AMPHIPHILIC PERFLUOROALKYLATED DERIVATIVES OF ALIPHATIC TRIOLS: HEMOCOMPATIBILITY AND EFFECT ON PERFLUOROCARBON EMULSION

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Dedicated to the memory of Professor Miloš Hudlický.

Two sets of amphiphilic perfluoroalkylated aliphatic triols were prepared in a two-step synthesis: a protected glycerol, 4-hydroxymethyl-2,2-dimethyl-1,3-dioxolane (**1**) and protected 2-hydroxymethyl-2-methylpropane-1,3-diol, 5-hydroxymethyl-2,2,5-trimethyl-1,3-dioxane (**11**) were fluoroalkylated with racemic 2-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)- (**2**), or 2-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)- (**3**) or 2-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononyl)oxirane (**4**) using boron trifluoride diethyl etherate as a catalyst to afford intermediates **5**–**7** and **12**–**14**, which were deprotected by re-acetalization to the target triols $HOCH_2CH(OH)CH_2OCH_2CH(OH)CH_2CF_2(CF_2)_nCF_3$ (n = 2, 4, 6) **8**–**10** and $(OHCH_2)_2C(CH_3)CH_2OCH_2CH(OH)CH_2CF_2(CF_2)_nCF_3$ (n = 2, 4, 6) **15**–**17**. Regioselectivity of competitive fluoroalkylation of propane-1,2-diol and butane-1,3-diol appeared to be considerably dependent on the catalyst up to 93 rel.% for the preferential fluoroalkylation at the primary hydroxy group. Hemocompatibility of the triols **8**–**10** and **15**–**17**, which was very high for linear-chain amphiphiles **9** and **10**, showed particular dependence on the starting triol and perfluoroalkyl-chain length. All amphiphiles **8**–**10** and **15**–**17** displayed very good compatibility with perfluorodecalin–Pluronic F-68 water emulsion.

Keywords: Perfluoroalkyl epoxides; Fluoroalkylations; Fluorophilic triols; Regioselectivity of fluoroalkylations; Hemocompatibility; Fluorinated surfactants; Blood substituents; Oxygen carriers.

Perfluorocarbon (PFC) emulsions are prominent candidates for blood substitutes due to their ability to carry oxygen[1–6]. They can also be applied for cell cultures, diagnoses, and drug delivery systems[7]. The PFC liquids are im-

miscible with aqueous solutions and for intravascular use, they must be emulsified in an electrolyte solution containing appropriate one or more surface-active agents. Usually, a main surfactant is applied with co-emulsifiers. The co-surfactants are important constituents of emulsion systems that stabilize the emulsions by preventing flocculation or coalescence. As the classical (commercial) surfactants fitted with fatty acid chains have a weak affinity to PFCs, the surfactants that possess a fluorophilic rather than simply a lipophilic tail should be applied.

In the last years, some families of strongly amphiphilic molecules have been synthesized, whose molecular structures assemble perfluoroalkylated chains, spacers of various chain lengths, and junction units (ether, or ester groups) and hydrophilic heads derived from polyethylene glycol[8], polyols[9] (alditols) or saccharides[1–4,6,7].

In this paper, we focused on the synthesis of perfluoroalkylated amphiphiles derived from easily accessible triols as simplest new surfactants. Recently, we have developed a convenient method for fluoroalkylation of hydroxy compounds by reaction with perfluoroalkylated epoxides[10–13], which was successfully applied here to triols. The new surfactants were subjected to preliminary tests for hemocompatibility and co-emulsifying properties.

