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The enantioselective synthesis of dideoxy-tetrafluorinated hexoses

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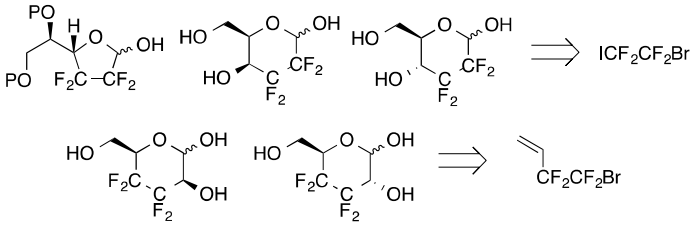

Abstract—Carbohydrates typically have low affinities to protein binding sites, and the development of carbohydrate mimetics with improved binding is therefore of interest. Tetrafluorination of monosaccharides is one of the strategies currently under investigation for that purpose. The synthesis of the required tetrafluorinated monosaccharides is achieved by a fluorinated building block approach. The enantioselective synthesis of tetrafluorinated hexose derivatives is described here, both in the pyranose and furanose form. 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-

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tetrafluoro-D-*erythro*-hexopyranose **5** is described, as well as 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, and proceeds in good to excellent yields. NMR and X-ray crystallographic analysis of the tetrafluorinated methyl pyranoside derivatives confirms their $^4C_1$ conformation.

1. Introduction

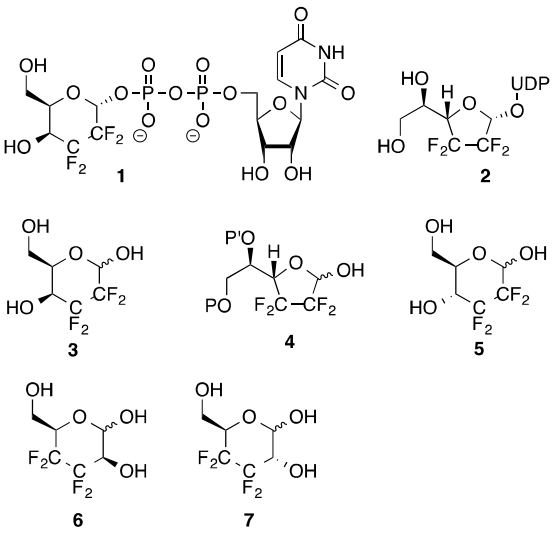
The pronounced hydrophilicity of carbohydrates is an inherent significant contributor to the typically low affinity found for protein-carbohydrate interactions.[1] This unfavorable factor has to be taken into account when developing inhibitors of carbohydrate processing enzymes or carbohydrate binding proteins starting from a carbohydrate structure, at least for non mechanism-based inhibitors. Given 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 non-fluorinated 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 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 from 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.

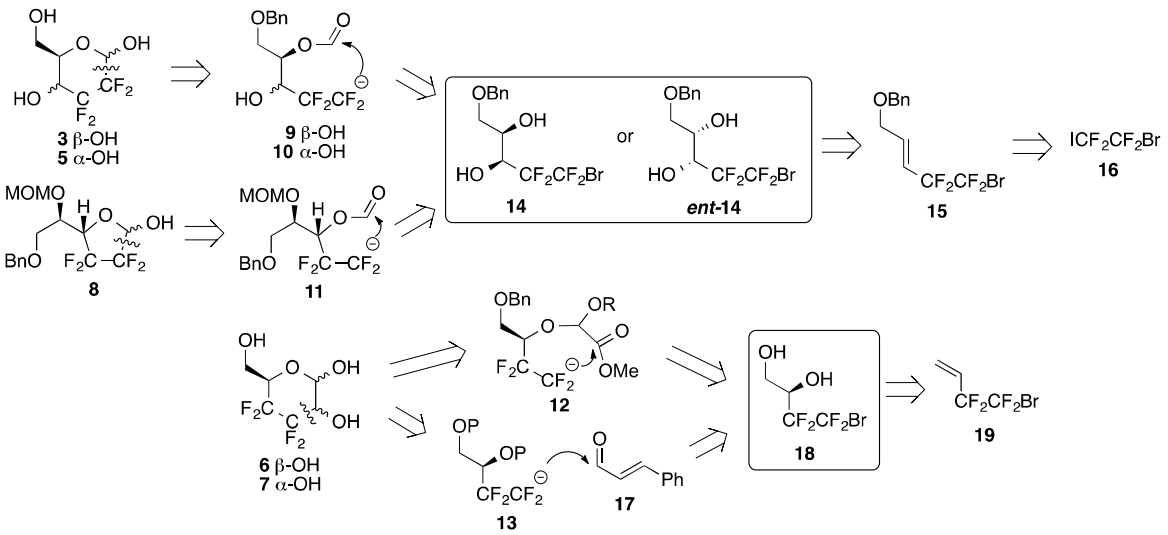
Chart 1. Dideoxy-tetrafluorinated UGM inhibitors **1** and **2**, and structures of the target monosaccharides **3**–**7**.



2. Results and Discussion

Retrosynthetic analysis

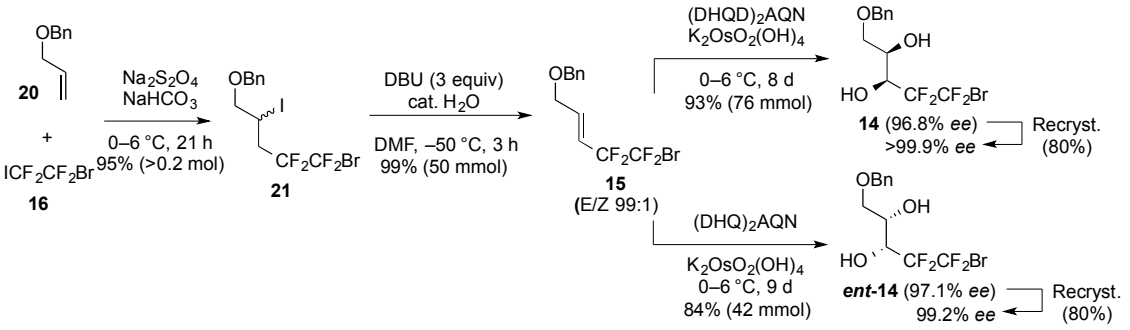
The synthesis of all compounds followed a fluorinated building block approach, with the sugars fluorinated at positions 2 and 3 (sugar numbering) originating from 1-bromo-2-iodotetrafluoroethane **16** (Scheme 1) and those at positions 3 and 4 from 4-bromo-3,3,4,4-tetrafluorobut-1-ene **19** (Scheme 1). Both fluorinated building blocks are commercially available. In all cases, the key step consisted of an intramolecular[21] or intermolecular[22,23,24] 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 centres 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]



Scheme 1. Retrosynthetic analysis for the dideoxy-tetrafluoro analogues.

Synthesis of the enantiopure *syn*-diols 14 (Scheme 2)

Following on from our earlier communication,[18] the synthesis of the diols **14** was optimized on large scale. Intermolecular atom transfer addition of the 2-bromotetrafluoroethyl radical, formed by sodium dithionite mediated single electron transfer, to benzyl allyl ether yielded the iodide **21** in excellent yield. Regioselective elimination through reaction of the most acidic proton led to alkene **15** in quantitative yield, and 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 invariably resulted in incomplete reaction. It was found that laboratory grade DMF (<0.2% H_2O) gave much better conversions than 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.



Scheme 2. Enantioselective synthesis of the key *syn*-diol intermediates.

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 chiral ligand.[18] Further optimization consisted of the development of a recrystallization protocol that resulted in virtually enantiopure material (>99% *e.e.*). 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 *e.e.*, which can then be recrystallized again to increase the enantiopurity. Recovery of the expensive ligand was easily achieved by a modified extraction method.[26]

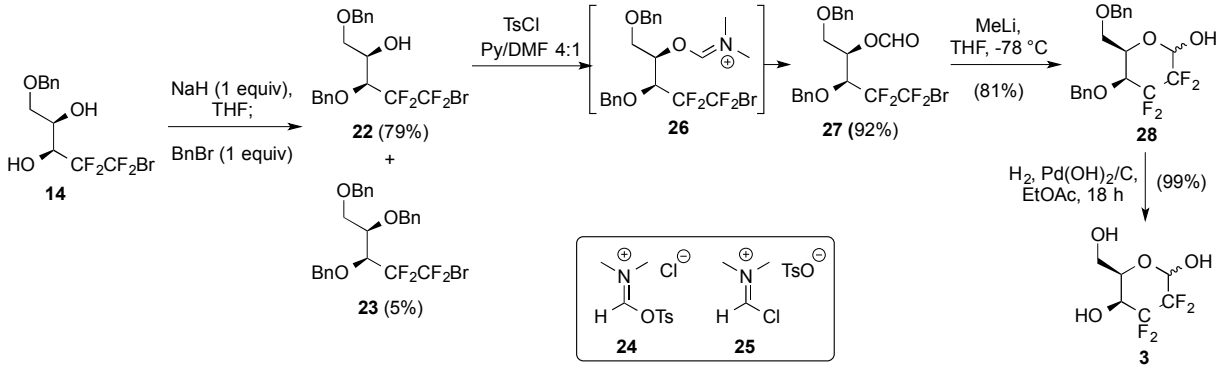
Formation of the enantiomeric diol *ent*-**14** was achieved by using a catalyst having the AQN spacer and the *pseudo*-enantiomeric DHQ ligand, which resulted in a 97% *e.e.,* which was increased to 99% by recrystallization. On a 14 g (40 mmol) scale, this transformation was achieved in an 84% yield,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

Pyranose ring formation: synthesis of the dideoxy-tetrafluoro "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] 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, simple workup consisting of extraction into hexane provided clean product suitable for the next step, with no chromatography necessary.



