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Enantioselective Synthesis of Dideoxy-tetrafluorinated Hexoses

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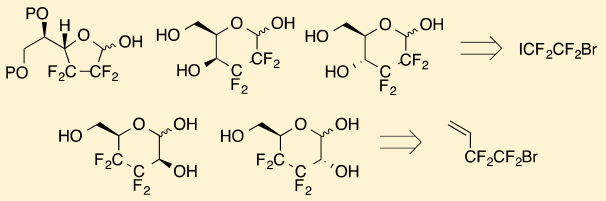
Supporting Information

ABSTRACT: Carbohydrates typically have low affinities to protein binding sites, and the development of carbohydrate mimetics with improved binding is therefore of interest. Tetrafluorination of monosaccharides is one of the strategies currently under investigation for that purpose. The synthesis of the required tetrafluorinated monosaccharides is achieved by a fluorinated building block approach. The enantioselective synthesis of tetrafluorinated hexose derivatives is described here, in both pyranose and furanose forms. In particular, the optimization of the enantioselective synthesis of the previously reported 2,3-dideoxy-2,2,3,3-tetrafluoro-D-*threo*-hexopyranose **3**, 2,3-dideoxy-2,2,3,3-tetrafluoro-D-*threo*-hexofuranose **4**, and 2,3-dideoxy-2,2,3,3-tetrafluoro-D-*erythro*-hexopyranose **5** is described as is the synthesis of two novel sugar derivatives, 3,4-dideoxy-3,3,4,4-tetrafluoro-D-*threo*-hexopyranose **6** and 3,4-dideoxy-3,3,4,4-tetrafluoro-D-*erythro*-hexopyranose **7**. The key step of all syntheses is a perfluoroalkyl lithium-mediated C−C bond formation, either intramolecular or intermolecular, which proceeds in good to excellent yields. NMR and X-ray crystallographic analyses of the tetrafluorinated methyl pyranoside derivatives confirm their $^4C_1$ conformation.

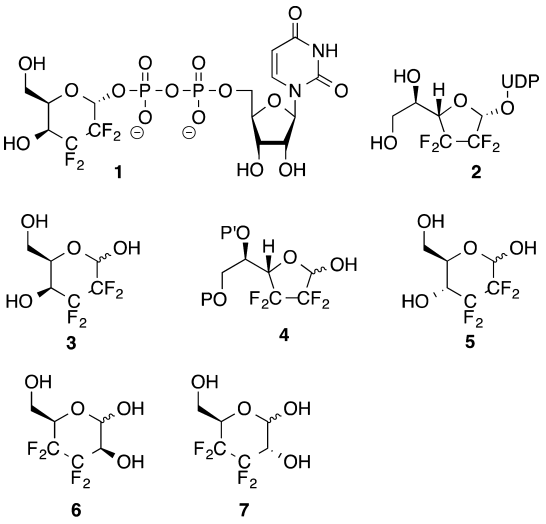


INTRODUCTION

The pronounced hydrophilicity of carbohydrates is an inherent significant contributor to the typically low affinity found for protein−carbohydrate interactions.[1] This unfavorable factor has to be taken into account when developing inhibitors of carbohydrate-processing enzymes or carbohydrate-binding proteins starting from a carbohydrate structure, at least for non-mechanism-based inhibitors. Given that carbohydrates play a central role in many fundamental processes[2] and that glycosylation of proteins and natural products can significantly alter their stability and/or biological activity,[3,4] the design of carbohydrate-based analogues with greater affinity to carbohydrate-processing proteins is of interest for use as probes or therapeutics.[2,5−9]

We are interested in investigating an approach in which the carbohydrate ring is modified by extensive fluorination. The rationale for this approach is that the combination of aqueous desolvation of perfluoroalkylidene groups[10] as well as attractive multipolar interactions mediated by the individual polar C−F bonds would positively contribute to the sugar-binding affinity and selectivity.[11,12] Such C−F-mediated polar interactions have been recognized and described in detail by Diederich et al.[13−15] Recently, our group and collaborators have described the synthesis and biological evaluation of dideoxy-tetrafluorinated uridine diphosphate (UDP)−Gal analogues **1** and **2** (Chart 1) as inhibitors of the enzyme UDP−galactopyranose mutase (UGM).[16] Inhibition assays and competition STD NMR experiments clearly showed that **2** possessed much higher affinities compared to its nonfluorinated parent, and that the tetrafluorinated structures occupied the same binding site. This was confirmed by structural studies using X-ray crystallography of the *Mycobacterium tuberculosis* UGM, which further revealed

Chart 1. Dideoxy-tetrafluorinated UGM Inhibitors 1 and 2 and Structures of the Target Monosaccharides 3−7



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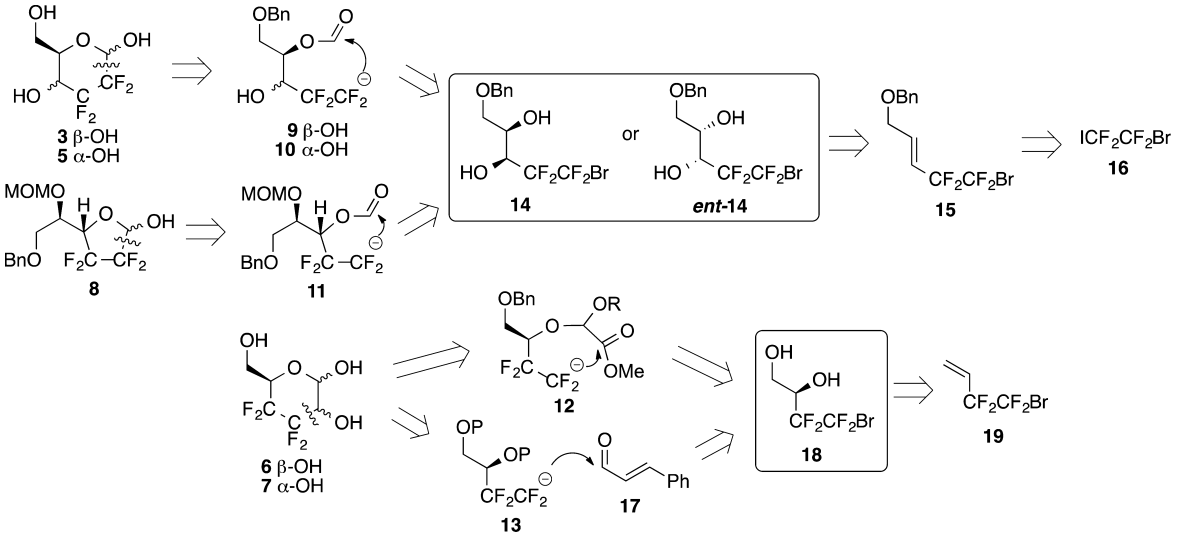
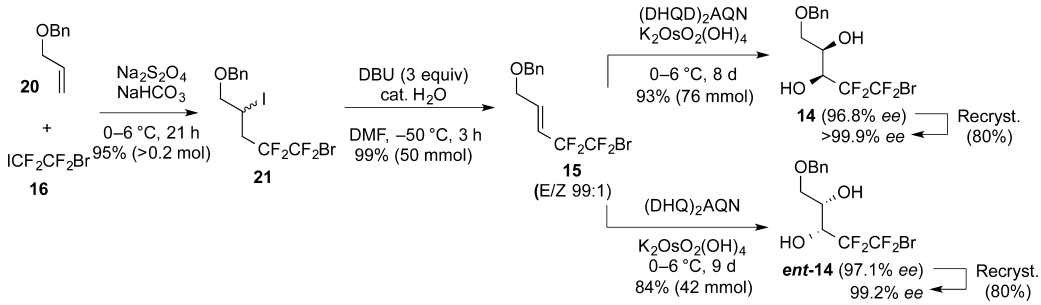
Scheme 1. Retrosynthetic Analyses for the Dideoxy-tetrafluoro Analogues



Scheme 2. Enantioselective Synthesis of the Key *syn*-Diol Intermediates



that binding of both **1** and **2** occurred with extensive substrate–enzyme interactions, including CF–F···H_2O interactions.[17] Hence, with the obvious caveat that sugar C–OH for C–F replacement will result in a loss of hydrogen-bond-donating capacity at these positions, these results demonstrate the potential of tetrafluorinated derivatives for investigation as potential carbohydrate mimetics as inhibitors of carbohydrate-processing enzymes.

Here, we describe in detail the synthesis of the four possible (contiguous) dideoxy-tetrafluorinated pyranose derivatives and, for one of these, the synthesis in the furanose form. Following our preliminary reports,[16,18] improved large-scale syntheses of 2,3-dideoxy-2,2,3,3-tetrafluoro-D-*threo*-hexopyranose[18] **3** and the corresponding (protected) 2,3-dideoxy-2,2,3,3-tetrafluoro-D-*threo*-hexofuranose[16] **4** are described. Further optimization in the synthesis of 2,3-dideoxy-2,2,3,3-tetrafluoro-D-*erythro*-hexopyranose[18] **5** is also detailed. This includes an improvement in enantiopurity to >99% ee. In addition, the syntheses of two novel dideoxy-tetrafluorinated monosaccharides, 3,4-dideoxy-3,3,4,4-tetrafluoro-D-*threo*-hexopyranose **6** and 3,4-dideoxy-3,3,4,4-tetrafluoro-D-*erythro*-hexopyranose **7**, are disclosed. Further evidence of the scarcely distorted $^4C_1$ chair conformation of these tetrafluorinated pyranoses[19,20] is also provided.

RESULTS AND DISCUSSION

Retrosynthetic Analysis. The synthesis of all compounds followed a fluorinated building block approach, with the sugars fluorinated at positions 2 and 3 (sugar numbering) originating from 1-bromo-2-iodotetrafluoroethane **16** (Scheme 1) and those at positions 3 and 4 from 4-bromo-3,3,4,4-tetrafluorobut-1-ene **19** (Scheme 1). Both fluorinated building blocks are commercially available. In all cases, the key step consisted of an intramolecular[21] or intermolecular[22−24] C–C bond formation, through perfluoroalkyl lithium intermediates **9**–**13**, all formed by MeLi-mediated halogen–lithium exchange. Two approaches are described for **6** and **7**. In all cases, chirality was introduced via asymmetric dihydroxylation, with enantiopure vicinal diol intermediates **14** and **18** obtained from alkenes **15** and **19**. The C4-diastereomers **3** and **5** both originated from a *syn*-diol, with **5** requiring inversion of configuration at one of the chiral centers of the diol. An alternative synthesis of **3** and **5** was recently described by Konno et al., using an intermolecular addition of the perfluoroalkyl anion derived from **19** with glyceraldehyde acetonide.[22]

Synthesis of the Enantiopure *syn*-Diols 14 (Scheme 2). Following from our earlier communication,[18] the synthesis of diols **14** was optimized on a large scale. Intermolecular atom transfer addition of the 2-bromotetrafluoroethyl radical, formed by sodium-dithionite-mediated single electron transfer, to benzyl allyl ether yielded iodide **21** in excellent yield. Regioselective elimination through reaction of the most acidic proton led to alkene **15** in quantitative yield, with virtually complete stereoselectivity. This reaction required extensive optimization to achieve this result, as product and starting material were not separable, and initial attempts at large-scale optimization invariably resulted in incomplete reaction. It was found that laboratory-grade DMF (<0.2% H_2O) gave much

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Scheme 3. Synthesis of the Pyranose Sugar Derivative 3

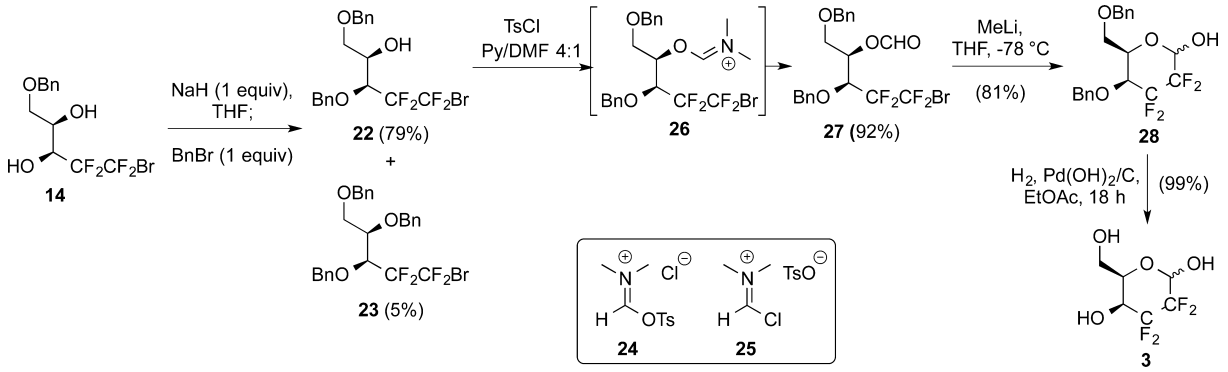
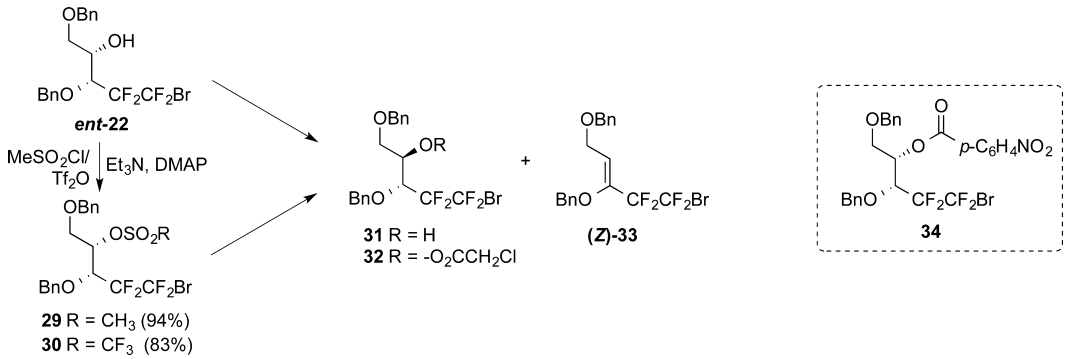


Table 1. Attempts To Effect C5 Alcohol Inversion



entry	starting material	conditions	product (yield)[a] (%)	% starting material
1	*ent*-**22**	DIAD, PPh_3, HCOOH, THF	no reaction	nd
2	*ent*-**22**	DIAD, PPh_3, $ClCH_2COH$, toluene	**32** (3%), (*Z*)-**33** (50%)	
3	*ent*-**22**	DIC, $Cu(OTf)_2$, HCOOH	no reaction	nd
4	*ent*-**22**	DIC, $Cu(OTf)_2$, PNB−OH	**34** (9%)	90
5	**29**	HCOOCs, DMF, 80 °C	(*Z*)-**33** (40%)	20
6	**29**	HCOOCs, DMAP, toluene, reflux	(*Z*)-**33** (50%)	0
7	**29**	HCOOH, CsF, DMF, 50 °C	(*Z*)-**33** (14%)	60
8	**30**	$NaNO_2$, DMF	**31** (33%), (*Z*)-**33** (22%)	0

[a]Isolated yield.

better conversions than did extra dry DMF (<0.005% H_2O). These conditions gave 99% yield of **15** on a 23 g (50 mmol) scale, with 99:1 *E*/*Z* selectivity. The low temperature was required to achieve high diastereoselectivity.

The previously established conditions for the Sharpless AD reaction with the deactivated[25] alkene **15** led to **14** in 97% ee using $(DHQD)_2AQN$ as the chiral ligand.[18] Further optimization consisted of the development of a recrystallization protocol that resulted in virtually enantiopure material (>99% ee). On a 25 g (75 mmol) scale, a 93% reaction yield and 80% recrystallization yield was obtained, which denotes an overall yield of 75%. In addition, recovery of the mother liquor provides more diol of inferior ee, which can then be recrystallized again to increase the enantiopurity. Recovery of the expensive ligand was easily achieved by a modified extraction method.[26]

Formation of the enantiomeric diol *ent*-**14** was achieved by using a catalyst having the AQN spacer and the pseudoenantiomeric DHQ ligand, which resulted in a 97% ee, which was increased to 99% by recrystallization. On a 14 g (40 mmol) scale, this transformation was achieved in an 84% yield, with an 80% yield for the recrystallization, accounting for an overall yield of 67%.

Pyranose Ring Formation: Synthesis of the Dideoxytetrafluoro "Galactopyranose" 3 (Scheme 3). The required selective benzylation is possible due to the increased acidity of the hydroxyl group proximal to the perfluoroalkyl moiety.[27] Thus, deprotonation was carried out using 1 equiv of a strong base (NaH) followed by treatment with 1 equiv of BnBr. The reaction has now been performed on a large scale (12 g, 30 mmol), giving a 79% yield. The dibenzylation product (**23**) was also isolated in 5% yield, and 16% yield of starting diol was recovered. None of the undesired "reverse" monobenzylation product has ever been observed, suggesting that the first benzylation proceeded with complete selectivity.

The next step is the formylation of the remaining hydroxyl group in **22**. Although this was previously achieved using diisopropyl carbodiimide (DIC) and formic acid in the presence of dimethylaminopyridine (DMAP), we serendipitously found that the use of a Vilsmeier−Haack-type reagent led to superior results. Activation of DMF with tosyl chloride in pyridine solvent is presumed to generate iminium salts **24** or **25** that then react with alcohol **22** to give the intermediate **26**.[28]

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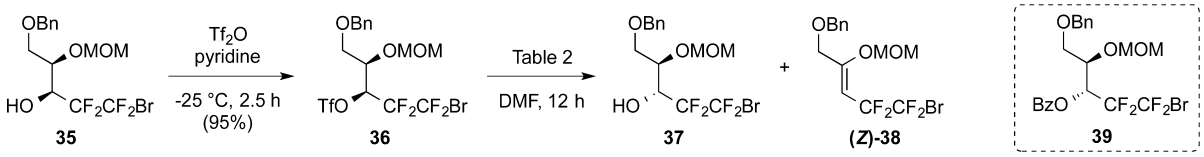
Table 2. Attempts To Effect C4 Alcohol Inversion



			products (yield)[a] (%)		
entry	reagent(s) (equiv)	temp (°C)	**37**	(*Z*)-**38**	% starting material
1	$NaNO_2$ (9.8)	25	13	0	53
2	$NaNO_2$ (9.8)	60	38	24	0
3	$NaNO_2$ (9.8), 15-c-5	60	39	29	0
4	$NaNO_2$ (9.8), Bu_4NBr	60	27	26	0
5	$NaNO_2$ (9.8)	40	52	33[a]	15
6	NaOBz (9.8)	60	15[c]	85	0
7	CCl_3CO_2Na (9.8)	60		38[a]	62
8	CF_3CO_2Na (9.8)	60	6	35[a]	60
9	CF_3CO_2Cs (3.2)[b]	60		28[a]	72

[a]Triflate **36** and alkene **38** were not separable, so in these cases, crude ratios are reported. [b]Solvent: butanone. [c]Yield of **39**.

Aqueous workup then results in hydrolysis and loss of dimethylamine to give the formate **27**, which was confirmed to proceed with retention of configuration. This reaction has been achieved in a 92% yield on a 12 g (25 mmol) scale and has been employed in favor of the DIC/HCO_2H method as it is more reliable, efficient, and uses cheaper reagents. More importantly, a simple workup consisting of extraction into hexane provided clean product suitable for the next step, with no chromatography necessary.

Finally, cyclization to give pyranose **28**, achieved in a yield of 81% on an 11 g (20 mmol) scale, and hydrogenolysis of the benzyl ethers gave the deprotected dideoxy-tetrafluorinated sugar **3** in 99% yield on a 1 g (3 mmol) scale.

Pyranose Ring Formation: Synthesis of the Dideoxy-tetrafluoro "Glucopyranose" 5. Using the strategy used for the synthesis of the dideoxy-tetrafluoro "galactose" **3**, the synthesis of the diastereomeric "glucose" **5** would require asymmetric dihydroxylation of (*Z*)-**15**. However, a highly diastereoselective synthesis of (*Z*)-**15** was expected to be cumbersome (separation with the *E*-isomer is not possible), and its asymmetric dihydroxylation would unlikely proceed with high enantioselectivity. Hence, a synthesis starting from (*E*)-**15** was envisaged that involved an inversion of configuration at one carbon center, for example, by opening of the corresponding epoxide. Unfortunately, all attempts to effect a Sharpless asymmetric epoxidation on the corresponding (*E*)-allylic alcohol failed (not shown), which led us to investigate inversion of configuration of the alcohol group at C4 in **14** or at C5 in *ent*-**14** (sugar numbering). Because S_N2 reactions next to perfluorinated carbon atoms are difficult, inversion at C5, through activation of the alcohol group in *ent*-**22** was investigated first (Table 1). Mitsunobu inversion[29,30] with formic acid gave no reaction (entry 1). With chloroacetic acid,[31] a tiny amount of inversion product **32** was isolated, in addition to the elimination product **33** (entry 2). The *Z*-configuration of **33** showed that elimination occurred at the activated alcohol stage. Isourea-mediated alcohol inversion also proceeds with inversion of stereochemistry,[32,33] but all attempts with *ent*-**22** led to recovered starting material (entry 3) or direct ester formation with retention of configuration (entry 4, leading to **34**). The relative configuration of **34** was proven by ester cleavage to give *ent*-**22** (not shown). Then, the alcohol group was activated as mesylate **29**. Reaction with cesium formate,[34,35] with[36] or without DMAP, only led to elimination (entries 5 and 6). Following a procedure by Otera using formic acid and CsF,[37] we observed only elimination product (entry 7). Finally, reacting the triflate **30** with sodium nitrite (entry 8) did give the desired inverted alcohol **31**, but it was again accompanied by elimination product as well as a range of decomposition products.

Clearly, the increased C−H acidity due to the fluorination, combined with the deactivation toward S_N2 reaction by the electronegative substitution pattern, promoted E2 elimination reaction, and this line of research was terminated. When the MOM-ether **35** became available (see below), inversion of the alcohol group next to the fluorination was investigated (Table 2). Activation as the corresponding triflate **36** was high-yielding, provided that short reaction times were employed given the lability of the MOM protecting group under the reaction conditions. Triflate **36** was noticeably more stable compared to triflate **30**, due to the electronegativity of the tetrafluoroalkylidene group.

Pleasingly, displacement with $NaNO_2$ at room temperature (entry 1) gave the inversion product, even if in low yield. However, no elimination product was observed, and starting material was recovered. Raising the temperature (entry 2) increased the yield of **37** but unfortunately also gave rise to the elimination side reaction. Again, the alkene configuration indicated that the elimination process took place from the starting material. The addition of a crown ether[38] (entry 3) or attempting to generate Bu_4NNO_2 (entry 4), which was reported as an effective nucleophile for triflate displacement,[39] did not lead to improved results. Lowering the temperature to an intermediate 40 °C did lead to a reasonable 52% yield (entry 5) but still with a substantial amount of elimination byproduct. Carboxylate-based nucleophiles were not successful. With benzoate,[40] a low yield of **39** was obtained, but the major product was the elimination byproduct (entry 6). With trichloro- and trifluoroacetates (entries 7−9), mainly elimination was observed for incomplete conversions, even with cesium trifluoroacetate.[41]

Hence, it was decided to return to the previously developed cyclic sulfate route (Scheme 4), in which the regioselectivity is due to the fluorination hampering S_N2 reactions in adjacent

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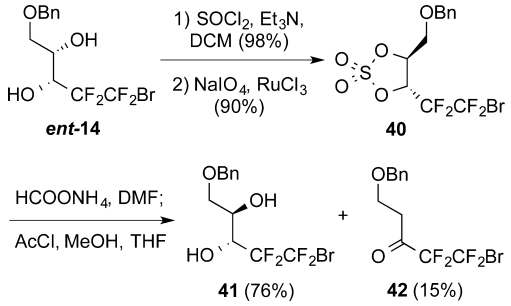
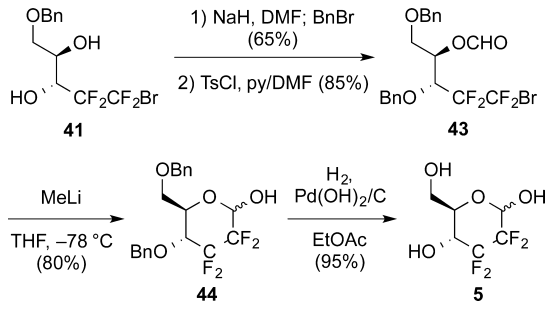
Scheme 4. Formation of the *anti*-Diol



positions.[18] The cyclic sulfate formation was further optimized to give excellent overall yield on a large scale (10 mmol), mainly achieved by modifying the workup procedure. The direct cyclic sulfate formation using SO_2Cl_2 was also investigated but only gave a 68% yield. As reported, the direct formation of the formate ester was shown to be low-yielding, due to its lability under the conditions of the required subsequent hydrolysis of the sulfate group. Hence, the reaction was optimized toward complete formate hydrolysis to obtain the *anti*-diol. After extensive efforts, it was found that non-aqueous conditions involving HCl generated in situ (AcCl, MeOH) were superior to the use of aqueous sulfuric acid. The use of 3 equiv of in situ generated HCl gave the desired *anti*-diol **41** in an acceptable yield on an 8 mmol scale. Interestingly, on this scale, ketone **42** was isolated as a byproduct, which presumably is formed via competitive elimination of the formate group followed by equilibration to the keto-tautomer.

Finally, with the *anti*-diol **41** in hand, completion of the synthesis of **5** was achieved in a manner similar to that shown for **3** (Scheme 5), via selective diol benzylation, which, given its

Scheme 5. Synthesis of the Pyranose Sugar Derivative 5

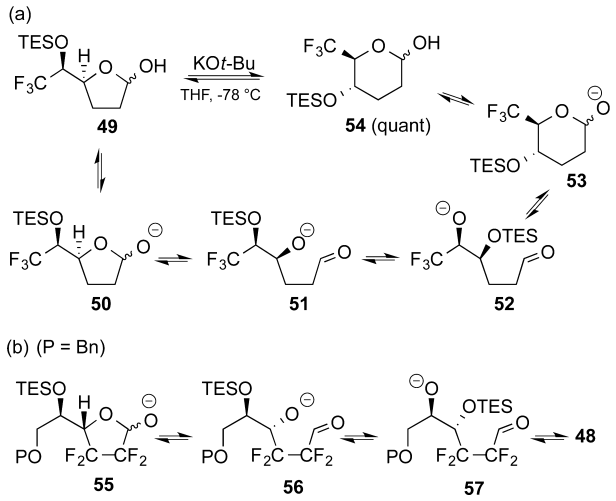


anti-stereochemistry, was lower-yielding than for the *syn*-diol as reported in Scheme 3, formate introduction, and anionic cyclization.

