Carbohydrate Research 339 (2004) 2177–2185

Novel perfluoroalkylated derivatives of D-galactopyranose and xylitol for biomedical uses. Hemocompatibility and effect on perfluorocarbon emulsions

Vladimír Církva,[a] Radek Polák,[a] Oldřich Paleta,[a,*] Karel Kefurt,[b] Jitka Moravcová,[b] Milan Kodíček[c] and Stanislav Forman[c]

[a]*Department of Organic Chemistry, Institute of Chemical Technology Prague, Technická 5, 166 28 Prague, Czech Republic*
[b]*Department of Chemistry of Natural Compounds, Institute of Chemical Technology Prague, Technická 5, 166 28 Prague, Czech Republic*
[c]*Department of Biochemistry and Microbiology, Institute of Chemical Technology Prague, Technická 5, 166 28 Prague, Czech Republic*

Received 4 March 2004; received in revised form 8 June 2004; accepted 26 June 2004
Available online 29 July 2004

Abstract—6-*O*-(4,4,5,5,6,6,7,7,7-Nonafluoro-2-hydroxyheptyl)-, 6-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-hydroxynonyl)-, and 6-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-hydroxyundecyl)-D-galactopyranose (**9**, **10**, and **11**, resp.) were prepared by a two-step synthesis including the reaction of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose with 2-[(perfluoroalkyl)methyl]oxiranes under catalysis with $BF_3{\cdot}Et_2O$. Similarly, 1-*O*-(4,4,5,5,6,6,7,7,7-nonafluoro-2-hydroxyheptyl)-, 1-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-hydroxynonyl)-, 1-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-hydroxyundecyl)-DL-xylitol (**18**, **19**, and **20**, resp.) were prepared by a two-step synthesis from the corresponding 1,2:3,4-di-*O*-isopropylidene-DL-xylitol. Most of the both types of fluoroalkylated carbohydrate derivatives **9**–**11** and **18**–**20** generally displayed very low level of hemolytic activity and excellent co-emulsifying properties on testing on perfluorodecalin-Pluronic F-68 microemulsions.

Keywords: Perfluoroalkyl epoxides; Fluorinated surfactants; 6-*O*-(Fluoroalkyl)-D-galactopyranoses; 1-*O*-(Fluoroalkyl)-DL-xylitol; Hemocompatibility; Microemulsion, stability

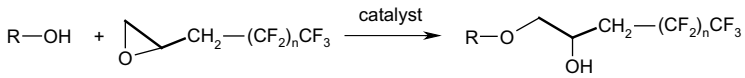
1. Introduction

The synthesis of amphiphilic molecules has been reported,[1,2] the molecular structures of which involve polyfluoroalkylated chains, spacers of various chain lengths, junction units (ether, or ester groups), and hydrophilic heads derived from polyethylene glycol, polyols (alditols), or saccharides. They have been proposed as biocompatible surfactants in the medical area[1,2] displaying unique properties for the formulation of colloidal systems including perfluorocarbon (PFC) emulsions, fluorinated vesicles, and other highly fluorinated self-assemblies with supramolecular structures.[3,4] Perfluoroalkylated biocompatible surfactants can be applied as oxygen carriers (including blood substitutes),[5,6] oxygen transporting gels for surgery, medium for cell cultures,[7] contrast agent for diagnosis by ultrasound imaging,[6] and drug delivery systems.[6]

Recently, perfluoroalkylated derivatives of D-galactose and DL-xylitol possessing an unsaturated spacer between the hydrophilic saccharide and hydrophobic perfluoroalkyls by a several-step synthesis have been reported.[1,2] Additionally, fluoroalkylated derivatives of D-glucose and D-galactose were synthesized by the one-step nucleophilic addition of protected carbohydrates to perfluorinated vinyl oligoether,[8] but their co-emulsifying properties were limited. In recent papers, we have published a convenient method for fluoroalkylation of hydroxy compounds[9,10] by their reaction with

* Corresponding author. Tel.: +420-22435-4284; fax: +420-22431-1082; e-mail: oldrich.paleta@vscht.cz

doi:10.1016/j.carres.2004.06.019



Scheme 1. Completely regioselective[10] reaction of hydroxy compounds with fluoroalkylated oxiranes.

perfluoroalkylated epoxides[11–13] according to a general scheme (Scheme 1).

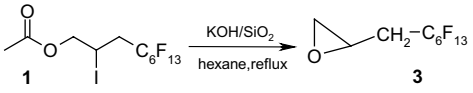
The reaction was applied to the preparation of sets of amphiphilic perfluoroalkylated triols,[9,14] tetritols,[11] and saccharides.[15,16]

This paper deals with a novel one-step synthesis of fluoroalkylated derivatives of D-galactopyranose and DL-xylitol as surfactants possessing the $–CH_2–CHOH–CH_2–$ spacer between the hydrophilic saccharide and hydrophobic perfluoroalkyl. The new surfactants were subjected to preliminary tests for hemocompatibility and co-emulsifying properties.

2. Results and discussion

2.1. Improved synthesis of 2-[(tridecafluorohexyl)-methyl]oxirane

Fluoroalkylated oxiranes **2–4** were used as fluorinated building blocks in this paper. A highly selective synthesis of the oxiranes from iodoacetate **1** has recently been developed (Scheme 2).[12] The last step, the epoxide formation, has to be carried out very carefully, but still small amounts of byproducts are formed. As an improvement, we have developed a completely selective synthesis of the most frequently used epoxide **3** by using potassium hydroxide anchored on silica gel surface (Table 1). No unsaturated byproducts[12] have been detected in the reaction mixture.



Scheme 2. Improved synthesis of 2-[(tridecafluorohexyl)methyl]oxirane **3**.

Table 1. Conditions of the improved synthesis of epoxide **3**

Reagent[a]	KOH/Silica gel (w/w)	Yield of **3** (%)	Time (min)
KOH	—	73.7	360
KOH/Silica gel	1:5	85.1	120
KOH/Silica gel	1:7.5	91.8	80
KOH/Silica gel	1:10	93.2	60
K_2CO_3[b]	—	34.5	600

[a] Molar ratio iodoacetate **1**/KOH was 1/2.2.
[b] Molar ratio iodoacetate **1**/K_2CO_3 was 1/2.2.

2.2. Fluoroalkylations of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose

The practicality of acid-catalyzed reactions of perfluoroalkylated epoxides **2–4** with alkane-α,ω-diols,[10,15] protected triols,[9] and partially protected tetritols[16] has opened a preparative pathway to the biosurfactants from pentitols and aldohexoses. As both primary and secondary hydroxy groups have appeared[9] to react with the epoxides **2–4**, it is necessary to let unprotected only one hydroxy group.

