Reactions of Difluoroenoxysilanes with Glycosyl Donors: Synthesis of Difluoro-C-glycosides and Difluoro-C-disaccharides**

Hatice Berber, Thierry Brigaud, Olivier Lefebvre, Richard Plantier-Royon, and Charles Portella*[a]

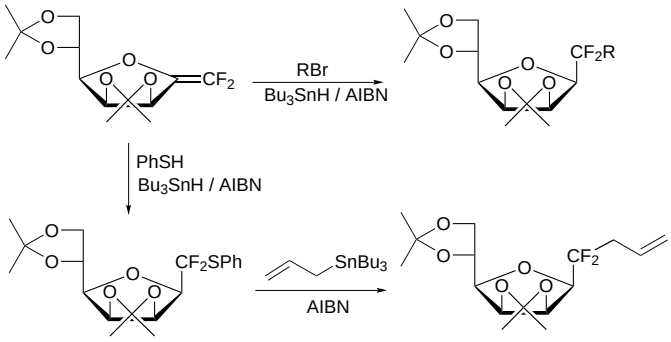
Abstract: Difluoroenoxysilanes, prepared from acylsilanes and trifluoromethyltrimethylsilane under fluoride activation, were glycosylated with some glycosyl donors (acylglycosides, glycals) to yield difluoro-C-glycosides with a difluoromethylene group in the place of the anomeric oxygen. This reaction strongly depends on the substituent in the 2-position of the glycosyl donor. Application of this methodology to a xylose-derived acylsilane led to the formation of difluoro-C-disaccharides as an isosteric O-glycosyl mimetic.

Keywords: C-glycosides · difluoroenol silyl ether · fluorine · glycosyl donor · silanes

Introduction

Difluoromethylene group has long been recognized as isopolar and bioisosteric to oxygen.[1] A lot of investigations were devoted to the synthesis of difluoro analogues of oxygen containing bioactive molecules, mainly of difluorophosphonates as phosphate mimics.[2] It was not surprising that carbohydrate chemists were interested in applying this concept to synthesize various substituted fluorinated sugars and nucleosides.[3] Though several groups reported on C-difluoromethylene containing groups grafted in other positions,[4] the grafting on the anomeric carbon to give difluoro-C-glycosides, was much less investigated, in spite of the potential interest of these compounds as non hydrolyzable glycoside mimics. Most of the methods of synthesis of C-glycosides, recently reviewed,[5] are not suitable for difluoro-C-glycosides, which need more specific methodologies.

The synthesis of difluoro-C-glycosides was first undertaken by Motherwell's group and then by ours although to a lesser extent than the Motherwell group. Motherwell's approach was based on derivatization of a 1-C-difluoromethylene sugar either as a radical acceptor[6] or, better, as a radical donor[7] after a suitable transformation (Scheme 1). The second way is more effective for C–C bond formation. The stereoselectivity of the radical addition is generally controlled by the configuration at C2.



Scheme 1. Synthesis of difluoro-C-glycosides according to Motherwell's approach.

The strategy we adopted is completely different, using a difluoroenoxysilane as a glycosyl acceptor. As we reported recently, a difluoroenoxysilane may be prepared quantitatively by the reaction of trifluoromethyltrimethylsilane (TFMTMS) with an acylsilane in a chain process initiated by *n*-tetrabutylammonium difluorotriphenylstannate (DFTPS) depicted in Scheme 2. The possibility to carry out the reaction in methylene chloride as the ideal solvent for Lewis acid activation of electrophilic substrates, allowed to form various difluoromethylene containing compounds in a one-pot process.[8–11]

Among several reactions already described, the Mukaiyama aldol reaction with ethanal dimethylacetal[8] and allylation with prenyl esters[9] prompted us to apply our methodology to glycoside and glycal derivatives, respectively, in order to have access to the interesting class of difluoro mimics of glycosides (Scheme 3).

In a preliminary account, we reported our initial results with tri-*O*-acetyl-D-glucal as glycosyl donor.[12] We have since

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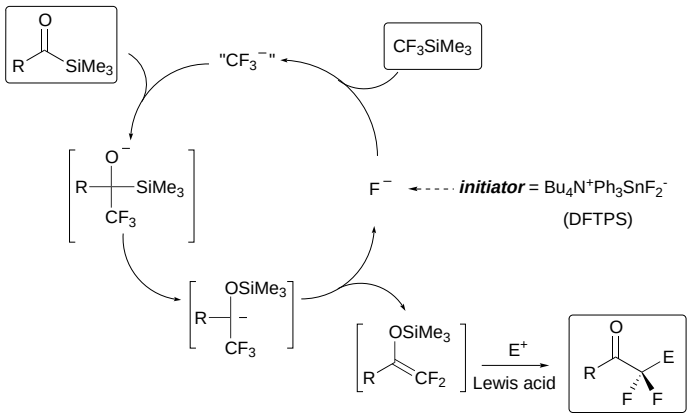
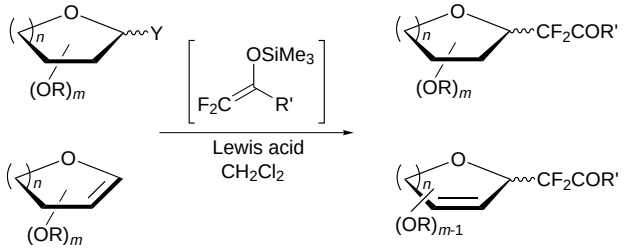


Scheme 2. Our strategy for the synthesis of difluorocarbonyl compounds from acylsilanes and TFMTMS under fluoride activation (solvent: CH_2Cl_2).



Scheme 3. Application of the methodology to glycosyl donors.

investigated other glycosyl donors, and observed that the C2 substituent of the acylglycoside plays a crucial role in the regioselectivity of the reaction. We report in this paper the full details of this study.

Results and Discussion

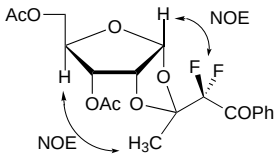
Acyl glycosides as glycosyl donors: Owing to its commercial availability, we started our study with compound **1a**. After preliminary observations, it appeared that the best way for a clean reaction would be to carry out two parallel preparations of the difluoroenoxysilane **3** and the activated (with $SnCl_4$) sugar derivative and to mix the content of the two flasks. Instead of the expected difluoro-C-riboside though, we obtained a product after purification which obviously resulted from a coupling with the non-anomeric carbon (Scheme 4, Table 1). The benzoxyl group at C2 does not seem to be

Table 1. Reaction of difluoroenoxysilanes **3** with D-ribofuranosyl donors.