Furanose Ring Formation: Synthesis of (Protected) Dideoxy-tetrafluoro "Galactofuranose". The synthesis of tetrafluorinated furanose **47** has been communicated as part of the synthesis of the UGM inhibitor **2**.[16] Briefly (Scheme 6), starting from **14**, selective silylation of the more nucleophilic alcohol[42,43] yielded the desired silyl ether **45** in good yield and selectivity (6% of the regioisomer and 10% of bis-silylated derivative, not shown). Formylation of **45** with TsCl/DMF never reached completion, no doubt due to the reduced nucleophilicity of the hydroxyl group in close proximity to the perfluoroalkyl group, but could be accomplished with the conventional formic acid/DIC method. Finally, MeLi-induced anionic cyclization led to the protected dideoxy-tetrafluoro furanose derivative **47**. However, a significant amount of the isomerized pyranose **48** was also isolated.

As shown in Scheme 7a, Kitazume had described a similar isomerization process in which deprotonation of the furanose

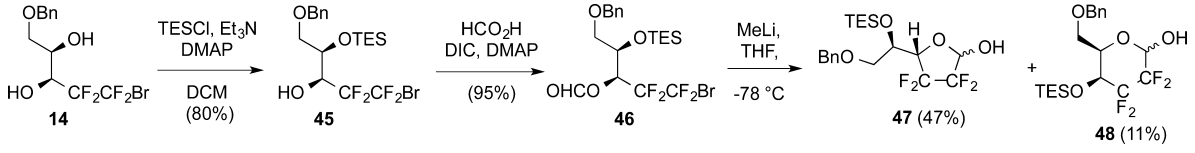
Scheme 7. Mechanism of the Silyl Migration



49 led to ring opening and silyl transfer, followed by cyclization to give the pyranose **54** in quantitative yield.[42,43] The direction of the equilibrium was explained by the thermodynamic driving force toward formation of the more stable pyranose form, with the equilibrium easily established due to an energetically favorable silyl migration (pK_a difference of the alcohols). Hence, formation of **48** (Scheme 7b) is similarly explained starting from anion **55**, which is obtained from the cyclization step. While the isomerization of **49** to give **54** was reported to be complete in 3 h at −78 °C, it is interesting to observe that the anionic cyclization step starting from **46** as described above (Scheme 6), which took 4.5 h at temperatures up to −60 °C, only led to the formation of **48** in 11% yield. This suggests a much slower isomerization process, due to the higher stability of anion **56** compared to that of anion **57**.

Indeed, in a separate experiment in which **47** was subjected to the Kitazume isomerization conditions (Scheme 8a), only minimal reaction to **48** was observed (TLC) at −78 °C, and quantitative conversion only occurred after warming the reaction mixture to room temperature overnight. This clearly confirms that the tetrafluorinated pyranose form is the more stable ring and, as expected, that the silyl migration from **56** to

Scheme 6. First-Generation Synthesis of the Tetrafluorinated Furanose with Rearranged Pyranose as a Side Product



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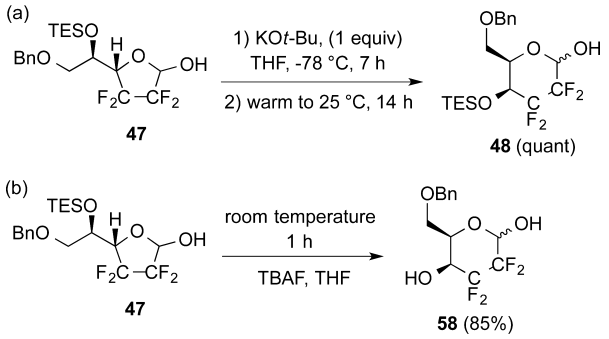
Scheme 8. Isomerization Experiments from Furanose 47



57 is an energetically unfavorable process with a low reaction rate at low temperature. Unfortunately, attempts to prevent the formation of **48** in the anionic cyclization reaction starting from **46** by decreasing the reaction temperature, or by shorter reaction times, only resulted in incomplete reaction.

The much larger stability of the tetrafluorinated pyranose was further confirmed by rapid isomerization upon silyl cleavage (Scheme 8b). Hence, to avoid the isomerization, a different protecting group was used (Scheme 9). Reaction of diol **14** with MOMCl led to the desired monoprotected **35** in 70% yield (contaminated with an additional 5% of **60**, which was separated after the next step). With **35** in hand, formylation of the remaining alcohol group and anionic cyclization gave the desired furanose **8** without any isomerization.

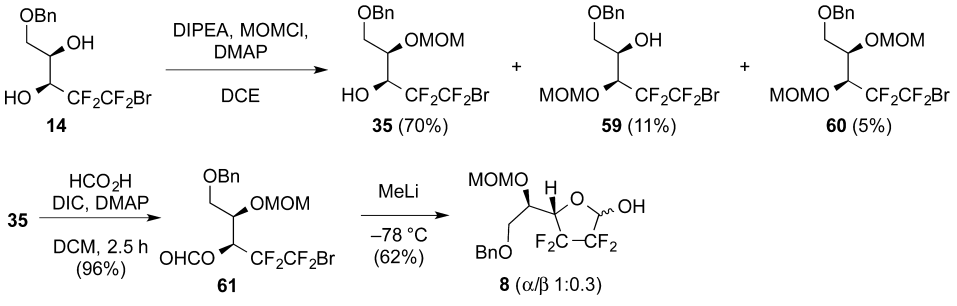
Pyranose Ring Formation: Synthesis of 6 and 7. Given the success of the anionic cyclization reaction, this strategy was initially investigated for the synthesis of the 3,3,4,4-tetrafluorinated sugar derivatives **6** and **7** (Scheme 10), which here required the formation of the C2−C3 bond. Hence, starting from the (racemic) alcohol derivative **62**, obtained in two steps as described previously,[26] functionalization with α-bromoacetate esters to obtain suitable cyclization precursors was required. Initially, alkylation with methyl bromoacetate **63** was carried out to investigate the cyclization on a simplified precursor **65**. Pleasingly, using the standard conditions, the 1-deoxysugar derivative **67** was obtained in very good yield and was isolated mainly as the hydrate, as shown. The structure of the hydrate was proven by X-ray crystallographic analysis (Figure 1). Unfortunately, subsequent functionalization of the anomeric position of **67** using radical bromination was unsuccessful (not shown).

Hence, the synthesis of precursor **66**, already containing an anomeric substituent, was envisioned. This was achieved in high yield by reaction of **62** with known bromoether **64**,[44] which was obtained by radical bromination of methyl methoxyacetate (not shown). Also, on this substrate, anionic cyclization proceeded in excellent yield, leading to an inseparable mixture of anomers. Subsequent reduction of the C2 keto group led to a mixture of four diastereomers, with the existing anomeric configuration directing the hydride attack.[45,46] Hence, the *cis*-1,2-disubstituted diastereomers ***β*-70** and ***α*-71** were obtained as major products, each as a 10:1 mixture with the other C2 epimer. Unfortunately, despite extensive efforts, a high-yielding and complete separation of these compounds was never achieved. In addition, anomeric deprotection proved to be difficult. Hence, a different approach involving intermolecular addition with **13** (cf. Scheme 1) leading directly to hemiacetal structures was investigated (Scheme 11).

In contrast to Konno's strategy,[22] which involved lithiation of **19** and reaction with a chiral aldehyde, the synthesis of **6**/**7** called for the use of a chiral lithiated fluorinated building block and an achiral aldehyde. Hence, **19** was converted to enantiopure monoprotected diol **72** on a large scale as described by us previously.[26] Analysis via the corresponding Mosher ester derivative confirmed its enantiopurity (>99% ee; see Supporting Information). Protection of the remaining alcohol was initially achieved by benzylation or *p*-methoxybenzylation, and while the generation of the corresponding lithiated species and intermolecular addition to cinnamaldehyde proved high-yielding (80%, not shown), it was decided, in the interest of atom economy, to protect the secondary alcohol as naphthylmethylidene acetal **73** (Scheme 11). Hence, DDQ-mediated oxidation of **72** under anhydrous conditions[47] led to **73** as a crystalline 1:1 mixture of diastereomers, which could be easily separated by column chromatography. Assignment of relative stereochemistry was achieved by X-ray crystallographic analysis of both isomers (see Supporting Information).

Starting from each acetal diastereomer, bromine−lithium exchange followed by reaction with cinnamaldehyde proceeds in excellent yields (80%), but in each case, an inseparable 1:1 mixture of alcohol diastereomers was obtained (not shown). Hence, on a large scale (7 g), the acetal diastereomers were not separated before lithiation and cinnamaldehyde addition, leading to **74** as a mixture of four diastereomers. These were not separated and directly subjected to acetal deprotection, leading to an inseparable mixture of *syn* and *anti* isomers **75** in 71% overall yield. An added advantage of this two-step procedure is that the small amount of MeLi/cinnamaldehyde addition product formed in the first step, which is inseparable from the addition products **74**, is easily removed after acetal cleavage. In addition, the ozonolysis step is not compatible with the naphthyl acetal protecting group. Finally, ozonolysis provided a mixture of sugar derivatives **6** and **7** in 97% yield

Scheme 9. Optimized Second-Generation Synthesis of the Furanose Derivative



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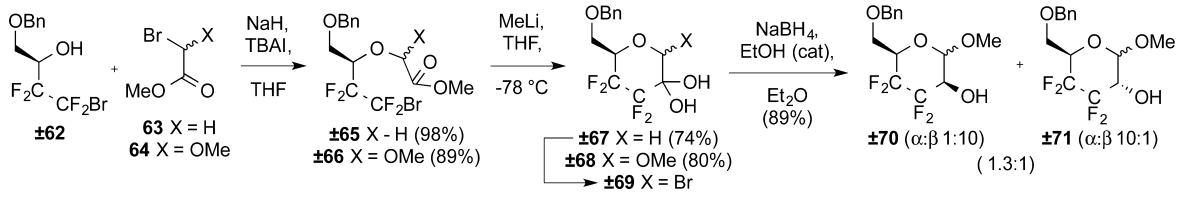
Scheme 10. Anionic Cyclization Strategy toward the Synthesis of 6 and 7



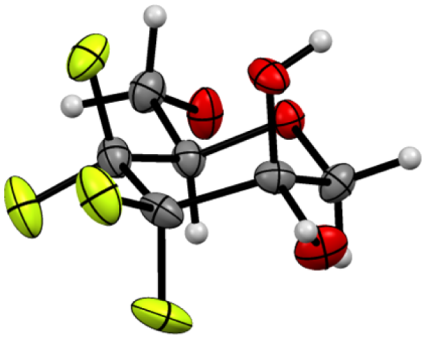
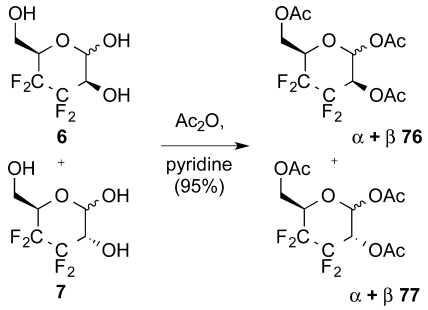


Figure 1. Crystal structure of **67**. Thermal probability ellipsoids are shown at the 50% probability level. The 6-*O*-Bn group is omitted for clarity.

Scheme 12. Acetylation of the Mixture To Attempt Separation



(89% on multigram scale) after removal of the benzaldehyde and DMSO byproducts by column chromatography. Unfortunately, separation of these sugar derivatives was not possible. Derivatization as the peracetates **76** and **77** proceeded in excellent yield (Scheme 12) but did not allow for a practical diastereomeric separation.

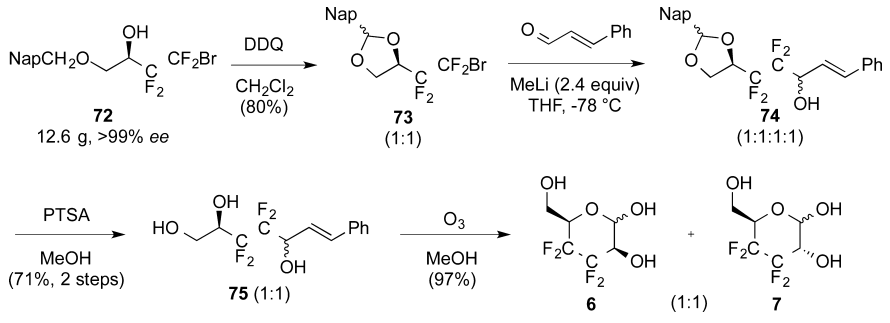
Interestingly, ***β*-77** could be obtained as pure crystals and analyzed by X-ray diffraction (see below). Analogous perbenzoylation was also achieved but proved equally ineffective in separating the C2-diastereomers (not shown).

During the extensive derivatization/separation efforts, it was noticed that very often the two diastereomers having the same anomeric configuration but different C2-stereochemistry were separable. Hence, a protection strategy aiming at selective glycoside formation was pursued. It was found that after 6-OH protection as silyl ether (Scheme 13), anomeric naphthylmethylation proceeded with excellent yield and *β*-selectivity.[18,48,49] Only low amounts (<3%) of *α*-anomers could be observed by ^{19}F NMR. Interestingly, 6.5% of presumably 2-naphthylmethylated "tetrafluoromannose" byproduct was formed during the reaction, whereas no regioisomer could be observed for the "gluco" analogue. TBDMS cleavage then gave the free naphthylmethyl glycosides **82** and **83**, which were separable by column chromatography. Finally, the individual sugar analogues **6** and **7** could be obtained after hydrogenolysis using Pearlman's catalyst.

Conformational Analysis. The conformation of carbohydrates is an important element in considering protein–carbohydrate interactions, and hence, conformational analysis of modified carbohydrates is of interest.[50,51] Solution-phase NMR studies (2D ^{1}H–^{19}F HOESY) of the spectra of both *α*- and *β*-methyl glycosides of **3** in $CDCl_3$ and D_2O have been reported previously and were consistent with a $^{4}C_1$ chair conformation.[19] These studies have been extended with the novel sugar derivatives described herein, and given the extensive spectral overlap of the free hemiacetals prevented clear analysis by 1D and 2D ^{1}H–^{19}F HOESY NMR, they were conducted with the corresponding methyl glycosides. The syntheses of the methyl glycosides are shown in Scheme 14. Anomeric alkylation of **44** with methyl iodide followed by benzyl hydrogenolysis led to the methyl glycoside derivatives ***α*-85** and ***β*-85**. For the 2-OH sugar derivatives, the mixture of **70** and **71**, obtained as described above, was subjected to hydrogenolysis, leading to ***β*-86**, which was obtained in pure form, and ***α*-87**, which could not be separated from small amounts of its *β*-anomer.

Clearly, the ^{1}H–^{1}H NOESY and ^{1}H–^{19}F HOESY analysis shown in Figure 2 shows that all methyl pyranoside structures adopt a $^{4}C_1$ conformation, both in deuterated chloroform and

Scheme 11. Intermolecular Addition Strategy for the Synthesis of 6 and 7



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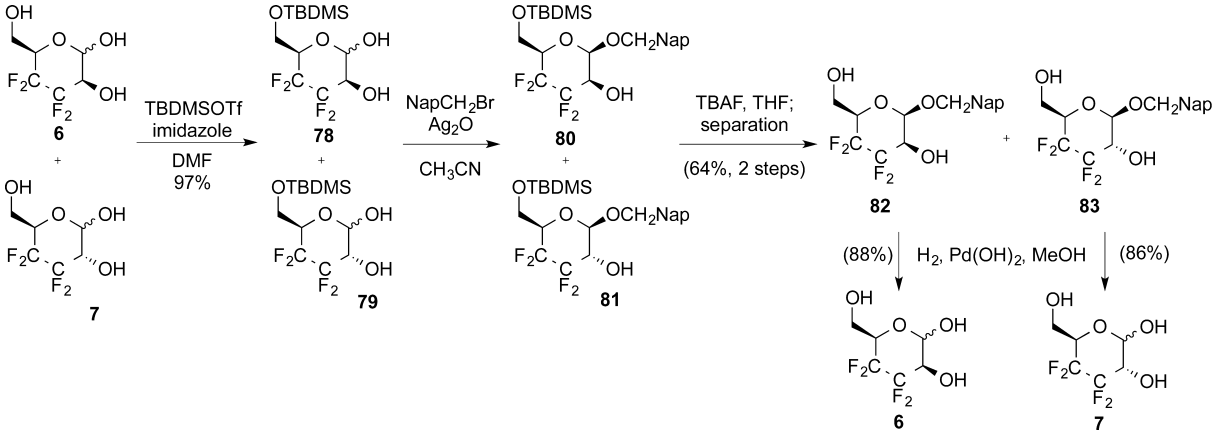
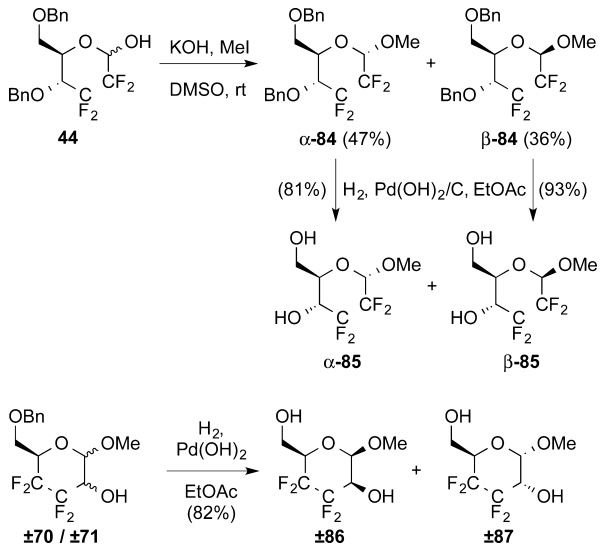
Scheme 13. Separation of 6 and 7



Scheme 14. Synthesis of the Methyl Glycosides



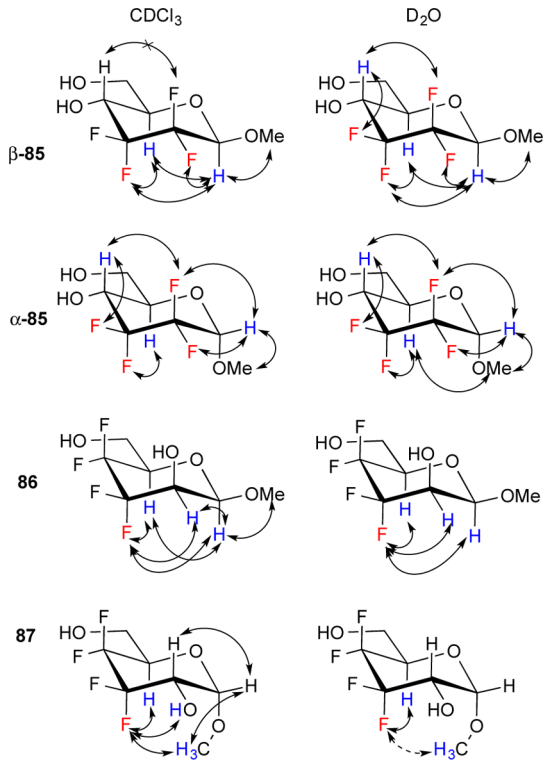
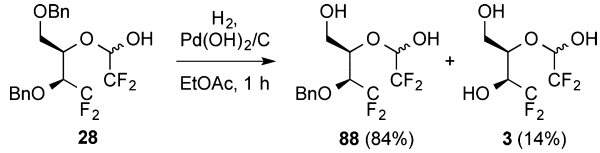


Figure 2. $^{1}H-^{1}H$ NOESY and $^{1}H-^{19}F$ HOESY analysis of **85**–**87**.

Scheme 15. Incomplete Hydrogenolysis Leading to 88



in water. This confirms the minimal influence of dideoxy-tetrafluorination on the monosaccharide chair conformation.

Crystal structure analysis of heavily fluorinated carbohydrate derivatives has also shown that the $^{4}C_{1}$ chair conformation is retained, with generally minimal distortion. Examples include the 1,6-dibenzoate ester of a hexafluorinated pyranose described by DiMagno,[11,12] as well as structures from our group such as **28**,[20] the α- and β-methyl glycosides of **3**,[19] and the UDP derivative **1**.[17] In addition to the structure of **67**, shown in Figure 1, the structures of the other crystalline sugar derivatives described above (***α*-58**, and ***β*-77**), as well as that of ***β*-88**, which was isolated after an incomplete hydrogenolysis of **28** (Scheme 15), were obtained and are shown in Figure 3. These crystal structures also show a relatively undistorted $^{4}C_{1}$ chair conformation. The crystal packing of all structures (see Supporting Information) shows that hydrogen bonding of the alcohol groups with oxygen-containing groups is maximized, an effect which presumably determines the anomeric configuration of the hemiacetals:[20] the benzyl ether **58** crystallizes as the α-anomer, while **88** and **77** are obtained as the β-anomer.

Pleasingly, both unprotected 3,3,4,4-tetrafluorinated sugar derivatives **6** and **7** proved to be crystalline (Figure 4), and crystallization was achieved from hexane/acetone. These are the first crystal structures of fully deprotected tetrafluorinated pyranoses. Both compounds crystallized as the β-anomer, with the hydroxymethyl group as the *gt*-rotamer. For **6**, the axial C2 hydroxyl group and C4 fluorine atom are somewhat splayed (13.7°). Their corresponding methyl glycosides were also crystallized and showed very similar conformations.

Where hydrogen bonding opportunities are present (O–H···O and less often O–H···F), these interactions dominate the packing arrangements (see Supporting Information for figures). In **6**, the high number of donors and the compact nature of the

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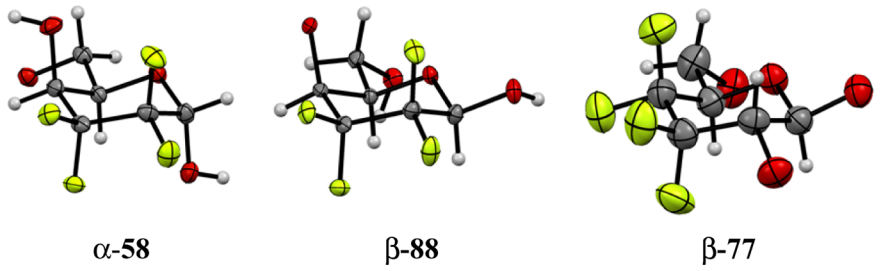

Figure 3. Crystal structures of tetrafluorinated sugar derivatives. Thermal probability ellipsoids are shown at the 50% probability level. The benzyl groups present in ***α*-58** (6-position) and ***β*-88** (4-position), as well as all three acetate groups in ***β*-77**, were removed for clarity. See Supporting Information for the complete crystal structures.

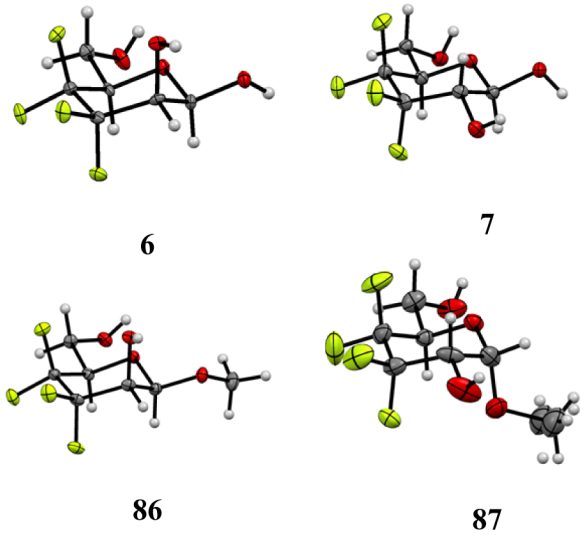

Figure 4. Crystal structures of **6** and **7** and methyl glycosides **86** and **87**. Thermal probability ellipsoids are shown at the 50% probability level. There is disorder at the **87** methyl group.

molecule allow for 3D network formation; however, the change of the 2-OH configuration is enough to disrupt this network such that **7** now forms 2D sheets in the *bc* plane. The arrangement in the third direction is now directed by weaker interactions with hydrophobic F surfaces stacking along the *a* axis, forming alternating hydrophilic and hydrophobic layers. Similar molecules **58** and **67** also form sheets (*bc* plane) with a layer structure characterized by interdigitating benzyl groups at the sheet interfaces. Compounds **82**, **86**, and **87** have supramolecular structures dominated by hydrogen-bonded ladder chains aligned in a manner that colocates the benzyl groups of adjacent chains, forming hydrophobic columns. This colocation of certain groups gives rise to a related colocation of the CF_2 groups. In **82**, hydrogen-bonded ladder chains are still dominant, but the larger nature of the naphthalene rings now gives rise to a more pronounced layer structure with pseudoparallel naphthalenes. Compounds *cis*-**73** and *trans*-**73** have structures dominated by interdigitation of the naphthalene rings forming hydrophobic layers. Interestingly, the change between *cis*/*trans* is enough to significantly change the level of interdigitation and switch the arrangement from herringbone to pseudoparallel. Compound ***β*-77** has neither hydrogen bonding opportunities nor peripheral aromatic rings, and its packing is thus directed by van der Waals interactions.

CONCLUSIONS

It has been shown that the intramolecular tetrafluoroalkylidene lithium addition to ester groups is a suitable method for the synthesis of tetrafluorinated monosaccharides, even on a large scale. The formation of both the C1−C2 (tetrafluorination at C2/C3) as well as the C2−C3 (tetrafluorination at C3/C4) bonds (sugar numbering) is possible. Controlling the protection group pattern allows selective formation of the furanose or the pyranose form. In addition, following the work of Konno for the synthesis of 2,2,3,3-tetrafluorinated pyranose derivatives, an intermolecular strategy is also demonstrated here for the synthesis of pyranose derivatives with tetrafluorination at C3/C4. For all sugar derivatives investigated, NMR and X-ray crystallographic analyses show that they exist in the $^4C_1$ conformation, with only minimal distortion from the ideal chair conformation. The monosaccharides synthesized will be of interest for the synthesis of carbohydrate mimetics for possible use as inhibitors or probes for carbohydrate-processing enzymes.

EXPERIMENTAL SECTION

All air/moisture-sensitive reactions were carried out under an inert atmosphere (Ar) in oven-dried glassware. Solvents distilled prior to use: CH_2Cl_2 (from CaH_2), THF (from Na and benzophenone), and MeCN (from CaH_2). Where appropriate, other reagents and solvents were purified by standard techniques. TLC was performed on aluminum-precoated plates coated with silica gel 60 with an F254 indicator; they were visualized under UV light (254 nm) and/or by staining with $KMnO_4$ (10% aq). Flash column chromatography was performed with silica gel (40−63 nm). Chemical shifts are reported in δ units using $CHCl_3$ as an internal standard. Fourier transform infrared spectra were measured using an ATR accessory using neat samples (solids and liquids). Electrospray mass spectra were run in HPLC methanol or MeCN. HRMS samples were run on an ESI-TOF MS or an ESI FT-ICR MS spectrometer. Optical rotations were measured at 589 nm, and all reducing carbohydrate derivatives were equilibrated in the used solvent for 3 days prior to measurement.