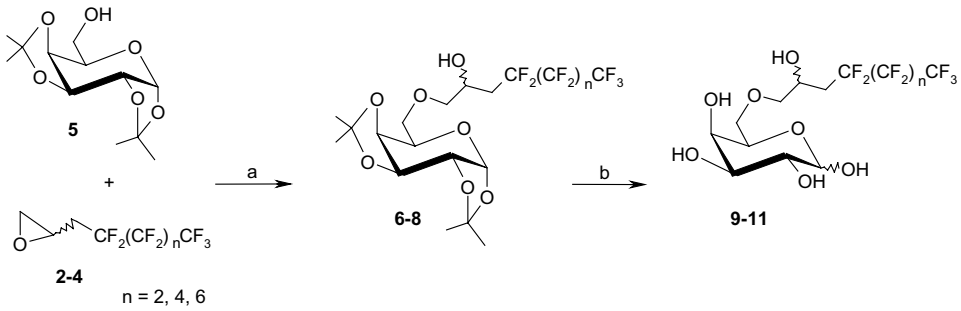
Protected galactose, that is 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[17] (**5**) was reacted with racemic 2-[(perfluoroalkyl)-methyl]oxiranes (**2–4**) in the presence of boron trifluoride diethyl etherate in diisopropyl ether as a solvent to afford monofluoroalkylated products **6–8** (Scheme 3) in good isolated yields of 70–73%. The attack of the oxirane ring in epoxides **2–4** by *O*-nucleophile **5** took place at the terminal carbon atom with the complete regioselectivity as observed previously.[10]

For the deprotection of fluoroalkylated compounds **6–8** to obtain the target fluoroalkylated D-galactopyranoses **9–11**, a variety of *O*-deisopropylidenation methods are available, for example, deprotection by iodine in methanol,[18] on an acidic ion-exchange resins[19,20] or using aluminum iodide.[21] The convenient deprotection method for fluoroalkylated triols,[9] that is transacetalization by methanol in the presence of hydrochloric acid cannot be applied to aldohexoses due to methoxylation at the anomeric position.[22] This effect can be attributed to the rather hydrophobic character conferred on molecule by the fluoroalkyl chain.[23] The best deprotection method for fluoroalkylated compounds **6–8** was using aqueous trifluoroacetic acid to afford the fluoroalkylated D-galactopyranoses **9–11** (Scheme 3) in high isolated yields of 85–90%.

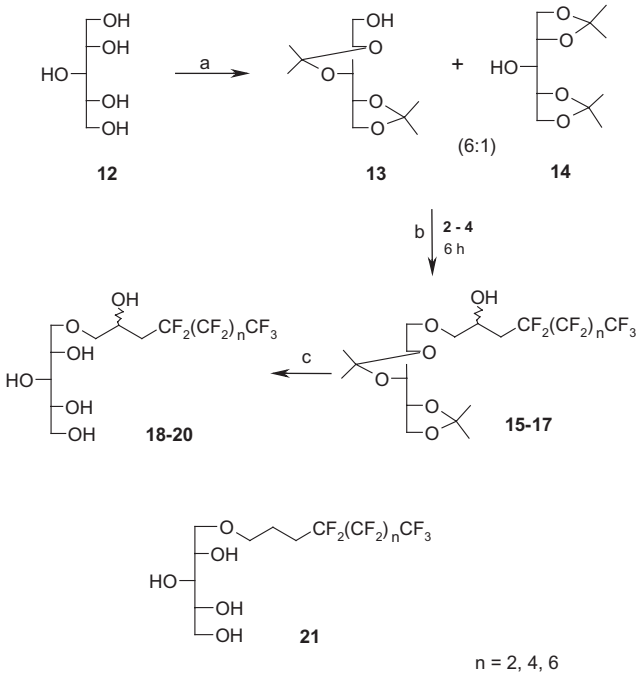
2.3. Fluoroalkylations of 1,2:3,4-di-*O*-isopropylidene-DL-xylitol

The protected xylitol, that is 1,2:3,4-di-*O*-isopropylidene-DL-xylitol[17,18] (**13**) was reacted with racemic 2-[(perfluoroalkyl)methyl]oxiranes (**2–4**) in the presence of boron trifluoride diethyl etherate in diisopropyl ether to afford monofluoroalkylated products **15–17** (Scheme 4) in good yields of 75–81%.

Due to marked difference in the reactivity of the primary and secondary hydroxy groups with the epoxide **3**, as reported for diols,[9] the product of the reaction of



Scheme 3. Preparation of perfluoroalkylated derivatives of D-galactopyranose. Reagents and conditions: (a) $BF_3{\cdot}Et_2O$, *i*-Pr_2O, reflux, 5 h; (b) CF_3CO_2H/H_2O (9:1), rt, 30 min.



Scheme 4. Preparation of perfluoroalkylated xylitols. Reagents and conditions: (a) acetone, H^+; (b) $BF_3{\cdot}Et_2O$, *i*-Pr_2O, reflux, 10 h; (c) CF_3CO_2H/H_2O (9:1), rt, 30 min.

the minor protected xylitol isomer **14** was not detected in the reaction mixture by proton NMR spectrum. A pattern signals appear after ca. 30 h reaction in the excess of the epoxide **3**.

The deprotection of fluoroalkylated compounds **15**–**17** was carried out by using aqueous trifluoroacetic acid[23] to afford the fluoroalkylated xylitols **18**–**20** (Scheme 4) in yields of 75–90%.

2.4. Testing of co-emulsifying properties and hemocompatibility

The novel sugar amphiphiles **9**–**11** and **18**–**20** were tested as co-surfactants for potential oxygen carriers. Co-surfactants for microemulsions are usually used[3,24–27] in amounts up to 10% relatively to the main emulsifier, for example, Pluronic F-68, and in positive case stabilize microemulsions. Preliminary testing was carried out using a reference microemulsion of perfluorodecalin emulsified with Pluronic F-68. Two kinds of testing were applied; the effects on microemulsion stability and hemolytic stability of erythrocytes in microemulsion media. In the standard microemulsion, Pluronic was gradually substituted with the sugar amphiphile tested and the state of the new emulsion under testing conditions visually evaluated. The xylitol derivative **21** was tested together with the compounds **9**–**11** and **18**–**20** as a standard[23] to verify reliability of the results with respect to the quality of hemoglobin used.

