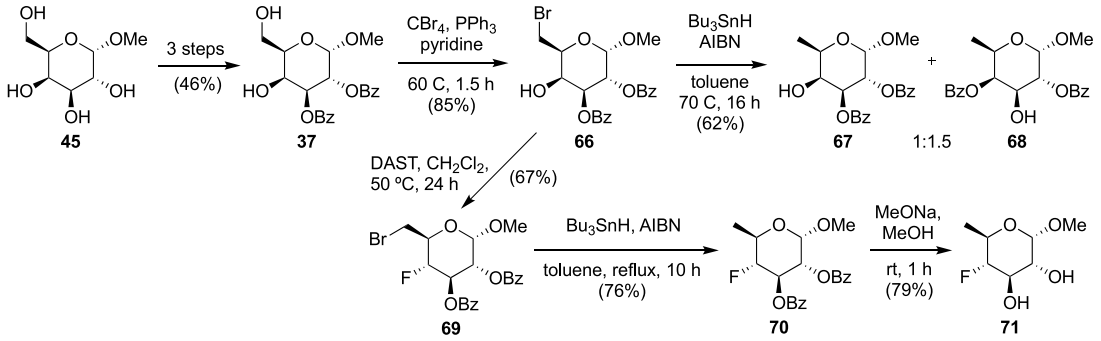
Scheme 6. Introduction of the 4,6-Dideoxy-4-fluoro Substitution (Fucose Stereochemistry)



Scheme 7. Introduction of the 4,6-Dideoxy-4-fluoro Substitution (Quinovose Stereochemistry)



used 2 equiv of methanesulfonyl chloride as the chloride source, bypassing the need to use hepatotoxic CCl_4.[91] In our hands, this afforded **64** in near-quantitative yield. Subsequent deoxyfluorination with DAST furnished **65** in 47% yield, possessing the desired 4-fluoro-6-chloro motif. Finally, application of the Bu_3SnH/AIBN reduction in refluxing toluene would afford the desired deoxygenated product D-**19**, this time in a much improved 70% yield (31% over three steps).

Introduction of 4,6-Dideoxy-4-fluoro Substitution (4-Deoxy-4-fluoroquinovose Stereochemistry). In contrast to dideoxyfluorination of unprotected methyl α-D-glucopyranoside **27** leading to the 4,6-dideoxy-4,6-difluorogalactose derivative in good yield (cf. Scheme 2), subjecting methyl α-D-galactopyranoside **45** to these conditions leads to a mixture of regioisomers. This mirrors the low-yielding monofluorination of **45** in which the 6-deoxy-6-fluorogalactose derivative could only be obtained in yields ranging from 20 to 25%,[92] compared to 60 to 70% for the corresponding process from the methyl glucoside **27** leading to 6-deoxy-6-fluoroglucose (not shown).[76] Hence, a direct deoxyfluorination strategy from unprotected methyl α-D-fucoside was not attempted. Instead, an approach involving protection of the alcohols at the 2- and 3-position was pursued. As shown in Scheme 1, Lindhorst et al. successfully deoxyfluorinated the 1,2,3-tribenzoylated L-fucoside **22**.[59] However, the high cost of D-fucose prevented us from using the same strategy, and a synthesis from methyl α-D-galactopyranoside **45** was carried out (Scheme 7) which was converted to the known methyl 2,3-di-*O*-benzoyl-α-D-galactopyranoside **37** in three steps.[93] Deoxygenation was envisioned via selective 6-bromination using an Appel reaction to give **66**. Adapting protocols from Cléophax and co-workers,[94] 1 equiv of CBr_4 was used to avoid any overhalogenation at OH-4. For large-scale reactions (3 g), precipitation and filtration of most of the triphenylphosphine oxide with Et_2O afforded a crude product easily purified by column chromatography to give the bromide **66** in 85% yield. However, radical reduction of **66** with Bu_3SnH led to a 1:1.5 mixture of the desired 2,3-dibenzoyl compound **67** and the migrated 2,4-dibenzoyl isomer **68**. This observation is consistent with a study by Roslund, Leino, and co-workers, who reported on the fast migration of benzoyl esters between positions 3 and 4.[95]

Instead, direct deoxyfluorination of **66** (7 g scale) using DAST in refluxing CH_2Cl_2 gave the bromofluorosugar **69** in 67% yield, consistent with the yield obtained by Lindhorst et al. on their fucose intermediate (cf. **22** → 25, Scheme 1).[59] Inversion of stereochemistry was determined by NMR analysis and was also unambiguously confirmed by X-ray crystallographic analysis of a single crystal (Figure 3). The bromide

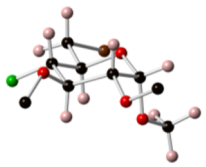


Figure 3. Crystal structure of methyl 4,6-dideoxy-2,3-di-*O*-benzoyl-6-bromo 4-fluoro-α-D-glucopyranoside **69** (benzoyl protecting groups have been removed for clarity).

group could now be reduced on large (8 g) scale without any risk of benzoyl migration to yield 76% of the deoxyfluorosugar **70**. Subsequent alcohol deprotection was easily performed with sodium methoxide to offer methyl 4-deoxy-4-fluoro-α-D-quinovoside **71** in 79% yield. Direct conversion of **69** into **71** by treatment with $LiAlH_4$ was not successful. Starting from **45**, application of the MsCl mediated deoxychlorination procedure, followed by C4-deoxyfluorination, and chloride reduction may result in an even higher yield for the

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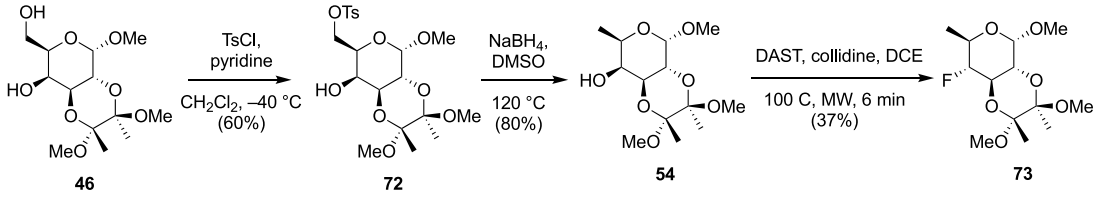
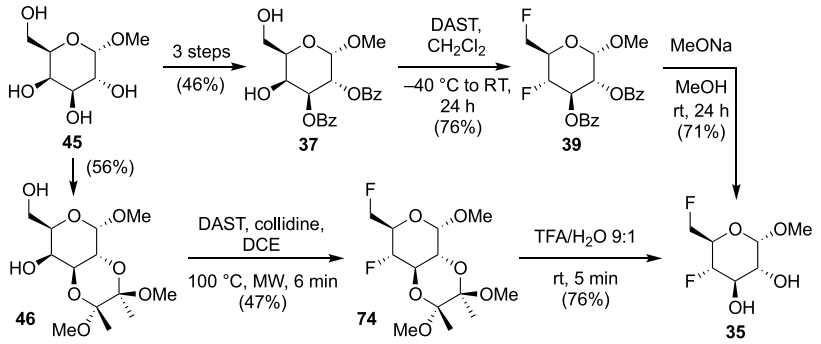
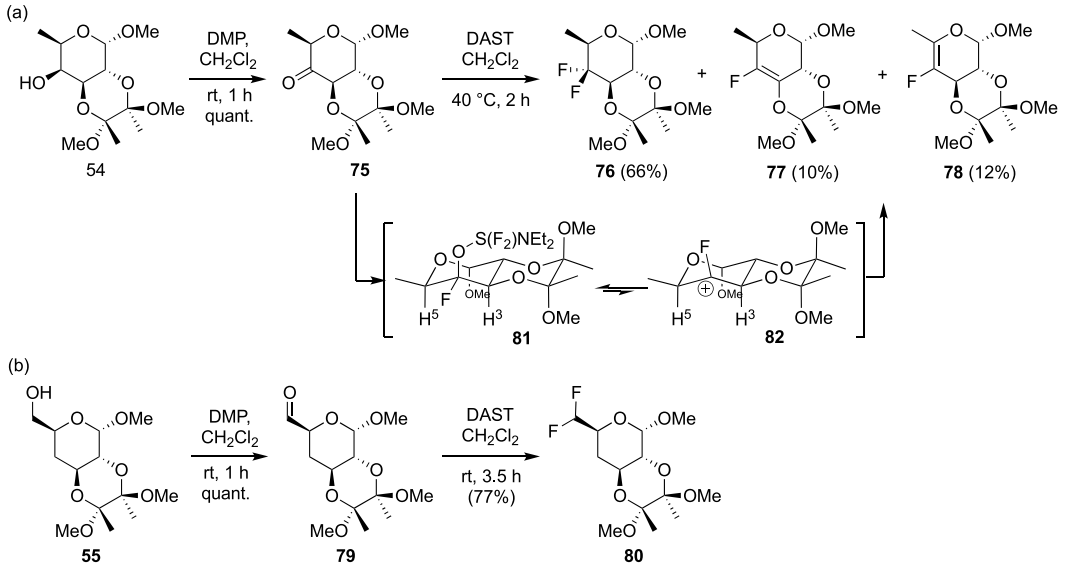
Scheme 8. 4,6-Dideoxy-4-fluoro Substitution (Quinovose Stereochemistry) Using BDA Protection



Scheme 9. Introduction of 4,6-Dideoxy-4,6-difluoro Substitution (Glucose Stereochemistry)



Scheme 10. Introduction of 4,6-Dideoxy-4,4-difluoro and -6,6-difluoro Substitution



deoxyfluorination reaction, given the higher electronegativity of Cl over Br, but was not attempted.

A shorter synthesis was also investigated (Scheme 8) based on the previously mentioned selective BDA protection of methyl α-D-galactopyranoside **45** (cf. Scheme 3 above) leading to **46**. At−40 °C, it was possible to selectively tosylate the 6-OH of **46** to give **72**; conducting the reaction at room temperature gave an inseparable mixture of mono- and ditosylated products. Subsequent hydride displacement of **72** gave D-fucose derivative **54**. Unfortunately, DAST-mediated deoxygenation was much less efficient compared to that of **66** (cf. Scheme 7), giving **73** in only 37% yield. Because of this drastic loss of yield in the final fluorination step, the approach using the 2,3-di-*O*-benzoyl-protected galactoside **37** is the preferred route for the synthesis.

Introduction of 4,6-Dideoxy-4,6-difluoro Substitution (Galactose Stereochemistry). The conversion of **27** to **28**, as reported in the literature[69] (cf. Scheme 2), has been carried out a number of times in our group and when conducted on large scale once led to a violent runaway reaction despite no external heating. It was suspected that the poor solubility of **27** in DAST played a role, and when solid particles remain present after the mixture is allowed to warm to room temperature, local heating of this exothermic reaction at the interface may lead to excessive HF evolution. Hence, given this safety risk, a safer reaction procedure was developed by simply using dichloromethane as reaction solvent, leading to a 46% yield on 5 g scale (not shown).

Introduction of 4,6-Dideoxy-4,6-difluoro Substitution (Glucose Stereochemistry). As shown in Scheme 2, the synthesis of methyl 4,6-difluoro-D-glucoside **39** involving the dibenzoate **37** had been reported by Esmurziev et al.[75] In our hands (Scheme 9), dideoxydifluorination to give **39** was achieved in 76% yield on 9 g scale, which afforded the desired 4,6-difluoroglucoside **35** upon deprotection with sodium methoxide also in 71% yield (25% overall).

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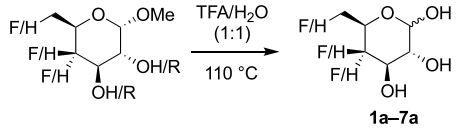
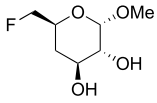
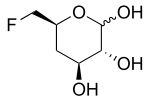
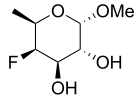
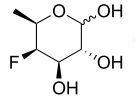
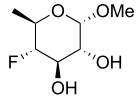
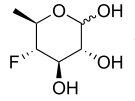
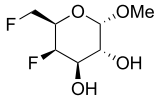
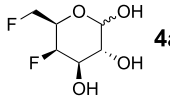
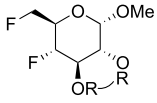
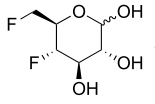
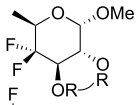
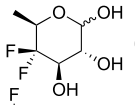
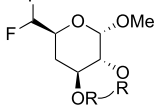
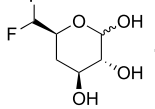
Table 1. Hydrolysis of the Methyl Glycosides to Free Dideoxyfluorosugars 1a−7a



1a–7a

Entry	Substrate	Hydrolysis product	t (h)	Yield (%)	TFA (%)[b]
1	 **10**	 **1a**	1.5	83	18
2	 **D-19**	 **2a**	3.5	83	22
3	 **71**	 **3a**	13	95	13
4	 **28**[a]	 **4a**	16	78	<1%
5	 **35** (R = H) **74** (R = BDA)	 **5a**	60 (36)	68 (55)	<1% (<1%)
6	 **76** (R = BDA)	 **6a**	21	61	<1%
7	 **80** (R = BDA)	 **7a**	3	51	N.D

[a]Synthesized according to ref 68. [b]Residual TFA in the isolated reducing sugar derivative, relative to the product.

As above, the use of the BDA protecting group to directly protect the galactoside positions 2 and 3 (**46**, cf Scheme 3) provided a means to avoid the three-step preparation of the deoxyfluorination substrate **37**. However, deoxyfluorination of **46** proved capricious with yields of **74** capped around 30% even when using a large molar excess of DAST (up to 6 equiv) and an elevated reaction temperature. As observed before, the less electron-withdrawing nature of the BDA group probably results in a more electron-rich sugar ring leading to rearrangement side reactions. The best yield was again obtained using the modified conditions reported by Wagner et al.[86] Up to 600 mg of diol **46** was treated with 3 equiv of both DAST and 2,4,6-collidine in 1,2-dichloroethane and heated at 100 °C under microwave irradiation for 6 min, yielding 47% of the desired compound **74**. Hydrolysis of the BDA protecting group in 4 M HCl in refluxing THF gave methyl glycoside **35** in 61% yield, with 9% of recovered starting material, but with TFA/H_2O, an improved 76% yield of **35** was obtained. Therefore, **35** could be obtained in a three-step synthesis from **45** in a 25% overall yield. Comparison of the two methods shows that, while the double deoxyfluorination of the benzoate-protected derivative **35** is clearly superior to that of the BDA derivative **46**, the overall yields of the different processes are very similar. In addition, the overall yield of the BDA approach will be higher if one is content to work with the initial diastereomeric mixture[82] of 2,3-BDA-protected galactosides obtained upon protection of **45**.

Introduction of 4,6-Dideoxy-4,4-difluoro and -6,6-Difluoro Substitution. The alcohols **54** and **55** (Scheme 10), obtained as a separable mixture in four steps from methyl α-D-galactopyranoside **45** as discussed above (cf. Scheme 3), were identified as precursors to introduce 4,6-dideoxy-4,4- and -6,6-difluorosubstitution. The alcohol groups of **54** and **55** were quantitatively oxidized with Dess−Martin periodinane to give **75** and **79**, which were then treated with 6 equiv of DAST to give the *gem*-difluorinated products **76** and **80** in good yields. The deoxyfluorination of **75** led to two fluoroalkene by-products **77** and **78** in 12% and 10% isolated yield, respectively, likely resulting from concomitant E2-elimination of H-3 or H-5 of the putative intermediate **81** by fluoride. Given that the reaction was conducted in nonpolar CH_2Cl_2, involvement of the possible intermediate **82**, which features a degree of stabilization by the fluorine atom,[96,97] is unlikely. No carbenium ion mediated rearrangement products were isolated. Hence, C4-*deoxo*fluorination gives a better yield than the C4-*deoxy*fluorination of **54** to **73** (cf. Scheme 8). C4-Deoxofluorination with an electron-withdrawing C6-substituent was not attempted, given the obvious risk for an elimination side reaction.

Deprotection and Access to the Reducing or Peracetylated Sugars. In order to obtain the fully

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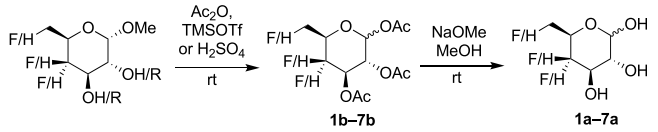
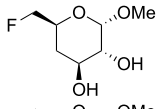
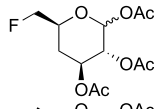
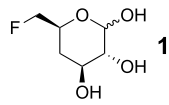
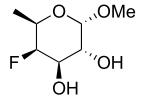
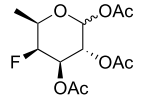
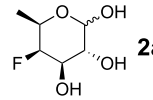
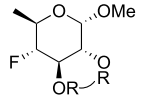
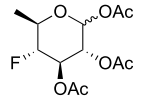
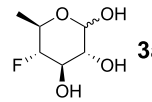
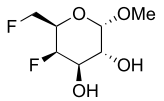
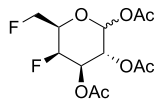
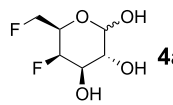
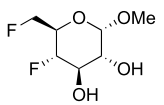
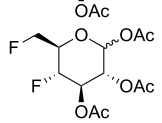
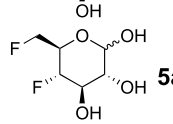
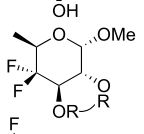
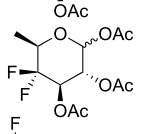
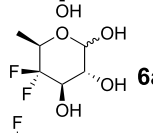
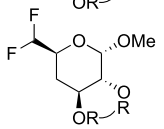
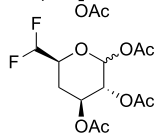
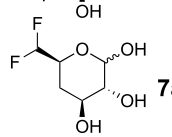
Table 2. Acetolysis/Zemplén Deprotection Strategy to Obtain Free Dideoxyfluorosugars 1a−7a



Entry	Substrate	Acetolysis product	Conditions (equiv)	Yield (%)	Zemplén product	Yield (%)
1	 **10**	 **1b**	TMSOTf (0.1)	89	 **1a**	73
2	 **D-19**	 **2b**	TMSOTf (0.1)	82	 **2a**	80
3	 **73** (R = BDA)	 **3b**	H_2SO_4 (1)	57[b]	 **3a**	90
4	 **28**[a]	 **4b**	H_2SO_4 (5)	74	 **4a**	78
5	 **35**	 **5b**	H_2SO_4 (3)	69[c]	 **5a**	65
6	 **76** (R = BDA)	 **6b**	H_2SO_4 (1)	48[b,d]	 **6a**	97
7	 **80** (R = BDA)	 **7b**	H_2SO_4 (1)	71[b]	 **7a**	60

[a]Synthesized according to ref 68. [b]Starting from **73**/**76**/**80**, the BDA protecting group was first removed using TFA/H_2O (9:1) at rt for 5 min, followed by evaporation. [c]13% of peracetylated open form sugar (**5c**) was also isolated. [d]7% of peracetylated open form sugar (**6c**) was also isolated.

deprotected reducing fluorinated sugars, the methyl glycosides were treated with a 1:1 mixture of trifluoroacetic acid and water while heating at reflux (Table 1).[92] The reaction time required highly depended on the fluorination pattern with the 4-deoxysugars being the fastest (entries 1 and 7), followed by the 6-deoxymonofluorosugars (entries 2 and 3) and the difluorosugars (entries 4−6). As expected,[4] hydrolysis was the slowest when an equatorial fluorine was present. For **74**, **76**, and **80**, TLC analysis indicated fast removal of the BDA protecting group under these conditions. The yields were good to excellent for the three monofluorosugars **10**, D-**19**, and **71** (entries 1−3), but as these required more polar eluents during chromatographic purification, it was difficult to remove residual TFA to a satisfactory level even after extensive evaporation or treatment with K_2CO_3. Therefore, further purification by peracetylation and column chromatography, followed by Zemplén deprotection, afforded the pure sugar derivatives **1a**−**3a** in 53, 58, and 75% yield, respectively (not shown). In contrast, compounds **4a**−**6a** could be obtained in moderate to good yields with less than 1% residual TFA. The preparation of **4a** was attempted from both the methyl glycoside **35** and the BDA-protected derivative **74** (entry 5), with the former approach giving the highest yield.

Given the moderate yields and the difficult removal of residual TFA, it was decided to achieve anomeric deprotection by a direct acetolysis reaction using acetic anhydride as solvent and either sulfuric acid or TMSOTf[98] as catalyst (Table 2). Excellent yields of 82−89% were obtained for monofluorinated substrates **1b** and **2b** using TMSOTf (entries 1 and 2), while 4,6-difluoro- products **4b** and **5b** were afforded in slightly lower 74 and 69% yields (entries 4 and 5).

When these conditions were applied to the BDA-protected 4,6-difluorinated methyl glycoside **74**, a complex mixture was obtained from which compound **5b** could only be obtained in 14−18% yield.

Consequently, substrates **73**, **76**, and **80** were first treated with TFA/H_2O (9:1) for 5 min at room temperature followed by evaporation to dryness. The crude mixtures were then subjected to the acetolysis conditions (H_2SO_4) to give the triacetylated derivatives **3b**, **6b**, and **7b** in 57%, 48%, and 71% yield, respectively (entries 3, 6, and 7). It should be noted that, in the case of **5b** and **6b**, byproducts in the acetylation reactions were isolated in non-negligible yields of 13% and 7%, respectively. These were identified as the pentaacetylated open forms **5c** and **6c** of the parent reducing sugars (Figure 4) Presumably the 5-OH group has a significantly reduced nucleophilicity due to the electron-withdrawing nature of the

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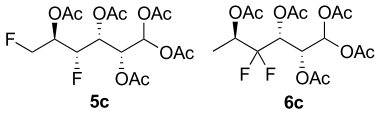


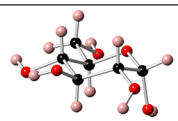
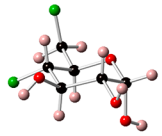
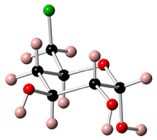
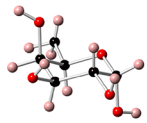
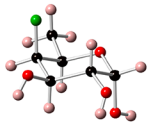
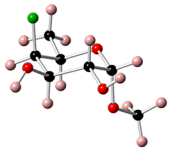
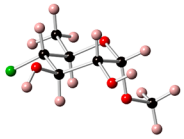
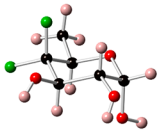
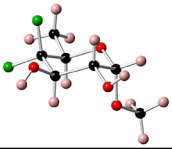
Figure 4. Structure of the acetolysis byproducts of 4,6-dideoxy-4,6-difluoro-D-glucose and 4,6-dideoxy-4,4-difluoro-D-*xylo*-hexose.

proximal fluorine substituents, causing a small amount of the open-chain form to exist as part of the solution equilibrium. Although not attempted, Zemplén deprotection of these byproducts is expected to return **5a** and **6a**.

Finally, all of the peracetylated pyranoses were then subjected to standard Zemplén deprotection, affording free sugars **1a**–**7a** in good to excellent yields with straightforward purification. Hence, the acetolysis strategy proved the method of choice to cleave the methyl glycosides.

Structural Characteristics and Anomer Preferences. Pleasingly, various monosaccharides proved crystalline, with all reducing sugars crystallizing as the α-anomer. Their crystal structures are given in Table 3, next to the crystal structures of α-D-glucopyranose **83** and α-L-fucopyranose **84** (shown in the D-configuration to facilitate comparison) as reference structures. Based on the Cremer–Pople parameters,[99] with azimuthal angles θ and radii Q approaching 0° and 0.57 Å, respectively, all structures are very close to a $^4C_1$ conformation (θ = 0° and Q = 0.57 Å represent the ideal values for a $^4C_1$

Table 3. Crystal Structures with Structural Data

Compound/structure	Average Ring Dihedral	Cremer-Pople[99,a]	Whitfield[100,b]	BFMP[101]
83[c] 	56.7 ± 4.0°	φ = 323.81° θ = 3.55° Q = 0.566 Å	0.945 $^4C_1$, 0.015 $B_{1,4}$, 0.092 $^OS_2$	$^Od_3$(1.55) $^2d_5$(1.90) $^4d_1$(3.41)
5a 	56.3 ± 5.3°	φ = 27.0(1.2)° θ = 6.56(13)° Q = 0.568(2) Å	0.939 $^4C_1$, 0.028 $B_{2,5}$, 0.120 $^3S_1$	$^Od_3$(1.81) $^4d_1$(3.24) $^2d_5$(4.94)
1a 	57.1 ± 1.3°	φ = 166(11)° θ = 1.4(2)° Q = 0.576(2) Å	0.952 $^4C_1$, 0.026 $^{O,3}B$, 0.004 $^5S_1$	$^4d_1$(0.07) $^Od_3$(0.15) $^2d_5$(0.40)
84[d] 	58.5 ± 2.0°	φ = 270.407° θ = 2.64° Q = 0.5932 Å	0.975 $^4C_1$, 0.001 $B_{1,4}$, 0.047 $^OS_2$	$^2d_5$(0.27) $^4d_1$(1.30) $^Od_3$(1.72)
2a 	56.4 ± 2.4°	φ = 79(6)° θ = 1.53(18)° Q = 0.566(2) Å	0.941 $^4C_1$, 0.008 $B_{2,5}$, 0.054 $^3S_1$	$^4d_1$(0.45) $^Od_3$(0.87) $^2d_5$(1.61)
19 	55.4 ± 3.9	φ = 20(4)° θ = 3.2(2)° Q = 0.552(2) Å	0.922 $^4C_1$, 0.079 $^{O,3}B$, 0.013 $^5S_1$	$^Od_3$(0.58) $^4d_1$(2.21) $^2d_5$(3.16)
71 	56.8 ± 4.7°	φ = 339(3)° θ = 4.1(3)° Q = 0.532(3) Å	0.947 $^4C_1$, 0.093 $^{O,3}B$, 0.018 $^1S_5$	$^Od_3$(1.14) $^2d_5$(3.03) $^4d_1$(3.82)
6a 	58.2 ± 2.3°	φ = 105(5)° θ = 3.2(3)° Q = 0.588(3) Å	0.969 $^4C_1$, 0.011 $^{2,5}B$, 0.050 $^3S_1$	$^4d_1$(0.50) $^2d_5$(1.39) $^Od_3$(1.85)
85[e] 	56.0 ± 4.3°	φ = 35(3)° θ = 4.1(2)° Q = 0.560(2) Å	0.933 $^4C_1$, 0.018 $B_{2,5}$, 0.098 $^3S_1$	$^Od_3$(1.49) $^4d_1$(2.05) $^2d_5$(3.70)

[a]Older database structures do not retain atom coordinate standard deviations, and thus, these cannot be calculated for the CP parameters. [b]http://6ring.bio.nrc.ca. [c]Structure from Mostad et al.[102] [d]Structure from Longchambon et al.[103] [e]Obtained from an incomplete hydrolysis reaction of **76**: see the Experimental Section for details.

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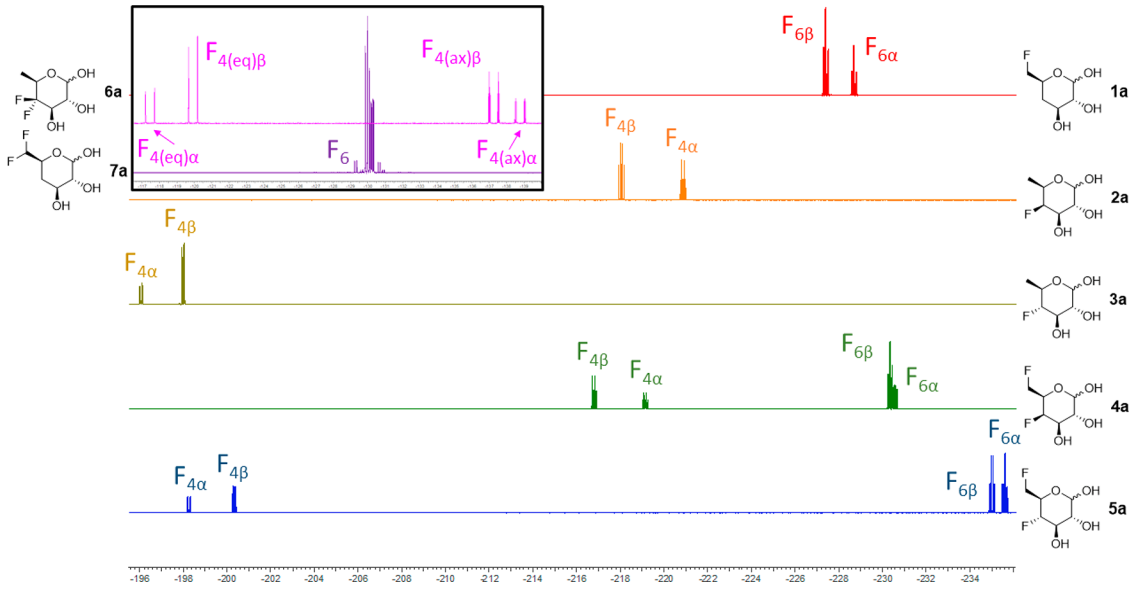

Figure 5. Comparison of ^{19}F NMR (470 MHz, D_2O) spectra of all synthesized 4,6-dideoxysugars **1a**−**7a**. Inset: Signals for **6a** and **7a** (CF_2 region).

conformation). The average ring dihedrals are between 56.3° and 58.2°, so very close to the ideal angle of 60° and very similar to the values for α-glucopyranose (56.7°) and α-fucopyranose (58.5°). The closeness to a $^4C_1$ chair structure is also apparent from their respective Whitfield linear combination of idealized IUPAC shapes,[100] which in all cases is clearly dominated by the $^4C_1$ chair conformation, and from the Woods[101] BFMP system, in which the three possible "d" reference planes all show very little distortion (all <5°, most <3°). As expected for small deviations, the Cremer−Pople meridian angles φ, indicating the distortion from the chair conformation, vary considerably, even between close analogues. This is also seen with the BFMP method: the $^0d_3$ plane is the best-fit plane for 4 of the 7 fluorinated structures, and the $^4d_1$ plane for the remaining three. α-Glucopyranose **83** and α-fucopyranose **84** show the $^0d_3$ plane and the $^2d_5$ plane as their best BFMP fit. While **5a**, the direct 4,6-difluorinated analogue of glucose, has the same best fit plane as glucose, this is not the case for fucose and its 4-deoxyfluorinated analogue. Interestingly, the reducing fluorosugars **2a** and **6a** do not have the same best fit plane as their methyl glycoside derivatives **19** and **76**: in both cases, a shift from $^4d_1$ to $^0d_3$ is observed. In contrast, the methyl glucoside structures **19**, **71**, and **76**, which differ in fluorination stereochemistry/number at C4, all have the same best fit plane ($^0d_3$). On the whole, this analysis clearly shows that 4,6-dideoxygenation combined with monofluorination at C4 or at C6, difluorination at C4, or difluorination at C4 and C6 does not cause appreciable ring distortion, even with different C4 stereochemistry. Regarding the C5−C6 conformation, α-D-glucose α-**83** crystallized in the *gt*-conformation, while its 4,6-difluorinated analogue **5a** crystallized as the *gg*-conformer.

The $^4C_1$ chair conformation is also apparent from the solution-phase NMR data, including vicinal coupling constants between C2 and F4 ($^3J_{C2-F4}$, Table S2) and small effects such as the Altona−Haasnoot rules,[104,105] as illustrated for $^3J_{H2-H3}$ in Table S3 for α- and β-4-fluorinated gluco- and galacto-configured analogues. The higher population of the C5−C6 *gg*-conformer for the 4,6-difluorinated glucose derivative **5a** compared to the galactose derivative **4a** was clearly exposed by its much higher $^3J_{H5-F6}$ value (±27 Hz vs ±14 Hz). Without a substituent at the 4-position as in **1a**, the $^3J_{H5-F6}$ value is an intermediate ±22 Hz.

The dispersion of the fluorine resonances of sugar derivatives **1a**−**7a** is shown in Figure 5. Some interesting trends can be observed. The F4 resonances of the *galacto*-configured compounds **2a** and **4a** are upfield (lower chemical shift) compared to those of the corresponding glucose analogues **3a** and **5a**, which can be explained by deshielding of the equatorial F by the antiperiplanar endocyclic C5−O5 bond[106] and shielding of the axial fluorine from hyperconjugation by the antiperiplanar C3−H3 and C5−H5 bonds.[107] The ^{19}F chemical shift values of the monodeoxyfluorinated 4-deoxy-4-fluoroglucose **87**[5,108] and -galactose **92**[109] show the same trend (not shown). Similarly, for the 4,4-difluorinated **6a**, the equatorial fluorine is deshielded compared to the axial fluorine substituent.

Conversely, the F6 resonance of the galacto-configured **4a** is downfield compared to that of the glucose analogue **5a**, with a smaller chemical shift difference. We suggest that this is consistent with the explanation given above for the F4 resonances: for **5a**, as reported above, the C5−C6 *gg* conformation featuring antiperiplanar C5−H5 and C6−F6 bonds is the most populated, leading to enhanced shielding of the "axial" C6−F6 by the C5−H5 bond. For **4a**, the *gt*/*tg* conformations will be the most populated, within the latter a deshielding effect from the antiperiplanar C5−O5 group takes place. The combined effects on F4 and F6 then explain the much larger chemical shift difference between F4 and F6 for **5a** compared to **4a**. The same trend is observed for 6-deoxy-6-fluoroglucose and 6-deoxy-6-fluorogalactose: the F6 resonance of the galacto-configured analogue (−229.9/−229.8 ppm) is downfield compared to that of the glucose analogue (−235.6/−234.9 ppm).