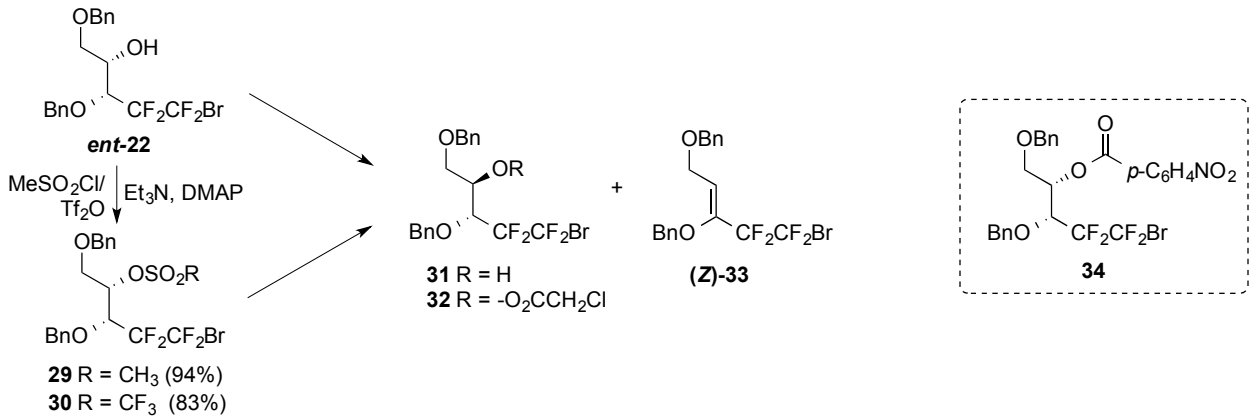
Scheme 3. Synthesis of the pyranose sugar derivative **3**.

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.

Following 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**. Given 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, next 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 5,6). Following a procedure by Ohara using formic acid and CsF,[37] only elimination product was observed (entry 7). Finally, reacting the triflate **30** with sodium nitrite (entry 8) did give the desired inverted alcohol **31**, but again accompanied by elimination product, as well as a range of decomposition products.

Table 1. Attempts to effect C5 alcohol inversion

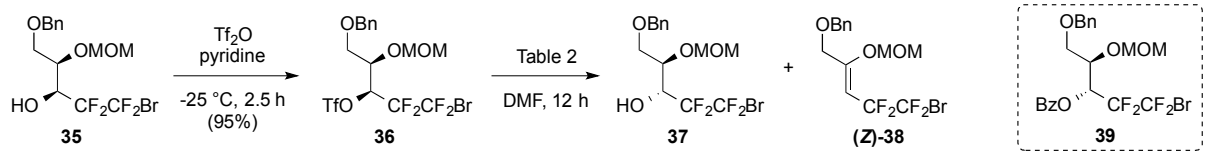


Entry	s.m.	Conditions	Product (yield)[a] (%)	s.m.
1	***ent*-22**	DIAD, PPh_3, HCOOH, THF	No reaction	n.d.
2	***ent*-22**	DIAD. PPh_3, $ClCH_2COH$, toluene	**32** (3%), **(*Z*)-33** (50%)	-
3	***ent*-22**	DIC, $Cu(OTf)_2$; HCOOH	No reaction	n.d.
4	***ent*-22**	DIC, $Cu(OTf)_2$; PNB-OH	**34** (9%)	90%
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.

Clearly, the increased C–H acidity due to the fluorination, combined with the deactivation towards 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 short reaction times were employed given the lability of the MOM protecting group under the reaction conditions. The triflate **36** was noticeably more stable compared to the triflate **30**, due to the electronegativity of the tetrafluoroalkylidene group.

Table 2. Attempts to effect C4 inversion.



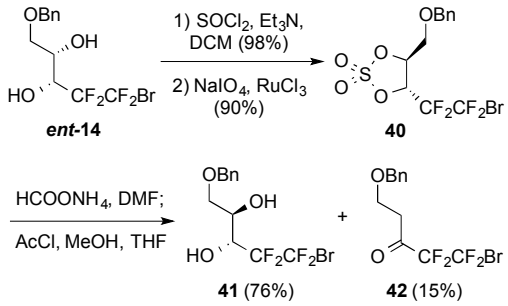
Entry	Reagent(s) (equiv)	Temp (°C)	Products (yield)[a] (%)		
			37	**(*Z*)-38**	s.m.
1	$NaNO_2$ (9.8)	25	13	0	53
2	$NaNO_2$ (9.8)	60	38	24	0
3	$NaNO_2$ (9.8), 15-c-5	60	39	29	0
4	$NaNO_2$ (9.8), Bu_4NBr	60	27	26	0
5	$NaNO_2$ (9.8)	40	52	33[a]	15
6	NaOBz (9.8)	60	15	85	0
7	CCl_3CO_2Na (9.8)	60	-	38[a]	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.

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]

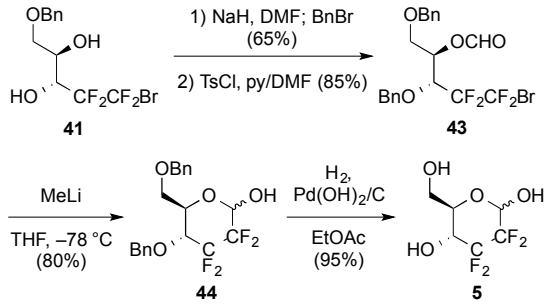
Hence, it was decided to return to the previously developed cyclic sulfate route (Scheme 4), which regioselectivity is due to the fluorination hampering S_N2 reactions in adjacent positions.[18] The cyclic sulfate formation itself was further optimized to give excellent overall yield on large-scale (10 mmol), mainly achieved by modifying the work-up 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 towards 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 acceptable yield on 8 mmol scale. Interestingly, on this scale, the 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.



Scheme 4. Formation of the *anti*-diol.

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

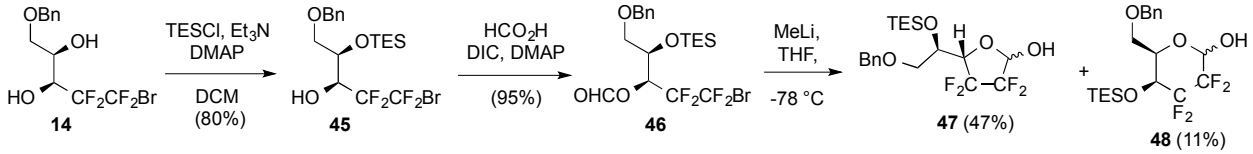
stereochemistry, was lower-yielding than for the *syn*-diol as reported in Scheme 3, formate introduction and anionic cyclization.



Scheme 5. Synthesis of the pyranose sugar derivative **5.**

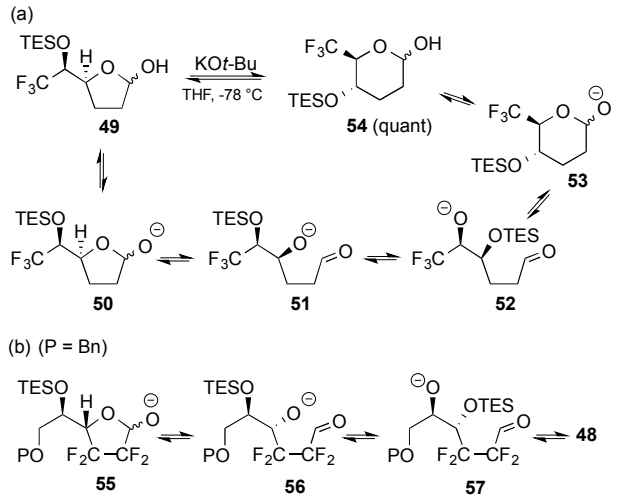
Furanose ring formation: synthesis of (protected) dideoxy-tetrafluoro "galactofuranose"

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.



Scheme 6. First generation synthesis of the tetrafluorinated furanose, with rearranged pyranose as side-product.

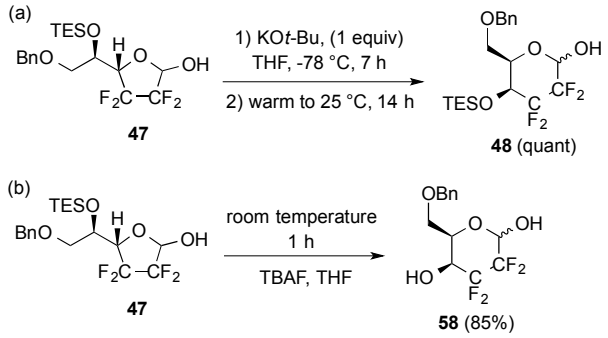
As shown in Scheme 7(a), Kitazume had described a similar isomerization process in which deprotonation of the furanose **49** led to ring opening and silyl transfer, followed by cyclization to give the pyranose **54**, in quantitative yield.[42,43] The direction of the equilibrium was explained by the thermodynamic driving force towards 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**.



Scheme 7. Mechanism of the silyl migration.

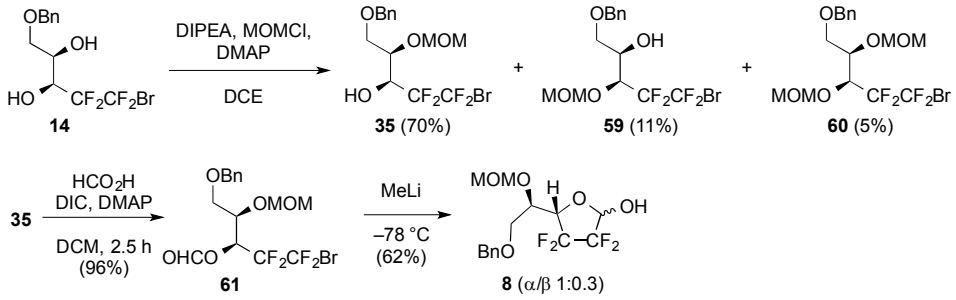
Indeed, in a separate experiment in which **47** was subjected to the Kitazume isomerization conditions (Scheme 8 (a)), only minimal reaction to **48** was observed (TLC) at –78 °C, and quantitative conversion only occurred after warming up the reaction mixture to room temperature overnight. This clearly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



Scheme 8. Isomerization experiments from the furanose 47

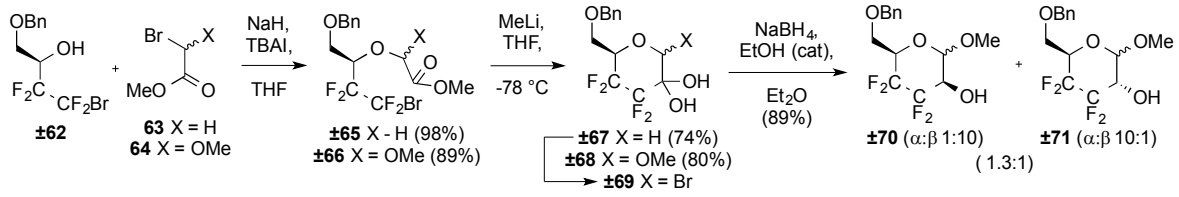
The much larger stability of the tetrafluorinated pyranose was further confirmed by rapid isomerization upon silyl cleavage (Scheme 8 (b)). Hence, to avoid the isomerization, a different protecting group was used (Scheme 9). Reaction of diol **14** with MOMCl led to the desired monoprotected **35** in 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.



