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De Novo Synthesis of Racemic 4-Deoxy-4,4-difluoro- and 2,4-Dideoxy-2,4,4-trifluorohexosides

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A range of racemic 4-deoxy-4,4-difluorinated carbohydrates were prepared by using a diversity-oriented de novo synthesis starting with three commercially available two-carbon building blocks. A common *gem*-difluorinated glycal was prepared in 35 % yield in seven steps, from which five different 4-deoxy-4,4-difluoro- and 4-deoxy-2,4,4-trifluorohexopyranosides were accessed using well-established functional group manipulations.

Introduction

Nature relies on weak interactions such as hydrogen bonds to construct complex supramolecular architectures; this is best illustrated with the three-dimensional structures of enzymes or nucleic acids. Inspired by these systems, chemists have exploited non-covalent interactions to advance synthesis and catalysis as well as the field of selective molecular recognition.[1] The growing prevalence of fluorinated pharmaceuticals,[2] agrochemicals,[3] and materials[4] in our daily life underscores the need to further understand the effects of fluorine substitution for archetypical molecules.[5] Various groups have studied the ability of the C–F bond to engage in hydrogen bonding both in the solid state and in solution.[6] NMR spectroscopy has unveiled the existence of C–F···H–X hydrogen bonds between carbon-bound fluorine and intramolecular H-bond donors.[7–9] For these investigations, carbohydrate-derived 1,3-diaxial and 1,2-*cis*-fluoroalcohols are ideal probes by virtue of their rigid ring structure (Figure 1a).[7,8] No information is available on the effect of *gem*-difluorination on C–F···H–O bonding, so we initiated a study aimed at accessing representative 4-deoxy-4,4-difluorohexopyranosides (±)-**1** and (±)-**2** for interrogation using NMR spectroscopy (Figure 1b). A comparative study with the corresponding monofluorinated structural analogs[10] will allow us to gain further insight into the strength and persistence of C–F···H–O bonding in these systems. Currently, such investigations are hampered by the lack of efficient synthetic routes to the desired probes. Herein we present a diversity-oriented approach towards a series of novel racemic 4,4-difluorinated hexopyranosides.

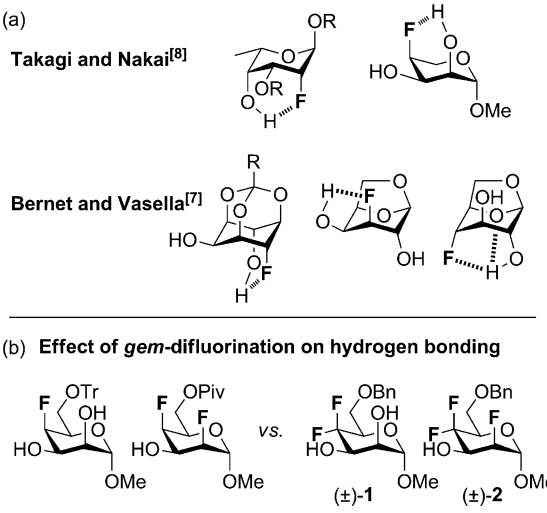

Figure 1. (a) Previously observed C–F···H–O bonds in fluorinated carbohydrates;[7,8] (b) fluorinated carbohydrates **(±)-1** and (±)-**2** as novel probes to investigate the effect of geminal fluorination on C–F···H–O.

The installation of a difluoromethylene group at a late stage is synthetically challenging. Electrophilic fluorination allows for the preparation of 2,2-difluoro sugars from 2-fluoroglycals only,[11] and nucleophilic fluorination of carbonyl groups with diethylaminosulfur trifluoride (DAST)[12] can suffer from side reactions resulting from neighboring group participation, migration, or elimination.[13] Alternatively, *gem*-difluorinated monosaccharides can be prepared by de novo synthesis, whereby the highly functionalized molecular core is assembled from small building blocks, one of them featuring the key difluoromethylene motif.[14,15] Hitherto, only two racemic de novo syntheses of 4-deoxy-4,4-difluorohexosides have been re-

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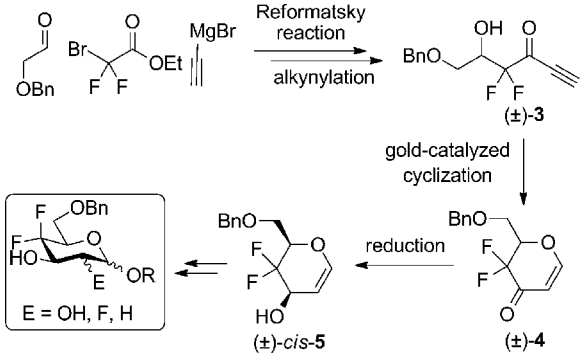
ported. In 1993, Taguchi and co-workers described the synthesis of 4-deoxy-4,4-difluoro-*threo*-hexopyranosides in eight steps with an overall yield of 16%, featuring a Diels–Alder reaction as the key cyclization step.[15c] More recently, Percy and co-workers described the synthesis of 4-deoxy-4,4-difluoromannoses and -alloses in six steps with overall yields of up to 17%, applying a ring-closing metathesis reaction as their key step.[15a] Based on our past experience on the development of novel fluorination reactions[16] and the synthesis of fluorinated carbohydrate analogs,[17] we conceive a robust de novo synthesis of a range of novel racemic 4-deoxy-4,4-difluorohexopyranosides starting with three commercially available two-carbon precursors. We have demonstrated that dihydropyranone (±)-**4** is accessible by a four-step protocol with a 6-*endo*-*dig* gold-catalyzed cyclization of ynone (±)-**3** as the key reaction (Scheme 1).[16e] In addition, Taguchi and co-workers reported that stereoselective reduction of (±)-**4** under Luche conditions leads to key *cis*-glycal (±)-*cis*-**5**.[15c] With these two precedents, we surmise that a subsequent diversity-oriented functionalization of (±)-*cis*-**5** by electrophilic additions to the enolic double bond should give access to a range of diversely substituted racemic 4-deoxy-4,4-difluorohexopyranosides inclusive of the desired methyl α-D/L-talopyranosides (±)-**1** and (±)-**2**.

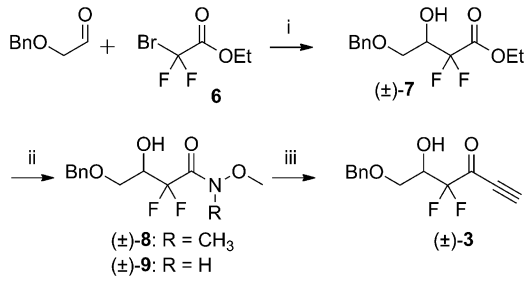


Scheme 1. Synthetic plan.

Results and Discussion

Optimization of the Preparation of the Key Intermediate: *syn*-Glycal (±)-*cis*-5

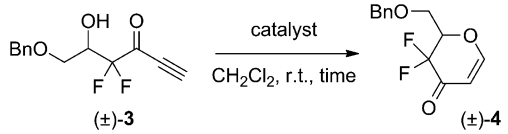
Our study commenced with the preparation of ynone (±)-**3** from three two-carbon building blocks (Scheme 2). The use of rigorously dried solvents led to an improvement in the previously reported Reformatsky reaction of ethyl bromodifluoroacetate (**6**) with (benzyloxy)acetaldehyde. β-Hydroxy ester (±)-**7** was delivered in 77% yield after 16 h at room temperature (ref.[16e] 57%). To ensure selective monoaddition of the Grignard reagent, Weinreb amide (±)-**8** was prepared in 85% yield by treating ester (±)-**7** with *N*,*O*-dimethylhydroxylamine hydrochloride.[16e] Demethylated (±)-**9** was formed as a side product (9% yield). Addition of ethynylmagnesium bromide to (±)-**8** gave quantitatively difluorinated terminal ynone (±)-**3**. This three-step synthesis of (±)-**3** is a significant improvement (65% overall yield) over the previously reported preparation (9% overall yield[16e]).



Scheme 2. Preparation of ynone (±)-**3**. Reagents and conditions: (i) Zn dust, CuCl, $BF_3{\cdot}OEt_2$, THF/Et_2O, 0 °C to r.t., 16 h, 77%; (ii) NHMeOMe·HCl, $AlMe_3$, THF, –78 °C to r.t., 1 h, (±)-**8** (85%), (±)-**9** (9%); (iii) ethynylmagnesium bromide, THF, 0 °C, 5 h, quantitative.

Treatment of (±)-**3** with four successive portions of gold(III) chloride (2.5 mol-%) afforded the corresponding 5,5-difluoro-5,6-dihydropyran-4-one (±)-**4** in 75% yield after 2 d (Table 1, Entry 1).[16e] The use of gold(I) chloride also required four additions (2.5 mol-% portions), but the yield was reduced to 67% (Table 1, Entry 2). When chloro(triphenylphosphane)gold(I) (1 mol-%) and silver triflate (2 mol-%) were used (Table 1, Entry 3), starting material (±)-**3** was completely consumed within 1 h and (±)-**4** was isolated in 49% yield. The yield was raised to 63–66% upon treatment with (SIPr)AuCl[18] [SIPr = 1,3-bis(2,6-diisopropylphenyl)imidazolin-2-ylidene] (1 mol-%) and silver triflate (2 mol-%) at room temperature or 0 °C (Table 1, Entries 4 and 5). The highest yield (87%) was obtained with 1 mol-% of the Gagosz catalyst[19] ($Ph_3PAuNTf_2$) (Table 1, Entry 6).

Table 1. Cyclization of (±)-**3**.

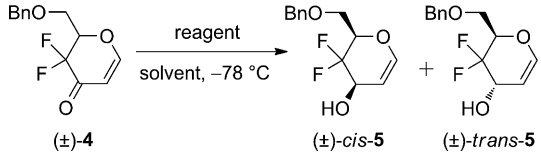


Entry	Catalyst	Time [h]	Yield [%]
1	10 mol-% $AuCl_3$	48	75
2	10 mol-% AuCl	48	67
3	1 mol-% Ph_3PAuCl / 2 mol-% AgOTf	1	49
4	1 mol-% (SIPr)AuCl / 2 mol-% AgOTf	1	63
5	1 mol-% (SIPr)AuCl / 2 mol-% AgOTf	1 (0 °C)	66
6	1 mol-% $Ph_3PAuNTf_2$	24	87

Taguchi and co-workers described the reduction of dihydropyranone (±)-**4** under Luche conditions (cerium chloride heptahydrate and sodium borohydride) and obtained (±)-*cis*-**5** and (±)-*trans*-**5** in 81% yield as a 94:6 *cis*/*trans* mixture.[15c] In our hands, the selectivity of this reaction dropped to 90:10 and the yield to 60% (Table 2, Entry 1). A complex mixture of products was observed when (±)-**4** was treated with L-Selectride. The highest diastereoselectivity (*cis*/*trans* = 92:8) was observed upon reduction with di-

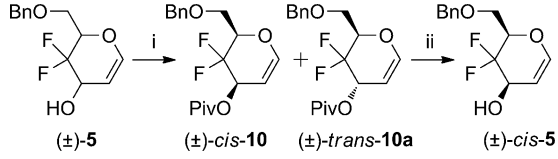
isobutylaluminum hydride (DIBAL) in dichloromethane (63% yield; Table 2, Entry 2), and the highest yield of 81% with DIBAL in toluene (*cis*/*trans* = 87:13; Table 2, Entry 3).

Table 2. Reduction of pyranone (±)-**4**.



Entry	Reagent	Solvent	Yield [%]	*cis*/*trans*
1	$NaBH_4/CeCl_3·7H_2O$	MeOH	60	90:10
2	DIBAL	CH_2Cl_2	63	92:8
3	DIBAL	toluene	81	87:13

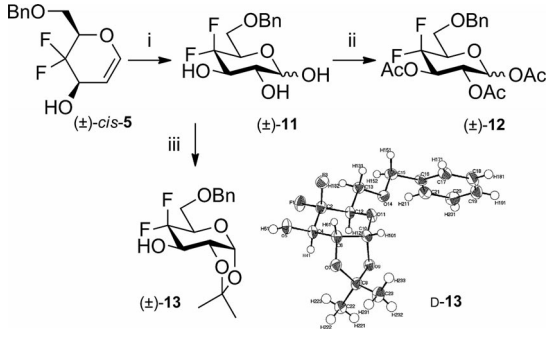
Hydroxyglycals (±)-*cis*-**5** and (±)-*trans*-**5** could not be separated by silica gel chromatography. Therefore, a 92:8 mixture of (±)-*cis*-**5**/(±)-*trans*-**5** was transformed into pivalates (±)-*cis*-**10**/(±)-*trans*-**10** by treatment with pivaloyl chloride in pyridine. Chromatography on silica gel gave (±)-*cis*-**10** (75% yield), a mixture of (±)-*cis*-**10** and (±)-*trans*-**10** (24% yield), and a pure sample of *trans*-**10** (Scheme 3). Deprotection of (±)-*cis*-**10** with 1,8-diazabicycloundec-7-ene (DBU) proceeded quantitatively to afford pure (±)-*cis*-**5**. With pure *syn*-glycal (±)-*cis*-**5** in hand, we started the diversity-oriented functionalization.



Scheme 3. Preparation of pure *syn*-glycal (±)-*cis*-**5**. Reagents and conditions: (i) PivCl, pyridine, 0 °C to r.t., 16 h, 75% of (±)-*cis*-**5**, 24% of (±)-*cis*-**5**/(±)-*trans*-**5**, and a sample of pure (±)-*trans*-**5**; (ii) DBU, MeOH, r.t., 16 h, >95%.