The influence of the anomeric configuration on the fluorine resonances, albeit a smaller effect, is also apparent: for all equatorial F4 substituents, including that of the 4,4-difluorinated **6a**, the chemical shift is upfield (lower chemical shift) for the β-anomer compared to the α-anomer, while for the axial F4 substituents it is the other way around: the α-

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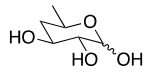
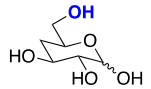
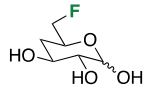
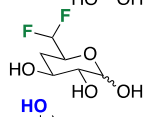
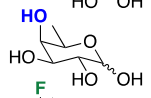
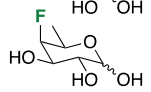
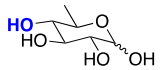
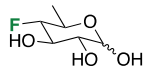
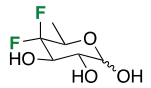
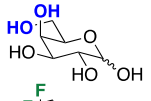
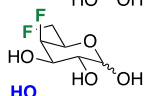
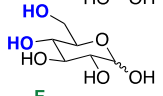
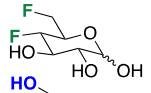
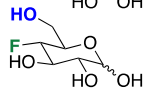
Table 4. Relative Proportions of α/β Anomers at Equilibrium in D_2O

Entry	Sugar		%α	δ_{H3}/δ_{H5} (α) δ_{H3}/δ_{H5} (β)	$(\delta_{H3}+\delta_{H5})_\alpha$ $(\delta_{H3}+\delta_{H5})_\beta$	$\Delta G°_{obs}(\alpha\rightarrow\beta)$ (kcal/mol)
1		**86**	27	3.76/4.02 3.55/3.62	7.72 7.17	−0.59
2		**93**	31	3.81/3.95 3.59/3.57	7.76 7.16	–0.47
3		**1a**	33	3.83/4.14 3.62/3.79	7.97 7.41	−0.42
4		**7a**	39	3.83/4.14 3.63/3.80	7.97 7.43	−0.29
5		**84**	31	3.71/4.05 3.49/3.66	7.76 7.15	−0.47
6		**2a**	34	3.80/4.13 3.60/3.76	7.93 7.36	−0.39
7		**89**	31	3.51/3.75 3.28/3.35	7.26 6.63	–0.47
8		**3a**	34	3.77/3.94 3.60/3.58	7.71 7.18	−0.39
9		**6a**	39	3.91/4.16 3.75/3.80	8.07 7.55	−0.27
10		**92**	33 (31)[a]	3.71/3.94 3.50/3.56	7.65 7.06	−0.42 (–0.47)[a]
11		**4a**	40	3.84/4.28 3.65/3.96	8.12 7.61	−0.24
12		**83**	38 (35)[a]	3.3.57/3.69 3.34/3.32	7.26 6.66	−0.29 (–0.37)[a]
13		**5a**	45	3.87/4.06 3.70/3.75	7.93 7.45	−0.12
14		**87**	43 (44)[a]	3.84/3.88 3.67/3.55	7.72 7.22	−0.17 (−0.14)[a]

[a]Ratios as reported by Murphy et al.[110]

anomer displays the upfield resonance. The published chemical shift data for monodeoxyfluorinated 4-deoxy-4-fluoroglucose **87**[5,108] and -galactose **92**[109] also show this trend. In the study of a series of fluorinated glucose derivatives (equatorial fluorine substituents), Giguere had noted that the ^{19}F resonances for the β-anomers occur at lower field than these of the α-anomers, except for F4,[20] and our data are consistent with this. For F6, in all cases the α-anomer does display an upfield chemical shift, regardless of C4 stereochemistry. We have no explanation for this observation, although for the 6-fluorinated compounds, it is noted that the $^3J_{H5-F6}$ values of the α-anomer are always larger than those of the β-anomer, which suggests a larger shielding of $F6_\alpha$, consistent with a lower chemical shift.

Next, the anomeric ratio of the reducing sugars **1a**−**7a** was analyzed. Samples were prepared in duplicate to a concentration of 64 μmol of substrate in D_2O (0.75 mL) and monitored by ^1H NMR until the ratio of anomers at 25 °C reached equilibrium. The time taken for equilibration was typically 1 d or less, but samples were left to further equilibrate for at least 3 d. The anomeric ratios were then obtained by ^{19}F quantitative integration (qNMR), and the corresponding $-\Delta G°$ ($-\Delta G°_{obs}$) values were then calculated from K_{eq} according to eq 1.

$$K_{eq} = \frac{[\alpha]}{[\beta]} = e^{-\Delta G°/RT} \quad (1)$$

The data are listed in Table 4, which is augmented with the data for a number of nonfluorinated "parent" sugars and a number of monodeoxyfluorinated sugars for comparison, and the ratios are discussed using Figures 6 and 7.

There is a clear correlation between the number of fluorines and the anomeric ratio, as illustrated in Figure 6 for all 4,6-dideoxygenated derivatives. The parent 4,6-dideoxygenated **86**, synthesized from methyl 4,6-dideoxy-4,6-dichloro-galactopyr-

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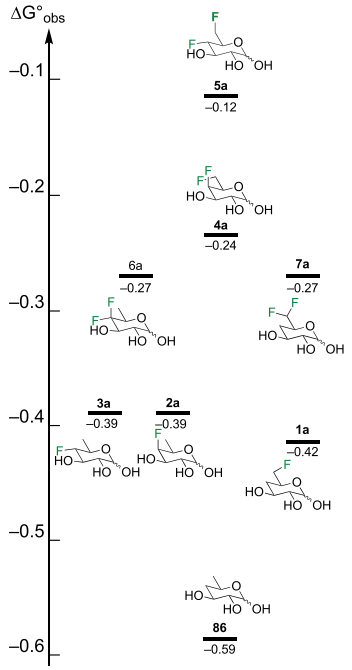

Figure 6. Free energy change corresponding to anomeric inversion of 4,6-dideoxygenated mono- and difluorinated sugar derivatives (D_2O, less negative $\Delta G°$ value equals higher α-anomer population).

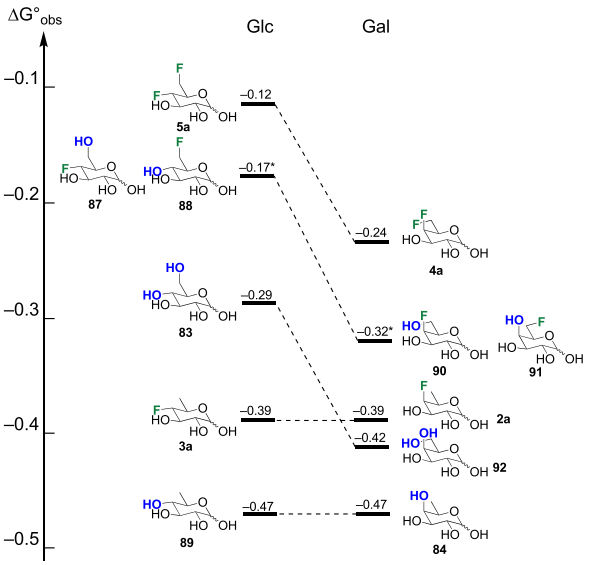

Figure 7. Comparison (dotted line) of the anomeric ratio differerences (expressed as their corresponding anomerization free energy change) between glucose and their corresponding galactose derivatives (D_2O, less negative $\Delta G°$ value equals higher α-anomer population). *These values were taken from ref 100.

anose **29** (cf. Scheme 2) *via* tin-mediated radical reduction and subsequent acetolysis to deprotect the anomeric position, followed by global Zemplen deprotection (not shown),[88] has by far the lowest anomeric ratio, and monofluorination at the 4- (**2a**, **3a**) or 6-position (**1a**) leads to an increase in α-anomer population. Geminal difluorination at these positions leads to a further increase (**6a**, **7a**). For these derivatives, there is very little or no difference between fluorination at the 4- and 6-positions. With difluorination present at the 4-and 6-positions, the anomeric ratio is further increased. The dependence of the anomeric ratio on the C4-configuration is discussed using Figure 7.

In all cases, it can be seen from Figure 7 that OH → F exchange leads to an increase in α-anomer population. Murphy already showed that this was the case for monodeoxyfluorination of glucose and galactose at both the 4- and 6-positions (compare **83** with **87** and **88** and compare **92** with **90** and **91**).[110] Here, it can be seen that monodeoxyfluorination of **87** and **88** to **5a** and of **90** and **91** to **4a** also leads to such an increase. Equally, 4-deoxyfluorination of quinovose (**89** to **3a**) and fucose (**84** to **2a**) leads to an increase in (α/β)-anomer ratio.

In general, galactose-configured derivatives display a lower α-anomer population compared to their respective glucose-configured diastereomers, with approximately the same free energy difference. However, this does not hold when the 6-position is unsubstituted: quinovose **89** and fucose **84** have the same anomeric ratio, as have their respective 4-deoxyfluorinated derivatives **2a** and **3a**.

This was further explored by correlating the free energy change upon anomerization with chemical shift data of H3 and H5, which were shown by Murphy to be correlated.[110] The chemical shift data utilized in the Murphy analysis are the chemical shift differences of (H3 + H5) of the derivatives with the (H3 + H5) chemical shift values of their parent sugars. Although the subtraction of the chemical shift values of the parent sugar derivatives does not change any correlation coefficients, it does facilitate comparison of the relative effect of the fluorination upon anomer ratio between different series. In this regard, the anomeric ratios of the "parent" pyranoses 4-deoxyglucose **93** (Table 4, entry 2), fucose **84** (entry 5), quinovose **89** (entry 7), galactose (**92**), glucose (**83**), and 4-deoxy-4-fluoroglucose (**87**) were also determined by ^1H or ^{19}F qNMR, while the data for 6-deoxy-6-fluoroglucose (**88**), 4-deoxy-4-fluorogalactcose (**90**), and 6-deoxy-6-fluorogalactcose (**91**) were taken from the Murphy report.

In Figure 8, the plot of $\Delta G°_{obs}$ vs the sum of the chemical shift values of all sugar derivatives involved (the 4,6-dideoxygenated *xylo*-hexopyranose derivatives α-**86** and α-**1a**−α-**7a**, the nonfluorinated C4- or C6-deoxygenated sugars α-**84**, α-**89**, and α-**93**, the parent glucose and galactose α-**83** and α-**92**, and the C4/C6 monodeoxyfluorinated sugars α-**87** and α-**88**−α-**90**) are shown. There is clearly no correlation

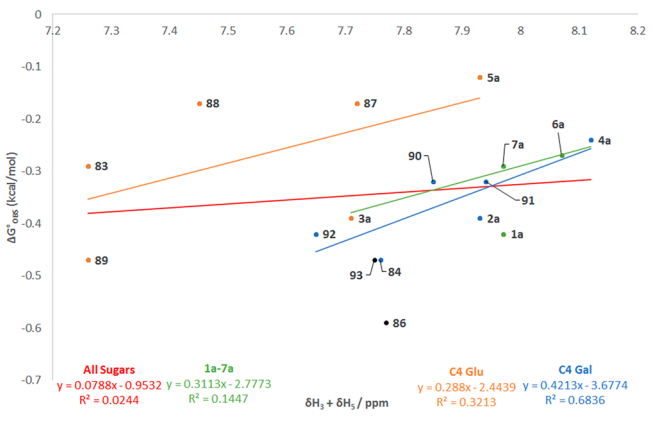

Figure 8. Plot of $\Delta G°_{obs}$ vs chemical shift values of **1a**−**7a** and **83**, **84**, and **86**−**93**. Values for **88**, **90** and **91** taken from ref.[110] Only the α-anomers are shown; the data for the β-anomers is given in the Supporting Information (Figure S1).

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observed for the data set at a whole (red trendline), with little correlation observed for the fluorinated 4,6-dideoxygenated *xylo*-hexopyranose derivatives α-**1a**-α-**7a** (green trendline). However, the trendline of sugars having C4-*gluco* stereochemistry (**83**, **89**, **88**, **3a**, **87**, **5a**, orange) shows an improved correlation coefficient, which is even higher for the C4-*galacto* configured compounds (**92**, **84**, **90**, **2a**, **91**, **4a**, blue).

Further dissection of these data revealed that categorizing the set by both the presence/absence of substitution at C6, and by stereochemistry at C4, affords excellent correlations for three of the four series, as shown in Figure 9A. Only the *gluco*-configured series has a correlation coefficient of less than 0.9, with the *galacto*, *fuco*, and *quinovo* series having coefficients greater than 0.96. Figure 9B shows the same correlations, but now the chemical shift values of H3 and H5 of the parent hydroxylated compounds (galactose **92**, glucose **83**, fucose **84**, and quinovose **89**) are subtracted from the sum of the H3 and H5 chemical shifts of the corresponding analogues, according to the Murphy analysis. This indicates the relative effect of the substitution on the anomeric ratio, and in accord with Murphy's observation, a given chemical shift change causes a higher α/β ratio for *galacto*-configured derivatives (with a very pronounced effect in the fucose series). An unexpected observation is that the 4,4-difluorinated compound **6a** correlates well with both the *quinovo* and *fuco* series.

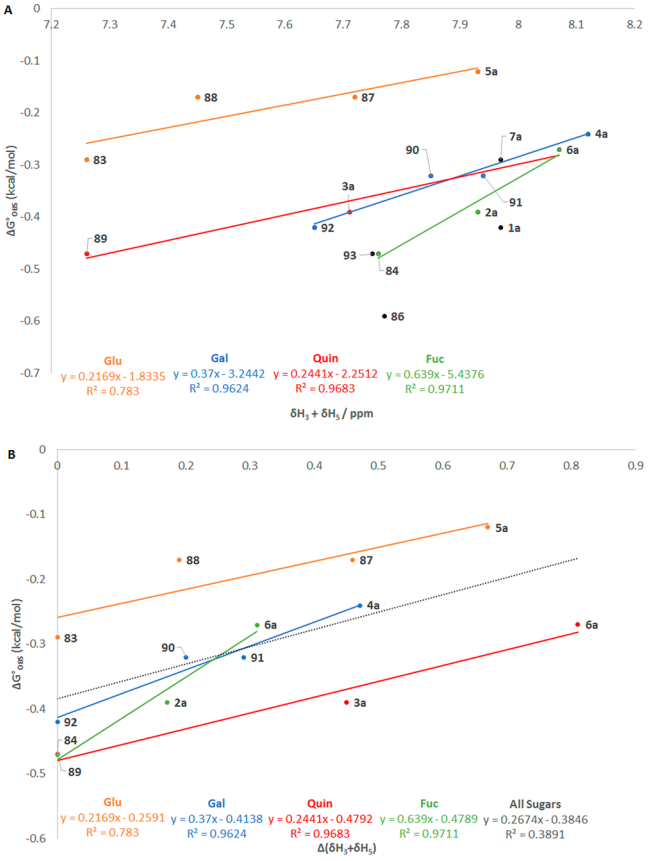

Figure 9. Plots of (A) ΔG°_{obs} vs chemical shift values of **1a**−**7a** and **83**, **84**, and **86**−**93** and (B) ΔG°_{obs} vs chemical shift difference of **1a**−**7a** and **83**, **84**, and **86**−**93** from the "parent" pyranose. Trendlines have been calculated for the four different parent series (Glu, Gal, Quin, and Fuc) and for the whole data set. Values for **88**, **90**, and **91** taken from ref110. Only the α-anomers are shown; the data for the β-anomers are given in the Supporting Information (Figure S2).

We were also interested if the 4,6-difluorinated derivatives **4a** and **5a** would correlate with Murphy's previously published *gluco* and *galacto* series. Figure 10 shows that when the values of **4a** and **5a** are added to this larger data set, it can be seen that an excellent fit is obtained.

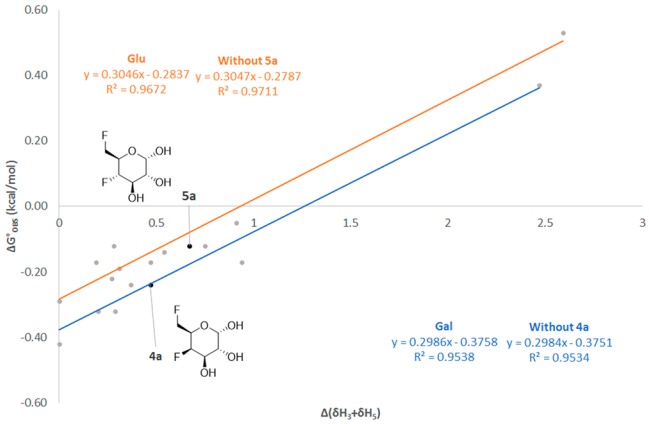

Figure 10. ΔG°_{obs} vs chemical shift differencefor compounds **4a** and **5a** superimposed onto the Murphy[100] data. Trendlines have been calculated with and without compounds **4a** and **5a**. For compounds **83**, **87**, and **92**, we have used our experimental values. Only the α-anomers are shown, and a fully annotated plot and the data for the β-anomers are given in the Supporting Information (Figures S4 and S5).

CONCLUSION

The synthesis of a series of 4,6-dideoxygenated monosaccharides with all possible mono- and difluorination motifs at these positions has been achieved, and their structural characteristics investigated. While the 4,6-dideoxy-4,6-difluorinated galactose derivative was obtained via a modification of Somawardhana's excellent direct regioselective bis-deoxyfluorination of methyl-α-D-glucopyranoside,[68,69] the synthesis of other known targets was reinvestigated and typically improved with regards to overall yield and/or number of syntetic steps. In all cases, the starting materials were cheap/nonexpensive methyl-α-D-gluco or -galactopyranoside.

The use of protecting groups was avoided in the synthesis of the 4,6-dideoxy-6-fluoro- and the 4,6-dideoxy-4-fluoro-D-fucose derivative by exploiting selective deoxychlorination methodology at either the 4- or the 6-position. In the latter case, the chloride served as protecting group to allow selective deoxyfluorination at the 4-position before reduction to the deoxy moiety. The use of an efficient yet old and rarely used 6-deoxychlorination method,[91] avoiding the use of Appel conditions (CCl_4, PPh_3), added to the synthetic efficiency on larger scale. For glucose stereochemistry, as in 4-deoxy-4-fluoro-D-quinovose, protection of the 2,3-positions was still required, with the benzoate protecting group being superior over the BDA protecting group in terms of deoxyfluorination yield, but with the latter allowing a shorter synthesis in similar overall yield (or higher yield if the use of 2,3-BDA isomers is tolerated). Hence, there is a clear tendency for the deoxyfluorination yields to be higher when electron-withdrawing groups are present, which is attributed to the decreased availability of the ring oxygen lone pairs to initiate ring contraction side reactions. The synthesis of the novel

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geminal difluorinated derivatives was also achieved with 2,3-BDA protection. The deoxofluorination yields were excellent overall, although deoxofluorination of the C4-ketone also gave rise to two regioisomeric elimination side products.

Anomeric deprotection using aqueous TFA proceeded in all cases, although, predictably, it was lower yielding with substrates with an increased fluorine content. The use of acetolysis conditions followed by Zemplen deprotection was also successful, with similar overall yields.

Seven crystal structures were obtained of methyl anomers and reducing sugars, involving five fluorination motifs. A comparison involving Cremer−Pople, Whitfield, and Woods BFMP parameters clearly indicated that these fluorination motifs did not cause appreciable $^4C_1$-chair distortion, at least not more than their corresponding hydroxylated sugars. The chair conformation was also apparent from NMR analysis in aqueous solution. The fluorine chemical shifts of all sugars showed nice dispersion between −196 and −235 ppm (C−F groups) and −116 and −139 ppm (CF_2 groups), and their relative chemical shift values, including that of the 6-fluorinated compounds, could be explained by the extent of "axial" disposition of the C−F bond. There is also a consistent chemical shift difference whether the anomeric position is α- or β-configured, for which we have no explanation yet.

The anomeric ratios in aqueous solution were quantified using a qNMR protocol. In all cases, the α/β-ratio increased with increasing fluorine content. Surprisingly, there is very little difference in anomeric ratio between regioisomers. Equally surprising is the dependence on C4-stereochemistry: with 4,6-difluorination, the gluco-configured sugar has a higher α-anomer content, which was also observed for the monodeoxy-fluorinated derivatives: both 4- and 6-deoxyfluoroglucose show a higher α/β-ratio than the corresponding 4- and 6-deoxyfluorogalactose derivatives. In all these cases, the anomeric ratio difference is very similar compared to that of glucose and galactose. However, the anomeric ratio of 4-deoxyfluorofucose and 4-deoxyfluoroquinovose is the same. The anomeric ratios and the sum of the H3 and H5 chemical shift values according to Murphy's method[110] show good to excellent correlations when taking into account both the extent of deoxygenation and stereochemistry present at C4. There is also an excellent fit of the two 4,6-difluorinated sugars with Murphy's data.

These sugars will be useful as building blocks for glycorandomization of aglycones leading to bioactive compounds including macrolide antibiotics for screening studie,[57,111−114] or as probes for enzymatic and biosynthethesis studies.[115]

EXPERIMENTAL SECTION

4-Deoxy-D-glucose (**93**), L-fucose (**84**), D-quinovose (**89**), D-glucose (**83**), D-galactose (**92**), and 4-deoxy-4-fluoro-D-glucose (**87**) were commercially available and used as received.

General Conditions. All air/moisture sensitive-reactions were carried out under an inert atmosphere (Ar or N_2) in dried glassware. Dry CH_2Cl_2, THF, MeOH, and MeCN were purchased from commercial suppliers and used as received. In all cases, heating of reaction mixtures was achieved by aluminum heating blocks using a thermostat. TLC was performed on aluminum-precoated plates coated with silica gel 60 with an F254 indicator, visualized under UV light (254 nm), and/or by staining with $KMnO_4$ (10% aq) or H_2SO_4/EtOH + 0.4% (w/v) *N*-(1-naphthyl)ethylenediamine dihydrochloride, followed by brief heating. Flash column chromatography was performed with Sigma-Aldrich 60 silica gel (40−63 μm) unless otherwise noted. All reported solvent mixtures are volume measurements. ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded at room temperature on a Bruker Ultrashield 400 or 500 MHz spectrometer. ^{1}H and ^{13}C chemical shifts (δ) are quoted in ppm relative to residual solvent peaks as appropriate ($CDCl_3$ 7.27 and 77.0 ppm; CD_3OD 3.31 and 49.15 ppm; acetone-d_6 2.05 and 29.32 ppm; D_2O 4.64 ppm). ^{19}F spectra were externally referenced to $CFCl_3$. The coupling constants (J) are given in hertz (Hz). The NMR signals were designated as follows: s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sxt (sextet), spt (septet), m (multiplet), or a combination of the above. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments. ACD/Laboratories (2020.1.2, v S15S41) was used for processing spectral data. IR spectra were recorded in the range 4000−500 cm^{-1} on Thermo Scientific Nicolet iS5 as films or solids, and absorption peaks are given in cm^{-1}. Optical rotations were collected on an Optical Activity PolAAr 2001 machine. Samples of reducing sugar derivatives were allowed to equilibrate for 24 h before optical rotation measurement. HRMS spectra were obtained on a Bruker Daltonics MaXis time-of-flight (TOF) mass spectrometer. Low resolution electrospray mass spectra were recorded with a Waters Acquity TDQ mass tandem quadrupole mass spectrometer.

General Procedure A for the Deprotection of Methyl Glycosides. A solution of methyl glycoside (1 equiv) in TFA/H_2O (1:1, 0.3 M) was heated to 110 °C and stirred for the noted time. The reaction was cooled to rt and concentrated *in vacuo*. Purification by chromatography (MeOH/CH_2Cl_2) afforded the reducing sugars **1a**−**7a**.

General Procedure B for the Acetolysis of Protected Sugars. To a solution of protected sugar (1 equiv) in Ac_2O (20 equiv) was cooled to 0 °C. TMSOTf (0.1−0.2 equiv) or H_2SO_4(1−5 equiv) was added, and the reaction allowed to warm to rt and stirred for 16 h. The reaction was diluted with EtOAc and then quenched by the slow addition of satd $NaHCO_{3(aq)}$. The phases were separated, and the organic layer washed with satd $NaHCO_{3(aq)}$. The combined aqueous layers were re-extracted with EtOAc, and then the combined organic phases were washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. Purification by chromatography (EtOAc/hexane or EtOAc/petroleum ether) afforded the acetylated sugars **1b**−**7b**.

General Procedure C for the Zemplén Deprotection of Acetylated Sugars. To a solution of acylated sugar (1 equiv) in MeOH (0.2 M) was added NaOMe (0.3 equiv). The reaction was stirred for 2 h and then neutralized by the addition of Amberlite IR120 H-form ion-exchange resin (pH 7). The resin was then filtered off, and the beads were washed with MeOH. The filtrate was concentrated *in vacuo*. Purification by chromatography (MeOH/CH_2Cl_2 or MeOH/EtOAc) afforded the reducing sugars **1a**−**7a**.

*4,6-Dideoxy-6-fluoro-D-xylo-hexopyranose (**1a**). From **1b**.* Using general procedure C with **1b** (140 mg, 0.48 mmol), purification by chromatography (5% MeOH/CH_2Cl_2) afforded **1a** as an off-white powder (57 mg, 0.35 mmol, 73%).

*From **10**.* Using general procedure A with **10** (500 mg, 2.78 mmol) for 90 min, purification by chromatography (8−10% MeOH/CH_2Cl_2) afforded **1a** as a colorless solid (383 mg, 2.31 mmol, 83%) with 18% TFA by ^{19}F NMR: mp (postcolumn) 144−145 °C; $[\alpha]_D^{24}$ +75.7 (c 0.27, MeOH); IR (neat) 3351 (br), 2933 (w), 1446 (w), 1067 (s), 1009 (s), 978 (s), 832 (s) cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD, 45/55 α/β) δ 5.15 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.44 (1H, d, J = 7.7 Hz, $H_{1\beta}$), 4.42 (1H, ddd, J = 47.4, 10.0, 3.2 Hz, $H_{6a\beta}$), 4.39 (1H, ddd, J = 47.7, 9.9, 3.3 Hz, $H_{6a\alpha}$), 4.38 (1H, ddd, J = 47.8, 10.0, 5.5 Hz, $H_{6b\beta}$), 4.35 (1H, ddd, J = 47.8, 9.9, 5.1 Hz, $H_{6b\alpha}$), 4.27−4.17 (1H, m, $H_{5\alpha}$), 3.90 (1H, ddd, J = 11.4, 9.4, 5.2 Hz, $H_{3\alpha}$), 3.76 (1H, ddddd, J = 19.9, 11.9, 5.5, 3.2, 2.1 Hz, $H_{5\beta}$), 3.61 (1H, ddd, J = 11.5, 9.0, 5.2 Hz, $H_{3\beta}$), 3.28 (1H, dd, J = 9.4, 3.7 Hz, $H_{2\alpha}$), 3.04 (1H, dd, J = 9.0, 7.7 Hz, $H_{2\beta}$), 1.91 (1H, ddd, J = 12.6, 5.0, 2.3 Hz, $H_{4(eq)\alpha}$), 1.89 (1H, ddd, J = 12.6, 5.2, 2.0 Hz, $H_{4(eq)\beta}$), 1.43 (1H, dt, J = 12.7, 11.7 Hz, $H_{4(ax)\beta}$), 1.42 (1H, td, J = 12.4, 11.6 Hz, $H_{4(ax)\alpha}$) ppm; ^{1}H NMR (500 MHz, D_2O, α/β 33:67) δ 5.14 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.46 (1H, d, J = 7.8 Hz, $H_{1\beta}$), 4.43 (1H, ddd, J = 46.9, 10.4, 2.4 Hz, $H_{6a\beta}$), 4.41 (1H, ddd, J = 46.9, 10.5, 2.6 Hz, $H_{6a\alpha}$), 4.33 (1H, ddd, J = 47.4, 10.5, 5.2

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Hz, $H_{6b\alpha}$), 4.32 (1H, ddd, J = 47.6, 10.4, 5.8 Hz, $H_{6b\beta}$), 4.14 (1H, ddddd, J = 23.9, 12.4, 5.2, 2.6, 2.4 Hz, $H_{5\alpha}$), 3.83 (1H, br ddd, J = 11.3, 9.7, 5.2 Hz, $H_{3\alpha}$), 3.79 (1H, dddt, J = 21.6, 12.1, 5.7, 2.3 Hz, $H_{5\beta}$), 3.62 (1H, ddd, J = 11.4, 9.4, 5.2 Hz, $H_{3\beta}$), 3.32 (1H, dd, J = 9.7, 3.8 Hz, $H_{2\alpha}$), 3.02 (1H, dd, J = 9.4, 7.9 Hz, $H_{2\beta}$), 1.87 (1H, br dddd, J = 12.8, 5.2, 2.3, 0.3 Hz, $H_{4(eq)\alpha}$), 1.84 (1H, br ddd, J = 12.9, 5.2, 2.1 Hz, $H_{4(eq)\beta}$), 1.39 (1H, td, J = 12.6, 11.4 Hz, $H_{4(ax)\alpha}$), 1.37 (1H, dt, J = 12.6, 11.9 Hz, $H_{4(ax)\beta}$) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, CD_3OD) δ 5.15 (1H, d, J = 3.6 Hz, $H_{1\alpha}$), 4.43 (1H, d, J = 7.7 Hz, $H_{1\beta}$), 4.42 (1H, dd, J = 9.9, 3.1 Hz, $H_{6a\beta}$), 4.39 (1H, dd, J = 9.9, 3.3 Hz, $H_{6a\alpha}$), 4.37 (1H, dd, J = 9.8, 5.5 Hz, $H_{6b\beta}$), 4.35 (1H, dd, J = 9.9, 5.0 Hz, $H_{6b\alpha}$), 4.22 (1H, ddt, J = 12.2, 5.1, 2.7 Hz, $H_{5\alpha}$), 3.90 (1H, ddd, J = 11.4, 9.4, 5.1 Hz, $H_{3\alpha}$), 3.76 (1H, dddd, J = 11.9, 5.4, 3.2, 2.1 Hz, $H_{5\beta}$), 3.61 (1H, ddd, J = 11.5, 9.0, 5.2 Hz, $H_{3\beta}$), 3.28 (1H, dd, J = 9.4, 3.7 Hz, $H_{2\alpha}$), 3.04 (1H, dd, J = 9.1, 7.7 Hz, $H_{2\beta}$), 1.91 (1H, ddd, J = 12.5, 5.1, 2.2 Hz, $H_{4(eq)\alpha}$), 1.89 (1H, ddd, J = 12.6, 5.3, 2.0 Hz, $H_{4(eq)\beta}$), 1.43 (1H, dt, J = 12.6, 11.8 Hz, $H_{4(ax)\beta}$), 1.42 (1H, td, J = 12.3, 11.5 Hz, $H_{4(ax)\alpha}$) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, D_2O) δ 5.14 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.46 (1H, d, J = 7.9 Hz, $H_{1\beta}$), 4.43 (1H, dd, J = 10.4, 2.4 Hz, $H_{6a\beta}$), 4.41 (1H, dd, J = 10.4, 2.5 Hz, $H_{6a\alpha}$), 4.33 (1H, dd, J = 10.3, 5.2 Hz, $H_{6b\alpha}$), 4.32 (1H, dd, J = 10.4, 5.8 Hz, $H_{6b\beta}$), 4.14 (1H, ddt, J = 12.3, 5.1, 2.4 Hz, $H_{5\alpha}$), 3.83 (1H, ddd, J = 11.4, 9.7, 5.1 Hz, $H_{3\alpha}$), 3.79 (1H, ddt, J = 12.0, 5.8, 2.3 Hz, $H_{5\beta}$), 3.62 (1H, ddd, J = 11.5, 9.2, 5.2 Hz, $H_{3\beta}$), 3.32 (1H, dd, J = 9.7, 3.7 Hz, $H_{2\alpha}$), 3.02 (1H, dd, J = 9.2, 7.9 Hz, $H_{2\beta}$), 1.87 (1H, br ddd, J = 12.8, 5.2, 2.3 Hz, $H_{4(eq)\alpha}$), 1.84 (1H, ddd, J = 12.9, 5.2, 2.1 Hz, $H_{4(eq)\beta}$), 1.39 (1H, br q, J = 12.4 Hz, $H_{4(ax)\alpha}$), 1.37 (1H, dt, J = 12.4, 11.9 Hz, $H_{4(ax)\beta}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, CD_3OD) δ 98.6 ($C_{1\beta}$), 94.8 ($C_{1\alpha}$), 86.2 (d, J_{C-F} = 171.2 Hz, $C_{6\alpha}$), 85.8 (d, J_{C-F} = 171.9 Hz, $C_{6\beta}$), 78.2 ($C_{2\beta}$), 75.7 ($C_{2\alpha}$), 72.2 ($C_{3\beta}$), 72.1 (d, J_{C-F} = 18.9 Hz, $C_{5\beta}$), 68.6 ($C_{3\alpha}$), 67.9 ($C_{5\alpha}$), 35.4 (d, J_{C-F} = 6.2 Hz, $C_{4\alpha}$ or $C_{4\beta}$), 35.3 (d, J_{C-F} = 6.2 Hz, $C_{4\alpha}$ or $C_{4\beta}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 96.1 ($C_{1\beta}$), 92.7 ($C_{1\alpha}$), 85.0 (d, J_{C-F} = 167.6 Hz, $H_{6\alpha}$), 84.7 (d, J_{C-F} = 167.9 Hz, $C_{6\beta}$), 75.7 ($C_{2\beta}$), 72.9 ($C_{2\alpha}$), 70.8 (d, J_{C-F} = 18.6 Hz, $C_{5\beta}$), 70.1 (d, J_{C-F} = 0.7 Hz, $C_{3\beta}$), 67.1 (d, J_{C-F} = 18.1 Hz, $C_{5\alpha}$), 66.7 (d, J_{C-F} = 0.7 Hz, $C_{3\alpha}$), 32.72 (d, J_{C-F} = 6.7 Hz, $C_{4\alpha}$), 32.69 (d, J_{C-F} = 6.9 Hz, $C_{4\beta}$) ppm; ^{19}F NMR (470 MHz, CD_3OD) δ −229.7 (td, J = 47.6, 20.0 Hz, $F_{6\beta}$), −230.9 (td, J = 47.7, 21.8 Hz, $F_{6\alpha}$) ppm; ^{19}F NMR (470 MHz, D_2O) δ −227.6 (td, J = 47.3, 21.6 Hz, $F_{6\beta}$), −228.9 (td, J = 47.4, 24.0 Hz, $F_{6\alpha}$) ppm; $^{19}F(^1H)$ NMR (470 MHz, CD_3OD) δ −229.7 (s, $F_{6\beta}$), −230.9 (s, $F_{6\alpha}$) ppm; $^{19}F(^1H)$ NMR (470 MHz, D_2O) δ −227.7 (s, $F_{6\beta}$), −229.0 (s, $F_{6\alpha}$) ppm; HRMS (ES^+) for $C_6H_{11}FNaO_4$ $[M + Na]^+$ calcd 189.0534 found 189.0534.