The results summarized in Table 2 show that the effect of the co-emulsifier on microemulsion stability is strongly dependent on both the saccharide moiety and the length of the perfluoroalkyl chain. Generally, the derivatives **9**–**11** of the cyclic D-galactopyranose showed lower co-emulsifying effect than the derivatives **18**–**20** containing the open-chained xylitol (Table 2). Compounds **9** and **18** possessing the shortest perfluoroalkyl displayed the lowest and insufficient co-emulsification and therefore they were not further tested. The best results were obtained with D-galactopyranose derivatives **9**–**11** bearing medium–long perfluoroalkyl (C_6F_{13}) chains, while longer perfluoroalkyl in **11** caused collapse of the microemulsion. This is in contrast to the xylitol derivatives **19** and **20** where the microemulsion was stable up to 80% of the substitution of Pluronic for the both co-emulsifiers (Table 2). The long-term stability of the microemulsions was tested for 6 weeks at room temperature mimicking a long-term storage. The results (Table 3) generally show better co-emulsifying effect for the derivatives of D-galactose than that of xylitol. As shown in Table 4, all compounds and concentrations tested showed that addition of erythrocytes does not cause coalescence of the microemulsions or hemolysis of the erythrocytes (Table 5). Amphiphiles bearing perfluorohexyl or perfluorooctyl (**10**, **11**, **19**, and **20**) moiety displayed no hemolysis up to 80% substitution of Pluronic. Among them, perfluorohexyl derivative of xylitol

Table 2. Stability of the emulsions after centrifugation

	Emulsifier	Substitution of Pluronic F-68 by tested emulsifiers (% w/v PF-68)				
		20%	40%	60%	80%	100%
		Stability of the emulsion				
9	[D-Galactose-6-*O*-yl]-CH_2–CHOH–CH_2–$CF_2CF_2CF_2CF_3$	+	–	nt	nt	nt
10	[D-Galactose-6-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_2CF_3$	+	+	+	+	nf
11	[D-Galactose-6-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_3CF_3$	–	–	–	–	nf
18	[Xylitol-1-*O*-yl]-CH_2–CHOH–CH_2–$CF_2CF_2CF_{22}CF_3$	+	–	–	nt	nt
19	[Xylitol-1-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_2CF_3$	+	+	+	+	–
20	[Xylitol-1-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_3CF_3$	+	+	+	+	nf
21	[Xylitol-1-*O*-yl]-CH_2–CH_2–CH_2–$CF_2CF_2CF_2CF_2CF_2CF_3$	+	+	+	+	–

Plus value means no apparent change of emulsion; minus value means colaps of the emulsion; nt—not tested; nf—the emulsion was not formed.

Table 3. Long-term stability of the emulsions for 6 weeks at rt

	Emulsifier	Substitution of Pluronic F-68 by tested emulsifiers (% w/v PF-68)				
		20%	40%	60%	80%	100%
		Stability of the emulsion				
10	[D-Galactose-6-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_2CF_3$	+	+	+	+	nf
11	[D-Galactose-6-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_3CF_3$	+	+	+	+	nf
19	[Xylitol-1-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_2CF_3$	+	+	–	–	–
20	[Xylitol-1-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_3CF_3$	+	+	+	+	nf
21	[Xylitol-1-*O*-yl]-CH_2–CH_2–CH_2–$CF_2CF_2CF_2CF_2CF_2CF_3$	+	+	+	+	–

Plus value means no apparent change of emulsion; minus value means colaps of the emulsion; nf—the emulsion was not formed.

Table 4. Stability of the emulsions for 6 h after mixing with erythrocytes at 37 °C

	Emulsifier	Substitution of Pluronic F-68 by tested emulsifiers (% w/v PF-68)				
		20%	40%	60%	80%	100%
		Stability of the emulsion				
10	[D-Galactose-6-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_2CF_3$	+	+	+	+	nf
11	[D-Galactose-6-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_3CF_3$	+	+	+	+	nf
19	[Xylitol-1-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_2CF_3$	+	+	+	+	–
20	[Xylitol-1-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_3CF_3$	+	+	+	+	nf
21	[Xylitol-1-*O*-yl]-CH_2–CH_2–CH_2–$CF_2CF_2CF_2CF_2CF_2CF_3$	+	+	+	+	+

Plus value means no apparent change of emulsion; minus value means colaps of the emulsion; nf—the emulsion was not formed.

Table 5. Hemocompatibility (range of hemolysis, %) of the new amphiphilic compounds

	Emulsifier	Substitution of Pluronic F-68 by tested emulsifiers (% w/v PF-68)				
		20%	40%	60%	80%	100%
		Range of hemolysis (%)				
9	[D-Galactose-6-*O*-yl]-CH_2–CHOH–CH_2–$CF_2CF_2CF_2CF_3$	9	27	nt	nt	nt
10	[D-Galactose-6-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_2CF_3$	0	1	0	0	nf
11	[D-Galactose-6-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_3CF_3$	0	0	0	0	nf
19	[Xylitol-1-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_2CF_3$	1	1	0	0	0
20	[Xylitol-1-*O*-yl]-CH_2–CHOH–CH_2–$CF_2(CF_2CF_2)_3CF_3$	0	0	0	nt	nt
21	[Xylitol-1-*O*-yl]-CH_2–CH_2–CH_2–$CF_2CF_2CF_2CF_2CF_2CF_3$	0	0	0	0	0

19, which is a mixture of two diastereoisomers with a stereogenic center CH(OH) in fluoroalkyl chain showed no hemolysis at 100% substitution of Pluronic, that is equally as racemic analogue **21**. Thus, the stereoisomers of both compounds **19** and **21** must be nonhemolytic under the conditions tested. It can be concluded that compound **19**, which is much easier accessible than its nonhydroxylated analogue **21**, can also be used as hemolytic standard.

In conclusion, we reported herein a novel standard compound **19** for an assessment hemocompatibility and the co-emulsifying properties.

3. Experimental

3.1. General methods

The temperature data were not corrected. Distillations of high boiling compounds were carried out on a Vacuumbrand RC5 high vacuum oil pump. GC analyses were performed on Micromat HRGC 412 (Nordion Analytical; 25 m glass capilary column, SE-30); nitrogen was used as carrier gas. NMR spectra were recorded on a Bruker 400 AM (FT, ^{19}F at 376.5 MHz) and Bruker WP 80 SY (FT, ^{19}F at 75 MHz) instruments using Me_4Si and $CFCl_3$ as the internal standards. Chemical shifts are quoted in ppm (δ-scale; s singlet, br s broad singlet; d doublet, t triplet, m multiplet), coupling constants J in Hz.

Chemicals used were as follows: fluoroalkyl epoxides **2–4** were prepared according to our procedure;[12] 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**5**) and 1,2:3,4-di-*O*-isopropylidene-DL-xylitol (**13**) were prepared according to Refs. 17,23,27; diisopropyl ether was dried with sodium and further purified by distillation; boron trifluoride diethyl etherate (Lachema) was distilled before use; acetone, petroleum ether, tetrahydrofuran, chloroform, MeOH (all Aldrich) were dried before use; trifluoroacetic acid (Aldrich); silica gel (60–100 μm, Merck).

