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Stereoselectivity of the nucleophilic F-alkylation of carbonylated carbohydrates

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Abstract

The addition of F-alkyl organometallics to carbonylated carbohydrates **1**–**3** was carried out using trimethylsilyl or bromomagnesium reagents. The results are strongly dependent upon both the nature of the metal and of the substrate. Compounds **1** and **2** were transformed with high stereoselectivity into the L-ido adduct using F-organomagnesium reagents, whereas the D-allo adduct was obtained with complete stereoselectivity using fluoride activated addition of F-organosilanes on compound **3**. Comparison with literature data emphasizes the enhanced stereoselectivity exhibited by perfluoroorganometallic reagents. The difference between the stereoselectivity of the addition of magnesium versus silyl reagents was attributed to chelation effects.

Carbohydrates, renewable raw materials, are attractive building blocks for the synthesis of a wide range of products. They are involved as 'chirons' in the synthesis of enantiomerically pure compounds.[1] Their polyhydroxylic functionality brings about a hydrophilic character exploited in the surfactant field.[2] On the other hand, fluorinated derivatives of carbohydrates have attracted the attention of organic and bioorganic chemists, due to the properties induced by fluorine. Weakly fluorinated sugars, containing one or two fluorine atoms, were widely studied as part of bioactive molecules.[3] More recently, synthesis of some deoxytrifluorosugars[4,5] or *C*-trifluoromethyl sugars including nucleoside analogues,[6,7] were reported. Some highly fluorinated carbohydrates (containing a perfluoroalkyl chain longer than CF_3) were synthesized as surfactants, for example for the formulation of biocompatible oxygen carriers.[8] Most of the reported carbohydrate derived fluorinated surfactants contain a hydrocarbon spacer between the hydrophilic sugar moiety and the F-alkyl chain, due especially to two main reasons: (i) some syntheses were based on *O*- or *S*-alkylation or -glycosidation with F-alkyl alkanols or -thiols on which the F-alkyl group is necessarily branched at a remote position from the functional carbon[9] (the hydroxyl group is highly deactivated in alcohols such as F-alkylmethanol); (ii) other syntheses involved radical F-alkylation of *O*-allyl derivatives or glycal derivatives.[10]

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Within a program on the synthesis and applications of new fluorinated carbohydrates derivatives, we have undertaken the study of the direct grafting of an F-alkyl chain (including CF_3) onto the sugar carbon backbone by radical[11] or nucleophilic[12] F-alkylation. This paper deals with the F-alkylation and trifluoromethylation of carbonylated derivatives **1**–**3** with F-organomagnesium reagents and F-alkyl trimethylsilanes (F-alkyl TMS). Comparison of the two types of reagents, and on the other hand, comparison with the reported results on the addition of non-fluorinated nucleophiles is discussed to emphasize the specific behaviour of the fluorinated reagents.

1. Results

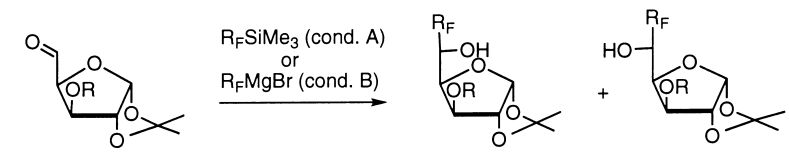
1.1. Starting compounds and reagents

Two types of carbonylated substrates were considered, which vary by the nature of a hydroxyl protecting group or the carbonyl function. 3-*O*-Benzyl- and 3-*O*-allyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanoses **1** and **2**, and 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose **3** were prepared according to conventional procedures from D-glucose. To simplify the following description, we will subsequently name these compounds 'pentodialdoses' and '3-oxo-glucose', respectively.

The reagent used as a source of nucleophilic trifluoromethyl was trifluoromethyltrimethylsilane (TFMTMS),[13] prepared according to reported procedures.[14] Long chain F-alkylations were carried out with F-organomagnesium bromides,[15] prepared in situ from F-alkyliodides and ethylmagnesium bromide, or with F-alkyltrimethylsilane,[16] in order to compare the influence of the metal on the stereoselectivity.

1.2. Additions on the 'pentodialdoses'

The trifluoromethylation of **1** and **2** with TFMTMS was carried out at 0°C in methylene chloride and induced with a catalytic amount of *n*-tetrabutylammonium difluorotriphenylstannate (DFTPS).[17] These conditions, already used in this laboratory,[18] gave better results than conventional solvent and catalyst (ether or THF, TBAF). The results are reported in Scheme 1 and Table 1 (entries 1–3), including a literature result about the use of trifluoromethylzinc iodide (under sonication) as the nucleophilic source (entry 3),[5] to emphasize the effectiveness of TFMTMS methodology. The addition to **1**, yielded quantitatively a mixture of intermediate silyl ethers which was easily hydrolyzed to give a mixture of the two epimeric L-ido and D-gluco derivatives **4** and **5** with an 80/20 ratio. The epimers were separated by chromatography and the stereochemical assignment was based on literature data. The minor D-gluco derivative **5** is a crystalline compound whose X-ray structure and specific rotation has been already reported.[5]



Scheme 1.

Table 1
F-Alkylation of 1,2-*O*-isopropylidene-3-*O*-alkyl-α-D-*xylo*-pentodialdo-1,4-furanoses

Entry	Substrate	R_F-M	Conditions[a/]	L-ido/D-gluco[c/]	Yield[d/] (%)
1	**1**	CF_3SiMe_3	A	**4/5** = 80/20	95
2	**2**	CF_3SiMe_3	A	**6/7** = 88/12	98
3	**1**	CF_3I / Zn	b/	**4/5** = 72/28	47
4	**1**	C_4F_9MgBr	B	**8a/9a** = >95/<5	64
5	**1**	$C_6F_{13}MgBr$	B	**8b/9b** = >95/<5	57
6	**2**	C_4F_9MgBr	B	**10a/11a** = >95/<5	68
7	**2**	$C_6F_{13}MgBr$	B	**10b/11b** = >95/<5	60
8	**1**	$C_4F_9SiMe_3$	A[e/]	**8a/9a** = 85/15	65

[a/] Conditions A: (i) R_FSiMe_3 (1.1 eq), $Bu_4N^+Ph_3SnF_2^-$ (cat.), CH_2Cl_2 , r.t.; (ii) H_3O^+ or TBAF. Conditions B: (i) R_FMgBr (1.2 eq), Et_2O, -45°C; (ii) H_3O^+. [b/] see ref. 5. [c/] determined by integration of H-1 signals on the crude product. [d/] isolated pure product (yield of separated epimers for entries 1,2 and 8). [e/] similar results were obtained when the reaction was carried out at -45°C (**8a/9a** = 80/20).