*1,2,3-Tri-O-acetyl-4,6-dideoxy-6-fluoro-D-xylo-hexopyranoside (**1b**).* Using general procedure B with **10** (500 mg, 2.78 mmol) and TMSOTf (0.1 equiv) purification by chromatography (25% EtOAc/petroleum ether) afforded **1b** as a colorless oil (720 mg, 2.46 mmol, 89%): IR (neat) 2963 (w), 1746 (s), 1371 (m), 1219 (s), 1069 (m), 930 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, α/β 64:33) δ 6.37 (1H, d, J = 3.6 Hz, $H_{1\alpha}$), 5.68 (0.5H, d, J = 8.0 Hz, $H_{1\beta}$), 5.32 (1H, td, J = 10.9, 5.1 Hz, $H_{3\alpha}$), 5.12−5.00 (2H, m, $H_{2\alpha}$, $H_{2\beta}$, $H_{3\beta}$), 4.48 (0.5H, ddd, J = 47.3, 10.0, 3.6 Hz, $H_{6a\beta}$), 4.45 (1H, ddd, J = 47.4, 10.1, 3.4 Hz, $H_{6a\alpha}$), 4.44 (0.5H, ddd, J = 46.8, 10.4, 4.4 Hz, $H_{6b\beta}$), 4.40 (1H, ddd, J = 47.1, 10.2, 4.4 Hz, $H_{6b\alpha}$), 4.29−4.14 (1H, m, $H_{5\alpha}$), 3.92 (0.5H, ddddd, J = 19.7, 12.0, 4.5, 3.5, 2.2 Hz, $H_{5\beta}$), 2.25 (1H, ddd, J = 12.8, 5.2, 2.4 Hz, $H_{4(eq)\alpha}$), 2.20 (0.5H, ddd, J = 13.1, 5.0, 2.2 Hz, $H_{4(eq)\beta}$), 2.15 (3H, s, $COCH_{3\alpha}$), 2.11 (1.5H, s, $COCH_{3\beta}$), 2.06 (3H, s, $COCH_{3\alpha}$), 2.05 (3H, s, 2 × $COCH_{3\beta}$), 2.03 (3H, s, $COCH_{3\alpha}$), 1.81−1.69 (1.5H, m, $H_{4(ax)\alpha}$, $H_{4(ax)\beta}$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 170.3 (CO_α), 170.2 (CO_β), 169.9 (CO_α), 169.6 (CO_β), 169.1 (CO_β), 169.0 (CO_α), 92.1 ($C_{1\beta}$), 90.1 ($C_{1\alpha}$), 83.7 (d, J_{C-F} = 174.6 Hz, $C_{6\alpha}$), 83.3 (d, J_{C-F} = 174.6 Hz, $C_{6\beta}$), 71.05 (d, J_{C-F} = 21.3 Hz, $C_{5\beta}$), 71.03 ($C_{2\beta}$), 70.5 ($C_{3\beta}$), 70.0 ($C_{2\alpha}$), 68.6 (d, J_{C-F} = 20.5 Hz, $H_{5\alpha}$), 67.2 ($C_{3\alpha}$), 31.1 (d, J_{C-F} = 6.6 Hz, $C_{4\alpha}$), 30.9 (d, J_{C-F} = 5.9 Hz, $C_{4\beta}$), 21.0 ($COCH_{3\alpha}$), 20.89 ($COCH_{3\alpha}$), 20.86 ($COCH_{3\beta}$), 20.8 ($COCH_{3\beta}$), 20.7 ($COCH_{3\beta}$), 20.6 ($COCH_{3\alpha}$) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −230.3 (td, J = 46.8, 19.1 Hz, $F_{6\beta}$), −230.8 (td, J = 46.8, 20.8 Hz, $F_{6\alpha}$) ppm; $^{19}F(^1H)$ NMR (376 MHz, $CDCl_3$) δ −230.4 (0.5F, s, $F_{6\beta}$), −230.9 (s, $F_{6\alpha}$) ppm; HRMS (ES^+) for $C_{12}H_{17}FNaO_7$ $[M + H]^+$ calcd 315.0851 found 315.0855.

*4-Deoxy-4-fluoro-D-fucose (**2a**). From **2b**.* Using general procedure C with **2b** (270 mg, 0.92 mmol), purification by chromatography (5% $MeOH/CH_2Cl_2$) afforded **2a** as a colorless solid (123 mg, 0.74 mmol, 80%).

*From D-**19**.* Using general procedure A with D-**19** (500 mg, 2.78 mmol) for 3.5 h, purification by chromatography (8−10% $MeOH/CH_2Cl_2$) afforded **2a** as a colorless solid (383 mg, 2.31 mmol, 83%) with 22% residual TFA (^{19}F NMR integration): mp (postcolumn) 183−185 °C; $[\alpha]_D^{25}$ +67.9 (c 0.48, MeOH); IR (neat) 3334 (br), 2937 (w), 1419 (w), 1076 (s), 1033 (s), 960 (s) cm^{-1}; ^1H NMR (500 MHz, CD_3OD, α/β 50:50) δ 5.11 (1H, d, J = 3.6 Hz, H1α), 4.51 (1H, br ddt, J = 50.7, 2.7, 0.4 Hz, $H_{4\alpha}$), 4.452 (1H, br ddd, J = 50.3, 3.0, 0.4 Hz, $H_{4\beta}$), 4.445 (1H, dd, J = 7.7, 1.1 Hz, $H_{1\beta}$), 4.19 (1H, dq, J = 29.8, 6.8 Hz, $H_{5\alpha}$), 3.85 (1H, ddd, J = 29.3, 10.2, 2.7 Hz, $H_{3\alpha}$), 3.73 (1H, dq, J = 27.4, 6.5 Hz, $H_{5\beta}$), 3.69 (1H, dd, J = 10.2, 3.7. 0.9 Hz, $H_{2\alpha}$), 3.55 (1H, ddd, J = 29.5, 9.9, 3.0 Hz, $H_{3\beta}$), 3.43 (1H, ddd, J = 9.9, 7.8, 1.5 Hz, $H_{2\beta}$), 1.29 (3H, dd, J = 6.6, 0.6 Hz, $H_{6\beta}$), 1.23 (3H, dd, J = 6.7, 0.6 Hz, $H_{6\alpha}$) ppm; ^1H NMR (500 MHz, D_2O, α/β: 34:66) δ 5.10 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.57 (1H, br dd, J = 50.1, 2.8 Hz, $H_{4\alpha}$), 4.50 (1H, br dd, J = 49.9, 2.9 Hz, $H_{4\beta}$), 4.49 (1H, dd, J = 7.9, 1.1 Hz, $H_{1\beta}$), 4.13 (1H, dq, J = 30.7, 6.7 Hz, $H_{5\alpha}$), 3.80 (1H, ddd, J = 29.9, 10.4, 2.7 Hz, $H_{3\alpha}$), 3.76 (1H, dq, J = 28.5, 6.6 Hz, $H_{5\beta}$), 3.67 (1H, ddd, J = 10.4, 3.7, 1.3 Hz, $H_{2\alpha}$), 3.60 (1H, ddd, J = 30.3, 10.1, 2.8 Hz, $H_{3\beta}$), 3.35 (1H, ddd, J = 10.1, 7.9, 1.4 Hz, $H_{2\beta}$), 1.17 (3H, dd, J = 6.6, 0.6 Hz, $H_{6\beta}$), 1.13 (3H, dd, J = 6.7, 0.6 Hz, $H_{6\alpha}$) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, CD_3OD) δ 5.11 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.51 (1H, dt, J = 2.7, 0.4 Hz, $H_{4\alpha}$), 4.453 (1H, br d, J = 2.8 Hz, $H_{4\beta}$), 4.452 (1H, d, J = 7.7 Hz, $H_{1\beta}$), 4.19 (1H, br q, J = 6.6 Hz, $H_{5\alpha}$), 3.85 (1H, dd, J = 10.2, 2.7 Hz, $H_{3\alpha}$), 3.73 (1H, br q, J = 6.6 Hz, $H_{5\beta}$), 3.69 (1H, dd, J = 10.2, 3.7 Hz, $H_{2\alpha}$), 3.55 (1H, dd, J = 9.8, 2.7 Hz, $H_{3\beta}$), 3.43 (1H, dd, J = 9.9, 7.6 Hz, $H_{2\beta}$), 1.29 (3H, d, J = 6.6 Hz, $H_{6\beta}$), 1.23 (3H, d, J = 6.7 Hz, $H_{6\alpha}$) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, D_2O) δ 5.10 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.57 (1H, br d, J = 2.7 Hz, $H_{4\alpha}$), 4.51 (1H, br d, J = 2.9 Hz, $H_{4\beta}$), 4.49 (1H, d, J = 8.0 Hz, $H_{1\beta}$), 4.13 (1H, q, J = 6.7 Hz, $H_{5\alpha}$), 3.80 (1H, dd, J = 10.4, 2.7 Hz, $H_{3\alpha}$), 3.76 (1H, q, J = 6.6 Hz, $H_{5\beta}$), 3.67 (1H, dd, J = 10.4, 3.9 Hz, $H_{2\alpha}$), 3.60 (1H, dd, J = 10.0, 2.8 Hz, $H_{3\beta}$), 3.36 (1H, dd, J = 10.0, 7.9 Hz, $H_{2\beta}$), 1.17 (3H, d, J = 6.6 Hz, $H_{6\beta}$), 1.13 (3H, d, J = 6.7 Hz, $H_{6\alpha}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, CD_3OD) δ 98.4 ($C_{1\beta}$), 94.32 ($C_{1\alpha}$), 94.26 (d, J_{C-F} = 180.7 Hz, $C_{4\alpha}$), 93.4 (d, J_{C-F} = 181.4 Hz, $C_{4\beta}$), 74.0 (d, J_{C-F} = 18.6 Hz, $C_{3\beta}$), 73.7 ($C_{2\beta}$), 70.6 (d, J_{C-F} = 18.8 Hz, $C_{5\beta}$), 70.4 (d, J_{C-F} = 2.2 Hz, $C_{2\alpha}$), 70.2 (d, J_{C-F} = 18.4 Hz, $C_{3\alpha}$), 66.1 (d, J_{C-F} = 18.8 Hz, $C_{5\alpha}$), 16.5 (d, J_{C-F} = 5.5 Hz, $C_{6\beta}$), 16.3 (d, J_{C-F} = 6.0 Hz, $C_{6\alpha}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 95.9 ($C_{1\beta}$), 92.9 (d, J_{C-F} = 177.4 Hz, $C_{4\alpha}$), 92.21 ($C_{1\alpha}$), 92.15 (d, J_{C-F} = 179.1 Hz, $C_{4\beta}$), 71.7 (d, J_{C-F} = 18.4 Hz, $C_{3\beta}$), 71.6 (d, J_{C-F} = 0.7 Hz, $C_{2\beta}$), 69.4 (d, J_{C-F} = 18.4 Hz, $C_{5\beta}$), 68.08 (d, J_{C-F} = 18.1 Hz, $C_{3\alpha}$), 68.06 (d, J_{C-F} = 2.2 Hz, $C_{2\alpha}$), 65.2 (d, J_{C-F} = 18.6 Hz, $C_{5\alpha}$), 14.9 (d, J_{C-F} = 5.5 Hz, $C_{6\beta}$), 14.8 (d, J_{C-F} = 5.7 Hz, $C_{6\alpha}$) ppm; ^{19}F NMR (470 MHz, CD_3OD) δ −219.5 (dt, J = 50.2, 28.5 Hz, $F_{4\beta}$), −222.7 (dt, J = 50.9, 29.6 Hz, $F_{4\alpha}$) ppm; ^{19}F NMR (470 MHz, D_2O) δ −218.2 (1F, br dtd, J = 49.7, 29.3, 0.7 Hz, $F_{4\beta}$), −221.1 (1F, br dtd, J = 50.1, 30.7, 1.1 Hz, $F_{4\alpha}$) ppm; $^{19}F(^1H)$ NMR (470 MHz, CD_3OD) δ −219.5 (0.4F, s, $F_{4\beta}$), −222.7 (1F, s, $F_{4\alpha}$) ppm; $^{19}F(^1H)$ NMR (470 MHz, D_2O) δ −218.2 (s, $F_{4\beta}$), −221.1 (s, $F_{4\alpha}$) ppm; HRMS (ES^+) for $C_6H_{11}FNaO_4$ $[M + Na]^+$ calcd 189.0534 found 189.0536.

*1,2,3-Tri-O-acetyl-4-deoxy-4-fluoro-D-fucopyranoside (**2b**).* Using general procedure B with D-**19** (128 mg, 0.71 mmol) and TMSOTf (0.1 equiv), purification by chromatography (20% EtOAc/hexane) afforded **2b** as a colorless oil (170 mg, 0.58 mmol, 82%). IR (neat) 2987 (w), 1735 (s), 1367 (m), 1208 (s), 1069 (s), 927 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, α/β 91/9)δ 6.34 (1H, d, J = 3.6 Hz, $H_{1\alpha}$), 5.68 (0.1H, dd, J = 8.3, 0.7 Hz, $H_{1\beta}$), 5.38 (1H, ddd, J = 10.9, 3.6, 1.1 Hz, $H_{2\alpha}$), 5.27 (1H, ddd, J = 26.3, 10.9, 2.5 Hz, $H_{3\alpha}$), 5.00 (0.1H, ddd, J = 27.3. 10.4, 3.7 Hz, $H_{3\beta}$), 4.74 (1H, dd, J = 50.1, 2.5 Hz, $H_{4\alpha}$), 4.66 (0.1H, dd, J = 49.8, 2.7 Hz, $H_{4\beta}$), 4.17 (1H, dq, J = 28.5, 6.6 Hz, $H_{5\alpha}$), 3.87 (0.1H, dq, J = 25.8, 6.6 Hz, $H_{5\beta}$), 2.14 (3H, s, OAc_α), 2.13 (3H, s, OAc_α), 2.12 (0.3H, s, OAc_β), 2.11 (0.3H, s, OAc_β), 2.05 (0.3H, s, OAc_β), 2.03 (OAc_α), 1.38 (0.3H, d, J = 6.6 Hz, $H_{6\beta}$), 1.32 (3H, d, J = 6.6 Hz, $H_{6\alpha}$) ($H_{2\beta}$ not resolved) ppm; $^{13}C\{^1H\}$

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NMR (101 MHz, $CDCl_3$) δ 170.5 (CO_α), 169.7 (CO_α), 169.23 (CO_β), 169.22 (CO_β), 169.0 (CO_α), 91.9 ($C_{1\beta}$), 89.8 ($C_{1\alpha}$), 89.1 (d, J_{C-F} = 186.3 Hz, $C_{4\alpha}$), 71.8 (d, J_{C-F} = 18.3 Hz, $C_{3\beta}$), 70.3 (d, J_{C-F} = 19.1 Hz, $C_{5\beta}$), 68.4 (d, J_{C-F} = 18.3 Hz, $C_{3\alpha}$), 67.7 ($C_{2\beta}$), 67.4 (d, J_{C-F} = 19.1 Hz, $C_{5\alpha}$), 66.1 (d, J_{C-F} = 2.2 Hz, $C_{2\alpha}$), 20.9 (OAc_α), 20.81 (OAc_β), 20.79 (OAc_α), 20.7 (OAc_β), 20.6 (OAc_β), 20.5 (OAc_α), 15.6 (2 × C, d, J_{C-F} = 5.9 Hz, $C_{6\alpha}$, $C_{6\beta}$) ppm (one CO_β and $C_{4\beta}$ not observed); ^{19}F NMR (376 MHz, $CDCl_3$) δ −217.5 (0.1F, dt, J = 50.3, 26.9 Hz, $F_{4\beta}$), −219.8 (1F, dt, J = 50.3, 27.7 Hz, $F_{4\alpha}$) ppm; ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ −217.6 (s, $F_{4\beta}$), −219.9 (s, $F_{4\alpha}$) ppm; HRMS (ES$^+$) for $C_{12}H_{17}FNaO_7$ $[M + Na]^+$ calcd 315.0851 found 315.0850.

*4-Deoxy-4-fluoro-D-quinovose (**3a**). From **3b**.* Using general procedure C with **3b** (292 mg, 1.00 mmol), purification by chromatography (5% MeOH/CH_2Cl_2) afforded **3a** as a colorless solid (150 mg, 0.90 mmol, 90%).

*From **71**.* Using general procedure A with **71** (500 mg, 2.78 mmol) for 17 h, purification by chromatography (8−10% MeOH/CH_2Cl_2 afforded **3a** as a colorless solid (438 mg, 2.64 mmol, 95%) with 13% residual TFA (^{19}F NMR integration): mp (postcolumn) 117−119 °C; $[\alpha]_D^{25}$ +38.6 (*c* 0.49, MeOH); IR (neat) 3343 (br), 2937 (w), 1373 (m), 1089 (s), 998 (s) cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD, α/β 50:50) δ 5.03 (1H, t, J = 3.7 Hz, $H_{1\alpha}$), 4.48 (1H, d, J = 7.8 Hz, $H_{1\beta}$), 4.05−3.97 (1H, m, $H_{5\alpha}$), 3.87 (1H, ddd, J = 50.8, 9.5, 8.7 Hz, $H_{4\beta}$), 3.83 (1H, ddd, J = 13.2, 9.4, 8.7 Hz, $H_{3\alpha}$), 3.82 (1H, ddd, J = 53.2, 9.3, 8.7 Hz, $H_{4\alpha}$), 3.56 (1H, ddd, J = 15.4, 9.4, 8.7 Hz, $H_{3\beta}$), 3.54 (1H, dqd, J = 9.5, 6.1, 2.4 Hz, $H_{5\beta}$), 3.40−3.35 (1H, m, $H_{2\alpha}$), 3.15 (1H, ddd, J = 9.4, 7.8, 0.8 Hz, $H_{2\beta}$), 1.29 (3H, dd, J = 6.2, 1.4 Hz, $H_{6\alpha}$), 1.23 (3H, dd, J = 6.2, 1.2 Hz, $H_{6\beta}$) ppm; ^{1}H NMR (500 MHz, D_2O, α/β 34:66) δ 5.03 (1H, t, J = 3.6 Hz, $H_{1\alpha}$), 4.52 (1H, d, J = 8.0 Hz, $H_{1\beta}$), 3.99−3.91 (1H, m, $H_{5\alpha}$), 3.92 (1H, ddd, J = 50.4, 9.5, 8.9 Hz, $H_{4\beta}$), 3.91 (1H, ddd, J = 52.6, 9.6, 8.7 Hz, $H_{4\alpha}$), 3.77 (1H, dddd, J = 15.3, 9.8, 8.8, 0.5 Hz, $H_{3\alpha}$), 3.60 (1H, ddd, J = 15.3, 9.5, 8.8 Hz, $H_{3\beta}$), 3.58 (1H, dqd, J = 9.5, 6.2, 2.5 Hz, $H_{5\beta}$), 3.44 (1H, ddd, J = 9.8, 3.9, 0.9 Hz, $H_{2\alpha}$), 3.15 (1H, ddd, J = 9.6, 8.0, 0.9 Hz, $H_{2\beta}$), 1.18 (3H, dd, J = 6.2, 1.5 Hz, $H_{6\beta}$), 1.15 (3H, dd, J = 6.0, 1.1 Hz, $H_{6\alpha}$) ppm; ^{1}H{^{19}F} NMR (500 MHz, CD_3OD) δ 5.03 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.49 (1H, d, J = 7.8 Hz, $H_{1\beta}$), 4.05−3.97 (1H, m, $H_{5\alpha}$), 3.87 (1H, dd, J = 9.4, 8.8 Hz, $H_{4\beta}$), 3.85−3.79 (2H, m, $H_{3\alpha}$, $H_{4\alpha}$), 3.56 (1H, dd, J = 9.4, 8.8 Hz, $H_{3\beta}$), 3.54 (1H, dq, J = 9.4, 6.1 Hz, $H_{5\beta}$), 3.40 (1H, m, $H_{2\alpha}$), 3.16 (1H, dd, J = 9.4, 7.8 Hz, $H_{2\beta}$), 1.29 (3H, d, J = 6.1 Hz, $H_{6\beta}$), 1.23 (3H, d, J = 6.3 Hz, $H_{6\alpha}$) ppm; ^{1}H{^{19}F} NMR (500 MHz, D_2O) δ 5.03 (1H, d, J = 3.9 Hz, $H_{1\alpha}$), 4.52 (1H, d, J = 8.0 Hz, $H_{1\beta}$), 3.98−3.88 (3H, m, $H_{4\alpha}$, $H_{4\beta}$, $H_{5\alpha}$), 3.78 (1H, dd, J = 9.8, 8.6 Hz, $H_{3\alpha}$), 3.60 (1H, dd, J = 9.6, 8.9 Hz, $H_{3\beta}$), 3.58 (1H, dq, J = 9.5, 6.2 Hz, $H_{5\beta}$), 3.44 (1H, dd, J = 9.8, 3.9 Hz, $H_{2\alpha}$), 3.15 (1H, J = 9.5, 8.0 Hz, $H_{2\beta}$), 1.18 (3H, d, J = 6.2 Hz, $H_{6\beta}$), 1.15 (3H, d, J = 5.9 Hz, $H_{6\alpha}$) ppm; ^{13}C{^{1}H} NMR (126 MHz, CD_3OD) δ 98.2 (d, J_{C-F} = 1.4 Hz, $C_{1\beta}$), 96.8 (d, J_{C-F} = 181.9 Hz, $C_{4\alpha}$), 96.2 (d, J_{C-F} = 182.2 Hz, $C_{4\beta}$), 93.6 (d, J_{C-F} = 1.7 Hz, $C_{1\alpha}$), 76.3 (d, J_{C-F} = 8.3 Hz, $C_{2\beta}$), 75.9 (d, J_{C-F} = 17.9 Hz, $C_{3\beta}$), 73.8 (d, J_{C-F} = 7.9 Hz, $C_{2\alpha}$), 72.9 (d, J_{C-F} = 17.6 Hz, $C_{3\alpha}$), 70.6 (d, J_{C-F} = 24.7 Hz, $C_{5\beta}$), 65.7 (d, J_{C-F} = 24.1 Hz, $C_{5\alpha}$), 17.9 ($C_{6\alpha}$ and C_{6b}(bs)) ppm; ^{13}C{^{1}H} NMR (126 MHz, D_2O) δ 95.7 ($C_{1\beta}$), 94.5 (d, J_{C-F} = 179.8 Hz, $C_{4\alpha}$), 94.1 (d, J_{C-F} = 180.0 Hz, $C_{4\beta}$), 91.8 ($C_{1\alpha}$), 73.8 (d, J_{C-F} = 8.8 Hz, $C_{2\beta}$), 73.6 (d, J_{C-F} = 17.9 Hz, $C_{3\beta}$), 71.1 (d, J_{C-F} = 8.1 Hz, $C_{2\alpha}$), 70.9 (d, J_{C-F} = 17.6 Hz, $C_{3\alpha}$), 69.3 (d, J_{C-F} = 24.8 Hz, $C_{5\beta}$), 64.8 (d, J_{C-F} = 24.3 Hz, $C_{5\alpha}$), 16.36 ($C_{6\beta}$), 16.34 ($C_{6\alpha}$) ppm; ^{19}F NMR (470 MHz, CD_3OD) δ −197.5−197.7 (m, $F_{4\alpha}$), −199.3 (ddquin, J = 50.8, 15.4, 1.4 Hz, $F_{4\beta}$) ppm; ^{19}F NMR (470 MHz, D_2O) δ −119.2−196.4 (m, $F_{4\alpha}$), −198.2 (app ddspt, J = 50.4, 15.4, 1.4 Hz, $F_{4\beta}$) ppm; ^{19}F{^{1}H} NMR (470 MHz, CD_3OD) δ −197.6 (s, $F_{4\alpha}$), −199.3 (s, $F_{4\beta}$) ppm; ^{19}F{^{1}H} NMR (470 MHz, D_2O) δ −196.3 (s, $F_{4\alpha}$), −198.3 (s, $F_{4\beta}$) ppm; HRMS (ES$^+$) for $C_6H_{11}FNaO_4$ $[M + Na]^+$ calcd 189.0534 found 189.0538.

*1,2,3-Tri-O-acetyl-4-deoxy-4-fluoro-D-quinovopyranoside (**3b**).* To **73** (42 mg, 0.14 mmol) was added a solution of TFA/H_2O (9:1, 0.5 mL). The colorless mixture was stirred for 10 min, over which time it turned bright yellow. The solution was concentrated *in vacuo* and redissolved in Ac_2O (0.27 mL, 2.80 mmol). The solution was cooled to 0 °C, and concd H_2SO_4 (10 μL, 0.14 mmol) was added. The mixture was stirred for 16 h. The reaction was diluted with CH_2Cl_2 (10 mL) and quenched by the addition of satd $NaHCO_{3(aq)}$ (20 mL). The phases were separated, and the aqueous phase extracted with CH_2Cl_2 (3 × 20 mL). the combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by chromatography (20% EtOAc/hexane) afforded **3b** as a colorless oil (24 mg, 0.08 mmol, 57%, α/β 76:24): IR (neat) 3655 (w), 2981 (m), 1749 (s), 1369 (m), 1208 (s), 1031 (s), 943 (m), 899 (m) cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$,) δ 6.24 (1H, t, J = 3.4 Hz, $H_{1\alpha}$), 5.71 (1H, d, J = 8.3 Hz, $H_{1\beta}$), 5.55 (1H, ddd, J = 13.1, 10.4, 8.8 Hz, $H_{3\alpha}$), 5.32 (1H, ddd, J = 14.0, 9.6, 9.0 Hz, $H_{3\beta}$), 5.06 (1H, ddd, J = 9.7, 8.4, 0.5 Hz, $H_{2\beta}$), 5.01 (1H, ddd, J = 10.3, 3.8, 0.9 Hz, $H_{2\alpha}$), 4.17 (1H, ddd, J = 50.0, 9.4, 9.1 Hz, $H_{4\beta}$), 4.15 (1H, ddd, J = 49.3, 9.7, 9.1 Hz, $H_{4\alpha}$), 4.09−4.00 (1H, m, $H_{5\alpha}$), 3.75 (1H, dqd, J = 9.8, 6.1, 2.5 Hz, $H_{5\beta}$), 3.05 (3H, s, OAc_α), 2.11 (6H, s, OAc_α, OAc_β), 2.09 (3H, s, OAc_β), 2.04 (3H, OAc_β), 2.02 (3H, s, OAc_α), 1.40 (3H, dd, J = 6.2, 1.4 Hz, $H_{6\beta}$), 1.36 (3H, dd, J = 5.9, 1.3 Hz, $H_{6\alpha}$) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.94 (CO_α), 169.93 (CO_β), 169.8 (CO_α), 169.4 (CO_β), 169.00 (CO_α), 168.96 (CO_β), 91.7 (d, J_{C-F} = 187.1 Hz, $C_{4\alpha}$), 91.5 ($C_{1\beta}$), 91.3 (d, J_{C-F} = 187.8 Hz, $C_{4\beta}$), 88.9 (d, J_{C-F} = 1.5 Hz, $C_{1\alpha}$), 72.6 (d, J_{C-F} = 20.5 Hz, $C_{3\beta}$), 70.50 (d, J_{C-F} = 8.1 Hz, $C_{2\beta}$), 70.48 (d, J_{C-F} = 24.2 Hz, $C_{5\beta}$), 69.7 (d, J_{C-F} = 20.5 Hz, $C_{3\alpha}$), 69.3 (d, J_{C-F} = 8.8 Hz, $C_{2\alpha}$), 67.5 (d, J_{C-F} = 23.5 Hz, $C_{5\alpha}$), 20.9 (OAc_α), 20.80 (OAc_β), 20.78 (OAc_α), 20.7 (OAc_β), 20.6 (OAc_β), 20.5 (OAc_α), 17.2 ($C_{6\alpha}$), 17.1 ($C_{6\beta}$) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −197.1 to −197.4 (m, $F_{4\alpha}$), −198.9 (br dd, J = 50.3, 13.9 Hz, $F_{4\beta}$) ppm; ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ −197.3 (1F, s, $F_{4\alpha}$), −199.0 (0.29F, s, $F_{4\beta}$) ppm; HRMS (ES+) for $C_{12}H_{17}FNaO_7$, calcd 315.0851, found 315.0852.

*4,6-Dideoxy-4,6-difluoro-D-galactose (**4a**). From **4b**.* Using general procedure C with **4b** (729 mg, 2.35 mmol), purification by chromatography (10% MeOH/CH_2Cl_2) afforded **4a** as a white powder (337 mg, 1.83 mmol, 78%).