Synthesis of 4-Deoxy-4,4-difluoro-D/L-glucopyranoses

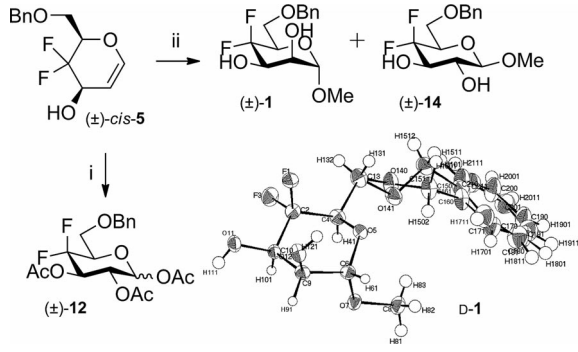
Dihydroxylation of (±)-*cis*-**5** under the standard Upjohn conditions (OsO_4, NMO) led to a 1:1 anomeric mixture of *gluco*-configured triol (±)-**11** in 75% yield (Scheme 4). The yield was improved to 80% when the reaction was carried out with a stoichiometric amount of osmium tetroxide and tetramethylethylenediamine (TMEDA) in dichloromethane at –78 °C. Acetylation of (±)-**11** delivered triacetate (±)-**12** in 96% yield as a 3:1 α/β mixture. The anomers of (±)-**12** were assigned by the upfield shift for H–C(1) of the β-D/L-anomers and its large *J*(1,2) coupling of 8.5 Hz, but could not be separated by silica gel chromatography. Treatment of (±)-**11** with 2,2-dimethoxypropane and $TsOH·H_2O$ in acetone gave isopropylidene acetal (±)-**13** in 63% yield. The structure of (±)-**13** was confirmed by X-ray analysis; only D-**13** is depicted in Scheme 4.



Scheme 4. Synthesis of 4-deoxy-4,4-difluoro-D/L-glucopyranoses (±)-**12** and (±)-**13** and X-ray structure of isopropylidene acetal (±)-**13**. Reagents and conditions: (i) OsO_4, TMEDA, CH_2Cl_2, –78 °C, 16 h, 80%; (ii) Ac_2O, DMAP, pyridine, r.t., 16 h, 96%; (iii) $CMe_2(OMe)_2$, $TsOH·H_2O$, acetone, r.t., 63%.

Synthesis of 4-Deoxy-4,4-difluoro-D/L-mannopyranoses

In attempts to obtain 4-deoxy-4,4-difluoro-D/L-mannopyranoses, glycal (±)-*cis*-**5** was treated with *meta*-chloroperbenzoic acid (*m*-CPBA) in water. This reaction delivered, after subsequent acetylation, an anomeric mixture of *gluco*-configured triacetate (±)-**12** as the only isolable product (16%) (Scheme 5). However, when performing the oxidation with *m*-CPBA in methanol, methyl α-D/L-mannopyranoside (±)-**1** was obtained in 41% yield, along with 28% of β-D/L-*gluco* isomer (±)-**14**, evidencing the intermediate formation of epimeric 1,2-epoxides. Diastereoisomers (±)-**1** and (±)-**14** were easily separated by silica gel chromatography. The α-D/L-*manno* configuration of (±)-**1** is evidenced by a small *J*(1,2) value (1.6 Hz) and by the downfield shift of H-3 (3.78–3.68 ppm) and H-5 (δ =3.90 ppm). Crystallization of (±)-**1** from ethyl acetate and hexane gave crystals suitable for X-ray analysis, which confirmed the α-D/L-*manno* configuration of (±)-**1**; only D-**1** is depicted in Scheme 5.

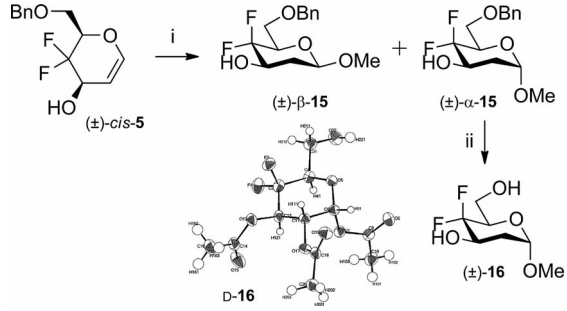


Scheme 5. Synthesis and X-ray analysis of 4-deoxy-4,4-difluoro-α-D/L-mannopyranoside (±)-**1**. Reagents and conditions: (i) 1. *m*-CPBA, H_2O, 0 °C to r.t., 16 h; 2. Ac_2O, pyridine, r.t., 16 h, 16%; (ii) *m*-CPBA, MeOH, 0 °C to r.t., 16 h, (±)-**1** (41%), (±)-**14** (28%).

Synthesis of 2,4-Dideoxy-4,4-difluoro-D/L-*threo*-hexopyranosides

Treatment of (±)-*cis*-**5** with HCl in methanol and chromatographic separation on silica gel delivered methyl 2,4-dideoxy-4,4-difluoro-α-D/L-hexopyranoside (±)-α-**15** and its β-D/L-anomer (±)-β-**15** in 83 and 10% yield, respectively

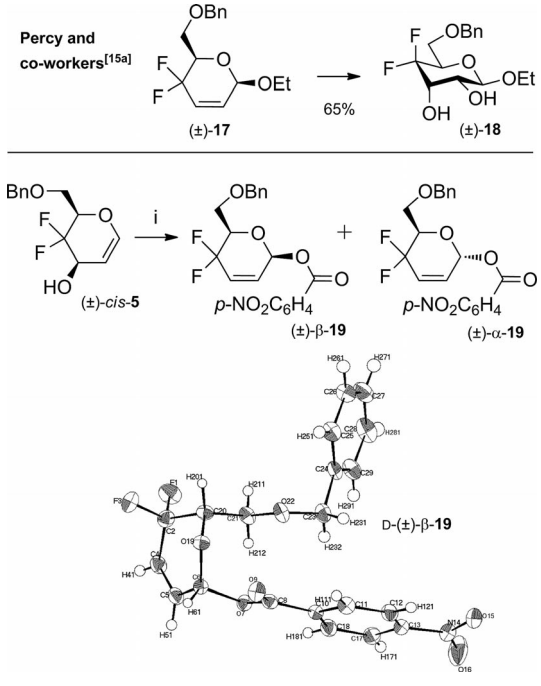
(Scheme 6). Hydrogenation of (±)-α-**15** delivered diol (±)-**16** in quantitative yield. X-ray crystal analysis of (±)-**16** confirmed the structural assignment; only D-**16** is depicted in Scheme 6.



Scheme 6. Synthesis and X-ray analysis of 2,4-dideoxy-4,4-difluoro-α-D/L-*threo*-hexopyranoside (±)-**16**. Reagents and conditions: (i) 37% HCl, THF/MeOH, 40 °C, 20 h, (±)-α-**15** (83%), (±)-β-**15** (10%); (ii) H_2, 10% Pd/C, MeOH, r.t., 3 h, >95%.

Synthesis towards 4-Deoxy-4,4-difluoro-D/L-allopyranoses

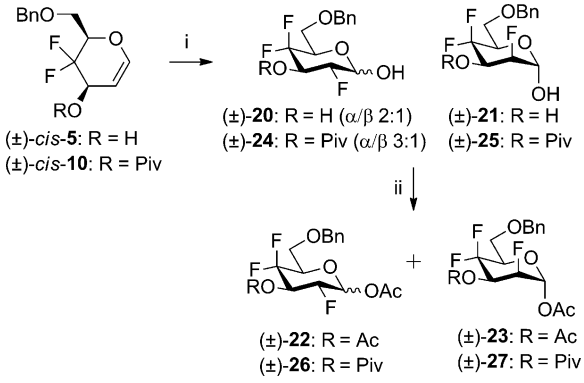
Percy and co-workers reported that the dihydroxylation of 2,3-unsaturated (±)-**17** delivers 4-deoxy-4,4-difluoro-β-D/L-allopyranoside (±)-**18** in good yields (Scheme 7).[15a] To assess the ability of (±)-*cis*-**5** to engage in S_N2' substitution under standard Mitsunobu conditions, (±)-*cis*-**5** was treated with *para*-nitrobenzoic acid, diisopropyl azodicarboxylate (DIAD), and triphenylphosphane. This transformation led to a 2:1 mixture of desired α/β-D/L-hex-2-enopyranosides (±)-β-**19**/(±)-α-**19** in 89% yield. Silica gel chromatography allowed partial separation of the anomers, affording 42% of pure (±)-β-**19** and 15% of pure (±)-α-**19**. Single-crystal analysis of major β-D/L anomer (±)-β-**19** allowed unambiguous structural assignment; only D-β-**19** is depicted in Scheme 7. The pyranosyl ring of crystalline D-β-**19** adopts a ^5S conformation with a pseudoequatorial ester moiety and an axial benzyloxymethyl group. 4-Deoxy-4,4-difluoro-D/L-allopyranoses should be accessible by applying the conditions of Percy and co-workers[15a] to (±)-β-**19**.



Scheme 7. Synthesis of anomeric hex-2-enopyranosides (±)-β-**19** and (±)-α-**19** and X-ray structure of (±)-β-**19**. Reagents and conditions: (i) *p*-NO_2BzOH, PPh_3, DIAD, toluene, r.t., 24 h, (±)-β-**19** (42%), (±)-α-**19** (15%).

Synthesis of 2,4-Dideoxy-2,4,4-trifluoro-D/L-hexopyranoses

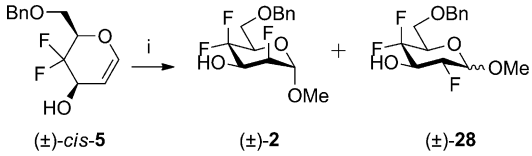
Following procedures reported by Wong and Dax,[20] fluorination of glycal (±)-*cis*-**5** was attempted using Selectfluor in a mixture of nitromethane and water at room temperature (Scheme 8). Only trace amounts of trifluorinated products were formed within 16 h; prolonged reaction times of up to 5 d did not lead to a satisfactory conversion. At 60 °C, the reaction went to completion within 16 h when using 1.2 equiv. of Selectfluor in a 1:5 mixture of nitromethane/water. A 3:2 mixture of α/β-D/L-glucopyranose (±)-**20** (α/β = 2:1) and α-D/L-mannopyranose (±)-**21** was identified by ^{19}F NMR spectroscopy of the crude mixture. Acetylation of the crude product and chromatographic separation on silica gel delivered α/β-D/L-glucopyranosyl acetates (±)-**22** (α/β = 2:1) and α-D/L-mannopyranosyl acetate (±)-**23** in 55 and 38% yield, respectively. Inspired by the work of Dax and co-workers,[20b] pivaloylated glycal (±)-*cis*-**10** was treated with Selectfluor to improve the diastereoselectivity. ^{19}F NMR spectroscopic analysis of the crude product indicated a 5:1 ratio of (±)-**24** (α/β = 3:1)/(±)-**25**. Acetylation and chromatographic separation delivered (±)-**26** (α/β = 3:1) and (±)-**27** in 53 and 15% yield, respectively.



Scheme 8. Synthesis of 2,4,4-trifluoro-D/L-hexopyranoses (±)-**20**–**27**. Reagents and conditions: (i) Selectfluor, $MeNO_2/H_2O$ (1:5), 80 °C, 16 h; (ii) Ac_2O, DMAP, pyridine, CH_2Cl_2, r.t., 16 h, (±)-**22** (55%, α/β = 2:1), (±)-**23** (38%), (±)-**26** (53%, α/β = 3:1), (±)-**27** (15%).

To get direct access to 2,4,4-trifluorinated methyl α-D/L-mannopyranoside (±)-**2**, glycal (±)-*cis*-**5** was treated with Selectfluor in a 1:3 mixture of nitromethane/methanol for 16 h at 60 °C (Scheme 9). Silica gel chromatography gave the desired mannopyranoside (±)-**2** in 19% yield together with the *gluco*-anomers (±)-α-**28** (14%) and (±)-β-**28**

(35%). The α-D/L-*manno* configuration of (±)-**2** is evidenced by a small J(1,2) value (1.6 Hz), the downfield shift of H-3 (δ = 4.17–4.01 ppm) and H-5 (δ = 4.10 ppm), a large ^3J(H-3,F) (27 Hz), and a distinctly smaller ^3J(H-1,F) (9 Hz).



(±)-*cis*-**5** (±)-**2** (±)-**28**

Scheme 9. Synthesis of 2,4-dideoxy-2,4,4-trifluorohexopyranosides (±)-**2**, (±)-α-**28**, and (±)-β-**28**. Reagents and conditions: (i) Selectfluor, $MeNO_2$/MeOH (1:3), 80 °C, 16 h, (±)-**2** (19%), (±)-α-**28** (14%), (±)-β-**28** (35%).

The ^{19}F NMR spectra of trifluorides (±)-**2** and (±)-**28** exhibit characteristic J(F,F) couplings. Besides the large $^2J(F_{ax}\text{-}4,F_{eq}\text{-}4)$ of 250 Hz, (±)-**2** shows $^{1F}J(F\text{-}2,F_{ax}\text{-}4)$ of 20 Hz (see ref.[10,21]) and $^4J(F\text{-}2,F_{eq}\text{-}4)$ of 3 Hz (bent W arrangement), whereas (±)-α-**28** and (±)-β-**28** show $^4J(F\text{-}2,F_{eq}\text{-}4)$ of 14 Hz (flat W arrangement; see ref.[22]) and $^4J(F\text{-}2,F_{ax}\text{-}4)$ of 3 Hz (bent W arrangement).