Scheme 9. Optimized second generation synthesis of the furanose derivative.

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).



Scheme 10. Anionic cyclization strategy towards the synthesis of **6** and **7**.

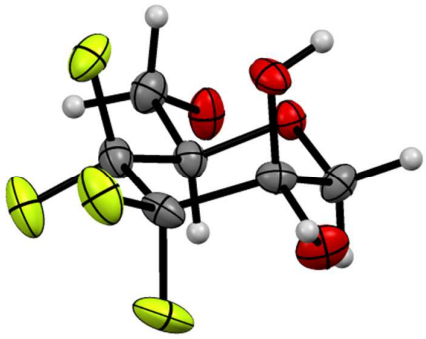
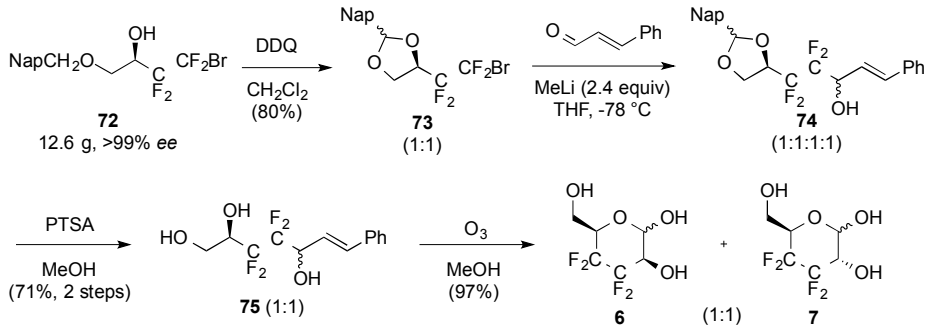


Figure 1. Crystal structure of **67**. Thermal probability ellipsoids are shown at the 50% probability level. The 6-*O*-Bn group is omitted for clarity.

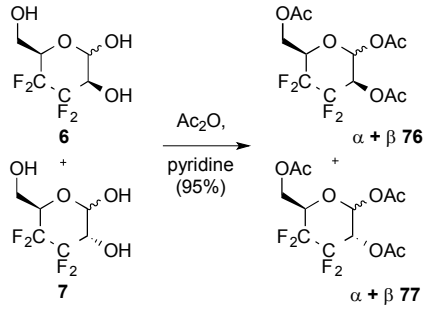
Hence, the synthesis of the precursor **66**, already containing an anomeric substituent, was envisioned. This was achieved in high yield by reaction of **62** with known bromoether **64**,[44] which was obtained by radical bromination of methyl methoxyacetate (not shown). Also on this substrate, anionic 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 product, 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 hemi-acetal 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 large scale as described by us previously.[26] Analysis *via* the corresponding Mosher ester derivative confirmed its enantiopurity (>99% *ee*, see SI). 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 SI).



Scheme 11. Intermolecular addition strategy for the synthesis of **6** and **7**.

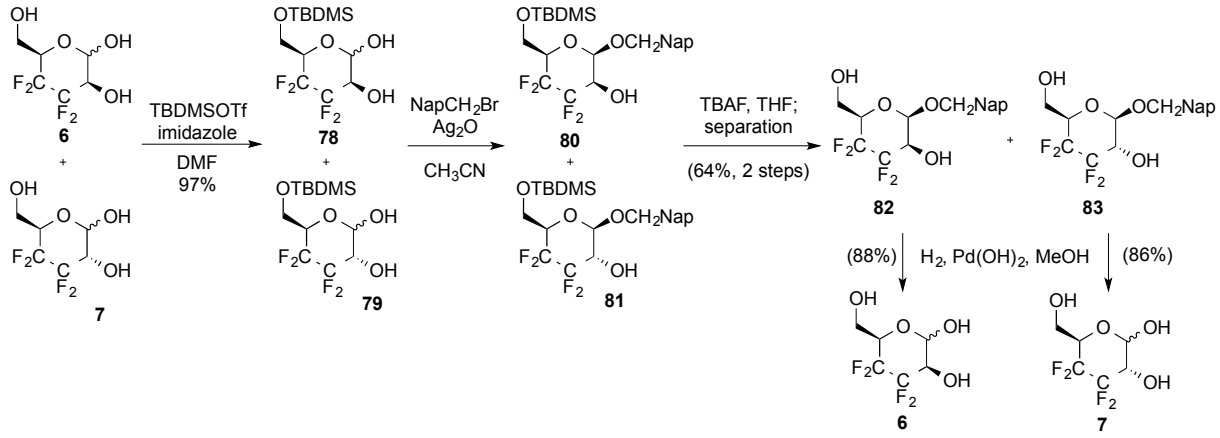
Starting from each acetal diastereomer, bromine-lithium exchange followed by reaction with cinnamaldehyde proceeds in excellent yields (80%), but in each case an inseparable 1:1 mixture of alcohol diastereomers was obtained (not shown). Hence, on large scale (7 g) the acetal diastereomers were not separated 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 2-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 (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 per-acetates **76** and **77** proceeded in excellent yield (Scheme 12), but did not allow for a practical diastereomeric separation.



Scheme 12. Acetylation of the mixture to attempt separation.

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

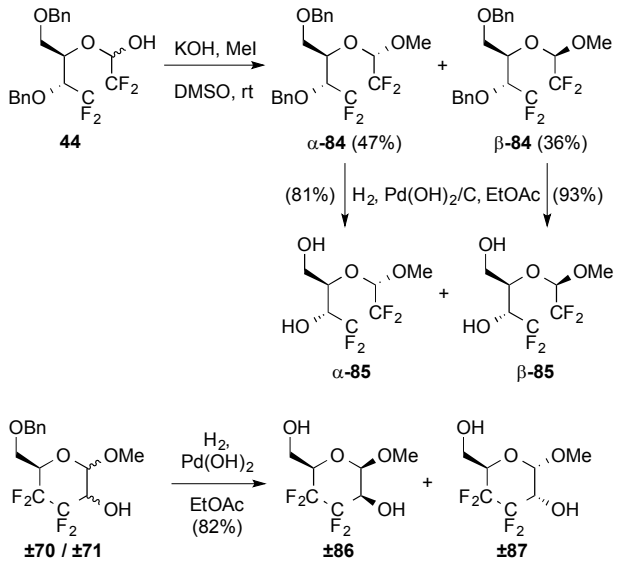
During the extensive derivatization/separation efforts, it was noticed that very often the two diastereomers having the same anomeric configuration but different C2 stereochemistry were separable. Hence, a protection strategy aiming at selective glycoside formation was pursued. It was found that after 6-OH protection as silyl ether (Scheme 13), anomeric napthylmethylation proceeded with excellent yield and β-selectivity.[48,49,18] 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.



Scheme 13. Separation of **6** and **7**.

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 studies (2D ^{1}H-^{19}F HOESY) 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 hemi-acetals prevented clear analysis by 1D and 2D ^{1}H-^{19}F HOESY-NMR, 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.



Scheme 14. Synthesis of the methyl glycosides.

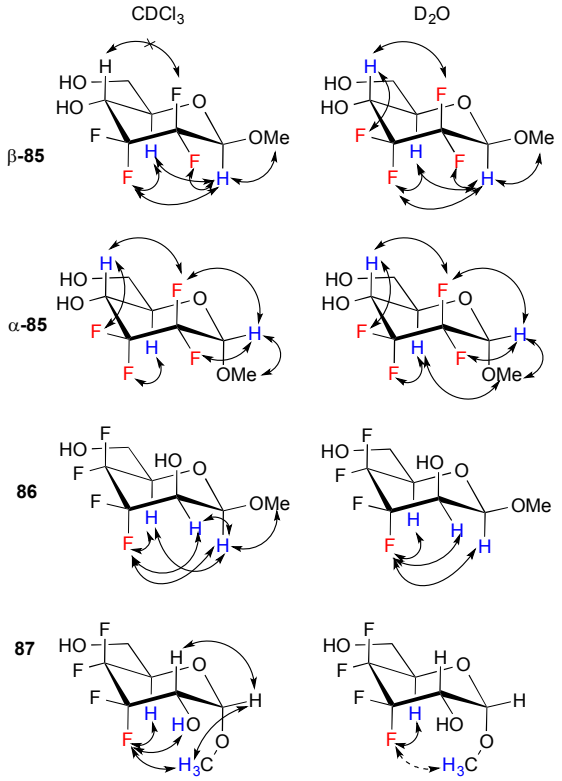
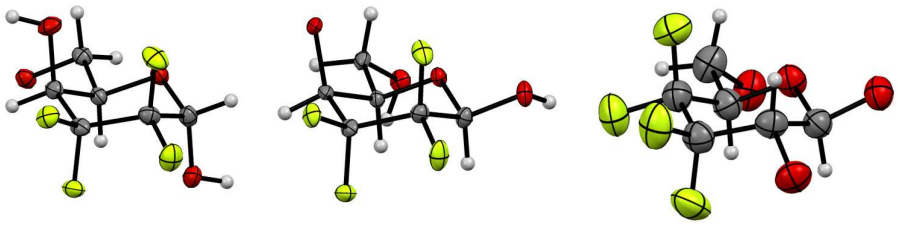


Figure 2. ^{1}H-^{1}H NOESY and ^{1}H-^{19}F HOESY analysis of 85–87.