*From **28**.* Using general procedure A with **28** (1.93 g, 9.74 mmol), purification by chromatography (5−8% MeOH/CH_2Cl_2) afforded **4a** as a pale yellow solid (1.40 g, 7.60 mmol, 78%) with <1% TFA (^{19}F NMR integration): mp (postcolumn) 172−174 °C; $[\alpha]_D^{25}$ + 75.0 (*c* 0.64, MeOH); IR (neat) 3402 (br), 2978 (w), 1411 (w), 1148 (m), 1099 (s), 1019 (s), 924 (m) cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD, α/β 58/42) δ 5.18 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.76 (1H, br dd, J = 51.2, 2.7 Hz, $H_{4\alpha}$), 4.70 (1H, br dd, J = 51.0, 2.8 Hz, $H_{4\beta}$), 4.58 (1H, ddd, J = 46.1, 9.5, 5.7 Hz, $H_{6a\beta}$), 4.57 (1H, ddd, J = 46.1, 9.5, 5.7 Hz, $H_{6a\alpha}$), 4.523 (1H, dddd, J = 47.5, 9.5, 6.7, 1.2 Hz, $H_{6b\beta}$), 4.518 (1H, dd, J = 7.7, 1.2 Hz, $H_{1\beta}$), 4.47 (1H, dddd, J = 47.5, 9.5, 6.7, 1.3 Hz, $H_{6b\alpha}$), 4.31 (1H, br dddd, J = 30.5, 13.2, 6.7, 5.7 Hz, $H_{5\alpha}$), 3.92 (1H, dddd, J = 28.2, 12.6, 6.7, 5.7 Hz, $H_{5\beta}$), 3.88 (1H, ddd, J = 29.3, 10.2, 2.7 Hz, $H_{3\alpha}$), 3.73 (1H, ddd, J = 10.2, 3.7, 1.1 Hz, $H_{2\alpha}$), 3.60 (1H, ddd, J = 29.5, 10.0, 2.8 Hz, $H_{3\beta}$), 3.48 (1H, ddd, J = 10.0, 7.7, 1.5 Hz, $H_{2\beta}$) ppm; ^{1}H NMR (500 MHz, D_2O, α/β 40:60) δ5.20 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.81 (1H, br dd, J = 50.8, 2.8 Hz, $H_{4\alpha}$), 4.74 (1H, br dd, J = 50.4, 2.8 Hz, $H_{4\beta}$), 4.56 (1H, dd, J = 7.9, 1.0 Hz, $H_{1\beta}$), 4.50 (1H, dddd, J = 47.5, 10.1, 7.2, 1.0 Hz, $H_{6b\beta}$), 4.28 (1H, dddd, J = 31.6, 17.2, 6.9, 4.0 Hz, $H_{5\alpha}$), 3.96 (1H, ddddd, J = 29.1, 11.3, 7.2, 4.1, 3.8 Hz, $H_{5\beta}$), 3.84 (1H, ddd, J = 29.5, 10.4, 2.8 Hz, $H_{3\alpha}$), 3.73 (1H, ddd, J = 10.4, 3.8, 1.2 Hz, $H_{2\alpha}$), 3.65 (1H, ddd, J = 29.9, 10.0, 2.8 Hz, $H_{3\beta}$), 3.42 (1H, ddd, J = 9.9, 8.1, 1.3 Hz, $H_{2\beta}$) ppm; $H_{6a\alpha}$, $H_{6b\alpha}$ and $H_{6a\beta}$ are obscured by the residual solvent peak. ^{1}H{^{19}F} NMR (500 MHz, CD_3OD) δ 5.18 (1H, d, J = 3.6 Hz, $H_{1\alpha}$), 4.76 (1H, br d, J = 2.7 Hz, $H_{4\alpha}$), 4.70 (1H, dd, J = 2.8, 0.5 Hz, $H_{4\beta}$), 4.58 (1H, dd, J = 9.5, 5.3 Hz, $H_{6a\beta}$), 4.57 (1H, dd, J = 9.5, 5.7 Hz, $H_{6a\alpha}$), 4.523 (1H, dd, J = 9.5, 6.8 Hz, $H_{6b\beta}$), 4.519 (1H, d, J = 7.7 Hz, $H_{1\beta}$), 4.47 (1H, dd, J = 9.5, 6.9 Hz, $H_{6b\alpha}$), 4.31 (1H, br dd, J = 6.7, 5.7 Hz, $H_{5\alpha}$), 3.92 (1H, dd, J = 6.8, 5.3 Hz, $H_{5\beta}$), 3.87 (1H, dd, J = 10.2, 2.7 Hz, $H_{3\alpha}$), 3.73 (1H, dd, J = 10.2, 3.7 Hz, $H_{2\alpha}$), 3.60 (1H, dd, J = 9.9, 2.8 Hz, $H_{3\beta}$), 3.48 (1H, dd, J = 9.9, 7.7 Hz, $H_{2\beta}$) ppm; ^{1}H{^{19}F} NMR (500 MHz, D_2O) δ 5.20 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.81 (1H, br d, J = 2.7 Hz, $H_{4\alpha}$), 4.75 (1H, br d, J = 2.7 Hz, $H_{4\beta}$), 4.58 (1H, ddd, J = 10.3, 4.1, 1.8 Hz, $H_{6b\alpha}$), 4.56 (1H, d, J = 8.0 Hz, $H_{1\beta}$), 4.50 (1H, dd, J = 10.2, 7.1 Hz, $H_{6b\beta}$), 4.28 (1H, dd, J = 7.0, 4.1 Hz, $H_{5\alpha}$), 3.96 (1H, dd, J = 7.2, 4.1 Hz, $H_{5\beta}$), 3.84 (1H, dd, J = 10.4, 2.8 Hz, $H_{3\alpha}$), 3.74 (1H, dd, J = 10.4, 3.7 Hz,

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$H_{2\alpha}$), 3.65 (1H, dd, J = 10.0, 2.8 Hz, $H_{3\beta}$), 3.42 (1H, dd, J = 10.0, 7.9 Hz, $H_{2\beta}$) ppm; $H_{6a\alpha}$ and $H_{6a\beta}$ are obscured by the residual solvent peak. $^{13}C\{^1H\}$ NMR (101 MHz, CD_3OD) δ 98.6 ($C_{1\beta}$), 94.4 ($C_{1\alpha}$), 91.4 (dd, J_{C-F} = 179.7, 5.9 Hz, $C_{4\alpha}$), 90.5 (dd, J_{C-F} = 180.1, 6.2 Hz, $C_{4\beta}$), 82.9 (dd, J_{C-F} = 168.0, 6.6 Hz, $C_{6\alpha}$), 82.6 (dd, J_{C-F} = 168.7, 5.9 Hz, $C_{6\beta}$), 73.8 ($C_{2\beta}$), 73.5 (d, J_{C-F} = 17.6 Hz, $C_{3\beta}$), 73.3 (dd, J_{C-F} = 22.7, 17.6 Hz, $C_{5\beta}$), 70.5 (d, J_{C-F} = 2.2 Hz, $C_{2\alpha}$), 69.8 (d, J_{C-F} = 18.3 Hz, $C_{3\alpha}$), 69.0 (dd, J_{C-F} = 23.1, 18.0 Hz, $C_{5\alpha}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 96.1 ($C_{1\beta}$), 92.4 ($C_{1\alpha}$), 90.3 (dd, J_{C-F} = 177.3, 7.0 Hz, $C_{4\alpha}$), 89.3 (dd, J_{C-F} = 178.0, 7.3 Hz, $C_{4\beta}$), 82.4 (dd, J_{C-F} = 166.7, 6.0 Hz, $C_{6\alpha}$), 82.0 (dd, J_{C-F} = 166.7, 5.7 Hz, $C_{6\beta}$), 71.8 (dd, J_{C-F} = 20.9, 17.3 Hz, $C_{5\beta}$), 71.6 ($C_{2\beta}$), 71.3 (d, J_{C-F} = 18.1 Hz, $C_{3\beta}$), 68.1 (d, J_{C-F} = 2.2 Hz, $C_{2\alpha}$), 67.70 (dd, J_{C-F} = 20.6, 17.3 Hz, $C_{5\alpha}$), 67.69 (d, J_{C-F} = 17.6 Hz, $C_{3\alpha}$) ppm; ^{19}F NMR (470 MHz, CD_3OD) δ −219.1 (1F, dddq, J = 51.2, 29.5, 28.2, 1.2 Hz, $H_{4\beta}$), −222.0 (1F, dddq, J = 51.1, 30.5, 29.3, 1.0 Hz, $F_{4\alpha}$), −232.5 (1F, ddd, J = 47.5, 46.1, 12.4 Hz, $F_{6\beta}$), −232.6 (1F, dddd, J = 47.6, 46.8, 13.5, 0.6 Hz, $F_{6\alpha}$) ppm; ^{19}F NMR (470 MHz, D_2O) δ −217.0 (1F, dtq, J = 50.4, 29.7, 1.1 Hz, $F_{4\beta}$), 219.4 (1F, ddddd, J = 50.8, 31.6, 29.3, 3.6, 0.7 Hz, $F_{4\alpha}$), −230.6 (1F, dddd, J = 57.9, 45.4, 15.3, 2.5 Hz, $F_{6\beta}$), −230.8 (1F, dddd, J = 47.6, 45.4, 17.2, 3.9 Hz, $F_{6\alpha}$) ppm; $^{19}F(^1H)$ NMR (470 MHz, CD_3OD) δ −219.0 (1F, s, $F_{4\beta}$), −221.9 (1F, s, $F_{4\alpha}$), −232.3 (1F, s, $F_{6\beta}$), −232.5 (1F, s, $F_{6\alpha}$) ppm; $^{19}F(^1H)$ NMR (470 MHz, D_2O) δ −216.9 (1F, d, J = 2.5 Hz, $F_{4\beta}$), −219.2 (1F, d, J = 3.9 Hz, $F_{4\alpha}$), −230.4 (1F, d, J = 2.5 Hz, $F_{6\beta}$), −230.7 (1F, d, J = 3.9 Hz, $F_{6\alpha}$) ppm; HRMS (ES^+) for $C_6H_{10}F_2NaO_4$ $[M + Na]^+$ calcd 207.0439, found 207.0439. Spectroscopic data corresponds with the literature.[116]

*1,2,3-Tri-O-acetyl-4,6-dideoxy-4,6-difluoro-D-galactopyranoside (**4b**).* Using general procedure B from **28** (1.50 g, 8.15 mmol) and H_2SO_4 (5 equiv), purification by chromatography (25% EtOAc/petroleum ether) afforded **4b** as an off-yellow amorphous solid (1.87 g, 6.03 mmol, 74%): mp (postcolumn) 91−92 °C; IR (neat) 2981 (w), 1746 (s), 1374 (s), 1209 (s), 1010 (s), 899 (s) cm^{-1}; Data for the major (α) anomer: ^1H NMR (400 MHz, $CDCl_3$, α/β 98:2) δ 6.40 (1H, d, J = 3.6 Hz, H_1), 5.41 (1H, ddd, J = 10.9, 3.6, 1.2 Hz, H_2), 5.30 (1H, ddd, J = 26.2, 10.9, 2.5 Hz, H_3), 5.02 (1H, dd, J = 50.3, 2.3 Hz, H_4), 4.58 (1H, ddd, J = 46.1, 9.4, 6.6 Hz, H_{6a}), 4.54 (1H, dddd, J = 46.2, 9.4, 6.1, 1.2 Hz, H_{6b}), 4.29 (1H, dddd, J = 28.9, 10.9, 6.6, 6.1 Hz, H_5), 2.17 (3H, s, OAc), 2.14 (3H, s, OAc), 2.04 (3H, s, OAc) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 170.3 (CO), 169.6 (CO), 168.7 (CO), 89.5 (C_1), 85.9 (dd, J_{C-F} = 185.6, 5.1 Hz, C_4), 79.9 (dd, J_{C-F} = 170.2, 6.6 Hz, C_6), 69.5 (dd, J_{C-F} = 25.3, 18.7 Hz, C_5), 67.7 (d, J_{C-F} = 17.6 Hz, C_3), 66.1 (d, J_{C-F} = 2.2 Hz, C_2), 20.8 (OAc), 20.7 (OAc), 20.5 (OAc) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −219.6 (1F, dt, J = 50.3, 27.7 Hz, F_4), −232.4 (1F, td, J = 46.4, 11.3 Hz, F_6) ppm; $^{19}F(^1H)$ NMR (376 MHz, $CDCl_3$) δ −219.8 (1F, s, F_4), −232.5 (1F, s, F_6) ppm; Selected data for the minor (β) anomer: ^1H NMR (400 MHz, $CDCl_3$) δ 5.73 (1H, dd, J = 8.3, 0.9 Hz, H_1) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −217.6 (1F, dt, J = 50.3, 27.7 Hz, F_4) ppm; $^{19}F(^1H)$ NMR (376 MHz, $CDCl_3$) δ −217.8 (1F, s, F_4) ppm; HRMS (ES^+) for $C_{12}H_{16}F_2NaO_7$ $[M + Na]^+$ calcd 333.0756 $[M + H]^+$ found 333.0755.

*4,6-Dideoxy-4,6-difluoro-D-glucose (**5a**). From **5b**.* Using general procedure C with **5b** (413 mg, 1.33 mmol), purification by chromatography (10% MeOH/CH_2Cl_2) afforded **5a** as a white powder (158 mg, 0.86 mmol, 65%).

*From **35**.* Using general procedure A with **35** (1.03 g, 5.20 mmol) for 60 h, purification by chromatography (3−6% MeOH/CH_2Cl_2) afforded **5a** as a white powder (650 mg, 3.53 mmol, 68%) with <1% TFA (^{19}F NMR integration).

*From **74**.* Using general procedure A with **74** (130 mg, 0.42 mmol) for 36 h, purification by chromatography (4−8% MeOH/CH_2Cl_2) afforded **5a** as an off-white solid (42 mg, 0.23 mmol, 55%) with <1% TFA (^{19}F NMR integration): mp (postcolumn) 117−119 °C; $[\alpha]_D^{24}$ +53.5 (*c* 0.91, MeOH), lit.[20] +48.2 (*c* 1.0, MeOH); IR (neat) 3355 (br. s), 3288 (br. s), 2958 (w), 1149 (s), 1130 (s), 1081 (s), 1054 (s) cm^{-1}; ^1H NMR (500 MHz, CD_3OD, α/β 64:36) δ 5.11 (1H, t, J = 3.5 Hz, $H_{1\alpha}$), 4.61 (1H, ddt, J = 47.8, 10.4, 2.0 Hz, $H_{6a\beta}$), 4.59 (1H, dddd, J = 47.5, 10.4, 3.7, 1.7 Hz, $H_{6a\alpha}$), 4.56 (1H, dddd, J = 47.5, 10.4, 4.1, 1.8 Hz, $H_{6b\beta}$), 4.543 (1H, ddt, J = 48.1, 10.4, 1.7 Hz, $H_{6b\alpha}$), 4.542 (1H, dd, J = 7.9, 0.5 Hz, $H_{1\beta}$), 4.24 (1H, dt, J 50.9, 8.8 Hz, $H_{4\beta}$), 4.22 (1H, dt, J 50.9, 8.7 Hz, $H_{4\alpha}$), 4.03−4.13 (1H, m, $H_{5\alpha}$), 3.92 (1H, dt, J 16.3, 9.3 Hz, $H_{3\alpha}$), 3.60−3.64 (1H, m, $H_{5\beta}$), 3.65 (1H, dddd, J = 16.3, 9.5, 8.7, 0.8 Hz, $H_{3\beta}$), 3.38 (1H, ddd, J 9.6, 3.7, 0.9 Hz, $H_{2\alpha}$), 3.17 (1H, ddd, J 9.3, 7.8, 0.7 Hz, $H_{2\beta}$) ppm; ^1H NMR (500 MHz, D_2O, α/β 45:55) δ 5.12 (1H, t, J = 3.5 Hz, $H_{1\alpha}$), 4.67−4.48 (4H, m, $H_{6\alpha}$, $H_{6\beta}$), 4.59 (1H, dd, J = 8.0, 0.5 Hz, $H_{1\beta}$), 4.28 (2H, ddd, J = 50.7, 10.1, 8.9 Hz, $H_{4\alpha}$, $H_{4\beta}$), 4.06 (1H, dddddd, J = 28.0, 10.1, 4.1, 3.6, 1.8, 0.5 Hz, $H_{5\alpha}$), 3.87 (1H, dt, J = 15.9, 9.3 Hz, $H_{3\alpha}$), 3.75 (1H, ddddd, J = 25.8, 10.0, 3.9, 2.6, 2.1 Hz, $H_{5\beta}$), 3.70 (1H, dddd, J = 15.7, 9.6, 8.8, 0.8 Hz, $H_{3\beta}$), 3.46 (1H, ddd, J = 9.9, 3.8, 0.9 Hz, $H_{2\alpha}$), 3.17 (1H, ddd, J = 9.6, 8.0, 0.9 Hz, $H_{2\beta}$) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, CD_3OD) δ 5.11 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.52−4.62 (4H, m, $H_{6a\alpha}$ + $H_{6b\alpha}$ + $H_{6a\beta}$ + H6$_{b\beta}$), 4.54 (1H, d, J = 7.9 Hz, $H_{1\beta}$), 4.24 (1H, t, J = 8.8 Hz, $H_{4\beta}$), 4.22 (1H, t, J = 8.8 Hz, $H_{4\alpha}$), 4.08 (1H, ddd, J = 10.2, 3.8, 1.5 Hz, $H_{5\alpha}$), 3.92 (1H, t, J = 9.3 Hz, $H_{3\alpha}$), 3.68 (1H, ddd, J = 10.0, 4.1, 1.8 Hz, $H_{5\beta}$), 3.65 (1H, t, J = 9.0 Hz, $H_{3\beta}$), 3.38 (1H, dd, J = 9.6, 3.7 Hz, $H_{2\alpha}$), 3.17 (1H, dd, J = 9.3, 7.8 Hz, $H_{2\beta}$) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, D_2O) δ 5.12 (1H, d, J = 3.9 Hz, $H_{1\alpha}$), 4.60 (1H, dd, J = 11.0, 3.5 Hz, $H_{6a\alpha}$), 4.59 (1H, d, J = 8.0 Hz, $H_{1\beta}$), 4.59 (1H, dd, J = 10.9, 2.0 Hz, $H_{6a\beta}$), 4.55 (1H, dd, J = 10.9, 3.2 Hz, $H_{6b\beta}$), 4.54 (1H, dd, J = 11.0, 1.1 Hz, $H_{6b\alpha}$), 4.28 (2H, dd, J = 10.0, 8.9 Hz, $H_{4\alpha}$, $H_{4\beta}$), 4.06 (1H, dddd, J = 10.0, 3.5, 1.8, 0.5 Hz, $H_{5\alpha}$), 3.87 (1H, dd, J = 9.9, 8.8 Hz, $H_{3\alpha}$), 3.75 (1H, ddd, J = 10.0, 3.9, 2.0 Hz, $H_{5\beta}$), 3.70 (1H, dd, J = 9.6, 8.8 Hz, $H_{3\beta}$), 3.46 (1H, dd, J = 9.9, 3.8 Hz, $H_{2\alpha}$), 3.17 (1H, dd, J = 9.6, 8.0 Hz, $H_{2\beta}$) ppm; ^{13}C NMR (101 MHz, CD_3OD) δ 98.4 (d, J_{C-F} = 1.5 Hz, $C_{1\beta}$), 94.0 (d, J_{C-F} = 1.8 Hz, $C_{1\alpha}$), 90.2 (dd, J_{C-F} = 182.3, 7.3 Hz, $C_{4\alpha}$), 89.9 (dd, J_{C-F} = 181.9, 7.3 Hz, $C_{4\beta}$), 83.1 (d, J_{C-F} = 173.1 Hz, $C_{6\alpha}$), 82.7 (d, J_{C-F} = 172.4 Hz, $C_{6\beta}$), 76.0 (d, J_{C-F} = 8.8 Hz, $C_{2\beta}$), 75.9 (d, J_{C-F} = 18.0 Hz, $C_{3\beta}$), 73.7 (dd, J_{C-F} = 24.2, 18.3 Hz, $C_{5\beta}$), 73.4 (bd, J_{C-F} = 8.1 Hz, $C_{2\alpha}$), 72.9 (d, J_{C-F} = 17.2 Hz, $C_{3\alpha}$), 69.3 (dd, J_{C-F} = 23.8, 18.0 Hz, $C_{5\alpha}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 96.0 (d, J_{C-F} = 1.2 Hz, $C_{1\beta}$), 92.0 (d, J_{C-F} = 1.4 Hz, $C_{1\alpha}$), 88.1 (dd, J_{C-F} = 180.5, 7.2 Hz, $C_{6\alpha}$), 87.9 (dd, J_{C-F} = 180.8, 7.3 Hz, $C_{6\beta}$), 81.6 (d, J_{C-F} = 168.3 Hz, $C_{4\alpha}$), 81.4 (d, J_{C-F} = 168.6 Hz, $C_{4\beta}$), 73.6 (d, J_{C-F} = 17.9 Hz, $C_{3\beta}$), 73.4 (d, J_{C-F} = 8.8 Hz, $C_{2\beta}$), 71.7 (dd, J_{C-F} = 24.3, 17.9 Hz, $C_{5\beta}$), 70.9 (d, J_{C-F} = 18.1 Hz, $C_{3\alpha}$), 70.8 (d, J_{C-F} = 8.3 Hz, $C_{2\alpha}$), 67.6 (dd, J_{C-F} = 24.1, 17.4 Hz, $C_{5\alpha}$) ppm; ^{19}F NMR (470 MHz, CD_3OD) δ −199.6 to −199.4 (1F, m, $F_{4\alpha}$, a dd, J = 51.0, 16.2 was observed), −201.4 to −201.2 (1F, m, $F_{4\beta}$, a dd, J = 51.0, 16.2 Hz was observed), −236.6 (1F, td, J = 47.7, 25.0 Hz, $F_{6\beta}$), −237.3 (1F, td, J = 47.8, 26.9 Hz, $F_{6\alpha}$) ppm; ^{19}F NMR (470 MHz, D_2O) δ −198.5 (1F, ddddtd, J = 50.8, 15.8, 4.0, 3.1, 1.7, 0.8 Hz, $F_{4\alpha}$), −200.6 (1F, ddddt, J = 50.8, 15.7, 3.6, 1.8, 0.7 Hz, $F_{4\beta}$), −235.2 (1F, td, J = 47.1. 25.9 Hz, $F_{6\beta}$), −235.8 (1F, dddd, J = 47.6, 46.8, 27.9, 0.7 Hz. $F_{6\alpha}$) ppm; $^{19}F(^1H)$ NMR (470 MHz, CD_3OD) δ −199.5 (1F, s, $F_{4\alpha}$), −201.3 (1F, s, $F_{4\beta}$), −236.6 (1F, s, $F_{6\beta}$), −237.4 (1F, s, $F_{6\alpha}$) ppm; $^{19}F(^1H)$ NMR (470 MHz, D_2O) δ −198.4 (1F, s, $F_{4\alpha}$), −200.5 (1F, s, $F_{4\beta}$), −235.1 (1F, s, $F_{6\beta}$), −235.7 (1F, s, $F_{6\alpha}$) ppm; MS (ESI+) 207.3 $[M + Na]^+$. Physical and spectroscopic values are consistent with the literature.[20]

*1,2,3-Tri-O-acetyl-4,6-dideoxy-4,6-difluoro-D-glucopyranoside (**5b**) and 1,1,2,3,5-Penta-O-acetyl-4,6-dideoxy-4,6-difluoro-D-glucose (**5c**).* Using general procedure B with **35** (506 mg, 2.55 mmol) and H_2SO_4 (3 equiv), purification by chromatography (20−50% EtOAc/hexane) afforded first **5b** as a colorless oil (543 mg, 1.75 mmol, 69%) and then the peracetylated open chain form **5c** as a white powder (135 mg, 0.33 mmol, 13%).

*Data for **5b**.* IR (neat) 2970 (w), 1712 (s), 1372 (m), 1225 (s), 1013 (s), 913 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, α/β 88:12) δ 6.32 (1H, t, J = 3.3 Hz, $H_{1\alpha}$), 5.74 (1H, d, J = 8.3 Hz, $H_{1\beta}$), 5.62 (1H, app dt, J = 13.8, 9.7 Hz, $H_{3\alpha}$), 5.39 (1H, dddd, J = 14.8, 9.5, 8.9, 0.6 Hz, $H_{3\beta}$), 5.07 (1H, ddd, J = 9.4, 8.3, 0.4 Hz, $H_{2\beta}$), 5.02 (1H, ddd, J = 10.3, 3.7, 0.9 Hz, $H_{2\alpha}$), 4.76−4.50 (6H, m, $H_{4\alpha}$, $H_{4\beta}$, $H_{6\alpha}$, $H_{6\beta}$), 4.08 (1H, dddt, J = 26.5, 10.3, 4.2, 2.2 Hz, $H_{5\alpha}$), 3.82 (1H, ddtd, J = 25.4, 10.0, 3.0, 2.0 Hz, $H_{5\beta}$), 2.18 (3H, s, OAc_α), 2.11 (3H, s, OAc_α), 2.11 (3H, s, OAc_β), 2.10 (3H, s, OAc_β), 2.04 (3H, s, OAc_β), 2.02 (3H, s, OAc_α) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.74 (CO_α), 169.69 (CO_β), 169.5 (CO_α), 169.1 (CO_β), 168.7 (CO_β), 168.6 (CO_α), 91.4 ($C_{1\beta}$), 88.8 ($C_{1\alpha}$), 85.2 (dd, J_{C-F} = 187.1, 8.1 Hz, $C_{4\alpha}$),

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85.0 (dd, J_{C-F} = 187.4, 7.7 Hz, $C_{4\beta}$), 80.1 (d, J_{C-F} = 176.1 Hz, $C_{6\alpha}$), 79.9 (d, J_{C-F} = 176.1 Hz, $C_{6\beta}$), 72.7 (dd, J_{C-F} = 24.2, 18.3 Hz, $C_{5\beta}$), 72.3 (d, J_{C-F} = 19.8 Hz, $C_{3\beta}$), 70.3 (dd, J_{C-F} = 23.5, 18.3 Hz, $C_{5\alpha}$), 69.9 (d, J_{C-F} = 8.1 Hz, $C_{2\beta}$), 69.4 (d, J_{C-F} = 19.8 Hz, $C_{3\alpha}$), 68.7 (d, J_{C-F} = 8.1 Hz, $C_{2\alpha}$), 20.6 (OAc_α), 20.5 (OAc_α), 20.4 (OAc_β), 20.3 (OAc_β), 20.2 (OAc_α) (One OAc_β signal not resolved) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −199.3 (1F, br dd, J = 50.3, 13.8 Hz, $F_{4\alpha}$), −200.9 (1F, br dd, J = 51.2, 14.8 Hz, $F_{4\beta}$), −236.8 (1F, td, J = 46.8, 25.4 Hz, $F_{6\beta}$), −237.1 (1F, td, J = 46.8, 26.5 Hz, $F_{6\alpha}$) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −199.1 (1F, s, $F_{4\alpha}$), −200.75 (1F, s, $F_{4\beta}$), −236.7 (1F, s, $F_{6\beta}$), −237.0 (1F, s, $F_{6\alpha}$) ppm; HRMS (ES+) for $C_{12}H_{16}F_2NaO_7$ $[M + Na]^+$ calcd 333.0756, found 333.0761. Spectroscopic data corresponds with the literature.[58,117]

Data for ***5c****:* mp (postcolumn) 111−113 °C; $[\alpha]_D^{25}$ −12.3 (*c* 0.55, $CHCl_3$); IR (neat) 2947 (w), 1738 (s), 1370 (m), 1215 (s), 1011 (m), 963 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.94 (1H, br d, J = 4.6 Hz, H_1), 5.50 (1H, ddd, J = 5.7, 4.6, 0.7 Hz, H_2), 5.46 (1H, ddd, J = 27.5, 5.7, 2.0 Hz, H_3), 5.03 (1H, ddd, J = 47.4, 8.9, 1.8 Hz, H_4), 5.05−4.94 (1H, m, H_5), 4.64 (1H, ddt, J = 46.7, 10.8, 2.6 Hz, H_{6a}), 4.61 (1H, ddt, J = 47.7, 10.8, 2.2 Hz, H_{6b}), 2.11−2.09 (15H, m, 5 × CH_3) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, $CDCl_3$) δ 6.94 (1H, d, J = 4.4 Hz, H_1), 5.50 (1H, dd, J = 5.8, 4.6 Hz, H_2), 5.45 (1H, dd, J = 5.8, 2.1 Hz, H_3), 5.04 (1H, dd, J = 9.0, 2.2 Hz, H_4), 5.00 (1H, dt, J = 8.8, 2.4 Hz, H_5), 4.64 (1H, dd, J = 10.8, 2.6 Hz, H_{6a}), 4.62 (1H, dd, J = 10.8, 2.4 Hz, H_{6b}), 2.19−2.09 (15H, m, 5 × CH_3) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 169.7 (*C*O), 169.6 (*C*O), 169.5 (*C*O), 168.1 (2 × *C*O), 87.2 (dd, J_{C-F} = 181.1, 6.1 Hz, C_4), 85.9 (C_1), 80.4 (dd, J_{C-F} = 174.3, 2.6 Hz, C_6), 70.1 (d, J_{C-F} = 3.1 Hz, C_2), 68.0 (dd, J_{C-F} = 60.6, 18.7 Hz, C_5), 66.7 (d, J_{C-F} = 17.2 Hz, C_3), 20.7 (CH_3), 20.54 (2 × CH_3), 20.46 (CH_3), 20.4 (CH_3) ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ −209.4 (1F, br ddd, J = 46.1, 27.2, 7.5 Hz, F_4), −237.7 (1F, br td, J = 47.2, 25.8 Hz, F_6) ppm; $^{19}F\{^1H\}$ NMR (470 MHz, $CDCl_3$) δ −209.5 (1F, d, J = 1.1 Hz, F_4), −237.8 (1F, d, J = 1.1 Hz, F_6) ppm; HRMS (ES^+) for $C_{16}H_{22}F_2NaO_{10}$ $[M + H]^+$ calcd 435.1073 found 435.1076.

*4,6-Dideoxy-4,4-difluoro-D-xylo-hexopyranose (****6a****). From* ***6b****.* Using general procedure C with **6b** (192 mg, 0.52 mmol), purification by chromatography (5% MeOH/EtOAc) afforded **6a** as a white amorphous solid (113 mg, 0.61 mmol, 97%).

From ***76****.* Using general procedure A with **76** (325 mg, 1.04 mmol) for 21 h, purification by chromatography (5% $MeOH/CH_2Cl_2$) and further purification by recrystallization (Et_2O) afforded **6a** as colorless needles (116 mg, 0.63 mmol, 61%) with <1% TFA (^{19}F NMR integration): mp (Et_2O) 135−145 °C; $[\alpha]_D^{24}$ +80.4 (*c* 0.72, MeOH); IR (neat) 3347 (br), 2942 (w), 1441 (w), 1246 (w), 1048 (s), 978 (s), 926 (m), 859 (m) cm^{-1}; ^1H NMR (500 MHz, CD_3OD, α/β 60:40) δ 5.09 (1H, t, J = 3.1 Hz, $H_{1\alpha}$), 4.55 (1H, dd, J = 7.9, 0.9 Hz, $H_{1\beta}$), 4.17 (1H, dq, J = 23.6, 6.5 Hz, $H_{5\alpha}$), 3.93 (1H, ddd, J = 20.6, 10.0, 6.5 Hz, $H_{3\alpha}$), 3.75 (1H, dq, J = 22.2, 6.3 Hz, $H_{5\beta}$), 3.67 (1H, ddd, J = 20.7, 9.8, 6.6 Hz, $H_{3\beta}$), 3.56 (1H, ddd, J = 10.0, 3.7, 1.6 Hz, $H_{2\alpha}$), 3.23 (1H, ddd, J = 9.8, 7.9, 2.0 Hz, $H_{2\beta}$), 1.26 (3H. br d, J = 6.3 Hz, $H_{6\beta}$), 1.21 (3H, br d, J = 6.5 Hz, $H_{6\alpha}$) ppm; ^1H NMR (500 MHz, D_2O, α/β 39:61) δ 5.11 (1H, br dd, J = 3.8, 2.5 Hz, $H_{1\alpha}$), 4.60 (1H, dd, J = 8.1, 1.0 Hz, $H_{1\beta}$), 4.16 (1H, dq, J = 24.2, 6.5 Hz, $H_{5\alpha}$), 3.91 (1H, ddd, J = 20.7, 10.2, 6.2 Hz, $H_{3\alpha}$), 3.80 (1H, dq, J = 23.0, 6.3 Hz, $H_{5\beta}$), 3.75 (1H, ddd, J = 20.8, 10.0, 6.3 Hz, $H_{3\beta}$), 3.59 (1H, ddd, J = 10.2, 3.8, 1.7 Hz, $H_{2\alpha}$), 3.29 (1H, ddd, J = 10.0, 8.0, 2.0 Hz, $H_{2\beta}$), 1.16 (3H, d, J = 6.4 Hz, $H_{6\beta}$), 1.13 (3H, d, J = 6.5 Hz, $H_{6\alpha}$) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, CD_3OD) δ 5.09 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.55 (1H, d, J = 7.9 Hz, $H_{1\beta}$), 4.17 (1H, q, J = 6.5 Hz, $H_{5\alpha}$), 3.93 (1H, d, J = 10.0 Hz, $H_{3\alpha}$), 3.75 (1H, q, J = 6.4 Hz, $H_{5\beta}$), 3.67 (1H, d, J = 9.8 Hz, $H_{3\beta}$), 3.56 (1H, dd, J = 10.0, 3.7 Hz, $H_{2\alpha}$), 3.32 (1H, dd, J = 9.8, 7.9 Hz, $H_{2\beta}$), 1.26 (3H, d, J = 6.4 Hz, $H_{6\beta}$), 1.21 (3H, d, J = 6.5 Hz, $H_{6\alpha}$) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, D_2O) δ 5.11 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.60 (1H, d, J = 8.0 Hz, $H_{1\beta}$), 4.16 (1H, q, J = 6.5 Hz, $H_{5\alpha}$), 3.91 (1H, d, J = 10.2 Hz, $H_{3\alpha}$), 3.80 (1H, q, J = 6.5 Hz, $H_{5\beta}$), 3.75 (1H, d, J = 9.9 Hz, $H_{3\beta}$), 3.59 (1H, dd, J = 10.2, 3.8 Hz, $H_{2\alpha}$), 3.29 (1H, dd, J = 9.9, 8.0 Hz, $H_{2\beta}$), 1.16 (3H, d, J = 6.5 Hz, $H_{6\beta}$), 1.13 (3H, d, J = 6.5 Hz, $H_{6\alpha}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, CD_3OD) δ 120.1 (dd, J_{C-F} = 250.7, 248.9 Hz, $C_{4\alpha}$), 119.4 (dd, J_{C-F} = 251.6, 248.0 Hz, $C_{4\beta}$), 98.2 ($C_{1\beta}$), 94.0 ($C_{1\alpha}$), 75.4 (d, J_{C-F} = 8.2 Hz, $C_{2\beta}$), 74.5 (t, J_{C-F} = 20.4 Hz, $C_{3\beta}$), 72.7 (d, J_{C-F} = 7.3 Hz, $C_{2\alpha}$), 71.6 (t, J_{C-F} = 20.0 Hz, $C_{3\alpha}$), 70.9 (dd, J_{C-F} = 30.4, 24.1 Hz, $C_{5\beta}$), 66.0 (dd, J_{C-F} = 30.0, 24.5 Hz, $C_{5\alpha}$), 12.2 (d, J_{C-F} = 5.5 Hz, $C_{6\beta}$), 12.0 (d, J_{C-F} = 5.6 Hz, $C_{6\alpha}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 118.4 (t, J_{C-F} = 249.6 Hz, $C_{4\alpha}$), 117.9 (t, J_{C-F} = 249.8 Hz, $C_{4\beta}$), 95.7 d, J_{C-F} = 1.0 Hz, $C_{1\beta}$), 91.9 (br s, $C_{1\alpha}$), 73.1 (d, J_{C-F} = 8.1 Hz, $C_{2\beta}$), 72.2 (t, J_{C-F} = 20.7 Hz, $C_{3\beta}$), 70.3 (d, J_{C-F} = 7.4 Hz, $C_{2\alpha}$), 69.54 (dd, J_{C-F} = 30.6, 24.2 Hz, $C_{5\beta}$), 69.54 (t, J_{C-F} = 20.2 Hz, $C_{3\alpha}$), 64.9 (dd, J_{C-F} = 29.8, 24.3 Hz, $C_{5\alpha}$), 10.7 (d, J_{C-F} = 5.3 Hz, $C_{6\beta}$), 10.6 (d, J_{C-F} = 5.5 Hz, $C_{6\alpha}$) ppm; ^{19}F NMR (471 MHz, CD_3OD) δ −118.8 (1F, br ddd, J = 245.9, 6.1, 2.1 Hz, $F_{4\alpha(eq)}$), −121.3 (1F, dd, J = 246.1, 6.6 Hz, $H_{4\beta(eq)}$), −139.5 (1F, dt, J = 246.1, 21.6 Hz, $F_{4\beta(ax)}$), −141.3 (1F, dddd, J = 245.9, 23.6, 20.6, 1.1 Hz, $H_{4\alpha(ax)}$) ppm; ^{19}F NMR (470 MHz, D_2O) δ −117.6 (1F, dddd, J = 245.3, 6.1, 2.5, 0.7 Hz, $F_{4\alpha(eq)}$), −120.0 (1F, br dd, J = 245.3, 6.3 Hz, $F_{4\beta(eq)}$), −137.4 (1F, br dt, J = 245.3, 21.9 Hz, $F_{4\beta(ax)}$), −138.9 (1F, dddd, J = 245.3, 23.6, 21.1, 1.4 Hz, $F_{4\alpha(ax)}$) ppm; $^{19}F\{^1H\}$ NMR (471 MHz, CD_3OD) δ −118.8 (1F, d, J = 245.9 Hz, $F_{4\alpha(eq)}$), −121.9 (1F, d, J = 246.1 Hz, $F_{4\beta(eq)}$), −139.5 (1F, d, J = 246.1 Hz, $F_{4\beta(ax)}$), −141.3 (1F, d, J = 245.9 Hz, $F_{4\alpha(ax)}$) ppm; $^{19}F\{^1H\}$ NMR (470 MHz, D_2O) δ −117.6 (1F, d, J = 245.3 Hz, $F_4(eq)_\alpha$), −120.0 (1F, d, J = 245.3 Hz, $F_4(eq)_\beta$), −137.4 (1F, d, J = 245.3 Hz, $F_4(ax)_\beta$), −138.9 (1F, d, J = 245.3 Hz, $F_4(ax)_\alpha$) ppm; HRMS (ES+) for $C_6H_{10}F_2NaO_4$ calcd 207.0439, found 207.0444.