Table 2
Selected ^1H and ^{13}C NMR data[a] for compounds **4**–**10**

Products	R_F	R	δ_{OH} (ppm)	$\delta_{H\text{-}3}$ (ppm)	$\delta_{C\text{-}5}$ (ppm)
4 (L-*ido*)	CF_3	OBn	3.49	3.80	68.8
5 (D-*gluco*)	CF_3	OBn	3.55	4.06	69.8
6 (L-*ido*)	CF_3	OAll	3.10	3.75	68.7
7 (D-*gluco*)	CF_3	OAll	3.44-3.69	3.97	70.3
8a (L-*ido*)	C_4F_9	OBn	3.31	3.77	67.8
9a (D-*gluco*)	C_4F_9	OBn	4.09	4.09	70.1
10a (L-*ido*)	C_4F_9	OAll	3.39	3.75	68.0
10b (L-*ido*)	C_6F_{13}	OAll	3.17	3.72	67.6

[a/] All spectra were recorded in C_6D_6

The assumption that the same stereoselectivity was obtained for the allyl derivative **2**, giving the corresponding allyl L-ido/D-gluco **6**/**7** as a 88/12 mixture, is consistent with good correlation in the ^1H NMR and ^{13}C NMR data of **6**/**7** versus **4**/**5** (Table 2). In particular, H-3 and C-5 are more shielded ($\Delta\delta$ at 0.25 and 1.5 ppm, respectively) for L-ido derivatives, and the hydroxylic proton is coupled only for the D-gluco derivatives. The relative shielding of H-3 and the coupling of the hydroxylic proton are consistent with similar observations in non-fluorinated derivatives in this series.[19,20]

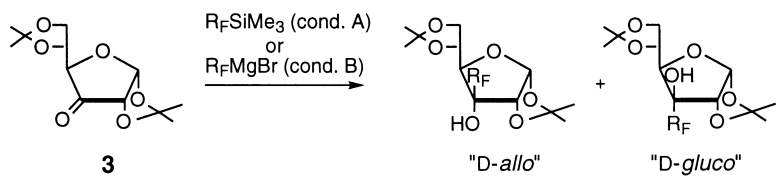
Addition of **1** or **2** to a solution of F-organomagnesium reagents in ether at −45°C gave the results

depicted in Scheme 1 and Table 1 (entries 4–7). The addition gave highly stereoselectively the L-ido adducts **8** and **10**, since the minor D-gluco epimers **9** and **11** could be observed only as traces in the NMR spectra.

The actual yields did not exceed 68%, but the reaction was very clean and the yield versus the converted starting material is quantitative. Changing the experimental conditions (time and/or temperature) did not improve the conversion. In order to assess the role of the F-alkyl chain versus the nature of the metal on the stereoselectivity of the addition, F-butyltrimethylsilane was added to **1** under conditions similar to the ones used for trifluoromethylation and at −45°C. A diastereoselectivity comparable to that observed in the addition of TFMTMS was observed (**8a**/**9a**=80/20), but the conversion and the yields were in the same range as for the addition of R_FMgBr (Table 1, entries 8–9).

1.3. Addition on '3-oxo-glucose'

The results obtained when the same reagents were reacted in the same conditions with **3** are depicted in Scheme 2 and Table 3. As above, the long chain reagents gave partial conversion and high selectivity (yield versus converted starting material; entries 2–4). In contrast to the addition to **1** and **2**, silyl reagents add with complete stereoselectivity to the β-face, giving the D-allose derivative **12** or **13** as a unique isolable and observable product, whereas a mixture of epimers D-allo and D-gluco (**13**/**14**=75/25) was obtained from magnesium reagents. The two epimers were easily separated by silica gel chromatography. We have already given the spectral features of the trifluoromethyl D-allo derivative **12**.[7]



3 "D-*allo*" "D-*gluco*"

Scheme 2.

The configuration of the other F-alkyl derivatives was assigned according to correlations with **12** and to the following observations (Table 4): (i) the hydroxylic proton is more shielded (Δδ at 1.3 ppm) in the D-allose series; (ii) a splitting of H-2 signal (J=1.1 Hz) and C-5 signal (J=5.9 Hz) was observed for the long F-alkyl branched D-allose derivatives **13a** and **13b**, probably because of a coupling through space with fluorine; (iii) C-3 and C-5 for all derivatives of D-glucose series are more deshielded (Δδ at 1.5

Table 3
F-Alkylation of 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose **3**

Entry	R_FM	Conditions[a/]	D-allo/D-gluco[b/]	Yield[c/] (%)
1	CF_3SiMe_3	A	**12** (100/0)	88
2	C_4F_9MgBr	B	**13a**/**14a** = 78/22	68
3	$C_6F_{13}MgBr$	B	**13b**/**14b** = 73/27	59
4	$C_4F_9SiMe_3$	A	**13a** (100/0)	70

[a/] see Table 1. [b/] determined by integration of H-1 signals on the crude product. [c/] isolated pure product (yield of separated epimers for entries 2 and 3).

Table 4
Selected NMR data for compounds **12**–**14**

Substrate	R_F	δ_{OH}	$\delta_{H\text{-}2}$	$\delta_{C\text{-}3}$	$\delta_{C\text{-}5}$	$\delta_{CF2\alpha}$
12	CF_3	3.31	4.60 d	80.1 t, J = 28.0 Hz	72.8	
13a	C_4F_9	3.41	4.76 dt	81.0 t, J = 25.6 Hz	72.9 d, J = 5.9 Hz	-114.75 -120.10
14a	C_4F_9	4.63	4.60 d	82.5 t, J = 23.4 Hz	74.9	-112.55
13b	C_6F_{13}	3.43	4.73 dt	80.7 t, J = 23.4 Hz	72.5 d, J = 5.9 Hz	-113.75 -119.00
14b	C_6F_{13}	4.66	4.60 d	82.6 t, J = 23.6 Hz	75.0	-111.99 -112.75

and 2.5 ppm, respectively) than for D-allose derivatives; (iv) the difluoromethylene linked to C-3 is more deshielded for D-gluco derivatives (cis relation to the oxygen at C-2).

2. Discussion

Two major observations can be drawn from these results. The yields of trifluoromethylation with TFMTMS are quantitative, and the conversion is not complete with long chain F-alkyl reagents, whatever the associated metal. In contrast, the nature of the metal is responsible for the stereochemical course of the addition, and the relative stereochemistry depends on the substrate: high stereoselectivity is observed with magnesium reagents for pentodialdoses substrates, with silyl reagents for 3-oxo glucose substrates.

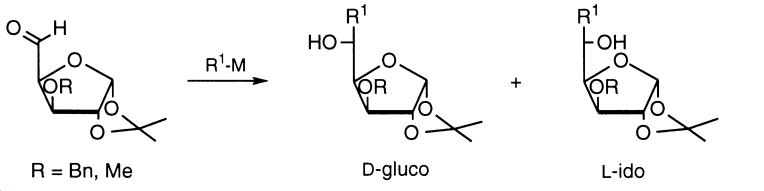
The lower conversion in additions with long chain reagents may be related to a slower attack of a highly oxygenated substrate by a highly hydrophobic reagent. Such an explanation is consistent with the limited stability of F-organometallic reagents.[15] The specific stereochemical behaviour of each substrate deserves separate discussion, as does a comparison with the literature data to determine the specificity of the additions on fluorinated nucleophiles.