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

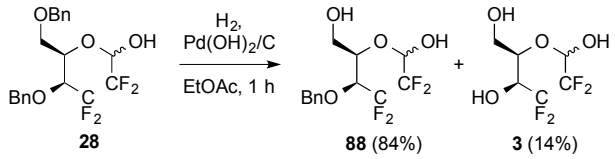
confirms the minimal influence of dideoxy-tetrafluorination on the monosaccharide chair conformation.

Crystal structure analysis of heavily fluorinated carbohydrate derivatives have also shown that the $^4C_1$ 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 shown in Figure 3. These crystal structures also show a relatively undistorted $^4C_1$ chair conformation. The crystal packing of all structures (see SI) shows that hydrogen bonding of the alcohol groups with oxygen containing groups is maximized, an effect which presumably determines the anomeric configuration of the hemi-acetals:[20] the benzyl ether **58** crystallizes as the α-anomer, while **88** and **77** are obtained as the β-anomer.



α-58 **β-88** **β-77**

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 SI for the complete crystal structures.



Scheme 15. Incomplete hydrogenolysis leading to **88**.

Pleasingly, both unprotected 3,3,4,4-tetrafluorinated sugar derivatives **6** and **7** proved 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.

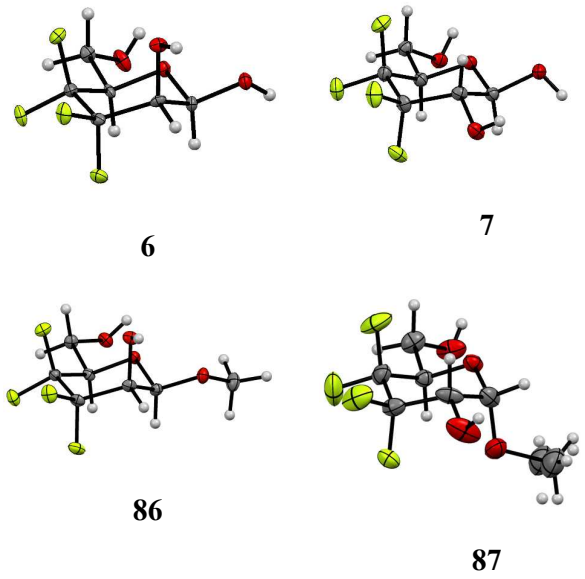


Figure 4. Crystal structures of **6** and **7** and methyl glycosides **86** and **87**. Thermal probability ellipsoids are shown at the 50% probability level. There is disorder at the **87** methyl group.

Where hydrogen bonding opportunities are present (O-H…O and less often O-H…F) these interactions dominate the packing arrangements (see SI for figures). In **6** the high number of donors and the compact nature of the molecule allows for 3D network formation, however, change of 2-OH

configuration is enough to disrupt this network such that **7** now forms 2D sheets in the bc plane. The arrangement in the 3rd direction is now directed by weaker interactions with hydrophobic F surfaces stacking along the a axis forming alternating hydrophilic and hydrophobic layers. The similar molecules **58** and **67** also form sheets (bc plane) with a layer structure characterised 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 co-locates the benzyl groups of adjacent chains forming hydrophobic columns. This co-location of certain groups gives rise to a related co-location 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 pseudo parallel 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 pseudo-parallel. 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 large scale. Both the formation of the C1–C2 (tetrafluorination at C2/C3) as well as the C2–C3 (tetrafluorination at C3/C4) bonds (sugar numbering) are 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 analysis shows 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 aluminium-precoated plates coated with silica gel 60 with an F254 indicator; visualised 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 (FT-IR) spectra were measured using an ATR accessory using neat samples (solids and liquids). Electrospray mass spectra were ran 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 three 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. Aq. HCl (1M, 170 mL)

was then added and the resultant 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]

*(3S,4R)-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) was 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 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 d. Na_2SO_3 (100 g) was added and the mixture stirred for 2 h at 0 °C to r.t. before being treated with H_2O (175 mL). Extraction was carried out into EtOAc (3 × 350 mL). The combined organic phases were washed with HCl (2M, 2 × 75 mL) then brine (75 mL), before being dried ($MgSO_4$), filtered and concentrated to give a yellow solid (96.8% *e.e.*). 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 d at r.t. and the resultant crystals filtered and washed with hexane to give a white solid (20.54 g, 75%, >99.9% *e.e.*). 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 (2M, aq), then extracted into EtOAc (2 × 270 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated to give impure $(DHQD)_2AQN$ as red solid. Column chromatography (DCM/MeOH 85:15) gave recovered $(DHQD)_2AQN$ (1.29 g, 92%) as a yellow/orange solid.

*(3R,4S)-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) was 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 d. Na_2SO_3 (60 g) was added and the reaction mixture stirred for 2 h at 5 °C to r.t. 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 (2M, 2 × 40 mL) 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% *e.e*). This was suspended in hexane and heated to 40 °C, then Et_2O was added until dissolution occurred. The solution was allowed to stand for 7 d, 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% *e.e.*). Mp 84–86 ºC (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) 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.

*(3S,4R)-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 r.t. for 22 h. Aq. NH_4Cl (sat., 180 mL) was added and the resultant mixture stirred at r.t. for 30 min, before extraction was carried out into 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 tri-benzyl 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]

*(3S,4R)-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 r.t. 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 r.t. 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 (sat., 75 mL) was added to the reaction mixture, which was then stirred for 30 min, while allowing to warm to r.t. The mixture was diluted with H_2O (150 mL) 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 r.t. 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]

*(2S,3R)-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 r.t. 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.

*(2S,3R)-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 r.t. for 14.5 h. The reaction was diluted with DCM (9 mL) and the solid pyridinium 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<u>H</u>CH_2), 4.75 (1H, d, *J* 11.0 Hz, C<u>H</u>HPh), 4.69 (1H, d, *J* 11.0 Hz, CH<u>H</u>Ph), 4.58 (1 H, d, *J* 11.5 Hz, C<u>H</u>HPh), 4.53 (2H, d, *J* 12.0 Hz, CH<u>H</u>Ph), 4.51 (1H, dt, *J* 17.6, 4.5 Hz, C<u>H</u>CF_2), 3.83 (1H, dd, *J* 11.0, 4.5 Hz, C<u>H</u>HOBn), 3.77 (1H, dd, *J* 11.5, 6.0 Hz, CH<u>H</u>OBn); ^{13}C NMR (101 MHz, $CDCl_3$) δ 129.0 (<u>C</u>H_{Ar} × 3), 129.0 (<u>C</u>H_{Ar} × 2), 129.0 (<u>C</u>H_{Ar} × 2), 128.8 (<u>C</u>H_{Ar} × 2), 128.7 (<u>C</u>H_{Ar}), 128.3 (<u>C</u>H_{Ar} × 2), 83.2 (<u>C</u>HCH_2), 76.3 (<u>C</u>H_2Ph), 74.1 (<u>C</u>H_2Ph), 67.4 (<u>C</u>H_2OBn); ^{19}F NMR (282 MHz, $CDCl_3$) δ -63.3 (s, C<u>F</u>$_2$Br), -75.1 (s, C<u>F</u>$_3$), -110.9 (d, *J* 275 Hz, C<u>F</u>FCH), -120.4 (dd, *J* 274, 18 Hz, CF<u>F</u>CH); HRMS (ES+): for $C_{20}H_{18}{}^{79}BrF_7O_5SNa^+$ $[M + Na]^+$ calcd.604.9839; found 604.9823.

*(2R,3R)-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 dissolution, DIAD (114 μL, 0.58 mmol) was then added and stirring continued at r.t. 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<u>H</u>CH_2), 4.75 (1H, d, *J* 10.7 Hz, C<u>H</u>HPh), 4.69 (1H, d, *J* 10.8 Hz, CH<u>H</u>Ph), 4.56 (1H, d, *J* 11.9 Hz, C<u>H</u>HPh), 4.50 (1H, d, *J* 11.9 Hz, CH<u>H</u>Ph), 4.38 (1H, dt, *J* 16.6, 5.9 Hz, C<u>H</u>CF_2), 4.05 (1H, d, *J* 14.9 Hz, C<u>H</u>HCl), 3.99 (1H, d, *J* 14.9 Hz, CH<u>H</u>Cl), 3.86 (1H, dd, *J* 11.3, 6.0 Hz, C<u>H</u>HOBn), 3.78 (1H, dd, *J* 11.3, 2.8 Hz, CH<u>H</u>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 × <u>C</u>H_{Ar}), 128.4 (<u>C</u>H_{Ar}), 128.2 (2C, 2 × <u>C</u>H_{Ar}), 127.9 (<u>C</u>H_{Ar}), 127.7 (2C, 2 × <u>C</u>H_{Ar}), 75.4 (<u>C</u>H_2Ph), 75.3 (dd, *J* 27, 21 Hz, <u>C</u>HCF_2), 73.4 (<u>C</u>H_2Ph), 72.3 (<u>C</u>HCH_2), 67.6 (<u>C</u>H_2OBn), 40.6 (<u>C</u>H_2Cl); ^{19}F NMR (282 MHz, $CDCl_3$) δ -63.1 (d, *J* 5 Hz, CF<u>F</u>Br), -63.2 (s, C<u>F</u>FBr), -111.0 (d, *J* 274 Hz, C<u>F</u>FCH), -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, CHCH$_2$), 4.88 (2H, s, CHHPh + CHHPh), 4.47 (2H, s, CHHPh + CHHPh), 4.12 (1H, t, *J* 2.2 Hz, CHHOBn), 4.11 (1H, t, *J* 2.2 Hz, CHHOBn); ^{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 (CHCH$_2$), 75.8 (CH$_2$Ph × 2), (dd, *J* 26, 22 Hz, CCF$_2$), 73.5 (CH$_2$Ph), 66.5 (CH$_2$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.

*(3S,4R)-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 (1M 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, CHCF$_2$), 4.74 (1H, d, *J* 7.1 Hz, CHHOMe), 4.70 (1H, d, *J* 7.1 Hz, CHHOMe), 4.64 (1H, d, *J* 11.6 Hz, CHHPh), 4.53 (1H, d, *J* 11.6 Hz, CHHPh), 4.23 (1H, dd, *J* 11.1, 5.1 Hz, CHCH$_2$), 3.77 (1H, dd, *J* 10.1, 5.1 Hz, CHHOBn), 3.67 (1H, dd, *J* 10.1, 6.6 Hz,

CHHOBn), 3.38 (3H, s, CH$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.2 (C_{Ar}), 128.5 (CH_{Ar} × 2), 128.0 (CH_{Ar}), 127.8 (CH_{Ar} × 2), 97.4 (CH_2OMe), 77.8 (t, *J* 26 Hz, $CHCF_2$), 73.6 (CH_2Ph), 72.7 ($CHCH_2$), 67.7 (CH_2OBn), 56.2 (CH_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.