5-Benzyloxy-1-bromo-1,1,2,2-tetrafluoro-3-iodopentane (21). A solution of **20** (29.5 g, 199 mmol) in MeCN/H_2O (1:1, 200 mL) was sonicated for 15 min under N_2 and then cooled to 0 °C. Neat **16** (67.8 g, 221 mmol) was then added. The mixture was treated with $NaHCO_3$ (8.36 g, 99.5 mmol) and $Na_2S_2O_4$ (17.3 g, 99.5 mmol) and stirred at 4−6 °C for 21 h. H_2O (140 mL) was added, and the mixture was extracted into Et_2O (3 × 240 mL). The combined organic extracts were washed with brine (2 × 400 mL), dried ($MgSO_4$), filtered, and concentrated to give iodide **21** as an orange oil (86.3 g, 95%); NMR data matched those previously reported.[18]

***(E)*-5-Benzyloxy-1-bromo-1,1,2,2-tetrafluoropent-3-ene (15).** Iodide **21** (23.2 g, 50.9 mmol) was dissolved in laboratory reagent-grade DMF (83 mL) and cooled to −50 °C. DBU (23.6 mL, 158 mmol) was added slowly. Stirring was continued at −50 to −55 °C for 3 h. Aqueous HCl (1 M, 170 mL) was then added and the resultant

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mixture extracted quickly into Et_2O (4 × 230 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated to give an orange oil. Column chromatography (petroleum ether/Et_2O 96:4) gave alkene **15** as a cloudy oil (16.41 g, 99%, *E*/*Z* 99:1); NMR data matched those previously reported.[18]

(3*S*,4*R*)-5-Benzyloxy-1-bromo-1,1,2,2-tetrafluoropentan-3,4-diol (14). To a stirred solution of *t*-BuOH/H_2O (1:1, 700 mL) were added $(DHQD)_2AQN$ (1.33 g, 1.52 mmol), $K_3Fe(CN)_6$ (75.2 g, 229 mmol), K_2CO_3 (31.6 g, 229 mmol), and $K_2OsO_2(OH)_4$ (224 mg, 609 μmol). H_2O (30 mL) was added, which dissolved most of the solids. $MeSO_2NH_2$ (7.24 g, 76.2 mmol) was then added, and the mixture was cooled to 0 °C. Alkene **15** (24.91 g, 76.2 mmol) was then added. The resultant mixture was stirred at 4−6 °C for 8 days. Na_2SO_3 (100 g) was added, and the mixture stirred for 2 h at 0 °C to rt before being treated with H_2O (175 mL). Extraction was carried out in EtOAc (3 × 350 mL). The combined organic phases were washed with HCl (2 M, 2 × 75 mL) then brine (75 mL), before being dried ($MgSO_4$), filtered, and concentrated to give a yellow solid (96.8% ee). Column chromatography (petroleum ether/EtOAc 65:35) gave diol **14** as a white solid (25.61 g, 93%). This white solid was suspended in hexane and gently heated to 40 °C, then Et_2O was added until dissolution occurred. The solution was allowed to stand for 4 days at rt, and the resultant crystals were filtered and washed with hexane to give a white solid (20.54 g, 75%, > 99.9% ee): mp 96−97 °C; $[\alpha]_D$ −1.7 (*c* 0.54, $CHCl_3$, 23 °C); NMR data matched those previously reported.[18]

The acidic extracts from the workup were combined and neutralized with NaOH (2 M, aq) and then extracted into EtOAc (2 × 270 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated to give impure $(DHQD)_2AQN$ as a red solid. Column chromatography (DCM/MeOH 85:15) gave recovered $(DHQD)_2AQN$ (1.29 g, 92%) as a yellow/orange solid.

(3*R*,4*S*)-5-Benzyloxy-1-bromo-1,1,2,2-tetrafluoropentan-3,4-diol (*ent*-14). To a stirred solution of *t*-BuOH/H_2O (1:1, 400 mL) were added $(DHQ)_2AQN$ (655 mg, 0.84 mmol), $K_3Fe(CN)_6$ (41.6 g, 126 mmol), K_2CO_3 (17.4 g, 126 mmol), and $K_2OsO_2(OH)_4$ (124 mg, 337 μmol). H_2O (15 mL) was added, which dissolved most of the solids. $MeSO_2NH_2$ (4.00 g, 42.1 mmol) was added and the reaction mixture cooled to 0 °C. Alkene **14** (13.8 g, 42.1 mmol) was added. The resultant mixture was stirred at 4−6 °C for 9 days. Na_2SO_3 (60 g) was added, and the reaction mixture was stirred for 2 h at 5 °C to rt. H_2O (40 mL) was then added and extraction carried out into Et_2O (3 × 210 mL). The combined organic phases were washed with aq HCl (2 M, 2 × 40 mL) and then brine (40 mL), before being dried ($MgSO_4$), filtered, and concentrated to give a yellow solid. Column chromatography (petroleum ether/EtOAc 70:30) gave diol *ent*-**14** as a white solid (3.57 g, 84%, 97.1% ee). This was suspended in hexane and heated to 40 °C, and then Et_2O was added until dissolution occurred. The solution was allowed to stand for 7 days, and the resultant crystals were filtered and washed with a small amount of hexane to give a white solid (7.73 g, 51%, 99.2% ee): mp 84−86 °C (hexane/Et_2O); $[\alpha]_D$ +1.7 (*c* 0.5, $CHCl_3$, 25 °C); NMR data matched those previously reported.[18]

The acidic extracts from the workup were combined and neutralized with aq NaOH (2M) and then extracted into EtOAc (2 × 150 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give impure $(DHQ)_2AQN$ as an orange solid.

(3*S*,4*R*)-3,5-Dibenzyloxy-1-bromo-1,1,2,2-tetrafluoropentan-4-ol (22). Diol **14** (11.7 g, 32.4 mmol) was dissolved in THF (200 mL) and cooled to 0 °C. NaH (60% in mineral oil, 1.30 g, 32.4 mmol) was added followed by stirring at 0 °C for 1 h. BnBr (3.85 mL, 32.4 mmol) was added and the resultant solution stirred at 0 °C to rt for 22 h. Aqueous NH_4Cl (saturated, 180 mL) was added and the resultant mixture stirred at rt for 30 min, before extraction was carried out in EtOAc (4 × 250 mL). The combined organic phases were washed with brine (2 × 800 mL), dried ($MgSO_4$), filtered, and concentrated to give a pale yellow oil. Column chromatography (petroleum ether/EtOAc 95:5) gave alcohol **22** as a colorless oil (11.5 g, 79%) and tribenzyl ether **23** as a colorless oil (970 mg, 5%). Data for **22**: $[\alpha]_D$ −30.8 (*c* 0.5, $CHCl_3$, 25 °C); NMR data matched those previously reported.[18] Data for (3*S*,4*R*)-3,4,5-tribenzyloxy-1-bromo-1,1,2,2-tetrafluoropentane (**23**): $[\alpha]_D$ −4.2 (*c* 0.5, $CHCl_3$, 24 °C); NMR data matched those previously reported.[18]

(3*S*,4*R*)-3,5-Dibenzyloxy-1-bromo-4-formyloxy-1,1,2,2-tetrafluoropentane (27). TsCl (6.94 g, 36.4 mmol) was dissolved in pyridine (66 mL) and cooled to 0 °C. DMF (22 mL) was added and the resultant solution stirred at rt for 20 min. The solution was then cooled to 0 °C, and a solution of alcohol **22** (11.7 g, 26.0 mmol) in pyridine (22 mL) was added dropwise. The resultant solution was stirred at rt for 1.5 h before being cooled to 0 °C. H_2O (120 mL) was added and extraction carried out into hexane (3 × 120 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give formate **27** as a pale yellow oil (11.4 g, 92%): $[\alpha]_D$ −26.2 (*c* 0.4, $CHCl_3$, 23 °C); NMR data matched those previously reported.[18]

4,6-Di-*O*-benzyl-2,3-dideoxy-2,2,3,3-tetrafluoro-*threo*-hexopyranose (28). Formate **27** (10.7 g, 22.3 mmol) was dissolved in dry DCM (120 mL) and filtered through a pad of $MgSO_4$ directly into the reaction flask, while concentrating the filtrate with a stream of N_2. The resultant oil was dried under high vacuum for 16 h before being dissolved in THF (210 mL) and cooled to −78 °C. MeLi (1.6 M in Et_2O, 13.3 mL, 21.2 mmol) was added very slowly dropwise. The resultant solution was stirred at −78 °C for 4.5 h. At this temperature, aq NH_4Cl (saturated, 75 mL) was added to the reaction mixture, which was then stirred for 30 min, while being allowed to warm to rt. The mixture was diluted with H_2O (150 mL) and then extracted into EtOAc (3 × 520 mL), dried ($MgSO_4$), filtered, and concentrated to give a white solid. Column chromatography (petroleum ether/acetone 90:10 then 75:25) gave **28** as a white solid (7.20 g, 81%): mp 98−103 °C ($CHCl_3$); $[\alpha]_D$ +4.60 (*c* 0.511, acetone, 22 °C); NMR data matched those previously reported.[18]

2,3-Dideoxy-2,2,3,3-tetrafluoro-*threo*-hexopyranose (3). Pyranose **28** (1.2 g, 3.0 mmol) was dissolved in EtOAc (24 mL). $Pd(OH)_2/C$ (20 wt %, 958 mg, 1.8 mmol) was added and the resultant mixture flushed with H_2. Stirring under H_2 atmosphere (balloon) at rt was continued for 18 h before the reaction mixture was filtered through Celite, which was washed with plenty of EtOAc. The solvent was concentrated to give **3** as a white foam (654 mg, 99%): $[\alpha]_D$ +36.7 (*c* 0.533, acetone, 22 °C); NMR data matched those previously reported.[18]

(2*S*,3*R*)-2-(1,3-Dibenzyloxy-5-bromo-4,4,5,5-tetrafluoro)-pentyl Methanesulfonate (29). To a stirred solution of *ent*-**22** (372 mg, 0.82 mmol, 1 equiv) in CH_2Cl_2 (4.1 mL) were added NEt_3 (0.29 mL, 2.1 mmol) and DMAP (10 mg, 0.082 mmol, 0.1 equiv). MsCl (0.083 mL, 1.07 mmol) was added dropwise at 0 °C. The reaction was stirred at 0 °C to rt for 2.5 h and then filtered. The filtrate was washed with H_2O (4 mL) and brine (2 × 4 mL), and the organic phase was dried (Na_2SO_4). Column chromatography (petroleum ether/EtOAc 70/30) gave the product **29** as transparent gel (409 mg, 94%): R_f 0.38 (petroleum ether/EtOAc 80/20); $[\alpha]_D$ +8.18 (*c* 0.55, $CHCl_3$, 29.5 °C); IR (neat) 2878 (w), 1455 (m), 1359 (s), 1175 (s), 1079 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31−7.57 (10H, m, H_{Ar}), 5.19 (1H, app td, *J* = 5.6, 3.8 Hz, C<u>H</u>CH_2), 4.84 (1H, d, *J* = 11.0 Hz, C<u>H</u>HPh), 4.76 (1H, d, *J* = 10.9 Hz, CH<u>H</u>Ph), 4.51−4.68 (3H, m, C<u>H</u>HPh, CH<u>H</u>Ph, C<u>H</u>CF_2), 3.83−4.02 (2H, m, C<u>H</u>HOBn, CH<u>H</u>OBn), 3.00 (3H, s, C<u>H</u>$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.8 (C_{Ar}), 135.7 (C_{Ar}), 128.3 (CH_{Ar} × 2), 128.24 (CH_{Ar} × 2), 128.15 (CH_{Ar}), 128.0 (CH_{Ar} × 2), 127.8 (CH_{Ar}), 127.6 (CH_{Ar} × 2), 76.2−76.9 (<u>C</u>HCH_2), 76.0 (<u>C</u>H_2Ph), 75.3 (1 C, s), 73.7 (1 C, dd, *J* = 28, 20 Hz, <u>C</u>HCF_2), 73.2 (<u>C</u>H_2Ph), 67.5 (<u>C</u>H_2OBn) 38.1 (<u>C</u>H_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −63.23 (s, C<u>F</u>$_2$Br), −111.02 (d, *J* = 275.1 Hz, C<u>F</u>FCH), −120.21 (dd, *J* = 270.8, 17.2 Hz, CF<u>F</u>CH); ES^+MS *m*/*z* 551 and 553 $[M + Na]^+$; HRMS (ES+) for $C_{20}H_{21}{}^{79}Br_1F_4O_5S_1Na_1$ $[M + Na]^+$ calcd 551.0121, found 551.0130.

(2*S*,3*R*)-2-(1,3-Dibenzyloxy-5-bromo-4,4,5,5-tetrafluoro)-pentyl Trifluoromethanesulfonate (30). Alcohol **22** (480 mg, 1.06 mmol, not enantiopure) was dissolved in DCM (1.7 mL) and treated with pyridine (172 μL, 2.12 mmol). The reaction was cooled to 0 °C, and Tf_2O (357 μL, 2.12 mmol) was added dropwise while stirring vigorously. The mixture was stirred for 2 h at 0 °C then at rt for 14.5 h. The reaction was diluted with DCM (9 mL) and the solid pyridinium

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triflate filtered off. The resultant solution was washed with cold (~0 °C) water (3 × 8 mL), dried ($MgSO_4$), filtered, and concentrated to give a brown liquid. Chromatographic purification (petroleum ether/Et_2O 90:10) gave **30** as a colorless oil (512 mg, 83%): R_f 0.20 (petroleum ether/EtOAc 70:30); IR (neat) 3034 (w), 2928 (br, w), 2881 (w), 2362 (w), 1416 (m), 1212 (s), 1144 (s), 925 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28−7.43 (10H, m, H_{Ar}), 5.20 (1H, dd, J = 10.0, 4.5 Hz, C$\underline{H}$CH$_2$), 4.75 (1H, d, J = 11.0 Hz, C$\underline{H}$HPh), 4.69 (1H, d, J = 11.0 Hz, CH$\underline{H}$Ph), 4.58 (1 H, d, J = 11.5 Hz, C$\underline{H}$HPh), 4.53 (2H, d, J = 12.0 Hz, CH$\underline{H}$Ph), 4.51 (1H, dt, J = 17.6, 4.5 Hz, C$\underline{H}$CF$_2$), 3.83 (1H, dd, J = 11.0, 4.5 Hz, C$\underline{H}$HOBn), 3.77 (1H, dd, J = 11.5, 6.0 Hz, CH$\underline{H}$OBn); ^{13}C NMR (101 MHz, $CDCl_3$) δ 129.0 (C$\underline{H}_{Ar}$ × 3), 129.0 (C$\underline{H}_{Ar}$ × 2), 129.0 (C$\underline{H}_{Ar}$ × 2), 128.8 (C$\underline{H}_{Ar}$ × 2), 128.7 (C$\underline{H}_{Ar}$), 128.3 (C$\underline{H}_{Ar}$ × 2), 83.2 (C$\underline{H}$CH$_2$), 76.3 (C$\underline{H}_2$Ph), 74.1 (C$\underline{H}_2$Ph), 67.4 (C$\underline{H}_2$OBn); ^{19}F NMR (282 MHz, $CDCl_3$) δ −63.3 (s, CF$_2$Br), −75.1 (s, CF$_3$), −110.9 (d, J = 275 Hz, CFFCH), −120.4 (dd, J = 274, 18 Hz, CFFCH); HRMS (ES+) for $C_{20}H_{18}{}^{79}BrF_7O_5SNa^+$ [M + Na]$^+$ calcd 604.9839, found 604.9823.

(2*R*,3*R*)-2-(1,3-Dibenzyloxy-5-bromo-4,4,5,5-tetrafluoro)-pentyl Chloroacetate (32). Alcohol **22** (131 mg, 0.29 mmol, not enantiopure) was dissolved in toluene (2.9 mL) and treated with PPh_3 (152 mg, 0.58 mmol) and chloroacetic acid (55 mg, 0.58 mmol). The reaction was stirred until dissolved; DIAD (114 μL, 0.58 mmol) was then added and stirring continued at rt overnight. The reaction mixture was then concentrated to give a residue, which was purified by column chromatography (petroleum ether/EtOAc 95:5 to 0:100) to give (*Z*)-**33** as a colorless oil (63 mg, 50%) and ester **32** as a colorless oil (5 mg, 3%). Data for **32**: R_f 0.38 (petroleum ether/EtOAc 90:10); IR (neat) 3033 (w), 2952 (w), 2875 (w), 1768 (m), 1152 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27−7.43 (10H, m, H_{Ar}) 5.50 (1H, td, J = 5.5, 2.8 Hz, C$\underline{H}$CH$_2$), 4.75 (1H, d, J = 10.7 Hz, C$\underline{H}$HPh), 4.69 (1H, d, J = 10.8 Hz, CH$\underline{H}$Ph), 4.56 (1H, d, J = 11.9 Hz, C$\underline{H}$HPh), 4.50 (1H, d, J = 11.9 Hz, CH$\underline{H}$Ph), 4.38 (1H, dt, J = 16.6, 5.9 Hz, C$\underline{H}$CF$_2$), 4.05 (1H, d, J = 14.9 Hz, C$\underline{H}$HCl), 3.99 (1H, d, J = 14.9 Hz, CH$\underline{H}$Cl), 3.86 (1H, dd, J = 11.3, 6.0 Hz, C$\underline{H}$HOBn), 3.78 (1H, dd, J = 11.3, 2.8 Hz, CH$\underline{H}$OBn); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2 (C═O), 137.4 (C$_{Ar}$), 136.1 (C$_{Ar}$), 128.5 (4C, 4 × C$\underline{H}_{Ar}$), 128.4 (C$\underline{H}_{Ar}$), 128.2 (2C, 2 × C$\underline{H}_{Ar}$), 127.9 (C$\underline{H}_{Ar}$), 127.7 (2C, 2 × C$\underline{H}_{Ar}$), 75.4 (C$\underline{H}_2$Ph), 75.3 (dd, J = 27, 21 Hz, C$\underline{H}$CF$_2$), 73.4 (C$\underline{H}_2$Ph), 72.3 (C$\underline{H}$CH$_2$), 67.6 (C$\underline{H}_2$OBn), 40.6 (C$\underline{H}_2$Cl); ^{19}F NMR (282 MHz, $CDCl_3$) δ −63.1 (d, J = 5 Hz, CFFBr), −63.2 (s, CFFBr), −111.0 (d, J = 274 Hz, CFFCH), −119.3 (ddd, J = 274, 17, 6 Hz, CFFCH); ES$^+$MS m/z 549.1 [M + Na]$^+$ 549.0, HRMS (ES+) for $C_{21}H_{20}BrClF_4O_4Na^+$ [M + Na]$^+$ calcd 549.0062, found 549.0062. Data for (*Z*)-3,5-dibenzyloxy-1-bromo-1,1,2,2-tetrafluoropent-3-ene ((*Z*)-**33**): R_f 0.57 (petroleum ether/EtOAc 90/10); IR (neat) 3033 (w), 2860 (w), 1673 (w), 1455 (m), 1233 (m), 1147 (s), 1082 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28−7.63 (10H, m, H_{Ar}), 6.00 (1H, t, J = 6.6 Hz, C$\underline{H}$CH$_2$), 4.88 (2H, s, C$\underline{H}$HPh + CH$\underline{H}$Ph), 4.47 (2H, s, C$\underline{H}$HPh + CH$\underline{H}$Ph), 4.12 (1H, t, J = 2.2 Hz, C$\underline{H}$HOBn), 4.11 (1H, t, J = 2.2 Hz, CH$\underline{H}$OBn); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.2 (C$_{Ar}$), 136.4 (C$_{Ar}$), 128.6 (CH$_{Ar}$ × 2), 128.5 (CH$_{Ar}$ × 2), 128.3 (CH$_{Ar}$), 128.1 (CH$_{Ar}$), 127.94 (CH$_{Ar}$ × 2), 127.88 (CH$_{Ar}$ × 2), 123.5 (C$\underline{H}$CH$_2$), 75.8 (C$\underline{H}_2$Ph × 2), (dd, J = 26, 22 Hz, C$\underline{C}$F$_2$), 73.5 (C$\underline{H}_2$Ph), 66.5 (C$\underline{H}_2$OBn); ^{19}F NMR (282 MHz, $CDCl_3$) δ −64.08 (t, J = 5.4 Hz, CF$_2$CF$_2$Br), −110.87 (br s, CF$_2$Br); ES$^+$MS m/z 450.2 and 452.2 [M + NH$_4$]$^+$, 1:1 ratio; HRMS (ES+) for $C_{19}H_{17}{}^{79}Br_1F_4O_2Na_1$ (M + Na)$^+$ calcd 455.0240, found 455.0232.

(3*S*,4*R*)-3-(5-Benzyloxy-4-(methoxymethyl)oxy-1-bromo-1,1,2,2-tetrafluoro)pentyl Trifluoromethanesulfonate (36). Alcohol **35** (420 mg, 1.04 mmol, not enantiopure) was dissolved in DCM (6 mL) and treated with pyridine (168 μL, 2.07 mmol). The reaction was then cooled to −35 °C before the dropwise addition of Tf_2O (1 M in DCM, 1.56 mL, 1.56 mmol). Stirring was continued at −25 °C for 2.5 h, after which time the reaction was allowed to warm to room temperature. H_2O (12 mL) and aq $NaHCO_3$ (12 mL) were then added, and the resultant mixture was extracted into DCM (2 × 24 mL). The combined organic phases were dried (Na_2SO_4), filtered, and concentrated to give a yellow oil, which was diluted in DCM and filtered through silica. The silica plug was washed with plenty of DCM, and the resultant combined DCM was concentrated to give triflate **36** as a pale yellow oil (527 mg, 95%): R_f 0.47 (petroleum ether/EtOAc 80:20); IR (neat) 2900 (w), 1418 (m), 1212 (s), 1135 (s), 1086 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28−7.43 (5H, m, H_{Ar}), 5.66 (1H, td, J = 10.4, 4.0 Hz, C$\underline{H}$CF$_2$), 4.74 (1H, d, J = 7.1 Hz, C$\underline{H}$HOMe), 4.70 (1H, d, J = 7.1 Hz, CH$\underline{H}$OMe), 4.64 (1H, d, J = 11.6 Hz, C$\underline{H}$HPh), 4.53 (1H, d, J = 11.6 Hz, CH$\underline{H}$Ph), 4.23 (1H, dd, J = 11.1, 5.1 Hz, C$\underline{H}$CH$_2$), 3.77 (1H, dd, J = 10.1, 5.1 Hz, C$\underline{H}$HOBn), 3.67 (1H, dd, J = 10.1, 6.6 Hz, CH$\underline{H}$OBn), 3.38 (3H, s, C$\underline{H}_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.2 (C$_{Ar}$), 128.5 (C$\underline{H}_{Ar}$ × 2), 128.0 (C$\underline{H}_{Ar}$), 127.8 (C$\underline{H}_{Ar}$ × 2), 97.4 (C$\underline{H}_2$OMe), 77.8 (t, J = 26 Hz, C$\underline{H}$CF$_2$), 73.6 (C$\underline{H}_2$Ph), 72.7 (C$\underline{H}$CH$_2$), 67.7 (C$\underline{H}_2$OBn), 56.2 (C$\underline{H}_3$); ^{19}F NMR (282 MHz, $CDCl_3$) δ −63.8 (d, J = 185 Hz, CFFBr), −64.6 (d, J = 185 Hz, CFFBr), −74.0 (br s, CF$_3$), −112.7 (d, J = 275 Hz, CFFCH), −113.9 (d, J = 279 Hz, CFFCH); EIMS m/z 490.9 [M − MOM]$^{+\bullet}$; HRMS (ES+) for $C_{15}H_{16}{}^{81}BrF_7O_6SNa^+$ [M + Na]$^+$ calcd 560.9616, found 560.9623.

(3*R*,4*R*)-5-(Benzyloxy)-1-bromo-4-(methoxymethyl)oxy-1,1,2,2-tetrafluoropentan-3-ol (37). Triflate **27** (69 mg, 0.13 mmol, not enantiopure) was dissolved in DMF (1 mL) and cooled to 0 °C. $NaNO_2$ (89 mg, 1.28 mmol) was added and the reaction stirred at 60 °C for 17 h. The resultant mixture was diluted with H_2O (2 mL) and extracted into DCM (4 × 2 mL). The combined organic phases were dried (Na_2SO_4), filtered, and concentrated to give a pale yellow oil. Column chromatography (petroleum ether/EtOAc 90:10 to 80:20) gave alkene (*Z*)-**38** as a colorless oil (12 mg, 24%) and alcohol **37** as a pale yellow oil (20 mg, 38%). Data for **37**: R_f 0.19 (petroleum ether/EtOAc 80:20); IR (neat) 3415 (w, br), 2940 (w), 2360 (w), 1152 (s), 1101 (s), 1030 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29−7.44 (5H, m), 4.77 (1H, d, J = 7.1 Hz, OC$\underline{H}$HO), 4.74 (1H, d, J = 7.1 Hz, OCH$\underline{H}$O), 4.59 (2H, s, C$\underline{H}$HPh, CH$\underline{H}$Ph), 4.47 (1H, ddt, $^3J_{H-F}$ 22.2, J = 8.6, 3.5 Hz, C$\underline{H}$CF$_2$), 4.28 (1H, d, J = 8.6 Hz, O$\underline{H}$), 4.02 (1H, q, J = 3.5 Hz, C$\underline{H}$CH$_2$), 3.89 (1H, dd, J = 10.6, 4.0 Hz, C$\underline{H}$HOBn), 3.83 (1H, dd, J = 10.1, 3.5 Hz, CH$\underline{H}$OBn), 3.43 (3H, s, C$\underline{H}_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.0 (C$_{Ar}$), 128.6 (C$\underline{H}_{Ar}$ × 2), 128.1 (C$\underline{H}_{Ar}$), 127.9 (C$\underline{H}_{Ar}$ × 2), 96.8 (OC$\underline{H}_2$O), 75.6 (C$\underline{H}$CH$_2$), 74.0 (C$\underline{H}_2$Ph), 70.7 (t, J = 3 Hz, C$\underline{H}_2$OBn), 70.6 (dd, J = 28, 22 Hz, C$\underline{H}$CF$_2$), 56.1 (C$\underline{H}_3$); ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.7 (dd, J = 181, 9 Hz, CFFBr), −63.9 (d, J = 176 Hz, CFFBr), −114.7 (d, J = 271 Hz, CFFCH), −124.7 (dt, J = 266, 9 Hz, CFFCH); ES$^+$MS m/z 468.0 [^{79Br}M + MeCN + Na]$^+$; HRMS (ES+) for $C_{14}H_{17}BrF_4O_4Na^+$ [M + Na]$^+$ calcd 427.0139, found 427.0148. Data for (*Z*)-5-benzyloxy-1-bromo-4-(methoxymethyl)oxy-1,1,2,2-tetrafluoropent-3-ene ((*Z*)-**38**): R_f 0.47 (petroleum ether/EtOAc 80:20); IR (neat) 2919 (w), 1675 (m), 1153 (s), 1082 (s), 1002 (s), 914 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29−7.43 (5H, m, H_{Ar}), 5.13 (2H, s, C$\underline{H}_2$OMe), 5.01 (1H, t, J = 14.1 Hz, C$\underline{H}$), 4.57 (2H, s, C$\underline{H}_2$Ph), 4.21 (2H, t, J = 1.8 Hz, C$\underline{H}_2$OBn), 3.49 (3H, s, C$\underline{H}_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9 (t, J = 5 Hz, C$\underline{O}$MOM), 137.1 (C$_{Ar}$), 128.6 (C$\underline{H}_{Ar}$ × 2), 128.1 (C$\underline{H}_{Ar}$), 127.9 (C$\underline{H}_{Ar}$ × 2), 96.7 (t, J = 25 Hz, C$\underline{H}$), 93.9 (C$\underline{H}_2$OMe), 72.2 (C$\underline{H}_2$Ph), 67.6 (C$\underline{H}_2$OBn), 56.8 (C$\underline{H}_3$); ^{19}F NMR (282 MHz, $CDCl_3$) δ −66.2 (2F, t, J = 9 Hz, CF$_2$Br), −104.4 (2F, m, CF$_2$CH); ES$^+$MS m/z 409.0 [M + Na]$^+$; HRMS (ES+) for $C_{14}H_{15}BrF_4O_3Na^+$ [M + Na]$^+$ calcd 409.0033, found 409.0034.