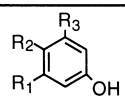
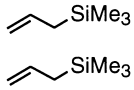
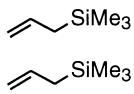
*2.1. Stereoselectivity of the F-alkylation of the 'pentodialdoses' **1** and **2***

Several papers have reported on the addition of various non-fluorinated nucleophilic reagents to **1** or related compounds. The results and references are summarized in Table 5. We can ignore the first reported result[21] (entry 1) which is in complete disagreement with the other literature data, probably because the isolation of the L-ido derivative was performed by crystallization, possibly ignoring the epimer in the mother liquor. Considering the other data, we can deduce the following observations:

(i) magnesium reagents generally gave the L-ido derivative[19,20,22,23] stereoselectively (entries 2–5);
(ii) this stereoselectivity may be improved with addition of Lewis acid such as titanium tetrachloride or zinc chloride (entry 2) or be reversed by increasing the size of the counter metal by addition of crown ether (entry 3) or titanium tetraisopropoxide (entry 5); and

Table 5
Organometallic additions on 'pentodialdo' derivatives: literature data

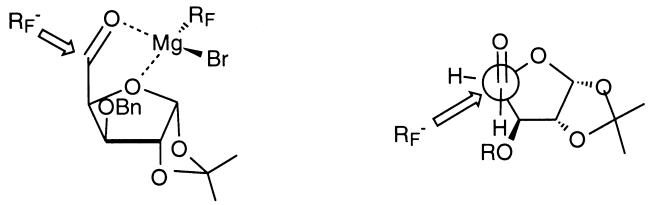


Entry	Nucleophilic reagent	Conditions	D-gluco / L-ido	Réf
1	CH_3MgI	Et_2O, Δ	0/100	21
2	CH_3MgBr	Et_2O, r.t. Et_2O, r.t., $ZnCl_2$ Et_2O, -78°C, $TiCl_4$	37/63 23/77 18/82	22
3	CH_3MgI	Et_2O, r.t. Et_2O, r.t., 12-crown-4 Et_2O, r.t., 18-crown-6	30/70 67/33 83/17	23
4	PhMgBr	THF, 0°C	8/92	20
5		EtMgBr, CH_2Cl_2, 0°C $Ti(OiPr)_4$, Toluène, r.t.	3/97 97/3	19
6		CH_2Cl_2, $TiCl_4$ CH_2Cl_2, $BF_3.Et_2O$	4/96 96/4	24
7		DMF-H_2O, $Yb(OTf)_3$ CH_2Cl_2,-78°C, $SnCl_4$	6/94 88/12	25

(iii) silyl reagents (entries 6 and 7) gave a high L-ido selectivity only with added oxygenophilic chelating Lewis acid.[24,25]

All of these observations are consistent with a chelated transition state giving rise to L-ido selectivity. Our results can also be explained in terms of chelated (with F-alkylmagnesium bromide; Scheme 3) or non-chelated (with F-alkyl TMS) transition states and have not to be distinguished from this point of view. What is noteworthy is that the stereoselectivity with fluorinated reagents is higher than with non-fluorinated ones for both magnesium and silicon reagents. We have obtained a quasi complete L-ido selectivity with the magnesium reagent without needing to add further chelating Lewis acid. On the other hand, the selectivity of the addition of the non-chelating TFMTMS or F-alkyl TMS is similar to or better than that of chelating non-fluorinated alkylmagnesium reagents. Hence, we have to consider further stereoelectronic interactions due to the presence of fluorine atoms. In the chelated transition state (F-alkylmagnesium), the usual steric hindrance favours the exo-face attack, moreover the endo-face attack is inhibited by electronic hindrance between the oxygen-rich endo-face and the fluorine atoms. To explain the stereoselectivity observed in absence of chelation (F-alkyl TMS) we propose an empirical transition state model depicted in Scheme 3, different to the classical Felkin–Anh model which would

give reversed stereoselectivity. In such a model, the increased electronic interaction between the carbonyl oxygen and the heterocyclic oxygen is balanced by avoiding a strong interaction between the entering F-alkyl group and the alkoxy group on C-3. Another point to take into account is the bulkiness of the actual nucleophilic reagent: the 'R_F^-' is in fact delivered by a hypervalent fluorosilicon intermediate[13] more sterically demanding than a naked R_F^- (which would be unstable due to β- or -α-elimination). Hence, both electronic and steric factors would control the stereochemical outcome of the R_F–TMS reagents.



Scheme 3.

*2.2. Stereoselectivity of the F-alkylation of the 3-oxo-derivative **3***

A general feature of nucleophilic attack on 3-oxo-glucose and, more generally, to corresponding derivatives with an unsaturated sp^2 C-3, is its high preference for the β-face, due to steric interactions with the substituent at C-2.[26] It is noteworthy that such a high stereoselectivity was observed with F-alkyl nucleophiles only in the F-alkylsilane series, whereas the magnesium reagents led to an important amount of the epimeric D-glucose derivative. Thus, in contrast to the reactions with the 'pentodialdo' derivatives, if a chelation of magnesium occurred, it would allow an α-attack and counteract the steric strain.

Some comparisons with the reaction of classical magnesium reagents may be of interest. Non-bulky reagents like methyl-, phenyl- or vinylmagnesium bromide gave a completely stereoselective β-face addition with good yields.[27] As soon as a β-hydrogen is available on the reagent, poor yields of addition were obtained and the reduction of the carbonyl group leading to D-allose and D-glucose competes. The yield of addition as well as the β-stereoselectivity of reduction are increased if magnesium bromide is added to the medium and if the reaction is carried out at low temperature.[28] Thus it seems that the latter conditions induce a 'protection' against hydride transfer from the α-face, probably by its selective complexation with magnesium bromide. We can assume that, in the absence of a possible competitive reduction, a similar complexation of the F-alkylmagnesium reagent allows an intramolecular F-alkyl group transfer from the α-face.

Even if a more satisfactory interpretation cannot be given, it is noteworthy that, for the first time, without any additional salt, a substantial amount of the unusual adduct epimer, resulting from an α-addition was isolated. Hence, as for the 'pentodialdo' derivatives, the addition of F-alkylmagnesium reagents to 3-oxo-glucose derivative follows a particular behaviour compared to the hydrogenated reagents.

3. Conclusion

Besides the synthesis and characterization of new *C*-F-alkylated carbohydrate derivatives, this study emphasizes the stereochemical course of nucleophilic F-alkylation compared to alkylation. The stereochemistry depends strongly on the nature of the counter metal. In particular, the results highlight the

complete stereoselectivity of addition of F-alkylmagnesium reagents on pentodialdose, due to the usual chelated transition state and stereoelectronic effect of the F-alkyl chain. Even with F-alkylsilanes, where chelation may not be invoked, the stereoselectivity is higher than that usually observed with non-fluorinated magnesium reagents. The F-alkyl nucleophiles also exhibit a particular character toward the addition on the 3-oxo-glucose derivative, where complete stereoselectivity is observed, here, with silane reagents, and where the chelated magnesium species counteracts the β-face preference. Deprotection of the long F-alkyl chain compounds and the study of their amphiphilic properties will be reported in a forthcoming paper.

4. Experimental section

4.1. General methods

All reactions were performed under a constant flow of dry argon. Commercial dichloromethane (Fluka puriss) and ether (SDS) were used without further purification. Merck silica gel F_{254} (0.2 nm) was used for TLC plates, detection being carried out by spraying with an alcoholic solution of phosphomolybdic acid, followed by heating. Flash column chromatography was performed on silica gel Merck Art. 9385 Kieselgel 60 (0.04–0.063 μm). Melting points were determined with a Buchi apparatus. IR spectra were recorded with an IR^{TM} plus MIDAC spectrophotometer and are expressed in cm^{-1}. NMR spectra were recorded on a Brücker AC 250 spectrometer (250 MHz for ^{1}H, 62.5 MHz for ^{13}C and 235.36 MHz for ^{19}F). Chemical shifts are expressed in parts per million from TMS (^{1}H and ^{13}C) or $CFCl_3$ as an internal reference. Coupling constants are in Hz and splitting pattern abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Optical rotations were determined with a Perkin–Elmer 241 polarimeter. Elemental analyses were performed with a Perkin–Elmer CHN 2400 apparatus. Mass spectra were recorded on a Fison VG Autospec spectrometer.