3.2. Preparation of emulsions

Perfluorodecalin (0.125 mL) was mixed with isotonic Tris–HCl buffer of pH 7.4 and Pluronic F-68 (block co-polymer of polyoxypropylene and polyoxyethylene, 5% w/v) as a standard emulsifier and the mixture was sonicated for 15 s to afford 0.5 mL of an emulsion. (For a more detailed description of the testing procedures see Ref. 28.)

3.2.1. Testing of co-emulsifying properties. In the preparation of an emulsion (see above), Pluronic F-68 was partially or completely substituted by the tested co-emulsifier; if any apparent phase separation of water and perfluorodecalin phases did not appear immediately after finishing the test, the emulsion was considered to be stable. Stable emulsions in the test are indicated as '+', unstable emulsion are denoted marked by the sign '–'. Stabilities of the mixtures were tested under three different conditions: (1) stability during centrifugation: the emulsion was centrifuged for 5 min at 400*g*; (2) long-term stability at room temperature: the emulsion was gently stirred (magnetic spinbar) for 6 weeks; (3) stability of the emulsion in the presence of erythrocytes: the emulsion was mixed with erythrocytes and gently stirred (magnetic spinbar) at 37 °C for 6 h.

3.2.2. Hemocompatibility testing[23,27,28]. Human erythrocytes (from a healthy donor, stored in a refrigerator not longer than 1 week) were washed by isotonic Tris–HCl buffer. Packed erythrocytes (0.5 mL) were added to the emulsion of perfluorodecalin (see above), the mixture was then gently stirred at 37 °C for 6 h and after that shortly centrifuged. The amount of the extracellular hemoglobin in the water phase was determined spectrophotometrically and used as a measure of hemolytic activity of the co-emulsifier tested.

3.2.3. Improved preparation of 2-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)oxirane (3). Modified KOH was prepared as follows: Saturated water solution of KOH was mixed with silica gel (L60/100), then toluene was added and the mixture was evaporated on rotary evaporator. The water residue was removed under vacuum (130–150 °C/53 Pa) for 10 h.

The reactions were carried out in a double-neck round-bottomed flask equipped with a Dimroth condenser that was connected with atmosphere by a drying tube. The apparatus was flushed with argon then charged with KOH/silica gel, iodoacetate **1** (1.03 g; 1.9 mmol), and hexane (10 mL) (for the ratio of reagents see Table 1). The mixture was gently refluxed while stirring. The advance of the reaction was periodically checked by GC and ^{19}F NMR. Then the reaction flask was equipped with a jacketed short packed column (Berle saddles, column 4 cm) and a fraction receiver (a head) and the reaction mixture was fractionally distilled. For yields, see Table 1. The analysis of the product **3** (GC, NMR) confirmed the absence of unsaturated by-products.

3.3. Fluoroalkylated derivatives of D-galactopyranose (compounds 6–8 and 9–11)

3.3.1. General procedure for the reaction of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (5) with 2-[(perfluoroalkyl)methyl]oxiranes 2–4 (products 6–8). A mixture of 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (**5**) (5.21 g, 20 mmol), epoxide **2–4** (20 mmol), diisopropyl ether (40 g, 0.39 mol), and boron trifluoride etherate (43 mg, 0.3 mmol) was heated at reflux for 5 h while stirring (complete conversion of epoxide). The mixture was filtered, solvent was evaporated, and crude yellowish oil product was purified on a silica gel column (5 g, elution with petroleum ether/acetone 4:1). Slightly yellow viscous products **6–8** were obtained in 99% purity (check by ^{19}F NMR).

3.3.2. 1,2:3,4-Di-*O*-isopropylidene-6-*O*-(4,4,5,5,6,6,7,7,7-nonafluoro-2-hydroxyheptyl)-α-D-galactopyranose (6). Yield 7.8 g (73%); bp 141–143 °C/0.67 Pa; ^1H NMR ($CDCl_3$): δ, 2 diastereoisomers, A (53% rel.), B (47% rel.): 1.34, 1.35, 1.45, 1.51 (4×s, 12H, 4×CH_3), 2.26,

2.36 (2×m, 2H, CH_2CF_2), 3.36, 3.37 (2×br s, 1H, OH), 3.48, 3.55 (2×dd, 1H(H(a), A, B), ^2J 10.5, ^3J 6.6, CH_2O), 3.60, 3.67 (2×dd, 1H(H(b), B, A), ^2J 10.5, ^3J 4, CH_2O), 3.69, 3.73 (2×dd, 1H(H(a), B, A), ^2J 6, $^3J_{5,6}$ 3.5, H-6), 3.71, 3.72 (2×ddd, 1H(A, B), $^3J_{5,6}$ 6, $^3J_{5,6}$ 3.5, $^3J_{4,5}$ 2, H-5), 4.00, 4.01 (2×t, 1H(H(b), A, B), ^2J 6, $^3J_{5,6}$ 6, H-6), 4.25, 4.27 (2×dd, 1H(B, A), $^3J_{3,4}$ 8, $^3J_{4,5}$ 2, H-4), 4.26 (m, 1H, CH), 4.34, 4.35 (2×dd, 1H(B, A), $^3J_{1,2}$ 5, $^3J_{2,3}$ 2.5, H-2), 4.63, 4.64 (2×dd, 1H(A, B), $^3J_{3,4}$ 8, $^3J_{2,3}$ 2.5, H-3), 5.54, 5.55 (2×d, 1H(B, A), $^3J_{1,2}$ 5, H-1); ^{13}C NMR ($CDCl_3$): δ 24.47, 24.94, 25.98, 26.00 (4×s, 4×CH_3), 34.55, 34.71 (2×t, C-A, C-B, $^2J_{CF}$ 21, C_2CF_2), 64.12, 64.47 (2×s, C-B, C-A, CH), 66.80, 67.21 (2×s, C-B, C-A, C-5), 70.06, 70.70 (2×s, C-A, C-B, C-6), 70.58, 70.65 (2×s, C-B, C-A, C-4), 70.81 (s, C-3), 71.30 (s, C-2), 74.95, 75.21 (2×s, C-B, C-A, CH_2O), 96.43 (s, C-1), 108.85, 109.62 (2×s, 2C_q), 105.03–125.06 (m, CF_2 and CF_3); ^{19}F NMR ($CDCl_3$): δ −81.34 (t, 3F, $^3J_{FF}$ 10, CF_3), −113.12 (m, 2F, CF_2CH_2), −122.21 (m, 2F, CF_2), −126.43 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{19}H_{25}F_9O_7$: C, 42.55; H, 4.70; F, 31.88. Found: C, 42.61; H, 4.64; F, 32.08.