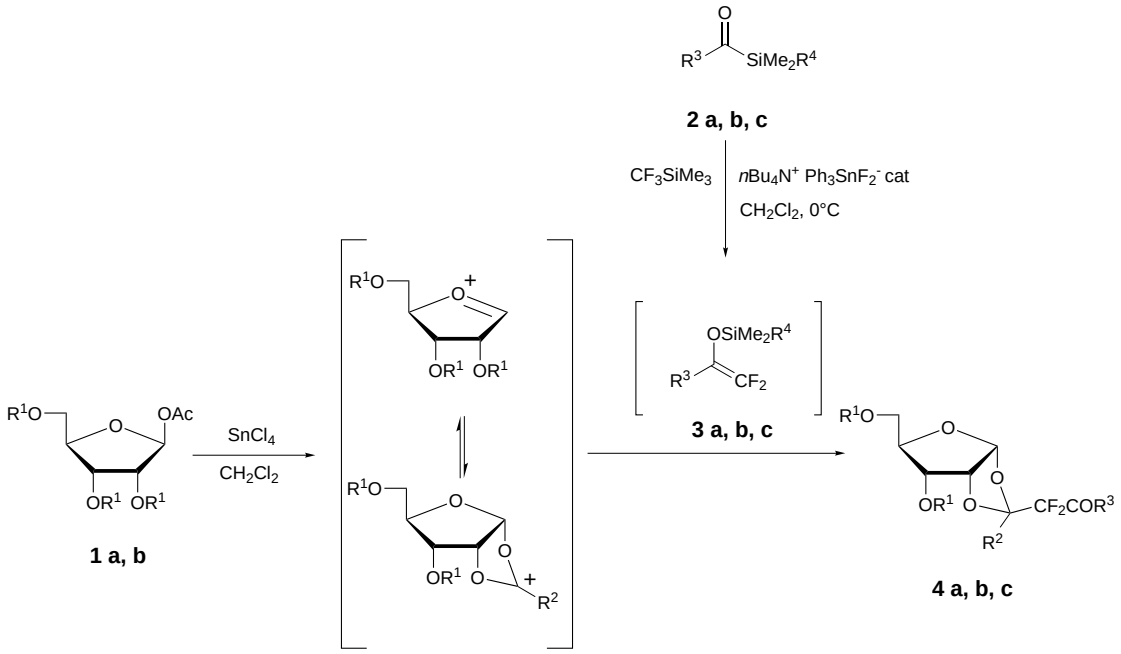
Donor	Acceptor	R^1	R^2	R^3	R^4	**4** (%)[a]
1a	**3a** (1 equiv)	Bz	Ph	Ph	Me	**4a** (55)
1a	**3a** (2 equiv)	Bz	Ph	Ph	Me	**4a** (61)
1a	**3b** (1.2 equiv)	Bz	Ph	Ph	*t*Bu	**4a** (52)
1a	**3c** (1.2 equiv)	Bz	Ph	Me	Me	**4b** (66)
1b	**3a** (1.2 equiv)	Ac	Me	Ph	Me	**4c** (45)

[a] Isolated yield.

responsible for the observed regioselectivity since the corresponding peracetylated ribose **1b** gave similar results. In both cases, the reaction was stereoselective, giving rise to *exo* compounds as shown by NOE experiments on **4c**. The structure of the difluoroenoxysilane **3** seems to be of little



4c



Scheme 4. Reaction of difluoroenoxysilanes **3** with D-ribofuranosyl donors (see Table 1).

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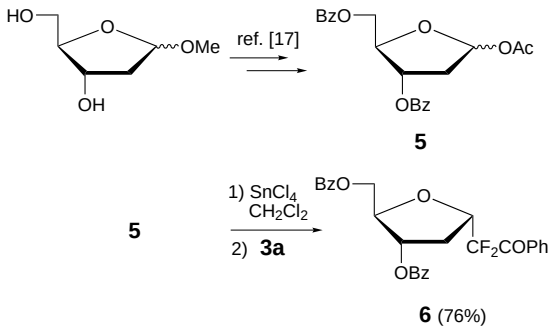
importance, as similar regioselectivity and yields are obtained from both benzoylsilane and acetylsilane.

If the nucleophilic attack of the non-anomeric carbon is a well known side reaction in the Koenigs–Knorr syntheses of glycosides, the regioselectivity is not a trivial question in C-glycosylation using enolsilyl ethers. Contrasting results were reported for the reaction of **1a** or its tri-*O*-benzyl analogue with various silylenol ethers derived from simple ketones[13, 14] or α-heteroatom substituted silylenol ethers,[15] showing that the regioselectivity strongly depends on the structure of the enol ether, mainly those derived from acyclic ketones.

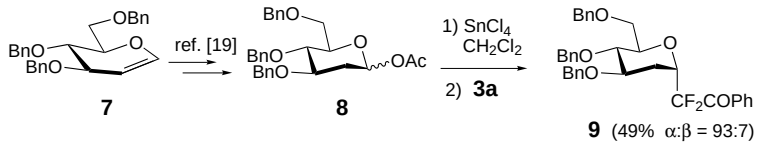
As a silicon–tin exchange was proposed to be responsible for the non-anomeric attack on **1** activated with tin tetrachloride in non-fluorinated series,[15] we assumed a different regioselectivity using boron trifluoride as activator. Unfortunately, O-glycosylation rather than C-glycosylation occurred with this Lewis acid.[16]

Since the substituent at C2 is rather problematic for C-glycosylation of difluoroenoxysilanes, it was interesting to investigate the 2-deoxy series. Using the conditions which converted compound **1** into the orthoester such as compound **4** (activation with $SnCl_4$), acetyl 3,5-di-*O*-benzoyl-2-deoxy-D-*erythro*-pentofuranoside (**5**)[17] was converted in good yields into the corresponding difluoro-C-glycoside **6** (Scheme 5). The α anomer was obtained with a stereoselectivity greater than 95%, this reaction being more stereoselective than the analogous hydrogenated enoxysilane derived from acetophenone.[18] The α configuration was attributed by comparison of NMR data with similar compounds[18] and confirmed by NOE experiments on analogue **13** (see below).



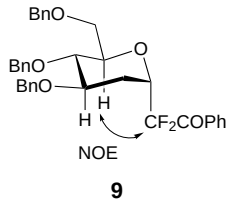
Scheme 5. Reaction of difluoroenoxysilane **3a** with a 2-deoxy glycofuranosyl donor leading to a 2-deoxy difluoro-C-glycoside.

The glycosylations were also attempted on acyl pyranosides. Penta-*O*-acetyl-D-glucopyranose treated with difluoroenoxysilane derived from **2a** in the presence of tin tetrachloride proved to be unreactive. Acetyl tetra-*O*-benzyl-D-glucopyranoside gave a complex mixture under the same conditions. In the 2-deoxy pyranose series, acetyl 3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hexopyranoside (**8**) prepared from tri-*O*-benzyl-D-glucal (**7**)[19] gave the corresponding difluoro-C-glycopyranoside **9** (Scheme 6) in moderate yields under



Scheme 6. Reaction of difluoroenoxysilane **3a** with a 2-deoxypyranosyl donor.

$SnCl_4$ activation. The major compound was observed to have α configuration (93:7, as determined by ^{19}F NMR spectroscopy) which was further confirmed by NMR studies. The vicinal coupling constants between H1 and H2 (6.3 and 5.2 Hz) revealed no axial–axial correlation (9 Hz) and irradiation of the two axial protons H3 and H5 induced a nuclear Overhauser effect on the two fluorine.

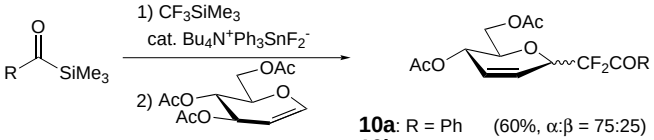


It is noteworthy that this C-glycosylation works only with 2-deoxy derivatives. We already observed that the reactivity of difluoroenoxysilanes depends strongly on the structure of the electrophilic substrate. For example, efficient coupling were observed with α-methyl benzyl bromide and dimethylallyl esters,[9] but not with benzyl bromide and allyl esters, respectively. These examples led us to conclude that the reaction works with highly stabilized electrophilic substrates. Similarly, an alkoxy group destabilizes the oxocarbenium intermediate and the reaction is favored in the 2-deoxy systems. This tentative qualitative explanation could be further confirmed by computational treatment.