*1,2,3-Tri-O-acetyl-4,6-dideoxy-4,4-difluoro-D-xylo-hexopyranoside (****6b****) and 1,1,2,3,5-Penta-O-acetyl-4,6-dideoxy-4,4-difluoro-D-xylo-hexose (****6c****).* A solution of **76** (448 mg, 1.43 mmol) in THF/H_2O (9:1, 5 mL) was stirred for 5 min, then concentrated *in vacuo*. The brown residue was then redissolved in Ac_2O (2.7 mL), and cooled to 0 °C. concd H_2SO_4 (80 μL, 1.43 mmol) was added, and the reaction warmed to rt and stirred for 48 h. The reaction was diluted with EtOAc (20 mL) and quenched by the slow addition of satd $NaHCO_{3(aq)}$ (20 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (50 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by chromatography (Biotage Isolera One, 10 g KP-Sil, gradient 0−15% EtOAc/cyclohexane) afforded first **6b** as a colorless oil (212 mg, 0.68 mmol, 48%) and then the peracetylated open chain form **6c** as a white powder (41 mg, 0.10 mmol, 7%).

Data for ***6b****:* IR (neat) 2999 (w), 1755 (s), 1371 (m), 1205 (s), 1061 (s), 938 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, α/β 87:13) δ 6.32 (1H, dd, J = 3.6, 2.5 Hz, $H_{1\alpha}$), 5.75 (1H, dd, J = 8.4, 0.8 Hz, $H_{1\beta}$), 5.59 (1H, ddd, J = 19.8, 10.7, 4.5 Hz, $H_{3\alpha}$), 5.37 (1H, ddd, J = 19.7, 10.2, 5.0 Hz, $H_{3\beta}$), 5.23 (1H, ddd, J = 10.2, 8.3, 1.5 Hz, $H_{2\beta}$), 5.19 (1H, ddd, J = 10.7, 3.7, 1.3 Hz, $H_{2\alpha}$), 4.16 (1H, dq, J = 22.3, 6.4 Hz, $H_{5\alpha}$), 3.87 (1H, dq, J = 21.2, 6.4 Hz, $H_{5\beta}$), 2.18 (3H, s, $COCH_{3\alpha}$), 2.17 (3H, s, $COCH_{3\alpha}$), 2.15 (3H, s, $COCH_{3\beta}$), 2.21 (3H, s, $COCH_{3\beta}$), 2.04 (3H, s, $COCH_{3\beta}$), 2.02 (3H, s, $COCH_{3\alpha}$), 1.37 (3H, d, J = 6.4 Hz, $H_{6\beta}$), 1.33 (3H, d, J = 6.4 Hz, $H_{6\alpha}$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.7 (CO_α), 169.6 (CO_β), 169.4 (CO_α), 169.0 (CO_β), 168.9 (CO_β), 168.7 (CO_α), 116.4 (dd, J_{C-F} = 253.1, 251.6 Hz, $C_{4\alpha}$), 115.9 (dd, J_{C-F} = 254.6, 252.4 Hz, $C_{4\beta}$), 91.4 (d, J_{C-F} = 1.5 Hz, $C_{1\beta}$), 88.9 ($C_{1\alpha}$), 71.1 (dd, J_{C-F} = 30.1, 25.0 Hz, $C_{5\beta}$), 70.4 (dd, J_{C-F} = 22.0, 19.1 Hz, $C_{3\beta}$), 69.6 (d, J_{C-F} = 8.1 Hz, $C_{2\beta}$), 68.6 (d, J_{C-F} = 7.3 Hz, $H_{2\alpha}$), 68.1 (dd, J_{C-F} = 29.3, 25.0 Hz, $C_{5\alpha}$), 67.6 (d, J_{C-F} = 22.0, 19.1 Hz, $C_{3\alpha}$), 20.6 ($COCH_{3\alpha}$), 20.7 ($COCH_{3\beta}$), 20.48 ($COCH_{3\alpha}$), 20.45 ($COCH_{3\beta}$), 20.38 ($COCH_{3\beta}$), 20.35 ($COCH_{3\alpha}$), 11.3 (d, J_{C-F} = 5.9 Hz, $C_{6\alpha}$) ppm ($C_{6\beta}$ obscured by $C_{6\alpha}$); ^{19}F NMR (376 MHz, $CDCl_3$) δ −117.2 (1F, br d, J = 249.7 Hz, $F_{4(eq)\alpha}$), −119.6 (1F, br dd, J = 249.7, 4.3 Hz, $F_{4(eq)\beta}$), −133.8 (1F, dt, J = 249.7, 20.8 Hz, $F_{4(ax)\beta}$), −135.0 (1F, dt, J = 249.7, 20.8 Hz, $F_{4(ax)\alpha}$) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −117.2 (1F, d, J = 249.7 Hz, $F_{4(eq)\alpha}$), −119.6 (1F, d, J = 249.7 Hz, $F_{4(eq)\beta}$), −133.8 (1F, d, J = 249.7 Hz, $F_{4(ax)\alpha}$), −135.0 (1F, d, J = 249.7 Hz, $F_{4(ax)\alpha}$) ppm; HRMS (ES^+) for $C_{12}H_{16}F_2NaO_7$ $[M + Na]^+$ calcd 333.0756 found 333.0754.

Data for ***6c****:* mp (postcolumn) 114−116 °C; $[\alpha]_D^{25}$ −23.4 (*c* 0.47, $CHCl_3$); IR (neat) 2968 (w), 1759 (s), 1743 (s), 1374 (s), 1127 (s), 1044 (s), 979 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.86 (1H, d, J = 5.4 Hz, H_1), 5.70 (1H, dd, J = 5.4, 2.7 Hz, H_2), 5.62−5.50 (1H, m,

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H_3), 5.09 (1H, ddq, J = 14.4, 9.7, 6.5 Hz, H_5), 2.13 (3H, s, CH_3), 2.11 (3H, s, CH_3), 2.09 (3H, s, CH_3), 2.07 (3H, s, CH_3), 2.06 (3H, s, CH_3), 1.31 (3H, d, J = 6.5 Hz, H_6) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.5 (*C*O), 169.21 (*C*O), 169.16 (*C*O), 168.13 (*C*O), 168.05 (*C*O), 119.5 (t, J_{C-F} = 251.6 Hz, C_4), 86.0 (C_1), 67.3 (C_2), 66.2 (dd, J_{C-F} = 33.0, 29.3 Hz, C_5), 65.5 (dd, J_{C-F} = 31.5, 27.9 Hz, C_3), 20.8 (*C*H_3), 20.52 (*C*H_3), 20.49 (*C*H_3), 20.45 (*C*H_3), 20.4 (*C*H_3), 12.1 (t, J_{C-F} = 2.9 Hz, C_6) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −120.6 (1F, ddd, J = 277.4, 15.6, 10.4 Hz, F_{4a}), −121.3 (1F, ddd, J = 277.4, 13.9, 10.4 Hz, F_{4b}) ppm; $^{19}F(^1H\}$ NMR (376 MHz, $CDCl_3$) δ −120.6 (1F, d, J = 277.4 Hz, F_{4a}), −121.3 (1F, d, J = 277.4 Hz, F_{4b}) ppm; HRMS (ES^+) for $C_{16}H_{22}F_2NaO_{10}$ $[M + H]^+$ calcd 435.1073 found 435.1080.

*4,6-Dideoxy-6,6-difluoro-D-xylo-hexopyranose (**7a**). From **7b**.* Using general procedure C with **7b** (726 mg, 2.34 mmol), purification by chromatography (8% MeOH/CH_2Cl_2) afforded **7a** as an off-white powder (257 mg, 1.40 mmol, 60%).

*From **80**.* Using general procedure A with **80** (280 mg, 0.90 mmol) for 3 h, purification by chromatography (8−10% MeOH/CH_2Cl_2) afforded **7a** as a colorless solid (85 mg, 0.46 mmol, 51%): mp (postcolumn)118−119 °C; $[\alpha]_D^{25}$ +46.7 (*c* 0.61, MeOH); IR (neat) 3300 (br), 2941 (w), 1428 (w), 1025 (s), 993 (s), 861 (m) cm^{-1}; ^1H NMR (500 MHz, CD_3OD, α/β 56:44) δ 5.79 (1H, td, J = 55.6, 3.8 Hz, $H_{6\beta}$), 5.75 (1H, td, J = 55.7, 3.7 Hz, $H_{6\alpha}$), 5.17 (1H, d, J = 3.6 Hz, $H_{1\alpha}$), 4.46 (1H, d, J = 7.7 Hz, $H_{1\beta}$), 4.16 (1H, br tddd, J = 12.0, 10.0, 3.5, 2.6 Hz, $H_{5\alpha}$), 3.89 (1H, ddd, J = 11.4, 9.4, 5.1 Hz, $H_{3\alpha}$), 3.75 (1H, br ddddd, J = 12.0, 10.7, 10.4, 3.8, 2.2 Hz, $H_{5\beta}$), 3.61 (1H, ddd, J = 11.5, 9.1, 5.1 Hz, $H_{3\beta}$), 3.29 (1H, dd, J = 9.4, 3.6 Hz, $H_{2\alpha}$), 3.06 (1H, dd, J = 9.1, 7.7 Hz, $H_{2\beta}$), 2.00 (1H, br dd, J = 11.9, 4.6 Hz, $H_{4\alpha(eq)}$), 1.99 (1H, ddt, J = 12.7, 5.0, 1.7 Hz, $H_{4\beta(eq)}$), 1.50 (1H, app q, J = 12.1 Hz, $H_{4\beta(ax)}$), 1.46 (1H, app q, J = 12.1 Hz, $H_{4\alpha(ax)}$) ppm; ^1H NMR (500 MHz, D_2O, α/β 39:61) δ 5.780 (1H, td, J = 54.8, 3.3 Hz, $H_{6\beta}$), 5.776 (1H, td, J = 54.8, 3.1 Hz, $H_{6\alpha}$), 5.17 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.49 (1H, d, J = 7.9 Hz, $H_{1\beta}$), 4.14 (1H, app qt, J = 12.0, 2.6 Hz, $H_{5\alpha}$), 3.83 (1H, ddd, J = 11.4, 9.7, 5.2 Hz, $H_{3\alpha}$), 3.80 (1H, tddd, J = 11.8, 10.9, 3.1, 2.2 Hz, $H_{5\beta}$), 3.63 (1H, ddd, J = 11.4, 9.3, 5.2 Hz, $H_{3\beta}$), 3.35 (1H, dd, J = 9.8, 3.7 Hz, $H_{2\alpha}$), 3.05 (1H, dd, J = 9.3, 7.9 Hz, $H_{2\beta}$), 2.00 (1H, br ddd, J = 12.7, 5.1, 2.4 Hz, $H_{4(eq)\alpha}$), 1.98 (1H, br ddd, J = 12.6, 5.2, 2.0 Hz, $H_{4(eq)\beta}$), 1.44 (1H, dt, J = 12.7, 11.8 Hz, $H_{4(ax)\beta}$), 1.43 (1H, td, J = 12.5, 11.6 Hz, $H_{4(ax)\alpha}$) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, CD_3OD) δ 5.80 (1H, d, J = 3.8 Hz, $H_{6\beta}$), 5.75 (1H, d, J = 3.8 Hz, $H_{6\alpha}$), 5.17 (1H, d, J = 3.6 Hz, $H_{1\alpha}$), 4.46 (1H, d, J = 7.7 Hz, $H_{1\beta}$), 4.16 (1H, dddd, J = 12.3, 3.6, 2.4, 0.5 Hz, $H_{5\alpha}$), 3.89 (1H, ddd, J = 11.4, 9.4, 5.1 Hz, $H_{3\alpha}$), 3.75 (1H, ddd, J = 12.0, 3.8, 2.2 Hz, $H_{5\beta}$), 3.61 (1H, ddd, J = 11.5, 9.1, 5.1 Hz, $H_{3\beta}$), 3.29 (1H, dd, J = 9.4, 3.6 Hz, $H_{2\alpha}$), 3.06 (1H, dd, J = 9.1, 7.7 Hz, $H_{2\beta}$), 1.995 (1H, br ddd, J = 12.5, 5.1, 2.6 Hz, $H_{4\alpha(eq)}$), 1.985 (1H, br ddd, J = 12.5, 5.1, 2.2 Hz, $H_{4\beta(eq)}$), 1.50 (1H, app q, J = 12.1 Hz, $H_{4\beta(ax)}$), 1.46 (1H, app q, J = 12.1 Hz, $H_{4\alpha(ax)}$) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, D_2O) δ 5.783 (1H, d, J = 3.2 Hz, $H_{6\beta}$), 5.779 (1H, d, J = 2.7 Hz, $H_{6\alpha}$), 5.17 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 4.49 (1H, d, J = 7.9 Hz, $H_{1\beta}$), 4.14 (1H, dt, J = 12.3, 2.7 Hz, $H_{5\alpha}$), 3.83 (1H, ddd, J = 11.4, 9.8, 5.1 Hz, $H_{3\alpha}$), 3.80 (1H, ddd, J = 11.8, 3.1, 2.2 Hz, $H_{5\beta}$), 3.63 (1H, ddd, J = 11.5, 9.3, 5.2 Hz, $H_{3\beta}$), 3.35 (1H, dd, J = 9.7, 3.7 Hz, $H_{2\alpha}$), 3.05 (1H, dd, J = 9.2, 8.0 Hz, $H_{2\beta}$), 2.00 (1H, ddd, J = 12.7, 4.9, 2.2 Hz, $H_{4(eq)\alpha}$), 1.98 (1H, ddd, J = 12.8, 5.1, 2.1 Hz, $H_{4(eq)\beta}$), 1.44 (1H, dt, J = 12.6, 12.0 Hz, $H_{4(ax)\beta}$), 1.42 (1H, td, J = 12.4, 11.8 Hz, $H_{4(ax)\alpha}$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, CD_3OD) δ 117.1 (t, J_{C-F} = 241.2 Hz, $C_{6\alpha}$), 116.5 (t, J_{C-F} = 241.5 Hz, $C_{6\beta}$), 98.8 ($C_{1\beta}$), 94.8 ($C_{1\alpha}$), 78.0 ($C_{2\beta}$), 75.5 ($C_{2\alpha}$), 72.3 (t, J_{C-F} = 25.9 Hz, $C_{5\beta}$), 71.7 ($C_{3\beta}$), 68.2 (t, J_{C-F} = 25.8 Hz, $C_{5\alpha}$), 68.0 ($C_{3\alpha}$), 33.1 (t, J_{C-F} = 3.1 Hz, $C_{4\alpha}$), 33.0 (t, J_{C-F} = 3.0 Hz, $C_{4\beta}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 115.0 (t, J_{C-F} = 241.2 Hz, $C_{6\alpha}$), 114.4 (t, J_{C-F} = 241.4 Hz, $C_{6\beta}$), 96.4 ($C_{1\beta}$), 92.9 ($C_{1\alpha}$), 75.7 ($C_{2\beta}$), 72.9 ($C_{2\alpha}$), 70.5 (t, J_{C-F} = 24.6 Hz, $C_{5\beta}$), 69.7 ($C_{3\beta}$), 66.9 (t, J_{C-F} = 24.0 Hz, $C_{5\alpha}$), 66.2 ($C_{3\alpha}$), 31.1−31.0 (m, $C_{4\alpha}$, $C_{4\beta}$) ppm; ^{19}F NMR (470 MHz, CD_3OD) δ −128.8 (1F, ddd, J = 290.0, 55.4, 10.0 Hz, $F_{6a\beta}$), −129.0 (1F, ddd, J = 289.0, 55.7, 10.4 Hz, $F_{6a\alpha}$), −132.5 (1F, dddd, J = 290.0, 55.8, 11.1, 1.1 Hz, $F_{6b\beta}$), −132.6 (1F, ddd, J = 289.0, 55.9, 12.0 Hz, $H_{6b\alpha}$) ppm; ^{19}F NMR (470 MHz, D_2O) δ −129.7 (1F, ddd, J = 287.9, 54.7, 11.8 Hz, $F_{6a\beta}$), −130.0 (1F, ddd, J = 286.5, 54.7, 11.4 Hz, $F_{6a\alpha}$), −130.5 (1F, ddd, J = 287.9, 54.9, 10.9 Hz, $F_{6b\beta}$), −130.7 (1F, ddd, J = 286.5, 54.7, 12.2 Hz, $F_{6b\alpha}$) ppm; $^{19}F(^1H\}$ NMR (470 MHz, CD_3OD) δ −128.9 (1F, d, J = 290.0 Hz, $F_{6a\beta}$), −129.1 (1F, d, J = 289.0 Hz, $F_{6a\alpha}$), −132.5 (1F, d, J = 290.0 Hz, $F_{6b\beta}$), −132.7 (1F, d, J = 289.0 Hz, $F_{6b\alpha}$) ppm; $^{19}F(^1H\}$ NMR (470 MHz, D_2O) δ −129.8 (1F, d, J = 287.9 Hz, $F_{6a\beta}$), −130.1 (1F, d, J = 286.5 Hz, $F_{6a\alpha}$), −130.5 (1F, d, J = 287.9 Hz, $F_{6b\beta}$), −130.8 (1F, d, J = 286.5 Hz, $F_{6b\alpha}$) ppm; HRMS (ES-) for $C_6H_9F_2O_4$ $[M - H]^-$ calcd 183.0474, found 183.0475.

*1,2,3-Tri-O-acetyl-4,6-dideoxy-6,6-difluoro-D-xylo-hexopyranoside (**7b**).* A solution of **80** (1.15 g, 3.68 mmol) in TFA/H_2O (9:1, 12 mL) was stirred for 5 min and then concentrated *in vacuo*. The residue was redissolved in Ac_2O (6.95 mL) and cooled to 0 °C. Concentrated H_2SO_4 (0.20 mL, 3.68 mmol) was added, and then the reaction was warmed to rt and stirred for 24 h. The solution was diluted with EtOAc (30 mL) and quenched by the slow addition of satd $NaHCO_{3(aq)}$ (30 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic phases were washed with brine (100 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by chromatography (Biotage Isolera One, 20% EtOAc/cyclohexane) afforded **7b** as a colorless oil (809 mg, 2.61 mmol, 71%): IR (neat) 2971 (w), 1742 (s), 1370 (m), 1210 (s), 1057 (s), 917 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, α/β 85:15) δ 6.38 (1H, d, J = 3.6 Hz, $H_{1\alpha}$), 5.81 (1H, ddd, J = 56.0, 54.5, 3.4 Hz, $H_{6\beta}$), 5.75 (1H, ddd, J = 56.0, 54.4, 3.4 Hz, $H_{6\alpha}$), 5.68 (1H, d, J = 7.6 Hz, $H_{1\beta}$), 5.32 (1H, ddd, J = 11.4, 10.4, 5.3 Hz, $H_{3\alpha}$), 5.05 (1H, dd, J = 10.3, 3.6 Hz, $H_{2\alpha}$), 4.23−4.11 (1H, m $H_{5\alpha}$), 3.97−3.85 (1H, m, $H_{5\beta}$), 2.35 (1H, ddd, J = 12.7, 5.1, 2.4 Hz, $H_{4(eq)\alpha}$), 2.33−2.26 (1H, m, $H_{4(eq)\beta}$), 2.17 (3H, s, OCH_3^{α}), 2.12 (3H, s, OCH_3^{β}), 2.07 (3H, s, OCH_3^{α}), 2.06 (3H, s, OCH_3^{β}), 2.06 (3H, s, OCH_3^{β}), 2.04 (3H, s, OCH_3^{α}), 1.78 (1H, app q, J = 12.5 Hz, $H_{4(ax)\alpha}$) ($H_{2\beta}$,$H_{3\beta}$, $H_{4(ax)\beta}$ obscured by major anomer) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2 (CO_α), 169.9 (CO_α), 168.8 (CO_α), 113.8 (dd, J_{C-F} = 245.0, 242.1 Hz, $C_{6\alpha}$), 92.0 ($C_{1\beta}$), 89.8 ($C_{1\alpha}$), 70.8 ($C_{2\beta}$), 69.9 ($C_{2\alpha}$), 69.7 ($C_{3\beta}$), 68.9 (dd, J_{C-F} = 28.6, 26.4 Hz, $H_{5\alpha}$), 66.5 ($C_{3\alpha}$), 28.3 (dd, J_{C-F} = 4.4, 2.9 Hz, $C_{4\alpha}$), 20.9 (OCH_3^{α}), 20.82 (OCH_3^{α}), 20.76 (OCH_3^{β}), 20.6 (OCH_3^{β}), 20.5 (OCH_3^{α}) ($C_{5\beta}$, $C_{4\beta}$ and one OCH_3^{β} unresolved) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −127.1 (1F, ddd, J = 293.0, 53.8, 6.9 Hz, $F_{6a\beta}$), −127.3 (1F, ddd, J = 293.0, 55.5, 8.7 Hz, $F_{6a\alpha}$), −132.2 (1F, ddd, J = 293.0, 55.5, 12.1 Hz, $F_{6b\beta}$), −132.6 (1F, ddd, J = 293.0, 55.5, 13.9 Hz, $F_{6b\alpha}$) ppm; $^{19}F(^1H\}$ NMR (376 MHz, $CDCl_3$) δ −127.2 (1F, d, J = 293.0 Hz, $F_{6a\beta}$), −127.4 (1F, d, J = 293.0 Hz, $F_{6a\alpha}$), −132.2 (1F, d, J = 293.0 Hz, $F_{6b\beta}$), −132.6 (1F, d, J = 293.0 Hz, $F_{6b\alpha}$) ppm; HRMS (ES^+) for $C_{12}H_{16}F_2NaO_7$ $[M + Na]^+$ calcd 333.0756, found 333.0753.

*Methyl 4,6-Dideoxy-6-fluoro-α-D-xylo-hexopyranoside (**10**).* This is a known compound;[58] however, no characterization data have been described. To a solution of **60** (2.37 g, 11.0 mmol) in toluene (80 mL) was added Bu_3SnH (7.40 mL, 27.5 mmol) and AIBN (200 mg, 0.88 mmol). The reaction mixture was refluxed at 115 °C for 16 h and then concentrated *in vacuo* to afford a yellow oil. Purification by chromatography (10% K_2CO_3/silica,[118] 10% MeOH/CH_2Cl_2) afforded **10** as an off-white powder (1.75 g, 9.71 mmol, 88%): mp (postcolumn) 104−106 °C; $[\alpha]_D^{24}$ +157.6 (*c* 0.49, MeOH); IR (neat) 3300 (br), 2941 (w), 1430 (w), 1118 (m), 1026 (s), 927 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.84 (1H, d, J = 3.9 Hz, H_1), 4.45 (1H, ddd, J = 47.1, 9.9, 3.8 Hz, H_{6a}), 4.41 (1H, ddd, J = 47.6, 9.9, 5.1 Hz, H_{6b}), 4.02 (1H, ddddd, J = 20.8, 12.0, 5.1, 3.6, 2.5 Hz, H_5), 3.89 (1H, dddd, J = 11.5, 9.3, 5.1, 2.1 Hz, H_3), 3.44 (3H, s, OCH_3), 3.42 (1H, td, J = 9.8, 3.9 Hz, H_2), 2.52 (1H, d, J = 2.5 Hz, 3-OH), 2.09 (1H, d, J = 10.3 Hz, 2-OH), 1.98 (1H, ddd, J = 12.8, 5.1, 2.1 Hz, $H_{4(eq)}$), 1.53 (1H, app q, J = 12.2 Hz, $H_{4(ax)}$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 99.7 (C_1), 84.6 (d, J_{C-F} = 173.1 Hz, C_6), 74.2 (C_2), 68.7 (C_3), 67.0 (d, J_{C-F} = 20.5 Hz, C_5), 55.5 (OCH_3), 32.9 (d, J_{C-F} = 6.6 Hz, C_4) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −228.4 (ddd, J = 47.6, 47.2, 20.8 Hz, F_6) ppm; $^{19}F(^1H\}$ NMR (376 MHz, $CDCl_3$) δ −228.4 (s, F_6) ppm; HRMS (ES^+) $C_7H_{13}FNaO_4$ $[M + Na]^+$ calcd 203.0690 found 203.0691.

*Methyl 4-Deoxy-4-fluoro-α-D-fucopyranoside (D-**19**). From **62**.* A solution of **62** (414 mg, 1.18 mmol) in THF (6 mL) was cooled to 0

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°C. A solution of $LiAlH_4$ (1 M in THF, 4.27 mL, 4.72 mmol) was added dropwise, turning the light brown solution colorless. The reaction was heated to 80 °C and stirred for 3 h. The reaction was cooled to rt and quenched by the slow addition of satd Rochelle's $salt_{(aq)}$ (10 mL). The emulsion was diluted with EtOAc (10 mL) and stirred for 2 h. The phases were separated, and the aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (50 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by chromatography (50−100% EtOAc/hexane then 2% MeOH/EtOAc) afforded first **63** as a colorless oil (33 mg, 0.19 mmol, 16%) followed by D-**19** as a white solid (7 mg, 0.04 mmol, 4%).

*From **65**.* to a solution of **65** (1.78 g, 8.27 mmol) in toluene (40 mL) was added AIBN (543 mg, 3.31 mmol) and Bu_3SnH (4.45 mL, 16.5 mmol). The yellow solution was heated to 120 °C and stirred for 16 h, before being cooled to rt. The mixture was concentrated *in vacuo* and the yellow residue dissolved in MeCN (50 mL). The organic phase was washed with hexane (3 × 50 mL) and then concentrated *in vacuo* to yield an off-white solid. Purification by chromatography (10% acetone/hexane) afforded D-**19** as a white solid (1.04 g, 5.77 mmol, 70%): mp (postcolumn) 141−143 °C; $[\alpha]_D^{25}$ +165.6 (*c* 0.40, $CHCl_3$), lit. (enantiomer)[62] $[\alpha]_D^{25}$ −191.2 (*c* 1.0, MeOH); IR (neat) 3472 (m), 3428 (m), 2934 (w), 1452 (w), 1345 (m), 1105 (m), 1017 (s), 993 (s), 956 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.81 (1H, d, J = 3.2 Hz, H_1), 4.59 (1H, dd, J = 50.6, 2.7 Hz, H_4), 3.94 (1H, dq, J = 29.7, 6.7 Hz, H_5), 3.88−3.78 (2H, m, H_2, H_3), 3.44 (3H, s, OCH_3), 2.58 (1H, s, 3-OH), 2.27 (1H, d, J = 7.8 Hz, 2-OH), 1.33 (3H, d, J = 6.7 Hz, H_6) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 99.4 (C_1), 91.8 (d, J_{C-F} = 181.9 Hz,C_4), 70.3 (d, J_{C-F} = 18.3 Hz, C_3), 69.5 (d, J_{C-F} = 2.2 Hz, C_2), 65.2 (d, J_{C-F} = 19.1 Hz, C_5), 55.7 (OCH_3), 15.8 (d, J_{C-F} = 5.1 Hz, C_6) ppm; ^{19}F NMR (376 MHz, $CDCl_3$), δ −221.9 (dt, J = 50.6, 29.7 Hz, F_4) ppm; $^{19}F(^1H)$ NMR (346 MHz, $CDCl_3$) δ −221.8 (s, F_4) ppm; HRMS (ES^+) for $C_7H_{13}FNaO_4$ $[M + Na]^+$ calcd 203.0690 found 203.0688. Physical and spectroscopic data are consistent with the enantiomer.[62]

*Methyl 4,6-Dideoxy-4,6-difluoro-α-D-galactopyranoside (**28**).* A suspension of **27** (5.00 g, 25.7 mmol) in CH_2Cl_2 (25 mL) under Ar was cooled to 0 °C. DAST (20.4 mL, 154.2 mmol) was added dropwise. The solution was allowed to slowly warm to rt and stirred for 90 h. The solution was cooled to 0 °C and quenched by the slow addition of MeOH (60 mL) and addition of silica powder (6 mL). The mixture was stirred for 30 min over which time it warmed to rt. The mixture was concentrated *in vacuo*. Purification by chromatography (10−25% acetone/CH_2Cl_2) afforded **28** as a white powder (2.33 g, 11.76 mmol, 46%). $[\alpha]_D^{21}$ +166.6(*c* 0.53, EtOH), lit.[69] $[\alpha]_D^{22}$ +282.9 (EtOH); IR (neat) 3357 (br), 2953 (w), 1350 (w), 1191 (m), 1097 (s), 1056 (s), 913 (s) cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 4.81 (1H, br dd, J = 51.2, 2.7 Hz, H_4), 4.76 (1H, d, J = 3.2 Hz, H_1), 4.62 (1H, ddd, J = 46.0, 9.5, 4.9 Hz, H_{6a}), 4.52 (1H, dddd, J = 47.8, 9.5, 7.1, 1.1 Hz, H_{6b}), 4.21 (1H, d, J = 4.2 Hz, 3-OH), 4.09 (1H, br dddd, J = 30.4, 14.4, 7.1, 4.8 Hz, H_5), 3.85 (1H, dddd, J = 29.0, 10.0, 6.1, 2.7 Hz, H_3), 3.77−3.70 (2H, m, H_2 and 2-OH), 3.38 (3H, s, OCH_3) ppm; ^1H NMR (400 MHz, $CDCl_3$) δ 4.89 (1H, d, J = 3.3 Hz, H_1), 4.85 (1H, dd, J = 50.9, 2.3 Hz, H_4), 4.63 (1H, ddd, J = 46.1, 9.5, 6.0 Hz, H_{6a}), 4.58 (1H, dddd, J = 46.8, 9.5, 6.5, 1.0 Hz, H_{6b}), 4.07 (1H, ddt, J = 30.1, 12.6, 6.5 Hz, H_6), 3.94−3.78 (2H, m, H_2 and H_3), 3.48 (3H, s, OCH_3), 2.43 (1H, br s, 2-OH or 3-OH), 2.13 (1H, br d, J = 6.4 Hz, 2-OH or 3-OH) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, acetone-d_6) δ 100.7 (C_1), 90.3 (dd, J_{C-F} = 179.7, 6.6 Hz, C_4), 82.2 (dd, J_{C-F} = 167.3, 6.6 Hz, C_6), 69.6 (d, J_{C-F} = 2.9 Hz, C_2), 69.2 (d, J_{C-F} = 17.6 Hz, C_3), 68.5 (33, J_{C-F} = 22.0, 17.6 Hz, C_5), 55.2 (OCH_3) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 99.3 (C_1), 88.6 (dd, J_{C-F} = 181.6, 5.5 Hz, C_4), 81.0 (dd, J_{C-F} = 169.5, 6.6 Hz, C_6), 69.8 (d, J_{C-F} = 17.6 Hz, C_3), 69.6 (d, J_{C-F} = 2.9 Hz, C_2), 67.9 (dd, J_{C-F} = 23.8, 18.0 Hz, C_5), 55.9 (OCH_3) ppm; ^{19}F NMR (376 MHz, acetone-d_6) δ −220.0 (1F, dtt, J = 20.3, 29.5, 5.2 Hz, F_4), −230.2 (1F, td, J = 46.8, 15.6 Hz, F_6) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −221.3 (1F, dt, J = 51.2, 29.9 Hz, F_4), −231.2 (1F, td, J = 46.8, 12.1 Hz, F_6) ppm; $^{19}F(^1H)$ NMR (376 MHz, acetone-d_6) δ −219.9 (1F, s, F_4), −230.1 (1F, s, F_6) ppm; $^{19}F(^1H)$ NMR (376 MHz, $CDCl_3$) δ −221.2 (1F, s, F_4), −231.0 (1F, s, F_6) ppm. These NMR data correspond to the data in the literature.[68,69]

*Methyl 4,6-Dideoxy-4,6-difluoro-α-D-glucopyranoside (**35**). From **39**.* To a solution of **39** (6.52 g, 16.0 mmol) in MeOH/CH_2Cl_2 (1:1, 100 mL) was added NaOMe in MeOH (25% w/w, 10 drops). The mixture was stirred for 16 h. The reaction was neutralized by the addition of 4 M $HCl_{(aq)}$ (pH 7). The solution was concentrated *in vacuo* to afford a yellow oil. Purification by chromatography (3−8% MeOH/CH_2Cl_2) afforded **35** as a white crystalline solid (2.24 g, 11.3 mmol, 71%).