(4*S*,5*R*)-4-((Benzyloxy)methyl)-5-(2-bromo-1,1,2,2-tetrafluoroethyl)-2,2-dioxo-1,3-dioxa-2-thiolane (40). Diol *ent*-**14** (4.79 g, 13.3 mmol) was dissolved in DCM (60 mL) and cooled to 0 °C. Et_3N (7.42 mL, 53.2 mmol) was added, followed by the dropwise addition of $SOCl_2$ (1.94 mL, 26.6 mmol) over 9 min. The reaction was stirred at 0 °C for 25 min then diluted with cold Et_2O (90 mL). H_2O (180 mL) was added, and the layers were separated. The aqueous phase was extracted into Et_2O (4 × 180 mL), and the resultant organic phases were combined and washed with brine (4 × 180 mL), dried (Na_2SO_4), filtered, and concentrated to give a dark brown oil. The oil was dissolved in Et_2O and filtered through silica, which was washed with plenty of Et_2O. Concentration of the filtrate gave a brown oil. Column chromatography (petroleum ether/Et_2O 90:10) gave the corresponding sulfite as an oil (5.27 g, 98%). The sulfite (4.3 g, 10.6 mmol) was dissolved in H_2O (25 mL), MeCN (17 mL), and CCl_4 (17 mL) and then immediately cooled to 0 °C. $NaIO_4$ (2.71 g, 12.7 mmol) and

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$RuCl_3 \cdot xH_2O$ (55 mg) were added, and the reaction was stirred vigorously at 0 °C to rt for 16 h. The resultant mixture was diluted with Et_2O (50 mL) and then stirred for 5 min. The aqueous phase was then separated and extracted into Et_2O (3 × 80 mL). The combined organic phases were washed with H_2O (80 mL), dried (Na_2SO_4), filtered, and concentrated to give a red oil. Column chromatography (petroleum ether/Et_2O 75:25) gave sulfate **40** as a colorless oil, which after storage in the refrigerator for several days became a solid (4.0 g, 90%): $[\alpha]_D$ −37.1 (*c* 0.5, $CHCl_3$, 27 °C); NMR spectra are in agreement with reported data.[18]

(3*R*,4*R*)-5-Benzyloxy-1-bromo-1,1,2,2-tetrafluoropentan-3,4-diol (41). Sulfate **40** (3.52 g, 8.32 mmol) was dissolved in DMF (65 mL) and treated with HCO_2NH_4 (1.05 g, 16.6 mmol). The reaction was stirred at 80 °C for 4 h before being concentrated under reduced pressure. The resultant oil was dissolved in THF (45 mL) and treated with acetyl chloride (2 M in MeOH, 12.5 mL, 25.0 mmol). The reaction mixture was stirred at rt for 30 min before being quenched with $NaHCO_3$. Stirring was continued for 20 min before the reaction was filtered and washed with EtOAc. Concentration of the filtrate gave a yellow residue. Column chromatography (petroleum ether/EtOAc 85:15 then 70:30) gave ketone **42** as a yellow oil (439 mg, 15%), sulfate **40** as a yellow oil (82 mg, 2.3%), the corresponding 4-formate **89** as a yellow oil (38 mg, 1.2%), and desired diol **41** as an oily solid (2.27 g, 76%). Data for **41**: $[\alpha]_D$ +21.7 (*c* 0.5, $CHCl_3$, 26 °C); NMR spectra are in agreement with reported data.[18] Data for (3*R*,4*R*)-5-benzyloxy-1-bromo-3-hydroxy-1,1,2,2-tetrafluoropentan-4-yl formate (**89**): $[\alpha]_D$ −3.0 (*c* 0.6, $CHCl_3$, 24 °C); NMR spectra are in agreement with reported data.[18] Data for 5-benzyloxy-1-bromo-1,1,2,2-tetrafluoropentan-3-one (**42**): R_f 0.54 (hexane/EtOAc 80:20); IR (neat) 2873 (w), 1756 (m), 1163 (s), 1098 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28−7.40 (5H, m, H_{Ar}), 4.55 (2H, s, $C\underline{H}_2Ph$), 3.82 (2H, t, *J* = 6.1 Hz, $C\underline{H}_2OBn$), 3.07 (2H, t, *J* = 6.1 Hz, $C\underline{H}_2C{=}O$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.4 (t, *J* = 28 Hz, $\underline{C}{=}O$), 137.7 ($\underline{C}q_{Ar}$), 128.4 ($\underline{C}H_{Ar}$ × 2), 127.8 ($\underline{C}H_{Ar}$), 127.7 ($\underline{C}H_{Ar}$ × 2), 73.4 ($\underline{C}H_2Ph$), 63.4 ($\underline{C}H_2OBn$), 38.7 ($\underline{C}H_2C{=}O$); ^{19}F NMR (282 MHz, $CDCl_3$) δ −64.8 (2F, br s), −116.8 (2F, br s); CI^+MS *m*/*z* 344.1 $[M + H]^+$; HRMS (ESI−) for $C_{12}H_{10}BrF_4O_2$ $[M - H]^-$ calcd 340.9800, found 340.9802.

(3*R*,4*R*)-3,5-Dibenzyloxy-1-bromo-1,1,2,2-tetrafluoropentan-4-ol (90). Diol **41** (1.88 g, 5.19 mmol) was dissolved in DMF (200 mL) and cooled to 0 °C. NaH (60% in mineral oil, 208 mg, 5.19 mmol) was added and stirring continued at 0 °C for 1 h. BnBr (617 μL, 5.19 mmol) was added and stirring continued at 0 °C to rt for 20 h. Aqueous NH_4Cl (saturated, 25 mL) was added and the resultant mixture stirred at rt for 30 min. Extraction was carried out in EtOAc (4 × 40 mL). The combined organic phase was washed with brine (2 × 130 mL), dried ($MgSO_4$), filtered, and concentrated to give a yellow oil. Column chromatography (petroleum ether/EtOAc 90:10 then 70:30) gave alcohol **90** as a colorless oil (1.53 g, 65%), trisbenzyl ether **91** as a colorless oil (288 mg, 10%), and starting diol **41** as a colorless oil (394 mg, 21%). Data for **90**: $[\alpha]_D$ +21.7 (*c* 0.3, $CHCl_3$, 26 °C); NMR spectra are in agreement with reported data.[18] Data for (3*R*,4*R*)-3,4,5-tribenzyloxy-1-bromo-1,1,2,2-tetrafluoropentane **91**: $[\alpha]_D$ +11.6 (*c* 0.4, $CHCl_3$, 25 °C); NMR spectra are in agreement with reported data.[18]

(2*R*,3*R*)-2-(1,3-Dibenzyloxy-5-bromo-4,4,5,5-tetrafluoro)-pentyl Formate (43). TsCl (1.02 g, 3.82 mmol) was dissolved in pyridine (9.8 mL) and cooled to 0 °C. DMF (3.25 mL) was added and the resultant solution stirred at 0 °C for 15 min and then at rt for 30 min. The solution was then cooled to 0 °C, and a solution of alcohol **90** (1.72 g, 3.82 mmol) in pyridine (3 mL) was added dropwise and washed with pyridine (0.25 mL). The resultant solution was stirred at rt for 1.5 h before being cooled to 0 °C. H_2O (20 mL) was added followed by extraction into hexane (4 × 20 mL). The combined organic phases were dried (Na_2SO_4), filtered, and concentrated to give a pale yellow oil. Column chromatography (petroleum ether/EtOAc 95:5 then 80:20) gave formate **43** as a colorless oil (1.56 g, 85%) and starting alcohol **90** as a colorless oil (165 mg, 10%): $[\alpha]_D$ +15.2 (*c* 0.66, $CHCl_3$, 25 °C); NMR spectra are in agreement with reported data.[18]

4,6-Di-*O*-benzyl-2,3-dideoxy-2,2,3,3-tetrafluoro-D-*erythro*-hexopyranose (44). Formate **43** (1.46 g, 3.23 mmol) was dissolved in dry DCM (20 mL) and filtered through a pad of $MgSO_4$ directly into the reaction flask, while the filtrate was concentrated with a stream of argon. The resultant oil was dried under high vacuum for 16 h before being dissolved in THF (30 mL) and cooled to −78 °C. MeLi (1.22 M in Et_2O, 2.65 mL, 3.23 mmol) was added very slowly dropwise. The resultant solution was stirred at −78 °C for 4.5 h. At −78 °C, aq NH_4Cl (saturated, 10 mL) was added to the reaction mixture, which was then stirred for 20 min, while allowing to warm to rt. The mixture was diluted with H_2O (20 mL) then extracted into EtOAc (3 × 75 mL), dried ($MgSO_4$), filtered, and concentrated to give a white solid. Column chromatography (petroleum ether/acetone 90:10 then 75:25) gave **44** as a colorless oil (1.04 g, 80%): $[\alpha]_D$ +77.1 (*c* 0.529, acetone, 22 °C); NMR spectra are in agreement with reported data.[18]

2,3-Dideoxy-2,2,3,3-tetrafluoro-D-*erythro*-hexopyranose (5). Pyranose **44** (470 mg, 1.17 mmol) was dissolved in EtOAc (9 mL) and treated with $Pd(OH)_2/C$ (249 mg, 0.47 mmol). The resultant mixture was flushed with H_2 and then stirred under H_2 for 3.5 h before being filtered through Celite, which was was washed with plenty of EtOAc. Concentration gave a colorless oil. Column chromatography (petroleum ether/acetone 55:45) followed by HPLC (hexane/acetone 50:50) gave pyranose **5** as a colorless oil (244 mg, 95%, α/β 1:1): $[\alpha]_D$ +60.7 (*c* 0.516, acetone, 22 °C); NMR spectra are in agreement with reported data.[18]

6-Benzyloxy-4-triethylsilyl-2,3-dideoxy-2,2,3,3-tetrafluoro-D-*threo*-hexopyranose (48). Furanose **47** (130 mg, 0.31 mmol) was dissolved in THF (6 mL) and cooled to −78 °C. *t*-BuOK (38 mg, 0.31 mmol) was added. The resultant mixture was stirred at −78 °C for 7 h and allowed to warm to rt for 14 h. Aqueous HCl (1M, 0.33 mL) was added and then H_2O (1 mL). The volatile components were removed under reduced pressure, and the resultant aqueous phase was extracted into EtOAc (3 × 8 mL). The combined organic phases were washed with aq $NaHCO_3$ (10 mL) and brine (10 mL) before being dried ($MgSO_4$), filtered, and concentrated to give a colorless oil. Column chromatography (petroleum ether/acetone 80:20) gave **48** (α/β 1:1) as a white waxy solid (130 mg, quant): R_f 0.21 (petroleum ether/acetone 95:5); mp 40−44 °C (Et_2O); $[\alpha]_D$ +31.7 (*c* 0.567, acetone, 22 °C); IR (neat) 3412 (br, w), 2956 (m), 2879 (m), 1456 (w), 1197 (m), 1151 (s), 1123 (s), 1079 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29−7.42 (10H, m, H_{Ar} × 10), 5.30 (1H, dd, *J* = 8.7, 6.1 Hz, H-1_α), 4.86 (1H, dd, *J* = 13.9, 3.6 Hz, H-1_β), 4.55−4.61 (3H, m, $C\underline{H}HPh$ × 3), 4.53 (1H, d, *J* = 11.8 Hz, $C\underline{H}HPh$), 4.49 (1H, m, H-5_α), 4.12 (2H, m, H-$4_{\alpha+\beta}$), 3.91 (1H, m, H-5_β), 3.60−3.70 (4H, m, H-$6_{\alpha+\beta}$ and H-$6'_{\alpha+\beta}$), 0.96 (9H, t, *J* = 8.0 Hz, $C\underline{H}_{3\ \alpha/\beta}$ × 3), 0.95 (9H, t, *J* = 7.9 Hz, $C\underline{H}_{3\beta/\alpha}$), 0.58−0.73 (12H, m, $CH_3C\underline{H}_2$ × 6); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.4 ($C_{Ar\ \alpha/\beta}$), 137.3 ($C_{Ar\ \beta/\alpha}$), 128.5 (4C, $\underline{C}H_{Ar}$ × 4), 128.0 (4C, $\underline{C}H_{Ar}$ × 4), 128.0 (2C, $\underline{C}H_{Ar}$ × 2), 91.3−92.5 (2C, m, C-$1_{\alpha+\beta}$), 73.7 (2C, $\underline{C}H_2Ph_{\alpha+\beta}$), 73.2 (d, *J* = 6 Hz, C-5_β), 69.6−70.9 (2C, m, C-$4_{\alpha+\beta}$), 68.8 (d, *J* = 5 Hz, C-5_α), 67.8 (C-$6_{\ \alpha/\beta}$), 67.2 (C-$6_{\beta/\alpha}$), 6.5 (6C, $\underline{C}H_3$ × 6), 4.6 (6C, s, $CH_3C\underline{H}_2$ × 6), $\underline{C}F_2\underline{C}F_2$ not observed; ^{19}F NMR (282 MHz, $CDCl_3$) δ −118.8 (ddt, *J* = 271, 16, 9 Hz), −119.3 (ddt, *J* = 269, 14, 8 Hz), −120.4 (dt, *J* = 271, 5 Hz), −128.1 (m, *J* = 269 Hz can be observed), −129.8 (m, *J* = 270 Hz can be observed), −134.1 (m, *J* = 271 Hz can be observed), −135.9 (br d, *J* = 260 Hz), −137.8 (m, *J* = 260 Hz can be observed); ES^+MS *m*/*z* 447 $[M + Na]^+$; HRMS (ES+) for $C_{19}H_{28}F_4NaO_4Si^+$ $[M + Na]^+$ calcd 447.1585, found 447.1577.

6-*O*-Benzyl-2,3-dideoxy-2,2,3,3-tetrafluoro-D-*threo*-hexopyranose (58). Furanose **47** (128 mg, 0.30 mmol) was dissolved in THF (0.4 mL) at rt, and TBAF (1 M in THF, 300 μL, 0.30 mmol) was added dropwise. The reaction was stirred at rt for 1 h and concentrated. The resultant oil was purified by column chromatography (hexane/acetone 70:30) to give pyranose **58** as a white solid (79 mg, 85%): R_f 0.05 (petroleum ether/EtOAc 85:15); mp 120−126 °C (CH_2Cl_2); $[\alpha]_D$ +27.0 (*c* 0.505, acetone, 22 °C); IR (neat) 3383 (m, br), 2931 (w), 2876 (w), 1454 (w), 1117 (s), 1063 (s) cm^{-1}, ^1H NMR (400 MHz, acetone-d_6) [OH peaks only] δ 6.71 (1H, m, O$\underline{H}$-1_α), 4.94−5.21 (2H, m, O$\underline{H}$-$4_{\alpha+\beta}$), 2.83 (1H, br s, O$\underline{H}$-1_β) [D_2O exchange]

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δ 7.23−7.42 (10H, m, $\underline{H}_{Ar}$), 5.30 (1H, dd, J = 9.2, 6.5 Hz, H-1$_\alpha$), 5.00 (1H, dt, J = 13.1, 3.6 Hz, H-1$_\beta$), 4.52−4.62 (5H, m, $CH_2Ph_{\alpha+\beta}$, H-5$_\alpha$), 4.09−4.23 (2H, m, H-4$_{\alpha+\beta}$), 4.02 (1H, dtd, J = 8.0, 4.0, 2.0 Hz, H-5$_\beta$), 3.81 (2H, dd, J = 9.8, 6.0 Hz, H-6$_{\alpha+\beta}$), 3.71 (1H, ddd, J = 9.9, 6.3, 1.4 Hz, H-6′$_\beta$), 3.67 (1H, ddd, J = 9.9, 6.4, 1.5 Hz, H-6′$_\alpha$); ^{13}C NMR (101 MHz, acetone-d_6) δ 139.5 ($\underline{C}_{Ar}$), 139.4 ($\underline{C}_{Ar}$), 129.2 (4C, $\underline{C}H_{Ar}$ × 4), 128.5 (4C, $\underline{C}H_{Ar}$ × 4), 128.4 (2C, $\underline{C}H_{Ar}$ × 2), 93.2−92.2 (m, C-1$_{\alpha+\beta}$), 73.91 ($\underline{C}H_2Ph_{\alpha/\beta}$), 73.86 ($\underline{C}H_2Ph_{\beta/\alpha}$), 73.6 (d, J = 7 Hz, C-5$_\beta$), 70.1 (t, J = 21 Hz, C-4$_{\alpha/\beta}$), 69.8 (t, J = 20 Hz, C-4$_{\beta/\alpha}$), 69.0 (C-6$_{\alpha/\beta}$), 68.8 (C-6$_{\beta/\alpha}$), 68.6 (d, J = 6 Hz, C-5$_\alpha$); ^{19}F NMR (282 MHz, acetone-d_6) δ −117.6 (ddt, J = 265, 17, 9 Hz), −118.4 (ddt, J = 266, 15, 8, Hz), −119.8 (d, J = 268 Hz), −129.4 (dd, J = 268, 8 Hz), −131.6 (dt, J = 268, 11 Hz), −133.2 (dtt, J = 267, 10, 4 Hz), −136.0 (br d, J = 259 Hz), −137.1 (dt, J = 258, 13 Hz). ES$^+$MS m/z 333 [M + Na]$^+$; HRMS (ES+) for $C_{13}H_{14}F_4NaO_4^+$ [M + Na]$^+$ calcd 333.0720, found 333.0717.

(3*S*,4*R*)-5-(Benzyloxy)-1-bromo-4-((methoxymethyl)oxy)-1,1,2,2-tetrafluoropentan-3-ol (35). Diol **14** (933 mg, 2.58 mmol) was dissolved in DCE (10 mL) and cooled to 0 °C. The mixture was treated with MOMCl (235 μL, 3.10 mmol), DIPEA (540 μL, 3.10 mmol), and DMAP (32 mg, 258 μmol) and was stirred at 0 °C for 1 h and then at 83 °C for 5 h. The brown reaction mixture was then washed with aq $NaHCO_3$ (saturated, 9 mL), which was extracted into DCM (3 × 9 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give a brown oil. Column chromatography (petroleum ether/EtOAc 97:3 to 78:22) gave a pale yellow oil (787 mg) containing bis-MOM ether **60** (55 mg, 5%) and desired alcohol **35** (732 mg, 70%) and an oil/solid mixture (226 mg) containing undesired alcohol **59** (120 mg, 11%) and starting diol **14** (106 mg, 11%). The compounds were separated on a smaller scale for analytical purposes. Data for **35**: R_f 0.40 (petroleum ether/EtOAc 70:30); $[\alpha]_D$ +0.2 (c 0.5, $CHCl_3$, 25 °C); IR (neat) 3421 (br, w), 2941 (w), 2900 (w), 1152 (s), 1128 (s), 1078 (s), 1033 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16−7.38 (5H, m, $\underline{H}_{Ar}$), 4.64−4.70 (2H, m, OC$\underline{H}$HO, OCH$\underline{H}$O), 4.47−4.54 (2H, m, C$\underline{H}$HPh, CH$\underline{H}$Ph), 4.31 (1H, dddt, J = 22.2, 10.1, 3.0, 1.5 Hz, C$\underline{H}$OH), 4.11 (1H, tt, J = 6.6, 2.0 Hz, C$\underline{H}CH_2$), 3.53−3.69 (2H, m, C$\underline{H}$HOBn, CH$\underline{H}$OBn), 3.32 (3H, s, $\underline{C}H_3$), 3.05 (1H, d, J = 10.1 Hz, O$\underline{H}$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.5 (C_{Ar}), 128.5 ($\underline{C}H_{Ar}$), 127.9 ($\underline{C}H_{Ar}$), 127.6 ($\underline{C}H_{Ar}$), 96.7 (O$\underline{C}H_2$O), 73.5 ($\underline{C}H_2$Ph), 72.4 ($\underline{C}HCH_2$), 68.7 ($\underline{C}H_2$OBn), 67.7 (dd, J = 29, 20 Hz, $\underline{C}$HOH), 56.2 ($\underline{C}H_3$); ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.7 (dd, J = 176, 9 Hz), −63.8 (d, J = 176 Hz), −113.6 (d, J = 266 Hz), −126.4 (ddd, J = 271, 21, 9 Hz); ES$^+$MS m/z 427.1 [M + Na]$^+$; HRMS (ES+) for $C_{14}H_{17}BrF_4O_4Na^+$ [M + Na]$^+$ calcd 427.0139, found 427.0134. Data for (3*S*,4*R*)-5-benzyloxy-1-bromo-3-(methoxymethyl)oxy-1,1,2,2-tetrafluoropentan-4-ol (**59**): R_f 0.29 (petroleum ether/EtOAc 70:30); $[\alpha]_D$ −28.9 (c 0.5, $CHCl_3$, 26 °C); IR (neat) 3465 (br, w), 2905 (w), 2867 (w), 1130 (s), 1095 (s), 1028 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.42 (5H, m), 4.74 (2H, s C$\underline{H}$HOMe + CH$\underline{H}$OMe), 4.57 (2H, s, C$\underline{H}$HPh + CH$\underline{H}$Ph), 4.37 (1H, dd, $^3J_{H-F}$ 21.7, J = 8.6 Hz, C$\underline{H}CF_2$), 4.18 (1H, t, J = 6.3 Hz, C$\underline{H}CH_2$), 3.66 (1H, s, C$\underline{H}$HOBn) 3.65 (1H, s, CH$\underline{H}$OBn), 3.39 (3H, s, $\underline{C}H_3$), 3.12 (1H, d, J = 10.1 Hz, O$\underline{H}$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.6 ($\underline{C}_{Ar}$), 128.5 (CH_{Ar} × 2), 127.9 (CH_{Ar}), 127.8 (CH_{Ar} × 2), 98.7 ($\underline{C}H_2$OMe), 74.5 (dd, J = 26, 23 Hz, $\underline{C}HCF_2$), 73.4 ($\underline{C}H_2$Ph), 70.0 ($\underline{C}H_2$OBn), 67.8 ($\underline{C}HCH_2$), 56.8 ($\underline{C}H_3$); ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.7 (d, J = 181 Hz), −63.4 (d, J = 176 Hz), −112.5 (d, J = 275 Hz), −117.5 (dd, J = 275, 13 Hz); ES$^+$MS m/z 427.1 [M + Na]$^+$; HRMS (ES+) for $C_{14}H_{17}BrF_4O_4Na^+$ [M + Na]$^+$ calcd 427.0139, found 427.0134. Data for (3*S*,4*R*)-5-benzyloxy-1-bromo-3,4-di(methoxymethyl)oxy-1,1,2,2-tetrafluoropentane (**60**): R_f 0.46 (petroleum ether/EtOAc 70:30); $[\alpha]_D$ +6.1 (c 0.5, $CHCl_3$, 25 °C); IR (neat) 2936 (w), 2898 (w), 1134 (s), 1107 (s), 1075 (s), 1025 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.40 (5H, m), 4.79 (1H, d, J = 7.1 Hz, C$\underline{H}$HOMe), 4.74−4.77 (2H, m. CH$\underline{H}$OMe + C$\underline{H}$HOMe), 4.73 (1H, d, J = 6.6 Hz, C$\underline{H}$HOMe), 4.58 (1H, d, J = 12.1 Hz, C$\underline{H}$HPh), 4.55 (1H, d, J = 12.1 Hz, CH$\underline{H}$Ph), 4.45 (1H, ddd, J = 17.3, 7.5, 2.0 Hz, C$\underline{H}CF_2$), 4.15 (1H, td, J = 6.1, 1.5 Hz, C$\underline{H}CH_2$), 3.70 (2H, d, J = 6.1 Hz, C$\underline{H}$HOBn + CH$\underline{H}$OBn), 3.44 (3H, s, $\underline{C}H_3$), 3.39 (3H, s, $\underline{C}H_3$′); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.7 ($\underline{C}_{Ar}$), 128.4 ($\underline{C}H_{Ar}$ × 2), 127.8 ($\underline{C}H_{Ar}$), 127.7 ($\underline{C}H_{Ar}$ × 2), 98.7 ($\underline{C}H_2$OMe), 97.3 ($\underline{C}H_2$OMe), 74.5 ($\underline{C}HCH_2$), 73.4 ($\underline{C}H_2$Ph), 73.5 (dd, J = 26, 20 Hz, $\underline{C}HCF_2$), 68.7 ($\underline{C}H_2$OBn), 56.8 ($\underline{C}H_3$), 55.9 ($\underline{C}H_3$′); ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.7 (d, J = 185 Hz), −63.4 (d, J = 181 Hz), −112.2 (d, J = 271 Hz), −118.2 (dd, J = 275, 17 Hz); ES$^+$MS m/z 471.1 [M + Na]$^+$; HRMS (ES+) for $C_{16}H_{21}BrF_4O_5Na^+$ [M + Na]$^+$ calcd 471.0401, found 471.0402.