Tri-*O*-acetyl-D-glucal as glycosyl donor: Glucals are good electrophilic substrates for glycosylation of carbon nucleophiles.[5] They were first used, for glycosylation of enoxysilanes by Fraser-Reid's group in 1981,[20] who reported high yields of the coupling product under boron trifluoride activation. Further examples with 2-substituted glycals[21] as well as with ketene silyl acetals[22] show invariably a stereoselective α coupling. With glycals, the anomeric C–C bond formation was concomitant to an allylic rearrangement, giving 2,3-unsaturated-C-glycosides.

We applied the above conditions to the glycosylation of difluoroenoxysilanes in a fully one-pot procedure starting from acylsilanes, as depicted in Scheme 7.

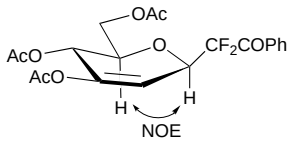
Tri-*O*-acetyl-D-glucal was converted in good overall yields into 2,3-unsaturated-C-difluoro-glycosides **10**. Regardless of the starting acylsilane, the reaction gave a mixture of anomers with a diastereomeric ratio similar to those already reported by Fraser-Reid for the hydrogenated analogues. The α configuration was attributed to the major diastereomer after



10a: R = Ph (60%, α:β = 75:25)
10b: R = CH_3 (60%, α:β = 77:23)
10c: R = C_8H_{17} (63%, α:β = 80:20)

Scheme 7. Reaction of difluoroenoxysilanes with tri-*O*-acetyl-D-glucal.

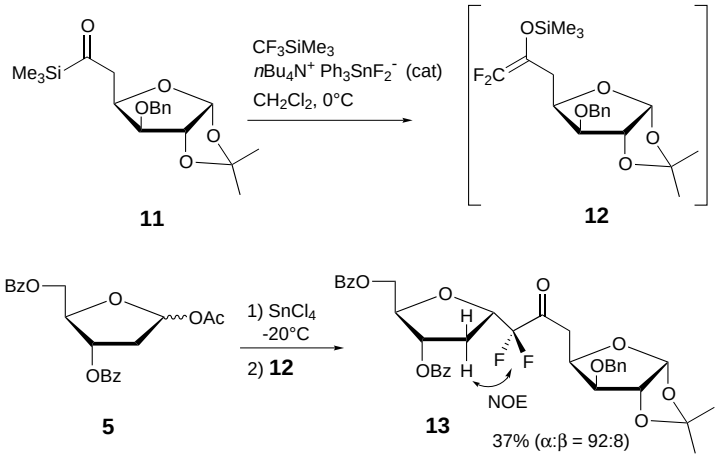
NMR analysis of separated anomers by analogy to the hydrogenated analogues[23] and was confirmed by NOE experiments. Irradiation of H1 induces a 8% nuclear Overhauser effect on H5 in the case of the minor isomer, whereas no effect was observed for the major one.



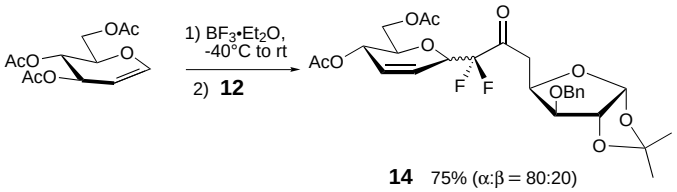
10a (minor β anomer)

These observations show that the difluoromethylene group has no effect on the stereochemical outcome of the glycosylation using D-glucal derivatives.

Application to the synthesis of difluoro-C-disaccharides: A lot of methodologies are available for the synthesis of C-disaccharides, which need a suitable functionalized sugar.[5] Except for the radical coupling proposed by Motherwell,[6b] there is no report on the synthesis of difluoro-C-disaccharides as interesting nonhydrolyzable mimics of disaccharides. To prepare such compounds with the methodology we report here, we need difluoroenoxysilanes prepared from carbohydrate-derived acylsilanes. We reported the synthesis of this type of acylsilanes some years ago,[24, 25] and we propose to exemplify the feasibility of the synthesis of difluoro-C-disaccharides starting from the acylsilane **11**, which was synthesized from D-xylose,[25] and the two types of glycosyl donors studied above. The results are depicted in Schemes 8 and 9.



Scheme 8. Application to a carbohydrate derived difluoroenoxysilane in the 2-deoxy furanose series.



Scheme 9. Application to a carbohydrate derived difluoroenoxysilane in the D-glucal series.

The reaction with the acetyl 2-deoxy-D-*erythro*-pentofuranoside **5** gave the expected disaccharide **13** in a moderate yield via the difluoroenoxysilane **12**; the major product was the α anomer (92:8, ^{19}F NMR). The irradiation of H2 on the β face shows a NOE on H3 and H1 (10%) but no effect on the two fluorine atoms. On the other hand, irradiation of H2 on the α face induces a significant NOE on the two fluorine atoms.

The application of the methodology to the glucal donor gave the C-disaccharide type compound **14** with a similar α stereoselectivity. In the latter case, the reaction was optimized by activation of the glycosyl donor prior to mixing with the in situ prepared difluoroenoxysilane giving interesting overall preparative yields for such a multistep process.

Conclusion

Several conclusions may be drawn from this work. Acylsilanes precusors are good candidates for the synthesis of difluoro-C-glycosides and -C-disaccharides. This family of compounds has a a high potential as glycosides mimics to enhance the biochemical properties. If glucal-type donors showed a similar reactivity with difluoroenoxysilanes and their hydrogenated analogues, the chemistry of acyl glycosides with these difluorinated acceptors is more subtle and problematic, good results being obtained only with 2-deoxy glycosides.

Although the results reported here are far from an exhaustive investigation on the glycosyl donors and acceptors, and activation conditions, one can consider that they are representative of a new general strategy to reach the difluoro-C-glycosidic linkage. This strategy is completely different from the radical approach of Motherwell. The availability of these two complementary methodologies should encourage bioorganic chemists to undertake the evaluation of this undoubtedly interesting class of compounds.

Experimental Section

General: Melting points are uncorrected. Optical rotations were determined with a Perkin–Elmer Model 241 polarimeter. FTIR spectra were recorded on a MIDAC Corporation Spectrafile IR™ apparatus. ^1H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker AC 250 or AC 500 in $CDCl_3$ or CD_3OD as the solvent. Tetramethylsilane ($\delta = 0.00$) or $CHCl_3$ ($\delta = 7.27$) were used as internal standards for ^1H and ^{13}C NMR spectra and $CFCl_3$ for ^{19}F NMR spectra. MS data were obtained on a JEOL D 300 apparatus at 70 eV in the electron impact mode. Elemental analyses were performed with a Perkin–Elmer CHN 2400 apparatus. All reactions were monitored by TLC (Merck silica gel F 254) or GC. GC analyses were performed on a HP 6890 chromatograph equipped with a polydimethylsiloxane HP ultra I column and a flame ionization detector. HPLC separations were performed on a HP 1100 Series chromatograph with a LiChrospher Si 60 (5 μm) column. Silica gel Merck 9385 (40–63 μm) was used for flash chromatography. All reactions

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were carried out under dry argon atmosphere. THF was dried and freshly distilled over sodium/benzophenone. Diethyl ether (SDS Purex for analyses) and dichloromethane (Fluka over molecular sieves) were obtained from commercial sources and used without further purification.