*From **74**.* A solution of **74** (859 mg, 2.75 mmol) in TFA/H_2O (9:1, 10 mL) was stirred for 5 min at rt and then concentrated *in vacuo*. Purification by chromatography (5% MeOH/CH_2Cl_2) afforded **35** as a brown oil (414 mg, 2.09 mmol, 76%, including 8 mol % of TFA): mp 80−83 °C, lit.[77] 93−94 °C (EtOAc/hexane); $[\alpha]_D^{21}$+142.2 (*c* 0.23, $CHCl_3$), lit.[77] $[\alpha]_D$ +142.0 (*c* 1.02 $CHCl_3$); IR (neat) 3379 (br), 2919 (w), 1456 (w), 1015 (s), 900 (m) cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 4.70 (1H, t, J = 3.5 Hz, H_1), 4.61 (3H, m, H_6 + OH, a coupling constant of 49.8 Hz [doublet] was observed for H_6), 4.25 (1H, ddd, J = 51.2, 10.1, 8.7 Hz, H_4), 3.78−4.02 (3H, m, H_3, H_5, OH), 3.40−3.46 (1H, m, H_2), 3.38 (3H, s, OCH_3) ppm; ^1H NMR (400 MHz $CDCl_3$) δ 4.82 (1H, t, J = 3.6 Hz, H_1), 4.65 (2H, dm, a coupling constant of 47.2 Hz [doublet] was observed, H_6), 4.38 (1H, ddd, J = 51.0, 10.3, 8.7 Hz, H_4), 3.99 (1H, dt, J = 15.7, 9.1 Hz, H_3), 3.89 (1H, ddq, J = 26.0, 10.0, 3.2 Hz, H_5), 3.59 (1H, td, J = 9.1, 3.6 Hz, H_2), 3.48 (3H, s, OCH_3), 2.82 (1H, br s, 3-OH), 2.28 (1H, br d, J = 9.1 Hz, 2-OH) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, acetone-d_6) δ 100.9 (d, J_{C-F} = 1.5 Hz, C_1), 89.8 (dd, J_{C-F} = 182.3, 8.1 Hz, C_4), 82.5 (d, J_{C-F} = 172.0 Hz, C_6), 73.04 (C_2), 73.00 (d, J_{C-F} = 25.3 Hz, C_3), 69.1 (dd, J_{C-F} = 24.6, 19.1 Hz, C_5), 55.7 (OCH_3) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 99.0 (C_1), 87.9 (dd, J_{C-F} = 183.4, 7.3 Hz, C_4), 81.0 (d, J_{C-F} = 174.6 Hz, C_6), 72.9 (d, J_{C-F} = 17.6 Hz, C_3), 71.9 (d, J_{C-F} = 8.1 Hz, C_2), 68.2 (dd, J_{C-F} = 23.5, 18.3 Hz, C_5), 55.8 (OCH_3) ppm; ^{19}F NMR (376 MHz, acetone-d_6) δ −198.3 (1F, br dd, J = 51.2, 16.5 Hz, F_4), −235.5 (1F, td, J = 48.2, 26.5 Hz, F_6) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −199.2 (1F, br dd, J = 51.0, 15.7 Hz, F_4), −235.5 (1F, td, J = 47.2 26.0 Hz, F_6) ppm; $^{19}F(^1H)$ NMR (376 MHz, acetone-d_6) δ −198.3 (1F, s, F_4), −235.5 (1F, s, F_6) ppm; HRMS (ES^+) for $C_7H_{12}F_2NaO_4$ $[M + Na]^+$ calcd 221.0596 found 221.0594. NMR data in acetone d_6 correspond to literature data.[77]

*Methyl 2,3-Di-O-benzoyl-4,6-dideoxy-4,6-difluoro-α-D-glucopyranoside (**39**).* A suspension of **37**[93] (8.90 g, 22.1 mmol) in CH_2Cl_2 (10 mL) was cooled to −40 °C. DAST (25.5 mL, 193 mmol) was added, and the mixture was stirred for 24 h, over which time it was allowed to reach rt. The mixture was diluted with CH_2Cl_2 (70 mL) and cooled to 0 °C. The reaction was quenched by the addition of MeOH (20 mL), warmed to rt, and stirred for 2 h. The solution was washed with satd $NaHCO_{3(aq)}$ (100 mL), H_2O (100 mL), and brine (100 mL), dried ($MgSO_4$), and concentrated *in vacuo* to afford a yellow oil. Purification by chromatography (0−20% EtOAc/hexane) afforded **39** as a colorless foam (6.84 g, 16.8 mmol, 76%): $[\alpha]_D^{21}$ +154.6 (*c* 0.53, $CHCl_3$, lit.[75] $[\alpha]_D^{22}$ +29.4, *c* 2.0, $CHCl_3$);IR (neat) 2958 (w), 1723 (s), 1602 (w), 1452 (m), 1270 (s), 1025 (s), 918 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05−7.95 (4H, m, Ar_H), 7.57−7.49 (2H, m, Ar_H), 7.44−7.35 (4H, m, Ar_H), 6.11 (1H, dt, J = 14.4, 9.3 Hz, H_3), 5.21−5.14 (2H, m, H_1, H_2), 4.77 (1H, ddd, J = 50.7, 9.9, 9.1 Hz, H_4), 4.83−4.64 (2H, m, H_6), 4.20−4.05 (1H, m, H_5), 3.47 (3H, s, OCH_3) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 165.8 (CO), 165.6 (CO), 133.5 (Ar_C), 133.3 (Ar_C), 129.9 (Ar_C), 129.8 (Ar_C), 129.3 (Ar_C), 128.9 (Ar_C), 128.5 (Ar_C), 128.4 (Ar_C), 97.0 (C_1), 86.0 (dd, J_{C-F} = 187.4, 7.7 Hz, C_4), 80.8 (d, J_{C-F} = 175.3 Hz, C_6), 71.3 (d, J_{C-F} = 7.3 Hz, C_2), 70.4 (d, J_{C-F} = 20.5 Hz, C_3), 68.0 (dd, J_{C-F} = 23.1, 18.7 Hz, C_5), 55.8 (OCH_3) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −197.9 (1F, br dd, J = 49.4, 17.7 Hz, H_4), −235.9 (1F, ddd, J = 48.6, 46.8, 26.0 Hz, F_6) ppm; $^{19}F(^1H)$ NMR (376 MHz, $CDCl_3$) δ −198.0 (1F, s, F_4), −235.9 (1F, s, F_6) ppm; LRMS (ESI+) 407.4 $[M + H]^+$. NMR data correspond to literature data.[75]

*Methyl 6-O-tert-Butyldimethylsilyl-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-galactopyranoside (**47**).* To a solution of **46**[80] (8.80 g, 28.5 mmol) in DMF (100 mL) was added imidazole

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(85.6 mmol, 5.82 g). The solution was cooled to 0 °C, and TBDMSCl (4.73 g, 31.4 mmol) was added portionwise. The mixture was stirred for 15 min at this temperature, warmed to rt, and stirred for 1 h. The reaction was quenched by the addition of H_2O (4 mL). The mixture was extracted with Et_2O and pentane (9:1, 2 × 100 mL). The combined organic phases were washed with H_2O and brine, dried ($MgSO_4$), and concentrated *in vacuo*. Purification by chromatography (20−30% EtOAc/petroleum ether) afforded **47** as a colorless solid (10.1 g, 23.9 mmol, 84%): mp (postcolumn) 112−114 °C; $[\alpha]_D^{27}$ −39.3 (*c* 0.36, $CHCl_3$); IR (neat) 3474 (br, w), 2951 (m), 2856 (w), 1472 (w), 1376 (w), 1255 (w), 1119 (s), 1037 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.80 (1H, d, J = 3.6 Hz, H_1), 4.21 (1H, dd, J = 10.3, 3.6 Hz, H_2), 4.06 (1H, dd, J = 10.3, 3.1 Hz, H_3), 4.04−4.01 (1H, m, H_4), 3.90 (1H, dd, J = 12.4, 8.4 Hz, H_{6a}), 3.84−3.77 (2H, m, H_5, H_{6b}), 3.42 (3H, s, OCH_3), 3.27 (3H, s, OCH_3^{BDA}), 3.25 (3H, s, OCH_3^{BDA}), 2.56 (1H, t, J = 1.1 Hz, 4-OH), 1.34 (3H, s, $C(CH_3)^{BDA}$), 1.32 (3H, s, $C(CH_3)^{BDA}$), 0.91 (9H, s, $C(CH_3)_3$), 0.10 (6H, s, $Si(CH_3)_2$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 100.11 ($C(CH_3)^{BDA}$), 100.09 ($C(CH_3)^{BDA}$), 98.3 (C_1), 70.7 (C_5), 67.9 (C_4), 66.5 (C_3), 65.2 (C_2), 62.5 (C_6), 55.0 (OCH_3), 47.92 (OCH_3^{BDA}), 47.89 (OCH_3^{BDA}), 25.9 ($C(CH_3)_3$), 18.3 ($C(CH_3)_3$), 17.8 ($C(CH_3)^{BDA}$), 17.7 ($C(CH_3)^{BDA}$), −5.5 ($Si(CH_3)_2$) ppm; HRMS (ES^+) for $C_{19}H_{38}NaO_8Si$ $[M + Na]^+$ calcd 445.2228 found 445.2240.

*Methyl 6-O-tert-Butyldimethylsilyl-4-O-phenoxythiocarbonyl-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl]-α-D-galactopyranoside (**48**).* To a solution of **47** (9.16 g, 21.7 mmol) and DMAP (6.62 g, 54.3 mmol) in MeCN (12 mL) was added *O*-phenyl chlorothionoformate (3.90 mL, 28.0 mmol). The mixture was stirred for 15 h. The mixture was concentrated *in vacuo*, and the residue was redissolved in Et_2O (150 mL) and washed with H_2O (3 × 100 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. Purification by chromatography (10−15% EtOAc/petroleum ether) afforded **48** as a colorless foam (10.3 g, 18.4 mmol, 85%): $[\alpha]_D^{27}$ −13.6 (*c* 0.44, $CHCl_3$); IR (neat) 2951 (w), 2856 (w), 1490 (w), 1369 (w), 1277 (m), 1198 (s), 1115 (s), 1037 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49−7.39 (2H, m, Ar_H), 7.31−7.26 (1H, m, Ar_H), 7.16−7.12 (2H, m, Ar_H), 5.97 (1H, dd, J = 3.3, 1.1 Hz, H_4), 4.80 (1H, d, J = 3.6 Hz, H_1), 4.28 (1H, dd, J = 10.5, 3.3 Hz, H_3), 4.08 (1H, dd, J = 10.5, 3.6 Hz, H_2), 4.08−4.04 (1H, m, H_5), 3.79 (1H, dd, J = 10.3, 6.5 Hz, H_{6a}), 3.70 (1H, dd, J = 10.3, 6.9 Hz, H_{6b}), 3.44 (3H, s, OCH_3), 3.28 (3H, s, OCH_3^{BDA}), 3.25 (3H, s, OCH_3^{BDA}), 1.34 (3H, s, $C(CH_3)^{BDA}$), 1.29 (3H, s, $C(CH_3)^{BDA}$), 0.91 (9H, s, $C(CH_3)_3$), 0.10 (3H, s, $Si(CH)_3$), 0.09 (3H, s, $Si(CH_3)$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 194.6 (CS), 153.5 (Ar_C), 129.4 (Ar_C), 126.3 (Ar_C), 121.8 (Ar_C), 100.2 ($C(CH_3)^{BDA}$), 100.0 ($C(CH_3)^{BDA}$), 98.2 (C_1), 78.8 (C_4), 70.3 (C_5), 66.8 (C_2), 65.3 (C_3), 61.5 (C_6), 55.3 (OCH_3), 48.1 (OCH_3^{BDA}), 48.0 (OCH_3^{BDA}), 25.9 ($C(CH_3)_3$), 18.3 ($C(CH_3)_3$), 17.8 ($C(CH_3)^{BDA}$), 17.7 ($C(CH_3)^{BDA}$), −5.36 ($Si(CH_3)$), −5.49 ($Si(CH_3)$) ppm; HRMS (ES^+) for $C_{26}H_{42}NaO_9SSi$ $[M + Na]^+$ calcd 581.2211 found 581.2220.

*Methyl 6-O-tert-Butyldimethylsilyl-4-deoxy-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-xylo-hexopyranoside (**49**).* A mixture of **48** (5.89 g, 10.9 mmol) and Et_3SiH (60 mL) was brought to reflux. Benzoyl peroxide (526 mg, 2.17 mmol) was added, and the reaction was heated under reflux for 30 min. A further portion of benzoyl peroxide (526 mg, 2.17 mmol) was added and the reflux continued for a further 1.5 h. The reaction was cooled to rt and the Et_3SiH removed *in vacuo*. The crude residue was dissolved in CH_2Cl_2 (100 mL) and washed with 1 M NaOH (2 × 100 mL) and brine (100 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. Purification by chromatography (8−10% EtOAc/petroleum ether) afforded **49** as an amorphous white solid (2.73 g, 6.71 mmol, 62%): mp (postcolumn) 77−78 °C; $[\alpha]_D^{27}$ −53.6 (*c* 0.79, $CHCl_3$); IR (neat) 2952 (w), 2857 (w), 1463 (w), 1375 (w), 1253 (w), 1196 (w), 1121 (s), 1085 (s), 1037 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.77 (1H, d, J = 3.4 Hz, H_1), 4.15 (1H, ddd, J = 11.8, 10.1, 4.8 Hz, H_3), 3.86 (1H, dddd, J = 11.4, 5.9, 5.1, 2.2 Hz, H_5), 3.69 (1H, dd, J = 10.4, 5.9 Hz, H_{6a}), 3.68 (1H, dd, J = 10.1, 3.4 Hz, H_2), 3.58 (1H, dd, J = 10.4, 5.1 Hz, H_{6b}), 3.40 (3H, s, OCH_3), 3.28 (3H, s, OCH_3^{BDA}), 3.26 (3H, s, OCH_3^{BDA}), 1.90 (1H, ddd, J = 12.4, 4.8, 2.2 Hz, H_4(eq)), 1.52 (1H, app q, J = 11.9 Hz, H_4(ax)), 1.35 (3H, s, $C(CH_3)^{BDA}$), 1.30 ($C(CH_3)^{BDA}$), 0.90 (9H, s, $C(CH_3)_3$), 0.072 (3H, s, $SI(CH_3)$), 0.068 (3H, s, $Si(CH_3)$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 100.2 ($C(CH_3)^{BDA}$), 99.5 ($C(CH_3)^{BDA}$), 98.4 (C_1), 71.0 (C_2), 69.1 (C_5), 65.9 (C_6), 63.7 (C_3), 54.8 (OCH_3), 47.9 (OCH_3^{BDA}), 47.8 (OCH_3^{BDA}), 32.5 (C_4), 25.9 ($C(CH_3)_3$), 18.4 ($C(CH_3)_3$), 17.9 ($C(CH_3)^{BDA}$), 17.8 ($C(CH_3)^{BDA}$), −5.3 ($Si(CH_3)$), −5.4 ($Si(CH_3)$) ppm; HRMS (ES^+) for $C_{19}H_{38}NaO_7Si$ $[M + Na]^+$ calcd 429.2279 found 429.2285.

*Mixture of Methyl 4-O-Benzoyl-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-fucopyranoside (**52**) and Methyl 6-O-Benzoyl-4-deoxy-2,3-O-((2′S,3′S)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-xylo-hexopyranoside (**53**).* To a solution of **50**[82] (7.00 g, 17.7 mmol) in chlorobenzene (26.5 mL) were added triisopropylsilane thiol (0.190 mL, 0.883 mmol) and di-*tert*-butyl peroxide (1.61 mL, 8.83 mmol). The reaction mixture was heated at reflux for 1.5 h before being cooled down to rt. The mixture was concentrated *in vacuo*. Purification by chromatography (40% Et_2O/petroleum ether) afforded an inseparable mixture of **52** and **53** as a colorless oil (6.39 g, 16.1 mmol, 91%, **52**/**53** 42:58): HRMS (ES+) for $C_{20}H_{28}NaO_8$,$[M + Na]^+$ calcd 419.1676, found 419.1676.

Selected data for **52**: ^1H NMR (400 MHz, $CDCl_3$) δ 8.14−8.09 (2H, m, Ar_H), 7.61−7.55 (1H, m, Ar_H), 7.51−7.42 (2H, m, Ar_H), 5.40 (1H, dd, J = 3.1, 1.0 Hz, H_4), 4.86 (1H, d, J = 3.3 Hz, H_1), 4.33 (1H, dd, J = 10.6, 3.3 Hz, H_2), 4.28 (1H, dd, J = 10.6, 3.3 Hz, H_3), 4.25−4.14 (1H, m, H_5), 3.46 (3H, s, OCH_3), 3.29 (3H, s, OCH_3^{BDA}), 3.26 (3H, s, OCH_3^{BDA}), 1.33 (3H, s, $(C(CH_3)^{BDA}$), 1.21 (3H, d, J = 6.6 Hz, H_6), 1.15 (3H, s, $(C(CH_3)^{BDA}$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 166.7 (CO), 132.9 (Ar_C), 130.5 (Ar_C), 130.0 (Ar_C), 128.3 (Ar_C), 100.1 ($C(CH_3)^{BDA}$), 99.8 ($C(CH_3)^{BDA}$), 98.6 (C_1), 72.3 (C_4), 65.8 (C_5), 65.7 (C_2), 64.9 (C_3), 55.3 (OCH_3), 48.0−47.8 (2 × OCH_3^{BDA}), 17.8 ($C(CH_3)^{BDA}$), 17.6 ($C(CH_3)^{BDA}$), 16.3 (C_6) ppm;

Selected data for **53**: ^1H NMR (400 MHz, $CDCl_3$) δ 8.09−8.04 (2H, m, Ar_H), 7.61−7.55 (1H, m, Ar_H), 7.51−7.42 (2H, m, Ar_H), 4.82 (1H, d, J = 3.4 Hz, H_1), 4.39 (2H, d, J = 4.9 Hz, H_6), 4.25−4.14 (2H, m, H_3, H_5,), 3.74 (1H, dd, J = 10.2, 3.6 Hz, H_2), 3.43 (3H, s, OCH_3), 3.29 (3H, s, OCH_3^{BDA}), 3.28 (3H, s, OCH_3^{BDA}), 1.95 (1H, ddd, J = 12.3, 4.8, 2.2 Hz, $H_{4(eq)}$), 1.73 (1H, app q, J = 12.0 Hz, $H_{4(ax)}$), 1.36 (3H, s, $(C(CH_3)^{BDA}$), 1.31 (3H, s, $(C(CH_3)^{BDA}$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 166.3 (CO), 133.1 (Ar_C), 129.9 (Ar_C), 129.7 (Ar_C), 128.4 (Ar_C), 100.3 ($C(CH_3)^{BDA}$), 99.7 ($C(CH_3)^{BDA}$), 98.6 (C_1), 70.7 (C_2), 66.5 (2 × C, C_5, C_6), 63.4 (C_3), 55.0 (OCH_3), 48.0−47.8 (2 × OCH_3^{BDA}), 32.2 (C_4), 17.9 ($C(CH_3)^{BDA}$), 17.8 ($C(CH_3)^{BDA}$) ppm;

*Methyl 2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-fucopyranoside (**54**) and Methyl 4-Deoxy-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-xylo-hexopyranoside (**55**).* From the 42:58 mixture of benzoates **52**/**53** obtained above: to a solution of **52**/**53** (7.56 g, 19.1 mmol) in MeOH (75 mL) was added a solution of NaOMe (25 wt %, 0.65 mL, 2.86 mmol). The mixture was stirred at rt for 16 h. A further portion of NaOMe (25 wt %, 0.65 mL, 2.86 mmol) was added, and the reaction was stirred at rt for a further 4 h then at 50 °C for 2.5 h. The reaction was neutralized with Amberlite IR120-H^+ and then filtered and concentrated *in vacuo*. Purification by chromatography (40−70% EtOAc/petroleum ether) afforded a first fraction containing unreacted **52** (900 mg, 2.27 mmol, 12%), a second fraction containing mainly **54** but contaminated with a small amount of **55**, and a third fraction containing pure **55** as an off-white amorphous solid (2.99 g, 10.2 mmol, 54%). Unreacted **52** was resubmitted to deprotection using 1 equiv of MeONa and heating at 60 °C for 3 h to reach completion. This was combined with the impure fraction and purified by chromatography (30−60% EtOAc/petroleum ether) to give pure **54** as a colorless oil (2.07 g 7.08 mmol, 37%).

Synthesis of **54** from **72**: To a solution of **72** (1.51 g, 3.26 mmol) in DMSO (20 mL) was added $NaBH_4$ (270 mg, 7.18 mmol). The suspension was heated to 120 °C for 3 h and then cooled to 0 °C. The reaction was quenched by the slow addition of 2 M HCl (10 mL), warmed to rt, and diluted with H_2O (20 mL). The aqueous phase was extracted with Et_2O (5 × 40 mL), and the combined organic extracts

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were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by chromatography (20% EtOAc/hexane) afforded **54** as a colorless oil (809 mg, 2.77 mmol, 80%).

Synthesis of **55** from **49**: To **49** (2.69 g, 6.62 mmol) was added a solution of TBAF in THF (1 M, 7.90 mL, 7.90 mmol). The mixture was stirred for 1 h. The THF was removed *in vacuo*, and the residue redissolved in CH_2Cl_2 (100 mL) and washed with satd $NH_4Cl_{(aq)}$ (150 mL), brine (150 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by chromatography (60−70% EtOAc/petroleum ether) afforded **55** as an off-white amorphous solid (1.65 g, 5.64 mmol, 85%).

*Data for **54**:* $[\alpha]_D^{27}$ −42.7 (*c* 0.66, $CHCl_3$, lit.[119] (enantiomer): $[\alpha]_D^{22}$ +40, c 1.0 $CHCl_3$); IR (neat) 3489 (br), 2938 (w), 2833 (w), 1453 (w), 1369 (m), 1115 (s), 1030 (s), 999 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.76 (1H, d, J = 3.6 Hz, H_1), 4.16 (1H, dd, J = 10.5, 3.6 Hz, H_2), 4.07 (1H, dd, J = 10.5, 3.2 Hz, H_3), 3.96 (1H, qd, J = 6.7, 1.0 Hz, H_5), 3.76 (1H, dd, J = 3.2, 1.0 Hz, H_4), 3.41 (3H, s, OCH_3), 3.26 (3H, s, OCH_3^{BDA}), 3.24 (3H, s, OCH_3^{BDA}), 1.33 (3H, s, CH_3^{BDA}), 1.31 (3H, s, CH_3^{BDA}), 1.31 (3H, d, J = 6.6 Hz, H_6) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 100.10 ($C(CH_3)^{BDA}$), 100.07 ($C(CH_3)^{BDA}$), 98.3 (C_1), 70.4 (C_4), 66.6 (C_3), 66.2 (C_5), 65.0 (C_2), 55.1 (OCH_3), 47.9 (2 × OCH_3^{BDA}), 17.8 ($C(CH_3)^{BDA}$), 17.7 ($C(CH_3)^{BDA}$), 16.1 (C_6) ppm; HRMS for $C_{13}H_{24}NaO_7$ $[M + Na]^+$ calcd 315.1414 found 315.1416. NMR data correspond to literature (of enantiomer).[119]

*Data for **55**:* mp 64−66 °C (postcolumn); $[\alpha]_D^{27}$ −53.1 (*c* 0.78, $CHCl_3$); IR (neat) 3511 (br, w), 2934 (w), 2879 (w), 1446 (w), 1375 (m), 1221 (m), 1114 (s), 1020 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.79 (1H, d, J = 3.6 Hz, H_1), 4.17 (1H, ddd, J = 11.7, 10.1, 5.0 Hz, H_3), 3.93 (1H, ddt, J = 12.0, 6.2, 2.9 Hz, H_5), 3.68 (1H, dd, J = 10.1, 3.6 Hz, H_2), 3.67 (1H, dd, J = 11.5, 3.3 Hz, H_{6a}), 3.59 (1H, dd, J = 11.5, 6.6 Hz, H_{6b}), 3.42 (3H, s, OCH_3), 3.271 (3H, s, OCH_3^{BDA}), 3.268 (3H, s, OCH_3^{BDA}), 1.79 (1H, ddd, J = 12.4, 4.9, 2.4 Hz, $H_{4(eq)}$), 1.61 (1H, app q, J = 12.0 Hz, $H_{4(ax)}$), 1.35 (3H, s, $C(CH_3)^{BDA}$), 1.29 (3H, s, $C(CH_3)^{BDA}$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 100.2 ($C(CH_3)^{BDA}$), 99.6 ($C(CH_3)^{BDA}$), 98.5 (C_1), 70.9 (C_2), 68.9 (C_5), 65.3 (C_6), 63.3 (C_3), 55.0 (OCH_3), 47.89 (OCH_3^{BDA}), 47.85 (OCH_3^{BDA}), 31.6 (C_4), 17.9 ($C(CH_3)^{BDA}$), 17.8 ($C(CH_3)^{BDA}$) ppm; HRMS (ES^+) for $C_{13}H_{24}NaO_7$ $[M + Na]^+$ calcd 315.1414 found 315.1416.

*Methyl 4,6-Dideoxy-6-fluoro-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-xylo-hexopyranoside (**56**).* Into a microwave vial was added a solution of **55** (100 mg, 0.342 mmol) in 1,2-dichloroethane (0.7 mL). 2,4,6-Collidine (54.7 μL, 0.411 mmol) and DAST (50.3 μL, 0.411 mmol) were then added, and the vial was sealed and placed in a microwave reactor. The reaction mixture was irradiated for 4 min at 100 °C, cooled to rt, quenched with MeOH, and then concentrated *in vacuo*. Purification by chromatography (20% EtOAc/hexane) afforded **56** as a pale-yellow oil (81 mg, 0.275 mmol, 80%): $[\alpha]_D^{24}$ −14.8 (*c* 0.39, $CHCl_3$); IR (neat) 2950 (w), 1374 (w), 1117 (s), 1036 (s), 884 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.81 (1H, d, J = 3.4 Hz, H_1), 4.43 (1H, ddd, J = 47.3, 9.9, 3.6 Hz, H_{6a}), 4.40 (1H, ddd, J = 47.6, 9.9, 5.1 Hz, H_{6b}), 4.18 (1H, ddd, J = 11.7, 10.2, 5.0 Hz, H_3), 4.06 (1H, ddddd, J = 20.8, 12.0, 5.1, 3.6, 2.9 Hz, H_5), 3.71 (1H, dd, J = 10.1, 3.5 Hz, H_2), 3.42 (3H, s, OCH_3), 3.27 (3H, s, OCH_3^{BDA}), 3.26 (3H, s, OCH_3^{BDA}), 1.83 (1H, ddd, J = 12.4, 4.9, 2.5 Hz, $H_{4(eq)}$), 1.65 (1H, app q, J = 12.1 Hz, $H_{4(ax)}$), 1.35 (3H, s, CH_3^{BDA}), 1.29 (3H, s, CH_3^{BDA}) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 100.2 ($C(CH_3)^{BDA}$), 99.6 ($C(CH_3)^{BDA}$), 98.6 (C_1), 84.7 (d, J_{C-F} = 173.1 Hz, C_6), 70.6 (C_2), 67.2 (d, J_{C-F} = 19.8 Hz, C_5), 63.2 (C_3), 55.1 (OCH_3), 47.90 (OCH_3^{BDA}), 47.86 (OCH_3^{BDA}), 30.8 (d, J_{C-F} = 6.6 Hz, C_4), 17.84 ($C(CH_3)^{BDA}$), 17.75 ($C(CH_3)^{BDA}$) ppm; ^{19}F NMR (378 MHz, $CDCl_3$) δ −228.3 (td, J = 46.8, 20.8 Hz, F_6) ppm; $^{19}F\{^1H\}$ NMR (378 MHz, $CDCl_3$) δ −228.1 (s, F_6) ppm; HRMS (ES^+) for $C_{13}H_{23}FNaO_6$ $[M + H]^+$ calcd 317.1371 found 317.1376.

*Mixture of Methyl 4-O-Benzoyl-2,3-O-((2′S,3′S)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-fucopyranoside (**57**) and Methyl 6-O-Benzoyl-4-deoxy-2,3-O-((2′S,3′S)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-xylo-hexopyranoside (**58**).* To a solution of **51** (1.05 g, 2.64 mmol) in chlorobenzene (4 mL) were added triisoproylsilane thiol (28 μL, 0.13 mmol) and di-*tert*-butyl peroxide (0.24 mL, 1.32 mmol). The mixture was heated to 140 °C for 1.5 h and then cooled to rt. The mixture was concentrated *in vacuo*. Purification by chromatography (40% Et_2O/petroleum ether) afforded an inseparable mixture of **57** and **58** as a colorless oil (868 mg, 2.19 mmol, 83%, **57**/**58** 80:20): HRMS (ES+) for $C_{20}H_{28}NaO_8$,$[M + Na]^+$ calcd 419.1676, found 419.1686.

Selected data for **57**: ^1H NMR (400 MHz, $CDCl_3$) δ 8.18−8.11 (2H, m, Ar_H), 7.62−7.53 (1H, m, Ar_H), 7.49−7.40 (2H, m, Ar_H), 5.50 (1H, br d, J = 2.6 Hz, H_4), 4.89 (1H, d, J = 3.4 Hz, H_1), 4.80 (1H, dd, J = 11.7, 3.1 Hz, H_3), 4.66 (1H, dd, J = 11.7, 3.4 Hz, H_2), 4.12 (1H, br q, J = 6.6 Hz, H_5), 3.46 (3H, s, OCH_3), 3.41 (3H, s, OCH_3^{BDA}), 2.95 (3H, s, OCH_3^{BDA}), 1.35 (3H, s, $C(CH_3)^{BDA}$), 1.30 (3H, s, $C(CH_3)^{BDA}$), 1.16 (3H, d, J = 6.6 Hz, H_6) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 165.8 (CO), 133.2 (Ar_C), 129.9 (Ar_C), 129.8 (Ar_C), 128.4 (Ar_C), 101.5 ($C(CH_3)^{BDA}$), 101.4 ($C(CH_3)^{BDA}$), 99.1 (C_1), 72.0 (C_4), 68.8 (C_2), 67.8 (C_3), 65.5 (C_5), 55.5 (OCH_3), 48.4 (OCH_3^{BDA}), 48.1 (OCH_3^{BDA}), 19.1 ($C(CH_3)^{BDA}$), 19.0 ($C(CH_3)^{BDA}$), 16.3 (C_6) ppm;

Selected data for **58**: ^1H NMR (400 MHz, $CDCl_3$) δ 8.07−8.02 (2H, m, Ar_H), 7.62−7.53 (1H, m, Ar_H), 7.49−7.40 (2H, m, Ar_H), 4.85 (1H, d, J = 3.3 Hz, H_1), 4.60 (1H, dt, J = 11.1, 4.7 Hz, H_3), 4.40−4.32 (2H, m, H_6), 4.06 (1H, dd, J = 11.1, 3.4 Hz, H_2), 3.43 (3H, s, OCH_3), 3.40 (3H, s, OCH_3^{BDA}), 3.34 (3H, s, OCH_3^{BDA}), 2.10 (1H, ddd, J = 12.3, 4.6, 2.1 Hz, $H_{4(eq)}$), 1.50 (1H, app q, J = 11.7 Hz, $H_{4(ax)}$), 1.38 (3H, s, $C(CH_3)^{BDA}$), 1.37 (3H, s, $C(CH_3)^{BDA}$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 166.3 (CO), 133.1 (Ar_C), 129.8 (Ar_C), 129.6 (Ar_C), 128.4 (Ar_C), 101.6 ($C(CH_3)^{BDA}$), 101.4 ($C(CH_3)^{BDA}$), 99.0 (C_1), 73.8 (C_2), 66.5 (C_6), 66.2 (C_3), 66.1 (C_5), 55.2 (OCH_3), 48.1 (OCH_3^{BDA}), 48.0 (OCH_3^{BDA}), 34.2 (C_4), 18.9 ($C(CH_3)^{BDA}$) ppm (one $C(CH_3)^{BDA}$) signal not observed).

*Methyl 4,6-Dideoxy-4-chloro-6-fluoro-α-D-galactopyranoside (**60**).* A solution of **59**[76] (610 mg, 3.11 mmol) in CH_2Cl_2 (10 mL) and pyridine (3 mL) was cooled to −78 °C. SO_2Cl_2 (1.05 mL, 13.0 mmol) was added, and the mixture was stirred for 30 min at this temperature and a further 90 min during which time it was allowed to warm to rt. The reaction was then cooled to 0 °C, a solution of NaI (930 mg, 6.20 mmol) in MeOH/H_2O (1:1, 6 mL) was added, and the resulting orange mixture stirred at rt for 30 min. The mixture was then concentrated *in vacuo* and the residue dissolved in $CHCl_3$. The organic phase was washed with satd $NaHCO_{3(aq)}$ (30 mL) and the aqueous phase re-extracted with $CHCl_3$ (3 × 30 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to afford a brown solid. Purification by chromatography (Biotage Isolera One, 5−9% MeOH/CH_2Cl_2) afforded **60** as a pale orange solid (400 mg, 1.86 mmol, 60%): mp (postcolumn) 133−134 °C; $[\alpha]_D^{27}$ +205.2 (*c* = 0.97, $CHCl_3$); IR (neat) 3419 (br), 2917 (w), 1456 (w), 1347 (m), 1093 (w), 1011 (s), 886 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.88 (1H, d, J = 3.9 Hz, H_1), 4.60 (1H, ddd, J = 47.0, 9.7, 6.7 Hz, H_{6a}), 4.57 (1H, ddd, J = 46.1, 9.7, 5.3 Hz, H_{6b}), 4.42 (1H, dd, J = 3.7, 1.2 Hz, H_4), 4.29 (1H, dddd, J = 12.7, 6.7, 5.3, 1.2 Hz, H_5), 4.01 (1H, ddd, J = 9.8, 6.5, 3.7 Hz, H_3), 3.86 (1H, td, J = 9.5, 3.9 Hz, H_2), 3.48 (3H, s, OCH_3), 2.55 (1H, d, J = 6.9 Hz, 3-OH), 2.17 (1H, d, J = 9.4 Hz, 2-OH) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 99.3 (C_1), 82.5 (d, J_{C-F} = 170.2 Hz, C_6), 69.8 (C_3), 69.4 (C_2), 67.9 (d, J_{C-F} = 24.2 Hz, C_5), 61.7 (d, J_{C-F} = 5.1 Hz, C_4), 55.8 (OCH_3) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −229.9 (ddd, J = 47.0, 46.1, 12.7 Hz, F_6) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −229.9 (s, F_6) ppm; HRMS (ES^+) for $C_7H_{12}{}^{35}ClFNaO_4$ $[M + Na]^+$ calcd 237.0300 found 237.0300.