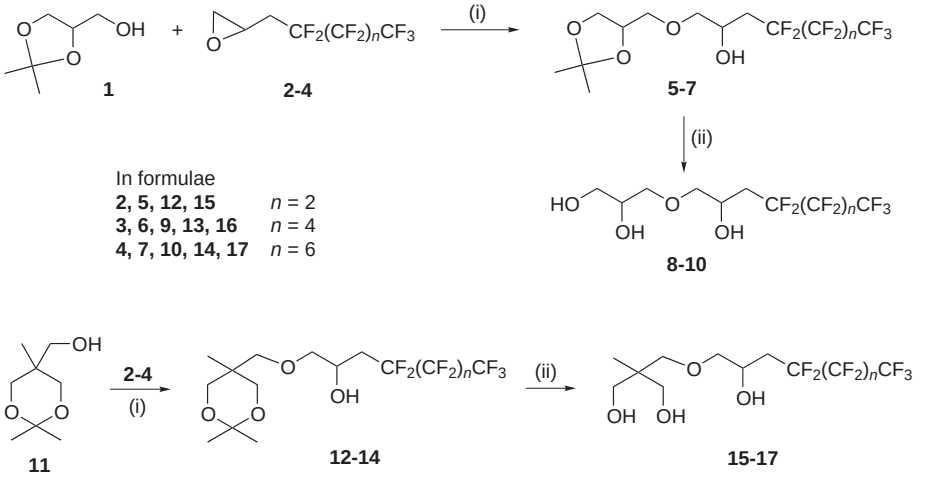
RESULTS AND DISCUSSION

Preparations of Fluoroalkylated Triols ***8–10*** *and* ***15–17***

The success in acid-catalyzed reactions of epoxide **3** with alkanols and alkane-α,ω-diols[11–13] has opened a preparative route to the synthesis of potential biosurfactants. To obtain monoperfluoroalkylated products of polyhydroxy compounds, it has been necessary to use their protected derivatives containing only one free hydroxy group. Thus, protected glycerol, *i.e.* 4-hydroxymethyl-2,2-dimethyl-1,3-dioxolane[14] (**1**) and a protected 2-hydroxymethyl-2-methyl-1,3-propanediol, *viz.* 5-hydroxymethyl-2,2,5-trimethyl-1,3-dioxane[15] (**11**) were reacted with racemic perfluoroalkylated epoxides **2**–**4** in the presence of boron trifluoride diethyl etherate as a strong Lewis-acid catalyst (Scheme 1) to afford monofluoroalkylated products **5**–**7** and **12**–**14** in good yields of 77–83%. The attack of the oxirane ring in epoxides **2**–**4** by *O*-nucleophiles **1** and **11** took place at the terminal carbon atom with the complete regioselectivity.

For the deprotection of fluoroalkylated compounds **5**–**7** and **12**–**14** to obtain the target fluoroalkylated triols **8**–**10** and **15**–**17**, a variety of methods

is available, *e.g.* deprotection with mineral acids in organic solvents[16,17] or diluted trifluoroacetic acid[18], on ion exchangers[19,20] or with aluminum iodide[21]. In our experience, the best deprotection method appeared to be the transacetalization with methanol in the presence of hydrochloric acid[22], which eased workup of the reaction mixture and afforded the end products **8**–**10** and **15**–**17** in high isolated yields of 85–89%.



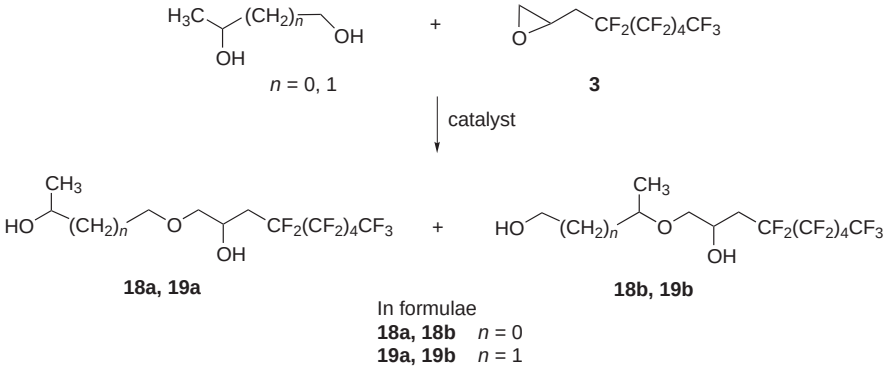
(i) $BF_3 \cdot Et_2O$, 90 °C, 2 h; (ii) conc. HCl, CH_3OH, reflux, 2 h