*(3R,4R)-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}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.44 (5H, m), 4.77 (1H, d, *J* 7.1 Hz, OCHHO), 4.74 (1H, d, *J* 7.1 Hz, OCHHO), 4.59 (2H, s, CHHPh, CHHPh), 4.47 (1H, ddt, $^3J_{H\text{-}F}$ 22.2, *J* 8.6, 3.5 Hz, $CHCF_2$), 4.28 (1H, d, *J* 8.6 Hz, OH), 4.02 (1H, q, *J* 3.5 Hz, $CHCH_2$), 3.89 (1H, dd, *J* 10.6, 4.0 Hz, CHHOBn), 3.83 (1H, dd, *J* 10.1, 3.5 Hz, CHHOBn), 3.43 (3H, s, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.0 (C_{Ar}), 128.6 (CH_{Ar} × 2), 128.1 (CH_{Ar}), 127.9 (CH_{Ar} × 2), 96.8 (OCH_2O), 75.6 ($CHCH_2$), 74.0 (CH_2Ph), 70.7 (t, *J* 3 Hz, CH_2OBn), 70.6 (dd, *J* 28, 22 Hz, $CHCF_2$), 56.1 (CH_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-tetrafluoro-pent-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}; ^{1}H 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, $\underline{C}$OMOM), 137.1 (C_{Ar}), 128.6 ($\underline{C}H_{Ar}$ × 2), 128.1 ($\underline{C}H_{Ar}$), 127.9 ($\underline{C}H_{Ar}$ × 2), 96.7 (t, *J* 25 Hz, $\underline{C}$H), 93.9 ($\underline{C}H_2$OMe), 72.2 ($\underline{C}H_2$Ph), 67.6 ($\underline{C}H_2$OBn), 56.8 ($\underline{C}H_3$); ^{19}F NMR (282 MHz, $CDCl_3$) δ -66.2 (2F, t, *J* 9 Hz, C$\underline{F}_2$Br), -104.4 (2F, m, C$\underline{F}_2$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.

*(4S,5R)-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 mins. 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 separated. The aqueous phase was extracted into Et_2O (4 × 180 mL) and the resultant organic phases 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 $RuCl_3$•xH_2O (55 mg) were added, and the reaction was stirred vigorously at 0 °C to r.t. for 16 h. The resultant mixture was diluted with Et_2O (50 mL) 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 fridge 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]

*(3R,4R)-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 (2M in MeOH, 12.5 mL, 25.0 mmol). The reaction mixture was stirred at r.t. 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$\underline{H}_2$Ph), 3.82 (2H, t, *J* 6.1 Hz, C$\underline{H}_2$OBn), 3.07 (2H, t, *J* 6.1 Hz, C$\underline{H}_2$C=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 ($\underline{C}H_2$Ph), 63.4 ($\underline{C}H_2$OBn), 38.7 ($\underline{C}H_2$C=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.

*(3R,4R)-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 r.t. for 20 h. Aq. NH_4Cl (sat., 25 mL) was added and the resultant mixture stirred at r.t. for 30 min. Extraction was carried out into 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%), tris-benzyl 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]

*(2R,3R)-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 then r.t. 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 r.t. 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 concentrating the filtrate 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 (sat., 10 mL) was added to the reaction mixture, which was then stirred for 20 min, while allowing to warm to r.t. 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 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 r.t. for 14 h. Aq. HCl (1M, 0.33 mL) was added, 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<u>H</u>HPh × 3), 4.53 (1H, d, *J* 11.8 Hz, C<u>H</u>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<u>H</u>$_{3\ \alpha/\beta}$ × 3), 0.95 (9H, t, *J* 7.9 Hz, C<u>H</u>$_{3\beta/\alpha}$), 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, <u>C</u>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-$5_\beta$), 69.6–70.9 (2C, m, C-$4_{\alpha+\beta}$), 68.8 (d, *J* 5 Hz, C-$5_\alpha$), 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 r.t. and TBAF (1M in THF, 300 µL, 0.30 mmol) was added dropwise. The reaction was stirred at r.t. for 1 h, then 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} ^{1}H 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] δ 7.23–7.42 (10H, m, $\underline{H}_{Ar}$), 5.30 (1H, dd, *J* 9.2, 6.5 Hz, H-1_α), 5.00 (1H, dt, *J* 13.1, 3.6 Hz, H-1_β), 4.52–4.62 (5H, m, $CH_2Ph_{\alpha+\beta}$, H-5_α), 4.09–4.23 (2H, m, H-$4_{\alpha+\beta}$), 4.02 (1H, dtd, *J* 8.0, 4.0, 2.0 Hz, H-5_β), 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_α); ^{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.

*(3S,4R)-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) then 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, then 83 °C for 5 h. The brown reaction mixture was then washed with aq. $NaHCO_3$ (sat., 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}; ^1H 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, C$\underline{H}_3$), 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}; ^1H 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, $^3J_{H\text{-}F}$ 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, C$\underline{H}_3$), 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, CHCF$_2$), 73.4 (CH$_2$Ph), 70.0 (CH$_2$OBn), 67.8 (CHCH$_2$), 56.8 (CH$_3$); ^{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, CHHOMe), 4.74–4.77 (2H, m. CHHOMe + CHHOMe), 4.73 (1H, d, *J* 6.6 Hz, CHHOMe), 4.58 (1H, d, *J* 12.1 Hz, CHHPh), 4.55 (1H, d, *J* 12.1 Hz, CHHPh), 4.45 (1H, ddd, *J* 17.3, 7.5, 2.0 Hz, CHCF$_2$), 4.15 (1H, td, *J* 6.1, 1.5 Hz, CHCH$_2$), 3.70 (2H, d, *J* 6.1 Hz, CHHOBn + CHHOBn), 3.44 (3H, s, CH$_3$), 3.39 (3H, s, CH$_3$'); ^{13}C NMR (101 MHz, CDCl$_3$) δ 137.7 (C$_{Ar}$), 128.4 (CH$_{Ar}$ × 2), 127.8 (CH$_{Ar}$), 127.7 (CH$_{Ar}$ × 2), 98.7 (CH$_2$OMe), 97.3 (CH$_2$OMe), 74.5 (CHCH$_2$), 73.4 (CH$_2$Ph), 73.5 (dd, *J* 26, 20 Hz, CHCF$_2$), 68.7 (CH$_2$OBn), 56.8 (CH$_3$), 55.9 (CH$_3$'); ^{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.

*(3S,4R)-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 then treated with formic acid (470 µL, 12.5 mmol) dropwise. The mixture was then stirred at r.t. for 2.5 h before being diluted with DCM (25 mL) and aq. HCl (1M, 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) 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, CHO), 7.28–

7.44 (5H, m, H_{Ar}), 6.00 (1H, dt, $^{3}J_{H\text{-}F}$ 19.3, *J* 3.3 Hz, C<u>H</u>CF_2), 4.75 (1H, d, *J* 7.1 Hz, C<u>H</u>HOMe), 4.72 (1H, d, *J* 6.9 Hz, CH<u>H</u>OMe), 4.54 (1H, d, *J* 11.7 Hz, C<u>H</u>HPh), 4.50 (1H, d, *J* 11.7 Hz, CH<u>H</u>Ph), 4.27 (1H, ddt, *J* 7.2, 5.2, 2.1 Hz, C<u>H</u>CH_2), 3.66 (1H, dd, *J* 9.7, 5.2 Hz, C<u>H</u>HOBn), 3.47 (1H, dd, *J* 9.7, 7.4 Hz, CH<u>H</u>OBn), 3.39 (3H, s, C<u>H</u>$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3 (<u>C</u>HO), 137.3 (C_{Ar}), 128.4 (2 × <u>C</u>H_{Ar}), 127.9 (2 × <u>C</u>H_{Ar}), 97.0 (<u>C</u>H_2OMe), 73.7 (<u>C</u>H_2Ph), 72.7 (<u>C</u>HCH_2), 68.1 (<u>C</u>H_2OBn), 65.7 (dd, *J* 31, 20 Hz, <u>C</u>HCF_2), 56.1 (<u>C</u>H_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ -64.0 (d, *J* 185 Hz, C<u>F</u>FBr), -64.6 (d, *J* 176 Hz, CF<u>F</u>Br), -112.2 (d, *J* 275 Hz, C<u>F</u>FCH), -119.5 (dd, *J* 275, 17 Hz, CF<u>F</u>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) then 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 (70 mL) and cooled to –78 °C. MeLi (1.6M in Et_2O, 4.3 mL, 6.88 mmol) was added very slowly, dropwise. The mixture was stirred at –78 °C for 5 h then treated with aq. NH_4Cl (sat., 35mL). After stirring for 0.5 h while being allowed to warm to r.t., the mixture was diluted with H_2O (45mL) 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, 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<u>H</u>HOMe$_{x+y}$ + CH<u>H</u>OMe$_{x+y}$), 4.65 (1.3H, m, H-4_{x+y}), 4.52–4.60 (2.6H, m, C<u>H</u>HPh$_{x+y}$ + CH<u>H</u>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<u>H</u>$_{3x}$), 3.38 (0.9H, s, C<u>H</u>$_{3y}$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.4 (<u>C</u>$_{Ary}$), 137.3 (<u>C</u>$_{Arx}$), 128.4, 128.4, 127.9, 127.8, 127.7, 127.7 (<u>C</u>H$_{Arx+y}$), 97.3 (<u>C</u>H_2OMe$_x$), 96.8 (<u>C</u>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.