4.2. F-Alkylation with R_FSiMe_3 — general procedure

The carbonylated compound (2 to 10 mmol) was dissolved in anhydrous dichloromethane (5 mL/mmol) and the reaction was cooled to 0°C. Then, TFMTMS or $C_4F_9SiMe_3$ (1.1 equiv.) and a catalytic amount of *n*-tetrabutylammonium difluorotriphenylstannate were added. The reaction was warmed to room temperature and stirred until completion of the reaction. The reaction mixture was treated with a 2 M aqueous HCl solution (reaction of **1** and **2**) or the crude product in methanol was treated with one equivalent of TBAF (reaction of **3**). After partition between aqueous NH_4Cl and dichloromethane, the organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was analyzed by NMR to determine the epimers proportions (see Table 1). Separation of the epimers or purification by flash chromatography yielded the F-alkylated compounds.

4.3. Perfluoroalkylation with R_FMgBr — general procedure

To a solution of perfluoroalkyl iodide (1.2 equiv.) in ether (3 mL/mmol) cooled to −45°C and protected from light was added dropwise ethylmagnesium bromide (1.2 equiv.). The reaction was stirred at −45°C for 0.5 h. The carbonylated compound (dehydrated by azeotropic distillation with toluene just before use) (2 to 10 mmol, 1 equiv.), was dissolved in ether (2 mL/mmol) and added dropwise to the reaction mixture. The reaction temperature was left to rise slowly to −10°C. After 2 h, the reaction was washed

with a saturated solution of ammonium chloride (2×20 mL) and the aqueous layer was extracted with ether (2×20 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated. The perfluoroalkylated compound was purified (separated) by flash chromatography.

*4.4. 3-O-Benzyl-6-deoxy-6,6,6-trifluoro-1,2-O-isopropylidene-β-L-ido- and -α-D-glucofuranose **4** and **5***

Conditions A: yield 1.2 g, 95% (**4**/**5**=80/20). Chromatography (petroleum ether/CH_2Cl_2 50/50).

4: oil. $[\alpha]^{20}_D=-29.5$ (*c* 0.48, $CHCl_3$). [Lit. $[\alpha]^{23}_D=-31.0$ (*c* 0.74, $CHCl_3$).] IR (film): 3462; 2997; 1265; 1128. MS (EI) m/z: 348 ($M^{+\bullet}$, 1); 333 (5); 290 (24); 128 (32); 91 (100); 85 (94); 65 (56); 59 (70). ^{1}H NMR ($CDCl_3$) δ: 1.32 (s, 3H, CH_3); 1.48 (s, 3H, CH_3); 3.28 (s, 1H, OH); 4.07 (d, 1H, J=3.0 Hz, H-3); 4.35 (m, 2H, H-4, H-5); 4.51 (d, 1H, J_{AB}=11.4 Hz, CH_2–Ph); 4.64 (d, 1H, $J_{2,1}$=3.8 Hz, H-2); 4.68 (d, 1H, J_{AB}=11.4 Hz, CH_2–Ph); 5.98 (d, 1H, $J_{1,2}$=3.8 Hz, H-1); 7.32–7.41 (m, 5H, Ph). ^{1}H NMR (C_6D_6) δ: 1.09 (s, 3H, CH_3); 1.33 (s, 3H, CH_3); 3.49 (s, 1H, OH); 3.80 (d, 1H, J=3.5 Hz, H-3); 4.04 (d, 1H, J_{AB}=11.4 Hz, CH_2–Ph); 4.15 (d, 1H, J_{AB}=11.4 Hz, CH_2–Ph); 4.26 (d, 1H, $J_{2,1}$=3.8 Hz, H-2); 4.39 (m, 1H, H-5); 4.45 (dd, 1H, $J_{4,5}$=5.3 Hz, $J_{4,3}$=3.4 Hz, H-4); 5.76 (d, 1H, $J_{1,2}$=3.8 Hz, H-1); 7.10–7.14 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$) δ: 26.2 (CH_3); 26.7 (CH_3); 68.4 (q, $^2J_{C,F}$=31.5 Hz, C-5); 72.2 (CH_2–Ph); 76.4 (C-4); 81.8 (C-2); 82.7 (C-3); 104.9 (C-1); 112.4 (Cq isopropylidene); 124.0 (q, $J_{C,F}$=281.6 Hz, CF_3); 127.8–128.4 (C-o, C-m, C-p); 136.4 (C-ipso). ^{13}C NMR (C_6D_6) δ: 68.8 (q, $J_{C,F}$=29.5 Hz, C-5). ^{19}F NMR ($CDCl_3$) δ: −77.88 (d, 3F, $J_{F,H}$=7.6 Hz, CF_3). Anal. calcd for $C_{16}H_{19}O_5F_3$ (348.34): C, 55.17; H, 5.46. Found: C, 55.09; H, 5.29.

5: m.p. 97°C (petroleum ether); $[\alpha]^{20}_D=-38.6$ (*c* 0.12, $CHCl_3$). [Lit. $[\alpha]^{23}_D=-37.6$ (*c* 1.00, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$) δ: 1.26 (s, 3H, CH_3); 1.43 (s, 3H, CH_3); 4.16 (d, 1H, J=8.0 Hz, OH); 4.18 (d, 1H, J=3.0 Hz, H-3); 4.24 (dd, 1H, $J_{4,5}$=4.6 Hz, $J_{4,3}$=3.0 Hz, H-4); 4.34 (m, 1H, H-5); 4.48 (d, 1H, J_{AB}=11.0 Hz, CH_2–Ph); 4.56 (d, 1H, $J_{2,1}$=3.8 Hz, H-2); 4.60 (d, 1H, J_{AB}=11.0 Hz, CH_2–Ph); 5.94 (d, 1H, $J_{1,2}$=3.8 Hz, H-1); 7.25–7.40 (m, 5H, Ph). ^{1}H NMR (C_6D_6) δ: 1.07 (s, 3H, CH_3); 1.33 (s, 3H, CH_3); 3.55 (d, 1H, J=6.6 Hz, OH); 4.06 (d, 1H, $J_{3,4}$=2.8 Hz, H-3); 4.11 (d, 1H, J_{AB}=11.5 Hz, CH_2–Ph); 4.18 (d, 1H, J_{AB}=11.5 Hz, CH_2–Ph); 4.24 (d, 1H, $J_{2,1}$=3.7 Hz, H-2); 4.40 (m, 1H, H-5); 4.24 (dd, 1H, $J_{4,5}$=5.8 Hz, $J_{4,3}$=2.8 Hz, H-4); 5.81 (d, 1H, $J_{1,2}$=3.7 Hz, H-1); 7.06–7.16 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$) δ: 26.1 (CH_3); 26.6 (CH_3); 69.9 (q, $^2J_{C,F}$=30.0 Hz, C-5); 72.7 (CH_2–Ph); 75.4 (C-4); 81.5 (C-2); 83.8 (C-3); 104.9 (C-1); 112.2 (Cq isopropylidene); 124.5 (q, J=283.0 Hz, CF_3); 128.1–128.8 (C-o, C-m, C-p); 136.0 (C-ipso). ^{13}C NMR (C_6D_6) δ: 69,8 (q, $J_{C,F}$=30.8 Hz, C-5). ^{19}F NMR ($CDCl_3$) δ: −77.63 (d, 3F, $J_{F,H}$=7.6 Hz, CF_3).