Starting materials: The following starting materials were obtained from commercial sources and were used without further purification: Acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**1a**), 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose (**1b**), acetyltrimethylsilane (**2c**), 3,4,6-tri-*O*-benzyl-D-glucal (**7**), 3,4,6-tri-*O*-acetyl-D-glucal. The following starting materials were prepared according to literature procedures: benzoyltrimethylsilane (**2a**),[26] *n*-tetrabutylammonium difluorotriphenylstanate,[27] Acetyl-3,5-di-*O*-benzoyl-2-deoxy-D-*erythro*-pentofuranoside (**5**),[17] acetyl-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hexopyranose (**8**),[19] 3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-5-C-trimethylsilylcarboxy-α-D-*arabino*-pentofuranose (**11**).[25]

General procedure for C-difluoro glycosylation

In situ preparation of the difluoroenoxysilane (3): A catalytic amount of *n*-tetrabutylammonium difluorotriphenylstanate (54 mg, 0.075 mmol) was added under argon and protected from light at −20 °C to a solution of acylsilane **2** (1.5 mmol) and trifluoromethyltrimethylsilane (TFMTMS) (0.3 mL, 1.89 mmol) in CH_2Cl_2 (5 mL). After stirring for 5 min at −20 °C, the reaction mixture was stirred for another 20 min at room temperature. The formation of the difluoroenoxysilane was monitored by GC.

$BF_3 \cdot Et_2O$ activation of the glycosyl donor: A solution of glycosyl donor (1 equiv) in CH_2Cl_2 (5 mL) was added to a solution of difluoroenoxysilane **3** at room temperature and the reaction mixture was cooled to −20 °C before dropwise addition of $BF_3 \cdot Et_2O$ (2 equiv). The reaction mixture was stirred at rt until completion of the reaction. The reaction mixture was quenched by addition of a saturated $NaHCO_3$ solution (10 mL). The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL), and the organic layer was washed with brine, dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The crude product was purified by silicagel column chromatography.

$SnCl_4$ activation of the glycosyl donor: Tin tetrachloride (1.5 equiv, 1M solution in CH_2Cl_2) was added dropwise under dry argon at rt to a solution of glycosyl donor (1 equiv) in CH_2Cl_2 (5 mL). After 30 min stirring at rt, a solution of difluoroenoxysilane **3** was slowly added and the reaction was monitored by TLC. After stirring overnight at rt, the reaction was quenched by a saturated aqueous $NaHCO_3$ solution (10 mL). After extraction with Et_2O (4 × 30 mL), the organic layer was washed with brine, dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The crude product was purified by silicagel column chromatography.

3,5-Di-*O*-benzoyl-1,2-*O*-[2,2-difluoro-3-oxo-1,3-diphenylprop-1-ylidene]-α-D-ribofuranose (4a): The reaction was performed according to the general procedure with $SnCl_4$ activation of the glycosyl donor from **1a** (1.5 mmol). Purification by flash chromatography (PE/EtOAc 9:1) yielded a solid (0.55 g, 61%). M.p. 48–49 °C; $[\alpha]_{21}^{D} = +122.2$ ($c = 1.01$ in chloroform); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 3.78$ (ddd, ^3J(H,H) = 9.2, 4.4, 3.3 Hz, 1H; H4), 4.27 (dd, ^3J(H,H) = 12.3, 4.4 Hz, 1H; H5), 4.50 (dd, ^3J(H,H) = 12.3, 3.3 Hz, 1H; H′5), 4.94 (dd, ^3J(H,H) = 9.2, 5.3 Hz, 1H; H3), 5.24 (dd, ^3J(H,H) = 5.3, 4.2 Hz, 1H; H2), 6.18 (d, ^3J(H,H) = 4.2 Hz, 1H; H1), 7.30–8.20 (m, 20H; 4Ph); ^{13}C NMR ($CDCl_3$): $\delta = 62.1$ (C5), 72.5 (C4), 76.2 (C3), 79.6 (C2), 106.5 (C1), 110.5 (t, ^2J(C,F) = 27 Hz, C-acetal), 114.5 (t, ^1J(C,F) = 263 Hz, CF_2), 127.6–134.8 (C-arom), 165.3, 165.9 (C=O benzoyl), 188.2 (t, ^2J(C,F) = 28.5 Hz, C=O); ^{19}F NMR ($CDCl_3$): $\delta = -110.8$ (d, ^2J(F,F) = 278.5 Hz), −110.1 (d, ^2J(F,F) = 278.5 Hz); IR: $\tilde{\nu} = 1726$ (C=O ester), 1271 (C–O), 1097 cm^{-1} (C–F); MS (70 eV, EI): *m*/*z* (%): 600 (0.01) $[M]^+$, 445 (49) $[M-155]^+$, 201 (74), 105 (100); elemental analysis calcd (%) for $C_{34}H_{26}O_8F_2$ (600.57): C 68.00, H 4.33; found C 67.86, H 4.73.

3,5-Di-*O*-benzoyl-1,2-*O*-(2,2-difluoro-3-methyl-3-oxo-1-phenylprop-1-ylidene)-α-D-ribofuranose (4b): The reaction was performed according to the general procedure with $SnCl_4$ activation of the glycosyl donor from **1a** (0.5 mmol). Purification by flash chromatography (PE/EtOAc 3:1) yielded an oil (0.18 g, 66%). $[\alpha]_{22}^{D} = +145.5$ ($c = 1.12$ in chloroform); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 2.20$ (t, ^4J(H,F) = 1.9 Hz, 3H; CH_3), 3.84 (ddd, ^3J(H,H) = 9.2, 4.6, 3.4 Hz, 1H; H4), 4.31 (dd, J(H,H) = 12.6, 4.6 Hz, 1H; H5), 4.51 (dd, J(H,H) = 12.6, 3.4 Hz, 1H; H′5), 4.99 (dd, ^3J(H,H) = 9.2, 5.3 Hz, 1H; H3), 5.33 (dd, ^3J(H,H) = 5.3, 4.2 Hz, 1H; H2), 6.29 (d, ^3J(H,H) = 4.2 Hz, 1H; H1), 7.32–8.03 (m, 15H; 3Ph); ^{13}C NMR ($CDCl_3$): $\delta = 26.2$ (CH_3), 62.2 (C5), 72.4 (C4), 76.2 (C3), 79.5 (C2), 106.5 (C1), 109.9 (t, ^2J(C,F) = 26.1 Hz, C-acetal), 113.4 (t, ^1J(C,F) = 264.8 Hz, CF_2), 127.1–134.1 (C-arom), 165.3, 165.8 (C=O benzoyl), 196.9 (t, ^2J(C,F) = 28.7 Hz, C=O); ^{19}F NMR ($CDCl_3$): $\delta = -119.0$ (d, ^2J(F,F) = 263.2 Hz), −118.5 (d, ^2J(F,F) = 263.2 Hz); IR: $\tilde{\nu} = 1730$ (C=O ester), 1278 (C–O), 1140 cm^{-1} (C–F); MS (70 eV, EI): *m*/*z* (%): 538 (0.01) $[M]^+$, 445 (74) $[M-155]^+$, 201 (78), 105 (100); elemental analysis calcd (%) for $C_{29}H_{24}O_8F_2$ (538.14): C 64.68, H 4.49; found C 65.09, H 4.16.