SCHEME 1

Regioselectivity of the Fluoroalkylation on Primary and Secondary Hydroxy Groups

The aim of this study has been to verify, whether the reactivities of primary and secondary hydroxy groups (in polyhydroxy compounds) in fluoroalkylation by the epoxides **2**–**4** are sufficiently different so that the protection of secondary hydroxy groups in reacting substrates is not necessary. Propane-1,2-diol with vicinal hydroxy groups and butane-1,3-diol with more remote hydroxy groups were used as model compounds. The fluoroalkylations were performed with epoxide **3** possessing a medium perfluoroalkyl-chain length under catalysis by several Lewis-acid catalysts. The results are summarized in Table I and Scheme 2. Different catalytic activity in the fluoroalkylation is demonstrated by the overall yields of products **18** or **19**: boron trifluoride diethyl etherate appeared to be the most efficient catalyst (yields 96 and 90%, respectively; entries 2 and 6), while titanium(IV) isopropoxide (entries 4 and 7) gave only patterns of products.

The regioselectivity in the fluoroalkylations is strongly dependent on the catalyst and specifically on the diol structure. Generally, the best regioselectivity was obtained under catalysis by magnesium perchlorate (entries 1 and 5) affording relative amounts of regioisomeric products in ratios **18a**/**18b** = 82 : 18 and **19a**/**19b** = 93 : 7. In contrast, lithium perchlorate or titanium(IV) isopropoxide (entries 3 and 7) had more a nivelling than selectivity effect on fluoroalkylations affording regioisomeric mixtures with *ca* 55 : 45 ratio of the products **18a**/**18b** or **19a**/**19b**. From the point of view of diol structure, the regioselectivity on butane-1,3-diol was apparently better when boron trifluoride or magnesium perchlorate catalysts were used.



SCHEME 2

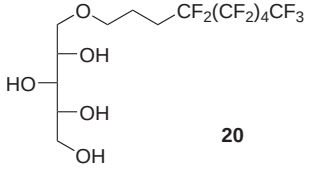
TABLE I
Regioselectivity of the fluoroalkylation of diols by perfluoroalkyl epoxide **3**

Entry No.	Diol	Catalyst	Regioisomeric products	rel.%	Yield %
1	CH_3–CHOH–CH_2OH	$Mg(ClO_4)_2$	**18a**/**18b**	82 : 18	66
2	CH_3–CHOH–CH_2OH	$BF_3{\cdot}Et_2O$	**18a**/**18b**	64 : 36	97
3	CH_3–CHOH–CH_2OH	$LiClO_4$	**18a**/**18b**	57 : 43	52
4	CH_3–CHOH–CH_2OH	$Ti(i\text{-}PrO)_4$	**18a**/**18b**	0	0
5	CH_3–CHOH–CH_2–CH_2OH	$Mg(ClO_4)_2$	**19a**/**19b**	93 : 7	64
6	CH_3–CHOH–CH_2–CH_2OH	$BF_3{\cdot}Et_2O$	**19a**/**19b**	74 : 26	90
7	CH_3–CHOH–CH_2–CH_2OH	$Ti(i\text{-}PrO)_4$	**19a**/**19b**	56 : 44	3

Hemocompatibility of the New Amphiphiles

The amphiphilic perfluoroalkylated triols **8**–**10** and **15**–**17** prepared in this work possess two or one stereogenic centers thus giving the possibility of the existence of two pairs of enantiomers for structures **8**–**10** (diastereoisomer ratio 52 : 48, ^{19}F NMR) and one pair of enantiomers for the structures **15**–**17**. The principle of the biochemical acting of bio-surfactants is their biological inertness. It is very probable that also configurational isomers would display close bioinert properties and that it is not necessary to separate them for preliminary biocompatibility testing.