*4.5. 3-O-Allyl-6-deoxy-6,6,6-trifluoro-1,2-O-isopropylidene-β-L-ido- and -α-D-glucofuranose **6** and **7***

Conditions A: yield 0.65 g, 98% (**6**/**7**=88/12). Chromatography (petroleum ether/EtOAc 90/10).

6: oil. $[\alpha]^{18}_D=-30.0$ (*c* 1.12, $CHCl_3$). IR (film): 3462; 3086; 2997; 1379; 1140; 1028. MS (EI) m/z: 299 (M+1, 20); 283 (100); 241 (23); 113 (33); 85 (40); 59 (42). ^{1}H NMR (C_6D_6) δ: 1.12 (s, 3H, CH_3); 1.32 (s, 3H, CH_3); 3.10 (s, 1H, OH); 3.65 (ddt, 1H, J=12.6 Hz, J=6.1 Hz, J=1.1 Hz, H-α allyl); 3.75 (d, 1H, $J_{3,4}$=3.4 Hz, H-3); 3.82 (ddt, 1H, J=12.6 Hz, J=5.3 Hz, J=1.1 Hz, H-α allyl); 4.21 (m, 1H, H-5); 4.26 (dd, 1H, $J_{4,5}$=5.3 Hz, $J_{3,4}$=3.4 Hz, H-4); 4.30 (d, 1H, $J_{2,1}$=3.8 Hz, H-2); 5.06 (m, 2H, H-γ allyl); 5.63 (ddt, 1H, J=16.0 Hz, J=11.0 Hz, J=5.7 Hz, H-β allyl); 5.72 (d, 1H, $J_{1,2}$=3.8 Hz, H-1). ^{13}C NMR (C_6D_6) δ: 26.3 (CH_3); 26.9 (CH_3); 68.7 (q, $^2J_{C,F}$=31.0 Hz, C-5); 71.2 (C-α); 76.8 (C-4); 82.4 (C-2); 82.9 (C-3); 105.2 (C-1); 112.6 (Cq isopropylidene); 118.2 (C-γ); 124.4 (q, J=281.6 Hz, CF_3); 133.3 (C-β). ^{19}F NMR (C_6D_6) δ: −77.95 (d, 3F, $J_{F,H}$=6.5 Hz, CF_3). Anal. calcd for $C_{12}H_{17}O_5F_3$ (298.25): C, 48.32; H, 5.70. Found: C, 48.38; H, 5.86.

7: paste. ^{1}H NMR ($CDCl_3$) δ: 1.26 (s, 3H, CH_3); 1.41 (s, 3H, CH_3); 3.97 (ddt, 1H, J=12.0 Hz, J=6.1 Hz, J=1.4 Hz, H-α allyl); 4.07–4.15 (m, 3H, OH, H-3, H-α allyl); 4.21 (m, 1H, H-4); 4.34 (m, 1H, H-5); 4.51 (d, 1H, $J_{2,1}$=3.8 Hz, H-2); 5.20 (m, 2H, H-γ allyl); 5.82 (ddt, 1H, J=16.0 Hz, J=11.0 Hz, J=5.7 Hz, H-β allyl); 5.93 (d, 1H, $J_{1,2}$=3.8 Hz, H-1). ^{1}H NMR (C_6D_6) δ: 1.07 (s, 3H, CH_3); 1.33 (s, 3H, CH_3); 3.44–3.69 (m, 3H, OH, H-α allyl); 3.97 (d, 1H, $J_{3,4}$=2.8 Hz, H-3); 3.97 (d, 1H, $J_{2,1}$=3.7 Hz, H-2); 4.27–4.44 (m, 2H, H-4, H-5); 5.20 (m, 2H, H-γ allyl); 5.55 (m, 1H, H-β allyl); 5.80 (d, 1H, $J_{1,2}$=3.7 Hz, H-1). ^{13}C NMR ($CDCl_3$) δ: 26.1 (CH_3); 26.6 (CH_3); 70.1 (q, $^2J_{C,F}$=31.0 Hz, C-5); 71.3 (C-α); 75.4 (C-4); 81.7 (C-2); 83.6 (C-3); 104.8 (C-1); 112.1 (Cq isopropylidene); 122.2 (C-γ); 124.4 (q, J=281.0 Hz, CF_3); 132.7 (C-β). ^{13}C NMR (C_6D_6) δ: 70.3 (dd, $J_{C,F}$=31.0 Hz, C-5). ^{19}F NMR ($CDCl_3$) δ: −77.88 (d, 3F, $J_{F,H}$=7.6 Hz, CF_3).

*4.6. 3-O-Benzyl-6-deoxy-6,6-difluoro-6-C-perfluoropropyl-1,2-O-isopropylidene-β-L-ido- and -α-D-glucofuranose **8a** and **9a***

Conditions A: yield 0.42 g, 65% (**8a**/**9a**=85/15). Conditions B: yield 2.91 g, 64% (**8a**/**9a**=>95/<5). Chromatography (petroleum ether/EtOAc 85/15).

8a: white solid: m.p. 60°C. $[\alpha]^{20}_D$=−2.6 (*c* 1.6, $CHCl_3$). IR (KBr): 3462; 2967; 1228; 1064; 1028; 864. MS (EI) m/z: 498 ($M^{+\bullet}$, 8); 483 (100); 440 (43); 423 (32); 333 (38); 249 (34); 149 (28); 129 (77); 113 (27). ^{1}H NMR (C_6D_6) δ: 1.07 (s, 3H, CH_3); 1.30 (s, 3H, CH_3); 3.31 (s, 1H, OH); 3.77 (m, 1H, H-3); 3.99 (d, 1H, J_{AB}=11.8 Hz, CH_2–Ph); 4.14 (d, 1H, J_{AB}=11.8 Hz, CH_2–Ph); 4.22 (d, 1H, $J_{2,1}$=3.4 Hz, H-2); 4.52 (m, 2H, H-4, H-5); 5.70 (d, 1H, $J_{1,2}$=3.4 Hz, H-1); 7.03–7.12 (m, 5H, Ph). ^{13}C NMR (C_6D_6) δ: 26.3 (CH_3); 26.8 (CH_3); 67.8 (dd, $J_{C,F}$=29.0 Hz, $J_{C,F}$=21.0 Hz, C-5); 72.2 (OCH_2); 76.4 (C-4); 82.4 (C-2); 83.2 (C-3); 105.2 (C-1); 112.5 (Cq isopropylidene); 127.6–128.7 (C-o, C-m, C-p); 137.2 (C-ipso). ^{19}F NMR (C_6D_6) δ: −81.11 (t, 3F, J=10.0 Hz, CF_3); −119.61 (dm, 1F, J_{AB}=278.5 Hz, CFa); −122.25 (dm, 1F, J_{AB}=290.0 Hz, CFb); −123.14 (dm, 1F, J_{AB}=290.0 Hz, CFb′); −125.23 (dm, 1F, J_{AB}=278.5 Hz, CFc); −125.90 (dm, 1F, J_{AB}=278.5 Hz, CFa′); −127.00 (dm, 1F, J_{AB}=278.5 Hz, CFc′). Anal. calcd for $C_{19}H_{19}O_5F_9$ (498.34): C, 45.82; H, 3.84. Found: C, 46.08; H, 3.97.