3.3.3. 1,2:3,4-Di-*O*-isopropylidene-6-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-hydroxynonyl)-α-D-galactopyranose (7). Yield 9.2 g (72%); ^{1}H NMR ($CDCl_3$): δ, 2 diastereoisomers, A (54% rel.), B (46% rel.): 1.33, 1.36, 1.46, 1.51 (4×s, 12H, 4×CH_3), 2.28, 2.34 (2×m, 2H, CH_2CF_2), 3.33, 3.38 (2×br s, 1H, OH), 3.47, 3.54 (2×dd, 1H(H(a), A, B), ^2J 10.5, ^3J 6.6, CH_2O), 3.61, 3.66 (2×dd, 1H(H(b), B, A), ^2J 10.5, ^3J 4, CH_2O), 3.70, 3.74 (2×dd, 1H(H(a), B, A), ^2J 6, $^3J_{5,6}$ 3.5, H-6), 3.70, 3.72 (2×ddd, 1H(A, B), $^3J_{5,6}$ 6, $^3J_{5,6}$ 3.5, $^3J_{4,5}$ 2, H-5), 4.02, 4.03 (2×t, 1H(H(b), A, B), ^2J 6, $^3J_{5,6}$ 6, H-6), 4.26, 4.28 (2×dd, 1H(B, A), $^3J_{3,4}$ 8, $^3J_{4,5}$ 2, H-4), 4.29 (m, 1H, CH), 4.33, 4.34 (2×dd, 1H(B, A), $^3J_{1,2}$ 5, $^3J_{2,3}$ 2.5, H-2), 4.65, 4.67 (2×dd, 1H(A, B), $^3J_{3,4}$ 8, $^3J_{2,3}$ 2.5, H-3), 5.55, 5.57 (2×d, 1H(B, A), $^3J_{1,2}$ 5, H-1); ^{13}C NMR ($CDCl_3$): δ 24.45, 24.92, 25.95, 26.02 (4×s, 4×CH_3), 34.57, 34.73 (2×t, C-A, C-B, $^2J_{CF}$ 21, C_2CF_2), 64.14, 64.45 (2×s, C-B, C-A, CH), 66.81, 67.22 (2×s, C-B, C-A, C-5), 70.08, 70.68 (2×s, C-A, C-B, C-6), 70.55, 70.72 (2×s, C-B, C-A, C-4), 70.83 (s, C-3), 71.32 (s, C-2), 74.93, 75.22 (2×s, C-B, C-A, CH_2O), 96.44 (s, C-1), 108.81, 109.64 (2×s, 2C_q), 105–125 (m, CF_2 and CF_3); ^{19}F NMR ($CDCl_3$): δ −81.46 (t, 3F, $^3J_{FF}$ 10, CF_3), −113.29 (m, 2F, CF_2CH_2), −122.25 (m, 2F, CF_2), −124.42 (m, 4F, 2×CF_2), −126.51 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{21}H_{25}F_{13}O_7$: C, 39.63; H, 3.96; F, 38.81. Found: C, 39.72; H, 3.93; F, 38.92.

3.3.4. 1,2:3,4-Di-*O*-isopropylidene-6-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-hydroxyundecyl)-α-D-galactopyranose (8). Yield 10.3 g (70%); ^{1}H NMR ($CDCl_3$): δ, 2 diastereoisomers, A (53% rel.), B (47% rel.): 1.34, 1.37, 1.47, 1.52 (4×s, 12H, 4×CH_3), 2.29, 2.33 (2×m, 2H, CH_2CF_2), 3.31, 3.42 (2×br s, 1H, OH), 3.48, 3.55 (2×dd, 1H(H(a), A, B), ^2J 10.5, ^3J 6.6, CH_2O), 3.62, 3.68 (2×dd, 1H(H(b), B, A), ^2J 10.5, ^3J 4, CH_2O), 3.71, 3.75 (2×dd, 1H(H(a), B, A), ^2J 6, $^3J_{5,6}$ 3.5, H-6), 3.71, 3.73 (2×ddd, 1H(A, B), $^3J_{5,6}$ 6, $^3J_{5,6}$ 3.5, $^3J_{4,5}$ 2, H-5), 4.05, 4.08 (2×t, 1H(H(b), A, B), ^2J 6, $^3J_{5,6}$ 6, H-6), 4.28, 4.31 (2×dd, 1H(B, A), $^3J_{3,4}$ 8, $^3J_{4,5}$ 2, H-4), 4.33 (m, 1H, CH), 4.35, 4.37 (2×dd, 1H(B, A), $^3J_{1,2}$ 5, $^3J_{2,3}$ 2.5, H-2), 4.66, 4.68 (2×dd, 1H(A, B), $^3J_{3,4}$ 8, $^3J_{2,3}$ 2.5, H-3), 5.56, 5.58 (2×d, 1H(B, A), $^3J_{1,2}$ 5, H-1); ^{13}C NMR ($CDCl_3$): δ 24.47, 24.95, 25.96, 26.04 (4×s, 4×CH_3), 34.56, 34.72 (2×t, C-A, C-B, $^2J_{CF}$ 21, C_2CF_2), 64.15, 64.47 (2×s, C-B, C-A, CH), 66.82, 67.24 (2×s, C-B, C-A, C-5), 70.06, 70.65 (2×s, C-A, C-B, C-6), 70.53, 70.70 (2×s, C-B, C-A, C-4), 70.81 (s, C-3), 71.33 (s, C-2), 74.94, 75.25 (2×s, C-B, C-A, CH_2O), 96.45 (s, C-1), 108.82, 109.65 (2×s, 2C_q), 105–125 (m, CF_2 and CF_3); ^{19}F NMR ($CDCl_3$): δ −81.58 (t, 3F, $^3J_{FF}$ 10, CF_3), −113.47 (m, 2F, CF_2CH_2), −122.34 (m, 2F, CF_2), −124.82 (m, 6F, 3×CF_2), −125.02 (m, 2F, CF_2), −126.51 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{23}H_{25}F_{17}O_7$: C, 37.51; H, 3.42; F, 43.86. Found: C, 37.42; H, 3.48; F, 44.03.

3.3.5. General procedure for the deprotection of 1,2:3,4-di-*O*-isopropylidene-6-*O*-(fluoroalkyl)-α-D-galactopyranoses 6–8 (products 9–11). A mixture of fluoroalkylated 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose **6–8** (10 mmol) in 10% aqueous TFA (30 mL) was stirred for 30 min at rt when the conversion was complete. The reaction mixture was concentrated to dryness, petroleum ether (25 mL) added, and evaporated (×2). The crude product crystallized from a mixture THF–chloroform (1:3) as a white foam to afford after recrystallization pure product (**9–11**) in 99% purity (check by ^{19}F NMR).