Conclusions

In summary, we have implemented a diversity-oriented de novo synthesis of a range of different 4-deoxy-4,4-difluoro-D/L-hexoses. Key glycal (±)-*cis*-**5** was synthesized in seven steps as a single diastereomer with a vastly improved overall yield of 35%. By using the Gagosz catalyst for the gold-catalyzed cyclization reaction, we were able to lower the catalyst loading (from 10 to 1 mol-%), to raise the yield (from 75 to 87%), and to avoid sequential addition of the catalyst. Glycal (±)-*cis*-**5** successfully delivered five different *gem*-difluorinated hexose analogs in good yield by using well-established functionalization reactions. With the exception of the 4,4-difluoroglucosides and the 4,4-difluoromannosides, the di- and trifluorinated carbohydrates reported herein are novel. Amongst them, target methyl α-D/L-talopyranosides (±)-**1** and (±)-**2** were accessed in eight steps with an overall yield of 14 and 7%, respectively. NMR spectroscopic investigations of (±)-**1** and (±)-**2** to elucidate the strength and persistence of intramolecular C–F···H–O bonds are currently ongoing in our laboratory and will be reported in due course.

Experimental Section

General: All reactions requiring anhydrous conditions were conducted in dried apparatus under an inert atmosphere of argon or nitrogen. Solvents were dried and purified before use according to standard procedures. All reactions were monitored by TLC using Merck Kiesegel 60 F254 plates. Visualizations of the reaction components was achieved by using UV fluorescence (254 nm) and $KMnO_4$ stain. Column chromatography was carried out over Merck silica gel C60 (40–60 μm) or by using a Biotage SP4 automated chromatography system using commercially available Biotage SNAP cartridges KP-sil. All ^{1}H NMR spectra were recorded in deuterated solvents using Bruker DPX400, AV400, and AV500 spectrometers. ^{13}C NMR spectra were recorded in deuterated solvents using Bruker DPX400, AV400, and AV500 spectrometers with a carbon-13 cryoprobe. ^{19}F spectra (both with and without proton decoupling) were recorded with Bruker AV400 and AV500 spectrometers. ^{1}H and ^{13}C NMR spectra are reported as chemical shifts (δ) in parts per million (ppm) relative to the solvent peak using the Bruker internal referencing procedure (edlock). ^{19}F NMR spectra are referenced relative to $CFCl_3$ in $CDCl_3$. The following abbreviations are used to describe multiplicities, s = singlet, d = doublet, t = triplet, q = quartet, br. = broad, m = multiplet. Low- and high-resolution mass spectra were recorded with a Bruker MicroTof spectrometer using positive or negative electrospray ionization (ESI+/ESI–). IR spectra were recorded as thin films on NaCl plates, neat or in solution in $CHCl_3$ or CH_2Cl_2 with a Bruker Tensor 27 FTIR spectrometer. Absorptions are measured in wavenumbers (cm^{-1}) and only peaks of interest are reported.

Ethyl (±)-4-(Benzyloxy)-2,2-difluoro-3-hydroxybutanoate [(±)-7]:[16e] A suspension of zinc dust (0.40 g, 6.0 mmol) and copper(I) chloride (60 mg, 0.6 mmol) in freshly dried diethyl ether/tetrahydrofuran (4:1) (12.5 mL) was vigorously stirred for 1 h at room temperature and treated with ethyl bromodifluoroacetate (0.25 mL, 2.0 mmol), freshly prepared benzyloxy acetaldehyde (0.31 mL, 2.2 mmol), and boron trifluoride diethyl ether (0.27 mL, 2.2 mmol). The suspension was stirred overnight and filtered through Celite, and the solvents were evaporated. Purification by column chromatography on silica gel (hexane/EtOAc, 85:15 to 80:20) afforded alcohol (±)-**7** (0.42 g, 77%) as a colorless oil. R_f = 0.31 (hexane/EtOAc, 75:25). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.29 (m, 5 H, Ph), 4.56 (s, 2 H, CH_2Ph), 4.30–4.20 (m, 1 H, 3-H), 4.24 (q, J = 7.1 Hz, 2 H, OCH_2Me), 3.98 (br. d, J = 6.1 Hz, 1 H, OH), 3.72 (dd, J = 10.1, 4.6 Hz, 1 H, 4-H_A), 3.68 (dd, J = 10.1, 6.1 Hz, 1 H, 4-H_B), 1.25 (t, J = 7.1 Hz, 3 H, Me) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.2 [t, ^2J(C,F) = 32 Hz, C=O], 137.3 (C of Ph), 128.7, 128.2, 128.0 (5 CH of Ph), 113.8 [dd, ^1J(C,F) = 257, 254 Hz, CF_2], 73.9 (*C*H_2Ph), 70.9 [dd, ^2J(C,F) = 26, 25 Hz, C-3], 67.9 [t, ^3J(C,F) = 3 Hz, C-4], 63.2 (O*C*H_2Me), 13.0 (Me) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –115.2 [ddd, ^2J(F,F) = 263 Hz, J = 8, 6 Hz, 1 F], –120.0 [ddd, ^2J(F,F) = 263 Hz, J = 13, 4 Hz, 1 F] ppm. HRMS (ESI): calcd. for $C_{18}H_{22}F_2NaO_4^+$ [M + Na]$^+$ 297.0909; found 297.0898.

Amidation of (±)-7: A suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (2.93 g, 30 mmol) in tetrahydrofuran (40 mL) was cooled to 0 °C, treated dropwise with trimethylaluminum (2 M in toluene, 15 mL, 30 mmol), allowed to reach room temperature leading to a transparent solution. This solution was cooled to –78 °C, treated with a solution of (±)-**7** (2.74 g, 10 mmol) in tetrahydrofuran (10 mL), stirred for 15 min at –78 °C and for 1 h at 0 °C, and diluted with 1.5 M HCl (30 mL). The aqueous mixture was extracted with ethyl acetate (3 × 30 mL). Combined organic layers were dried with magnesium sulfate, filtered, and concentrated. Purification by column chromatography on silica gel (hexane/EtOAc, 30:70 to 70:30) afforded amide (±)-**8** (2.46 g, 85%) and side product (±)-**9** (0.26 g, 9%).

(±)-4-(Benzyloxy)-2,2-difluoro-3-hydroxy-*N*-methoxy-*N*-methylbutanamide [(±)-8]:[16e] Colorless solid. R_f = 0.35 (hexane/EtOAc, 50:50); m.p. 65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 5 H, Ph), 4.58 (d, J = 12.0 Hz, 1 H, CH_APh), 4.54 (d, J = 12.0 Hz, 1 H, CH_BPh), 4.45 [dddd, ^3J(H,F) = 15.4, 8.7 Hz, J = 6.1, 4.5 Hz, 1 H, 3-H], 3.76 (dd, J = 10.2, 4.4 Hz, 1 H, 4-H_A), 3.72 (s, 3 H, OMe), 3.68 (dd, J = 10.4, 6.3 Hz, 1 H, 4-H_B), 3.29 (br. s, 1 H, OH), 3.17 (br. s, 3 H, NMe) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ =

161.3 (m, C=O), 137.5 (C of Ph), 128.4, 127.9, 127.8 (5 CH of Ph), 115.6 [dd, ^1J(C,F) = 259, 257 Hz, CF_2], 73.6 (CH_2Ph), 71.0 [dd, ^2J(C,F) = 26, 24 Hz, C-3], 68.3 [dd, ^3J(C,F) = 5, 2 Hz, C-4], 62.0 (OMe), 33.0 (NMe) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –113.8 [d, ^2J(F,F) = 270 Hz, 1 F], –117.2 [dd, ^2J(F,F) = 270 Hz, J = 11 Hz, 1 F] ppm. HRMS (ESI): calcd. for $C_{13}H_{17}F_2NNaO_4^+$ [M + Na]$^+$ 312.1018; found 312.1014.

(±)-4-(Benzyloxy)-2,2-difluoro-3-hydroxy-*N*-methoxybutanamide [(±)-9]: Colorless solid. R_f = 0.23 (hexane/EtOAc, 50:50); m.p. 93 °C. IR ($CHCl_3$): $\tilde{\nu}$ = 3176 (O-H/N–H), 1688 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): δ = 7.38–7.24 (m, 5 H, Ph), 4.54 (s, 2 H, CH_2Ph), 4.37–4.26 (m, 1 H, 3-H), 3.72 (dd, J = 10.3, 4.2 Hz, 1 H, 4-H_A), 3.70 (s, 3 H, OMe), 3.61 (dd, J = 10.3, 7.1 Hz, 1 H, 4-H_B) ppm. ^{13}C NMR (101 MHz, CD_3OD): δ = 161.3 [t, ^2J(C,F) = 28 Hz, C=O], 138.2 (C of Ph), 128.4, 128.0, 127.8 (5 CH of Ph), 116.2 [t, ^1J(C,F) = 256 Hz, CF_2], 73.5 (CH_2Ph), 70.1 [t, ^2J(C,F) = 24 Hz, C-3], 68.9 [t, ^3J(C,F) = 3 Hz, C-4], 63.4 (OMe) ppm. ^{19}F NMR (376 MHz, CD_3OD): δ = –119.1 [dd, ^2J(F,F) = 263 Hz, J = 10 Hz, 1 F], –122.6 [dd, ^2J(F,F) = 263 Hz, J = 11 Hz, 1 F] ppm. HRMS (ESI): calcd. for $C_{12}H_{15}F_2NNaO_4^+$ [M + Na]$^+$ 298.0861; found 298.0859.

(±)-6-(Benzyloxy)-4,4-difluoro-5-hydroxyhex-1-yn-3-one [(±)-3]:[16e] A solution of amide (±)-**8** (1.74 g, 6.0 mmol) in tetrahydrofuran (12 mL) was cooled to 0 °C, treated with ethynylmagnesium bromide (0.5 M in tetrahydrofuran, 36 mL, 18 mmol), stirred at 0 °C for 1 h, and poured into cold 1 M HCl (30 mL). The aqueous phase was extracted with diethyl ether (3 × 20 mL). Combined organic layers were washed with brine (50 mL), dried with magnesium sulfate, filtered, and concentrated. Purification through a short pad of silica gel (3 cm; hexane/EtOAc, 32:68) gave ynone (±)-**3** (1.55 g, >95%) as a yellowish oil. Important: Ynone (±)-**3** is very sensitive to silica gel (no product was obtained from acidic silica gel). R_f = 0.30 (hexane/Et_2O, 50:50). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.30 (m, 5 H, Ph), 4.56 (s, 2 H, CH_2Ph), 4.41–4.29 (m, 2 H, 2 6-H), 3.77–3.67 (m, 1 H, 5-H), 3.59 (s, 1 H, C≡CH), 3.13 (br. d, J = 4.7 Hz, 1 H, OH) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.0 [dd, ^2J(C,F) = 35, 33 Hz, C=O], 136.9 (C of Ph), 128.6, 128.1, 127.9 (5 CH of Ph), 114.3 [dd, ^1J(C,F) = 258, 256 Hz, CF_2], 85.7 (C-2), 78.0 (C-1), 73.7 (CH_2Ph), 70.3 [dd, ^2J(C,F) = 27, 25 Hz, C-5], 67.5 [t, ^3J(C,F) = 3 Hz, C-6] ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –115.1 [dd, ^2J(F,F) = 265 Hz, J = 8 Hz, 1 F], –120.4 [dd, ^2J(F,F) = 265 Hz, J = 13 Hz, 1 F] ppm. HRMS (ESI–): calcd. for $C_{13}H_{11}F_2O_3^+$ [M – H]$^-$ 253.0676; found 253.0680.

1,5-Anhydro-6-*O*-benzyl-2,4-dideoxy-4,4-difluoro-D/L-*glycero*-hex-2-en-3-ulose [(±)-4]:[16e] Triphenylphosphanegold(I) bis(trifluoromethanesulfonyl)imidate (3.8 mg, 0.005 mmol, 1 mol-%) was added to a solution of ynone (±)-**3** (127 mg, 0.50 mmol) in dichloromethane (5 mL). The mixture was stirred for 24 h at room temperature and filtered through Celite. Evaporation of the filtrate and purification by column chromatography on silica gel (hexane/EtOAc, 80:20) gave pyranone (±)-**4** (110 mg, 87%) as a colorless oil. R_f = 0.34 (hexane/Et_2O, 60:40). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (d, J = 6.1 Hz, 1 H, 1-H), 7.42–7.30 (m, 5 H, Ph), 5.61 [ddd, J = 5.8 Hz, ^4J(H,F) = 3.0, 2.9 Hz, 1 H, 2-H], 4.65–4.47 (m, 1 H, 5-H), 4.64 (d, J = 12.1 Hz, 1 H, CH_APh), 4.61 (d, J = 12.1 Hz, 1 H, CH_BPh), 4.01 (dd, J = 11.4, 2.8 Hz, 1 H, 6-H_A), 3.96 (dd, J = 11.4, 6.8 Hz, 1 H, 6-H_B) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.6 [t, ^2J(C,F) = 25 Hz, C-3], 163.6 (C-1), 136.9 (C of Ph), 128.6, 128.1, 127.8 (5 CH of Ph), 108.3 [t, ^1J(C,F) = 255 Hz, C-4], 104.9 [t, ^3J(C,F) = 2 Hz, C-2], 80.7 [t, ^2J(C,F) = 28 Hz, C-5], 73.9 (CH_2Ph), 65.8 [t, ^3J(C,F) = 4 Hz, C-6] ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –122.4 [ddd, ^2J(F,F) = 282 Hz, J = 16, 2 Hz, 1 F], –123.2 [ddd, ^2J(F,F) = 282 Hz, J = 14, 2 Hz, 1 F] ppm. HRMS (ESI): calcd. for $C_{13}H_{12}F_2NaO_3^+$ [M + Na]$^+$ 277.0652; found 277.0647.