*(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 then quenched with sat. aq. NH_4Cl (5 mL), diluted with Et_2O (50 mL) and washed with water (25 mL) and brine (25 mL). The etheral 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 of 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); ^{1}H 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 ($\underline{C}H_2CO_2Me$), 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 drying with N_2 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 (1.6M 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 sat. aq. NH_4Cl (5 mL) then allowed to warm up 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); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.29 (10H, m, H_{Ar}), 4.64 (1H, d, *J* 11.9 Hz, C<u>H</u>HPh, hydrate), 4.69–4.57 (2H, m, C<u>H</u>$_2$Ph ketone), 4.57 (1H, d, *J* 12.0 Hz, CH<u>H</u>Ph, hydrate), 4.43 (1H, ddd, *J* 15.4, 3.3, 1.0 Hz, C<u>H</u>HC=O), 4.32 (1H, ddd, *J* 15.5, 3.9, 0.9 Hz, CH<u>H</u>C=O), 4.24 (1H, ddtt, $^3J_{H\text{-}F}$ 22.2, *J* 7.5, 2.6, 1.2 Hz, C<u>H</u>CF_2 ketone), 3.99–3.76 (5H, m, C<u>H</u>CF_2, C<u>H</u>HOBn, C<u>H</u>HC$(OH)_2$, hydrate and C<u>H</u>$_2$OBn ketone), 3.75 (1H, dd, *J* 11.2, 7.6 Hz, CH<u>H</u>OBn, hydrate), 3.65 (1H, ddd, *J* 12.6, 3.4, 1.1 Hz, CH<u>H</u>C<u>(</u>$OH)_2$, 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, <u>C</u>$(OH)_2$), 77.1 (t, *J* 23.4 Hz, CF_2<u>C</u>H hydrate), 74.1 (<u>C</u>H_2Ph), 73.9 (<u>C</u>H_2Ph hydrate), 71.4 (<u>C</u>H_2C=O), 71.2 (d, *J* 2.9 Hz, <u>C</u>$H_2C(OH)_2$), 66.0 (br. s., <u>C</u>H_2OBn 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)-(2S,2'R)-Methyl (1-benzyloxy-4-bromo-3,3,4,4-tetrafluorobutan-2-yl)oxy-2-methoxyacetate (±**66a**) and (Rac)-(2R,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 then quenched with sat. aq. NH_4Cl (2.5 mL), diluted with Et_2O (25 mL) and washed with water (10 mL) and brine (10 mL). The etheral 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<u>H</u>CO_2Me, minor isomer), 5.10 (1H, s, C<u>H</u>CO_2Me, major isomer), 4.63–4.48 (6H, m, 2×C<u>H</u>$_2$Ph and 2×C<u>H</u>CF_2), 3.89–3.75 (4H, m, 2×CHC<u>H</u>$_2$O), 3.77 (3H, s, OC<u>H</u>$_3$, major isomer), 3.71 (3H, s, OC<u>H</u>$_3$, minor isomer), 3.47 (3H, s, OC<u>H</u>$_3$, minor isomer), 3.46 (3H, s, OC<u>H</u>$_3$, 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 (<u>C</u>HCO_2Me), 99.5 (<u>C</u>HCO_2Me), 74.6 (t, *J* 24.9 Hz, <u>C</u>HCF_2), 74.3 (dd, *J* 26.3, 23.4 Hz, <u>C</u>HCF_2), 73.7 (<u>C</u>H$_2$Ph), 73.6 (<u>C</u>H$_2$Ph), 68.8 (CH<u>C</u>H$_2$O), 68.5 (CH<u>C</u>H$_2$O), 55.0 (O<u>C</u>H$_3$), 54.7 (O<u>C</u>H$_3$), 52.4 (O<u>C</u>H$_3$), 52.3 (O<u>C</u>H$_3$) (2×CF_2 not resolved); ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.4 (m, *J* 180.5 Hz, C<u>F</u>FBr, minor isomer), –62.9 (m, *J* 180.5 Hz, C<u>F</u>FBr, major isomer), –63.4 (m, *J* 180.5 Hz, CF<u>F</u>Br, minor isomer), –63.5 (d, *J* 180.5 Hz, CF<u>F</u>Br, major isomer), –113.4 (m, *J* 275.1 Hz, CHC<u>F</u>F, minor isomer), –114.3 (dd, *J* 275.1, 8.6 Hz, CHC<u>F</u>F, major isomer), –116.4 (dd, *J* 275.1, 8.6 Hz, CHCF<u>F</u>, major isomer), –117.7 (dt, *J* 275.1, 10.8 Hz, CHCF<u>F</u>, minor isomer). MS (EI) *m*/*z* (%) 329 and 331 ($(M - MeOCHCO_2Me^{\bullet})^+$, 4), 251 and 253 (6), 103 ($MeOCHCO_2Me^+$, 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-glycero-hex-2-ulopyranoside (±68). A solution of the ester **±66** in DCM was filtered through $MgSO_4$ while drying with N_2 then dried under high vacuum overnight. The ester **±66** (484 mg, 1.12 mmol, 1 equiv) was dissolved in dry THF (10 mL) then cooled to –78 °C. MeLi (1.6M 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 sat. aq. NH_4Cl (5 mL) then allowed to warm up 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<u>H</u>OMe minor anomer), 4.65 (2H, d, *J* 12.0 Hz, 2×C<u>H</u>HPh), 4.63–4.57 (2H, m, 2×CH<u>H</u>Ph), 4.55 (1H, d, *J* 2.9 Hz, C<u>H</u>OMe major anomer), 4.38–4.26 (1H, m, C<u>H</u>CF_2 minor anomer), 4.10–3.98 (1H, m, C<u>H</u>CF_2, major anomer), 3.97–3.89 (2H, m, 2×C<u>H</u>HOBn), 3.78 (2H, dd, *J* 11.1, 7.6 Hz, 2×CH<u>H</u>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 (<u>C</u>HOMe, minor anomer), 99.9 (d, *J* 4.4 Hz, <u>C</u>HOMe, major anomer), 73.9 (<u>C</u>H_2Ph), 73.8 (<u>C</u>H_2Ph), 72.7 (t, *J* 24.9 Hz, <u>C</u>HCF_2, major anomer), 68.0 (t, *J* 24.5 Hz, <u>C</u>HCF_2, minor anomer), 66.0 (br. s., <u>C</u>H_2OBn), 65.8 (br. s., <u>C</u>H_2OBn), 57.8 (O<u>C</u>H_3, major anomer), 56.3 (O<u>C</u>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 – –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.

*(Rac)-methyl 6-O-benzyl-3,4-dideoxy-3,3,4,4-tetrafluoro-**β**-threo-hexopyranoside (**±β-70**) and the α-erythro-hexopyranoside (**±α-71**).* To a solution of **±68** (500 mg, 1.47 mmol, 1 equiv) in dry Et_2O (10 mL) was 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. 1 equiv of $NaBH_4$ was added and the resultant mixture was stirred overnight then 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, C<u>H</u>HPh), 4.60 (1H, dd, *J* 11.9, 1.9 Hz, CH<u>H</u>Ph), 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, OC<u>H</u>$_3$), 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 (<u>C</u>H$_2$Ph), 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 (O<u>C</u>H$_3$) (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 – –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, C<u>H</u>HPh), 4.60 (1H, dd, *J* 11.9, 1.9 Hz, CH<u>H</u>Ph), 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, OC<u>H</u>$_3$), 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 (<u>C</u>H$_2$Ph), 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 (O<u>C</u>H$_3$) (2×CF_2 not resolved); ^{19}F NMR (282 MHz, $CDCl_3$) δ–128.1 (dd, *J* 254.0, 21.5 Hz), –133.1 – –131.4 (3F, m). HRMS (MS+) for $C_{14}H_{16}F_4NaO_4$ $(M + Na)^+$ calcd 347.0877, found 347.0879.

*(2R)-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 1h. The solvents were reduced *in vacuo* to yield a crude residue which was taken up in sat. 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).

*(4R)-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 MS 4Å (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 5h 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 is rinsed with $CHCl_3$ (300 mL) and layers are partitioned. The aqueous layer was extracted with $CHCl_3$ (300 mL) and the combined organic extracts were washed with sat. 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); ^1H 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, C<u>H</u>OO), 4.83 (1H, dddd, $^3J_{HF}$ 17.4, $^3J_{HH}$ 7.2, $^3J_{HF}$ 6.8, $^3J_{HH}$ 6.6 Hz, C<u>H</u>CF_2), 4.49 (1H, dd, $^2J_{HH}$ 9.2, $^3J_{HH}$ 7.2 Hz, C<u>H</u>HCHO), 4.34 (1H, dd, $^2J_{HH}$ 9.2, $^3J_{HH}$ 6.6 Hz, CH<u>H</u>CHO); ^{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, $^{1}J_{CF}$ 311.8, $^{2}J_{CF}$ 39.5 Hz, $\underline{C}F_2$), 114.2 (ddt, $^{1}J_{CF}$ 262.0, $^{1}J_{CF}$ 256.1, $^{2}J_{CF}$ 32.2 Hz, $\underline{C}F_2$), 106.0 ($\underline{C}$HOO), 72.3 (dd, $^{2}J_{CF}$ 30.7, $^{2}J_{CF}$ 20.5 Hz, $\underline{C}$HCF2), 65.3 ($\underline{C}H_2$CHO); ^{19}F NMR (282MHz, $CDCl_3$): δ –63.8 (dd, $^{2}J_{FF}$ 182.7, $^{3}J_{FF}$ 7.5 Hz, C$\underline{F}$FBr), –64.9 (dd, $^{2}J_{FF}$ 182.7, $^{3}J_{FF}$ 5.9 Hz, CF$\underline{F}$Br), –118.0 (dt, $^{2}J_{FF}$ 271.3 , *J* 5.9 Hz, CHOC$\underline{F}$F), –123.1 ppm (ddd, $^{2}J_{FF}$ 271.3, $^{3}J_{HF}$ 17.2, $^{3}J_{FF}$ 7.5 Hz, CHOCF$\underline{F}$); 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 (400MHz, $CDCl_3$): 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, C$\underline{H}$OO), 4.85–4.72 (1H, m, C$\underline{H}CF_2$), 4.60 (1H, dd, $^{2}J_{HH}$ 9.5, $^{3}J_{HH}$ 2.3 Hz, C$\underline{H}$HCHO), 4.27 ppm (1H, dd, $^{2}J_{HH}$ 9.5, $^{3}J_{HH}$ 7.7 Hz, CH$\underline{H}$CHO); ^{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, $^{1}J_{CF}$ 314.7, $^{1}J_{CF}$ 311.8, $^{2}J_{CF}$ 39.5 Hz, $\underline{C}F_2$), 113.5 (ddt, $^{1}J_{CF}$ 264.9, $^{1}J_{CF}$ 253.2, $^{2}J_{CF}$ 30.7 Hz, $\underline{C}F_2$), 106.4 ($\underline{C}$HOO), 72.6 (dd, $^{2}J_{CF}$ 33.7, $^{2}J_{CF}$ 22.0 Hz), 65.8 ($\underline{C}H_2$CHO); ^{19}F NMR (282MHz, $CDCl_3$): δ –63.2 (dd, $^{2}J_{FF}$ 181.1, *J* 8.1 Hz, C$\underline{F}$FBr), –64.2 (dd, $^{2}J_{FF}$ 181.1, *J* 4.8 Hz, CF$\underline{F}$Br), –115.3 (dt, $^{2}J_{FF}$ 269.0, *J* 5.0 Hz, CHOC$\underline{F}$F), –126.1 ppm (ddd, $^{2}J_{FF}$ 269.0, *J* 18.1, *J* 8.3 Hz, CHOCF$\underline{F}$); 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.