9a: ^{1}H NMR ($CDCl_3$) δ: 1.33 (s, 3H, CH_3); 1.49 (s, 3H, CH_3); 4.28 (m, 2H, OH, H-3); 4.38 (m, 1H, H-5); 4.56 (d, 1H, J_{AB}=11.0 Hz, CH_2–Ph); 4.65 (m, 2H, H-2, H-4); 4.68 (d, 1H, J_{AB}=11.0 Hz, CH_2–Ph); 6.02 (d, 1H, $J_{1,2}$=3.8 Hz, H-1); 7.27–7.37 (m, 5H, Ph). ^{1}H NMR (C_6D_6) δ: 1.08 (s, 3H, CH_3); 1.35 (s, 3H, CH_3); 4.05 (d, 1H, J_{AB}=11.3 Hz, CH_2–Ph); 4.09 (m, 2H, OH, H-3); 4.12 (d, 1H, J_{AB}=11.3 Hz, CH_2–Ph); 4.23 (d, 1H, $J_{2,1}$=3.8 Hz, H-2); 4.49 (ddd, 1H, J=4.9 Hz, J=3.2 Hz, J=1.8 Hz, H-4); 4.73 (m, 1H, H-5); 5.80 (d, 1H, $J_{1,2}$=3.8 Hz, H-1); 7.03–7.18 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$) δ: 26.1 (CH_3); 26.6 (CH_3); 69.8 (dd, $J_{C,F}$=25.6 Hz, $J_{C,F}$=21.7 Hz, C-5); 72.8 (OCH_2); 74.8 (C-4); 81.8 (C-2); 84.7 (C-3); 104.6 (C-1); 112.1 (Cq isopropylidene); 127.9–128.8 (C-o, C-m, C-p); 135.8 (C-ipso). ^{13}C NMR (C_6D_6) δ: 70.0 (dd, $J_{C,F}$=25.6 Hz, $J_{C,F}$=21.6 Hz, C-5). ^{19}F NMR ($CDCl_3$) δ: −81.39 (t, 3F, J=9.5 Hz, CF_3); −120.17 (dm, 1F, J_{AB}=282.3 Hz, CFa); −122.81 (dm, 1F, J_{AB}=297.5 Hz, CFb); −123.67 (dm, 1F, J_{AB}=297.5 Hz, CFb′); −125.63 (dm, 1F, J_{AB}=297.5 Hz, CFc); −126.56 (dm, 1F, J_{AB}=282.3 Hz, CFa′); −127.62 (dm, 1F, J_{AB}=297.5 Hz, CFc′).

*4.7. 3-O-Benzyl-6-deoxy-6,6-difluoro-6-C-perfluoropentyl-1,2-O-isopropylidene-β-L-idofuranose **8b***

Conditions B: yield 0.53 g, 57%. Chromatography (petroleum ether/EtOAc 85/15).

White solid: m.p. 62°C. $[\alpha]^{19}_D$=−21.3 (*c* 0.64, $CHCl_3$). IR (KBr): 3462; 2961; 1454; 1240; 1078. MS (EI) m/z: 598 ($M^{+\bullet}$, 5); 181 (67); 149 (98); 92 (81); 91 (100); 59 (39). ^{1}H NMR ($CDCl_3$) δ: 1.25 (s, 3H, CH_3); 1.41 (s, 3H, CH_3); 3.26 (s, 1H, OH); 4.00 (m, 1H, H-3); 4.43 (d, 1H, J_{AB}=11.4 Hz, CH_2–Ph);

4.44 (m, 2H, H-4, H-5); 4.57 (d, 1H, $J_{2,1}$=3.8 Hz, H-2); 4.61 (d, 1H, J_{AB}=11.4 Hz, CH_2–Ph); 5.99 (d, 1H, $J_{1,2}$=3.8 Hz, H-1); 7.20–7.30 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$) δ: 26.2 (CH_3); 26.8 (CH_3); 67.6 (dd, $^2J_{C,F}$=27.6 Hz, $^2J_{C,F}$=21.7 Hz, C-5); 72.3 (OCH_2); 75.7 (C-4); 81.9 (C-2); 83.1 (C-3); 104.9 (C-1); 112.5 (Cq isopropylidene); 127.9–128.7 (C-o, C-m, C-p); 135.1 (C-ipso). ^{19}F NMR ($CDCl_3$) δ: −81.11 (t, 3F, J=9.8 Hz, CF_3); −112.59 (dm, 1F, J_{AB}=282.0 Hz, CFa); −121.76 (m, 3F, CF_2b, CFc); −122.16 (m, 1F, CFc′); −122.54 (m, 1F, CFd); −122.86 (m, 1F, CFd′); −125.60 (dm, 1F, J_{AB}=282.0 Hz, CFa′); −126.25 (dm, 1F, J_{AB}=286.9 Hz, CFe); −127.25 (dm, 1F, J_{AB}=286.9 Hz, CFe′). Anal. calcd for $C_{21}H_{19}O_5F_{13}$ (598.36): C, 42.14; H, 3.17. Found: C, 42.23; H, 3.29.

*4.8. 3-*O*-Allyl-6-deoxy-6,6-difluoro-6-*C*-perfluoropropyl-1,2-*O*-isopropylidene-β-*L*-idofuranose* **10a**

Conditions B: yield 1.6 g, 68%. Chromatography (petroleum ether/EtOAc 80/20).

Syrup. $[\alpha]^{20}_D$=−24.0 (*c* 0.19, $CHCl_3$). IR (film): 3474; 2997; 2936; 1228; 1028. MS (EI) m/z: 448 ($M^{+\bullet}$, 7); 433 (97); 199 (33); 113 (100); 85 (65). ^{1}H NMR (C_6D_6) δ: 1.11 (s, 3H, CH_3); 1.35 (s, 3H, CH_3); 3.39 (s, 1H, OH); 3.50 (dt, 1H, J_{AB}=14.0 Hz, J=5.7 Hz, J=1.3 Hz, –OCH_2–); 3.66 (dt, 1H, J_{AB}=11.3 Hz, J=5.3 Hz, J=1.3 Hz, –OCH_2–); 3.74 (t, 1H, J=2.7 Hz, H-3); 4.22 (d, 1H, $J_{2,1}$=3.7 Hz, H-2); 4.53–4.65 (m, 2H, H-4, H-5); 4.94–5.10 (m, 2H,=CH_2); 5.59 (ddt, 1H, J=17.0 Hz, J=11.5 Hz, J=5.7 Hz, –CH=); 5.74 (d, 1H, $J_{1,2}$=3.7 Hz, H-1). ^{13}C NMR (C_6D_6) δ: 26.3 (CH_3); 26.9 (CH_3); 68.0 (dd, $^2J_{C,F}$=29.0 Hz, $^2J_{C,F}$=22.0 Hz, C-5); 71.0 (C-α); 76.6 (C-4); 82.6 (C-2); 83.2 (C-3); 105.2 (C-1); 112.5 (Cq isopropylidene); 117.5 (C-γ); 133.7 (C-β). ^{19}F NMR (C_6D_6) δ: −81.42 (t, 3F, J=11.4 Hz, CF_3); −120.36 (dm, 1F, J_{AB}=283.0 Hz, CFa); −126.40 (dm, 1F, J_{AB}=283.0 Hz, CFa′); −123.39 (m, 2F, CF_2b); −125.70 (dm, 1F, J_{AB}=290.0 Hz, CFc); −127.40 (dm, 1F, J_{AB}=290.0 Hz, CFc′). Anal. calcd for $C_{15}H_{17}O_5F_9$ (448.28): C, 40.17; H, 3.79; Found: C, 40.28; H, 3.82.