Reduction of (±)-4: A solution of hex-2-en-ulose (±)-**4** (2.2 g, 8.6 mmol) in dichloromethane (19 mL) was cooled to –78 °C, treated dropwise with diisobutylaluminum hydride (1 M in hexane, 13 mL), stirred for 30 min at –78 °C, and treated with saturated aqueous potassium sodium tartrate solution (5 mL). The emulsion was warmed to room temperature and extracted with diethyl ether (3 × 5 mL). Combined organic layers were washed with brine (10 mL), dried with magnesium sulfate, filtered, and concentrated in vacuo. Purification by column chromatography on silica gel (hexane/EtOAc, 85:15 to 75:25) afforded an 92:8 mixture of (±)-*cis*-**5** and (±)-*trans*-**5** (1.4 g, 63%) as a colorless oil.

Pivaloylation of (±)-*cis*-5 and (±)-*trans*-5: Pivaloyl chloride (2.4 mL, 20 mmol) was added to a solution of glycals (±)-*cis*-**5**/(±)-*trans*-**5** 92:8 (0.51 g, 2.0 mmol) in pyridine (20 mL). The solution was stirred overnight at 0 °C, warmed to room temperature, and treated carefully with saturated aqueous $NaHCO_3$ solution (5 mL). The aqueous phase was extracted with dichloromethane (3 × 5 mL). Combined organic layers were washed with brine (15 mL), dried with magnesium sulfate, filtered, and concentrated in vacuo. The two diastereomers could be partially separated by column chromatography on silica gel (hexane/EtOAc, 97:3 to 92:8) to afford an analytical sample of (±)-*trans*-**10**, a mixture of (±)-*cis*-**10** and (±)-*trans*-**10** (0.17 g, 24%), and (±)-*cis*-**10** (0.51 g, 75%).

1,5-Anhydro-6-*O*-benzyl-2,4-dideoxy-4,4-difluoro-3-*O*-pivaloyl-D/L-*threo*-hex-1-enitol [(±)-*cis*-10]: Colorless oil. R_f = 0.27 (hexane/EtOAc, 92:8). IR (neat): $\tilde{\nu}$ = 1738 (C=O), 1647 (C=C) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = **7**.40–7.29 (m, 5 H, Ph), 6.48 (br. d, J = 6.0 Hz, 1 H, 1-H), 5.45 [tdd, ^3J(H,F) = 8.5 Hz, J = 3.8, 1.6 Hz, 1 H, 3-H], 4.83 [td, ^4J(H,F) = 6.3 Hz, J = 6.3, 3.2 Hz, 1 H, 2-H], 4.65 (d, J = 12.0 Hz, 1 H, CH_APh), 4.60 (d, J = 12.0 Hz, 1 H, CH_BPh), 4.46–4.36 (m, 1 H, 5-H), 3.88 (dd, J = 11.0, 8.5 Hz, 1 H, 6-H_A), 3.82 [dt, J = 11.0, 1.7 Hz, ^4J(H,F) = 1.7 Hz, 1 H, 6-H_B], 1.19 (s, 9 H, CMe_3) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 177.1 (C=O), 145.2 (C-1), 137.3 (C of Ph), 128.5, 127.9, 127.8 (5 CH of Ph), 114.9 [dd, ^1J(C,F) = 254, 247 Hz, C-4], 97.8 [d, ^3J(C,F) = 3 Hz, C-2], 76.0 [t, ^2J(C,F) = 27 Hz, C-5], 73.7 (CH_2Ph), 65.9 [dd, ^3J(C,F) = 7, 2 Hz, C-6], 64.4 [dd, ^2J(C,F) = 33, 19 Hz, C-3], 38.9 (CMe_3), 26.9 (CMe_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –110.9 [dd, ^2J(F,F) = 258 Hz, J = 6 Hz, 1 F], –126.4 [dt, ^2J(F,F) = 258 Hz, J = 10 Hz, 1 F] ppm. HRMS (ESI): calcd. for $C_{18}H_{22}F_2NaO_4^+$ [M + Na]$^+$ 363.1378; found 363.1387.

1,5-Anhydro-6-*O*-benzyl-2,4-dideoxy-4,4-difluoro-3-*O*-pivaloyl-D/L-*erythro*-hex-1-enitol [(±)-*trans*-10]: Colorless crystals. R_f = 0.35 (hexane/EtOAc, 92:8); m.p. 57 °C. IR (CH_2Cl_2): $\tilde{\nu}$ = 1732 (C=O), 1645 (C=C) cm^{-1}. ^{1}H NMR (500 MHz, C_6D_6): δ = 7.34 (m, 2 H, 2 H of Ph), 7.25 (m, 2 H, 2 H of Ph), 7.19 (m, 1 H, 1 H of Ph), 6.23 (dd, J = 6.0, 1.0 Hz, 1 H, 1-H), 5.60–5.54 (m, 1 H, 3-H), 4.76 [q, J = ^4J(H,F) = 5.7 Hz, 1 H, 2-H], 4.51 [ddt, ^3J(H,F) = 26.5 Hz, J = 7.3, 1.9, ^3J(H,F) = 1.9 Hz, 1 H, 5-H], 4.36 (dd, J = 12.0 Hz, 1 H, CH_APh), 4.34 (dd, J = 12.0 Hz, 1 H, CH_BPh), 3.99 (dt, J = 11.0, 1.9 Hz, 1 H, 6-H_A), 3.84 (dd, J = 11.0, 7.3 Hz, 1 H, 6-H_B), 1.19 (s, 9 H, CMe_3) ppm. ^{13}C NMR (126 MHz, C_6D_6): δ = 176.4 (C=O), 147.3 (C-1), 138.3 (C of Ph), 128.6, 127.9, 127.8 (5 CH of Ph), 117.2 [dd, ^1J(C,F) = 254, 249 Hz, C-4], 97.2 [d, ^3J(C,F) = 4 Hz, C-2], 73.7 (CH_2Ph), 73.6 [dd, ^2J(C,F) = 30, 24 Hz, C-5], 66.8 (C-6), 63.7 [dd, ^2J(C,F) = 37, 31 Hz, C-3], 38.7 (CMe_3), 27.0 (CMe_3) ppm. ^{19}F{^{1}H} NMR (376 MHz, C_6D_6): δ = –121.5 (d, J = 259 Hz, 1 F), –123.2 (d, J = 259 Hz, 1 F) ppm. HRMS (ESI): calcd. for $C_{18}H_{22}F_2NaO_4^+$ [M + Na]$^+$ 363.1378; found 363.1374.

Preparation of Pure (±)-*cis*-5 from (±)-*cis*-10: 1,8-Diazabicycloundec-7-ene (0.039 mL, 0.26 mmol) was added to a solution of pivalate (±)-*cis*-**10** (47 mg, 0.13 mmol) in methanol (1 mL). The solution was stirred at room temperature overnight and the solvents were then evaporated. Purification by chromatography on silica gel (hexane/EtOAc, 85:15 to 75:25) gave hydroxyglycal (±)-*cis*-**5** (33 mg, >95%) as a colorless oil. R_f = 0.27 (hexane/EtOAc, 75:25). IR (neat): $\tilde{\nu}$ = 3406 (O-H), 1650 (C=C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.29 (m, 5 H, Ph), 6.45 (d, J = 6.0 Hz, 1 H, 1-H), 4.96–4.84 (m, 1 H, 2-H), 4.64 (d, J = 11.8 Hz, 1 H, CH_APh), 4.61 (d, J = 11.8 Hz, 1 H, CH_BPh), 4.38–4.21 (m, 2 H, 3–H and 5-H), 3.92 (d, J = 4.4 Hz, 2 H, 6-H), 2.83 (br. s, 1 H, OH) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.5 (C-1), 137.0 (C of Ph), 128.6, 128.4, 127.6 (5 CH of Ph), 116.1 [dd, ^1J(C,F) = 251, 249 Hz, C-4], 101.1 [d, ^3J(C,F) = 4 Hz, C-2], 75.3 [t, ^2J(C,F) = 28 Hz, C-5], 73.9 (CH_2Ph), 66.8 [dd, ^3J(C,F) = 6, 2 Hz, C-6], 64.6 [dd, ^2J(C,F) = 30, 21 Hz, C-3] ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –110.0 [br. d, ^2J(F,F) = 254 Hz, 1 F, F_{eq}], –129.0 [br. d, ^2J(F,F) = 254 Hz, 1 F, F_{ax}] ppm. HRMS (ESI): calcd. for $C_{13}H_{14}F_2NaO_3^+$ [M + Na]$^+$ 279.0803; found 279.0802.

6-*O*-Benzyl-4-deoxy-4,4-difluoro-α/β-D/L-*xylo*-hexopyranose [(±)-11]: A solution of glycal (±)-*cis*-**5** (53 mg, 0.20 mmol) and tetramethylethylene diamine (33 μL, 0.22 mmol) in dichloromethane (20 mL) was cooled –78 °C, treated with osmium tetroxide (53 mg, 0.21 mmol), and stirred for 16 h at –78 °C. After evaporation, a solution of the residue in methanol (5 mL) and concentrated HCl (0.1 mL) was stirred for 2 h. Evaporation and purification by column chromatography on silica gel (hexane/EtOAc, 15:85 to 10:90) gave a 3:1 anomeric mixture of (±)-**11** (46 mg, 80%) as a white solid. R_f = 0.24 (hexane/EtOAc, 14:86). IR (CH_2Cl_2): $\tilde{\nu}$ = 3378 (O-H) cm^{-1}. ^1H NMR (500 MHz, [D$_6$]DMSO; α/β = 3:1): δ = 7.39–7.29 (m, 5 H, Ph), 7.00 (d, J = 6.5 Hz, 0.25 H, 1-OH_β), 6.86 (d, J = 4.7 Hz, 0.75 H, 1-OH_α), 5.72 (d, J = 6.5 Hz, 0.25 H, 3-OH_β), 5.64 (d, J = 6.3 Hz, 0.75 H, 3-OH_α), 5.37 (d, J = 6.5 Hz, 0.25 H, 2-OH_β), 5.06 (dd, J = 6.9, 1.3 Hz, 0.75 H, 2-OH_α), 5.05–5.01 (m, 0.75 H, 1_α-H), 4.54–4.52 (m, 0.25 H, 1_β-H), 4.52 (s, 0.5 H, CH_2Ph_β), 4.51 (s, 1.5 H, CH_2Ph_α), 4.18 [ddd, ^3J(H,F) = 26.2 Hz, J = 7.6, 2.2 Hz, 0.75 H, 5_α-H], 3.95 [ddd, ^3J(H,F) = 25.0 Hz, J = 7.6, 2.2 Hz, 0.25 H, 5_β-H], 3.83–3.70 (m, 1.75 H, 3_α-H, 6_α-H_A and 6_β-H_A), 3.60 [ddd, ^3J(H,F) = 21.6 Hz, J = 10.0, 7.6 Hz, 0.25 H, 3_β-H], 3.54 (dd, J = 10.4, 7.9 Hz, 1 H, 6_α-H_B and 6_β-H_B), 3.38 (m, 0.75 H, 2_α-H), 3.14–3.08 (m, 0.25 H, 2_β-H) ppm. ^{13}C NMR (126 MHz, [D$_6$]DMSO; α/β = 3:1): δ = 138.0 (C of Ph), 128.3, 127.7, 127.5 (5 CH of Ph), 119.2 [t, ^1J(C,F) = 251 Hz, C-4_α], 118.7 [t, ^1J(C,F) = 250 Hz, C-4_β], 96.5 [d, ^4J(C,F) = 13 Hz, C-1_β], 92.2 [d, ^4J(C,F) = 11 Hz, C-1_α], 73.3 (m, C-2_β), 72.3 (CH_2Ph_β), 72.3 (CH_2Ph_α), 71.9 (m, C-3_β and C-5_β), 70.4 (C-2_α), 69.1 (m, C-3_α), 68.0 [dd, ^2J(C,F) = 28, 23 Hz, C-5_α], 66.4 [d, ^3J(C,F) = 6 Hz, C-$6_{\alpha\text{ and }\beta}$] ppm. $^{19}F\{H\}$ NMR (376 MHz, [D$_6$]DMSO; α/β = 3:1): δ = –115.0 (d, J = 244 Hz, 0.75 F, F_{eq}-4_α), –117.8 (d, J = 243 Hz, 0.25 F, F_{eq}-4_β), –133.5 (br. dd, J = 243, 23 Hz, 0.25 F, F_{ax}-4_β), –134.8 (dtt, J = 244, 24, 6 Hz, 0.75 F, F_{ax}-4_α) ppm. HRMS (ESI): calcd. for $C_{13}H_{16}F_2NaO_5^+$ [M + Na]$^+$ 313.0858; found 313.0859.