*(2R)-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) 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 NH_4Cl aq. (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 sat. 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 and 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 (400MHz, 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 (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) and 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 which solidified into an off-white solid on standing. The epimers were separated by the 3-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 17 h then 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, $^3J_{H\text{-}F3ax}$ 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, $^3J_{H\text{-}F4ax}$ 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-t-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) was 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 – –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 – –133.5 (m, **β-79**), –134.7 – –133.8 (m, **β-78**), –134.8 (ddd, $^{2}J_{FF}$ 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 then 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 ($CDCl_3$) and 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, $^{3}J_{HH}$ 4.7 Hz, OH-1β), 4.42 – 4.27 (1H, m, H-5α), 4.31 (1H, d, $^{3}J_{HH}$ 3.9 Hz, OH-1α), 4.12 – 3.94 (2H, m, H-2α, H-6_aβ), 4.04 (1H, dd, $^{2}J_{HH}$ 11.4, $^{3}J_{HH}$ 3.0 Hz, H-6_aα), 3.93 – 3.79 (3H, m, H-2β, H-5β, H-6_bβ), 3.87 (1H, dd, $^{2}J_{HH}$ 11.4, $^{3}J_{HH}$ 7.5 Hz, H-6_bα), 3.30 (1H, d, $^{3}J_{HH}$ 4.5 Hz, OH-2β), 2.81 (1H, d, $^{3}J_{HH}$ 11.4 Hz, OH-2α), 0.92 (9H, s, $CH_{3,tBu}$α), 0.91 (9H, s, $CH_{3,tBu}$β), 0.12 (6H, s, CH_3α), 0.11 (6H, s, CH_3β); ^{13}C NMR (101 MHz, $CDCl_3$) δ 116.1 – 110.1 (2 × CF_2, α + β), 95.0 (d, $^{3}J_{CF}$ 8.8 Hz, C-1β), 91.4 (d, $^{3}J_{CF}$ 8.8 Hz, C-1α), 73.9 (dd, $^{2}J_{CF}$ 26.4, 22.0 Hz, C-2β or C-5β), 71.9 (td, $^{2}J_{CF}$ 18.5, *J* 2.2 Hz, C-2β or C-5β), 69.0 (t, $^{2}J_{CF}$ 23.5 Hz, C-5α), 68.5 (t, $^{2}J_{CF}$ 19.4 Hz, C-2α), 59.8 – 59.6 (C-6α + β), 25.82 ($CH_{3,tBu}$α), 25.79 ($CH_{3,tBu}$β), 18.44 ($C_{q,tBu}$α), 18.37 ($C_{q,tBu}$β), -5.4 (2 × CH_3α + β), -5.46 (CH_3α), -5.5 (CH_3β); ^{19}F NMR (376 MHz, $CDCl_3$) δ –127.9 (dd, $^{2}J_{FF}$ 255.8, 20.8 Hz, α), –132.5 – –131.4 (m, α, 2×β), –133.3 (app. t, *J* 12.1 Hz, 2×α), –133.5 – –134.3 (m, *J* 257.5 Hz, β), –134.4 – –135.2 (m, *J* 261.8 Hz, β).

*2-Naphthylmethyl 6-O-t-butyldimethylsilyl-3,4-dideoxy-3,3,4,4-tetrafluoro-D-threo-hexopyra-nose (**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) was 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 then 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 (400MHz ,$CDCl_3$) 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 – –131.3 (m, 2 × C$\underline{F}$F), –134.3 – –133.4 (m, CF$\underline{F}$), –135.4 – –134.5 (m, CF$\underline{F}$); 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: ^{1}H 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 – –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 then 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); ^{1}H 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 – –129.9 (1F, m), –131.3 – –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); ^{1}H 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 – –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 then 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) and 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); ^{1}H 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 – –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 – –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 then 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) and 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); ^{1}H 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 – –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); {^{1}H}^{19}F NMR (282 MHz, acetone-d_6) δ –126.7 (d, *J* 253.6 Hz, Fβ), –132.6 – –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 r.t. for 20 min, then 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 into 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<u>H</u>HPh), 4.64 (1H, d, *J* 12.1 Hz, C<u>H</u>HPh), 4.58 (1H, d, *J* 11.1 Hz, CH<u>H</u>Ph), 4.51 (1H, d, *J* 12.1 Hz, CH<u>H</u>Ph), 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, C<u>H</u>$_3$); ^{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 (<u>C</u>H_{Ar} × 10), 97.9 (dd, *J* 35, 25 Hz, C-1), 75.2 (<u>C</u>H_2Ph), 73.6 (<u>C</u>H_2Ph), 73.3 (t, *J* 18 Hz, C-4), 69.0 (d, *J* 6 Hz, C-5), 67.6 (C-6), 56.0 (<u>C</u>H_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}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.16–7.44 (10H, m), 4.87 (1H, d, *J* 10.6 Hz, C<u>H</u>HPh), 4.66 (1H, d, *J* 12.1 Hz, C<u>H</u>HPh), 4.61 (1H, d, *J* 10.6 Hz, CH<u>H</u>Ph), 4.58–4.62 (1H, m, H-1), 4.55 (1H, d, *J* 12.1 Hz, CH<u>H</u>Ph), 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, C<u>H</u>$_3$); ^{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 (<u>C</u>H_{Ar} × 10), 97.9 (t, *J* 22 Hz, C-1), 75.3 (<u>C</u>H_2Ph), 73.6 (<u>C</u>H_2Ph), 73.7 (t, *J* 18 Hz, C-4), 73.2 (t, *J* 4 Hz, C-5), 67.7 (C-6), 58.0 (<u>C</u>H_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ -130.5–-130.3 (2F, m), -138.0–-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 then 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–-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 ($O\underline{C}H_3$) 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, $^2J_{F3eq,F3ax}$ 254.2Hz, $^3J_{F3eq,F2ax}$ 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, $^2J_{F3ax,F3eq}$ 254.2Hz, $^3J_{F3ax,F2eq}$ 15.4 Hz, $^3J_{F3ax,H4ax}$ 18.4 Hz, $^3J_{F3ax,F2ax}$ 6.0Hz, $^4J_{F3ax,H5ax}$≈3.0 Hz, F3ax), -134.6 (ddd, $^2J_{F2ax,F2eq}$ 272.3 Hz, $^3J_{F2eq,F3ax}$ 15.4 Hz, $^3J_{F2eq,F3eq}$ 10.4Hz, 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 – -130.7 (m, F3ax + F3eq), -

134.80 (ddd, $^{2}J_{F2eq,F2ax}$ 273.3Hz, $^{3}J_{F2eq,F3ax}$ 13.0 Hz, $^{3}J_{F2eq,F3eq}$ 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 then 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, O<u>H</u>-4), 4.80 (1H, m, H-1), 3.96–4.12 (2H, m, O<u>H</u>-6, H-4), 3.91 (1H, m, H-6), 3.80 (1H, m, H-6'), 3.64–3.54 (4H, m, C<u>H</u>$_3$, 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 (O<u>C</u>H$_3$); ^{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–-136.5 (2F, m); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.68 (1H, dd, $^{3}J_{H1ax,F2ax}$ 12.8 Hz, $J_{H1ax,F}$≈1 Hz, H1), 4.16 (1H, dddd, $^{3}J_{H4ax,F3ax}$ 14.1 Hz, $^{3}J_{H4ax,F3eq}$ 11.5 Hz, $^{3}J_{H4ax,H5ax}$ 9.9 Hz, $^{4}J_{H4ax,F2ax}$ 4.0 Hz, H4), 4.02 (1H, dd, $^{2}J_{H6,H6'}$ 12.5 Hz, ^{3}J$_{H6,H5ax}$ 2.6 Hz, H6), 3.93 (1H, dd, $^{2}J_{H6',H6}$ 12.5 Hz, $^{3}J_{H6',H5ax}$ 3.4 Hz, H6'), 3.60 (1H, dddd, $^{3}J_{H5ax,H4ax}$ 9.9 Hz, $^{3}J_{H5ax,H6'}$ 3.4, $^{3}J_{H5ax,H6}$ 2.6 Hz, $^{n}J_{H5ax,F}$≈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 (O<u>C</u>H$_3$) ppm; ^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$) δ -132.5 – -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, $^{3}J_{H1ax,F2ax}$ 13.9 Hz, $^{4}J_{H1ax,F3ax}$ 2.9 Hz, H1), 4.02 (1H, dddd, $^{3}J_{H4ax,H5ax}$ 10.2 Hz, $^{3}J_{H4ax,F3ax}$ 18.6 Hz, $^{3}J_{H4ax,F3eq}$ 8.4 Hz, $^{4}J_{H4ax,F2ax}$ 3.8 Hz, H4), 3.91 (1H, dd, $^{2}J_{H6,H6'}$ 12.7 Hz, $^{3}J_{H6,H5ax}$ 2.1 Hz, H6), 3.75 (1H, dd, $^{2}J_{H6,H6'}$ 12.7 Hz, $^{3}J_{H6',H5ax}$ 4.9 Hz, H6'), 3.67 (1H, dddd, $^{3}J_{H5ax,H4ax}$ 10.2 Hz, $^{3}J_{H5ax,H6}$ 2.1