All the triols **8**–**10** and **15**–**17** were subjected to a preliminary testing as potential co-surfactants for oxygen carriers (blood substitutes). Hemolytic activity of the new amphiphiles on human erythrocytes was tested using a reference microemulsion of Pluronic F-68 with perfluorodecalin mixed with erythrocytes. In this heterogeneous mixture, Pluronic was gradually substituted with the amphiphile tested and the amount of extracellular hemoglobin was determined spectrophotometrically in per cent as the hemolysis degree. This is a modification of the method previously reported[23]. Xylitol derivative[24] **20** was used as a reference amphiphile with well-defined structure not forming stereoisomers, which is a structural improvement of the reported[23] xylitol derivative having unsaturation in the spacer part which could cause a biochemical instability. Co-emulsifiers for microemulsions are usually used in amounts up to10% relatively to the main emulsifier, but the amphiphile **20** was tested as a reference compound up to 100% substitution of Pluronic F-68 emulsifier. It has been found[24] that biosurfactant **20** to be completely non-hemolytic in the whole concentration range (Table II).



20

The results of the hemocompatibility evaluation of the new amphiphiles **8**–**10** and **15**–**17** (Table II) showed that two structural effects on hemocompatibility can be found, *i.e.* (i) the perfluoroalkyl-chain length, (ii) linearity of chain or its branching in the hydrophilic part. The amphiphiles **8** and **15** having the shortest perfluorinated chain, *i.e.* perfluorobutyl, were hemolytic at any concentrations tested (Table II). Amphiphiles **9** and **10**

TABLE II
Hemocompatibility (range of hemolysis, %) of the new amphiphilic compounds **8**–**10** and **15**–**17**[a,b]

Co-emulsifier	Substitution of Pluronic F-68 by tested co-emulsifiers, w/v				
	20%	40%	60%	80%	100%
8	1	80	100	100	100
9	0	0	nt	0	nt
10	0	0	0	0	nt
15	10	10	12	12	nt
16	0	1.5	2	10	nt
17	0	0	1	3	nt
20	0	0	0	0	0

[a] Zero value means hemolysis below 0.5%; [b] nt, not tested.

possessing six- or eight-carbon perfluoroalkyls and linear-chain hydrophilic part were non-hemolytic in the whole range tested (up to 80%). This a contrast to amphiphiles **16** and **17** bearing branched hydrophilic part, which showed hemolytic activity only above 60 or 80% substitution of Pluronic F-68 in the emulsion. It comes out from the observations that the branched amphiphiles **16** and **17** are less hemocompatible than the non-branched **9** and **10** ones. As a conclusion, it can be stated that the amphiphiles **9**, **10**, **16** and **17** are hemocompatible up to 40% or higher concentrations, which are much higher than 5–10% usually applied[1–7] to co-emulsifiers.

Co-emulsifying Properties

For an assessment of the co-emulsifying properties of the new amphiphiles as biosurfactants we have developed very efficient centrifugation test[8] to shorten the period of testing. This preliminary testing has been based on a visual evaluation of the state of an emulsion. The results of the testing are summarized in Table III. With the exception of the amphiphile **8**, all the new amphiphiles **9**, **10**, **15**–**17** let the emulsion stable up to substitution of 80% of the Pluronic in the emulsions. Compound **8** formed stable co-emulsions up to 60% substitution of Pluronic content. Thus, the new amphiphiles **8**–**10** and **15**–**17** displayed very good to excellent co-emulsifying properties.

TABLE III
Emulsion stability during centrifugation[a]

Co-emulsifier	Substitution of Pluronic F-68 by tested co-emulsifiers, w/v				
	20%	40%	60%	80%	100%
8	+	+	–	–	–
9	+	+	nt	+	nt
10	+	+	+	+	nt
15	+	+	+	+	nt
16	+	+	+	–	nt
17	+	+	–	–	nt
20	+	+	+	+	+

[a] nt, not tested.

Conclusions

The synthesis of new perfluoroalkylated amphiphilic triols **8**–**10** and **15**–**17** with ether linkage in the hydrophilic part has been accomplished using a new protocol. Regioselectivity of fluoroalkylation at the primary and secondary hydroxy groups studied on 1,2- and 1,3-diols is different. All the amphiphiles **8**–**10** and **15**–**17** display excellent co-emulsifying properties when mixed with the Pluronic F-68-emulsified perfluorodecalin. The new amphiphiles have excellent (**9** and **10**) or very good (**16** and **17**) hemocompatibility. Thus, the compounds synthesized are suitable for further biochemical and pharmacological testing. The easily accessible surfactants **8**–**10** and **15**–**17** could find application in biomedical and technical areas.