3.3.6. 6-*O*-(4,4,5,5,6,6,7,7,7-Nonafluoro-2-hydroxyheptyl)-D-galactose (9). Yield 3.9 g (85%); mp 157–159 °C; ^{1}H NMR (D_2O/THF-d_8): δ, 2 diastereoisomers, A (53% rel.), B (47% rel.), 2.18–2.45 (m, 2H, CH_2CF_2), 3.32–3.45 (m, 1H, OH), 3.72–3.84 (m, 4H, CH_2O and H-6), 3.85–4.65 (m, 5H, H-1, H-2, H-3, H-4, H-5), 4.33–4.44 (m, 1H, CH), 4.85–5.02 (m, 4H, OH); ^{13}C NMR (D_2O/THF-d_8): δ 34.5, 34.8 (2×t, C-A, C-B, $^2J_{CF}$ 21, C_2CF_2), 62.1, 62.5 (2×s, CH), 68.3, 68.9, 69.4, 69.8, 70.4, 70.7, 72.1, 72.4, 75.1, 75.6 (10×s, 5×D-galactose ring carbons C-2, C-3, C-4, C-5, C-6), 74.1, 74.3 (2×s, CH_2O), 94.5, 98.9 (2×s, C-1), 105–125 (m, CF_2 and CF_3); ^{19}F NMR (D_2O/THF-d_8): δ −81.3 (t, 3F, $^3J_{FF}$ 10, CF_3), −113.1 (m, 2F, CF_2CH_2), −122.2 (m, 2F, CF_2), −126.4 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{13}H_{17}F_9O_7$: C, 34.22; H, 3.76; F, 37.48. Found: C, 34.20; H, 3.61; F, 37.61.

3.3.7. 6-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluoro-2-hydroxynonyl)-D-galactose (10). Yield 4.9 g (88%); mp 171–173 °C; ^{1}H NMR (D_2O/THF-d_8): δ, 2 diastereoisomers, A (54% rel.), B (46% rel.), 2.20–2.50 (m, 2H, CH_2CF_2), 3.31–3.44 (m, 1H, OH), 3.75–3.88 (m, 4H, CH_2O and H-6), 3.87–4.66 (m, 5H, H-1, H-2, H-3, H-4, H-5), 4.32–4.43 (m, 1H, CH), 4.83–5.05 (m, 4H, OH); ^{13}C NMR (D_2O/THF-d_8): δ 34.6, 34.9 (2×t, C-A, C-B, $^2J_{CF}$ 21, C_2CF_2), 62.2, 62.6 (2×s, CH), 68.4, 68.8, 69.4, 69.9, 70.4, 70.8, 72.1, 72.5, 75.2, 75.7 (10×s, 5×D-galactose ring carbons C-2, C-3, C-4, C-5, C-6), 74.4, 74.8 (2×s, CH_2O), 94.8, 99.5 (2×s, C-1), 105–125 (m, CF_2 and CF_3); ^{19}F NMR (D_2O/THF-d_8): δ −81.5 (t, 3F, $^3J_{FF}$ 10, CF_3), −113.3 (m, 2F, CF_2CH_2), −122.5 (m, 2F, CF_2), −124.8 (m, 4F, CF_2), −126.5 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{15}H_{17}F_{13}O_7$: C, 32.39; H, 3.08; F, 44.40. Found: C, 32.33; H, 3.19; F, 44.52.

3.3.8. 6-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoro-2-hydroxyundecyl)-D-galactose (11). Yield 5.9 g (90%); mp 176–178 °C; ^{1}H NMR (D_2O/THF-d_8): δ, 2 diastereoisomers, A (53% rel.), B (47% rel.), 2.15–2.55 (m, 2H, CH_2CF_2), 3.31–3.47 (m, 1H, OH), 3.73–3.83 (m, 4H, CH_2O and H-6), 3.81–4.64 (m, 5H, H-1, H-2, H-3, H-4, H-5), 4.35–4.48 (m, 1H, CH), 4.83–5.01 (m, 4H, OH); ^{13}C NMR (D_2O/THF-d_8): δ 34.4, 34.7 (2×t, C-A, C-B, $^2J_{CF}$ 21, C_2CF_2), 62.0, 62.6 (2×s, CH), 68.4, 68.8, 69.6, 69.9, 70.3, 70.7, 72.2, 72.4, 75.2, 75.9 (10×s, 5×D-galactose ring carbons C-2, C-3, C-4, C-5, C-6), 74.5, 74.9 (2×s, CH_2O), 94.1, 98.5 (2×s, C-1), 105–125 (m, CF_2 and CF_3); ^{19}F NMR (D_2O/THF-d_8): δ −81.6 (t, 3F, $^3J_{FF}$ 10, CF_3), −113.5 (m, 2F, CF_2CH_2), −122.5 (m, 2F, CF_2), −124.6 (m, 6F, CF_2), −125.4 (m, 2F, CF_2), −126.6 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{17}H_{17}F_{17}O_7$: C, 31.11; H, 2.61; F, 49.21. Found: C, 31.10; H, 2.72; F, 49.34.

3.4. Fluoroalkylated derivatives of DL-xylitol (compounds 15–17 and 18–20)

3.4.1. General procedure for the reaction of 1,2:3,4-di-*O*-isopropylidene-dl-xylitol (13) with 2-[(perfluoroalkyl)-methyl]oxiranes 2–4 (products 15–17). A mixture of 1,2:3,4-di-*O*-isopropylidene-DL-xylitol (**13**) (2.32 g, 10 mmol), epoxide **2–4** (10 mmol), diisopropyl ether (20 g, 0.2 mol) and boron trifluoride etherate (22 mg, 0.15 mmol) was heated at reflux for 10 h while stirring (complete conversion of epoxide, TLC check, petroleum ether/acetone 4:1). The solids were removed, solvent was evaporated, and crude yellow oil product was purified on a silica gel column (50 g, elution with petroleum ether/acetone 4:1). The viscous product (**15–17**) was obtained in 99% purity (check by ^{19}F NMR).