3,5-Di-*O*-acetyl-1,2-*O*-[2,2-difluoro-1-methyl-3-oxo-3-phenylprop-1-ylidene]-α-D-ribofuranose (4c): The reaction was performed according to the general procedure with $SnCl_4$ activation of the glycosyl donor from **1b** (1.58 mmol). Purification by flash chromatography (PE/EtOAc 7:3) yielded an oil (0.29 g, 44%). $[\alpha]_{22}^{D} = +80.7$ ($c = 0.71$ in chloroform); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.71$ (dd, ^4J(H,F) = 1.9, 1.5 Hz, 3H; CH_3), 2.08 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 4.13 (dd, ^3J(H,H) = 12.2, 5.0 Hz, 1H; H5), 4.24 (ddd, ^3J(H,H) = 9.2, 5.0, 2.3 Hz, 1H; H4), 4.37 (dd, ^3J(H,H) = 12.2, 2.3 Hz, 1H; H′5), 4.61 (dd, ^3J(H,H) = 9.2, 5.2 Hz, 1H; H3), 4.97 (dd, ^3J(H,H) = 5.2, 4.2 Hz, 1H; H2), 5.95 (d, ^3J(H,H) = 4.2 Hz, 1H; H1), 7.35–8.10 (m, 5H; Ph); ^{13}C NMR ($CDCl_3$): $\delta = 20.2$, 20.3, 20.6, 61.9 (C5), 71.7 (C4), 75.8 (C3), 78.9 (C2), 105.9 (C1), 111.0 (t, ^2J(C,F) = 25.6 Hz, C-acetal), 115.5 (t, ^1J(C,F) = 264.8 Hz, CF_2), 128.5–134.3 (C-arom), 169.8, 170.5 (C=O acetyl), 188.9 (t, ^2J(C,F) = 27.6 Hz, C=O); ^{19}F NMR ($CDCl_3$): $\delta = -112.8$ (d, ^2J(F,F) = 278.5 Hz), −112.2 (d, ^2J(F,F) = 278.5 Hz); IR: $\tilde{\nu} = 1746$ (C=O ester), 1233 (C–O), 1136 cm^{-1} (C–F); MS (70 eV, EI): *m*/*z* (%): 414 (13) $[M]^+$, 368 (39), 259 (48) $[M-155]^+$, 139 (69), 105 (100); elemental analysis calcd (%) for $C_{19}H_{20}O_8F_2$ (414.11): C 55.06, H 4.87; found C 54.71, H 4.63.

(3,5-Di-*O*-Benzoyl-2-deoxy-α-D-*erythro*-pentofuranosyl)-2,2-difluoro-1-phenylethanone (6): The reaction was performed according to the general procedure with $SnCl_4$ activation of the glycosyl donor from **5** (1.54 mmol). The reaction mixture was kept to −78 °C. Purification by flash chromatography (PE/EtOAc 9:1) yielded the α anomer (0.55 g, 75%) as an oil. $[\alpha]_{21}^{D} = +60.1$ ($c = 0.94$ in chloroform); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 2.52$ (ddd, J(H,H) = 14.5, 5.3, 4.0 Hz, 1H; H2), 2.94 (ddd, J(H,H) = 14.5, 8.9, 7.8 Hz, 1H; H′2), 4.46–4.66 (m, 3H, H5, H′5, H4), 4.97 (dddd, ^3J(H,F) = 15.3, 9.6, ^3J(H,H) = 8.9, 5.3, 1H; H1), 5.57 (dt, ^3J(H,H) = 7.8, 3.8 Hz, 1H; H3), 7.20–8.20 (m, 15H; 3Ph); ^{13}C NMR ($CDCl_3$): $\delta = 32.2$ (C2), 64.4 (C4), 75.0 (C5), 78.0 (dd, ^2J (C,F) = 29.5, 25.6 Hz, C1), 82.7 (C3), 116.6 (dd, ^1J (C,F) = 260.9, 256.9 Hz, CF_2), 128.4–134.4 (C-arom), 166.1 (2C=O), 189.4 (t, ^2J (C,F) = 27.6 Hz, C=O); ^{19}F NMR ($CDCl_3$): $\delta = -114.3$ (dd, ^2J(F,F) = 283.3, ^3J(H,F) = 15.7 Hz, 1F), −109.1 (dd, ^2J(F,F) = 283.3, ^3J(H,F) = 9.7 Hz, 1F); IR: $\tilde{\nu} = 1723$ (C=O), 1271 (C–O); 1098 cm^{-1} (C–F); MS (70 eV, EI): *m*/*z* (%): 480 (14) $[M]^+$, 460 (13), 421, 403, 236, 216 (100); elemental analysis calcd (%) for $C_{27}H_{22}O_6F_2$ (480.14): C 67.48, H 4.62; found C 67.10, H 4.46.

2-(3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranosyl)-2,2-difluoro-1-phenylethanone (9): The reaction was performed according to the general procedure with $SnCl_4$ activation from 0.5 mmol of **8**. The reaction mixture was kept to −78 °C. Purification by flash chromatography (PE/EtOAc 9:1) gave a mixture of anomers α:β = 93:7 (determined by ^{19}F NMR) an an oil (0.14 g, 49%). $[\alpha]_{24}^{D} = +14.4$ ($c = 0.39$ in chloroform); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.98$ (ddd, J(H,H) = 14.1, 7.3, 5.3 Hz, 1H; H2), 2.38 (ddd, J(H,H) = 14.1, 6.5, 4.2 Hz, 1H; H′2), 3.56 (dd, J(H,H) = 10.3, 3.8 Hz, 1H; H6), 3.58 (t, ^3J(H,H) = 6.0 Hz, 1H; H4), 3.66 (dd, J(H,H) = 10.3, 5.0, 1H; H′6), 3.93–4.03 (m, 2H; H3, H5), 4.30 (d, ^2J(H,H) = 12.2 Hz, 1H; H-benzyl), 4.37 (d, ^2J(H,H) = 12.2 Hz, 1H; H-benzyl), 4.45 (d, ^2J(H,H) = 12.4 Hz, 1H; H-benzyl), 4.42–4.54 (m, 1H; H1), 4.48 (d, ^2J(H,H) = 11.8 Hz, 1H; H-benzyl), 4.53 (d, ^2J(H,H) = 11.8 Hz, 1H; H-benzyl), 4.60 (d, ^2J(H,H) = 12.4 Hz, 1H; H-benzyl), 7.12–8.10 (m, 20H; 4Ph); ^{13}C NMR ($CDCl_3$): $\delta = 25.8$ (C2), 68.3 (C6), 69.8 (dd, ^2J (C,F) = 30.5, 23.6 Hz, C1), 71.5 (CH_2 benzyl), 73.1 (CH_2 benzyl), 73.2 (CH_2 benzyl), 74.9 (C4), 75.0, 75.1 (C3, C5), 118.0 (dd, ^1J (C,F) = 263.8, 256.0 Hz, CF_2), 127.5–138.2 (C-arom), 190.0 (dd, ^2J (C,F) = 28.6, 26.6 Hz, C=O); ^{19}F NMR ($CDCl_3$): α anomer: $\delta = -114.0$ (dd, ^2J(F,F) = 270.8, ^3J(H,F) = 19.1 Hz, 1F), −105.5 (dd, ^2J(F,F) = 270.8, ^3J(H,F) = 7.6 Hz, 1F); β anomer, $\delta = -112.1$ (dd, ^2J(F,F) = 270.8, ^3J(H,F) = 19.1 Hz, 1F), −105.0 (dd, ^2J(F,F) = 270.8, ^3J(H,F) = 7.6 Hz, 1F); IR: $\tilde{\nu} = 1705$ cm^{-1} (C=O); MS (70 eV, EI): *m*/*z* (%): 572 (3) $[M]^+$, 481 (39), 356 (36), 267 (40), 209 (100); elemental analysis calcd (%) for $C_{35}H_{34}O_5F_2$ (572.65): C 73.34, H 5.93; found C 72.84, H 5.94.