(3*S*,4*R*)-5-Benzyloxy-1-bromo-4-(methoxymethyl)oxy-1,1,2,2-tetrafluoropent-3-yl Formate (61). Alcohol **35** (3.16 g, 7.79 mmol) was dissolved in DCM (15 mL) and treated with DMAP (238 mg, 1.95 mmol) and DIC (1.93 mL, 12.5 mmol). The mixture was cooled to 0 °C and then treated with formic acid (470 μL, 12.5 mmol) dropwise. The mixture was then stirred at rt for 2.5 h before being diluted with DCM (25 mL) and aq HCl (1 M, 18 mL). The aqueous phase was separated and extracted into DCM (2 × 12 mL). The combined organic phases were washed with HCl (3 × 18 mL) and then brine (90 mL) before being dried ($MgSO_4$), filtered, and concentrated to give a residue, which was suspended in hexane, filtered, and concentrated to give a pale yellow oil. Column chromatography (petroleum ether/EtOAc 85:15) gave formate **61** as a colorless oil (3.25 g, 96%): R_f 0.33 (petroleum ether/EtOAc 80:20); $[\alpha]_D$ +7.4 (c 0.5, $CHCl_3$, 30 °C); IR (neat) 2950 (w), 2899 (w), 1740 (s), 1142 (s), 1080 (s), 1029 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (1H, s, C$\underline{H}$O), 7.28−7.44 (5H, m, $\underline{H}_{Ar}$), 6.00 (1H, dt, $^3J_{H-F}$ 19.3, J = 3.3 Hz, C$\underline{H}CF_2$), 4.75 (1H, d, J = 7.1 Hz, C$\underline{H}$HOMe), 4.72 (1H, d, J = 6.9 Hz, CH$\underline{H}$OMe), 4.54 (1H, d, J = 11.7 Hz, C$\underline{H}$HPh), 4.50 (1H, d, J = 11.7 Hz, CH$\underline{H}$Ph), 4.27 (1H, ddt, J = 7.2, 5.2, 2.1 Hz, C$\underline{H}CH_2$), 3.66 (1H, dd, J = 9.7, 5.2 Hz, C$\underline{H}$HOBn), 3.47 (1H, dd, J = 9.7, 7.4 Hz, CH$\underline{H}$OBn), 3.39 (3H, s, $\underline{C}H_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3 ($\underline{C}$HO), 137.3 (C_{Ar}), 128.4 (2 × $\underline{C}H_{Ar}$), 127.9 (2 × $\underline{C}H_{Ar}$), 97.0 ($\underline{C}H_2$OMe), 73.7 ($\underline{C}H_2$Ph), 72.7 ($\underline{C}HCH_2$), 68.1 ($\underline{C}H_2$OBn), 65.7 (dd, J = 31, 20 Hz, $\underline{C}HCF_2$), 56.1 ($\underline{C}H_3$); ^{19}F NMR (282 MHz, $CDCl_3$) δ −64.0 (d, J = 185 Hz, C$\underline{F}$FBr), −64.6 (d, J = 176 Hz, CF$\underline{F}$Br), −112.2 (d, J = 275 Hz, C$\underline{F}$FCH), −119.5 (dd, J = 275, 17 Hz, CF$\underline{F}$CH); ES$^+$MS m/z 454.9 [M + Na]$^+$; HRMS (ES+) for $C_{15}H_{17}BrF_4O_5Na^+$ [M + Na]$^+$ calcd 455.0088, found 455.0088.

6-*O*-Benzyl-5-*O*-(methoxymethyl)-2,3-dideoxy-2,2,3,3-tetrafluoro-D-*threo*-hexofuranose (8). Formate **61** (2.88 g, 6.88 mmol) was dissolved in anhydrous DCM (40 mL) and filtered through a pad of $MgSO_4$ directly into the reaction flask, while the filtrate was concentrated with a stream of N_2. The resultant oil was dried under high vacuum for 16 h before being dissolved in THF (70 mL) and cooled to −78 °C. MeLi (1.6 M in Et_2O, 4.3 mL, 6.88 mmol) was added dropwise very slowly. The mixture was stirred at −78 °C for 5 h then treated with aq NH_4Cl (saturated, 35 mL). After being stirred for 0.5 h while being allowed to warm to rt, the mixture was diluted with H_2O (45 mL) and extracted into EtOAc (3 × 75 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give a yellow oil. Column chromatography (petroleum ether/acetone 95:5 to 80:20) gave furanose **8** as a pale yellow oil (1.51 g, 62%, anomeric mixture ratio 1:0.3): R_f 0.24 (petroleum ether/acetone 80:20); IR (neat) 3344 (w, br) 2901 (w), 1139 (s), 1103 (m), 1018 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.42 (6.5H, m, $\underline{H}_{Ar}$), 5.48 (0.3H, d, J = 6.6 Hz, H-1$_y$), 5.31 (1H, d, J = 8.1 Hz, H-1$_x$), 4.70−4.80 (2.6H, m, C$\underline{H}$HOMe$_{x+y}$ + CH$\underline{H}$OMe$_{x+y}$), 4.65 (1.3H, m, H-4$_{x+y}$), 4.52−4.60 (2.6H, m, C$\underline{H}$HPh$_{x+y}$ + CH$\underline{H}$Ph$_{x+y}$), 4.05 (0.3H, q, J = 5.1 Hz, H-5$_y$), 4.00 (1H, t, J = 6.6 Hz, H-5$_x$), 3.62−3.77 (2.6H, m, 2 × H-6$_{x+y}$), 3.40 (3H, s, C$\underline{H}_{3x}$), 3.38 (0.9H, s, C$\underline{H}_{3y}$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.4 ($\underline{C}_{Ary}$), 137.3 ($\underline{C}_{Arx}$), 128.4, 128.4, 127.9, 127.8, 127.7, 127.7 ($\underline{C}H_{Arx+y}$), 97.3 ($\underline{C}H_2OMe_x$), 96.8 ($\underline{C}H_2OMe_y$), 96.2 (ddd, J = 38, 25, 3 Hz, C-1$_x$), 94.7 (dd, J = 38, 22 Hz, C-1$_y$), 79.5 (dd, J = 29, 22 Hz, C-4$_x$), 77.2 (dd, J = 29, 23 Hz, C-4$_y$) 73.6 (CH_2Ph_x), 73.5 (CH_2Ph_y), 73.3 (C-5$_y$), 73.1 (d, J = 6 Hz, C-5$_x$), 68.5 (C-6$_y$), 67.8 (C-6$_x$), 56.4 ($\underline{C}H_{3x}$), 55.8 ($\underline{C}H_{3y}$); ^{19}F NMR (282 MHz, $CDCl_3$) δ −115.9 (0.3F, dd, J = 246, 11 Hz, F$_y$), −116.9 (1F, dd, J = 249, 17 Hz, F$_x$), −124.8 (1F, d, J = 247 Hz, F$_x$), −125.0 (1F, dd, J = 241, 5 Hz, F$_x$), −125.9 (1F, m, J = 247 Hz can be observed, F$_x$), −127.7 (0.3F, d, J = 247 Hz, F$_y$), −130.5 (0.3F, d, J = 246 Hz, F$_y$), −131.2 (0.3F, dd, J = 246, 14 Hz. F$_y$); ES$^+$MS m/z 377.1 [M + Na]$^+$; HRMS (ES+) for $C_{15}H_{18}F_4O_5Na^+$ [M + Na]$^+$ calcd 377.0983, found 377.0985.

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(*rac*)-Methyl (1-benzyloxy-4-bromo-3,3,4,4-tetrafluoro)but-2-yloxyacetate (±65). To a suspension of NaH (60% mineral oil, 193 mg, 4.83 mmol, 1.6 equiv) in THF (5 mL) was added a solution of the alcohol **±62** (1.00 g, 3.02 mmol, 1 equiv) in THF (2.5 mL) at 0 °C. After the reaction mixture was stirred for 1 h at rt, methyl bromoacetate **63** (0.57 mL, 6.0 mmol, 2 equiv) was added dropwise at 0 °C followed by TBAI (335 mg, 0.91 mmol, 0.3 equiv). The resultant mixture was stirred at rt overnight and quenched with saturated aq NH_4Cl (5 mL), diluted with Et_2O (50 mL), and washed with water (25 mL) and brine (25 mL). The ethereal layer was dried over Na_2SO_4, filtered, and concentrated. The obtained crude was then subjected to column chromatography (petroleum ether/Et_2O 80:20) to give the desired ester **±65** (1.19 g, 98%) as a colorless oil: R_f 0.30 (petroleum ether/Et_2O 80:20); IR (neat cm^{-1}) 2955 (w), 1760 (m), 1217 (m), 1147 (s), 1100 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.28 (5H, m, H_{Ar}), 4.59 (1H, d, J = 11.9 Hz, C$\underline{H}$HPh), 4.55 (1H, d, J = 11.9 Hz, CH$\underline{H}$Ph), 4.41 (1H, d, J = 16.1 Hz, C$\underline{H}$HCO$_2$Me), 4.34 (1H, d, J = 16.2 Hz, CH$\underline{H}$CO$_2$Me), 4.30 (1H, dtd, J = 15.8, 7.2, 2.8 Hz, C$\underline{H}$CF$_2$), 3.93−3.83 (2H, m, CHC$\underline{H}_2$O), 3.72 (3H, s, C$\underline{H}_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5 (C═O), 137.3 ($C_{q,Ar}$), 128.5 (CH_{Ar}), 127.9 (CH_{Ar}), 127.6 (CH_{Ar}), 77.8 (dd, J = 27.8, 23.4 Hz, $\underline{C}$HCF$_2$), 73.8 ($\underline{C}H_2$Ph), 69.3 ($\underline{C}H_2$CO$_2$Me), 68.8 (CH$\underline{C}H_2$O), 51.9 ($\underline{C}H_3$) (2 × CF_2 not resolved); ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.7 (dd, J = 180.5, 8.6 Hz, C$\underline{F}$FBr), −63.5 (d, J = 180.5 Hz, CF$\underline{F}$Br), −112.8 (d, J = 275.1 Hz, C$\underline{F}$FCF$_2$Br), −120.6 (ddd, J = 275.1, 17.2, 8.6 Hz, CF$\underline{F}$CF$_2$Br); MS (ESI) m/z 425 and 427 $(M + Na)^+$ 1:1 ratio; HRMS (MS^+) for $C_{14}H_{15}{}^{79}BrF_4NaO_4$ $(M + Na)^+$ calcd 424.9982, found 424.9993.

(*rac*)-6-Benzyloxymethyl-4,4,5,5-tetrafluorodihydropyran-3,3-diol (±67) and (*rac*)-6-Benzyloxymethyl-4,4,5,5-tetrafluorodihydropyran-3-one (±67b). A solution of the ester **±65** in DCM was filtered through $MgSO_4$ while being dried with N_2 and then dried under high vacuum overnight, then **±65** (450 mg, 1.12 mmol, 1 equiv) was dissolved in dry THF (10 mL) and cooled to −78 °C. MeLi (1.6 M in Et_2O, 0.70 mL, 1.12 mmol, 1 equiv) was added at −78 °C dropwise and the reaction mixture stirred at−78 °C for 4−5 h. The reaction was quenched at −78 °C by adding saturated aq NH_4Cl (5 mL) and allowed to warm to rt. The resultant mixture was diluted with water (5 mL) and extracted with EtOAc (3 × 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. The obtained crude was then subjected to column chromatography (petroleum ether/Et_2O 80:20 to 40:60) to give a 1:10 mixture of the desired hexulose derivative **±67b** and its hydrate **±67** as a colorless oil (236 mg, 68%): R_f 0.25 (petroleum ether/Et_2O 40:60); IR (neat cm^{-1}) 3376 (w, br), 2929 (w), 1285 (m), 1124 (s), 1092 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 7.42−7.29 (10H, m, H_{Ar}), 4.64 (1H, d, J = 11.9 Hz, C$\underline{H}$HPh, hydrate), 4.69−4.57 (2H, m, C$\underline{H}_2$Ph ketone), 4.57 (1H, d, J = 12.0 Hz, CH$\underline{H}$Ph, hydrate), 4.43 (1H, ddd, J = 15.4, 3.3, 1.0 Hz, C$\underline{H}$HC═O), 4.32 (1H, ddd, J = 15.5, 3.9, 0.9 Hz, CH$\underline{H}$C═O), 4.24 (1H, ddtt, $^3J_{H-F}$ 22.2, J = 7.5, 2.6, 1.2 Hz, C$\underline{H}$CF$_2$ ketone), 3.99−3.76 (5H, m, C$\underline{H}$CF$_2$, C$\underline{H}$HOBn, C$\underline{H}$HC(OH)$_2$, hydrate and C$\underline{H}_2$OBn ketone), 3.75 (1H, dd, J = 11.2, 7.6 Hz, CH$\underline{H}$OBn, hydrate), 3.65 (1H, ddd, J = 12.6, 3.4, 1.1 Hz, CH$\underline{H}$C(OH)$_2$, hydrate); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.0 ($C_{q,Ar}$ hydrate, 137.0 ($C_{q,Ar}$), 128.6 (2 × CH_{Ar}), 128.2 (CH_{Ar}), 128.1 (CH_{Ar} hydrate), 128.0 (CH_{Ar} hydrate), 127.9 (CH_{Ar}), 91.6 (dd, J = 23.4, 20.5 Hz, $\underline{C}$(OH)$_2$), 77.1 (t, J = 23.4 Hz, CF$_2$$\underline{C}$H hydrate), 74.1 ($\underline{C}H_2$Ph), 73.9 ($\underline{C}H_2$Ph hydrate), 71.4 ($\underline{C}H_2$C═O), 71.2 (d, J = 2.9 Hz, $\underline{C}H_2$C(OH)$_2$), 66.0 (br s, $\underline{C}H_2$OBn ketone and hydrate) (2 × CF_2 not resolved); ^{19}F NMR (282 MHz, $CDCl_3$) δ −117.3 (dd, J = 279.4, 12.9 Hz), −124.3 (d, J = 257.9 Hz, hydrate), −126.5 (dt, J = 262.2, 12.9 Hz), −129.3 (dt, J = 262.2, 15.0 Hz, hydrate), −130.5 (d, J = 262.2 Hz, hydrate), −133.5 (ddd, J = 262.2, 21.5, 12.9 Hz), −144.3 (dt, J = 279.4, 12.9 Hz), −150.5 (d, J = 257.9 Hz, hydrate); MS (ESI) for **67** m/z 311 $(M + H)^+$, HRMS (MS^+) for $C_{13}H_{14}F_4NaO_4$ $(M + Na)^+$ calcd 333.0720, found 333.0714.

(*rac*)-(2*S*,2′*R*)-Methyl (1-Benzyloxy-4-bromo-3,3,4,4-tetrafluorobutan-2-yl)oxy-2-methoxyacetate (±66a) and (*rac*)-(2*R*,2′*R*)-Methyl (1-Benzyloxy-4-bromo-3,3,4,4-tetrafluorobutan-2-yl)oxy-2-methoxyacetate (±66b). To a suspension of NaH (60% mineral oil, 97 mg, 2.42 mmol, 1.6 equiv) in THF (3 mL) was added a solution of the alcohol **±62** (500 mg, 1.51 mmol, 1 equiv) in THF (1.5 mL) at 0 °C. After the reaction mixture was stirred for 1 h at rt, methyl bromomethoxyacetate **64** (553 mg, 3.02 mmol, 2 equiv) was added dropwise at 0 °C followed by TBAI (167 mg, 0.45 mmol, 0.3 equiv). The resultant mixture was stirred at rt overnight and quenched with saturated aq NH_4Cl (2.5 mL), diluted with Et_2O (25 mL), and washed with water (10 mL) and brine (10 mL). The ethereal layer was dried over Na_2SO_4, filtered, and concentrated. The obtained crude was then subjected to column chromatography (petroleum ether/Et_2O 80:20) to give the desired esters **±66a** and **±66b** as a 1:0.8 mixture of diastereoisomers and a colorless oil (581 mg, 89%): R_f 0.21 (petroleum ether/Et_2O 80:20); IR (neat cm^{-1}) 2951 (w), 1756 (m), 1205 (m), 1127 (s), 1094 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.28 (5H, m, H_{Ar}), 5.19 (1H, s, C$\underline{H}$CO$_2$Me, minor isomer), 5.10 (1H, s, C$\underline{H}$CO$_2$Me, major isomer), 4.63−4.48 (6H, m, 2 × C$\underline{H}_2$Ph and 2 × C$\underline{H}$CF$_2$), 3.89−3.75 (4H, m, 2 × CHC$\underline{H}_2$O), 3.77 (3H, s, OC$\underline{H}_3$, major isomer), 3.71 (3H, s, OC$\underline{H}_3$, minor isomer), 3.47 (3H, s, OC$\underline{H}_3$, minor isomer), 3.46 (3H, s, OC$\underline{H}_3$, major isomer); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7 (C═O), 166.4 (C═O), 137.1 ($C_{q,Ar}$), 137.2 ($C_{q,Ar}$), 128.5 (CH_{Ar}), 128.0 (CH_{Ar}), 127.8 (CH_{Ar}), 127.7 (CH_{Ar}), 99.6 ($\underline{C}$HCO$_2$Me), 99.5 ($\underline{C}$HCO$_2$Me), 74.6 (t, J = 24.9 Hz, $\underline{C}$HCF$_2$), 74.3 (dd, J = 26.3, 23.4 Hz, $\underline{C}$HCF$_2$), 73.7 ($\underline{C}H_2$Ph), 73.6 ($\underline{C}H_2$Ph), 68.8 (CH$\underline{C}H_2$O), 68.5 (CH$\underline{C}H_2$O), 55.0 (O$\underline{C}H_3$), 54.7 (O$\underline{C}H_3$), 52.4 (O$\underline{C}H_3$), 52.3 (O$\underline{C}H_3$) (2 × CF_2 not resolved); ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.4 (m, J = 180.5 Hz, C$\underline{F}$FBr, minor isomer), −62.9 (m, J = 180.5 Hz, C$\underline{F}$FBr, major isomer), −63.4 (m, J = 180.5 Hz, CF$\underline{F}$Br, minor isomer), −63.5 (d, J = 180.5 Hz, CF$\underline{F}$Br, major isomer), −113.4 (m, J = 275.1 Hz, CHC$\underline{F}$F, minor isomer), −114.3 (dd, J = 275.1, 8.6 Hz, CHC$\underline{F}$F, major isomer), −116.4 (dd, J = 275.1, 8.6 Hz, CHCF$\underline{F}$, major isomer), −117.7 (dt, J = 275.1, 10.8 Hz, CHCF$\underline{F}$, minor isomer); MS (EI) m/z (%) 329 and 331 ((M −MeOCHCO$_2$Me$^\bullet$)$^+$, 4), 251 and 253 (6), 103 (MeOCHCO$_2$Me$^+$, 9), 91 ($C_7H_7^+$, 100); HRMS (MS+) for $C_{15}H_{17}{}^{79}BrF_4NaO_5$ $(M + Na)^+$ calcd 455.0088, found 455.0081.

(*rac*)-Methyl 6-*O*-Benzyl-3,4-dideoxy-3,3,4,4-tetrafluoro-glycerohex-2-ulopyranoside (±68). A solution of the ester **±66** in DCM was filtered through $MgSO_4$ while being dried with N_2 and then dried under high vacuum overnight. The ester **±66** (484 mg, 1.12 mmol, 1 equiv) was dissolved in dry THF (10 mL) and cooled to −78 °C. MeLi (1.6 M in Et_2O, 0.70 mL, 1.12 mmol, 1 equiv) was added at −78 °C dropwise and the reaction mixture stirred at −78 °C for 5 h. The reaction was quenched at −78 °C by adding saturated aq NH_4Cl (5 mL) and allowed to warm to rt. The resultant mixture was diluted with water (5 mL) and extracted with EtOAc (3 × 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. The obtained crude was then subjected to column chromatography (petroleum ether/acetone 80:20 to 70:30) to give an 1.4:1 anomeric mixture of the desired hexulose **±68** as a colorless oil (282 mg, 78%): R_f 0.25 (petroleum ether/acetone 70:30); IR (neat cm^{-1}) 3396 (w, br), 2943 (w), 1288 (m), 1105 (s), 1025 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.28 (1H, m, H_{Ar}), 4.70 (1H, d, J = 5.4 Hz, C$\underline{H}$OMe minor anomer), 4.65 (2H, d, J = 12.0 Hz, 2 × CH$\underline{H}$Ph), 4.63−4.57 (2H, m, 2 × CH$\underline{H}$Ph), 4.55 (1H, d, J = 2.9 Hz, C$\underline{H}$OMe major anomer), 4.38−4.26 (1H, m, C$\underline{H}$CF$_2$ minor anomer), 4.10−3.98 (1H, m, C$\underline{H}$CF$_2$, major anomer), 3.97−3.89 (2H, m, 2 × CH$\underline{H}$OBn), 3.78 (2H, dd, J = 11.1, 7.6 Hz, 2 × CH$\underline{H}$OBn), 3.68 (3H, s, major anomer), 3.53 (3H, s, minor anomer); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.5 ($C_{q,Ar}$), 137.3 ($C_{q,Ar}$), 128.5 (CH_{Ar}), 128.5 (CH_{Ar}), 128.0 (CH_{Ar}), 127.9 (CH_{Ar}), 127.7 (CH_{Ar}), 127.6 (CH_{Ar}), 100.9 ($\underline{C}$HOMe, minor anomer), 99.9 (d, J = 4.4 Hz, $\underline{C}$HOMe, major anomer), 73.9 ($\underline{C}H_2$Ph), 73.8 ($\underline{C}H_2$Ph), 72.7 (t, J = 24.9 Hz, $\underline{C}$HCF$_2$, major anomer), 68.0 (t, J = 24.5 Hz, $\underline{C}$HCF$_2$, minor anomer), 66.0 (br s, $\underline{C}H_2$OBn), 65.8 (br s, $\underline{C}H_2$OBn), 57.8 (O$\underline{C}H_3$, major anomer), 56.3 (O$\underline{C}H_3$, minor anomer) (2 × CF_2 not resolved); ^{19}F NMR (282 MHz, $CDCl_3$) δ −122.8 (d, J = 266.5 Hz, major anomer), −123.0 (d, J = 266.5 Hz, minor anomer), −132.0 to −128.6 (4F, m), −145.2 (d, J = 266.5 Hz, minor anomer), −147.5 (dt, J = 266.5, 12.9 Hz, major anomer); HRMS (MS+) for $C_{14}H_{16}F_4NaO_5$ $(M + Na)^+$ calcd 363.0826, found 363.0831.

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(*rac*)-Methyl 6-*O*-Benzyl-3,4-dideoxy-3,3,4,4-tetrafluoro-β-*threo*-hexopyranoside (±β-70) and α-*erythro*-Hexopyranoside (±α-71). To a solution of ±**68** (500 mg, 1.47 mmol, 1 equiv) in dry Et_2O (10 mL) were added $NaBH_4$ (2.2 equiv) and 10 drops of EtOH. The reaction mixture was stirred at rt for 7 h, after which some starting material could still be observed by TLC. One equivalent of $NaBH_4$ was added, and the resultant mixture was stirred overnight, quenched with water (20 mL), and extracted with Et_2O (3 × 40 mL). Organic extracts were dried over $MgSO_4$, filtered, and concentrated to give a 1.3:1 mixture of ±**β-70** and ±**α-71** as a colorless oil (440 mg, 92%), which was used without any further purification for the next step. Data for mixture: IR (neat cm^{-1}) 3415 (w, br), 2939 (w), 1197 (m), 1102 (s), 1027 (s); MS (EI) *m*/*z* (%) 324 ($M^{+\bullet}$, 2), 305 (3), 292 (M − $MeOH^{+\bullet}$, 2), 291 (3), 107 (14), 105 (14), 91 ($C_7H_7^+$, 100). Data for ±**β-70**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.29 (5H, m, H_{Ar}), 4.71 (1H, dt, *J* = 3.7, 1.3 Hz, H-1), 4.65 (1H, d, *J* = 11.9 Hz, CHHPh), 4.60 (1H, dd, *J* = 11.9, 1.9 Hz, CHHPh), 4.17−4.09 (1H, m, H-2), 4.09−3.97 (1 H, m, H-5), 3.94 (1H, dd, *J* = 11.1, 3.0 Hz, H-6a), 3.82 (1H, dd, *J* = 11.0, 7.5 Hz, H-6b), 3.63 (3H, s, OCH_3), 2.66 (1H, d, *J* = 5.3 Hz, OH-2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.5 ($C_{q,Ar}$), 128.5 (2C, CH_{Ar}), 127.9 (CH_{Ar}), 127.5 (2C, CH_{Ar}), 99.5 (d, *J* = 8.8 Hz, C-1), 73.7 (CH_2Ph), 70.6 (dd, *J* = 31.0, 20.0 Hz, C-2), 68.6 (t, *J* = 19.8 Hz, C-5), 66.2 (C-6), 57.3 (OCH_3) (2 × CF_2 not resolved); ^{19}F NMR (282 MHz, $CDCl_3$) δ −121.5 (d, *J* = 275.1 Hz), −129.9 (d, *J* = 262.2 Hz), −131.4 to −133.1 (2F, m); HRMS (MS+) for $C_{14}H_{16}F_4NaO_4$ (M + Na)$^+$ calcd 347.0877, found 347.0882. Data for ±**α-71**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.29 (5H, m, H_{Ar}), 4.92 (1H, t, *J* = 4.2 Hz, H-1), 4.65 (1H, d, *J* = 11.9 Hz, CHHPh), 4.60 (1H, dd, *J* = 11.9, 1.9 Hz, CHHPh), 4.34−4.23 (1H, m, H-5), 4.09−3.97 (1H, m, H-2), 3.90 (1H, ddd, *J* = 11.1, 2.7, 0.6 Hz, H-6a), 3.75 (1H, dd, *J* = 11.1, 7.5 Hz, H-6b), 3.51 (3H, s, OCH_3), 2.72 (1H, d, *J* = 11.9 Hz, OH-2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.4 ($C_{q,Ar}$), 128.5 (2C, CH_{Ar}), 127.9 (CH_{Ar}), 127.7 (2C, CH_{Ar}), 98.0 (d, *J* = 8.8 Hz, C-1), 73.8 (CH_2Ph), 73.2 (dd, *J* = 27.8, 23.0 Hz, C-2), 67.5 (t, *J* = 24.2 Hz, C-5), 65.7 (C-6), 56.3 (OCH_3) (2 × CF_2 not resolved); ^{19}F NMR (282 MHz, $CDCl_3$) δ−128.1 (dd, *J* = 254.0, 21.5 Hz), −133.1 to −131.4 (3F, m); HRMS (MS+) for $C_{14}H_{16}F_4NaO_4$ (M + Na)$^+$ calcd 347.0877, found 347.0879.

(2*R*)-1-(2-Naphthylmethyl)oxy-4-bromo-3,3,4,4-tetrafluorobutane-2-ol (72). This alcohol was obtained from its corresponding naproxen ester **92**[26] (the optical rotation of **92** has not yet been reported: $[\alpha]_D$ +32.6 (*c* 0.478, $CHCl_3$, 23 °C)). To the ester **92** (20.1 g, 33.9 mmol, 1 equiv) in THF (200 mL) was added ground NaOH (14.9 g, 373 mmol, 11 equiv), and the reaction mixture was stirred at reflux for 1 h. The solvents were reduced in vacuo to yield a crude residue which was taken up in saturated aq $NaHCO_3$ (500 mL) and extracted with Et_2O (3 × 500 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated. Purification by flash chromatography (petroleum ether/Et_2O 80:20 to 70:30) afforded the desired enantiopure **72** (12.6 g, 33.0 mmol, 97%) as a white solid; NMR spectra are in agreement with reported data:[26] $[\alpha]_D$ +9.70 (*c* 0.505, $CHCl_3$, 22 °C).