*4.9. 3-*O*-Allyl-6-deoxy-6,6-difluoro-6-*C*-perfluoropentyl-1,2-*O*-isopropylidene-β-*L*-idofuranose* **10b**

Conditions B: yield 1.17 g, 60%. Chromatography (petroleum ether/EtOAc 80/20).

Syrup. $[\alpha]^{24}_D$=−36.0 (*c* 0.23, $CHCl_3$). IR (film): 3462; 2997; 2936; 1240; 1203; 1028. MS (EI) m/z: 548 ($M^{+\bullet}$, 16); 533 (91); 433 (37); 199 (61); 133 (100); 85 (84); 59 (70). ^{1}H NMR (C_6D_6) δ: 1.10 (s, 3H, CH_3); 1.35 (s, 3H, CH_3); 3.17 (d, 1H, J=2.4 Hz, OH); 3.46 (dt, 1H, J_{AB}=12.7 Hz, J=5.3 Hz, J=1.3 Hz, –OCH_2–); 3.63 (dt, 1H, J_{AB}=12.7 Hz, J=4.4 Hz, J=1.3 Hz, –OCH_2–); 3.72 (m, 1H, H-3); 4.18 (d, 1H, $J_{2,1}$=3.6 Hz, H-2); 4.56 (m, 1H, H-4); 4.60 (m, 1H, H-5); 5.01 (ddt, 2H, J_{trans}=17.0 Hz, J_{cis}=10.6 Hz, J=1.6 Hz, =CH_2); 5.55 (ddt, 1H, J=17.0 Hz, J=10.6 Hz, J=5.5 Hz, –CH=); 5.71 (d, 1H, $J_{1,2}$=3.6 Hz, H-1). ^{13}C NMR (C_6D_6) δ: 26.2 (CH_3); 26.8 (CH_3); 67.6 (dd, $^2J_{C,F}$=29.0 Hz, $^2J_{C,F}$=22.0 Hz, C-5); 71.2 (C-α); 75.9 (C-4); 82.1 (C-2); 83.0 (C-3); 104.9 (C-1); 112.5 (Cq isopropylidene); 118.5 (C-γ); 133.0 (C-β). ^{19}F NMR δ: −81.34 (t, 3F, J=10.0 Hz, CF_3); −120.25 (dm, 1F, J_{AB}=283.0 Hz, CFa); −122.35 (m, 3F, CF_2b, CFc); −122.67 (m, 1F, CFc′); −122.97 (m, 1F, CFd); −123.77 (m, 1F, CFd′); −126.06 (dm, 1F, J_{AB}=290.0 Hz, CFe); −126.07 (dm, 1F, J_{AB}=283.0 Hz, CFa′); −127.07 (dm, 1F, J_{AB}=290.0 Hz, CFe′). Anal. calcd for $C_{17}H_{17}O_5F_{13}$ (548.30): C, 37.22; H, 3.10. Found: C, 37.59; H, 3.10.

*4.10. 3-*C*-Trifluoromethyl-1,2:5,6-di-*O*-isopropylidene-α-*D*-allofuranose* **12**

Conditions A: yield 3.4 g, 88%. Chromatography (petroleum ether/EtOAc 80/20).

White solid: m.p. 76°C. $[\alpha]^{20}_D$=+23.0 (*c* 1.8, $CHCl_3$) IR (KBr): 3374; 2986; 1215; 1153; 1014; 877. MS (EI) m/z: 313 (100); 195 (22); 131 (30); 101 (96); 69 (39); 59 (68). ^{1}H NMR ($CDCl_3$) δ: 1.36 (s, 3H, CH_3); 1.39 (s, 3H, CH_3); 1.45 (s, 3H, CH_3); 1.61 (s, 3H, CH_3); 3.31 (s, 1H, OH); 3.94 (dd, 1H, $J_{6,6'}$=8.8

Hz, $J_{6,5}$=5.3 Hz, H-6); 4.00 (d, 1H, $J_{4,3}$=2.3 Hz, H-4); 4.11 (dd, 1H, $J_{6',6}$=8.8 Hz, $J_{6',5}$=6.1 Hz, H-6′); 4.34 (m, 1H, H-5); 4.60 (d, 1H, $J_{2,1}$=3.8 Hz, H-2); 5.83 (d, 1H, $J_{1,2}$=3.8 Hz, H-1). ^{13}C NMR ($CDCl_3$) δ: 26.1 (CH_3); 26.8 (3×CH_3); 67.2 (C-6); 72.8 (C-5); 79.1 (C-2); 80.1 (q, $^2J_{C,F}$=28.0 Hz, C-3); 81.4 (C-4); 104.0 (C-1); 109.8 (Cq isopropylidene); 113.8 (Cq isopropylidene); 124.2 (q, $^2J_{C,F}$=285.0 Hz, CF_3). ^{19}F NMR ($CDCl_3$) δ: −76.25 (s, 3F, CF_3). Anal. calcd for $C_{13}H_{19}O_6F_3$ (328.28): C, 47.56; H, 5.79. Found: C, 47.44; H, 5.54.

*4.11. 3-*C*-Perfluorobutyl-1,2:5,6-di-*O*-isopropylidene-α-*D*-allo- and -α-*D*-glucofuranose **13a** and **14a***

Conditions A: yield 0.26 g, 70% (**13a**/**14a**=100/0). Conditions B: yield 2.34 g, 68% (**13a**/**14a**=78/22). Chromatography (petroleum ether/EtOAc 90/10).

13a: white solid: m.p. 118°C (petroleum ether). $[\alpha]^{22}_D$=+21.9 (*c* 0.47, $CHCl_3$). IR (KBr): 3427; 2997; 1215; 1128; 1039; 827. MS (EI) m/z: 463 (100); 405 (24); 345 (22); 287 (18); 131 (73). ^{1}H NMR ($CDCl_3$) δ: 1.38 (s, 3H, CH_3); 1.43 (s, 3H, CH_3); 1.47 (s, 3H, CH_3); 1.63 (s, 3H, CH_3); 3.41 (s, 1H, OH); 3.98 (dd, 1H, $J_{6,6'}$=8.8 Hz, $J_{6,5}$=5.3 Hz, H-6); 4.06 (d, 1H, $J_{4,5}$=7.3 Hz, H-4); 4.13 (dd, 1H, $J_{6',6}$=8.8 Hz, $J_{6',5}$=6.1 Hz, H-6′); 4.56 (m, 1H, H-5); 4.76 (dd, 1H, $J_{2,1}$=4.2 Hz, $J_{2,F}$=1.1 Hz, H-2); 5.71 (d, 1H, $J_{1,2}$=4.2 Hz, H-1). ^{13}C NMR ($CDCl_3$) δ: 25.1 (CH_3); 26.4 (CH_3); 26.6 (CH_3); 26.7 (CH_3); 67.0 (C-6); 72.9 (d, J=5.9 Hz, C-5); 78.3 (m, C-2); 81.0 (t, $J_{C,F}$=25.6 Hz, C-3); 84.3 (C-4); 104.2 (C-1); 109.7 (Cq isopropylidene); 113.8 (Cq isopropylidene). ^{19}F NMR ($CDCl_3$) δ: −81.23 (t, 3F, J=11.5 Hz, CF_3); −114.15 (dq, 1F, J_{AB}=293.7 Hz, J=15.3 Hz, CFa); −117.89 (dm, 1F, J_{AB}=297.6 Hz, CFb); −120.10 (dq, 1F, J_{AB}=293.7 Hz, J=15.3 Hz, CFa′); −120.80 (dm, 1F, J_{AB}=297.6 Hz, CFb′); −126.08 (dm, 1F, J_{AB}=293.7 Hz, CFc); −127.05 (dm, 1F, J_{AB}=293.7 Hz, CFc′). Anal. calcd for $C_{16}H_{19}O_6F_9$ (478.31): C, 40.17; H, 4.00. Found: C, 40.57; H, 3.84.