*Methyl 4-Deoxy-4-fluoro-6-O-tosyl-α-D-galactopyranoside (**62**).* To a solution of **61**[120] (3.00 g, 8.61 mmol) in CH_2Cl_2 (16 mL) was added DAST (3.98 mL, 30.1 mmol). The dark brown solution was then heated to 50 °C and stirred for 16 h. The reaction was cooled to 0 °C and quenched by the addition of MeOH (50 mL). The solution was concentrated *in vacuo* to afford a dark yellow oil. Purification by chromatography (80−100% EtOAc/hexane) afforded **62** as an off-yellow amorphous solid (1.42 g, 4.06 mmol, 49%): mp (postcolumn) 99−100 °C; $[\alpha]_D^{25}$+75.5 (*c* 0.6, $CHCl_3$); IR (neat) 3364 (br), 2922

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(w), 1598 (w), 1450 (w), 1356 (s), 1173 (s), 1093 (m), 983 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (2H, dt, J = 8.4, 2.0 Hz, 2H, Ar_H), 7.38−7.34 (2H, m, Ar_H), 4.76 (1H, dd, J = 51.5, 2.6 Hz, H_4), 4.78 (1H, d, J = 3.4 Hz, H_1), 4.17 (2H, d, J = 6.4 Hz, H_6), 4.02 (1H, dt, J = 29.1, 6.4 Hz, H_5), 3.82 (1H, dddd, J = 27.8, 10.0, 6.2, 2.7 Hz, H_3), 3.81−3.73 (1H, m, H_2), 3.40 (3H, s, OCH_3), 3.01 (1H, d, J = 6.1 Hz, 3-OH), 2.60 (1H, d, J = 8.9 Hz, 2-OH), 2.46 (s, 3H, $ArCH_3$) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2 (Ar_c), 132.4 (Ar_c), 130.0 (Ar_c), 128.0 (Ar_c), 99.3 (C_1), 88.7 (d, J_{C-F} = 181.9 Hz, C_4), 69.4 (d, J_{C-F} = 16.1 Hz,C_3), 69.3 (C_2), 67.3 (d, J_{C-F} = 18.3 Hz, C_5), 67.3 (d, J_{C-F} = 6.6 Hz, C_6), 55.9 (OCH_3), 21.7 ($ArCH_3$) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −221.2 (ddd, J = 50.3, 29.5, 27.7 Hz, F_4) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −221.0 (s, F_4) ppm; HRMS: (ES^+) for $C_{14}H_{19}FNaO_7S$ $[M + Na]^+$ calcd. 373.0728 found 373.0735.

*Methyl 3,6-Anhydro-4-deoxy-4-fluoro-β-D-galactopyranoside (**63**).* A solution of **62** (472 mg, 1.35 mmol) in THF (7 mL) was cooled to 0 °C. $LiBEt_3H$ (1 M in THF, 4.05 mL, 4.05 mmol) was added dropwise, and the reaction was stirred at 0 °C for 2 h. The reaction was quenched by the addition of EtOAc (10 mL) and satd aq Rochelle's salt (20 mL) and stirred vigorously for 5 min. The phases were separated, and the aqueous phase was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (50 mL), dried ($MgSO_4$), and concentrated *in vacuo* to yield a pale-yellow oil. Purification by chromatography (50% EtOAc/hexane) afforded the title compound as a colorless oil (160 mg, 0.90 mmol, 67%): $[\alpha]_D^{25}$ +26.5 (*c* 0.39, $CHCl_3$); IR (neat) 3364 (br), 2922 (w), 1598 (w), 1450 (w), 1356 (s), 1173 (s), 1093 (m), 983 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.34 (1H, dd, J = 51.7, 2.1 Hz, H_4), 4.72 (1H, d, J = 2.6 Hz, H_1), 4.56 (1H, dd, J = 14.6, 5.4 Hz, H_3), 4.49 (1H, q, J = 3.0 Hz, H_5), 4.14 (1H, dd, J = 10.5, 1.7 Hz, H_{6a}), 4.03 (1H, dt, J = 10.5, 3.2 Hz, H_{6b}), 4.03−3.98 (1H, m, H_2), 3.55 (3H, s, OCH_3), 2.61 (1H, d, J = 1.3 Hz, 2-OH) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 96.7 (C_1), 90.1 (d, J_{C-F} = 190.7 Hz, C_4), 78.5 (d, J_{C-F} = 16.8 Hz, C_3), 74.7 (d, J_{C-F} = 23.5 Hz,C_5), 70.8 (d, J_{C-F} = 8.8 Hz, C_2), 69.2 (C_6), 57.3 (OCH_3) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −202.3 (dd, J = 52.0, 13.9 Hz,F_4) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −202.4 (s, F_4) ppm. HRMS could not be obtained.

*Methyl 6-Chloro-6-deoxy-α-D-glucopyranoside (**64**).* Adapting the method of Uzan et al.,[121] to a suspension of **27** (10.0 g, 51.4 mmol) in DMF (100 mL) was added methanesulfonyl chloride (7.96 mL, 103 mmol). The reaction was heated to 70 °C and stirred for 24 h. The reaction was cooled to rt and concentrated *in vacuo*. Purification by chromatography (2−5% MeOH/EtOAc) afforded **64** as a white powder (10.4 g, 48.9 mmol, 95%): mp (postcolumn)-114−116 °C, lit.[122] 111−112 °C (EtOH/EtOAc); $[\alpha]_D^{25}$ +148.5 (*c* 0.66, MeOH, lit.[122] $[\alpha]_D$ +151, MeOH); IR (neat) 3401 (m, br), 2918 (w), 2838 (w), 1434 (w), 1341 (m), 1144 (m), 1044 (w), 955 (m) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 5.22 (1H, d, J = 5.9 Hz, 4-OH), 4.92 (1H, d, J = 5.1 Hz, 1H, 3-OH), 4.84 (1H, d, J = 6.4 Hz, 2-OH), 4.56 (1H, d, J = 3.7 Hz, H_1), 3.85 (1H, dd, J = 11.6, 2.1 Hz, H_{6a}), 3.68 (1H, dd, J = 11.6, 6.2 Hz, H_{6b}), 3.52 (1H, ddd, J = 9.5, 6.2, 2.0 Hz, H_5), 3.42−3.33 (1H, m, H_3), 3.28 (3H, s, OCH_3), 3.20 (1H, ddd, J = 9.8, 6.3, 3.7 Hz, 1H, H_2), 3.06 (1H, ddd, J = 9.7, 8.7, 5.9 Hz, H_4) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 99.8 (C_1), 73.1 (C_3), 71.8 (C_2), 71.23 (C_4 or C_5), 71.21 (C_4 or C_5), 54.5 (OCH_3), 45.6 (C_6) ppm; HRMS: (ES^+) for $C_7H_{13}{}^{35}ClNaO_5$ $[M + Na]^+$ calcd.235.0344 found 235.0342. Physical and spectroscopic characteristics correspond to the literature.[122]

*Methyl 4,6-Dideoxy-6-chloro-4-fluoro-α-D-galactopyranoside (**65**).* A solution of **64** (20.0 g, 94.1 mmol) in CH_2Cl_2 (200 mL) was cooled to 0 °C. DAST (32.5 mL, 246 mmol) was added dropwise. The yellow mixture was heated to 50 °C and stirred for 16 h. The reaction was cooled to rt and poured into a vigorously stirred solution of satd aq $NaHCO_3$ (400 mL) and stirred for 30 min. The mixture was then concentrated *in vacuo* to afford an orange-colored solid. Purification by chromatography (70% EtOAc/hexane) afforded **65** as fluffy white needles (9.45 g, 44.0 mmol, 47%): mp 153−154 °C (postcolumn); $[\alpha]_D^{25}$ +160.4 (*c* 0.38, $CHCl_3$); IR (neat) 3331 (m, br), 2937 (w), 2848 (w), 1455 (w), 1363 (w), 1137 (m), 1047 (s), 992 (s), 927 (m) cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 4.80 (1H, ddd, J = 50.7, 2.8, 0.9 Hz, H_4), 4.75 (1H, d, J = 3.0 Hz, H_1), 3.95 (1H, dddt, J = 28.6, 7.8, 6.0, 0.7 Hz, H_5), 3.82 (1H, ddd, J = 28.5, 10.2, 2.6 Hz, H_3), 3.75 (1H, ddd, J = 10.2, 3.6, 1.8 Hz, H_2), 3.73 (1H, dd, J = 11.1, 6.0 Hz, H_{6a}), 3.64 (1H, ddd, J = 11.1, 7.8, 1.3 Hz, H_{6b}), 3.43 (3H, s, OCH_3) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, CD_3OD) δ 4.80 (1H, br d, J = 2.2 Hz, H_4), 4.75 (1H, d, J = 3.6 Hz, H_1), 3.94 (1H, ddt, J = 7.8, 6.0, 0.7 Hz, H_5), 3.82 (1H, dd, J = 10.2, 2.6 Hz, H_3), 3.75 (1H, dd, J = 10.3, 3.7 Hz, H_2), 3.73 (1H, dd, J = 11.1, 6.0 Hz, H_{6a}), 3.64 (1H, dd, J = 11.1, 7.6 Hz, H_{6b}), 3.43 (3H, s, OCH_3) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $MeOD_4$) δ 101.7 (C_1), 91.3 (d, J_{C-F} = 181.2 Hz, C_4), 71.2 (d, J_{C-F} = 17.9 Hz, C_5), 70.10 (d, J_{C-F} = 2.4 Hz, C_2), 70.06 (d, J_{C-F} = 17.9 Hz, C_3), 50.1 (OCH_3), 43.0 (d, J_{C-F} = 6.7 Hz, C_6) ppm; ^{19}F NMR (470 MHz, $MeOD_4$) δ −222.5 (dtquin, J = 50.7, 28.4, 0.9 Hz, F_4) ppm; $^{19}F(^1H)$ NMR (470 MHz, $MeOD_4$), δ −222.5 (s, F_4) ppm; HRMS (ES^+) for $C_7H_{12}{}^{35}ClFNaO_4[M + Na]^+$ calcd 237.0300, found 237.0304.

*Methyl 2,3-Di-O-benzoyl-6-deoxy-6-bromo-α-D-galactopyranoside (**66**).* A solution of **37** (3.00 g, 7.45 mmol) in pyridine (100 mL) was cooled to 0 °C. PPh_3 (3.91 g, 14.9 mmol) and CBr_4 (2.47 g, 7.45 mmol) were added, and the reaction was heated to 60 °C for 1.5 h. The reaction was cooled to rt and then quenched by the addition of MeOH (10 mL), and stirred for 10 min. The reaction mixture was concentrated *in vacuo* to afford an orange oil. The residue was then taken up and triturated in Et_2O (3 × 100 mL). The precipitate was dried *in vacuo* to afford a white solid. Purification by chromatography (25−50% EtOAc/petroleum ether) afforded **66** as a white solid (2.93 g, 6.30 mmol, 85%): mp (postcolumn) 47−49 °C; $[\alpha]_D^{24}$ +161.7 (*c* 0.71, $CHCl_3$); IR (neat) 3494 (br), 2934 (w), 1714 (s), 1451 (m), 1268 (s), 1070 (s), 706 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04−7.94 (4H, m, Ar_H), 7.57−7.48 (2H, m, Ar_H), 7.43−7.34 (4H, m, Ar_H), 5.74 (1H, dd, J = 10.6, 3.1 Hz, H_3), 5.63 (1H, dd, J = 10.6, 3.6 Hz, H_2), 5.18 (1H, d, J = 3.6 Hz, H_1), 4.49 (1H, br t, J = 3.2 Hz, H_4), 4.23 (1H, app t, J = 6.9 Hz, H_5), 3.64 (1H, dd, J = 10.2, 7.0 Hz, H_{6a}), 3.59 (1H, dd, J = 10.2, 7.2 Hz, H_{6b}), 3.49 (3H, s, OCH_3), 2.26 (1H, d, J = 3.6 Hz, 4-OH) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 166.1 (CO), 165.6 (CO), 133.5 (Ar_C), 133.3 (Ar_C), 129.83 (Ar_C), 129.76 (Ar_C), 129.3 (Ar_C), 129.2 (Ar_C), 128.5 (Ar_C), 128.4 (Ar_C), 97.6 (C_1), 70.9 (C_3), 69.9 (C_5), 68.7 (C_2), 68.3 (C_4), 55.7 (OCH_3), 29.7 (C_6) ppm; HRMS (ES^+) for $C_{21}H_{21}{}^{79}BrNaO_7[M + Na]^+$ calcd 487.0363 found 487.0367.

*Mixture of Methyl 2,3-Di-O-benzoyl-α-D-fucopyranoside (**67**) and Methyl 2,4-Di-O-benzoyl-α-D-fucopyranoside (**68**).* To a solution of **66** (2.63 g, 5.63 mmol) in toluene (100 mL) were added Bu_3SnH (2.29 mL, 8.48 mmol) and AIBN (0.046 g, 0.28 mmol). The reaction mixture was heated to 70 °C for 16 h and then concentrated *in vacuo* to afford a yellow oil. Purification by chromatography (10% K_2CO_3/silica w/w,[118] 35−50% EtOAc/petroleum ether) afforded an inseparable mixture of **67** and **68** as a white solid (1.34 g, 3.47 mmol, 62%, **67**/**68** 1:1.5).

*Selected data for **67**:* ^1H NMR (400 MHz, $CDCl_3$) δ 8.19−8.13 (3H, m, Ar_H), 8.12−8.08 (3H, m, Ar_H), 8.03−7.97 (4H, m, Ar_H), 7.64−7.56 (3H, m, Ar_H), 7.56−7.43 (8H, m, Ar_H), 7.42−7.34 (4H, m, Ar_H), 5.71 (1H, dd, J = 10.8, 3.1 Hz, H_3), 5.62 (1H, dd, J = 10.8, 3.8 Hz, H_2), 5.12 (1H, d, J = 3.3 Hz, H_1), 4.28−4.19 (1H, m H_5), 4.15 (1H, br d, J = 2.1 Hz, H_4), 3.43 (3H, s, OCH_3), 1.37 (3H, d, J = 6.6 Hz, H_6) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 166.9 (CO), 166.7 (CO), 166.1 (CO), 165.8 (CO), 133.42 (Ar_c), 133.36 (Ar_c), 133.3 (Ar_c), 133.2 (Ar_c), 130.0 (Ar_c), 129.9 (Ar_c), 129.8 (Ar_c), 129.7 (Ar_c), 129.54 (Ar_c), 129.45 (Ar_c), 129.43 (Ar_c), 129.40 (Ar_c), 128.6 (Ar_c), 128.43 (Ar_c), 128.42 (Ar_c), 128.4 (Ar_c), 97.5 (C_1), 71.6 (C_3), 70.8 (C_4), 68.9 (C_2), 65.4 (C_5), 55.5 (OCH_3), 16.0 (C_6) ppm. NMR data correspond to literature (enantiomer).[123]

*Selected data for **68**:* ^1H NMR (400 MHz, $CDCl_3$) δ 5.57 (1H, dd, J = 3.4, 1.0 Hz, H_4), 5.36 (1H, dd, J = 10.4, 3.7 Hz, H_2), 5.13 (1H, d, J = 3.7 Hz, H_1), 4.49 (1H, dd, J = 10.5, 3.5 Hz, H_3), 3.45 (3H, s, OCH_3), 1.26 (3H, d, J = 6.6 Hz, H_6) ppm (resonances for the benzoate protecting groups, and for C5, of **67** and **68** overlapped); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 97.7 (C_1), 74.3 (C_4), 72.3 (C_2), 67.5 (C_3), 65.0 (C_5), 55.6 (OCH_3), 16.3 (C_6) ppm (resonances for

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the benzoate protecting groups of **67** and **68** overlapped). NMR data correspond to literature (enantiomer).[124]

*Methyl 2,3-Di-O-benzoyl-4,6-dideoxy-4-fluoro-6-bromo-α-D-glucopyranoside (**69**).* A solution of **66** (7.30 g, 15.7 mmol) in CH_2Cl_2 (200 mL) was cooled to 0 °C. DAST (6.50 mL, 47.0 mmol) was added, and the mixture was heated to 50 °C. The mixture was stirred for 24 h and then cooled to rt. The reaction was quenched by the addition of MeOH (30 mL) and then concentrated *in vacuo*. The residue was redissolved in CH_2Cl_2 (100 mL), then washed with satd $NaHCO_{3(aq)}$ (2 × 100 mL) and H_2O (100 mL), then dried ($MgSO_4$) and concentrated *in vacuo* to afford a brown solid. Purification by chromatography (30% EtOAc/petroleum ether) afforded **69** as an off-white solid (4.92g, 10.5 mmol, 67%): mp (postcolumn) 126−127 °C; $[\alpha]_D^{24}$ +56.5 (*c* 0.68, $CHCl_3$); IR (neat) 2935 (w), 1723 (s), 1451 (m), 1272 (s), 1106 (s), 707 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04−7.97 (4H, m, Ar_H), 7.56−7.50 (2H, m, Ar_H), 7.43−7.36 (4H, m, Ar_H), 6.15−6.03 (1H, m, H_3), 5.20−5.15 (2H, m, H_1, H_2), 4.66 (1H, dt, J = 50.9, 9.5 Hz, H_4), 4.17 (1H, dddd, J = 9.7, 6.1, 3.6, 2.7 Hz, H_5), 3.79 (1H, dt, J = 11.4, 2.0 Hz, H_{6a}), 3.65 (1H, ddd, J = 11.4, 5.8, 0.6 Hz, H_{6b}), 3.49 (3H, s, OCH_3) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 165.8 (CO), 165.5 (CO), 133.5 (Ar_C), 133.3 (Ar_C), 129.9 (Ar_C), 129.8 (Ar_C), 129.2 (Ar_C), 128.8 (Ar_C), 128.44 (Ar_C), 128.38 (Ar_C), 97.0 (C_1), 89.0 (d, J_{C-F} = 188.5 Hz, C_4), 71.3 (d, J_{C-F} = 7.3 Hz, C_2), 70.1 (d, J_{C-F} = 19.8 Hz, C_3), 67.8 (d, J_{C-F} = 23.5 Hz, C_5), 55.8 (OCH_3), 31.4 (C_6) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ−196.9 (dd, J = 51.2, 13.0 Hz, F_4) ppm; HRMS (ES+) for $C_{21}H_{20}{}^{79}BrFNaO_6$ $[M + Na]^+$ calcd 489.0320, found 489.0316.

*Methyl 2,3-Di-O-benzoyl-4-deoxy-4-fluoro-α-D-quinovopyranoside (**70**).* To a solution of **69** (7.88 g, 16.9 mmol) in toluene (200 mL) were added Bu_3SnH (6.83 mL, 25.4 mmol) and AIBN (139 mg, 0.85 mmol). The reaction was heated to 115 °C and stirred for 10 h. The mixture was cooled to rt and then concentrated *in vacuo* to yield a yellow oil. Purification by chromatography (10% K_2CO_3/silica,[118] 10−50% EtOAc/petroleum ether) afforded **70** as a colorless oil (5.00 g, 12.9 mmol, 76%): $[\alpha]_D^{27}$ +154.4 (*c* 0.51, $CHCl_3$); IR (neat) 2936 (w), 1724 (s), 1451 (m), 1273 (s), 1095 (s), 1027 (m), 986 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04−7.96 (4H, m, Ar_H), 7.55−7.49 (2H, m, Ar_H), 7.43−7.35 (4H, m, Ar_H), 6.03 (1H, ddd, J = 13.6, 10.2, 9.2 Hz, H_3), 5.15 (1H, ddd, J = 10.2, 3.7, 0.8 Hz, H_2), 5.08 (1H, t, J = 3.4 Hz, H_1), 4.33 (1H, dt, J = 50.9, 9.5 Hz, H_4), 4.07 (1H, dqd, J = 9.5, 6.2, 3.9 Hz, H_5), 3.44 (3H, s, OCH_3), 1.43 (3H, dd, J = 6.2, 0.9 Hz, H_6) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 165.9 (CO), 165.7 (CO), 133.4 (Ar_C), 133.2 (Ar_C), 130.0 (Ar_C), 129.8 (Ar_C), 129.5 (Ar_C), 129.0 (Ar_C), 128.43 (Ar_C), 128.35 (Ar_C), 96.8 (C_1), 92.4 (d, J_{C-F} = 187.1 Hz, C_4), 71.8 (d, J_{C-F} = 8.1 Hz, C_2), 70.5 (d, J_{C-F} = 20.5 Hz, H_3), 64.8 (d, J_{C-F} = 23.5 Hz, C_5), 55.5 (OCH_3), 17.2 (C_6) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −196.0 (dd, J = 50.3, 13.9 Hz, F_4) ppm; HRMS (ES+) for $C_{21}H_{21}FNaO_6$, $[M + Na]^+$ calcd 411.1214, found 411.1219.

*Methyl 4-Deoxy-4-fluoro-α-D-quinovopyranoside (**71**).* To a solution of **70** (1.23 g, 3.16 mmol) in MeOH (50 mL) was added NaOMe in MeOH (25% v/v, 0.22 mL, 0.95 mmol). The reaction mixture was stirred at rt for 1 h and was then neutralized with Amberlite IR-120 (H^+) resin and filtered. The filtrate was concentrated *in vacuo* to afford a brown oil. Purification by chromatography (15−100% EtOAc/petroleum ether) afforded **71** as a white amorphous solid (451 mg, 2.50 mmol, 79%): mp (postcolumn) 99−100 °C; $[\alpha]_D^{25}$ +169.0 (*c* 1.0, MeOH); IR (neat)3425 (br), 2936 (w), 1450 (m), 1001 (s) cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 4.60 (1H, t, J = 3.5 Hz, H_1), 3.84 (1H, ddd, J = 49.4, 9.5, 8.7 Hz, H_4), 3.80−3.72 (2H, m, H_3, H_5), 3.41 (1H, dd, J = 9.5, 3.8 Hz, H_2), 3.40 (3H, s, OCH_3), 1.26 (3H, dd, J = 6.2, 1.4 Hz, H_6) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, CD_3OD) δ 4.60 (1H, d, J = 3.9 Hz, H_1), 3.84 (1H, dd, J = 9.4, 8.6 Hz, H_4), 3.77 (1H, dd, J = 9.4, 8.6 Hz, H_3), 3.76 (1H, dqd, J = 9.4, 6.1, 0.5 Hz, H_5), 3.41 (1H, dd, J = 9.6, 3.9 Hz, H_2), 3.40 (3H, s, OCH_3), 1.26 (3H, d, J = 6.1 Hz, H_6) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, CD_3OD) δ 100.9 (d, J_{C-F} = 2.0 Hz C_1), 96.3 (d, J_{C-F} = 182.0 Hz, C_4), 73.2 (d, J_{C-F} = 8.0 Hz, C_2), 72.8 (d, J_{C-F} = 8.0 Hz, C_3), 65.9 (d, J_{C-F} = 24.0 Hz, C_5), 55.6 (OMe), 17.5 (C_6) ppm; ^{19}F NMR (471 MHz, CD_3OD) δ −197.6 to −197.8 (m, F_4) ppm; $^{19}F\{^1H\}$ NMR (471 MHz, CD_3OD) δ −197.59 (s, F_4) ppm; HRMS (ES+) for $C_7H_{13}FNaO_4$ $[M + Na]^+$ calcd 203.0690, found 203.0685.

*Methyl 6-O-p-Toluenesulfonyl-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-galactopyransoside (**72**).* A solution of **46** (3.39 g, 11.0 mmol) in pyridine (30 mL) was cooled to −40 °C. TsCl (2.52 g, 13.2 mmol) was added portionwise, and the reaction stirred for 6 h. The reaction was quenched by the addition of MeOH (20 mL), and warmed to rt. The mixture was concentrated *in vacuo*. Purification by chromatography (35% EtOAc/hexane) afforded **72** as an amorphous white solid (3.05 g, 6.59 mmol, 60%): mp (postcolumn)67−69 °C; $[\alpha]_D^{27}$ −27.6 (*c* 0.53, $CHCl_3$); IR (neat) 3458 (br), 2947 (w), 2835 (w), 1449 (w), 1359 (m), 1083 (s), 1036 (s), 977 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84−7.78 (2H, m, Ar_H), 7.38−7.31 (2H, m, Ar_H), 4.74 (1H, d, J = 3.4 Hz, H_1), 4.26 (1H, dd, J = 10.5, 5.3 Hz, H_{6a}), 4.19 (1H, dd, J = 10.5, 7.2 Hz, H_{6b}), 4.11 (1H, dd, J = 10.4, 3.4 Hz, H_2), 4.07−4.00 (2H, m, H_3 and H_5), 3.96−3.91 (1H, m, H_4), 3.38 (3H, s, OCH_3), 3.25 (3H, s, $OCH_3{}^{BDA}$), 3.22 (3H, s, $OCH_3{}^{BDA}$), 2.45 (3H, s, $ArCH_3$), 2.31 (1H, br t, J = 1.4 Hz,4-OH), 1.32 (3H, s, $CH_3{}^{BDA}$), 1.29 (3H, s, $CH_3{}^{BDA}$) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.9 (Ar_C), 132.8 (Ar_C), 129.8 (Ar_C), 128.0 (Ar_C), 100.19 ($C(CH_3)^{BDA}$), 100.18 ($C(CH_3)^{BDA}$), 98.2 (C_1), 68.8 (C_6), 68.4 (C_5), 67.6 (C_4), 65.8 (C_3), 64.9 (C_2), 55.3 (OCH_3), 48.0 ($OCH_3{}^{BDA}$), 47.9 ($OCH_3{}^{BDA}$), 21.6 ($ArCH_3$), 17.72 ($C(CH_3)^{BDA}$), 17.65 ($C(CH_3)^{BDA}$) ppm; HRMS (ES^+) for $C_{20}H_{30}NaO_{10}S$ $[M + Na]^+$ calcd 485.1452 found 485.1460.

*Methyl 4-Deoxy-4-fluoro-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-quinovopyranoside (**73**).* To a solution of **54** (100 mg, 0.342 mmol) in anhydrous 1,2-dichloroethane (0.7 mL) were added 2,4,6-collidine (54.7 μL, 0.411 mmol, 1.2 equiv) and DAST (50.3 μL, 0.411 mmol, 1.2 equiv), and the vial was placed in a microwave. The reaction mixture was irradiated for 6 min at 100 °C, cooled to rt, quenched with MeOH, and then concentrated under vacuum. Column chromatography (10% EtOAc/hexane) afforded **73** as a light brown powder (37 mg, 0.126 mmol, 37%): mp (postcolumn)121−123 °C; $[\alpha]_D^{24}$ −92.7 (*c* 0.64, $CHCl_3$); IR (neat) 2986 (w), 1371 (m), 1131 (s), 1028 (s), 997 (s), 885 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.68 (1H, t, J = 3.6 Hz, H_1), 4.25−4.14 (1H, m, H_3), 4.13 (1H, dt, J = 50.5, 9.1 Hz, H_4), 3.89−3.71 (2H, m, H_2 and H_5), 3.43 (3H, s, OCH_3), 3.30 (3H, s, $OCH_3{}^{BDA}$), 3.26 (3H, s, $OCH_3{}^{BDA}$), 1.35 (3H, s, $CH_3{}^{BDA}$), 1.33 (3H, s, $CH_3{}^{BDA}$), 1.32 (3H, dd, J = 6.2, 1.2 Hz, H_6) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 100.0 ($C(CH_3)^{BDA}$), 99.3 ($C(CH_3)^{BDA}$), 97.6 (d, J_{C-F} = 1.5 Hz, C_1), 92.0 (d, J_{C-F} = 184.9 Hz, C_4), 68.0 (d, J_{C-F} = 8.1 Hz, C_2), 67.4 (d, J_{C-F} = 18.3 Hz, C_3), 65.6 (d, J_{C-F} = 24.2 Hz, C_5), 55.1 (OCH_3), 48.0 ($OCH_3{}^{BDA}$), 47.9 ($OCH_3{}^{BDA}$), 17.7 ($C(CH_3)^{BDA}$), 17.6 ($C(CH_3)^{BDA}$), 17.3 (C_6) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −199.0 (br dd, J = 15.6, 50.5 Hz, F_4) ppm; $^{19}F(^1H)$ NMR (376 MHz, $CDCl_3$) δ −199.1 (s, F_4) ppm; HRMS (ES^+) for $C_{13}H_{23}FNaO_6[M + Na]^+$ calcd 317.1371 found 317.1375.

*Methyl 4,6-Dideoxy-4,6-difluoro-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-glucopyranoside (**74**).* Into a microwave vial was added a solution of **46** (600 mg, 1.95 mmol) in 1,2-dichloroethane (2.6 mL). 2,4,6-Collidine (0.79 mL, 5.94 mmol) and DAST (0.73 mL, 5.94 mmol) were added, and the vial wassealed and placed in a microwave reactor. The mixture was irradiated at 100 °C for 8 min. The reaction was cooled to rt and then quenched by the addition of MeOH. The solution was concentrated *in vacuo*. Purification by chromatography (silica, 10−20% EtOAc/petroleum ether) and subsequent recrystallization of the resultant brown oil (EtOAc/hexane) afforded **74** as fine yellow needles (285 mg, 0.92 mmol, 47%): mp (EtOAc/hexane) 123−125 °C; $[\alpha]_D^{27}$ −76.9 (*c* 0.28, $CHCl_3$); IR (neat) 3352 (br, w), 2981 (m), 1462 (w), 1384 (w), 1116 (s), 1005 (s), 936 (m), 884 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.78 (1H, t, J = 3.4 Hz, H_1), 4.65 (1H, dddd, J = 47.2, 10.4, 3.6, 1.7 Hz, H_{6a}), 4.62 (1H, ddt, J = 47.4, 10.4, 2.0 Hz, H_{6b}), 4.55 (1H, ddd, J = 52.1, 9.7, 9.2 Hz, H_5), 4.28 (1H, dt, J = 15.5, 9.6 Hz, H_3), 3.97−3.83 (1H, m, H_5), 3.78 (1H, ddd, J = 10.3, 3.6, 1.1 Hz, H_2), 3.46 (3H, s, OCH_3), 3.31 (3H, s, $OCH_3{}^{BDA}$), 3.27 (3H, s, $OCH_3{}^{BDA}$), 1.36 (3H, s, $C(CH_3)^{BDA}$), 1.33 (3H, s, $C(CH_3)^{BDA}$) ppm;

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$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 100.0 ($C(CH_3)^{BDA}$), 99.5 ($C(CH_3)^{BDA}$), 97.9 (d, J_{C-F} = 1.5 Hz, C_1), 85.6 (dd, J_{C-F} = 184.5, 7.7 Hz, C_4), 81.1 (d, J_{C-F} = 174.6 Hz, C_6), 68.9 (dd, J_{C-F} = 23.8, 18.0 Hz, C_5), 67.5 (d, J_{C-F} = 8.1 Hz, C_2), 67.4 (d, J_{C-F} = 17.6 Hz, C_3), 55.5 (OCH_3), 48.0 (OCH_3^{BDA}), 47.9 (OCH_3^{BDA}), 17.63 ($C(CH_3)^{BDA}$), 17.60 ($C(CH_3)^{BDA}$) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −200.6 (1F, br dd, J = 52.0, 15.6 Hz, F_4), −235.2 (1F, td, J = 47.3, 26.9 Hz, F_6) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −200.5 (1F, s, F_4), −235.1 (1F, s, F_6) ppm; HRMS (ES^+) for $C_{13}H_{22}F_2NaO_6$ $[M + Na]^+$ calcd 335.1277 found 335.1282.

*Methyl 4,6-Dideoxy-4,4-difluoro-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-xylo-hexopyranoside (**76**), Methyl 4,6-Dideoxy-4-fluoro-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-erythro-hex-3-enopyranoside (**77**), and Methyl 4,6-Dideoxy-4-fluoro-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-L-threo-hex-4-enopyranoside (**78**).* To a solution of **54** (2.07 g, 7.08 mmol) in CH_2Cl_2 (70 mL) was added Dess−Martin periodinane (3.90 g, 9.21 mmol). The mixture was stirred for 90 min. The mixture was diluted with CH_2Cl_2 (30 mL) and washed with a saturated solution of $NaHCO_3$ and $Na_2S_2O_3$ (1:1, 100 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with a saturated solution of $NaHCO_3$ and $Na_2S_2O_3$ (1:1, 80 mL), dried ($MgSO_4$), and concentrated *in vacuo* to afford aldehyde **75** as a colorless syrup (2.06 g, 7.08 mmol, 100%), which was used without further purification.

To a solution of **75** (2.06 g, 7.08 mmol) in CH_2Cl_2 (20 mL) was added DAST (5.20 mL, 42.5 mmol). The solution was warmed to 40°c and stirred for 16 h. The mixture was cooled to rt and diluted with CH_2Cl_2. The reaction was quenched by the addition of satd $NaHCO_{3(aq)}$. The layers were separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic layers were washed with satd $NaHCO_{3(aq)}$, dried ($MgSO_4$), and concentrated *in vacuo*. Purification by chromatography (20−50% EtOAc/petroleum ether) afforded first compound **78** as a white gummy solid (248 mg, 0.85 mmol, 12%), then **76** as a pale-yellow oil (1.45 g, 4.64 mmol, 66%), and finally 77 as a colorless oil (207 mg, 0.71 mmol, 10%). The byproducts 77 and **78** could not be obtained free of residual impurities.

*Data for **76**:* $[\alpha]_D^{24}$ −82.0 (c 0.57, $CHCl_3$); IR (neat) 2948 (w), 1453 (w), 1371 (m), 1109 (s), 1022 (s), 987 (s), 919 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.76 (1H, t, J = 3.2 Hz, H_1), 4.27 (1H, ddd, J = 20.5, 10.6, 6.0 Hz, H_3), 3.99 (1H, ddd, J = 10.5, 3.6, 1.6 Hz, H_2), 3.94 (1H, dq, J = 22.7, 6.5 Hz, H_5), 3.45 (3H, s, OCH_3), 3.30 (3H, s, OCH_3^{BDA}), 3.27 (3H, s, OCH_3^{BDA}), 1.37 (3H, s, CH_3^{BDA}), 1.35 (3H, s, CH_3^{BDA}), 1.31 (3H, d, J = 6.5 Hz, H_6) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 117.0 (dd, J_{C-F} = 255.3, 250.9 Hz, C_4), 99.98 ($C(CH_3)^{BDA}$), 99.96 ($C(CH_3)^{BDA}$), 97.8 (C_1), 67.2 (C_2), 66.2 (dd, J_{C-F} = 19.8, 18.3 Hz, C_5), 66.1 (dd, J_{C-F} = 30.1, 24.5 Hz, C_3), 55.6 (OCH_3), 48.1 (OCH_3^{BDA}), 48.0 (OCH_3^{BDA}), 17.62 ($C(CH_3)^{BDA}$), 17.55 ($C(CH_3)^{BDA}$), 11.3 (d, J_{C-F} = 5.9 Hz, C_6) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −120.38 (1F, dt, J = 242.8, 3.5 Hz, $F_{4(eq)}$), −138.82 (1F, dt, J = 242.8, 21.7 Hz, $F_{4(ax)}$) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −120.37 (1F, d, J = 242.8 Hz, $F_{4(eq)}$), −138.82 (1F, d, J = 242.8 Hz, $F_{4(ax)}$) ppm; HRMS (ES^+) for $C_{13}H_{22}F_2NaO_6$ $[M + Na]^+$ calcd 335.1277 found 335.1280.