(4*R*)-1-Bromo-1,1,2,2-tetrafluoro-3,4-(2-naphthylmethylidenedioxy)-butane (73). To a mixture of **72** (12.0 g, 31.5 mmol, 1 equiv) and dried powdered 4 Å MS (26 g) in dry CH_2Cl_2 (300 mL) was added DDQ (9.29 g, 40.9 mmol, 1.3 equiv) at 0 °C under Ar atmosphere. The mixture was stirred for 5 h at rt, quenched with aqueous ascorbate buffer (L-ascorbic acid (0.7 g), citric acid monohydrate (1.2 g), and NaOH (0.92 g) in water (100 mL), 300 mL), and then filtered through Celite. The filter cake was rinsed with $CHCl_3$ (300 mL), and layers were partitioned. The aqueous layer was extracted with $CHCl_3$ (300 mL), and the combined organic extracts were washed with saturated aq $NaHCO_3$ (300 mL), dried over $MgSO_4$, and evaporated in vacuo. Purification by flash chromatography (petroleum ether/Et_2O 80:20) afforded a mixture of enantiopure acetal diastereoisomers **73** (9.57 g, 25.2 mmol, 80%) as a pale yellow solid. An analytical sample of pure diastereomers was obtained from racemic material. Data for *trans*-**73**: R_f 0.59 (petroleum ether/Et_2O 80:20); mp 86 °C ($CHCl_3$); IR (neat cm^{-1}) 3060 (w), 2903 (w), 1125 (s), 1088 (s), 897 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.95 (1H, m, H_{Ar}), 7.94−7.83 (3H, m, H_{Ar}), 7.59 (1H, dd, *J* = 8.5, 1.6 Hz, H_{Ar}), 7.56−7.50 (1H, m, H_{Ar}), 6.16 (1H, s, CHOO), 4.83 (1H, dddd, $^3J_{HF}$ = 17.4, $^3J_{HH}$ = 7.2, $^3J_{HF}$ = 6.8, $^3J_{HH}$ = 6.6 Hz, $CHCF_2$), 4.49 (1H, dd, $^2J_{HH}$ = 9.2, $^3J_{HH}$ = 7.2 Hz, CHHCHO), 4.34 (1H, dd, $^2J_{HH}$ = 9.2, $^3J_{HH}$ = 6.6 Hz, CHHCHO); ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.1 ($C_{q,Ar}$), 133.2 ($C_{q,Ar}$), 132.8 ($C_{q,Ar}$), 128.3 (CH_{Ar}), 128.5 (CH_{Ar}), 127.8 (CH_{Ar}), 126.4 (CH_{Ar}), 126.6 (CH_{Ar}), 126.8 (CH_{Ar}), 123.5 (CH_{Ar}), 116.8 (tt, $^1J_{CF}$ 311.8, $^2J_{CF}$ = 39.5 Hz, CF_2), 114.2 (ddt, $^1J_{CF}$ 262.0, $^1J_{CF}$ 256.1, $^2J_{CF}$ = 32.2 Hz, CF_2), 106.0 (CHOO), 72.3 (dd, $^2J_{CF}$ = 30.7, $^2J_{CF}$ = 20.5 Hz, CHCF2), 65.3 (CH_2CHO); ^{19}F NMR (282 MHz, $CDCl_3$) δ −63.8 (dd, $^2J_{FF}$ 182.7, $^3J_{FF}$ = 7.5 Hz, CFFBr), −64.9 (dd, $^2J_{FF}$ 182.7, $^3J_{FF}$ = 5.9 Hz, CFFBr), −118.0 (dt, $^2J_{FF}$ 271.3, *J* = 5.9 Hz, CHOCFF), −123.1 ppm (ddd, $^2J_{FF}$ 271.3, $^3J_{HF}$ = 17.2, $^3J_{FF}$ = 7.5 Hz, CHOCFF); MS (EI) *m*/*z* (%) 378 and 380 ($M^{+\bullet}$, 9), 377 and 379 ($(M - H^{\bullet})^+$, 5), 299 ($(M - Br^{\bullet})^+$, 5), 155 ($NAPCO^+$, 30), 128 ($NAP^{+\bullet}$, 100); HRMS (MS+) for $C_{15}H_{12}{}^{79}BrF_4O_2$ (M + H)$^+$ calcd 378.9957, found 378.9955. Data for *cis*-**73**: R_f 0.41 (petroleum ether/Et_2O 80:20); mp 82 °C ($CHCl_3$); IR (neat cm^{-1}) 3060 (w), 2906 (w), 1151 (s), 1076 (s), 818 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (1H, s, H_{Ar}), 7.93−7.83 (3H, m, H_{Ar}), 7.64 (1H, dd, *J* = 8.5, 1.2 Hz, H_{Ar}), 7.57−7.48 (2H, m, H_{Ar}), 6.02 (s, 1H, CHOO), 4.85−4.72 (1H, m, $CHCF_2$), 4.60 (1H, dd, $^2J_{HH}$ = 9.5, $^3J_{HH}$ = 2.3 Hz, CHHCHO), 4.27 ppm (1H, dd, $^2J_{HH}$ = 9.5, $^3J_{HH}$ = 7.7 Hz, CHHCHO); ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.2 ($C_{q,Ar}$), 132.7 ($C_{q,Ar}$), 132.8 ($C_{q,Ar}$), 128.4 (CH_{Ar}), 128.5 (CH_{Ar}), 127.8 (CH_{Ar}), 127.2 (CH_{Ar}), 126.8 (CH_{Ar}), 126.3 (CH_{Ar}), 123.7 (CH_{Ar}), 116.9 (ddt, $^1J_{CF}$ 314.7, $^1J_{CF}$ 311.8, $^2J_{CF}$ = 39.5 Hz, CF_2), 113.5 (ddt, $^1J_{CF}$ 264.9, $^1J_{CF}$ 253.2, $^2J_{CF}$ = 30.7 Hz, CF_2), 106.4 (CHOO), 72.6 (dd, $^2J_{CF}$ = 33.7, $^2J_{CF}$ = 22.0 Hz), 65.8 (CH_2CHO); ^{19}F NMR (282 MHz, $CDCl_3$) δ −63.2 (dd, $^2J_{FF}$ 181.1, *J* = 8.1 Hz, CFFBr), −64.2 (dd, $^2J_{FF}$ 181.1, *J* = 4.8 Hz, CFFBr), −115.3 (dt, $^2J_{FF}$ 269.0, *J* = 5.0 Hz, CHOCFF), −126.1 ppm (ddd, $^2J_{FF}$ 269.0, *J* = 18.1, *J* = 8.3 Hz, CHOCFF); MS (EI) *m*/*z* (%) 378 and 380 ($M^{+\bullet}$, 11), 377 and 379 ($(M - H^{\bullet})^+$, 7), 299 ($(M - Br^{\bullet})^+$, 6), 155 ($NAPCO^+$, 37), 128 ($NAP^{+\bullet}$, 100); HRMS (MS+) for $C_{15}H_{12}{}^{79}BrF_4O_2$ (M + H)$^+$ calcd 378.9957, found 378.9943.

(2*R*)-3,3,4,4-Tetrafluoro-7-phenylhept-6-ene-1,2,5-triol (75). To a solution of **73** (7.00 g, 18.5 mmol, 1 equiv) in THF (75 mL) was added cinnamaldehyde (5.58 mL, 44.3 mmol, 2.4 equiv) and then cooled to −78 °C. After 10 min, MeLi (1.5 M in Et_2O, 27.7 mL, 44.3 mmol, 2.4 equiv) was added dropwise and the reaction mixture was stirred for 2.5 h. The reaction was quenched with saturated aq NH_4Cl (100 mL) and extracted with Et_2O (3 × 300 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo and used without further purification. To a solution of the crude acetal (m_{th}: 7.98 g, 18.5 mmol, 1 equiv) in MeOH (200 mL) was added PTSA (318 mg, 1.85 mmol, 0.1 equiv), and the resultant mixture was stirred at rt for 5 h. The reaction mixture was quenched with saturated aq $NaHCO_3$ (100 mL), diluted with water (200 mL,) and extracted with EtOAc (4 × 250 mL). The combined organic layers were reduced in vacuo to 500 mL, washed with brine (150 mL), dried (Na_2SO_4), filtered, and concentrated to offer 14.3 g of crude material. Purification by column chromatography (petroleum ether/acetone, 75:25 to 50:50) afforded 3.88 g (13.2 mmol, 71% over two steps) of pure triol **75** as a 1:1 mixture of diastereoisomers as a white solid: R_f 0.26 (petroleum ether/acetone 65:35); IR (neat cm^{-1}) 3365 (br, m), 1257 (m), 1099 (s), 968 (m); ^{1}H NMR (400 MHz, acetone-d_6) δ 7.49 (4H, d, *J* = 7.6 Hz, H_{Ar}), 7.40−7.32 (4H, m, H_{Ar}), 7.32−7.24 (2H, m, H_{Ar}), 6.88 (2H, d, $^3J_{HH}$ = 15.9 Hz, H-7, both dia), 6.39 (1H, dd, $^3J_{HH}$ = 15.9, $^3J_{HH}$ = 6.0 Hz, H-6, dia 1), 6.37 (1H, dd, $^3J_{HH}$ = 15.9, $^3J_{HH}$ = 5.9 Hz, H-6, dia 2), 5.43 (2H, d, $^3J_{HH}$ = 6.2 Hz, OH-5, both dia), 5.23 (1H, d, $^3J_{HH}$ = 6.2 Hz, OH-2, dia 1), 5.17 (1H, d, $^3J_{HH}$ = 6.4 Hz, OH-2, dia 2), 4.94−4.80 (2H, m, H-5, both dia), 4.35−4.19 (2H, m, H-2, both dia), 4.14−3.97 (2H, m, OH-1, both dia), 3.95−3.83 (2H, m, H-6a, both dia), 3.80−3.67 (2H, m, H-6b, both dia); ^{13}C NMR (101 MHz, acetone-d_6) δ 137.4 ($C_{q,Ar}$), 135.2 (C-7, dia 1), 135.1 (C-7, dia 2), 129.6 (CH_{Ar}), 129.0 (CH_{Ar}), 127.6 (CH_{Ar}), 124.1 (C-6), 121.1−114.6 (4 × CF_2), 72.3 (dd, $^2J_{CF}$ = 25.7, 23.5 Hz, C-2 or C-5), 71.9 (dd, $^2J_{CF}$ = 26.4, 24.9 Hz,, C-2 or C-5), 71.9 (t, $^2J_{CF}$ = 24.3 Hz, C-2 or C-5), 71.7 (dd, $^2J_{CF}$ = 27.9, 23.5 Hz,, C-2 or C-5), 61.3 (C-1); ^{19}F NMR (376 MHz, acetone-d_6) δ −119.4 (app dt, *J* = 271.5, 6.5 Hz), −119.9

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(app dtd, J = 270.5, 6.6, 6.6, 1.4 Hz), −120.5 (app dt, J = 274.9, 6.9 Hz), −121.0 (app dt, J = 273.6, 6.8 Hz), −123.9 (ddd, J = 274.9, 16.4, 6.6 Hz), −124.9 (app ddd, J = 273.6, 17.5, 6.2 Hz), −125.5 (ddd, J = 271.5, 15.9, 6.6 Hz), −126.1 (app ddd, J = 270.5, 16.7, 5.8 Hz, 1F); {^{1}H}^{19}F NMR (376 MHz, acetone-d_6) δ −119.4 (dd, J = 271.5, 5.9 Hz), −119.9 (ddd, J = 270.5, 6.5, 2.2 Hz), −120.5 (dd, J = 274.9, 5.9 Hz), −121.0 (ddd, J = 273.6, 6.1, 2.2 Hz), −123.9 (dd, J = 274.9, 6.6 Hz), −124.9 (ddd, J = 273.6, 6.5, 2.7 Hz), −125.5 (dd, J = 271.5, 6.6 Hz), −126.1 (ddd, J = 270.5, 6.1, 2.7 Hz); HRMS (MS+) for $C_{13}H_{14}F_4NaO_3$ (M + Na)$^+$ calcd 317.0777, found 317.0771.

3,4-Dideoxy-3,3,4,4-tetrafluoro-D-*threo*-hexopyranose (6) and D-*erythro*-Hexopyranose (7). Ozone was bubbled through a solution of triol **75** (2.50 g, 8.50 mmol) in MeOH (75 mL) until a light blue color was obtained (20 min). O_2 was bubbled through to remove excess ozone (10 min); then Me_2S (6.24 mL, 85.0 mmol, 10 equiv) was added, and the reaction mixture was allowed to warm to rt and concentrated to offer 2.58 g of crude material. Purification by column chromatography (petroleum ether/acetone 60:40) afforded 1.67 g (7.59 mmol, 89%) of a pure 1:1 mixture of **6** (α/β 65:35) and **7** (68:32) as a colorless syrup that solidified into an off-white solid on standing. The epimers were separated by the three-step procedure as described.

(*rac*)-1,2,6-Tri-*O*-acetyl-3,4-dideoxy-3,3,4,4-tetrafluoro-*threo*-hexopyranoside (±76) and *erythro*-Hexopyranoside (±77). To a solution of ±**6** and ±**7** (1.20 g, 5.45 mmol, 1 equiv) in pyridine (12 mL) was added Ac_2O (1.86 mL, 19.6 mmol, 3.6 equiv). The resultant mixture was stirred at rt for 17 h and quenched with EtOH (10 mL). Volatiles were evaporated and then fully removed by azeotropic distillation with toluene and $CHCl_3$ to afford 1.79 g (5.18 mmol, 95%) of ±**76** and ±**77** as a colorless oil. Repeated column chromatography ($CHCl_3$/EtOAc 96:4) afforded 486 mg (1.40 mmol, 26%) of pure ±**77** as a 4:96 α/β mixture. Recrystallization was achieved from chloroform. Data for ±***β*-77**: R_f 0.52 ($CHCl_3$/EtOAc 90:10); mp 62 °C ($CHCl_3$); IR (neat cm^{-1}) 2973 (w), 1770 (m), 1750 (m), 1199 (s), 1056 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (1H, d, J = 8.6 Hz, H-1) 5.41 (1H, ddt, $^3J_{H-F3ax}$ 20.8, J = 8.6, 3.9 Hz, H-2) 4.47 (1H, dd, J = 12.2, 3.4 Hz, H-6$_a$) 4.32 (1H, dd, J = 12.2, 7.1 Hz, H-6$_b$) 4.18 (1H, ddddd, $^3J_{H-F4ax}$ 22.0, J = 7.1, 3.5, 3.4, 1.1 Hz, H-5) 2.18 (3H, s) 2.13 (3H, s) 2.09 (3H, s) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3 (C═O) 168.4 (C═O) 168.3 (C═O) 115.7−109.6 (2 × CF_2) 90.2 (d, J = 9.2 Hz, C-1) 71.4 (ddd, J = 27.1, 22.0, 2.6 Hz, C-5) 67.8 (dddd, J = 20.2, 16.9, 2.9, 1.5 Hz, C-2) 59.2 (dd, J = 4.6, 2.2 Hz, C-6) 20.6 (CH_3) 20.5 (CH_3) 20.2 (CH_3) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −128.04 (m, J = 258.6 Hz) −132.05 (m, J = 262.6 Hz) −132.26 (m, J = 258.6 Hz) −134.80 (ddd, J = 263.6, 14.8, 9.6 Hz) ppm; MS (ESI+) (m/z) 369 (M+Na)$^+$; HRMS (MS+) for $C_{12}H_{14}F_4NaO_7$ (M + Na)$^+$ calcd 369.0568, found 369.0575.

6-*O*-*tert*-Butyldimethylsilyl-3,4-dideoxy-3,3,4,4-tetrafluoro-D-*threo*-hexopyranose (78) and D-*erythro*-Hexopyranose (79). To a solution of sugars **6**/**7** (450 mg, 2.04 mmol, 1 equiv) in dry DMF (6.75 mL) were added imidazole (181 mg, 2.66 mmol, 1.3 equiv) and TBDMSOTf (0.563 mL, 2.45 mmol, 1.2 equiv) at 0 °C. The resultant mixture was stirred at rt for 2.5 h, diluted with brine (20 mL) and water (5 mL), extracted with EtOAc (4 × 50 mL), dried ($MgSO_4$), filtered, and concentrated. Purification by column chromatography (compound loaded as $CHCl_3$ solution, eluted with petroleum ether/Et_2O, 60:40) afforded 654 mg (1.96 mmol, 96%) of a pure 1:1 mixture of **78** (α/β 44:56) and **79** (51:49) as a colorless gummy solid. Another experiment starting from 880 mg (4.00 mmol) afforded 1.030 g (3.08 mmol, 77%): R_f 0.26 (petroleum ether/Et_2O, 60:40); IR (neat cm^{-1}) 3386 (w), 2932 (w), 1099 (s), 1034 (s), 834 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.43 (1H, q, J = 3.9 Hz, H-1, ***α*-79**), 5.35−5.40 (1H, m, H-1, ***α*-78**), 5.30 (1H, br s, OH-1, ***β*-79**), 5.03 (1H, br s, H-1, ***β*-78**), 4.86 (1H, br d, J = 7.8 Hz, ***β*-79**), 4.71 (1H, br d, J = 8.3 Hz, OH-1, ***β*-78**), 4.55 (1H, d, J = 3.1 Hz, OH-1, ***α*-79**), 4.47−4.28 (2H, m, H-5, ***α*-79**, H-5, ***α*-78**), 4.31 (1H, br s, OH-1, ***α*-78**), 4.14−3.95 (7H, m, H-2, H-6$_a$, ***α*-79**, H-6$_a$, ***β*-79**, H-2, H-6$_a$, ***α*-78**, H-2, H-6$_a$, ***β*-78**), 3.95−3.79 (7H, m, H-6$_b$, ***α*-79**, H-2, H-5, H-6$_b$, ***β*-79**, H-6$_b$, *α*-78, H-5, H-6$_b$, ***β*-78**), 3.34 (1H, br s, OH-2, ***β*-78**), 3.08 (1H, br d, J = 10.7 Hz, OH-2, ***α*-79**), 2.97 (1H, br s, OH-2, ***α*-78**), 0.92 (9H, s, $CH_{3,tBu}$), 0.92 (9H, s, $CH_{3,tBu}$), 0.91 (18H, s, $CH_{3,tBu}$), 0.12 (6H, s, CH_3), 0.12 (6H, s, CH_3), 0.11 (12H, s, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 94.9 (d, J = 9.5 Hz, C-1, ***β*-79**), 94.3 (d, J = 5.9 Hz, C-1, ***α*-78**), 92.9 (d, J = 7.3 Hz, C-1, ***β*-78**), 91.3 (d, J = 8.8 Hz, C-1, ***α*-79**), 74.2 (dd, J = 26.4, 22.0 Hz, C-5, ***β*-78**), 73.8 (dd, J = 25.7, 22.0 Hz, C-5, ***β*-79**), 71.6 (t, J = 17.6 Hz, C-2, ***β*-79**), 71.1 (dd, J = 32.3, 19.1 Hz, C-2, ***β*-78**), 70.9 (dd, J = 30.1, 19.1 Hz, C-2, ***α*-78**), 69.8 (dd, J = 27.1, 22.0 Hz, C-5, ***α*-78**), 68.9 (t, J = 23.9 Hz, C-5, ***α*-79**), 68.4 (t, J = 19.1 Hz, C-2, ***α*-79**), 59.9−59.5 (m, C-6, all isomers), 25.8 ($CH_{3,tBu}$), 25.8 ($CH_{3,tBu}$), 25.8 ($CH_{3,tBu}$), 18.5 ($C_{q,tBu}$), 18.4 ($C_{q,tBu}$), 18.3 ($C_{q,tBu}$), −5.5 (CH_3), −5.5 (CH_3), −5.6 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm −118.9 (m, $^2J_{FF}$ 273.5 Hz, ***α*-78**), −121.3 (m, $^2J_{FF}$ 274.8 Hz, ***β*-78**), −127.9 (dd, $^2J_{FF}$ 255.8, 20.8 Hz, ***α*-79**), −129.5 (dddd, $^2J_{FF}$ 265.3, 23.8, 15.4, 7.8 Hz, ***α*-78**), −130.0 (dddd, $^2J_{FF}$ 267.5, 24.1, 16.0, 8.9 Hz, ***β*-78**), −132.5 to −131.4 (6F, m, 2 × ***α*-78**, ***β*-78**, ***α*-79**, 2 × ***β*-79**), −133.3 (2F, app t, J = 12.1 Hz, ***α*-79**), −134.4 to −133.5 (m, ***β*-79**), −134.7 to −133.8 (m, ***β*-78**), −134.8 (ddd, $^2J_{FF}$ 262.1, 13.7, 8.5 Hz, ***β*-79**); HRMS (MS+) for $C_{12}H_{22}F_4NaO_4Si$ (M + Na)$^+$ calcd 357.1116, found 357.1109. An analytical pure sample of **79** was obtained from hydrogenolysis of a pure fraction of **81**: to a solution of **81** (36 mg, 0.076 mmol, 1 equiv) in MeOH (1 mL) was added $Pd(OH)_2$/C (20%, 11 mg, 0.165 mmol, 0.2 equiv), and H_2 was bubbled through the solution via a needle for 10 min. The reaction mixture was left stirring at rt under H_2 for 16 h, filtered over a pad of Celite, and concentrated in vacuo. Purification by column chromatography (petroleum ether/Et_2O, 60:40) afforded 25 mg (0.075 mmol, 99%) of **79** as 70:30 α/β mixture ($CDCl_3$) as a white solid: R_f 0.26 (petroleum ether/Et_2O, 60:40); $[\alpha]_D$ +61.1 (c 0.509, acetone, 22 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.43 (1H, q, J = 4.3 Hz, H-1α), 4.90−4.83 (1H, m, H-1β), 4.62 (1H, d, $^3J_{HH}$ = 4.7 Hz, OH-1β), 4.42−4.27 (1H, m, H-5α), 4.31 (1H, d, $^3J_{HH}$ = 3.9 Hz, OH-1α), 4.12−3.94 (2H, m, H-2α, H-6$_a\beta$), 4.04 (1H, dd, $^2J_{HH}$ = 11.4, $^3J_{HH}$ = 3.0 Hz, H-6$_a\alpha$), 3.93−3.79 (3H, m, H-2β, H-5β, H-6$_b\beta$), 3.87 (1H, dd, $^2J_{HH}$ = 11.4, $^3J_{HH}$ = 7.5 Hz, H-6$_b\alpha$), 3.30 (1H, d, $^3J_{HH}$ = 4.5 Hz, OH-2β), 2.81 (1H, d, $^3J_{HH}$ = 11.4 Hz, OH-2α), 0.92 (9H, s, $CH_{3,tBu}\alpha$), 0.91 (9H, s, $CH_{3,tBu}\beta$), 0.12 (6H, s, $CH_3\alpha$), 0.11 (6H, s, $CH_3\beta$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 116.1−110.1 (2 × CF_2, α + β), 95.0 (d, $^3J_{CF}$ 8.8 Hz, C-1β), 91.4 (d, $^3J_{CF}$ 8.8 Hz, C-1α), 73.9 (dd, $^2J_{CF}$ = 26.4, 22.0 Hz, C-2β or C-5β), 71.9 (td, $^2J_{CF}$ = 18.5, J = 2.2 Hz, C-2β or C-5β), 69.0 (t, $^2J_{CF}$ = 23.5 Hz, C-5α), 68.5 (t, $^2J_{CF}$ = 19.4 Hz, C-2α), 59.8−59.6 (C-6α + β), 25.82 ($CH_{3,tBu}\alpha$), 25.79 ($CH_{3,tBu}\beta$), 18.44 ($C_{q,tBu}\alpha$), 18.37 ($C_{q,tBu}\beta$), −5.4 (2 × $CH_3\alpha$ + β), −5.46 ($CH_3\alpha$), −5.5 ($CH_3\beta$); ^{19}F NMR (376 MHz, $CDCl_3$) δ −127.9 (dd, $^2J_{FF}$ 255.8, 20.8 Hz, α), −132.5 to −131.4 (m, α, 2 × β), −133.3 (app t, J = 12.1 Hz, 2 × α), −133.5 to −134.3 (m, J = 257.5 Hz, β), −134.4 to −135.2 (m, J = 261.8 Hz, β).