1,2,3-Tri-*O*-acetyl-6-*O*-benzyl-4-deoxy-4,4-difluoro-α/β-D/L-*xylo*-hexopyranose [(±)-12]: A solution of triols (±)-**11** (43 mg, 0.15 mmol) and acetic anhydride (1.8 mL, 15 mmol) in pyridine (6 mL) was treated with 4-(dimethylamino)pyridine (2 mg, 0.03 mmol) and stirred at room temperature overnight. Evaporation and purification by chromatography on silica gel (hexane/EtOAc, 85:15 to 65:35) afforded a 3:1 α/β mixture of triacetates (±)-**12** (60 mg, 96%) as a colorless oil. R_f = 0.29 (hexane/EtOAc, 75:25). IR (neat): $\tilde{\nu}$ = 1763 (C=O)cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$; α/β = 3:1): δ = 7.33 (m, 5 H, Ph), 6.42 [t, $J \approx {}^5J$(H,F) ≈ 2.7 Hz, 0.75 H, 1_α-H], 5.81 (d, J = 8.5 Hz, 0.25 H, 1_β-H), 5.61 [ddd, ^3J(H,F) = 19.6, 4.7 Hz, J = 10.7 Hz, 0.75 H, 3_α-H], 5.40 [ddd, ^3J(H,F) = 19.6, 5.4 Hz, J = 10.1 Hz, 0.25 H, 3_β-H], 5.27–5.22 (m, 0.25 H, 2_β-H), 5.21 (dd, J = 10.7, 3.5 Hz, 0.75 H, 2_α-H), 4.62 (d, J = 12.3 Hz, 0.75 H, CH_APh_α), 4.62 (d, J = 12.0 Hz, 0.25 H, CH_APh_β), 4.55 (d, J = 12.3 Hz, 0.75 H, CH_BPh_α), 4.53 (d, J = 12.0 Hz, 0.25 H, CH_BPh_β), 4.30 [ddd, ^3J(H,F) = 24.6 Hz, J = 6.9, 2.8 Hz, 0.75 H, 5_α-H], 4.01 [ddd, ^3J(H,F) = 23.0 Hz, J = 6.9, 2.8 Hz, 0.25 H, 5_β-H], 3.92–3.90 (m, 0.25 H, 6_β-H_A), 3.90 (dd, J = 11.0, 2.2 Hz, 0.75 H, 6_α-H_A), 3.73 (dd, J = 11.0, 6.9 Hz, 0.25 H, 6_β-H_B), 3.70 (dd, J = 11.4, 6.9 Hz, 0.75 H, 6_α-H_B), 2.18 (s, 2.25 H, OAc_α), 2.16 (s, 2.25 H, OAc_α), 2.14 (s, 0.75 H, OAc_β), 2.13 (s, 0.75 H, OAc_β), 2.04 (s, 0.75 H, OAc_β), 2.02 (s, 2.25 H, OAc_α) ppm. ^{13}C NMR (126 MHz, $CDCl_3$; α/β = 3:1): δ = 169.5 (C=$O_{2\alpha}$), 169.4 (C=$O_{2\alpha\text{ and }\beta}$), 169.0 (C=$O_{2\beta}$), 168.7 (C=$O_{2\beta}$), 168.6 (C=$O_{2\alpha}$), 137.5 ($C_\beta$ of Ph), 137.4 (C_α of Ph), 128.5–127.7 (5 $CH_{\alpha\text{ and }\beta}$ of Ph), 116.3 [t, ^1J(C,F) = 254 Hz, C-4_α], 115.9 [t, ^1J(C,F) = 255 Hz, C-4_β], 91.4 (C-1_β), 88.8 (C-1_α), 74.9 [dd, ^2J(C,F) = 29, 23 Hz, C-5_β], 73.7 (CH_2Ph_α), 73.6 (CH_2Ph_β), 72.1 [dd, ^2J(C,F) = 28, 23 Hz, C-5_α], 70.2 [dd, ^2J(C,F) = 22, 19 Hz, C-3_β], 69.5 [d, ^3J(C,F) = 4 Hz, C-2_β], 68.4 [d, ^3J(C,F) = 8 Hz, C-2_α], 66.7 [d, ^3J(C,F) = 5 Hz, C-6_β], 66.3 [dd, ^2J(C,F) = 22, 19 Hz, C-3_α], 66.0 [d, ^3J(C,F) = 5 Hz, C-6_α], 20.8 (Me_α), 20.7 (Me_β), 20.4 ($Me_{\alpha\text{ and }\beta}$), 20.3 ($Me_{\alpha\text{ and }\beta}$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$; α/β = 3:1): δ = –116.3 [d, ^2J(F,F) = 251 Hz, 0.75 F, 4_α-F_{eq}], –118.6 [dd, ^2J(F,F) = 251 Hz, J = 6 Hz, 0.25 F, 4_β-F_{eq}], –130.5 [dt, ^2J(F,F) = 251 Hz, J = 22 Hz, 0.25 F, 4_β-F_{ax}], –131.5 [ddd, ^2J(F,F) = 251 Hz, J = 24, 20 Hz, 0.75 F, 4_α-F_{ax}] ppm. HRMS (ESI): calcd. for $C_{19}H_{22}F_2NaO_8^+$ [M + Na]$^+$ 439.1175; found 439.1162.

6-*O*-Benzyl-4-deoxy-4,4-difluoro-1,2-*O*-isopropylidene-α-D/L-*xylo*-hexopyranose [(±)-13]: A solution of triols (±)-**11** (85 mg, 0.29 mmol) in acetone/2,2-dimethoxypropane (1:1, 1.2 mL) was treated with TsOH·H_2O (6 mg, 0.03 mmol) and stirred at room temperature overnight. After the addition of Amberlite-400 IR 93 (OH^- form), filtration, evaporation, and purification by column chromatography (hexane/EtOAc, 80:20 to 70:30) gave isopropylidene acetal (±)-**13** (60 mg, 63%) as a white solid. R_f = 0.52 (hexane/EtOAc, 67:33); m.p. 89 °C. IR (CH_2Cl_2): $\tilde{\nu}$ = 3398 (O-H) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.25 (m, 5 H, Ph), 5.66 (d, J = 4.6 Hz, 1 H, 1-H), 4.67 (d, J = 12.1 Hz, 1 H, CH_APh), 4.60 (d, J = 12.1 Hz, 1 H, CH_BPh), 4.35 (dd, J = 9.0, 4.4 Hz, 1 H, 2-H), 4.30–4.13 (m, 2 H, 3-H, 5-H), 3.87 (dd, J = 11.0, 3.6 Hz, 1 H, 6-H_A), 3.82 [dt, J = 10.3, 6.7 Hz, ^4J(H,F) = 6.7 Hz, 1 H, 6-H_B], 2.90 (br. s, 1 H, 3-HO), 1.59 (s, 3 H, Me), 1.38 (s, 3 H, Me) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.4 (C of Ph), 128.5, 127.9, 127.1 (5 CH of Ph), 116.9 [dd, ^1J(C,F) = 254, 252 Hz, C-4], 110.4 (CMe_2), 96.3 (C-1), 75.2 [d, ^3J(C,F) = 3 Hz, C-2], 73.6 (CH_2Ph), 70.9 [dd, ^2J(C,F) = 32, 25 Hz, C-5], 69.2 [dd, ^2J(C,F) = 31, 22 Hz, C-3], 66.7 [d, ^3J(C,F) = 8 Hz, C-6], 26.4, 25.5 (CMe_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –100.0 [ddd, ^2J(F,F) = 258 Hz, J = 15, 8 Hz, 1 F, F_{eq}], –123.7 [ddt, ^2J(F,F) = 258 Hz, J = 19, 4 Hz, 1 F, F_{ax}] ppm. HRMS (ESI): calcd. for $C_{16}H_{20}F_2NaO_5^+$ [M + Na]$^+$ 353.1171; found 353.1172.

***m*-CPBA Oxidation of (±)-*cis*-5:** A solution of 3-chloroperbenzoic acid (741 mg, 4.3 mmol) in methanol (2 mL) was added to a solution of glycal (±)-*cis*-**5** (360 mg, 1.4 mmol) in methanol (10 mL) at 0 °C. The solution was stirred for 6 h at 0 °C, treated dropwise with saturated aqueous $NaHCO_3$ solution (6 mL), stirred overnight at room temperature, and extracted with dichloromethane (3 × 10 mL). Combined organic layers were washed with brine (20 mL), dried with magnesium sulfate, filtered, and concentrated. Purification by column chromatography on silica gel (hexane/

EtOAc, 60:40 to 30:70) afforded (±)-**1** (175 mg, 41%) and (±)-**14** (118 mg, 28%).

Methyl 6-*O*-Benzyl-4-deoxy-4,4-difluoro-α-D/L-*lyxo*-hexopyranoside [(±)-1]: R_f = 0.18 (hexane/EtOAc, 60:40); m.p. 45 °C. IR (CH_2Cl_2): $\tilde{\nu}$ = 3409 (O-H) cm^{-1}. ^1H NMR (500 MHz, [D$_8$]THF): δ = 7.27–7.19 (m, 4 H, 4 H of Ph), 7.15 (tt, J = 7.2, 1.6 Hz, 1 H, 1 H of Ph), 4.61 [t, J = ^5J(H,F) = 1.6 Hz, 1 H, 1-H], 4.52 (d, J = 12.2 Hz, 1 H, CH_APh), 4.50 (d, J = 9.2 Hz, 1 H, 3-OH), 4.49 (d, J = 12.2 Hz, 1 H, CH_BPh), 4.02 (J = 6.2 Hz, 1 H, 2-OH), 3.90 [ddd, ^3J(H,F) = 25.4 Hz, J = 8.1, 2.0 Hz, 1 H, 5-H], 3.80 [ddd, J = 10.7, 1.8 Hz, ^4J(H,F) = 0.8 Hz, 1 H, 6-H$_A$], 3.78–3.68 (m, 2 H, 2-H, 3-H), 3.60 (dd, J = 10.8, 7.8 Hz, 1 H, 6-H$_B$), 3.30 (s, 3 H, OMe) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.7 (C of Ph), 128.4, 127.8, 127.4 (5 CH of Ph), 118.0 [t, ^1J(C,F) = 252 Hz, C-4], 100.5 (C-1), 73.6 (CH_2Ph), 70.7 [d, ^3J(C,F) = 7 Hz, C-2], 69.2 [dd, ^2J(C,F) = 28, 23 Hz, C-5], 67.2 [dd, ^2J(C,F) = 20, 18 Hz, C-3], 66.2 [d, ^3J(C,F) = 5 Hz, C-6], 55.6 (OMe) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –115.2 [d, ^2J(F,F) = 254 Hz, 1 F, F$_{eq}$], –129.3 [dt, ^2J(F,F) = 254 Hz, J = 25 Hz, 1 F, F$_{ax}$] ppm. HRMS (ESI): calcd. for $C_{14}H_{18}F_2NaO_5^+$ [M + Na]$^+$ 327.1015; found 327.1016.

Methyl 6-*O*-Benzyl-4-deoxy-4,4-difluoro-β-D/L-*xylo*-hexopyranoside [(±)-14]: R_f = 0.16 (hexane/EtOAc, 60:40). IR (CH_2Cl_2): $\tilde{\nu}$ = 3317 (O-H) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34 (m, 5 H, Ph), 4.65 (d, J = 12.0 Hz, 1 H, CH_APh), 4.57 (d, J = 12.0 Hz, 1 H, CH_BPh), 4.30 (d, J = 7.9 Hz, 1 H, 1-H), 3.97 (br. d, J = 10.1 Hz, 1 H, 6-H$_A$), 3.86–3.72 (m, 3 H, 3-H, 5-H, and 6-H$_B$), 3.61 (s, 3 H, OMe), 3.62–3.55 (m, 1 H, 2-H), 3.04 (br. s, 1 H, OH), 3.00 (br. s, 1 H, OH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.6 (C of Ph), 128.5, 127.8, 127.7 (5 CH of Ph), 117.1 [dd, ^1J(C,F) = 253, 251 Hz, C-4], 103.0 (C-1), 74.1 [dd, ^2J(C,F) = 29, 23 Hz, C-5], 73.8 (CH_2Ph), 73.0 (m, C-2, C-3), 65.5 [d, ^3J(C,F) = 5 Hz, C-6], 57.4 (OMe) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.9 [dd, ^2J(F,F) = 248 Hz, J = 7 Hz, 1 F, F$_{eq}$], –134.4 [dt, ^2J(F,F) = 248 Hz, J = 21 Hz, 1 F, F$_{ax}$] ppm. HRMS (ESI): calcd. for $C_{14}H_{18}F_2NaO_5^+$ [M + Na]$^+$ 327.1015; found 327.1017.

Acid-Catalyzed Addition of Methanol to (±)-*cis*-5: A solution of glycal (±)-*cis*-**5** (176 mg, 0.69 mmol) in tetrahydrofuran/methanol (7:2, 9 mL) was treated with concentrated hydrochloric acid (0.16 mL, 2.0 mmol), heated to 40 °C for 6 h, diluted with diethyl ether (10 mL), washed with saturated aqueous $NaHCO_3$ solution (3 × 5 mL), dried with magnesium sulfate, filtered, and concentrated. Purification by column chromatography (hexane/EtOAc, 67:33 to 34:66) gave (±)-α-**15** (165 mg, 83%) and (±)-β-**15** (19 mg, 10%).

Methyl 6-*O*-Benzyl-2,4-dideoxy-4,4-difluoro-α-D/L-*threo*-hexopyranoside [(±)-α-15]: Colorless oil. R_f = 0.44 (hexane/EtOAc, 60:40). IR (neat): $\tilde{\nu}$ = 3427 (O-H) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.27 (m, 5 H, Ph), 4.87 (br. s, 1 H, 1-H), 4.66 (d, J = 12.0 Hz, 1 H, CH_APh), 4.57 (d, J = 12.0 Hz, 1 H, CH_BPh), 4.21 [ddt, ^3J(H,F) = 20.0, 6.0 Hz, J = 12.0, 6.0 Hz, 1 H, 3-H], 4.03 [ddd, ^3J(H,F) = 25.3 Hz, J = 7.8, 2.5 Hz, 1 H, 5-H], 3.94 (br. d, J = 10.8 Hz, 1 H, 6-H$_A$), 3.72 (dd, J = 10.8, 7.7 Hz, 1 H, 6-H$_B$), 3.40 (s, 3 H, OMe), 2.21 [dddd, J = 13.0, 5.4, 1.0 Hz, ^4J(H,F) = 3.3 Hz, 1 H, 2-H$_{eq}$], 1.90 [td, J = 13.0 Hz, ^4J(H,F) = 3.4 Hz, 1 H, 2-H$_{ax}$] ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.9 (C of Ph), 128.4, 127.7, 127.6 (5 CH of Ph), 117.9 [dd, ^1J(C,F) = 251, 249 Hz, C-4], 97.9 (C-1), 73.6 (CH_2Ph), 69.4 [dd, ^2J(C,F) = 28, 23 Hz, C-5], 66.6 [d, ^3J(C,F) = 4 Hz, C-6], 65.9 [t, ^2J(C,F) = 21 Hz, C-3], 55.2 (OMe), 36.2 [d, ^3J(C,F) = 6 Hz, C-2] ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –120.8 [br. d, ^2J(F,F) = 242 Hz, 1 F, F$_{eq}$], –140.0 [ddd, ^2J(F,F) = 242 Hz, J = 25, 20 Hz, 1 F, F$_{ax}$] ppm. HRMS (ESI): calcd. for $C_{14}H_{18}F_2NaO_4^+$ [M + Na]$^+$ 311.1065; found 311.1064.