14a: oil. ^{1}H NMR ($CDCl_3$) δ: 1.34 (s, 3H, CH_3); 1.36 (s, 3H, CH_3); 1.46 (s, 3H, CH_3); 1.52 (s, 3H, CH_3); 4.00 (dd, $J_{6,6'}$=8.8 Hz, $J_{6,5}$=7.6 Hz, H-6); 4.10 (dd, $J_{6',6}$=8.8 Hz, $J_{6',5}$=7.6 Hz, H-6′); 4.47 (d, 1H, $J_{4,5}$=3.4 Hz, H-4); 4.54 (m, 1H, H-5); 4.60 (m, 1H, H-2); 4.63 (s, 1H, OH); 5.71 (d, 1H, $J_{1,2}$=3.4 Hz, H-1). ^{13}C NMR ($CDCl_3$) δ: 24.6 (CH_3); 25.9 (CH_3); 26.5 (CH_3); 26.8 (CH_3); 66.4 (C-6); 74.9 (C-5); 78.4 (C-2); 82.5 (t, $J_{C,F}$=23.4 Hz, C-3); 85.1 (C-4); 104.2 (C-1); 110.5 (Cq isopropylidene); 114.0 (Cq isopropylidene). ^{19}F NMR δ: −81.23 (t, 3F, J=10.5 Hz, CF_3); −112.55 (m, 2F, CF_2a); −119.67 (dm, 1F, J_{AB}=293.7 Hz, CFb); −120.88 (dm, 1F, J_{AB}=293.7 Hz, CFb′); −126.58 (m, 2F, CF_2c).

*4.12. 3-*C*-Perfluorohexyl-1,2:5,6-di-*O*-isopropylidene-α-*D*-allo- and -α-*D*-glucofuranose **13b** and **14b***

Conditions B: yield 2.5 g, 59% (**13b**/**14b**=73/27). Chromatography (petroleum ether/EtOAc 90/10).

13b: white solid: m.p. 123°C. $[\alpha]^{22}_D$=+19.1 (*c* 0.83, $CHCl_3$). IR (KBr): 3437; 2997; 1379; 1203; 1039; 864. MS (EI) m/z: 563 (81); 505 (19); 445 (13); 387 (18); 131 (100); 119 (100). ^{1}H NMR ($CDCl_3$) δ: 1.37 (s, 3H, CH_3); 1.42 (s, 3H, CH_3); 1.46 (s, 3H, CH_3); 1.62 (s, 3H, CH_3); 3.43 (s, 1H, OH); 3.94 (dd, 1H, $J_{6,6'}$=8.5 Hz, $J_{6,5}$=4.9 Hz, H-6); 4.04 (d, 1H, $J_{4,5}$=7.3 Hz, H-4); 4.09 (dd, 1H, $J_{6',6}$=8.5 Hz, $J_{6',5}$=6.1 Hz, H-6′); 4.50 (m, 1H, H-5); 4.73 (dd, 1H, $J_{2,1}$=4.2 Hz, $J_{2,F}$=1.8 Hz, H-2); 5.86 (d, 1H, $J_{1,2}$=4.2 Hz, H-1). ^{13}C NMR ($CDCl_3$) δ: 25.1 (CH_3); 26.4 (CH_3); 26.6 (CH_3); 26.7 (CH_3); 67.0 (C-6); 72.9 (d, J=5.9 Hz, C-5); 78.3 (m, C-2); 80.7 (t, $J_{C,F}$=25.6 Hz, C-3); 84.3 (C-4); 104.2 (C-1); 109.7 (Cq isopropylidene); 113.8 (Cq isopropylidene). ^{19}F NMR ($CDCl_3$) δ: −81.33 (t, 3F, J=9.5 Hz, CF_3); −113.75 (dq, 1F, J_{AB}=289.9 Hz, J=15.3 Hz, CFa); −116.00 (dm, 1F, J_{AB}=293.7 Hz, CFb); −119.00 (dm, 1F, J_{AB}=289.9 Hz, CFa′); −120.00 (dm, 1F, J_{AB}=293.7 Hz, CFb′); −122.37 (m, 2F, CF_2c); −123.03 (m, 2F, CF_2d); −126.53 (m, 2F, CF_2e). Anal. calcd for $C_{18}H_{19}O_6F_{13}$ (578.33): C, 37.28; H, 3.31. Found: C, 37.22; H, 2.96.

14b: oil. $[\alpha]^{25}_{D}$=+21.7 (*c* 0.59, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 1.36 (s, 3H, CH_3); 1.37 (s, 3H, CH_3); 1.48 (s, 3H, CH_3); 1.53 (s, 3H, CH_3); 3.98 (dd, 1H, $J_{6,6'}$=8.0 Hz, $J_{6,5}$=7.2 Hz, H-6); 4.13 (t, 1H, $J_{6',6}$=$J_{6',5}$=8.0 Hz, H-6′); 4.47 (d, 1H, $J_{4,5}$=3.8 Hz, H-4); 4.54 (m, 1H, H-5); 4.60 (m, 1H, H-2); 4.66 (s, 1H, OH); 5.94 (d, 1H, $J_{1,2}$=3.4 Hz, H-1). ^{13}C NMR ($CDCl_3$) δ: 24.6 (CH_3); 25.9 (CH_3); 26.6 (CH_3); 26.9 (CH_3); 66.4 (C-6); 75.0 (C-5); 78.3 (C-2); 82.6 (t, $J_{C,F}$=23.6 Hz, C-3); 85.1 (C-4); 104.2 (C-1); 110.6 (Cq isopropylidene); 114.0 (Cq isopropylidene). ^{19}F NMR ($CDCl_3$) δ: −81.42 (t, 3F, J=9.6 Hz, CF_3); −111.99 (dm, 1F, J_{AB}=288.0 Hz, CFa); −112.75 (dm, 1F, J_{AB}=288.0 Hz, CFa′); −118.73 (dm, 1F, J_{AB}=293.7 Hz, CFb); −119.91 (dm, 1F, J_{AB}=293.7 Hz, CFb′); −122.29 (m, 2F, CF_2c); −123.01 (m, 2F, CF_2d); −126.55 (m, 2F, CF_2e).

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