2-Naphthylmethyl 6-*O*-*tert*-Butyldimethylsilyl-3,4-dideoxy-3,3,4,4-tetrafluoro-D-*threo*-hexopyranose (80) and D-*erythro*-Hexopyranoside (81). To a solution of **78**/**79** (950 mg, 2.84 mmol, 1 equiv) in CH_3CN (17.5 mL) were added NAPBr (1.26 g, 5.68 mmol, 2 equiv) and Ag_2O (1.65 g, 7.10 mmol, 2.5 equiv). The reaction mixture was stirred at rt for 2 h, filtered through Celite, and concentrated. Purification by column chromatography (petroleum ether/Et_2O, 90:10 to 70:30) afforded 1.11 g (2.34 mmol, 82%) of a mixture of **80** and **81** alongside some 2-O-NAP isomers as a white solid. Analytical samples of pure **81** and of a pure mixture of **80** and **81** could be obtained. Data for **81**: R_f 0.44 (petroleum ether/Et_2O 70:30); $[\alpha]_D$ −30.1 (c 0.799, acetone, 23 °C); IR (neat cm^{-1}) 3442 (br, w), 3056 (w), 2930 (w), 1256 (m), 1102 (s), 1033 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91−7.80 (4H, m, H_{Ar}), 7.56−7.46 (3H, m, H_{Ar}), 5.12 (1H, d, $^2J_{HH}$ = 11.6 Hz, H-7$_a$), 4.85 (1H, d, $^2J_{HH}$ = 11.6 Hz, H-7$_b$), 4.65 (1H, br d, $^3J_{HH}$ = 7.9 Hz, H-1), 4.11−4.05 (1H, m, H-6$_a$), 4.03−3.81 (3H, m, H-2, H-5, H-6$_b$), 2.57 (1H, d, $^3J_{HH}$ = 4.5 Hz, OH-2), 0.96 (s, 9H, tBu), 0.16 (s, 3H, CH_3), 0.15 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.4 ($C_{q,Ar}$), 133.2 ($C_{q,Ar}$), 133.2 ($C_{q,Ar}$), 128.6 (CH_{Ar}), 127.9 (CH_{Ar}), 127.7 (CH_{Ar}), 127.5 (CH_{Ar}), 126.3 (CH_{Ar}), 126.4 (CH_{Ar}), 125.9 (CH_{Ar}), 116.8−110.3 (m, 2 × CF_2), 99.4 (d, $^4J_{CF}$ 9.2 Hz, C-1), 73.9 (dd, $^2J_{CF}$ = 24.9, 22.7 Hz, C-5), 71.4 ($\underline{C}H_2$Nap), 71.6−70.9 (C-2), 59.5 (d, J = 2.9 Hz, C-6), 25.8 ($CH_{3,tBu}$), 18.3 ($C_{q,tBu}$), −5.3 (CH_3), −5.5 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ −132.3 to −131.3 (m, 2 × C$\underline{F}$F), −134.3 to −133.4 (m, CF$\underline{F}$), −135.4

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to −134.5 (m, CFF); HRMS (MS+) for $C_{23}H_{30}F_4NaO_4Si$ $(M + Na)^+$ calcd 497.1742, found 497.1755. Data for **80**: R_f 0.33 (petroleum ether/Et_2O 70:30); unambiguous resonances ^1H NMR (400 MHz, $CDCl_3$) δ 7.91−7.79 (4H, m, CH_{Ar}), 7.57−7.46 (3H, m, CH_{Ar}), 5.13 (1H, d, $^2J_{HH}$ = 11.8 Hz, H-7$_a$), 4.83−4.79 (1H, m, H-1), 4.90 (1H, d, $^2J_{HH}$ = 11.8 Hz, H-7$_b$), 2.68 (1H, d, $^3J_{HH}$ = 5.3 Hz, OH-2), 0.98 (9H, s, $CH_{3,tBu}$), 0.18 (s, 3H, CH_3), 0.16 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.0 ($C_{q,Ar}$), 133.2 ($C_{q,Ar}$), 133.3 ($C_{q,Ar}$), 128.6 (CH_{Ar}), 127.9 (CH_{Ar}), 127.7 (2C, CH_{Ar}), 126.4 (2C, CH_{Ar}), 126.0 (CH_{Ar}), 96.4 (d, $^3J_{CF}$ 8.1 Hz), 74.6 (dd, $^2J_{CF}$ = 26.4, 23.5 Hz, C-5), 71.0 (dd, $^2J_{CF}$ = 30.8, 19.8 Hz, C-2), 70.8 (C-7), 59.8−59.6 (C-6), 25.8 ($CH_{3,tBu}$), 18.3 ($C_{q,tBu}$), −5.3 (CH_3), −5.4 (CH_3) (2 × $\underline{C}F_2$ not visible); ^{19}F NMR (376 MHz, $CDCl_3$) δ −120.8 (br d, $^2J_{FF}$ = 273.1 Hz, F-3$_{ax}$), −129.9 (dddd, $^2J_{FF}$ = 266.2, J = 22.5, 16.5, 8.7 Hz, F-3$_{eq}$), −132.0 to −133.6 (m, 2 × F-4).

2-Naphthylmethyl 3,4-Dideoxy-3,3,4,4-tetrafluoro-D-*threo*-hexopyranose (82) and D-*erythro*-Hexopyranoside (83). To the mixture of **80** and **81** (1.11 g, 2.34 mmol, 1 equiv), in THF (20 mL) at 0 °C was added TBAF (1 M in THF, 2.45 mL, 2.45 mmol, 1.05 equiv), and the resulting mixture was stirred at 0 °C for 1 h and concentrated. Purification by column chromatography ($CHCl_3/Et_2O$, 80:20, with the crude was loaded as a solution in pure $CHCl_3$) afforded 325 mg (0.902 mmol, 38%) of pure **82** as a white solid and 327 mg (0.908 mmol, 39%) of **83** together with a small amount of unknown impurities as a light brown solid. Data for **82**: R_f 0.26 ($CHCl_3/Et_2O$ 70:30); mp 160 °C ($CHCl_3$); $[\alpha]_D$ −48.2 (c 0.517, acetone, 22 °C); IR (neat cm^{-1}) 3444 (br, w), 3205 (br, w), 2925 (w), 1206 (m), 1113 (s), 1029 (s); ^1H NMR (400 MHz, acetone-d_6) δ 8.00−7.81 (4H, m, CH_{Ar}), 7.60−7.46 (3H, m, CH_{Ar}), 5.16 (1H, d, $^2J_{HH}$ = 12.0 Hz, H-7$_a$), 5.06−5.01 (1H, m, H-1), 4.97 (1H, d, ^3J = 5.0 Hz, OH-2), 4.94 (1H, d, $^2J_{HH}$ = 12.0 Hz, H-7$_b$), 4.34−4.21 (2H, m, H-2, OH-6), 4.04−3.86 (3H, m, H-5, 2 × H-6); ^{13}C NMR (101 MHz, acetone-d_6) δ 135.8 ($C_{q,Ar}$), 134.3 ($C_{q,Ar}$), 134.1 ($C_{q,Ar}$), 129.0 (CH_{Ar}), 128.8 (CH_{Ar}), 128.6 (CH_{Ar}), 127.8 (CH_{Ar}), 127.2 (CH_{Ar}), 127.0 (CH_{Ar}), 127.0 (CH_{Ar}), 117.3−111.3 (2 × CF_2), 99.3 (d, J = 8.4 Hz, C-1), 75.5 (dd, $^2J_{CF}$ = 27.7, 22.6 Hz, C-5), 71.7 (C-7), 72.1−71.4 (C-2), 59.4−59.2 (C-6); ^{19}F NMR (376 MHz, acetone-d_6) δ −120.1 (1F, br d, $^2J_{FF}$ = 266.2 Hz), −128.9 to −129.9 (1F, m), −131.3 to −133.1 (2F, m); MS (EI) m/z (%) 360 ($M^{+\bullet}$, 4), 141 (NAP^+, 100); HRMS (MS+) for $C_{17}H_{16}F_4NaO_4$ $(M + Na)^+$ calcd 383.0877, found 383.0878. Data for **83**: R_f 0.44 ($CHCl_3/Et_2O$ 70:30); $[\alpha]_D$ −37.7 (c 0.487, acetone, 22 °C); IR (neat cm^{-1}) 3398 (br, w), 3239 (br, w), 3060 (w), 2952 (w), 1290 (m), 1098 (s), 1023 (s); ^1H NMR (400 MHz, acetone-d_6) δ 7.96−7.83 (m, 4H, H_{Ar}), 7.58−7.46 (m, 3H, H_{Ar}), 5.72 (d, $^3J_{HH}$ = 6.4 Hz, 1H, OH-2), 5.15 (d, $^2J_{HH}$ = 12.0 Hz, 1H, H-7$_a$), 4.92 (d, $^2J_{HH}$ = 12.0 Hz, 1H, H-7$_b$), 4.82 (d, $^3J_{HH}$ = 8.0 Hz, 1H, H-1), 4.30 (dd, $^3J_{HH}$ = 6.9, 5.7 Hz, 1H, OH-6), 4.06−3.81 (m, 4H, H-2, H-5, 2 × H-6); ^{13}C NMR (101 MHz, acetone-d_6) δ 135.9 ($C_{q,Ar}$), 134.3 ($C_{q,Ar}$), 134.1 ($C_{q,Ar}$), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.6 (CH_{Ar}), 127.6 (CH_{Ar}), 127.1 (CH_{Ar}), 127.0 (CH_{Ar}), 126.9 (CH_{Ar}), 101.4 (d, J = 10.3 Hz, C-1), 74.3 (dd, $^2J_{CF}$ = 25.7, 22.0 Hz, C-5), 72.0 (t, J = 17.6 Hz, C-2), 71.9 (C-7), 59.0 (dd, J = 4.4, 1.5 Hz, C-6); ^{19}F NMR (376 MHz, acetone-d_6) δ −130.8 (app dddd, $^2J_{FF}$ = 255.8, $^3J_{HF}$ = 20.9, $^3J_{FF}$ = 13.9, 10.4 Hz), −131.3 to −132.3 (m, $^2J_{FF}$ = 260.1 Hz), −133.2 (dddd, $^2J_{FF}$ = 255.8, $^3J_{FF}$ = 15.6, 8.7, $^3J_{HF}$ = 6.9 Hz), −135.0 (ddd, $^2J_{FF}$ = 260.1, J = 13.9, 8.7 Hz); MS (EI) m/z (%) 360 ($M^{+\bullet}$, 2), 141 (NAP^+, 100); HRMS (MS+) for $C_{17}H_{16}F_4NaO_4$ $(M + Na)^+$ calcd 383.0877, found 383.0884.

3,4-Dideoxy-3,3,4,4-tetrafluoro-D-*threo*-hexopyranose (6). To a solution of **82** (330 mg, 0.916 mmol, 1 equiv) in MeOH (10 mL) was added $Pd(OH)_2/C$ (20%, 129 mg, 0.183 mmol, 0.2 equiv), and H_2 was bubbled through the solution via a needle for 10 min. The reaction mixture was left stirring at rt under H_2 for 17 h, filtered over a pad of Celite, and concentrated in vacuo. Purification by column chromatography (petroleum ether/acetone, 65:35 to 60:40) afforded 178 mg (0.809 mmol, 88%) of **6** as 63:37 α/β mixture (acetone-d_6) as a white solid: R_f 0.31 (petroleum ether/acetone 60:40); $[\alpha]_D$ +22.2 (c 0.562, acetone, 22 °C); IR (neat, cm^{-1}) 3370 (m, br), 2953 (w), 1195 (m), 1154 (s), 1068 (s); ^1H NMR (400 MHz, acetone-d_6) δ 6.11 (1H, dd, J = 4.6, 2.3 Hz, OH-1α, disappears after D_2O exchange), 5.96 (1H, d, J = 9.5 Hz, OH-1β, disappears after D_2O exchange), 5.28 (1H, t, J = 4.6 Hz, H-1α, simplifies to d, J = 5.7 Hz after D_2O exchange), 5.18 (2H, d, J = 5.8 Hz, OH-2α and OH-2β, disappears after D_2O exchange), 5.07−5.00 (1H, m, H-1β), 4.44−4.31 (1H, m, H-5α), 4.15−4.00 (3H, m, H-2α, H-2β and OH-6β, simplifies after D_2O exchange), 3.98 (1H, t, J = 5.8 Hz, OH-6α, disappears after D_2O exchange), 3.94−3.82 (1H, m, H-5β, H-6α and H-6β), 3.81−3.71 (2H, m, H-6α' and H-6β'); ^{13}C NMR (101 MHz, acetone-d_6) δ 95.6 (d, J = 5.9 Hz, C-1α), 94.3 (d, J = 7.3 Hz, C-1β), 74.9 (dd, J = 27.8, 22.0 Hz, C-5β), 72.2 (dd, J = 27.8, 19.0 Hz, C-2α), 72.1 (dd, J = 30.7, 17.6 Hz, C-2β), 70.6 (dd, J = 27.8, 20.5 Hz, C-5α), 59.2 (dd, J = 5.9, 2.9 Hz, C-6α or C-6β), 59.0 (dd, J = 5.9, 2.9 Hz, C-6α or C-6β) ppm; ^{19}F NMR (282 MHz, acetone-d_6) δ −118.2 (d, J = 266.5 Hz, α), −120.2 (d, J = 266.5 Hz, β), −131.9 to −129.1 (m, 3 × α and 2 × β), −134.1 (d, J = 259.5 Hz, β); $\{^1H\}^{19}F$ NMR (282 MHz, acetone-d_6) δ −118.2 (d, J = 266.5 Hz, α), −120.2 (dt, J = 266.5, 12.9 Hz, β), −131.9 to −129.1 (m, 3 × α and 2 × β), −134.1 (dt, J = 262.2, 12.9 Hz, β); MS (ESI) m/z 284 (M + Na + MeCN)$^+$, HRMS (MS^+) for $C_6H_8F_4NaO_4$ $(M + Na)^+$ calcd 243.0251, found 243.0248. A racemic mixture of **6** was recrystallized from hexane/acetone.

3,4-Dideoxy-3,3,4,4-tetrafluoro-D-*erythro*-hexopyranose (7). To a solution of **83** (297 mg, 0.824 mmol, 1 equiv) in MeOH (18 mL) was added $Pd(OH)_2/C$ (20%, 116 mg, 0.165 mmol, 0.2 equiv), and H_2 was bubbled through the solution via a needle for 10 min. The reaction mixture was left stirring at rt under H_2 for 16 h, filtered over a pad of Celite, and concentrated in vacuo. Purification by column chromatography (petroleum ether/acetone, 65:35 to 60:40) afforded 156 mg (0.709 mmol, 86%) of **7** as 36:64 α/β mixture (acetone-d_6) as a white solid: R_f 0.32 (petroleum ether/acetone 60:40); $[\alpha]_D$ +70.4 (c 0.465, acetone, 23 °C); IR (neat cm^{-1}) 3347 (m, br), 2955 (w), 1167 (m), 1099 (s), 1031 (s); ^1H NMR (400 MHz, acetone-d_6) δ 6.54 (1H, d, J = 6.8 Hz, OH-1β, disappears after D_2O exchange), 6.38 (1H, d, J = 4.8 Hz, OH-1α, disappears after D_2O exchange), 5.49 (1H, d, J = 6.3 Hz, OH-2β, disappears after D_2O exchange), 5.37 (1H, dt, J = 4.8, 4.3 Hz, H-1α, simplifies to t, J = 4.3 Hz after D_2O exchange), 4.80 (1H, dd, J = 7.7, 6.8 Hz, H-1β, simplifies to d, J = 7.7 Hz after D_2O exchange), 4.62 (1H, d, J = 10.4 Hz, OH-2α, disappears after D_2O exchange), 4.42−4.30 (1H, m, H-5α), 4.15 (1H, dd, J = 6.6, 5.8 Hz, OH-6β, disappears after D_2O exchange), 4.06 (1H, dd, J = 6.6, 5.8 Hz, OH-6α, disappears after D_2O exchange), 4.02−3.82 (4H, m, H-2α, H-5β, H-6α, H-6β), 3.80−3.65 (3H, m, H-2β, H-6α', H-6β'); ^{13}C NMR (101 MHz, acetone-d_6) δ 96.7 (d, J = 10.2 Hz, C-1β), 92.7 (d, J = 8.8 Hz, C-1α), 74.2 (dd, J = 26.3, 22.0 Hz, C-5β), 73.0 (t, J = 17.6 Hz, C-2β), 69.6 (t, J = 19.0 Hz, C-2α), 69.3 (t, J = 23.4 Hz, C-5α), 59.2−58.9 (m, C-6α and C-6β); ^{19}F NMR (282 MHz, acetone-d_6) δ −126.7 (dd, J = 253.6, 21.5 Hz, Fβ), −132.6 to −130.6 (m, 2 × Fα and Fβ), −132.5 (m, J = 262.2 Hz, Fβ), −133.2 (ddd, J = 257.9, 17.2, 8.6 Hz, Fα), −133.5 (m, J = 262.2 Hz, Fβ), −135.0 (m, J = 257.9 Hz, Fα); $\{^1H\}^{19}F$ NMR (282 MHz, acetone-d_6) δ −126.7 (d, J = 253.6 Hz, Fβ), −132.6 to −130.6 (m, 2 × Fα and Fβ), −132.5 (dd, J = 262.2, 12.9 Hz, Fβ), −133.2 (m, J = 253.6 Hz, Fα), −133.5 (dt, J = 262.2, 8.6 Hz, Fβ), −135.0 (m, J = 257.9 Hz, Fα); MS (ESI) m/z 284 (M + Na + MeCN)$^+$; HRMS (MS^+) for $C_6H_8F_4NaO_4$ $(M + Na)^+$ calcd 243.0251, found 243.0248. A sample of **7** was recrystallized from hexane/acetone, mp 165 °C (degradation).

Methyl 4,6-Di-*O*-benzyl-2,3-dideoxy-2,2,3,3-tetrafluoro-D-*erythro*-hexopyranoside (84). Pyranose **44** (227 mg, 0.57 mmol) was dissolved in DMSO and treated with ground KOH (64 mg, 1.14 mmol). The reaction was stirred at rt for 20 min, and MeI (142 μL, 2.28 mmol) was added dropwise. Stirring was continued for 2.5 h before the reaction was quenched with aq HCl (1M, 5 mL). Extraction was then carried out in EtOAc (4 × 7 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated to give an orange oil. Column chromatography (petroleum ether/acetone 90:10) followed by HPLC (toluene/hexane 75:25) gave pyranose ***α*-84** as a colorless oil (110 mg, 47%) and ***β*-84** as a colorless oil (84 mg, 36%). Data for ***α*-84**: R_f 0.31 (toluene); $[\alpha]_D$ +122.1 (c 0.4, $CHCl_3$, 26 °C); IR (neat) 2936 (w), 2870 (w), 1684 (w), 1210 (m), 1117 (s), 1064 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.15−7.43 (10H, m), 4.85 (1H, m, H-1), 4.85 (1H, d, J = 11.1 Hz, C$\underline{H}$HPh), 4.64 (1H, d, J =

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12.1 Hz, CHHPh), 4.58 (1H, d, J = 11.1 Hz, CHHPh), 4.51 (1H, d, J = 12.1 Hz, CHHPh), 4.00−4.09 (2H, m, H-4, H-5), 3.78 (1H, dd, J = 10.6, 3.0 Hz, H-6), 3.70 (1 H, d, J = 11.1 Hz, H-6′), 3.47 (3H, s, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.6 (C_{Ar}), 136.8 (C_{Ar}), 128.4, 128.1, 128.0, 127.8, 127.8 (CH_{Ar} × 10), 97.9 (dd, J = 35, 25 Hz, C-1), 75.2 (CH_2Ph), 73.6 (CH_2Ph), 73.3 (t, J = 18 Hz, C-4), 69.0 (d, J = 6 Hz, C-5), 67.6 (C-6), 56.0 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −119.0 (ddt, J = 272, 15, 8, Hz,), −126.6 (d, J = 260 Hz), −128.7 (d, J = 260 Hz), −134.9 (ddd, J = 272, 16, 9 Hz); ^{19}F{1H} NMR (282 MHz, $CDCl_3$) δ −119.0 (ddd, J = 272, 16, 7 Hz), −126.6 (ddd, J = 256, 16, 9 Hz), −128.7 (ddd, J = 257, 15, 7 Hz), −134.9 (ddd, J = 272, 16, 9 Hz); HRMS (ES+) for $C_{21}H_{22}F_4O_4Na^+$ [M + Na]$^+$ calcd 437.1346, found 437.1352. Data for **β-85**: R_f 0.23 (toluene); $[\alpha]_D$ +27.4 (c 0.8, $CHCl_3$, 26 °C); IR (neat) 2940 (w), 2872 (w), 1108 (s), 1065 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16−7.44 (10H, m), 4.87 (1H, d, J = 10.6 Hz, CHHPh), 4.66 (1H, d, J = 12.1 Hz, CHHPh), 4.61 (1H, d, J = 10.6 Hz, CHHPh), 4.58−4.62 (1H, m, H-1), 4.55 (1H, d, J = 12.1 Hz, CHHPh), 4.05 (1H, app td, J = 12.1, 10.6 Hz, H-4), 3.73−3.80 (2H, m, H-6, H-6′), 3.67−3.73 (1H, m, H-5), 3.66 (3H, s, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.7 (C_{Ar}), 136.6 (C_{Ar}), 128.5, 128.4, 128.2, 128.2, 127.8 (CH_{Ar} × 10), 97.9 (t, J = 22 Hz, C-1), 75.3 (CH_2Ph), 73.6 (CH_2Ph), 73.7 (t, J = 18 Hz, C-4), 73.2 (t, J = 4 Hz, C-5), 67.7 (C-6), 58.0 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −130.5 to −130.3 (2F, m), −138.0 to −137.8 (2F, m); ES$^+$MS 437.2 [M + Na]$^+$, 453.2 [M + K]$^+$; HRMS (ES+) for $C_{21}H_{22}F_4O_4Na^+$ [M + Na]$^+$ calcd 437.1346, found 437.1349, for $C_{21}H_{26}F_4O_4N^+$ [M + NH_4]$^+$ calcd 432.1792, found 432.1797.

Methyl 2,3-Dideoxy-2,2,3,3-tetrafluoro-α-D-*erythro*-hexopyranoside (α-85). Pyranose **α-84** (96 mg, 0.23 mmol) was dissolved in EtOAc (1.8 mL) and treated with $Pd(OH)_2$/C (49 mg, 92 μmol). The resultant mixture was flushed with H_2 and stirred under a H_2 atmosphere (balloon) for 22 h before being filtered through Celite. The Celite was washed with plenty of EtOAc, which was concentrated to give a colorless oil. Column chromatography (petroleum ether/acetone 70:30) gave pyranose **α-85** as a colorless oil (44 mg, 81%): R_f 0.14 (petroleum ether/acetone 70:30); $[\alpha]_D$ +126.0 (c 0.4, CH_3OH, 27 °C); ^{1}H NMR (400 MHz, acetone-d_6) δ 5.35 (1H, d, J = 7.1 Hz, OH-4), 4.97 (1H, dd, J = 8.3, 3.8 Hz, H-1), 4.04 (1H, m, H-4), 3.98 (1H, t, J = 5.6 Hz, OH-6), 3.75−3.93 (3H, m, H-5, H-6, H-6′), 3.47 (3H, s, CH_3); ^{13}C NMR (101 MHz, acetone-d_6) δ 98.5 (dd, J = 37, 26 Hz, C-1), 72.0 (d, J = 3 Hz, C-5), 67.6 (t, J = 19 Hz, C-4), 61.2 (C-6), 56.0 (OCH_3); ^{19}F NMR (282 MHz, acetone-d_6) δ −118.9 (dtd, J = 269, 9, 4 Hz), −130.3 to −129.8 (2F, m), −134.5 (dt, J = 270, 13 Hz); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.85 (1H, dd, $^3J_{H1eq,F2ax}$ = 8.0 Hz, $^4J_{H1eq,F3eq}$ = 4.7 Hz, H1), 4.10 (1H, dddd, $^3J_{H4ax,F3ax}$ = 18.4 Hz, $^3J_{H4ax,H5ax}$ = 9.7 Hz, $^3J_{H4ax,F3eq}$ = 7.4 Hz, $^4J_{H4ax,F2ax}$ = 3.8 Hz, H4), 3.94−3.91 (2H, m, H6 + H6′), 3.92 (1H, dddd, $^3J_{H5ax,H4ax}$ = 9.7 Hz, $^3J_{H5ax,H6}$ = 3.0 Hz, $^3J_{H5ax,H6'}$ = 3.0 Hz, $^4J_{H5ax,F3ax}$ = ≈ 3.0 Hz, H5) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 114.13 (dddd, J = 261.4, 252.6, 30.0, 20.7 Hz, C3), 110.67 (dddd, J = 272.8, 243.4, 29.0, 21.8 Hz, C2), 98.12 (dd, J = 36.7, 25.7 Hz, C1), 69.98 (d, J = 5.2 Hz, C5), 66.75 (t, J = 19.3 Hz, C4), 60.96 (C6), 56.29 (OCH_3) ppm; ^{19}F NMR (471 MHz, $CDCl_3$) δ-119.3 (ddddd, $^2J_{F2ax,F2eq}$ = 272.3 Hz, $^3J_{F2ax,F3eq}$ = 15.7 Hz, $^3J_{H1eq,F2ax}$ = 8.0 Hz, $^3J_{F2ax,F3ax}$ = 6.0 Hz, $^4J_{H4ax,F2ax}$ = 3.8 Hz, F2ax), −130.3 (ddddd, $^2J_{F3eq,F3ax}$ = 254.2 Hz, $^3J_{F3eq,F2ax}$ = 15.7 Hz, $^3J_{F3eq,F2eq}$ = 10.4 Hz, $^3J_{F3eq,H4ax}$ = 7.4 Hz, $^4J_{F3eq,H1eq}$ = 4.7 Hz, F3eq), −131.2 (ddddd, $^2J_{F3ax,F3eq}$ = 254.2 Hz, $^3J_{F3ax,F2eq}$ = 15.4 Hz, $^3J_{F3ax,H4ax}$ = 18.4 Hz, $^3J_{F3ax,F2ax}$ = 6.0 Hz, $^4J_{F3ax,H5ax}$ = ≈ 3.0 Hz, F3ax), −134.6 (ddd, $^2J_{F2ax,F2eq}$ = 272.3 Hz, $^3J_{F2eq,F3ax}$ = 15.4 Hz, $^3J_{F2eq,F3eq}$ = 10.4 Hz, F2eq) ppm; ^{1}H NMR (500 MHz, D_2O) δ 5.12 (1H, d, $^3J_{H1eq,F2ax}$ = 7.8 Hz, H1), 4.08 (1H, dddd, $^3J_{H4ax,F3ax}$ = 15.4 Hz, $^3J_{H4ax,F3eq}$ = 11.1 Hz, $^3J_{H4ax,H5ax}$ = 10.5 Hz, $^4J_{H4ax,F2ax}$ = 3.5 Hz, H4), 3.94 (1H, ddd, $^3J_{H5ax,H4ax}$ = 10.5 Hz, $^3J_{H5ax,H6'}$ = 4.6 Hz, $^3J_{H5ax,H6}$ = 1.8 Hz, H5), 3.91 (1H, dd, $^2J_{H6,H6'}$ = 12.6 Hz, $^3J_{H6,H5ax}$ = 1.8 Hz, H6), 3.83 (1H, dd, $^2J_{H6,H6'}$ = 12.6 Hz, $^3J_{H6',H5ax}$ = 4.6 Hz, H6′) ppm; ^{19}F NMR (471 MHz, D_2O) δ −119.97 (ddddd, $^2J_{F2ax,F2eq}$ = 273.3 Hz, $^3J_{H1eq,F2ax}$ = 7.8 Hz, $^3J_{F2ax,F3eq}$ = 7.1 Hz, $^4J_{H4ax,F2ax}$ = 3.5 Hz, $^3J_{F2ax,F3ax}$ = 2.2 Hz, F2ax), −129.5 to −130.7 (m, F3ax + F3eq), −134.80 (ddd, $^2J_{F2eq,F2ax}$ = 273.3 Hz, $^3J_{F2eq,F3ax}$ = 13.0 Hz, $^3J_{F2eq,F3eq}$ = 13.0 Hz, F2eq) ppm; ES$^+$MS 233.2 [M − H]$^-$; HRMS (ES+) for $C_7H_9F_4O_4^-$ [M − H]$^-$ calcd 233.0442, found 233.0441.