Methyl 6-*O*-Benzyl-2,4-dideoxy-4,4-difluoro-β-D/L-*threo*-hexopyranoside [(±)-β-15]: Colorless oil. R_f = 0.27 (hexane/EtOAc, 60:40). IR (neat): $\tilde{\nu}$ = 3426 (O-H) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.26 (m, 5 H, Ph), 4.66 (d, J = 11.9 Hz, 1 H, CH_APh), 4.58 (d, J = 11.9 Hz, 1 H, CH_BPh), 4.54 (br. d, J = 9.2 Hz, 1 H, 1-H), 4.01–3.85 (m, 2 H, 3-H, 6-H$_A$), 3.81–3.70 (m, 2 H, 5-H, 6-H$_B$), 3.28 (s, 3 H, OMe), 2.33–2.26 (m, 1 H, 2-H$_{eq}$), 1.84 (td, J = 12.2, 9.6 Hz, 1 H, 2-H$_{ax}$) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.8 (C of Ph), 128.5, 127.8, 127.7 (5 CH of Ph), 117.2 [dd, ^1J(C,F) = 253, 249 Hz, C-4], 100.2 (C-1), 74.0 [dd, ^2J(C,F) = 28, 23 Hz, C-5], 73.8 (CH_2Ph), 68.2 [t, ^2J(C,F) = 22 Hz, C-3], 67.0 [d, ^3J(C,F) = 4 Hz, C-6], 56.9 (OMe), 37.3 [d, ^3J(C,F) = 6 Hz, C-2] ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –123.6 [d, ^2J(F,F) = 243 Hz, 1 F, F$_{eq}$], –137.5 [dt, ^2J(F,F) = 243 Hz, J = 21 Hz, 1 F, F$_{ax}$] ppm. HRMS (ESI): calcd. for $C_{14}H_{18}F_2NaO_4^+$ [M + Na]$^+$ 311.1065; found 311.1066.

Methyl 2,4-Dideoxy-4,4-difluoro-α-D/L-*threo*-hexopyranoside [(±)-16]: A suspension of (±)-α-**15** (40 mg, 0.14 mmol) and Pd/C (10%, 16 mg, 0.015 mmol) in tetrahydrofuran (1 mL) was put under a hydrogen atmosphere by three evacuation–hydrogen pressure cycles, stirred for 5 h at room temperature, and filtered through Celite, and the solvents were evaporated. Purification by column chromatography on silica gel (hexane/EtOAc, 25:75) gave diol (±)-**16** (26 mg, >95%) as a white solid. R_f = 0.38 (hexane/EtOAc, 25:75). ^1H NMR (400 MHz, $CDCl_3$): δ = 4.78 (br. s, 1 H, 1-H), 4.11 [dddd, ^3J(H,F) = 20.6, 6.1 Hz, J = 11.8, 5.8 Hz, 1 H, 3-H], 3.92 (dd, J = 11.9, 1.8 Hz, 1 H, 6-H$_A$), 3.83 [ddd, ^3J(H,F) = 24.6 Hz, J = 7.9, 2.6 Hz, 1 H, 5-H], 3.74 (dd, J = 11.8, 7.9 Hz, 1 H, 6-H$_B$), 3.40 (s, 3 H, OMe), 3.30 (br. s, 2 H, 2 OH), 2.10 [dddd, J = 13.1, 5.6, 1.2 Hz, ^4J(H,F) = 3.4 Hz, 1 H, 2-H$_{eq}$], 1.89 [td, J = 12.7 Hz, ^4J(H,F) = 3.5 Hz, 1 H, 2-H$_{ax}$] ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 119.5 [dd, ^1J(C,F) = 251, 247 Hz, C-4], 99.4 (C-1), 72.2 [dd, ^2J(C,F) = 28, 23 Hz, C-5], 66.4 [t, ^2J(C,F) = 21 Hz, C-3], 59.6 [d, ^3J(C,F) = 6 Hz, C-6], 55.4 (OMe), 37.3 [d, ^3J(C,F) = 7 Hz, C-2] ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –118.3 [br. dt, ^2J(F,F) = 243 Hz, J = 3 Hz, 1 F, F$_{eq}$], –137.9 [ddd, ^2J(F,F) = 243 Hz, J = 24, 21 Hz, 1 F, F$_{ax}$] ppm. HRMS (ESI): calcd. for $C_7H_{12}F_2NaO_4^+$ [M + Na]$^+$ 221.0596; found 221.0596.

S_N2'-Addition of 4-Nitrobenzoic Acid to (±)-*cis*-5: A mixture of triphenylphosphane (1.10 g, 4.1 mmol), diisopropyl azodicarboxylate (1.24 mL, 4.2 mmol), and 4-nitrobenzoic acid (0.68 g, 4.1 mmol) in tetrahydrofuran (5 mL) was added dropwise to a solution of glycal (±)-*cis*-**5** (0.38 g, 1.5 mmol) in toluene (30 mL) at 0 °C. The mixture was stirred at room temperature for 24 h and diluted with a 1:1 mixture of dichloromethane (30 mL) and saturated aqueous $NaHCO_3$ solution (30 mL). The layers were separated, and the aqueous phase was extracted with dichloromethane. The combined organic layers were dried with magnesium sulfate, filtered, and concentrated. Purification by column chromatography on silica gel (hexane/EtOAc, 90:10 to 85:15) gave (±)-α-**19** (90 mg, 15%), a mixture of (±)-α-**19** and (±)-β-**19** (192 mg, 32%), and (±)-β-**19** (260 mg, 42%).

6-*O*-Benzyl-2,3,4-trideoxy-4,4-difluoro-1-*O*-(4-nitrobenzoyl)-α-D/L-*glycero*-hex-2-enopyranose [(±)-α-19]: Colorless solid. R_f = 0.45 (hexane/EtOAc, 80:20); m.p. 101 °C. IR (CH_2Cl_2): $\tilde{\nu}$ = 1730 (C=O), 1607 (C=C) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 9.14 (dt, J = 9.1, 2.2 Hz, 2 H, 2 H of C_6H_4), 8.83 (dt, J = 8.8, 1.9 Hz, 2 H, 2 H of C_6H_4), 7.41–7.30 (m, 5 H, Ph), 6.68 [t, J = ^5J(H,F) = 3.2 Hz, 1 H, 1-H], 6.34 (dd, J = 10.1, 3.5 Hz, 1 H, 2-H), 6.24 [t, ^3J(H,F) = 9.8 Hz, J = 9.8 Hz, 1 H, 3-H], 4.64 (d, J = 12.0 Hz, 1 H, CH_APh), 4.56 (d, J = 12.0 Hz, 1 H, CH_BPh), 4.51 [ddt, ^3J(H,F) = 21.9 Hz, J = 7.5 Hz, ^3J(H,F) = J = 2.9 Hz, 1 H, 5-H], 3.99 (dd, J = 11.4,

2.8 Hz, 1 H, 6-H_A), 3.76 (dd, J = 11.0, 7.6 Hz, 1 H, 6-H_B) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 163.3 (C=O), 150.9 (CNO_2), 137.6 (C of Ph), 134.6 (C of C_6H_4), 131.0 (2 CH of C_6H_4), 130.9 [t, ^3J(C,F) = 8.6 Hz, C-2], 128.4, 127.7, 127.6 (5 CH of Ph), 126.4 [dd, ^2J(C,F) = 32, 26 Hz, C-3], 123.7 (2 CH of C_6H_4), 112.6 [dd, ^1J(C,F) = 246, 236 Hz, C-4], 88.6 (C-1), 73.6 (CH_2Ph), 72.5 [dd, ^2J(C,F) = 32, 25 Hz, C-5], 66.3 [d, ^3J(C,F) = 6 Hz, C-6] ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –109.6 [ddd, ^2J(F,F) = 238 Hz, J = 22, 2 Hz, 1 F], –113.5 [ddd, ^2J(F,F) = 238 Hz, J = 9, 2 Hz, 1 F] ppm. HRMS (ESI): calcd. for $C_{20}H_{17}F_2NNaO_6^+$ [M + Na]$^+$ 428.0916; found 428.0917.

6-*O*-Benzyl-2,3,4-trideoxy-4,4-difluoro-1-*O*-(4-nitrobenzoyl)-β-D/L-*glycero*-hex-2-enopyranose [(±)-β-19]: Colorless solid. R_f = 0.39 (hexane/EtOAc, 80:20); m.p. 85 °C. IR (CH_2Cl_2): $\tilde{\nu}$ = 1740 (C=O), 1607 (C=C) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.26 (dt, J = 8.8, 1.9 Hz, 2 H, 2 H of C_6H_4), 8.20 (dt, J = 8.8, 1.9 Hz, 2 H, 2 H of C_6H_4), 7.39–7.30 (m, 5 H, Ph), 6.65 (br. s, 1 H, 1-H), 6.30 (dd, J = 10.7, 1.6 Hz, 1 H, 2-H), 6.24–6.17 (m, 1 H, 3-H), 4.55 (d, J = 12.0 Hz, 1 H, CH_APh), 4.52 (d, J = 12.0 Hz, 1 H, CH_BPh), 4.33 [dtd, ^3J(H,F) = 13.0, 7.6 Hz, J = 7.6, 3.5 Hz, 1 H, 5-H], 3.89 [ddd, J = 11.4, 4.7 Hz, ^4J(H,F) = 1.3 Hz, 1 H, 6-H_A], 3.82 (dd, J = 11.0, 8.2 Hz, 1 H, 6-H_B) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 162.9 (C=O), 150.8 (CNO_2), 137.4 (C of Ph), 134.4 (C of C_6H_4), 132.6 [t, ^3J(C,F) = 10 Hz, C-2], 131.1 (2 CH of C_6H_4), 128.4, 127.8, 127.5 (5 CH of Ph), 126.0 [t, ^2J(C,F) = 29 Hz, C-3], 123.6 (2 CH of C_6H_4), 112.9 [dd, ^1J(C,F) = 241, 238 Hz, C-4], 89.6 (C-1), 75.4 [dd, ^2J(C,F) = 31, 26 Hz, C-5], 73.5 (CH_2Ph), 67.1 [d, ^3J(C,F) = 4 Hz, C-6] ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –100.8 [ddd, ^2J(F,F) = 283 Hz, J = 12, 7 Hz], –109.2 [ddd, ^2J(F,F) = 283 Hz, J = 13, 5 Hz] ppm. HRMS (ESI): calcd. for $C_{20}H_{17}F_2NNaO_6^+$ [M + Na]$^+$ 428.0916; found 428.0916.

Preparation of 6-*O*-Benzyl-2,4-dideoxy-2,4,4-trifluoro-α/β-D/L-*xylo*-hexopyranose [(±)-20] and 6-*O*-Benzyl-2,4-dideoxy-2,4,4-trifluoro-α-D/L-*lyxo*-hexopyranose [(±)-21] by Fluorination of (±)-*cis*-5: A solution of Selectfluor (0.42 g, 1.2 mmol) and glycal (±)-*cis*-**5** (0.26 g, 1.0 mmol) in nitromethane/water (3:16, 19 mL:16 mL) was heated to 60 °C overnight and to 90 °C for 30 min. The mixture was cooled to room temperature, and the aqueous phase was extracted with diethyl ether (3 × 20 mL). Combined organic layers were dried with magnesium sulfate, filtered, and concentrated to afford (±)-α-**20**/(±)-β-**20**/(±)-**21** = 3:1:2. R_f = 0.38 (hexane/EtOAc, 66:34). ^{19}F{^{1}H} NMR [376 MHz, $CDCl_3$; (±)-α-**20**/(±)-β-**20**/(±)-**21** = 3:1:2]: δ = [(±)-α-**20**] –115.7 (dd, J = 254, 13 Hz, 0.5 F, F_{eq}-4), –130.8 (d, J = 254 Hz, 0.5 F, F_{ax}-4), –205.5 (d, J = 13 Hz, 0.5 F, F-2); [(±)-β-**20**] –117.9 (dd, J = 252, 13 Hz, 0.17 F, F_{eq}-4), –129.8 (d, J = 252 Hz, 0.17 F, F_{ax}-4), –203.8 (d, J = 13 Hz, 0.17 F, F-2); [(±)-**21**] –115.5 (d, J = 252 Hz, 0.33 F, F_{eq}-4), –128.5 (dd, J = 252, 21 Hz, 0.33 F, F_{ax}-4), –205.3 (d, J = 21 Hz, 0.33 F, F-2) ppm.

Acetylation of (±)-20/(±)-21: A solution of (±)-α-**20**/(±)-β-**20**/(±)-**21** (3:1:2, 170 mg, 0.58 mmol), acetic anhydride (0.16 mL, 1.7 mmol), pyridine (0.14 mL, 1.7 mmol) and 4-(dimethylamino) pyridine (4 mg, 0.03 mmol) in dichloromethane (0.6 mL) was stirred overnight at room temperature, and the solvents were then evaporated. Purification by column chromatography on silica gel (hexane/EtOAc, 85:15 to 60:40) afforded (±)-**22** (α/β = 2:1; 113 mg, 55%) and **23** (90 mg, 38%).