*Data for **77**:* IR (neat) 2951 (w), 1745 (w), 1377 (m), 1152 (s), 1051 (s), 959 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.82 (1H, dd, J = 4.4, 1.3 Hz, H_1), 4.53 (1H, ddd, J = 7.6, 4.3, 3.3 Hz, H_2), 4.44 (1H, qt, J = 6.6, 3.5 Hz, H_5), 3.52 (3H, s, OCH_3), 3.37 (3H, s, OCH_3^{BDA}), 3.34 (3H, s, OCH_3^{BDA}), 1.42 (3H, s, CH_3^{BDA}), 1.38 (3H, s, CH_3^{BDA}), 1.32 (3H, dd, J = 6.6, 1.7 Hz, H_6) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.5 (d, J_{C-F} = 259.7 Hz, C_4), 123.0 (d, J_{C-F} = 6.6 Hz, C_3), 100.5 ($C(CH_3)^{BDA}$), 99.6 ($C(CH_3)^{BDA}$), 97.0 (C_1), 63.3 (d, J_{C-F} = 1.5 Hz, C_2), 63.0 (d, J_{C-F} = 27.1 Hz, C_5), 56.0 (OCH_3), 48.9 (d, J_{C-F} = 1.5 Hz, OCH_3^{BDA}), 48.5 (OCH_3^{BDA}), 17.7 ($C(CH_3)^{BDA}$), 17.6 (C_6), 17.3 ($C(CH_3)^{BDA}$) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −152.1 (1F, br t, J = 5.2 Hz, F_4) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −152.1 (s, F_4) ppm; HRMS (ES^+) for $C_{13}H_{21}FNaO_6$ $[M + Na]^+$ calcd 315.1214 found 315.1217.

*Data for **78**:* IR (neat) 2951 (w), 1734 (w), 1379 (s), 1138 (s), 1038 (s), 996 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.86 (1H, dd, J = 2.6, 1.1 Hz, H_1), 4.78 (1H, app dquin, J = 9.5, 2.2 Hz, H_3), 4.07 (1H, ddd, J = 9.5, 2.7. 0.4 Hz, H_2), 3.48 (3H, s, OCH_3), 3.31 (3H, s, OCH_3^{BDA}), 3.26 (3H, s, OCH_3^{BDA}), 1.81 (3H, dd, J = 4.8, 2.1 Hz, H_6), 1.37 (3H, s, CH_3^{BDA}), 1.35 (3H, s, CH_3^{BDA}) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 138.7 (d, J_{C-F} = 245.8 Hz, C_4), 135.0 (d, J_{C-F} = 31.6 Hz, C_5), 100.8 ($C(CH_3)^{BDA}$), 100.0 ($C(CH_3)^{BDA}$), 98.4 (C_1), 68.1 (d, J_{C-F} = 6.6 Hz, C_2), 61.9 (d, J_{C-F} = 19.1 Hz, C_3), 56.1 (OCH_3), 47.98 (OCH_3^{BDA}), 47.96 (OCH_3^{BDA}), 17.8 ($C(CH_3)^{BDA}$), 17.7 ($C(CH_3)^{BDA}$), 12.7 (C_6) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −169.4 (br dd, J = 5.2, 3.5 Hz, F_4) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −169.5 (s, F_4) ppm; HRMS (ES^+) for $C_{13}H_{21}FNaO_6$ $[M + Na]^+$ calcd 315.1214 found 315.1215.

*Methyl 4,6-Dideoxy-6,6-difluoro-2,3-O-((2′R,3′R)-2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-xylo-hexopyranoside (**80**).* To a solution of **55** (2.70 g, 9.24 mmol) in CH_2Cl_2 (100 mL) was added Dess−Martin periodinane (4.31 g, 10.2 mmol). The mixture was stirred at rt for 1 h. The reaction mixture was diluted in CH_2Cl_2 (50 mL) and washed with a saturated solution of $NaHCO_3$ and $Na_2S_2O_3$ (1:1, 150 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 75 mL), and the combined organic layers were washed with a saturated solution of $NaHCO_3/Na_2S_2O_3$ (1:1, 120 mL), dried ($MgSO_4$), and concentrated *in vacuo* to afford aldehyde **79** as a colorless oil (2.68 g, 9.24 mmol) which was used without further purification.

To a solution of **79** (2.68 g, 9.24 mmol) in CH_2Cl_2 (26 mL) was added DAST (4.53 mL, 36.9 mmol). The solution was then stirred at 25 °C for 3.5 h. The mixture was diluted with CH_2Cl_2 (120 mL) and cooled to 0 °C, and then the reaction was quenched by slow addition of satd $NaHCO_{3(aq)}$ (75 mL). The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 75 mL). The combined organic layers were dried ($MgSO_4$) and then concentrated *in vacuo*. Purification by chromatography (25% Et_2O/petroleum ether) afforded **80** as a light yellow amorphous solid (2.23 g, 7.14 mmol, 77%): mp (postcolumn) 103−104 °C; $[\alpha]_D^{27}$ −60.4 (c 0.56, $CHCl_3$); IR (neat) 2949 (w), 1449 (w), 1377 (w), 1117 (m), 1063 (s), 1027 (s), 965 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.72 (1H, td, J = 55.6, 4.2 Hz, H_6), 4.83 (1H, d, J = 3.4 Hz, H_1), 4.17 (1H, ddd, J = 11.8, 10.2, 4.8 Hz, H_3), 4.06−3.93 (1H, m, H_5), 3.72 (1H, dd, J = 10.2. 3.6 Hz, H_2), 3.44 (3H, s, OCH_3), 3.29 (3H, s, OCH_3^{BDA}), 3.27 (3H, s, OCH_3^{BDA}), 2.03−1.94 (1H, m, $H_{4(eq)}$), 1.71 (1H, app q, J = 12.1 Hz, $H_{4(ax)}$), 1.36 (3H, s, CH_3^{BDA}), 1.30 (3H, s, CH_3^{BDA}) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 114.9 (t, J_{C-F} = 242.8 Hz, C_6), 100.3 ($C(CH_3)^{BDA}$), 98.7 ($C(CH_3)^{BDA}$), 98.7 (C_1), 70.5 (C_2), 67.7 (t, J_{C-F} = 26.4 Hz, C_5), 62.7 (br s, C_3), 55.3 (OCH_3), 47.94 (OCH_3^{BDA}), 47.92 (OCH_3^{BDA}), 28.6 (t, J_{C-F} = 3.3 Hz, C_4), 17.8 ($C(CH_3)^{BDA}$), 17.7 ($C(CH_3)^{BDA}$) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −127.0 (1F, ddd, J = 289.6, 55.5, 8.7 Hz, F_{6a}), −130.8 (1F, ddd, J = 289.6, 55.5, 10.4 Hz, F_{6b}) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −127.1 (1F, d, J = 289.6 Hz, F_{6a}), −130.9 (1F, d, J = 289.6 Hz, F_{6b}) ppm; HRMS (ES^+) for $C_{13}H_{22}F_2NaO_6[M + Na]^+$ calcd 335.1277 found 335.1272.

*Methyl 4,6-Dideoxy-4,4-difluoro-α-D-xylo-hexopyranoside (**85**).* To a solution of **76** (700 mg, 2.24 mmol) in H_2O (40 mL) was added Dowex 50 × 8 H^+ (20 mL). The reaction was heated to 100 °C and stirred for 5 h. The mixture was filtered and concentrated *in vacuo*. The residue was redissolved in TFA/H_2O (9:1, 2.5 mL) and heated to 75 °C for 22 h. Monitoring by TLC indicated an incomplete reaction, so a further portion of H_2O (0.75 mL) was then added, and the mixture heated to 100 °C for a further 7 h. The mixture was concentrated *in vacuo*. Purification by chromatography (40% acetone/petroleum ether afforded first unreacted methyl glycoside **85** as a light brown solid, then 300 mg of slightly impure **6a**. These were both further purified by recrystallization (Et_2O) to afford **85** as a crystalline white solid (61 mg, 0.31 mmol, 14%), and the corresponding reducing sugar **6a** as a crystalline white solid (142 mg, 0.77 mmol, 34%): mp 130−131 °C; $[\alpha]_D^{21}$ +89.3 (c 0.2, $CHCl_3$); IR (neat) 3418 (br), 2923 (w), 1354 (w), 1230 (m), 1097 (s), 1021 (s), 988 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.80 (1H, t, J = 3.3 Hz, H_1), 3.97 (1H, dddd, J = 19.7, 9.8, 5.8, 5.3 Hz, H_3), 3.93 (1H, dqd, J =

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23.2, 6.4, 0.5 Hz, H_5), 3.73 (1H, dddd, J = 9.8, 9.3, 3.9, 1.7 Hz, H_2), 3.47 (3H, s, OCH_3), 2.46 (1H, d, J = 5.1 Hz, 3-OH), 2.29 (1 H, d, J = 9.0 Hz, 2-OH), 1.32 (3H, d, J = 6.5 Hz, H_6) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, $CDCl_3$) δ 4.80 (1H, d, J = 3.8 Hz, H_1), 3.97 (1H, dd, J = 9.8, 5.3 Hz, H_3), 3.93 (1H, q, J = 6.5 Hz, H_5), 3.73 (1H, ddd, J = 9.8, 9.1, 3.8 Hz, H_2), 3.47 (3 H, s, OCH_3), 2.46 (1H, d, J = 5.5 Hz, 3-OH), 2.29 (1H, d, J = 9.1 Hz, 2-OH), 1.32 (3H, d, J = 6.5 Hz, H_6) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ 117.7 (t, J_{C-F}= 251.5 Hz, C_4), 98.9 (d, J_{C-F} = 1.0 Hz, C_1), 71.67 (d, J_{C-F} = 6.7 Hz, C_2), 71.65 (t, J_{C-F}= 20.0 Hz, C_3), 65.3 (dd, J_{C-F} = 29.7, 24.7 Hz, C_5), 55.9 (OCH_3), 11.4 (d, J_{C-F} = 5.5 Hz, C_6) ppm; ^{19}F NMR (471 MHz, $CDCl_3$) δ −118.1 (1F, ddd, J = 246.2, 6.1, 2.0 Hz, $F_{4(eq)}$), −139.7 (1F, ddd, J = 246.4, 22.5, 20.7 Hz, $F_{4(ax)}$) ppm; $^{19}F(^1H\}$ NMR (471 MHz, $CDCl_3$) δ −118.1 (1F, d, J = 246.4 Hz, $F_{4(eq)}$), −139.7 (1F, d, J = 246.0 Hz, $F_{4(ax)}$) ppm; HRMS (ESI+) for $C_7H_{12}F_2NaO_4$ $[M + Na]^+$ calcd 221.0601, found 221.0594.

*4,6-Dideoxy-D-xylo-hexopyranose (**86**).* Using general procedure C with **92** (220 mg, 0.80 mmol), purification by chromatography (10% $MeOH/CH_2Cl_2$) afforded **82** as a white powder (101 mg, 0.68 mmol, 86%): mp (postcolumn) 143−146 °C, lit.[125] 134−136 °C. Et_2O/MeOH; $[\alpha]_D^{25}$ +47.0 (c 0.61, MeOH), $[\alpha]_D^{21}$ +33.9 (c 0.33, H_2O), lit.[126] $[\alpha]_D^{20}$ +34 (c 1, H_2O); IR (neat) 3315 (br), 2971 (w), 2923 (w), 1443 (w), 1045 (s), 815 (s) cm^{-1}; ^1H NMR (500 MHz, CD_3OD, α/β 49:51) δ 5.08 (1H, d, J = 3.8 Hz, $H_{1\alpha}$), 4.39 (1H, d, J = 7.8 Hz, $H_{1\beta}$), 4.14 (1H, dqdd, J = 11.4, 6.3, 2.2, 0.3 Hz, $H_{5\alpha}$), 3.84 (1H, ddd, J = 11.4, 9.4, 5.0 Hz, $H_{3\alpha}$), 3.63 (1H, dqd, J = 11.5, 6.2, 2.0 Hz, $H_{5\beta}$), 3.55 (1H, ddd, J = 11.4, 9.0, 5.2 Hz, $H_{3\beta}$), 3.25 (1H, dd, J = 9.4, 3.7 Hz, $H_{2\alpha}$), 3.01 (1H, dd, J = 9.0, 7.8 Hz, $H_{2\beta}$), 1.94 (1H, ddd, J = 12.8, 4.9, 2.2 Hz, $H_{4(eq)\alpha}$), 1.92 (1H, ddd, J = 12.8, 5.2, 2.0, 0.3 Hz, $H_{4(eq)\beta}$), 1.31 (1H, dt, J = 12.8, 11.4 Hz, $H_{4(ax)\beta}$), 1.25 (1H, dt, J = 12.7, 11.5 Hz, $H_{4(ax)\alpha}$), 1.21 (3H, d, J = 6.2 Hz, $H_{6\beta}$), 1.14 (3H, d, J = 6.3 Hz, $H_{6\alpha}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, CD_3OD) δ 98.4 ($C_{1\beta}$), 94.7 ($C_{1\alpha}$), 78.3 ($C_{2\beta}$), 75.8 ($C_{2\alpha}$), 72.4 ($C_{3\beta}$), 69.3 ($C_{5\beta}$), 68.8 ($C_{3\alpha}$), 64.8 ($C_{5\alpha}$), 42.5 ($C_{4\alpha}$), 42.3 ($C_{4\beta}$), 21.52 ($C_{6\alpha}$), 21.50 ($C_{6\beta}$) ppm; ^1H NMR (500 MHz, D_2O, α/β 27:73) δ 5.06 (1H, d, J = 3.8 Hz, $H_{1\alpha}$), 4.40 (1H, d, J = 7.9 Hz, $H_{1\beta}$), 4.02 (1H, dqdd, J = 11.8, 6.2, 2.2, 0.5 Hz, $H_{5\alpha}$), 3.75 (1H, ddd, J = 11.5, 9.8, 5.0 Hz, $H_{3\alpha}$), 3.62 (1H, dqd, J = 11.3, 6.2, 2.0 Hz, $H_{5\beta}$), 3.55 (1H, ddd, J = 11.5, 9.2, 5.3 Hz, $H_{3\beta}$), 3.29 (1H, dd, J = 9.8, 3.8 Hz, $H_{2\alpha}$), 2.98 (1H, dd, J = 9.3, 7.9 Hz, $H_{2\beta}$), 1.91 (dddt, J = 12.9, 5.0, 2.3, 0.5 Hz, $H_{4(eq)\alpha}$), 1.88 (1H, ddd, J = 13.0, 5.2, 2.0 Hz, $H_{4(eq)\beta}$), 1.24 (dt, J = 13.0, 11.5 Hz, $H_{4(ax)\beta}$), 1.26−1.17 (1H, m, $H_{4(ax)\alpha}$), 1.08 (3H, d, J = 6.3 Hz, $H_{6\beta}$), 1.05 (3H, d, J = 6.3 Hz, $H_{6\alpha}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 95.9 ($C_{1\beta}$), 92.6 ($C_{1\alpha}$), 78.0 ($C_{2\beta}$), 73.2 ($C_{2\alpha}$), 70.4 ($C_{3\beta}$), 68.6 ($C_{5\beta}$), 66.9 ($C_{3\alpha}$), 64.6 ($C_{5\alpha}$), 40.0 ($C_{4\alpha}$), 39.9 ($C_{4\beta}$), 19.87 ($C_{6\alpha}$), 19.85 ($C_{6\beta}$) ppm; MS (ESI+) 171.4 $[M + Na]^+$. Spectroscopic data corresponds with the literature.[50]

*1,2,3-Tri-O-acetyl-4,6-dideoxy-D-xylo-hexopyranoside (**94**).* Using general procedure A with methyl 4,6-dideoxy-α-D-xylo-hexopyranoside[88] (565 mg, 3.48 mmol) and TMSOTf (0.2 equiv) afforded **92** as a light yellow oil (265 mg, 0.97 mmol, 28%): IR (neat) 2979 (w), 1741 (s), 1369 (m), 1212 (s), 1044 (s), 924 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, α/β 85:15) δ 6.29 (1H, d, J = 3.7 Hz, $H_{1\alpha}$), 5.66−5.63 (1H, m, $H_{1\beta}$), 5.27 (1H, ddd, J = 11.5, 10.4, 5.0 Hz, $H_{3\alpha}$), 5.02 (1H, dd, J = 10.3, 3.7 Hz, $H_{2\alpha}$), 4.13 (1H, dqd, J = 12.0, 6.1, 2.3 Hz, $H_{5\alpha}$), 3.81 (1H, dqd, J = 12.2, 6.1, 1.8 Hz, $H_{5\beta}$), 2.22 (1H, ddd, J = 12.9, 5.1, 2.3 Hz, $H_{4(eq)\alpha}$), 2.14 (3H, s, $COCH_{3\alpha}$), 2.11 (3H, s, $COCH_{3\beta}$), 2.05 (3H, s, $COCH_{3\alpha}$), 2.05 (3H, s, $COCH_{3\beta}$), 2.04 (3H, s, $COCH_{3\beta}$), 2.03 ($COCH_{3\alpha}$), 1.53 (1H, dt, J = 12.7, 11.7 Hz, $H_{4(ax)\alpha}$), 1.29 (3H, d, J = 6.1 Hz, $H_{6\beta}$), 1.23 (3H, d, J = 6.2 Hz, $H_{6\alpha}$) ($H_{2\beta}$, $H_{3\beta}$, $H_{4\beta}$ signals obscured by major anomer) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 170.4 (CO_α), 170.1 (CO_α), 169.3 (CO_α), 92.3 ($C_{1\beta}$), 90.4 ($C_{1\alpha}$), 70.4 ($C_{2\alpha}$), 67.7 ($C_{3\alpha}$), 66.1 ($C_{5\alpha}$), 37.7 ($C_{4\alpha}$), 37.5 ($C_{4\beta}$), 21.01 ($COCH_{3\alpha}$), 20.95 ($COCH_{3\alpha}$), 20.65 ($COCH_{3\alpha}$), 20.62 ($C_{6\alpha}$) (other signals not resolved) ppm; HRMS (ES^+) for $C_{12}H_{18}NaO_7[M + Na]^+$ calcd 297.0945 found 297.0945. Spectroscopic characteristics correspond to the literature.[127]

*D_2O NMR Data for Compounds **83**−**88** (Table 4). D-Glucose (**83**):* ^1H NMR (500 MHz, D_2O, α/β 38:62) δ 5.08 (1H, d, J = 3.8 Hz, $H_{1\alpha}$), 4.50 (1H, d, J = 8.0 Hz, $H_{1\beta}$), 3.75 (1H, dd, J = 12.3, 2.2 Hz, $H_{6a\beta}$), 3.69 (1H, dd, J = 12.4, 2.3 Hz, $H_{6a\alpha}$), 3.69 (1H, dddd, J = 10.0, 5.6, 2.3, 0.6 Hz, $H_{5\alpha}$), 3.61 (1H, dd, J = 12.4, 5.6 Hz, $H_{6b\alpha}$), 3.57 (1H, dd, J = 12.4, 5.8 Hz, $H_{6b\beta}$), 3.57 (1H, ddd, J = 9.8, 9.2, 0.3 Hz, $H_{3\alpha}$), 3.38 (1H, dd, J = 9.8, 3.8 Hz, $H_{2\alpha}$), 3.34 (1H, dd, J = 9.3, 8.9 Hz, $H_{3\beta}$), 3.32 (1H, ddd, J = 9.6, 5.7, 2.2 Hz, $H_{5\beta}$), 3.26 (1H, dd, J = 9.8, 9.2 Hz, $H_{4\alpha}$), 3.25 (1H, dd, J = 9.7, 9.0 Hz, $H_{4\beta}$), 3.09 (1H, dd, J = 9.3, 8.0 Hz, $H_{2\beta}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 95.9 ($C_{1\beta}$), 92.1 ($C_{1\alpha}$), 75.9 ($C_{5\beta}$), 75.7 ($C_{3\beta}$), 74.1 ($C_{2\beta}$), 72.7 ($C_{3\alpha}$), 71.44 ($C_{2\alpha}$), 71.40 ($C_{5\alpha}$), 69.60 ($C_{4\alpha}$), 69.56 ($C_{4\beta}$), 60.7 ($C_{6\beta}$), 60.5 ($C_{6\alpha}$) ppm.

*L-Fucose (L-**84**):* ^1H NMR (500 MHz, D_2O, α/β 31:69) δ 5.05 (1H, d, J = 4.0 Hz, $H_{1\alpha}$), 4.40 (1H, d, J = 7.9 Hz, $H_{1\beta}$), 4.05 (1H, qdd, J = 6.6, 1.1, 0.6 Hz, $H_{5\alpha}$), 3.71 (1H, dd, J = 10.5, 3.4 Hz, $H_{3\alpha}$), 3.67−3.65 (1H, m, $H_{4\alpha}$), 3.66 (1H, qd, J = 6.5, 1.1 Hz, $H_{5\beta}$), 3.61 (1H, dd, J = 10.4, 4.0 Hz, $H_{2\alpha}$), 3.60 (1H, ddd, J = 3.6, 1.0, 0.2 Hz, $H_{4\beta}$), 3.49 (1H, dd, J = 10.0, 3.6 Hz, $H_{3\beta}$), 3.30 (1H, ddd, J = 10.3, 7.9, 0.3 Hz, $H_{2\beta}$), 1.10 (3H, d, J = 6.5 Hz, $H_{6\beta}$), 1.06 (3H, d, J = 6.5 Hz, $H_{6\alpha}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 96.2 ($C_{1\beta}$), 92.2 ($C_{1\alpha}$), 72.9 ($C_{2\beta}$), 71.9 ($C_{4\alpha}$), 71.6 ($C_{2\beta}$), 71.4 ($C_{4\beta}$), 70.9 ($C_{5\beta}$), 69.2 ($C_{3\alpha}$), 68.1 ($C_{2\alpha}$), 66.3 ($C_{5\alpha}$), 15.5 (2 × C, $C_{6\alpha}$, and $C_{6\beta}$) ppm. (*ca* 4% of furanose form is also present). Data correspond to literature data.[128]

*4-Deoxy-4-fluoro-D-glucose (**87**):* ^1H NMR (500 MHz, D_2O, α/β 43:57) δ 5.09 (1H, t, J = 3.5 Hz, $H_{1\alpha}$), 4.54 (1H, d, J = 7.9 Hz, $H_{1\beta}$), 4.19 (2H, ddd, J = 51.0, 10.0, 8.9 Hz, $H_{4\alpha}$ + $H_{4\beta}$), 3.91−3.85 (1H, m, $H_{5\alpha}$), 3.84 (1H, dddd, J = 15.7, 9.8, 8.8, 0.3 Hz, $H_{3\alpha}$), 3.74 (1H, dt, J = 12.5, 2.2 Hz, $H_{6a\beta}$), 3.69 (1H, dt, J = 12.5, 2.4 Hz, $H_{6a\alpha}$), 3.67 (1H, ddd, J = 15.8, 9.5, 8.7 Hz, $H_{3\beta}$), 3.65 (1H, ddd, J = 12.6, 4.5, 1.8 Hz, $H_{6b\alpha}$), 3.61 (1H, ddd, J = 12.6, 5.3, 1.8 Hz, $H_{6b\beta}$), 3.55 (1H, ddt, J = 9.8, 5.2, 2.5 Hz, $H_{5\beta}$), 3.43 (1H, ddd, J = 9.9, 3.8, 0.8 Hz, $H_{2\alpha}$), 3.14 (1H, ddd, J = 9.4, 8.2, 0.9 Hz, $H_{2\beta}$) ppm; $^1H\{^{19}F\}$ NMR (500 MHz, D_2O) δ 5.09 (1H, d, J = 3.9 Hz, $H_{1\alpha}$), 4.54 (1H, d, J = 8.0 Hz, $H_{1\beta}$), 4.19 (2H, dd, J = 9.8, 8.8 Hz, $H_{4\alpha}$ + $H_{4\beta}$), 3.88 (1H, ddd, J = 9.9, 4.5, 2.6 Hz, $H_{5\alpha}$), 3.84 (1H, dd, J = 9.9, 8.8 Hz, $H_{3\alpha}$), 3.74 (1H, dd, J = 12.4, 2.1 Hz, $H_{6a\beta}$), 3.69 (1H, dd, J = 12.7, 2.6 Hz, $H_{6a\alpha}$), 3.67 (1H, dd, J = 9.5, 8.9 Hz, $H_{3\beta}$), 3.65 (1H, dd, J = 12.6, 4.7 Hz, $H_{6b\alpha}$), 3.61 (1H, dd, J = 12.3, 5.2 Hz, $H_{6b\beta}$), 3.55 (1H, ddd, J = 9.7, 5.2, 2.4 Hz, $H_{5\beta}$), 3.43 (1H, dd, J = 9.9, 3.8 Hz, $H_{2\alpha}$), 3.14 (1H, dd, J = 9.6, 8.0 Hz, $H_{2\beta}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 95.9 (d, J_{C-F} = 1.4 Hz, $C_{1\beta}$), 91.9 (d, J_{C-F} = 1.4 Hz, $C_{1\alpha}$), 89.1 (d, J_{C-F} = 179.8 Hz, $C_{4\alpha}$), 89.0 (d, J_{C-F} = 180.0 Hz, $C_{4\beta}$), 73.7 (d, J_{C-F} = 17.6 Hz, $C_{3\beta}$), 73.7 (d, J_{C-F} = 8.6 Hz, $C_{2\beta}$), 73.3 (d, J_{C-F} = 24.3 Hz, $C_{5\beta}$), 71.0 (d, J_{C-F} = 17.6 Hz, $C_{3\alpha}$), 70.9 (d, J_{C-F} = 8.1 Hz, $C_{2\alpha}$), 68.9 (d, J_{C-F} = 23.8 Hz, $C_{5\alpha}$), 60.1 ($C_{6\beta}$), 59.9 ($C_{6\alpha}$) ppm; ^{19}F NMR (470 MHz, D_2O) δ −198.2 (app dddtdt, J = 50.8, 15.7, 3.9, 2.2, 1.8, 0.8 Hz, $F_{4\alpha}$), −200.2 (app ddqt, J = 50.8, 15.7, 2.2, 1.8, 0.8 Hz, $F_{4\beta}$) ppm; $^{19}F(^1H\}$ NMR (470 MHz, D_2O) δ −198.3 (1F, s, $F_{4\alpha}$), −200.3 (1F, s, $F_{4\beta}$) ppm.

*D-Quinovose (**89**):* ^1H NMR (500 MHz, D_2O, α/β 31:69) δ 5.03 (1H, d, J = 3.8 Hz, $H_{1\alpha}$), 4.48 (1H, d, J = 8.0 Hz, $H_{1\beta}$), 3.75 (1H, dqd, J = 9.7, 6.2, 0.3 Hz, $H_{5\alpha}$), 3.51 (1H, dd, J = 9.8, 9.4 Hz, $H_{3\alpha}$), 3.39 (1H, dd, J = 9.8, 3.8 Hz, $H_{2\alpha}$), 3.35 (1H, dq, J = 9.5, 6.2 Hz, $H_{5\beta}$), 3.28 (1H, t, J = 9.4 Hz, $H_{3\beta}$), 3.10 (1H, dd, J = 9.5, 8.0 Hz, $H_{2\beta}$), 3.01 (1H, t, J = 9.3 Hz, $H_{4\beta}$), 2.99 (1H, t, J = 9.4 Hz, $H_{4\alpha}$), 1.14 (3H, d, J = 6.3 Hz, $H_{6\beta}$), 1.11 (3H, d, J = 6.3 Hz, $H_{6\beta}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 95.7 ($C_{1\beta}$), 91.9 ($C_{1\alpha}$), 75.4 ($C_{3\beta}$), 75.2 ($C_{4\alpha}$), 74.9 ($C_{4\beta}$), 74.3 ($C_{2\beta}$). 74.4 ($C_{3\alpha}$), 71.9 ($C_{5\beta}$), 71.7 ($C_{2\alpha}$), 67.4 ($C_{5\alpha}$), 16.7 (2 × C, $C_{6\alpha}$ and $C_{6\beta}$) ppm. Data correspond to literature data.[129]

*D-Galactose (**92**):* ^1H NMR (500 MHz, D_2O, α/β 33:67) δ 5.11 (1H, d, J = 3.8 Hz, $H_{1\alpha}$), 4.43 (1H, d, J = 7.9 Hz, $H_{1\beta}$), 3.94 (1H, dddd, J = 7.1, 5.3, 1.2, 0.6 Hz, $H_{5\alpha}$), 3.84 (1H, dd, J = 3.2, 1.1 Hz, $H_{4\alpha}$), 3.78 (1H, ddd, J = 3.6, 1.0, 0.3 Hz, $H_{4\beta}$), 3.71 (1H, dd, J = 10.4, 3.3 Hz, $H_{3\alpha}$), 3.65 (1H, dd, J = 10.3, 3.7 Hz, $H_{2\alpha}$), 3.63 (1H, dd, J = 11.6, 7.9 Hz, $H_{6a\beta}$), 3.61−3.57 (3H, m, $H_{6a\alpha}$, $H_{6b\beta}$), 3.56 (1H, ddd, J = 7.8, 4.4, 1.0 Hz, $H_{5\beta}$), 3.50 (1H, dd, J = 10.0, 3.6 Hz, $H_{3\beta}$), 3.34 (1H, ddd, J = 10.0, 7.9, 0.3 Hz, $H_{2\beta}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 98.4 ($C_{1\beta}$), 92.3 ($C_{1\alpha}$), 75.1 ($C_{5\beta}$), 72.8 ($C_{3\beta}$), 71.8 ($C_{2\beta}$), 70.5 ($C_{5\alpha}$), 69.3 ($C_{4\alpha}$), 69.1 ($C_{3\alpha}$), 68.7 ($C_{4\beta}$), 68.3 ($C_{2\alpha}$), 61.2 ($C_{6\alpha}$), 61.0 ($C_{6\beta}$) ppm.

*4-Deoxy-D-xylo-hexopyranose (**93**):* ^1H NMR (500 MHz, D_2O, α/β 31:69) δ5.11 (1H, d, J = 3.8 Hz, $H_{1\alpha}$), 4.42 (1H, d, J = 7.9 Hz, $H_{1\beta}$), 3.95 (1H, ddddd, J = 12.1, 6.1, 3.4, 2.3, 0.5 Hz, $H_{5\alpha}$), 3.80 (1H,

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ddd, J = 11.4, 9.7, 5.0 Hz, $H_{3\alpha}$), 3.59 (1H, ddd, J = 11.7, 9.2, 5.2 Hz, $H_{3\beta}$), 3.57 (1H, dddd, J = 11.4, 6.5, 3.3, 1.4 Hz, $H_{5\beta}$), 3.53 (1H, dd, J = 11.9, 3.3 Hz, $H_{6a\beta}$), 3.52 (1H, dd, J = 12.0, 3.4 Hz, $H_{6a\alpha}$), 3.45 (1H, dd, J = 11.9, 6.5 Hz, $H_{6b\beta}$), 3.43 (1H, dd, J = 11.9, 6.1 Hz, $H_{6b\alpha}$), 3.31 (1H, dd, J = 9.7, 3.8 Hz, $H_{2\alpha}$), 3.00 (1H, dd, J = 9.3, 7.8 Hz, $H_{2\beta}$), 1.84 (1H, dddt, J = 12.8, 5.2, 2.3, 0.5 Hz, $H_{4(eq)\alpha}$), 1.82 (1H, dddd, J = 12.8, 5.3, 1.7, 0.3 Hz, $H_{4(eq)\beta}$), 1.29 (1H, br app q, J = 12.1 Hz, $H_{4(ax)\alpha}$), 1.28 (1H, dt, J = 12.9, 11.5 Hz, $H_{4(ax)\beta}$) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, D_2O) δ 96.1 ($C_{1\beta}$), 92.7 ($C_{1\alpha}$), 76.0 ($C_{2\beta}$), 73.2 ($C_{2\alpha}$), 72.5 ($C_{5\beta}$), 70.4 ($C_{3\beta}$), 68.4 ($C_{5\alpha}$), 66.9 ($C_{3\alpha}$), 63.7 ($C_{6\alpha}$), 63.6 ($C_{6\beta}$), 34.2 (2 × C, $C_{4\alpha}$ and $C_{4\beta}$) ppm. Data correspond to literature data.[130]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00796.

^1H, ^{13}C, ^{19}F NMR spectra, including 2D data, of all novel compounds; methodology and qNMR spectra of compounds **1a**−**7a** and **83**, **84**, **86**, **87**, **89**, **92**, and **93**; crystallographic data of compounds **1a**, **2a**, **5a**, **6a**, D-**19**, **69**, **71**, and **85**; coupling constant analyses of **1a**−**7a** and some acetylated derivatives; companion graphs for Figures 8−10 showing the β-anomers; tabulated chemical shift data used to make Figures 8−10 (PDF)

Accession Codes

CCDC 1453093, 1473639, 1483644, 1504321, 1520462, 1578049, 1879623, and 2046059 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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