Hz, $^{3}J_{H5ax,H6'}$ 4.9 Hz, $^{n}J_{H5ax,F}$≈1 Hz, H5) ppm; ^{19}F NMR (471 MHz, D_2O) δ -132.0 (ddddd, $^{2}J_{F3ax,F3eq}$ 255.6 Hz, $^{3}J_{F3ax,H4ax}$ 18.6 Hz, $^{3}J_{F3ax,F2eq}$ 13.0 Hz, $^{3}J_{F3ax,F2ax}$ 3.8 Hz, $^{4}J_{F3ax,H1ax}$ 2.9 Hz, F3ax), -132.7 (dddd, $^{2}J_{F3eq,F3ax}$ 255.6 Hz, $^{3}J_{F3eq,F2ax}$ 12.2 Hz, $^{3}J_{F3eq,F2eq}$ 10.9 Hz, $^{3}J_{F3eq,H4ax}$ 8.4 Hz, F3eq), -137.1 (ddd, $^{2}J_{F2eq,F2ax}$ 258.3Hz, $^{3}J_{F2eq,F3ax}$ 13.0 Hz, $^{3}J_{F2eq,F3eq}$ 10.7 Hz, F2eq), -138.2 (ddddd, $^{2}J_{F2ax,F2eq}$ 258.3Hz, $^{3}J_{H1ax,F2ax}$ 13.9 Hz, $^{3}J_{F2ax,F3eq}$ 12.2 Hz, $^{3}J_{F2ax,F3ax}$ 3.8 Hz, $^{4}J_{H4ax,F2ax}$ 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 **±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, $OC\underline{H}_3$); ^{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 ($O\underline{C}H_3$); ^{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, $^{4}J_{H1ax,F3ax}$ 3.7 Hz, $^{3}J_{H1ax,H2eq}$ 1.6 Hz, $^{4}J_{H1ax,F3eq}$ 1.5 Hz, H1), 4.15 (1H, dddd, $^{3}J_{H2eq,F3ax}$ 6.2 Hz, $^{3}J_{H2eq,F3eq}$ 6.2 Hz, $^{4}J_{H2eq,F4eq}$ 6.2 Hz, $^{3}J_{H2eq,H1ax}$ 1.6 Hz, H2), 4.06 – 3.98 (2H, m, H6 +H6'), 3.91 (1H, dddd, $^{3}J_{H5ax,F4ax}$ 22.2 Hz, $^{3}J_{H5ax,H6'}$ 6.2 Hz, $^{4}J_{H5ax,F3ax}$≈5 Hz, $^{3}J_{H5ax,H6}$ 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, $^4J_{H6,F}$<1Hz, 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, $^{3}J_{H1eq,H2ax}$ 4.6 Hz, $^{4}J_{H1eq,F3eq}$ 4.2 Hz, 1H, H1), 4.17 dddd, $^{3}J_{H5ax,F4ax}$ 22.4 Hz, $^{3}J_{H5ax,H6'}$ 7.3 Hz, $^{3}J_{H5ax,H6}$ 3.4 Hz, $^{4}J_{H5ax,F3ax}$ 2.6 Hz, H5), 4.04 (1H, ddddd, $^{3}J_{H2ax,F3ax}$ 23.2 Hz, $^{3}J_{H2ax,OH}$ 12.0 Hz, $^{3}J_{H2ax,F3eq}$ 6.7 Hz, $^{3}J_{H2ax,H1eq}$ 4.6 Hz, $^{4}J_{H2ax,F4ax}$ 3.9 Hz, H2), 4.04 – 3.93 (2H, m, H6 + H6') ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ□□□□□□□– □□□□□ (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, $^{2}J_{F3ax,F3eq}$ 254.8 Hz, $^{3}J_{F3ax,H2ax}$ 23.2 Hz, $^{3}J_{F3ax,F4eq}$ 13.4 Hz, $^{3}J_{F3ax,F4ax}$ 9.1 Hz, $^{4}J_{F3ax,H5ax}$ 2.6 Hz, F3ax), -132.1 (ddddd, $^{2}J_{F3eq,F3ax}$ 254.8 Hz, $^{3}J_{F3eq,F4ax}$ 15.1 Hz, $^{3}J_{F3eq,F4eq}$ 8.6 Hz, $^{3}J_{F3eq,H2ax}$ 6.7 Hz, $^{4}J_{F3eq,H1eq}$ 4.2 Hz, F3eq), -132.2 (ddddd, $^{2}J_{F4ax,F4eq}$ 263.5 Hz, $^{3}J_{F4ax,H5ax}$ 22.4 Hz, $^{3}J_{F4ax,F3eq}$ 15.1 Hz, $^{3}J_{F4ax,F3ax}$ 9.1 Hz, $^{4}J_{F4ax,H2ax}$ 3.9 Hz, F4ax), -133.4 (ddd, $^{2}J_{F4eq,F4ax}$ 263.5 Hz, $^{3}J_{F4eq,F3ax}$ 13.4 Hz, $^{3}J_{F4eq,F3eq}$ 8.6 Hz, F4eq) ppm. ^{1}H NMR (500 MHz, D_2O) δ 4.98 (1H, dd, $^{3}J_{H1eq,H2ax}$ 4.4 Hz, $^{4}J_{H1eq,F3eq}$ 4.2 Hz, H1), 4.21 (1H, dddd, $^{3}J_{H2ax,F3ax}$ 22.6Hz, $^{3}J_{H2ax,F3eq}$ 6.8 Hz, $^{3}J_{H2ax,H1eq}$ 4.4 Hz, $^{4}J_{H2ax,F4ax}$ 3.8 Hz, H2), 4.18 (1H, dddd, $^{3}J_{H5ax,F4ax}$ 24.1 Hz, $^{3}J_{H5ax,H6'}$ 6.9 Hz, $^{3}J_{H5ax,H6}$ 3.4 Hz, $^{4}J_{H5ax,F3ax}$ 2.3 Hz, H5), 3.95 (1H, ddd, $^{2}J_{H6,H6'}$ 12.8 Hz, $^{3}J_{H6,H5ax}$ 3.4 Hz, $^{4}J_{H6,F}$ <1Hz, H6), 3.84 (1H, dd, $^{2}J_{H6',H6}$ 12.8 Hz, $^{3}J_{H6',H5ax}$ 6.9 Hz, H6') ppm; ^{19}F NMR (471 MHz, D_2O) δ -127.2 (ddddd, $^{2}J_{F3ax,F3eq}$ 252.5 Hz, $^{3}J_{F3ax,H2ax}$ 22.6 Hz, $^{3}J_{F3ax,F4eq}$ 13.0 Hz, $^{3}J_{F3ax,F4ax}$ 9.2 Hz, $^{4}J_{F3ax,H5ax}$ 2.3 Hz, F3ax), -131.7 (ddddd, $^{2}J_{F3eq,F3ax}$ 252.5 Hz, $^{3}J_{F3eq,F4ax}$ 14.9 Hz, $^{3}J_{F3eq,F4eq}$ 8.7 Hz, $^{3}J_{F3eq,H2ax}$ 6.8 Hz, $^{4}J_{F3eq,H1eq}$ 4.2 Hz, F3eq), -131.9 (ddddd, $^{2}J_{F4ax,F4eq}$ 262.2 Hz, $^{3}J_{F4ax,H5ax}$ 24.1 Hz, $^{3}J_{F4ax,F3eq}$ 14.9 Hz, $^{3}J_{F4ax,F3ax}$ 9.2 Hz, $^{4}J_{F4ax,H2ax}$ 3.8 Hz, F4ax), -133.4 (ddd, $^{2}J_{F4eq,F4ax}$ 262.2 Hz, $^{3}J_{F4eq,F3ax}$ 13.0 Hz, $^{3}J_{F4eq,F3eq}$ 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 then stirred under H_2 for 1 h. EtOAc (11 mL) was added followed by filtration through Celite® to give a colorless oil. Column chromatography (petrol

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 subsequently allowing to stand for several weeks. Data for the anomeric mixture (1:1) was achieved after equilibration in solvent. R_f 0.27 (petrol 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_2Ph), 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>-$1_{α+β}$), 5.31 (1H, m, H-$1_α$), 4.99 (1H, br. d, *J* 14.1 Hz, H-$1_β$), 4.88 (1H, d, *J* 11.1 Hz, C<u>H</u>HP$h_{α/β}$), 4.87 (1H, d, *J* 11.1 Hz, C<u>H</u>HP$h_{β/α}$), 4.72 (2H, d, *J* 11.1 Hz, CH<u>H</u>P$h_{α+β}$), 4.45 (1H, m, H-$5_α$), 4.12–4.21 (3H, m, H-$4_{α+β}$, O<u>H</u>-$6_β$), 4.05 (1H, dd, *J* 6.6, 5.1 Hz, O<u>H</u>-$6_α$), 3.92 (1H, tdt, *J* 6.4, 4.7, 2.1 Hz, H-$5_β$), 3.67–3.82 (4H, m, H-$6_{α+β}$, H-6'$_{α+β}$); ^{13}C NMR (101 MHz, acetone-d_6) δ (ppm) 138.9 (C_{Ar}α), 138.8 (C_{Ar}β), 129.2, 128.8, 128.8, 128.7, 128.7 (<u>C</u>H_{Ar} × 10), 92.1–93.5 (m, C-$1_{α+β}$), 76.3–77.4 (m, C-$4_{α+β}$), 75.9 (d, *J* 3 Hz, <u>C</u>H_2P$h_{α+β}$), 75.3 (d, *J* 6 Hz, C-$5_β$), 70.3 (*J* 6 Hz, C-$5_α$), 60.4 (C-$6_α$), 60.4 (C-$6_β$); ^{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.

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Supporting Information: Characterization data for known compounds, copies of ^{1}H, ^{13}C, ^{19}F NMR spectra of all novel compounds, copies of chiral HPLC chromatograms and X-ray crystallographic data for **±6**, **±7**, **58**, **±67**, **±*trans*-73**, **±*cis*-73**, **±77**, **82**, **±β-86**, **±α-87** and **88**. This material is available free of charge via the Internet at http://pubs.acs.org/.

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