2-(4,6-Di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enopyranosyl)-2,2-difluoro-1-phenylethanone (10a): The reaction was performed according to the

general procedure with $BF_3 \cdot Et_2O$ activation of the glycosyl donor from tri-*O*-acetyl-D-glucal (1.5 mmol). Purification by flash chromatography (PE/EtOAc 80:20) gave compound **10a** (60%) a mixture of anomers $\alpha:\beta =$ 75:25 (determined by ^{19}F NMR) as an oil. ^1H NMR (250 MHz, $CDCl_3$): major α anomer: $\delta = 2.00$ (s, 3H; $COCH_3$), 2.06 (s, 3H; $COCH_3$), 4.01–4.20 (m, 3H, H5, H6, H′6), 4.91 (ddd, $^3J(H,F) = 18.8$, 7.2 Hz, $^3J(H,H) = 1.8$ Hz, 1H; H1), 5.18 (dm, $^3J(H,H) = 6.9$ Hz, 1H; H4), 6.01–6.11 (m, 2H; H2, H3), 7.43–8.10 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$): major α anomer, $\delta = 20.5$ (CH_3), 20.8 (CH_3), 62.6 (C6), 64.4 (C4), 74.0 (C5), 74.8 (dd, ^2J (C,F) = 30.5, 26.6 Hz, C1), 115.8 (dd, ^1J (C,F) = 259.4, 251.3 Hz, CF_2), 123.9 (C3), 128.6–129.0 (C2, C-arom), 170.1 (C=O acetyl), 170.5 (C=O acetyl), 188.8 (t, ^2J (C,F) = 27.6 Hz, C=O); minor β anomer, $\delta = 20.5$ (CH_3), 20.8 (CH_3),62.4 (C6), 63.9 (C4), 71.2 (C5), 71.6 (dd, ^2J (C,F) = 26.6, 22.6 Hz, C1), 116.9 (dd, ^1J (C,F) = 264.8, 258.9 Hz, CF_2), 123.2 (C3), 128.6–129.0 (C2, C-arom), 170.1 (C=O acetyl), 170.5 (C=O acetyl), 189.8 (t, ^2J (C,F) = 27.6 Hz, C=O); ^{19}F NMR ($CDCl_3$): major α anomer, $\delta = -112.5$ (dd, $^2J(F,F) = 275.8$, $^3J(H,F) = 18.8$ Hz, 1F), −105.0 (dd, $^2J(F,F) = 275.8$ Hz, $^3J(H,F) = 7.2$ Hz, 1F); minor β anomer, $\delta = -115.3$ (dd, $^2J(F,F) = 270.8$, $^3J(H,F) = 15.3$ Hz, 1F); −108.5 (dd, $^2J(F,F) = 270.8$ Hz, $^3J(H,F) = 7.6$ Hz, 1F); elemental analysis calcd (%) for $C_{18}H_{18}O_6F_2$ (368.11): C 58.68, H 4.93; found C 58.69, H 4.70.

1-(4,6-Di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enopyranosyl)-1,1-difluoropropan-2-one (10b): The reaction was performed according to the general procedure with $BF_3 \cdot Et_2O$ activation of the glycosyl donor from tri-*O*-acetyl-D-glucal (1.5 mmol). Purification by flash chromatography (PE/EtOAc 85:15) gave compound **10b** (60%) a mixture of anomers $\alpha:\beta =$ 77:23 (determined by ^{19}F NMR) as an oil. ^1H NMR (250 MHz, $CDCl_3$): major α anomer: $\delta = 2.00$ (s, 3H; $COCH_3$), 2.02 (s, 3H; $COCH_3$), 2.33 (d, $^4J(H,F) = 1.9$ Hz, 3H; CH_3), 3.95–4.15 (m, 3H, H5, H6, H′6), 4.59 (ddd, $^3J(H,F) = 18.9$, 5.0 Hz, $^3J(H,H) = 2.7$ Hz, 1H; H1), 5.07 (dm, $^3J(H,H) =$ 7.2 Hz, 1H; H4), 5.86 (dm, $^3J(H,H) = 10.7$ Hz, 1H; H3), 6.04 (dt, $^3J(H,H) = 10.7$, 2.3 Hz, 1H; H2); ^{13}C NMR ($CDCl_3$): major α anomer: $\delta = 20.5$ (CH_3), 20.7 (CH_3), 25.4 (CH_3), 62.5 (C6), 63.8 (C4), 70.8 (dd, ^2J (C,F) = 31.3, 26.2 Hz, C1), 71.3 (C5), 115.1 (dd, ^1J (C,F) = 163.9, 257.7 Hz, CF_2), 122.9 (C3), 129.0 (C2), 170.0 (C=O acetyl), 170.4 (C=O acetyl), 197.9 (dd, ^2J (C,F) = 31.5, 25.6 Hz, C=O); minor β anomer: $\delta = 20.4$ (CH_3), 20.7 (CH_3), 26.0 (CH_3), 61.8 (C6), 64.3 (C4), 74.0 (C5), 114.0 (dd, ^1J (C,F) = 260.0, 254.2 Hz, CF_2), 123.5 (C3), 129.7 (C2), 169.8 (C=O acetyl), 170.2 (C=O acetyl); ^{19}F NMR ($CDCl_3$): major α anomer: $\delta = -120.8$ (dd, $^2J(F,F) = 261.3$, $^3J(H,F) = 18.9$ Hz, 1F), −110.8 (d, $^2J(F,F) = 261.3$ Hz, 1F); minor β anomer: $\delta = -123.2$ (dd, $^2J(F,F) = 265.1$, $^3J(H,F) = 15.2$ Hz, 1F), −114.5 (d, $^2J(F,F) = 265.1$ Hz, 1F); IR: $\tilde{\nu} = 1726$ cm^{-1} (C=O); MS (70 eV, EI): m/z (%): 445 (28) $[M]^+$, 201 (24), 105 (100), 77 (27); elemental analysis calcd (%) for $C_{13}H_{16}O_6F_2$ (306.09): C 68.00, H 4.36; found C 67.64, H 4.26.