3.4.2. 2,3:4,5-Di-*O*-isopropylidene-1-*O*-(4,4,5,5,6,6,7,7,7-nonafluoro-2-hydroxyheptyl)-DL-xylitol (15). Yield 3.8 g (75%); ^{1}H NMR ($CDCl_3$): δ, 2 diastereoisomers, A (52% rel.), B (48% rel.): 1.16, 1.18, 1.37, 1.43 (4×s, 12H, 4×CH_3), 2.02–2.48 (m, 2H, CH_2CF_2), 2.72 (s, 1H, OH), 3.30–4.60 (m, 10H, CH_2O, CH, 2×H-1, H-2, H-3, H-4, 2×H-5); ^{13}C NMR ($CDCl_3$): δ 21.73, 21.84 (2×s, 4×CH_3), 34.69 (t, $^2J_{CF}$ 21, C_2CF_2), 64.42 (s, CH), 66.73, 68.20 (2×s, C-1), 69.03 (s, C-2), 69.21 (s, C-5), 71.39 (s, CH_2O), 72.43 (s, C-3, C-4), 109.39 (s, 2×C_q), 104–122 (m, CF_2 and CF_3); ^{19}F NMR ($CDCl_3$): δ −81.39 (t, 3F, ^3J 8.7, CF_3), −114.07 (m, 2F, CF_2CH_2), −122.23 (m, 2F, CF_2), −126.61 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{18}H_{25}F_9O_6$: C, 42.53; H, 4.96; F, 33.63. Found: C, 42.56; H, 4.99; F, 33.72.

3.4.3. 2,3:4,5-Di-*O*-isopropylidene-1-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-hydroxynonyl)-DL-xylitol (16). Yield 4.6 g (76%); ^{1}H NMR ($CDCl_3$): δ, 2 diastereoisomers, A (53% rel.), B (47% rel.): 1.17, 1.19, 1.36, 1.42 (4×s, 12H, 4×CH_3), 2.10–2.45 (m, 2H, CH_2CF_2), 2.68 (s, 1H, OH), 3.27–4.59 (m, 10H, CH_2O, CH, 2×H-1, H-2, H-3, H-4, 2×H-5); ^{13}C NMR ($CDCl_3$): δ 21.75, 21.81 (2×s, 4×CH_3), 34.62 (t, $^2J_{CF}$ 21, C_2CF_2), 64.45 (s, CH), 66.71, 68.22 (2×s, C-1), 69.12 (s, C-2), 69.28 (s, C-5), 71.35 (s, CH_2O), 72.48 (s, C-3, C-4), 109.33 (s, 2×C_q), 102–125 (m, CF_2 and CF_3); ^{19}F NMR ($CDCl_3$): δ −81.41 (t, 3F, ^3J 8.7, CF_3), −114.54 (m, 2F, CF_2CH_2), −122.34 (m, 2F, CF_2), −123.31 (m, 2F, CF_2), −124.11 (m, 2F, CF_2), −126.61 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{20}H_{25}F_{13}O_6$: C, 39.48; H, 4.14; F, 40.60. Found: C, 39.52; H, 4.23; F, 40.75.

3.4.4. 2,3:4,5-Di-*O*-isopropylidene-1-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-hydroxyundecyl)-DL-xylitol (17). Yield 5.7 g (81%); ^{1}H NMR ($CDCl_3$): δ, 2 diastereoisomers, A (53% rel.), B (47% rel.): 1.16, 1.18, 1.35, 1.41 (4×s, 12H, 4×CH_3), 2.15–2.40 (m, 2H, CH_2CF_2), 2.69 (s, 1H, OH), 3.25–4.66 (m, 10H, CH_2O, CH, 2×H-1, H-2, H-3, H-4, 2×H-5); ^{13}C NMR ($CDCl_3$): δ 21.71, 21.79 (2×s, 4×CH_3), 34.65 (t, $^2J_{CF}$ 21, C_2CF_2), 64.44 (s, CH), 66.75, 68.24 (2×s, C-1), 69.13 (s, C-2), 69.29 (s, C-5), 71.32 (s, CH_2O), 72.47 (s, C-3, C-4), 109.35 (s, 2×C_q), 102–125 (m, CF_2 and CF_3); ^{19}F NMR ($CDCl_3$): δ −81.48 (t, 3F, ^3J 8.7, CF_3), −114.68 (m, 2F, CF_2CH_2), −122.31 (m, 2F, CF_2), −123.44 (m, 6F, 3×CF_2), −124.15 (m, 2F, CF_2), −126.69 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{22}H_{25}F_{17}O_6$: C, 37.30; H, 3.56; F, 45.59. Found: C, 37.35; H, 3.69; F, 45.68.

3.4.5. General procedure for the deprotection of 2,3:4,5-di-*O*-isopropylidene-1-*O*-(fluoroalkyl)xylitols 15–17 (products 18–20). A mixture of fluoroalkylated

1,2:3,4-di-*O*-isopropylidenexylitol **15**–**17** (5 mmol) in water solution of trifluoroacetic acid (15 mL, 1:9) was stirred for 30 min at rt when the conversion was complete. Reaction mixture was concentrated to dryness and a crude viscous product of brown color was dissolved in MeOH (15 mL) and treated with carbon black (2 g) at 50 °C for 0.5 h. After filtration, the solvent was evaporated and the viscous oil was heated to 60 °C/266 Pa for 12 h to afford the waxy product (**18**–**20**) in 99% purity (check by ^{19}F NMR).

3.4.6. 1-*O*-(4,4,5,5,6,6,7,7,7-Nonafluoro-2-hydroxyheptyl)-DL-xylitol (18). Yield 1.61 g (75%); ^{1}H NMR (CD_3OD): δ, 2 diastereoisomers, A (52% rel.), B (48% rel.), 2.10–2.60 (m, 2H, CH_2CF_2), 3.40–4.35 (m, 10H, H-1, H-2, H-3, H-4, H-5, CH_2O, CH), 4.85 (m, 5H, OH); ^{13}C NMR (CD_3OD): δ 35.57 (t, $^{2}J_{CF}$ 20, C_2CF_2), 64.31 (s, C-1), 65.14 (s, CH), 72.04 (s, C-2), 72.20, 72.34 (2×s, C-3), 73.77, 73.92 (2×s, C-4), 74.03 (s, C-5), 76.19 (s, CH_2O), 105–124 (m, CF_2 and CF_3); ^{19}F NMR (CD_3OD): δ −80.96 (t, 3F, ^{3}J 9, CF_3), −112.36 (m, 2F, CF_2CH_2), −121.50 (m, 2F, CF_2), −125.97 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{12}H_{17}F_9O_6$: C, 33.66; H, 4.00; F, 39.93. Found: C, 33.72; H, 4.12; F, 40.05.