Methyl 2,3-Dideoxy-2,2,3,3-tetrafluoro-β-D-*erythro*-hexopyranoside (β-85). Pyranose **β-84** (76 mg, 0.18 mmol) was dissolved in EtOAc (1.5 mL) and treated with $Pd(OH)_2$/C (38 mg, 72 μmol). The resultant mixture was flushed with H_2 and stirred under a H_2 atmosphere (balloon) for 3.5 h before being filtered through Celite. The Celite was washed with plenty of EtOAc, which was concentrated to give a colorless oil. Column chromatography (petroleum ether/acetone 70:30) gave pyranose **β-85** as a colorless oil (40 mg, 93%): R_f 0.10 (petroleum ether/acetone 70:30); $[\alpha]_D$ −21.2 (c 0.5, CH_3OH, 26 °C); IR (neat) 3337 (w, br), 2949 (w), 1232 (m), 1079 (s), 1037 (s), 1007 (s), 960 (s); ^{1}H NMR (400 MHz, acetone-d_6) δ 5.44 (1H, m, OH-4), 4.80 (1H, m, H-1), 3.96−4.12 (2H, m, OH-6, H-4), 3.91 (1H, m, H-6), 3.80 (1H, m, H-6′), 3.64−3.54 (4H, m, CH_3, H-5); ^{13}C NMR (101 MHz, acetone-d_6) δ 98.6 (td, J = 22, 3 Hz, C-1), 75.7 (d, J = 4 Hz, C-5), 67.9 (t, J = 19 Hz, C-4), 61.3 (C-6), 57.9 (OCH_3); ^{19}F NMR (282 MHz, acetone-d_6) δ −131.9 (1F, ddd, J = 252, 15, 10 Hz), −132.9 (1F, ddd, J = 254, 19, 10 Hz), −138.7 to −136.5 (2F, m); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.68 (1H, dd, $^3J_{H1ax,F2ax}$ = 12.8 Hz, $J_{H1ax,F}$ ≈ 1 Hz, H1), 4.16 (1H, dddd, $^3J_{H4ax,F3ax}$ = 14.1 Hz, $^3J_{H4ax,F3eq}$ = 11.5 Hz, $^3J_{H4ax,H5ax}$ = 9.9 Hz, $^4J_{H4ax,F2ax}$ = 4.0 Hz, H4), 4.02 (1H, dd, $^2J_{H6,H6'}$ = 12.5 Hz, $^3J_{H6,H5ax}$ = 2.6 Hz, H6), 3.93 (1H, dd, $^2J_{H6',H6}$ = 12.5 Hz, $^3J_{H6',H5ax}$ = 3.4 Hz, H6′), 3.60 (1H, dddd, $^3J_{H5ax,H4ax}$ = 9.9 Hz, $^3J_{H5ax,H6'}$ = 3.4, $^3J_{H5ax,H6}$ = 2.6 Hz, $^nJ_{H5ax,F}$ ≈ 1 Hz, H5) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 114.68 (dddd, J = 257.6, 254.4, 28.5, 20.8 Hz, C3), 110.88 (dddd, J = 266.1, 257.5, 24.0, 25.0 Hz, C2), 98.1 (dd, J = 25.9, 19.3 Hz, C1), 73.7 (dd, J = 3.3, 3.1 Hz, C5), 66.7 (t, J = 19.3 Hz, C4), 60.9 (C6), 58.46 (OCH_3) ppm; ^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$) δ −132.5 to −133.7 (m, F3ax + F3eq), −137.4 (ddd, J = 260.4 11.5 11.5, F2eq), −138.3 (ddd, J = 260.4 6.5 2.1, Hz, F2ax); ^{1}H NMR (500 MHz, D_2O) δ 4.93 (1H, dd, $^3J_{H1ax,F2ax}$ = 13.9 Hz, $^4J_{H1ax,F3ax}$ = 2.9 Hz, H1), 4.02 (1H, dddd, $^3J_{H4ax,H5ax}$ = 10.2 Hz, $^3J_{H4ax,F3ax}$ = 18.6 Hz, $^3J_{H4ax,F3eq}$ = 8.4 Hz, $^4J_{H4ax,F2ax}$ = 3.8 Hz, H4), 3.91 (1H, dd, $^2J_{H6,H6'}$ = 12.7 Hz, $^3J_{H6,H5ax}$ = 2.1 Hz, H6), 3.75 (1H, dd, $^2J_{H6,H6'}$ = 12.7 Hz, $^3J_{H6',H5ax}$ = 4.9 Hz, H6′), 3.67 (1H, dddd, $^3J_{H5ax,H4ax}$ = 10.2 Hz, $^3J_{H5ax,H6}$ = 2.1 Hz, $^3J_{H5ax,H6'}$ = 4.9 Hz, $^nJ_{H5ax,F}$ ≈ 1 Hz, H5) ppm; ^{19}F NMR (471 MHz, D_2O) δ −132.0 (ddddd, $^2J_{F3ax,F3eq}$ = 255.6 Hz, $^3J_{F3ax,H4ax}$ = 18.6 Hz, $^3J_{F3ax,F2eq}$ = 13.0 Hz, $^3J_{F3ax,F2ax}$ = 3.8 Hz, $^4J_{F3ax,H1ax}$ = 2.9 Hz, F3ax), −132.7 (dddd, $^2J_{F3eq,F3ax}$ = 255.6 Hz, $^3J_{F3eq,F2ax}$ = 12.2 Hz, $^3J_{F3eq,F2eq}$ = 10.9 Hz, $^3J_{F3eq,H4ax}$ = 8.4 Hz, F3eq), −137.1 (ddd, $^2J_{F2eq,F2ax}$ = 258.3 Hz, $^3J_{F2eq,F3ax}$ = 13.0 Hz, $^3J_{F2eq,F3eq}$ = 10.7 Hz, F2eq), −138.2 (ddddd, $^2J_{F2ax,F2eq}$ = 258.3 Hz, $^3J_{H1ax,F2ax}$ = 13.9 Hz, $^3J_{F2ax,F3eq}$ = 12.2 Hz, $^3J_{F2ax,F3ax}$ = 3.8 Hz, $^4J_{H4ax,F2ax}$ = 3.8 Hz, Fax) ppm; ES$^+$MS 233.2 [M − H]$^-$; HRMS (ES+) for $C_7H_9F_4O_4^-$ [M − H]$^-$ calcd 233.0442, found 233.0441.

Methyl 3,4-Dideoxy-3,3,4,4-tetrafluoro-β-*threo*-hexopyranoside (±β-86) and α-*erythro*-Hexopyranoside (±α-87). To a stirred solution of the hexose mixture of **±70** and **±71** (250 mg, 0.77 mmol, 1 equiv) in EtOAc (6 mL) under N_2 was added $Pd(OH)_2$ (0.1 equiv) at rt, and the reaction mixture was stirred under H_2 for 2.5 h. The reaction mixture was filtered through Celite, concentrated, and purified by column chromatography (petroleum ether/acetone 85:15 to 70:30) to afford 148 mg (0.63 mmol, 82%). Further purification by HPLC (petroleum ether/acetone 70:30) gave 62 mg of pure **±β-86** and 66 mg of impure **±α-87** as white solids. Data for **±β-86**: R_f 0.27 (petroleum ether/acetone 70:30); mp 154 °C (hexane/acetone); IR (neat cm^{-1}) 3195 (br w), 2946 (w), 1453 (m), 1068 (s), 1017 (s); ^{1}H NMR (400 MHz, acetone-d_6) δ 4.83 (1H, d, J = 5.6 Hz, OH-2, disappears upon D_2O exchange), 4.77 (1H, dt, J = 4.2, 1.5 Hz, H−1), 4.29 (1H, dd, J = 6.7, 5.4 Hz, OH-6, disappears upon D_2O exchange), 4.17−4.08 (1H, m, H−2), 3.98−3.77 (3H, m, H−5, H−6a and H−6b), 3.55 (3H, s, OCH_3); ^{13}C NMR (101 MHz, acetone-d_6) δ 101.1 (d, J = 8.8 Hz, C−1), 75.2 (dd, J = 26.3, 22.0 Hz, C−5), 71.4 (dd, J = 29.3, 19.0 Hz, C−2), 59.3−59.0 (m, C−6), 57.3 (OCH_3); ^{19}F NMR (282 MHz, acetone-d_6) δ −120.33 (d, J = 267.2 Hz), −129.53 (m, J = 262.1 Hz), −131.82 (d, J = 267.2 Hz), −132.46 (d, J = 262.1 Hz); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.74 (1H, ddd, $^4J_{H1ax,F3ax}$ = 3.7 Hz, $^3J_{H1ax,H2eq}$ = 1.6 Hz, $^4J_{H1ax,F3eq}$ = 1.5 Hz, H1), 4.15 (1H, dddd, $^3J_{H2eq,F3ax}$

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= 6.2 Hz, $^3J_{H2eq,F3eq}$ = 6.2 Hz, $^4J_{H2eq,F4eq}$ = 6.2 Hz, $^3J_{H2eq,H1ax}$ = 1.6 Hz, H2), 4.06−3.98 (2H, m, H6 + H6′), 3.91 (1H, dddd, $^3J_{H5ax,F4ax}$ = 22.2 Hz, $^3J_{H5ax,H6'}$ = 6.2 Hz, $^4J_{H5ax,F3ax}$ = ≈ 5 Hz, $^3J_{H5ax,H6}$ = 4.9 Hz, H5) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 99.79 (d, J = 8.0 Hz, C1), 73.73 (dd, J = 29.1, 22.2, Hz, C5), 70.82 (dd, J = 31.3, 20.1 Hz, C2), 58.87 (d, J = 2.9 Hz), 57.58 (O<u>C</u>H$_3$) ppm (2 × CF_2 not visible); ^{19}F NMR (471 MHz, $CDCl_3$) δ −121.1 (dddddd, $^2J_{F3ax,F3eq}$ = 273.3 Hz, $^3J_{F3ax,F4eq}$ = 13.7 Hz, $^3J_{F3ax,F4ax}$ = 8.8 Hz, $^3J_{H2eq,F3ax}$ = 6.2 Hz, $^4J_{H5ax,F3ax}$ = ≈ 5 Hz, $^4J_{H1ax,F3ax}$ = 3.7 Hz, F3ax), −129.3 (dddd, $^2J_{F4ax,F4eq}$ = 266.3 Hz, $^3J_{F4ax,H5ax}$ = 22.2 Hz, $^3J_{F4ax,F3eq}$ = 15.4 Hz, $^3J_{F4ax,F3ax}$ = 8.8 Hz, F4ax), −132.4 (ddddd, $^2J_{F3eq,F3ax}$ = 273.3 Hz, $^3J_{F3eq,F4ax}$ = 15.4 Hz, $^3J_{F3eq,F4eq}$ = 9.0 Hz, $^3J_{F3eq,H2eq}$ = 6.2 Hz, $^4J_{H1ax,F3eq}$ = 1.5 Hz, F3eq), −133.1 (dddd, $^2J_{F4eq,F4ax}$ = 266.3 Hz, $^3J_{F4eq,F3ax}$ = 13.7 Hz, $^3J_{F4eq,F3eq}$ = 9.0 Hz, $^4J_{H2eq,F4eq}$ = 6.2 Hz, F4eq) ppm; ^{1}H NMR (500 MHz, D_2O) δ 4.83 (1H, ddd, $^4J_{H1ax,F3ax}$ = 3.9 Hz, $^4J_{H1ax,F3eq}$ = 1.6 Hz, $^3J_{H1ax,H2eq}$ = 1.3 Hz, H1), 4.24 (1H, dddd, $^3J_{H2eq,F3ax}$ = 7.3 Hz, $^3J_{H2eq,F3eq}$ = 5.9 Hz, $^4J_{H2eq,F4eq}$ = 5.9 Hz, $^3J_{H2eq,H1ax}$ = 1.3 Hz, H2), 3.99 (1H, dddd, $^3J_{H5ax,F4ax}$ = 24.6 Hz, $^3J_{H5ax,H6'}$ = 7.3 Hz, $^3J_{H5ax,H6}$ = 3.7 Hz, $^4J_{H5ax,F3ax}$ = 3.7 Hz, H5), 3.96 (1H, ddd, $^2J_{H6,H6'}$ = 12.3 Hz, $^3J_{H6,H5ax}$ = 3.7 Hz, $^4J_{H6,F}$ < 1 Hz, H6), 3.83 (1H, dd, $^2J_{H6',H6}$ = 12.3 Hz, $^3J_{H6',H5ax}$ = 7.3 Hz, H6′) ppm; ^{19}F NMR (471 MHz, D_2O) δ −120.9 (dddddd, $^2J_{F3ax,F3eq}$ = 271.4 Hz, $^3J_{F3ax,F4eq}$ = 14.0 Hz, $^3J_{F3ax,F4ax}$ = 9.6 Hz, $^3J_{H2eq,F3ax}$ = 7.3 Hz, $^4J_{H1ax,F3ax}$ = 3.9 Hz, $^4J_{H5ax,F3ax}$ = 3.7 Hz, F3ax), −129.8 (dddd, $^2J_{F4ax,F4eq}$ = 264.3 Hz, $^3J_{F4ax,H5ax}$ = 24.6, $^3J_{F4ax,F3eq}$ = 16.0 Hz, $^3J_{F4ax,F3ax}$ = 9.6 Hz, Hz, F4ax), −132.4 (ddddd, $^2J_{F3eq,F3ax}$ = 271.4 Hz, $^3J_{F3eq,F4ax}$ = 16.0 Hz, $^3J_{F3eq,F4eq}$ = 10.1 Hz, $^3J_{F3eq,H2eq}$ = 5.9 Hz, $^4J_{H1ax,F3eq}$ = 1.6 Hz, F3eq), −133.4 (dddd, $^2J_{F4eq,F4ax}$ = 264.3 Hz, $^3J_{F4eq,F3ax}$ = 14.0 Hz, $^3J_{F4eq,F3eq}$ = 10.1 Hz, $^4J_{H2eq,F4eq}$ = 5.9 Hz, F4eq) ppm; MS (EI) *m/z* (%) 234 ($M^{+\bullet}$, 2), 203 ((M − $MeO^{\bullet}$)$^+$, 21), 183 ((M − $MeO^{\bullet}$ − HF)$^+$, 50), 182 ((M − MeOH − HF)$^{+\bullet}$, 26), 154 ((M − MeOH − HF − CO)$^{+\bullet}$, 46), 61 ($C_2H_5O_2^+$, 100); HRMS (MS+) for $C_7H_{10}F_4NaO_4$ (M + Na)$^+$ calcd 257.0407, found 257.0407. Data for **±α-87**: R_f 0.32 (petroleum ether/acetone 70:30); mp 86 °C (hexane/acetone); IR (neat cm^{-1}) 3393 (br w), 3026 (w), 2973 (w), 1208 (m), 1101 (s), 1066 (s); ^{1}H NMR (400 MHz, acetone-d_6) δ 4.93 (1H, t, J = 4.3 Hz, H-1), 4.90 (1H, d, J = 9.7 Hz, OH-2, disappears upon D_2O exchange), 4.29 (1H, t, J = 6.1 Hz, OH-6, disappears upon D_2O exchange), 4.17−3.97 (2H, m, H-2 + H-5), 3.96−3.87 (1H, m, H-6a, simplifies to dd, J = 11.9, 3.0 Hz after D_2O exchange), 3.83−3.72 (1H, m, H-6b, simplifies to dd, J = 12.0, 7.3 Hz after D_2O exchange), 3.44 (3H, s, O<u>C</u>H$_3$); ^{13}C NMR (101 MHz, acetone-d_6) δ 99.6 (d, J = 10.2 Hz, C-1), 69.7 (t, J = 23.4 Hz, C-2 or C-5), 69.6 (t, J = 18.5 Hz, C-2 or C-5), 58.7 (C-6), 56.4 (O<u>C</u>H$_3$); ^{19}F NMR (282 MHz, acetone-d_6) δ−126.9 (m, J = 253.6 Hz), −131.7 (d, J = 253.6 Hz), −132.2 (m, J = 262.2 Hz), −133.56 (m, J = 262.2 Hz); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.94 (1H, dd, $^3J_{H1eq,H2ax}$ = 4.6 Hz, $^4J_{H1eq,F3eq}$ = 4.2 Hz, 1H, H1), 4.17 dddd, $^3J_{H5ax,F4ax}$ = 22.4 Hz, $^3J_{H5ax,H6'}$ = 7.3 Hz, $^3J_{H5ax,H6}$ = 3.4 Hz, $^4J_{H5ax,F3ax}$ = 2.6 Hz, H5), 4.04 (1H, ddddd, $^3J_{H2ax,F3ax}$ = 23.2 Hz, $^3J_{H2ax,OH}$ = 12.0 Hz, $^3J_{H2ax,F3eq}$ = 6.7 Hz, $^3J_{H2ax,H1eq}$ = 4.6 Hz, $^4J_{H2ax,F4ax}$ = 3.9 Hz, H2), 4.04−3.93 (2H, m, H6 + H6′) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ115.5−110.7 (m, 2 × CF_2), 98.2 (dd, J = 9.4, 1.2 Hz, C1), 68.69 (ddd, J = 1.7, 18.4, 20.4 Hz, C5), 68.14 (ddd, J = 27.2, 21.5, 2.1 Hz, C2), 60.87 (dd, J = 3.9, 2.0 Hz, C6), 56.45 (O<u>C</u>H$_3$) ppm; ^{19}F NMR (471 MHz, $CDCl_3$) δ −128.1 (ddddd, $^2J_{F3ax,F3eq}$ = 254.8 Hz, $^3J_{F3ax,H2ax}$ = 23.2 Hz, $^3J_{F3ax,F4eq}$ = 13.4 Hz, $^3J_{F3ax,F4ax}$ = 9.1 Hz, $^4J_{F3ax,H5ax}$ = 2.6 Hz, F3ax), −132.1 (ddddd, $^2J_{F3eq,F3ax}$ = 254.8 Hz, $^3J_{F3eq,F4ax}$ = 15.1 Hz, $^3J_{F3eq,F4eq}$ = 8.6 Hz, $^3J_{F3eq,H2ax}$ = 6.7 Hz, $^4J_{F3eq,H1eq}$ = 4.2 Hz, F3eq), −132.2 (ddddd, $^2J_{F4ax,F4eq}$ = 263.5 Hz, $^3J_{F4ax,H5ax}$ = 22.4 Hz, $^3J_{F4ax,F3eq}$ = 15.1 Hz, $^3J_{F4ax,F3ax}$ = 9.1 Hz, $^4J_{F4ax,H2ax}$ = 3.9 Hz, F4ax), −133.4 (ddd, $^2J_{F4eq,F4ax}$ = 263.5 Hz, $^3J_{F4eq,F3ax}$ = 13.4 Hz, $^3J_{F4eq,F3eq}$ = 8.6 Hz, F4eq) ppm; ^{1}H NMR (500 MHz, D_2O) δ 4.98 (1H, dd, $^3J_{H1eq,H2ax}$ = 4.4 Hz, $^4J_{H1eq,F3eq}$ = 4.2 Hz, H1), 4.21 (1H, dddd, $^3J_{H2ax,F3ax}$ = 22.6 Hz, $^3J_{H2ax,F3eq}$ = 6.8 Hz, $^3J_{H2ax,H1eq}$ = 4.4 Hz, $^4J_{H2ax,F4ax}$ = 3.8 Hz, H2), 4.18 (1H, dddd, $^3J_{H5ax,F4ax}$ = 24.1 Hz, $^3J_{H5ax,H6'}$ = 6.9 Hz, $^3J_{H5ax,H6}$ = 3.4 Hz, $^4J_{H5ax,F3ax}$ = 2.3 Hz, H5), 3.95 (1H, ddd, $^2J_{H6,H6'}$ = 12.8 Hz, $^3J_{H6,H5ax}$ = 3.4 Hz, $^4J_{H6,F}$ < 1 Hz, H6), 3.84 (1H, dd, $^2J_{H6',H6}$ = 12.8 Hz, $^3J_{H6',H5ax}$ = 6.9 Hz, H6′) ppm; ^{19}F NMR (471 MHz, D_2O) δ −127.2 (ddddd, $^2J_{F3ax,F3eq}$ = 252.5 Hz, $^3J_{F3ax,H2ax}$ = 22.6 Hz, $^3J_{F3ax,F4eq}$ = 13.0 Hz, $^3J_{F3ax,F4ax}$ = 9.2 Hz, $^4J_{F3ax,H5ax}$ = 2.3 Hz, F3ax), −131.7 (ddddd, $^2J_{F3eq,F3ax}$ = 252.5 Hz, $^3J_{F3eq,F4ax}$ = 14.9 Hz, $^3J_{F3eq,F4eq}$ = 8.7 Hz, $^3J_{F3eq,H2ax}$ = 6.8 Hz, $^4J_{F3eq,H1eq}$ = 4.2 Hz, F3eq), −131.9 (ddddd, $^2J_{F4ax,F4eq}$ = 262.2 Hz, $^3J_{F4ax,H5ax}$ = 24.1 Hz, $^3J_{F4ax,F3eq}$ = 14.9 Hz, $^3J_{F4ax,F3ax}$ = 9.2 Hz, $^4J_{F4ax,H2ax}$ = 3.8 Hz, F4ax), −133.4 (ddd, $^2J_{F4eq,F4ax}$ = 262.2 Hz, $^3J_{F4eq,F3ax}$ = 13.0 Hz, $^3J_{F4eq,F3eq}$ = 8.7 Hz, F4eq) ppm; MS (EI) *m/z* (%) 234 ($M^{+\bullet}$, 1), 203 ((M − $MeO^{\bullet}$)$^+$, 11), 183 ((M − $MeO^{\bullet}$ − HF)$^+$, 14), 182 ((M − MeOH − HF)$^{+\bullet}$, 9), 154 ((M − MeOH − HF − CO)$^{+\bullet}$, 23), 61 ($C_2H_5O_2^+$, 100); HRMS (MS+) for $C_7H_{10}F_4NaO_4$ (M + Na)$^+$ calcd 257.0407, found 257.0401.

4-*O*-Benzyl-2,3-dideoxy-2,2,3,3-tetrafluoro-*threo*-hexopyranose (88). To a stirred solution of pyranose **28** (405 mg, 1.01 mmol) in EtOAc (8 mL) was added $Pd(OH)_2/C$ (107 mg, 0.20 mmol). The resultant mixture was flushed with H_2 and stirred under H_2 for 1 h. EtOAc (11 mL) was added, followed by filtration through Celite, to give a colorless oil. Column chromatography (petroleum ether/acetone 60:40) gave pyranose **88** as a foam (264 mg, 84%) and pyranose **3** as a colorless residue (32 mg, 14%). Recrystallization of **88** to give the β-anomer was achieved by dissolution in acetone and was subsequently allowed to stand for several weeks. Data for the anomeric mixture (1:1) was achieved after equilibration in solvent: R_f 0.27 (petroleum ether/acetone 60:40); mp 138−142 °C (acetone); $[\alpha]_D$ +32.6 (*c* 0.455, acetone, 22 °C); IR (neat) 3320 (w, br), 2892 (w), 1692 (m), 1116 (s), 1074 (s), 1046 (s) cm^{-1}. Data for the β-isomer: ^{1}H NMR (400 MHz, acetone-d_6) δ (ppm) 7.25−7.45 (5H, m, H_{Ar}), 6.67 (1H, br s, O<u>H</u>-1), 4.99 (1H, d, J = 13.6 Hz, H-1), 4.88 (1H, d, J = 11.1 Hz, C<u>H</u>HPh), 4.72 (1H, d, J = 11.1 Hz, CH<u>H</u>Ph), 4.18 (1H, m, H-4), 4.12 (1H, br t, J = 5.3 Hz, O<u>H</u>-6), 3.92 (1H, m, H-6), 3.73−3.82 (2 H, m); ^{13}C NMR (101 MHz, acetone-d_6) δ (ppm) 138.8 (C_{Ar}), 129.2 (<u>C</u>H$_{Ar}$ × 2), 128.9 (<u>C</u>H$_{Ar}$ × 2), 128.7 (<u>C</u>H$_{Ar}$), 93.1 (ddd, J = 26, 20, 3 Hz, C-1), 76.7 (dd, J = 29, 19 Hz, C-4), 76.0 (d, J = 3 Hz, <u>C</u>H$_2$Ph), 75.3 (d, J = 6 Hz, C-5), 60.4 (C-6); ^{19}F NMR (282 MHz, acetone-d_6) δ (ppm) −116.9 (d, J = 272 Hz), −130.8 (dt, J = 272, 10 Hz), −136.4 (dt, J = 259, 9 Hz), −137.7 (dtd, J = 259, 15, 15, 5 Hz). Data for the 1:1 α/β mixture: ^{1}H NMR (400 MHz, acetone-d_6) δ (ppm) 7.27−7.44 (10H, m, H_{Ar}), 6.62−6.75 (2H, m, O<u>H</u>-1$_{\alpha+\beta}$), 5.31 (1H, m, H-1$_\alpha$), 4.99 (1H, br d, J = 14.1 Hz, H-1$_\beta$), 4.88 (1H, d, J = 11.1 Hz, C<u>H</u>HPh$_{\alpha/\beta}$), 4.87 (1H, d, J = 11.1 Hz, C<u>H</u>HPh$_{\beta/\alpha}$), 4.72 (2H, d, J = 11.1 Hz, CH<u>H</u>Ph$_{\alpha+\beta}$), 4.45 (1H, m, H-5$_\alpha$), 4.12−4.21 (3H, m, H-4$_{\alpha+\beta}$, O<u>H</u>-6$_\beta$), 4.05 (1H, dd, J = 6.6, 5.1 Hz, O<u>H</u>-6$_\alpha$), 3.92 (1H, tdt, J = 6.4, 4.7, 2.1 Hz, H-5$_\beta$), 3.67−3.82 (4H, m, H-6$_{\alpha+\beta}$, H-6′$_{\alpha+\beta}$); ^{13}C NMR (101 MHz, acetone-d_6) δ (ppm) 138.9 ($C_{Ar}\alpha$), 138.8 ($C_{Ar}\beta$), 129.2, 128.8, 128.8, 128.7, 128.7 (<u>C</u>H$_{Ar}$ × 10), 92.1−93.5 (m, C-1$_{\alpha+\beta}$), 76.3−77.4 (m, C-4$_{\alpha+\beta}$), 75.9 (d, J = 3 Hz, <u>C</u>H$_2$Ph$_{\alpha+\beta}$), 75.3 (d, J = 6 Hz, C-5$_\beta$), 70.3 (J = 6 Hz, C-5$_\alpha$), 60.4 (C-6$_\alpha$), 60.4 (C-6$_\beta$); ^{19}F NMR (282 MHz, acetone-d_6) δ (ppm) −115.3 (ddt, J = 270, 13, 8 Hz, Fα), −116.9 (dspt, J = 271, 6, 6 Hz, Fβ), −118.7 (ddt, J = 266, 17, 9 Hz, Fα), −128.8 (m, J = 270 Hz can be observed, Fα), −130.8 (app dt, J = 272, 11 Hz, Fβ), −133.7 (dddd, J = 266, 16, 10, 6 Hz, Fα), −136.4 (m, J = 259 Hz can be observed, Fβ), −137.7 (dtd, J = 259, 15, 5 Hz, Fβ); ES$^+$MS *m/z* 374.1 [M + MeCN + Na]$^+$; HRMS (ES+) for $C_{13}H_{14}F_4O_4Na^+$ [M + Na]$^+$ calcd 333.0720, found 333.0720.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00302.

X-ray data (CIF)
Determination of enantioselectivities and conformational analysis (PDF)
Copies of spectra of novel compounds (PDF)
Crystallographic data (PDF)

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The authors declare no competing financial interest.

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