1-(4,6-Di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enopyranosyl)-1,1-difluorodecan-2-one (10c): The reaction was performed according to the general procedure with $BF_3 \cdot Et_2O$ activation of the glycosyl donor from tri-*O*-acetyl-D-glucal (1.5 mmol). Purification by flash chromatography (PE/EtOAc 85:15) gave compound **10c** (63%). The α and β isomers were obtained in proportions 80:20, respectively. α Isomer was isolated by recrystallisation in *n*-pentane and a fraction of pure β-anomer was obtained by flash chromatography. α Anomer: white solid; m.p. 48–49 °C; $[\alpha]_{24}^{D} = +73.0$ ($c = 1.0$ in chloroform); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 0.88$ (t, $^3J(H,H) = 6.5$ Hz, 3H; CH_3), 1.29 (m, 10H; $5CH_2$), 1.65 (tm, $^3J(H,H) =$ 7.2 Hz, 2H; CH_2), 2.06 (s, 3H; $COCH_3$), 2.10 (s, 3H; $COCH_3$), 2.72 (t, $^3J(H,H) = 7.2$ Hz, 2H; CH_2), 4.01–4.23 (m, 3H; H5, H′6, H6), 4.68 (ddd, $^3J(H,F) = 21.6$, 5.3 Hz, $^3J(H,H) = 2.3$ Hz, 1H; H1), 5.16 (dm, $^3J(H,H) =$ 6.9 Hz, 1H; H4), 5.99 (dm, $^3J(H,H) = 10.7$ Hz, 1H; H3), 6.09 (ddd, $^3J(H,H) = 10.7$ Hz, $^4J(H,H) = 2.3$ Hz, 1H; H2); ^{13}C NMR ($CDCl_3$): $\delta =$ 14.0 (CH_3), 20.6 (CH_3), 20.9 (CH_3), 22.5, 22.6, 28.9, 29.0, 29.3, 31.8, 37.8 (CH_2), 62.6 (C6), 63.9 (C4), 71.0 (dd, ^2J (C,F) = 29.5, 25.6 Hz, C1), 71.4 (C5), 115.4 (dd, ^1J (C,F) = 263.8, 257.9 Hz, CF_2), 123.2 (C2), 129.0 (C3), 170.2 (C=O acetyl), 170.5 (C=O acetyl), 200.3 (dd, ^2J (C,F) = 30.5, 24.6 Hz, C=O); ^{19}F NMR ($CDCl_3$): $\delta = -121.6$ (dd, $^2J(F,F) = 267.2$, $^3J(H,F) =$ 21.6 Hz, 1F), −110.4 (d, $^2J(F,F) = 267.2$ Hz, 1F); MS (70 eV, EI): m/z (%): 213 (30) $[M-191]^+$, 141 (100), 111 (78). β-anomer: colourless oil; $[\alpha]_{24}^{D} = +28.0$ ($c = 0.3$; chloroform); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 0.89$ (t, $^3J(H,H) = 6.7$ Hz, 3H; CH_3), 1.28 (m, 10H; $5CH_2$), 1.60 (tm, $^3J(H,H) =$ 7.1 Hz, 2H; CH_2), 2.06 (s, 3H; $COCH_3$), 2.10 (s, 3H; $COCH_3$), 2.67 (t, $^3J(H,H) = 7.1$ Hz, 2H; CH_2), 3.72 (dt, $^3J(H,H) = 9.1$, 4.2 Hz, 1H; H5), 4.18 (d, $^3J(H,H) = 4.2$ Hz, 2H; H6, H′6), 4.66 (ddm, $^3J(H,F) = 15.5$ Hz, $^3J(H,H) = 6.1$ Hz, 1H; H1), 5.28 (dm, $^3J(H,H) = 9.1$ Hz, 1H; H4), 5.93–6.02 (m, 2H; H2, H3); ^{13}C NMR ($CDCl_3$): $\delta = 14.0$ (CH_3), 20.6 (CH_3), 20.8 (CH_3), 22.4, 22.6, 28.9, 29.0, 29.3, 31.8, 38.4 (CH_2), 62.7 (C6), 64.5 (C4), 74.1 (C5), 74.6 (dd, ^2J (C,F) = 31.5, 27.6 Hz, C1), 114.2 (dd, ^1J (C,F) = 261.9, 254.0 Hz, CF_2), 123.8 (C2), 129.0 (C3), 170.0 (C=O acetyl), 170.5 (C=O acetyl), 200.9 (dd, ^2J (C,F) = 29.5, 25.6 Hz, C=O); ^{19}F NMR ($CDCl_3$): $\delta =$ −124.4 (dd, $^2J(F,F) = 261.1$, $^3J(H,F) = 15.5$ Hz, 1F), −114.2 (d, $^2J(F,F) =$ 261.1 Hz, 1F); MS (70 eV, EI): m/z (%): 213 (30) $[M-191]^+$, 141 (100), 111 (78).

2-(3,5-Di-*O*-benzoyl-2-deoxy-α-D-*erythro*-pentofuranosyl)-2,2-difluoro-1-(3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-pentofuranosyl)-ethanone (13): The reaction was performed according to the general procedure with $SnCl_4$ activation from **5** (0.5 mmol). The reaction mixture was kept to −20 °C. Purification by flash chromatography (PE/EtOAc 85:15) gave a mixture of anomers $\alpha:\beta = 92:8$ (determined by ^{19}F NMR) as a solid (0.13 g, 37%). M.p. 45–47 °C; $[\alpha]_{24}^{D} = +21.1$ ($c = 0.45$ in chloroform); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.33$ (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 2.47 (ddd, $J(H,H) = 14.9$, 5.2, 3.2 Hz, 1H; H9α), 2.78 (ddd, $J(H,H) = 14.9$, 8.8, 7.6 Hz, 1H; H9β), 3.30 (d, $J(H,H) = 6.8$ Hz, 2H; H5, H′5), 4.10 (d, $^3J(H,H) = 3.2$ Hz, 1H; H3), 4.35 (dd, $J(H,H) = 11.7$, 3.8, 1H; H12), 4.41–4.49 (m, 3H; H11, H′12, H-benzyl), 4.59–4.75 (m, 4H; H2, H4, H8, H′-benzyl), 5.50 (dt, $^3J(H,H) = 7.6$, 3.2 Hz, 1H; H10), 5.88 (d, $^3J(H,H) =$ 3.8 Hz, 1H; H1), 7.12–8.03 (m, 15H; 3Ph); ^{13}C NMR ($CDCl_3$): $\delta = 26.2$ (CH_3), 26.8 (CH_3), 31.7 (C9), 37.3 (C5), 64.3 (C12), 72.0 (CH_2 benzyl), 74.9 (C10), 75.3 (C4), 77.6 (dd, ^2J (C,F) = 32.1, 25.5 Hz, C1), 81.7 (C3), 82.4 (C2), 83.0 (C11), 104.5 (C1), 111.7 (C-acetal), 114.6 (dd, ^1J(C,F) = 261.8, 254.0 Hz, CF_2), 127.5–137.8 (C-arom), 166.0, 166.1 (C=O benzoyl), 198.5 (dd, ^2J(C,F) = 32.5, 26.5 Hz, C=O); ^{19}F NMR ($CDCl_3$): α anomer, $\delta =$ −125.2 (dd, $^2J(F,F) = 270.5$, $^3J(H,F) = 19.2$ Hz, 1F), −112.7 (dd, $^2J(F,F) =$ 270.5, $^3J(H,F) = 6.0$ Hz, 1F); β anomer, $\delta = -127.6$ (dd, $^2J(F,F) = 268.3$, $^3J(H,F) = 18.5$ Hz, 1F), −105.0 (dd, $^2J(F,F) = 268.3$, $^3J(H,F) = 3.3$ Hz, 1F); IR: $\tilde{\nu} = 1730$ cm^{-1} (C=O); MS (70 eV, EI): m/z (%): 665 (2) $[M-H]^+$, 651 (13) $[M-15]^+$, 501 (29), 447 (58), 428 (33), 337 (26), 325 (100), 277 (93); elemental analysis calcd (%) for $C_{36}H_{36}O_{10}F_2$ (666.67): C 64.86, H 5.41; found C 64.61, H 5.24.