1,3-Di-*O*-acetyl-6-*O*-benzyl-2,4-dideoxy-2,4,4-trifluoro-α/β-D/L-*xylo*-hexopyranose [(±)-22]: Colorless oil. R_f = 0.64 (hexane/EtOAc, 66:34). IR (neat): $\tilde{\nu}$ = 1766 (C=O) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$; α/β = 2:1): δ = 7.38–7.26 (m, 5 H, Ph), 6.51 [dd, J = 3.2 Hz, ^3J(H,F) = 2.3 Hz, 0.67 H, 1_α-H], 5.88 [dd, J = 8.1 Hz, ^3J(H,F) = 3.1 Hz, 0.33 H, 1_β-H], 5.69 [dtd, ^3J(H,F) = 20, 10.5, 4.8 Hz, J = 10.5 Hz, 0.67 H, 3_α-H], 5.60–5.43 (m, 0.33 H, 3_β-H), 4.74 [ddd, ^2J(H,F) = 49.0 Hz, J = 10.0, 3.8 Hz, 0.67 H, 2_α-H], 4.61 (d, J = 12.1 Hz, 1 H, CH_APh), 4.55 [dt, ^2J(H,F) = 50.9 Hz, J ≈ 8.8 Hz, 0.33 H, 2_β-H], 4.53 (d, J = 11.9 Hz, 0.33 H, CH_BPh_β), 4.53 (d, J = 12.1 Hz, 0.67 H, CH_BPh_α), 4.25 [ddd, ^3J(H,F) = 25 Hz, J = 6.8, 2.7 Hz, 0.67 H, 5_α-H], 4.03 [ddd, ^3J(H,F) = 22.8 Hz, J = 6.9, 2.7 Hz, 0.33 H, 5_β-H], 3.89 (br. d, J = 11.1 Hz, 1 H, 6-H_A), 3.70 (dd, J = 11.1, 6.9 Hz, 0.33 H, 6_β-H_B), 3.67 (dd, J = 11.1, 6.8 Hz, 0.67 H, 6_α-H_B), 2.21 (s, 3 H, OAc), 2.20 (s, 2 H, OAc_α), 2.19 (s, 1 H, OAc_β) ppm. ^{13}C NMR (126 MHz, $CDCl_3$; α/β = 2:1): δ = 169.4 ($C=O_\alpha$), 169.1 ($C=O_\beta$), 168.5 ($C=O_\alpha$), 168.4 ($C=O_\beta$), 137.4 (C of Ph_β), 137.4 (C of Ph_α), 128.5–127.0 (5 CH of Ph), 116.5 [ddd, ^1J(C,F) = 256, 254 Hz, ^3J(C,F) = 11 Hz, C-4_α], 116.1 [td, ^1J(C,F) = 254 Hz, ^3J(C,F) = 11 Hz, C-4_β], 90.8 [d, ^2J(C,F) = 24 Hz, C-1_β], 89.0 [d, ^2J(C,F) = 22 Hz, C-1_α], 87.6 [dd, ^1J(C,F) = 192 Hz, ^3J(C,F) = 7 Hz, C-2_β], 85.5 [dd, ^1J(C,F) = 195 Hz, ^3J(C,F) = 7 Hz, C-2_α], 74.8 [dd, ^2J(C,F) = 28, 23 Hz, C-5_β], 73.7 (CH_2Ph_α), 73.6 (CH_2Ph_β), 71.8 [dd, ^2J(C,F) = 27, 23 Hz, C-5_α], 70.1 [dt, ^2J(C,F) = 22, 20 Hz, C-3_β], 68.2 [dt, ^2J(C,F) = 21, 20 Hz, C-3_α], 65.8 [d, ^3J(C,F) = 5 Hz, C-6_α], 65.6 [d, ^3J(C,F) = 4 Hz, C-6_β], 20.8 (Me_α), 20.7 (Me_β), 20.4 (Me) ppm. ^{19}F NMR (376 MHz, $CDCl_3$; α/β = 2:1): δ = –115.7 [br. dd, ^2J(F,F) = 253 Hz, ^4J(F,F) = 13 Hz, 0.67 F, 4_α-F_{eq}], –117.9 [ddd, ^2J(F,F) = 252 Hz, ^4J(F,F) = 13 Hz, J = 5 Hz, 0.33 F, 4_β-F_{eq}], –129.8 [dtd, ^2J(F,F) = 252 Hz, J = 21 Hz, ^4J(F,F) = 3 Hz, 0.33 F, 4_β-F_{ax}], –130.8 [dtd, ^2J(F,F) = 253 Hz, J = 22 Hz, ^4J(F,F) = 2 Hz, 0.67 F, 4_α-F_{ax}], –203.8 [dtt, J = 51, 13, 3 Hz, ^4J(F,F) = 13, 3 Hz, 0.33 F, 2_β-F], –205.4 [dddd, J = 49 Hz, ^4J(F,F) = 13 Hz, J = 12 Hz, ^4J(F,F) = 2 Hz, 0.67 F, 2_α-F] ppm. HRMS (ESI): calcd. for $C_{17}H_{19}F_3NaO_6^+$ [M + Na]$^+$ 399.1026; found 399.1023.

1,3-Di-*O*-acetyl-6-*O*-benzyl-2,4-dideoxy-2,4,4-trifluoro-α-D/L-*lyxo*-hexopyranose [(±)-23]: Colorless oil. R_f = 0.22 (hexane/EtOAc, 80:20). IR (neat): $\tilde{\nu}$ = 1766 (C=O) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.29 (m, 5 H, Ph), 6.34 [br. d, ^3J(C,F) = 7.1 Hz, 1 H, 1-H], 5.40 [dddd, ^3J(H,F) = 28.3, 22.5, 5.4 Hz, J = 3.1 Hz, 1 H, 3-H], 4.78 [br. d, ^2J(H,F) = 48 Hz, 1 H, 2-H], 4.64 (d, J = 12.0 Hz, 1 H, CH_APh), 4.55 (d, J = 12.0 Hz, 1 H, CH_BPh), 4.25 [ddd, ^3J(H,F) = 24.2 Hz, J = 7.1, 2.2 Hz, 1 H, 5-H], 3.95 (dd, J = 11.2, 2.2 Hz, 1 H, 6-H_A), 3.76 (dd, J = 11.2, 7.1 Hz, 1 H, 6-H_B), 2.25 (s, 3 H, OAc), 2.18 (s, 3 H, OAc) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 169.6, 167.8 (C=O), 137.5 (C of Ph), 128.5, 127.9, 127.7 (5 CH of Ph), 115.3 [dd, ^1J(C,F) = 259, 249 Hz, C-4], 89.9 [d, ^2J(C,F) = 32 Hz, C-1], 85.7 [dd, ^1J(C,F) = 188 Hz, ^3J(C,F) = 8 Hz, C-2], 73.8 (CH_2Ph), 72.8 [dd, ^2J(C,F) = 28, 23 Hz, C-5], 66.4 [dt, ^2J(C,F) = 23, 17 Hz, C-3], 60.1 [d, ^3J(C,F) = 6 Hz, C-6], 20.8 (Me), 20.5 (Me) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –115.5 [br. d, ^2J(F,F) = 252 Hz, 4-F_{eq}], –128.6 [dq, ^2J(F,F) = 252 Hz, ^{1F}J(F,F) = 22 Hz, J = 22 Hz, 4-F_{ax}], –205.3 [ddtd, J = 49, 28, 22 Hz, ^{1F}J(F,F) = 22 Hz, J = 7 Hz, 2-F] ppm. HRMS (ESI): calcd. for $C_{17}H_{19}F_3NaO_6^+$ [M + Na]$^+$ 399.1026; found 399.1017.

Preparation of 6-*O*-Benzyl-2,4-dideoxy-2,4,4-trifluoro-3-*O*-pivaloyl-α/β-D/L-*xylo*-hexopyranose [(±)-24] and 6-*O*-Benzyl-2,4-dideoxy-2,4,4-trifluoro-3-*O*-pivaloyl-α-D/L-*lyxo*-hexopyranose [(±)-25] by Electrophilic Fluorination of (±)-*cis*-10: A solution of Selectfluor (0.58 g, 1.6 mmol) and glycal (±)-*cis*-**10** (0.46 g, 1.4 mmol) in nitromethane/water (1:5, 24 mL) was heated to 60 °C overnight and to 90 °C for 30 min. The mixture was cooled to room temperature and extracted with diethyl ether (3 × 20 mL). Combined organic layers were dried with magnesium sulfate, filtered, and evaporated to afford (±)-α-**24**/(±)-β-**24**/(±)-**25** = 9:3:2. R_f = 0.16 (hexane/EtOAc, 73:17). ^{19}F{^{1}H} NMR [376 MHz, $CDCl_3$; (±)-α-**24**/(±)-β-**24**/(±)-**25** = 9:3:2]: δ = [(±)-α-**24**] –115.8 (dd, J = 250, 13 Hz, 0.64 F, 4-F_{eq}), –131.8 (d, J = 250 Hz, 0.64 F, 4-F_{ax}), –204.0 (d, J = 13 Hz, 0.64 F, 2-F); [(±)-β-**24**] –118.2 (dd, J = 250, 13 Hz, 0.21 F, 4-F_{eq}),

–130.1 (d, J = 250 Hz, 0.21 F, 4-F_{ax}), –202.6 (d, J = 13 Hz, 0.21 F, 2-F); [(±)-**25**] –115.9 (d, J = 249 Hz, 0.14 F, 4-F_{eq}), –128.9 (dd, J = 249, 21 Hz, 0.14 F, 4-F_{ax}), –206.7 (d, J = 21 Hz, 0.14 F, 2-F) ppm.

Acetylation of (±)-24/(±)-25: A solution of crude (±)-α-**24**/(±)-β-**24**/(±)-**25** (9:3:2, 0.46 g, 1.4 mmol) and acetic anhydride (1.4 mL, 14 mmol) in pyridine (33 mL) was treated with 4-(dimethylamino)-pyridine (12 mg, 0.10 mmol), and stirred overnight, and the solvents were evaporated. Purification by column chromatography on silica gel (hexane/EtOAc, 90:10 to 60:40) gave (±)-**26** (α/β = 5:1; 0.30 g, 53%), a mixture of (±)-**26** and (±)-**27** (95 mg, 17%), and (±)-**27** (84 mg, 15%).

1-*O*-Acetyl-6-*O*-benzyl-2,4-dideoxy-2,4,4-trifluoro-3-*O*-pivaloyl-α/β-D/L-*xylo*-hexopyranose [(±)-26]: Colorless oil. R_f = 0.55 (hexane/EtOAc, 80:20). IR (CH_2Cl_2): $\tilde{\nu}$ = 1754 (C=O) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$; α/β = 5:1): δ = 7.41–7.30 (m, 5 H, Ph), 6.56 [dd, J = 3.8 Hz, ^3J(H,F) = 2.2 Hz, 0.83 H, 1_α-H], 5.93 [dd, J = 8.0 Hz, ^3J(H,F) = 3.3 Hz, 0.17 H, 1_β-H], 5.72 [dtd, ^3J(H,F) = 21.1, 10.1, 4.9 Hz, J = 10.1 Hz, 0.83 H, 3_α-H], 5.42–5.26 (m, 0.17 H, 3_β-H), 4.81 [dddd, ^3J(H,F) = 48.8 Hz, J = 10.0, 3.9 Hz, ^4J(H,F) = 1.3 Hz, 0.83 H, 2_α-H], 4.66 (d, J = 11.9 Hz, 0.17 H, CH_APh_β), 4.66 (d, J = 12.1 Hz, 0.83 H, CH_APh_α), ca. 4.68–4.48 (m, 0.17 H, 2_β-H), 4.58 (d, J = 12.0 Hz, 1 H, CH_BPh), 4.29 [ddd, ^3J(H,F) = 24.4 Hz, J = 6.9, 2.9 Hz, 0.83 H, 5_α-H], 4.07 [ddd, ^3J(H,F) = 22.8 Hz, J = 6.8, 2.9 Hz, 0.17 H, 5_β-H], 3.93 [ddd, J = 11.4, 2.9 Hz, ^4J(H,F) = 1.1 Hz, 1 H, 6-H_A], 3.76 (dd, J = 10.5, 6.8 Hz, 0.17 H, 6_β-H_B), 3.72 (dd, J = 11.3, 6.9 Hz, 0.83 H, 6_α-H_B), 2.26 (s, 0.51 H, OAc_β), 2.25 (s, 2.49 H, OAc_α), 1.33 (s, 9 H, CMe_3) ppm. ^{13}C NMR (126 MHz, $CDCl_3$; α/β = 5:1): δ = 177.2 (C=O of Piv_α), 176.7 (C=O of Piv_β), 168.5 (C=O of Ac_β), 168.5 (C=O of Ac_α), 137.4 (C of Ph_α), 137.4 (C of Ph_β), 128.5–127.8 (5 CH of Ph), 116.5 [td, ^1J(C,F) = 255 Hz, ^3J(C,F) = 11 Hz, C-4_α], C-4_β hidden by the noise, 90.9 [d, ^2J(C,F) = 25 Hz, C-1_β], 88.1 [d, ^2J(C,F) = 22 Hz, C-1_α], 87.6 [dd, ^1J(C,F) = 192 Hz, ^3J(C,F) = 8 Hz, C-2_β], 85.6 [dd, ^1J(C,F) = 188 Hz, ^3J(C,F) = 7 Hz, C-2_α], 74.9 [dd, ^2J(C,F) = 28, 22 Hz, C-5_β], 73.7 (CH_2Ph_α), 73.6 (CH_2Ph_β), 71.8 [dd, ^2J(C,F) = 27, 23 Hz, C-5_α], 70.0 (m, C-3_β), 68.0 [dt, ^2J(C,F) = 22, 19 Hz, C-3_α], 65.8 [d, ^3J(C,F) = 5 Hz, C-6_α], 65.7 [d, ^3J(C,F) = 4 Hz, C-6_β], 39.11 ($CMe_{3\alpha}$), 39.06 ($CMe_{3\beta}$), 26.88 ($CMe_{3\alpha}$), 26.86 ($CMe_{3\beta}$), 20.8 (Me_α), 20.7 (Me_β) ppm. ^{19}F NMR (376 MHz, $CDCl_3$; α/β = 5:1): δ = –115.9 [ddd, ^2J(F,F) = 253 Hz, ^4J(F,F) = 13 Hz, J = 3 Hz, 0.83 F, 4_α-F_{eq}], –118.0 [ddd, ^2J(F,F) = 254 Hz, ^4J(F,F) = 13 Hz, J = 5 Hz, 0.17 F, 4_β-F_{eq}], –130.0 [dtd, ^2J(F,F) = 253 Hz, J = 21 Hz, ^4J(F,F) = 4 Hz, 0.17 F, 4_β-F_{ax}], –131.1 [dtd, ^2J(F,F) = 254 Hz, J = 22 Hz, ^4J(F,F) = 3 Hz, 0.83 F, 4_α-F_{ax}], –204.1 [0.17 F, dtt, J = 51, 13, 4 Hz, ^4J(F,F) = 13, 4 Hz, 2_β-F], –205.9 [0.83 F, dddd, J = 49, 11 Hz, ^4J(F,F) = 13, 3 Hz, 2_α-F] ppm. HRMS (ESI): calcd. for $C_{20}H_{25}F_3NaO_6^+$ [M + Na]$^+$ 441.1495; found 441.1489.