EXPERIMENTAL

Boiling points were not corrected. GC analyses were performed on Micromat HRGC 412 (Nordion Analytical; 25 m glass capillary column, SE-30) and a Chrom 5 instrument (Laboratorní přístroje, Prague; FID, 380 × 0.3 cm column packed with silicone elastomer E-301 on Chromaton N-AW-DMCS (Lachema, Brno); nitrogen was used as carrier gas, detector/injector temperatures were 260/255 °C); the GC apparatus was connected to a Hewlett–Packard integrator (model 33990). NMR spectra were recorded on a Bruker 400 AM (FT, ^{19}F at 376.5 MHz) and a Bruker WP 80 SY (FT, ^{19}F at 75 MHz) instruments using TMS and $CFCl_3$ as the internal standards. Chemical shifts are quoted in ppm (δ-scale; s singlet, bs broad, d doublet, t triplet, q quadruplet, qi quintuplet, m multiplet), coupling constants *J* in Hz, solvents $CDCl_3$ and DMSO-d_6.

The chemicals used were as follows: fluoroalkyl epoxides **2**–**4** were prepared according to our procedure[11]; 4-hydroxymethyl-2,2-dimethyl-1,3-dioxolane (**1**) and 5-hydroxymethyl-2,2,5-trimethyl-1,3-dioxane (**11**) were prepared according to literature[14,15]; propane-1,2-diol and butane-1,3-diol were dried with sodium and further purified by distillation; boron trifluoride diethyl etherate (Lachema) was distilled before use; magnesium perchlorate (Aldrich); lithium perchlorate (Aldrich); silica gel L40/100 (Merck).

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 poly(oxypropylene) and poly(oxyethylene), 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.[25])

Hemocompatibility test[25]: Human erythrocytes (from a healthy donor, stored in a refrigerator not longer than 1 week) were washed with 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. (For a more detailed description of the procedure see ref.[25])

Testing of co-emulsifying properties: in the preparation of emulsion (see above), Pluronic F-68 was partly 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 (indicated as "+" in Table III). Unstable emulsion is marked by the sign "–" in Table III. Stability of the mixtures was tested by centrifugation: the emulsion was centrifuged at 400 *g* for 5 min.

Reaction of Perfluoroalkyl Epoxides **2**–**4** with Protected Triols **1** and **11**. General Procedure

In a round-bottomed flask (50 ml) equipped with a Dimroth reflux condenser connected with atmosphere through drying tube (KOH) and with magnetic spinbar, a mixture of protected triol (0.1 mol), epoxide **2**–**4** (50 mmol) and boron trifluoride etherate (71 mg, 0.5 mmol) was heated at 90 °C for 2 h while stirring (complete conversion of epoxide, the mixture has become clear). The unreacted protected triol was distilled off in vacuum and the distillation continued to obtain products **5**–**7** or **12**–**14**.