3.4.7. 1-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluoro-2-hydroxynonyl)-DL-xylitol (19). Yield 2.17 g (82%); ^{1}H NMR (CD_3OD): δ, 2 diastereoisomers, A (53% rel.), B (47% rel.), 2.11–2.58 (m, 2H, CH_2CF_2), 3.45–4.40 (m, 10H, H-1, H-2, H-3, H-4, H-5, CH_2O, CH), 4.77 (m, 5H, OH); ^{13}C NMR (CD_3OD): δ 35.59 (t, $^{2}J_{CF}$ 20, CH_2CF_2), 64.30 (s, C-1), 65.15 (s, CH), 72.01 (s, C-2), 72.18, 72.32 (2×s, C-3), 73.78, 73.91 (2×s, C-4), 74.02 (s, C-5), 76.17 (s, CH_2O), 105–124 (m, CF_2 and CF_3); ^{19}F NMR (CD_3OD): δ −81.14 (t, 3F, ^{3}J 9, CF_3), −113.02 (m, 2F, CF_2CH_2), −121.48 (m, 2F, CF_2), −122.59 (m, 2F, CF_2), −123.28 (m, 2F, CF_2), −125.93 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{14}H_{17}F_{13}O_6$: C, 31.83; H, 3.24; F, 46.75. Found: C, 31.75; H, 3.33; F, 46.62.

3.4.8. 1-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoro-2-hydroxyundecyl)-DL-xylitol (20). Yield 2.83 g (90%); ^{1}H NMR (CD_3OD): δ, 2 diastereoisomers, A (53% rel.), B (47% rel.), 2.12–2.55 (m, 2H, CH_2CF_2), 3.44–4.42 (m, 10H, H-1, H-2, H-3, H-4, H-5, CH_2O, CH), 4.75 (m, 5H, OH); ^{13}C NMR (CD_3OD): δ 35.57 (t, $^{2}J_{CF}$ 20, CH_2CF_2), 64.35 (s, C-1), 65.22 (s, CH), 72.05 (s, C-2), 72.19, 72.33 (2×s, C-3), 73.79, 73.92 (2×s, C-4), 74.03 (s, C-5), 76.19 (s, CH_2O), 105–124 (m, CF_2 and CF_3); ^{19}F NMR (CD_3OD): δ −81.05 (t, 3F, ^{3}J 9, CF_3), −112.95 (m, 2F, CF_2CH_2), −121.44 (m, 2F, CF_2), −122.58 (m, 6F, 3×CF_2), −123.32 (m, 2F, CF_2), −125.74 (m, 2F, CF_2CF_3); Anal. Calcd for $C_{16}H_{17}F_{17}O_6$: C, 30.59; H, 2.73; F, 51.41. Found: C, 30.72; H, 2.85; F, 51.56.

Acknowledgements

The authors thank the Atofina S.A. (former Elf Atochem S.A.) for the gift of perfluoroalkyl iodides. The research was supported by the Grant Agency of the Czech Republic (grant no 203/01/1131) and partly by the Ministry of Education of the Czech Republic (Project MSM 223100001). Elemental analyses and measurements of some NMR spectra were carried out in the Central Laboratories of the Institute of Chemical Technology, Prague; the authors thank their staff members for the kind assistance.

References

1. Riess, J. G.; Greiner, J. *Carbohydr. Res.* **2000**, *327*, 147–168.
2. Riess, J. G. *Chem. Rev.* **2001**, *101*, 2797–2919.
3. Guittard, F.; Geribaldi, S. *J. Fluorine Chem.* **2001**, *107*, 363–374.
4. Sawada, H. *J. Fluorine Chem.* **2003**, *121*, 111–130.
5. Lowe, K. C. *J. Fluorine Chem.* **2001**, *109*, 59–65.
6. Riess, J. G. *J. Fluorine Chem.* **2002**, *114*, 119–126.
7. Lowe, K. C. *J. Fluorine Chem.* **2002**, *118*, 19–26.
8. Paleta, O.; Dlouhá, I.; Kaplánek, R.; Kefurt, K.; Kodíček, M. *Carbohydr. Res.* **2002**, *337*, 2411–2418.
9. Církva, V.; Kaplánek, R.; Paleta, O.; Kodíček, M. *Collect. Czech. Chem. Commun.* **2002**, *67*, 1436–1448.
10. Církva, V.; Améduri, B.; Boutevin, B.; Paleta, O. *J. Fluorine Chem.* **1997**, *84*, 53–61.
11. Církva, V.; Gaboyard, M.; Paleta, O. *J. Fluorine Chem.* **2000**, *102*, 349–361.
12. Církva, V.; Améduri, B.; Boutevin, B.; Paleta, O. *J. Fluorine Chem.* **1997**, *83*, 151–158.
13. Církva, V.; Duchek, J.; Paleta, O. *J. Fluorine Chem.* **2003**, *121*, 101–104.
14. Kvícala, J.; Mouyrin, J.-C.; Paleta, O. *J. Fluorine Chem.* **2002**, *113*, 195–200.
15. Církva, V. Dissertation. Institute of Chemical Technology, Prague, 1998.
16. Kefurt, K.; Moravcová, J.; Bambasová, S.; Buchalová, K.; Vymetalíková, B.; Kefurtová, Z.; Staník, J.; Paleta, O. *Collect. Czech. Chem. Commun.* **2001**, *66*, 1665–1681.
17. Baggett, N.; Buck, K. W.; Foster, A. B.; Jefferis, R.; Rees, B. H.; Weber, J. M. *J. Chem. Soc.* **1965**, 3382–3387.
18. Szarek, W. A.; Zamojski, A.; Tiwari, K. N.; Ison, E. R. *Tetrahedron Lett.* **1986**, *27*, 3827–3830.
19. Baker, D. C.; Horton, D.; Tindall, C. G. *Carbohydr. Res.* **1972**, *24*, 192–197.
20. Coppola, G. M. *Synthesis* **1984**, 1021–1023.
21. Mandal, A. K.; Shrotri, P. Y.; Ghogare, A. D. *Synthesis*, **1986**, 221–222.
22. Guillod, F.; Greiner, J.; Riess, J. G. *Carbohydr. Res.* **1994**, *261*, 37–56.
23. Manfredi, A.; Abouhilale, S.; Greiner, J.; Riess, J. G. *Bull. Soc. Chim. Fr.* **1989**, 872–878.

24. Riess, J. G.; Greiner, J.. In *Carbohydrates as Organic Raw Materials II*; Descotes, G., Ed.; Weinheim: New York, 1993, pp 209–259, and references cited therein.
25. Krafft, M. P.; Riess, J. G. *Biochimie* **1998**, *80*, 489–514.
26. Greiner, J.; Riess, J. G.; Vierling, P. In *Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications*; Filler, R., Kobayashi, Y., Yagupolskii, L. M., Eds.; Elsevier: Amsterdam, 1993; pp 339–380.
27. Zarif, L.; Greiner, J.; Pace, S.; Riess, J. G. *J. Med. Chem.* **1990**, *33*, 1262–1269.
28. Kodíccek, M.; Forman, S.; Danková, K.; Paleta, O., in preparation.