1-*O*-Acetyl-6-*O*-benzyl-2,4-dideoxy-2,4,4-trifluoro-3-*O*-pivaloyl-α-D/L-*lyxo*-hexopyranose [(±)-27]: Colorless solid. R_f = 0.40 (hexane/EtOAc, 80:20); m.p. 108 °C. IR (CH_2Cl_2): $\tilde{\nu}$ = 1753 (C=O) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.29 (m, 5 H, Ph), 6.39 [br. d, ^3J(H,F) = 6.4 Hz, 1 H, 1-H], 5.41 [dddd, ^3J(H,F) = 28.4, 21.1 5.4 Hz, J = 3.2 Hz, 1 H, 3-H], 4.80 [br. d, ^2J(H,F) = 48.6 Hz, 1 H, 2-H], 4.69 (d, J = 12.0 Hz, 1 H, CH_APh), 4.66 (d, J = 12.0 Hz, 1 H, CH_BPh), 4.31 [ddd, ^3J(H,F) = 23.6 Hz, J = 7.3, 2.5 Hz, 1 H, 5-H], 4.00 (dd, J = 11.4, 2.5 Hz, 1 H, 6-H_A), 3.81 (dd, J = 11.4, 7.2 Hz, 1 H, 6-H_B), 2.23 (s, 3 H, OAc), 1.34 (s, 9 H, CMe_3) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 177.3 (C=O of Piv), 167.9 (C=O of Ac), 137.4 (C of Ph), 128.5, 127.9, 127.8 (5 CH of Ph), 115.3 [td, ^1J(C,F) = 259 Hz, ^3J(C,F) = 11 Hz, C-4], 90.1 [d, ^2J(C,F) = 32 Hz, C-1], 85.7 [dd, ^1J(C,F) = 188 Hz, ^3J(C,F) = 7 Hz, C-2], 73.8 (CH_2Ph), 72.9 [dd, ^2J(C,F) = 29, 23 Hz, C-5], 66.3 [dt, ^2J(C,F) = 22, 17 Hz, C-3], 66.1 [d, ^3J(C,F) = 6 Hz, C-6], 39.2 (CMe_3), 26.9 (CMe_3), 20.8 (Me) ppm. $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$): δ = –115.8 (dd, J = 252, 2 Hz, 1 F, 4-F_{eq}), –128.8 (dd, J = 252, 21 Hz, 1 F, 4-F_{ax}), –205.9 (dd, J = 21, 2 Hz, 1 F, 2-F) ppm. HRMS (ESI): calcd. for $C_{19}H_{22}F_2NaO_8^+$ [M + Na]$^+$ 441.1495; found 441.1494.

Fluorination of (±)-*cis*-5 in Methanol: A solution of Selectfluor (0.71 g, 2.0 mmol) and glycal (±)-*cis*-**5** (0.26 g, 1.0 mmol) in nitromethane/methanol (3:10, 13 mL) was heated to 60 °C for 16 h and to 90 °C for 30 min. The mixture was cooled to room temperature, diluted with water (30 mL), and extracted with diethyl ether (3 × 20 mL). Combined organic layers were dried with magnesium sulfate, filtered, and concentrated. Purification by column chromatography on silica gel (hexane/EtOAc, 87:13 to 60:40) afforded (±)-α-**28** (42 mg, 14%), (±)-**2** (57 mg, 19%), and (±)-β-**28** (107 mg, 35%).

Methyl 6-*O*-Benzyl-2,4-dideoxy-2,4,4-trifluoro-α-D/L-*lyxo*-hexopyranoside [(±)-2]: Colorless oil. R_f = 0.49 (hexane/EtOAc, 67:33). IR (neat): $\tilde{\nu}$ = 3402 (O-H) cm^{-1}. ^1H NMR (500 MHz, [D_6]acetone): δ = 7.42–7.28 (m, 5 H, Ph), 5.16 (d, J = 7.9 Hz, 1 H, OH), 4.98 [dt, ^3J(H,F) = 8.4 Hz, J = 1.6 Hz, ^5J(H,F) = 1.6 Hz, 1 H, 1-H], 4.72 [dddd, ^2J(H,F) = 48.5 Hz, J = 6.1 Hz, ^4J(H,F) = 3.1, 1.5 Hz, 1 H, 2-H], 4.66 (d, J = 12.0 Hz, 1 H, CH_APh), 4.62 (d, J = 12.0 Hz, 1 H, CH_BPh), 4.17–4.01 (m, 1 H, 3-H), 4.10 [ddd, ^3J(H,F) = 25.1 Hz, J = 7.5, 2.5 Hz, 1 H, 5-H], 3.93 [ddd, J = 11.1, 2.4 Hz, ^4J(H,F) = 1.1 Hz, 1 H, 6-H_A], 3.73 (dd, J = 11.1, 7.8 Hz, 1 H, 6-H_B), 3.47 (s, 3 H, OMe) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.8 (C of Ph), 128.4, 127.8, 127.6 (5 CH of Ph), 116.9 [dd, ^1J(C,F) = 254, 249 Hz, C-4], 97.7 [d, ^2J(C,F) = 30 Hz, C-1], 88.4 [dd, ^1J(C,F) = 177 Hz, ^3J(C,F) = 8 Hz, C-2], 73.8 (CH_2Ph), 69.7 [dd, ^2J(C,F) = 28, 23 Hz, C-5], 67.0 [ddd, ^2J(C,F) = 22, 20, 18 Hz, C-3], 66.3 [d, ^3J(C,F) = 5 Hz, C-6], 55.6 (OMe) ppm. ^{19}F NMR (376 MHz, [D_6]acetone): δ = –116.7 [br. d, ^2J(F,F) = 250 Hz, 1 F, F_{eq}-4], –132.2 [ddt, ^2J(F,F) = 250 Hz, J = 25, 20 Hz, ^{h1}J(F,F) = 20 Hz, 1 F, F_{ax}-4], –208.4 [ddddd, J = 51, 27 Hz, ^{h1}J(F,F) = 19 Hz, J = 9, 3 Hz, 1 F, F-2] ppm. HRMS (ESI): calcd. for $C_{14}H_{17}F_3NaO_4^+$ [M + Na]$^+$ 329.0971; found 329.0969.

Methyl 6-*O*-Benzyl-2,4-dideoxy-2,4,4-trifluoro-α-D/L-*xylo*-hexopyranoside [(±)-α-28]: Colorless oil. R_f = 0.54 (hexane/EtOAc, 67:33). IR (neat): $\tilde{\nu}$ = 3403 (O-H) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.29 (m, 5 H, H_{Ph}), 5.02 [t, J = 3.0 Hz, ^3J(H,F) = 3.0 Hz, 1 H, 1-H], 4.65 (d, J = 12.1 Hz, 1 H, CH_APh), 4.57 (d, J = 12.1 Hz, 1 H, CH_BPh), 4.50 [dddd, ^2J(H,F) = 49.0 Hz, J = 9.7, 3.7 Hz, ^4J(H,F) = 1.7 Hz, 1 H, 2-H], 4.33 [dddt, ^3J(H,F) = 20.0, 12.2 Hz, J = 9.6, 6.1 Hz, ^3J(H,F) = 6.1 Hz, 1 H, 3-H], 4.10 [ddd, ^3J(H,F) = 25.5 Hz, J = 7.6, 2.7 Hz, 1 H, 5-H], 3.92 [ddd, J = 11.1, 2.4 Hz, ^4J(H,F) = 1.1 Hz, 1 H, 6-H_A], 3.72 (ddd, J = 11.1, 7.7 Hz, 1 H, 6-H_B), 3.52 (s, 3 H, CH_3), 2.32 (d, J = 6.0 Hz, 1 H, OH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.6 (C_{Ph}), 128.4, 127.8, 127.5 (C_{HPh}), 117.2 [td, ^1J(C,F) = 253 Hz, ^3J(C,F) = 11 Hz, C-4], 96.8 [d, ^2J(C,F) = 20 Hz, C-1], 88.8 [dd, ^1J(C,F) = 191 Hz, ^3J(C,F) = 8 Hz, C-2], 73.6 (CH_2Ph), 69.5 [dd, ^2J(C,F) = 22, 20 Hz, C-5], 69.1 [dt, ^2J(C,F) = 27, 23 Hz, C-3], 66.0 [d, ^3J(C,F) = 5 Hz, C-6], 55.9 (CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –116.8 [ddd, ^2J(F,F) = 250 Hz, ^4J(F,F) = 13 Hz, J = 6 Hz, 1 F, 4-F_{eq}], –135.2 [dddd, ^2J(F,F) = 250 Hz, J = 25, 21 Hz, ^4J(F,F) = 3 Hz, 1 F, 4-F_{ax}], –205.9 [dtd, J = 50, 13 Hz, ^4J(F,F) = 13, 3 Hz, 1 F, 2-F] ppm. HRMS (ESI): calcd. for $C_{14}H_{17}F_3NaO_4^+$ [M + Na]$^+$ 329.0971; found 329.0972.

Methyl 6-*O*-Benzyl-2,4-dideoxy-2,4,4-trifluoro-β-D/L-*xylo*-hexopyranoside [(±)-β-28]: Colorless oil. R_f = 0.43 (hexane/EtOAc, 67:33). IR (neat): $\tilde{\nu}$ = 3399 (O-H) cm^{-1}. ^1H NMR (500 MHz,

$CDCl_3$): δ = 7.40–7.29 (m, 5 H, Ph), 4.65 (d, J = 12.0 Hz, 1 H, CH_APh), 4.60 (d, J = 12.0 Hz, 1 H, CH_BPh), 4.50 [dd, J = 7.7 Hz, ^3J(H,F) = 2.7 Hz, 1 H, 1-H], 4.29 [dddd, ^2J(H,F) = 50.5 Hz, J = 9.3, 7.5 Hz, ^4J(H,F) = 1.7 Hz, 1 H, 2-H], 4.10–3.97 (m, 1 H, 3-H), 3.96 (br. d, J = 10.8 Hz, 1 H, 6-H_A), 3.82 [ddd, ^3J(H,F) = 23.1 Hz, J = 7.3, 2.4 Hz, 1 H, 5-H], 3.75 [ddd, J = 10.8, 7.3 Hz, ^{h1}J(H,F) = 0.5 Hz, 1 H, 6-H_B], 3.63 (s, 3 H, OAc), 2.45 (br. s, 1 H, OH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.4 (C of Ph), 128.6, 128.0, 127.9 (5 CH of Ph), 117.2 [td, ^1J(C,F) = 253 Hz, ^3J(C,F) = 11 Hz, C-4], 100.8 [d, ^2J(C,F) = 23 Hz, C-1], 90.9 [dd, ^1J(C,F) = 188 Hz, ^3J(C,F) = 8 Hz, C-2], 73.9 (CH_2Ph), 72.8 [dd, ^2J(C,F) = 28, 23 Hz, C-5], 71.9 [dt, ^2J(C,F) = 22, 21 Hz, C-3], 66.4 [d, ^3J(C,F) = 5 Hz, C-6], 57.4 (OMe) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –118.9 [ddd, ^2J(F,F) = 250 Hz, ^4J(F,F) = 13 Hz, J = 7 Hz, 1 F, 4-F_{eq}], –128.8 [dtd, ^2J(F,F) = 250 Hz, J = 20 Hz, ^4J(F,F) = 3 Hz, 1 F, 4-F_{ax}], –205.9 [dtt, J = 50, 14, 3 Hz, ^4J(F,F) = 14, 3 Hz, 1 F, 2-F] ppm. HRMS (ESI): calcd. for $C_{14}H_{17}F_3NaO_4^+$ [M + Na]$^+$ 329.0971; found 329.0973.

CCDC-825987 [for (±)-**13**], -825988 [for (±)-**16**], -825989 [for (±)-**1**], and -825990 [for (±)-β-**19**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): ^{1}H, ^{13}C, and ^{19}F NMR spectra of all products.

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