2-(4,6-Di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enopyranosyl)-2,2-difluoro-1-(3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-pentofuranosyl)-ethanone (14): $BF_3 \cdot Et_2O$ (1.3 equiv, 0.39 mmol) was added dropwise at −40 °C under dry argon to a solution of tri-*O*-acetyl-D-glucal (1.1 equiv, 0.33 mmol) in CH_2Cl_2 (3 mL). After 15 min stirring at −40 °C, a solution of the difluoroenoxysilane **12** (0.30 mmol) was slowly added and the reaction was monitored by TLC (PE/EtOAc 4:1). After stirring 3 h at −40 °C, the reaction was quenched by a saturated $NaHCO_3$ solution (30 mL). After extraction with CH_2Cl_2 (4 × 30 mL), the organic layer was washed with brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude product was purified by silicagel column chromatography. Purification by flash chromatography (PE/EtOAc 4:1) gave **14** as a mixture of anomers ($\alpha:\beta = 80:20$, ^{19}F NMR) (0.13g, 75%). The two diastereoisomers were separated by HPLC on silica gel (hexane/EtOAc 3:1) and were fully characterized. Major α anomer: white solid; m.p. 83–84 °C; $[\alpha]_{22}^{D} = +23.9$ ($c = 0.36$ in chloroform); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 1.32$ (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 2.04 (s, 3H, $COCH_3$), 3.29 (d, $^3J(H,H) = 6.9$ Hz, 2H; H5, H′5), 4.00–4.08 (m, 3H, H12, H13, H′13), 4.13 (d, $^3J(H,H) = 3.4$ Hz, 1H; H3), 4.45 (d, $^2J(H,H) = 11.8$ Hz, 1H; H-benzyl), 4.59 (d, $^2J(H,H) = 11.8$ Hz, 1H; H-benzyl), 4.60 (d, $^3J(H,H) = 3.8$ Hz, 1H; H2), 4.56–4.68 (m, 2H; H4, H8), 5.11 (m, 1H; H11), 5.85 (d, $^3J(H,H) =$ 3.8 Hz, 1H; H1), 5.98 (dm, $^3J(H,H) = 10.7$ Hz, 1H; H10), 6.09 (dt, $J(H,H) = 10.7$, 2.3 Hz, 1H; H9), 7.20–7.35 (m, 5H; Ph); ^{13}C NMR ($CDCl_3$): $\delta = 20.5$ ($COCH_3$), 20.9 ($COCH_3$), 26.2 (CH_3), 26.8 (CH_3), 37.2 (C5), 62.6 (C13), 63.9 (C11), 70.9 (dd, ^2J (C,F) = 29.5, 25.2 Hz, C8), 71.5 (C12), 72.2 (CH_2 benzyl), 75.4 (C4), 81.7 (C3), 82.4 (C2), 104.4 (C1), 111.0 (C-acetal), 115.2 (dd, ^1J (C,F) = 263.8, 257.9 Hz, CF_2), 123.0 (C10), 127.8–128.4 (C-arom), 129.2 (C9), 137.2 (C-arom), 170.1, 170.6 (C=O acetyl), 197.9 (dd, ^2J (C,F) = 29.5, 25.6 Hz, C=O); ^{19}F NMR ($CDCl_3$): $\delta = -120.7$ (dd, $^2J(F,F) =$ 263.8, $^3J(H,F) = 20.8$ Hz, 1F), −111.1 (dd, $^2J(F,F) = 263.8$, $^3J(H,F) = 5.0$ Hz, 1F); IR: $\tilde{\nu} = 1744$ cm^{-1} (C=O); MS (70 eV, EI): m/z (%): 554 (0.1) $[M-H]^+$, 539 (9) $[M-15]^+$, 329 (27), 275 (95), 215 (66), 153 (100); HRMS (EI): calcd for $C_{27}H_{32}O_{10}F_2$ 554.1963, found 554.1956; $C_{27}H_{32}O_{10}F_2$ (554.20): calcd for C 58.46, H 5.82; found C 58.18, H 5.59. Minor β anomer: $[\alpha]_{22}^{D} = -12.7$ ($c = 0.30$ in chloroform); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 1.32$ (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 2.08 (s, 3H, $COCH_3$), 3.19 (d, $^3J(H,H) = 6.9$ Hz,

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2H; H5, H′5), 3.70 (ddd, ^3J(H,H) = 9.2, 5.0, 3.0 Hz, 1H; H12), 4.07 – 4.18 (m, 3H, H3, H13, H′13), 4.46 (d, ^2J(H,H) = 11.8 Hz, 1H; H-benzyl), 4.58 – 4.73 (m, 4H; H2, H4, H8, H′ benzyl), 5.30 (dm, ^3J(H,H) = 9.2 Hz, 1H; H11), 5.87 (d, ^3J(H,H) = 3.8 Hz, 1H; H1), 5.94 (dm, ^3J(H,H) = 10.8 Hz, 1H; H10), 6.00 (dm, ^3J(H,H) = 10.8 Hz, 1H; H9), 7.23 – 7.38 (m, 5H; Ph); ^{13}C NMR ($CDCl_3$): δ = 20.6 ($COCH_3$), 20.9 ($COCH_3$), 26.3 (CH_3), 26.8 (CH_3), 37.8 (C5), 62.6 (C13), 64.5 (C11), 72.1 (CH_2 benzyl), 74.1 (C12), 74.4 (dd, ^2J (C,F) = 31.5, 25.6 Hz, C8), 75.3 (C4), 81.9 (C3), 82.3 (C2), 104.5 (C1), 111.7 (C-acetal), 113.9 (dd, ^1J (C,F) = 261.9, 254.0 Hz, CF_2), 123.4 (C10), 127.8 – 128.0 (C-arom), 130.1 (C9), 137.2 (C-arom), 169.9, 170.7 (C=O acetyl), 198.5 (dd, ^2J(C,F) = 33.5, 23.6 Hz, C=O); ^{19}F NMR ($CDCl_3$): δ = – 125.4 (dd, ^2J(F,F) = 263.1, ^3J(H,F) = 16.8 Hz, 1F), – 113.9 (dd, ^2J(F,F) = 263.1, ^3J(H,F) = 5.2 Hz, 1F); IR: $\tilde{\nu}$ = 1744 cm^{-1} (C=O); MS (70 eV, EI): *m*/*z* (%): 554 (0.1) $[M - H]^+$, 539 (9) $[M - 15]^+$, 329 (27), 275 (95), 215 (66), 153 (100); elemental analysis calcd (%) for $C_{27}H_{32}O_{10}F_2$ (554.20): C 58.46, H 5.82; found C 58.08, H 5.57.

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