2,2-Dimethyl-4-(6,6,7,7,8,8,9,9,9-nonafluoro-4-hydroxy-2-oxanonyl)-1,3-dioxolane (**5**), yield 16.9 g (83%), b.p. 92–94 °C/6.6 Pa. ^{1}H NMR ($CDCl_3$), 2 diastereoisomers, A (52 rel.%), B (48 rel.%): 1.35 s, 6 H (CH_3); 1.41 s, 6 H (CH_3); 2.27 m, 2 H (CH_2CF_2); 2.31 m, 2 H (CH_2CF_2); 3.34 bs, 1 H (OH); 3.46 dd, 1 H(a), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 2.5 (CH_2O); 3.49 dd, 1 H(a), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 2.5 (CH_2O); 3.55 m, 2 H (OC**H**$_2$CHO); 3.57 m, 2 H (OC**H**$_2$CHO); 3.60 dd, 1 H(b), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 1.0 (CH_2O); 3.62 dd, 1 H(b), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 1.0 (CH_2O); 3.70 dd, 1 H(a), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 4.5 (CH_2OC); 3.72 dd, 1 H(a), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 4.5 (CH_2OC); 4.03 dd, 1 H(b), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 1.6 (CH_2OC); 4.05 dd, 1 H(b), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 1.6 (CH_2OC); 4.26 m, 2 H (CHO). ^{13}C NMR ($CDCl_3$): 25.04 s, 2 C (CH_3); 26.39 s, 2 C (CH_3); 34.30 t, 1 C, $^2J_{CF}$ = 21 (**C**H$_2$CF$_2$); 34.36 t, 1 C, $^2J_{CF}$ = 21 (**C**H$_2$CF$_2$); 64.05 t, 1 C, $^3J_{CF}$ = 3 (CHOH); 66.04 s, 1 C (**C**H$_2$OC); 66.07 s, 1 C (**C**H$_2$OC); 72.19 s, 1 C (OCH$_2$CHO); 72.34 s, 1 C (OCH$_2$CHO); 74.56 s, 1 C (CH_2O); 74.62 s, 1 C (CH_2O); 74.93 s, 1 C (CHO); 74.99 s, 1 C (CHO); 109.52 s, 1 C (CO_2); 109.56 s, 1 C (CO_2); 105–125 m, 4 C (CF_2 and CF_3). ^{19}F NMR

($CDCl_3$): –81.41 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –113.21 m, 2 F (CF_2CH_2); –122.35 m, 2 F (CF_2); –126.53 m, 2 F (C**F**$_2$CF$_3$). For $C_{13}H_{17}F_9O_4$ (408.3) calculated: 38.2% C, 4.2% H, 41.9% F; found: 38.7% C, 4.4% H, 40.3% F.

2,2-Dimethyl-4-(6,6,7,7,8,8,9,9,10,10,11,11,11-tridecafluoro-4-hydroxy-2-oxaundecyl)-1,3-dioxolane (**6**), yield 20.6 g (81%), b.p. 102–105 °C/5.3 Pa. ^{1}H NMR ($CDCl_3$), 2 diastereoisomers, A (52 rel.%), B (48 rel.%): 1.35 s, 6 H (CH_3); 1.41 s, 6 H (CH_3); 2.27 m, 2 H (CH_2CF_2); 2.31 m, 2 H (CH_2CF_2); 3.34 bs, 1 H (OH); 3.46 dd, 1 H(a), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 2.5 (CH_2O); 3.49 dd, 1 H(a), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 2.5 (CH_2O); 3.55 m, 2 H (OC**H**$_2$CHO); 3.57 m, 2 H (OC**H**$_2$CHO); 3.60 dd, 1 H(b), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 1.0 (CH_2O); 3.62 dd, 1 H(b), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 1.0 (CH_2O); 3.70 dd, 1 H(a), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 4.5 (CH_2OC); 3.72 dd, 1 H(a), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 4.5 (CH_2OC); 4.03 dd, 1 H(b), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 1.6 (CH_2OC); 4.05 dd, 1 H(b), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 1.6 (CH_2OC); 4.26 m, 2 H (CHO). ^{13}C NMR ($CDCl_3$): 25.04 s, 2 C (CH_3); 26.39 s, 2 C (CH_3); 34.30 t, 1 C, $^2J_{CF}$ = 21 (C**H**$_2$CF$_2$); 34.36 t, 1 C, $^2J_{CF}$ = 21 (C**H**$_2$CF$_2$); 64.05 t, 1 C, $^3J_{CF}$ = 3 (CHOH); 66.04 s, 1 C (C**H**$_2$OC); 66.07 s, 1 C (C**H**$_2$OC); 72.19 s, 1 C (OC**H**$_2$CHO); 72.34 s, 1 C (OC**H**$_2$CHO); 74.56 s, 1 C (CH_2O); 74.62 s, 1 C (CH_2O); 74.93 s, 1 C (CHO); 74.99 s, 1 C (CHO); 109.52 s, 1 C (CO_2); 109.56 s, 1 C (CO_2); 105–125 m, 6 C (CF_2 and CF_3). ^{19}F NMR ($CDCl_3$): –81.49 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –113.33 m, 2 F (CF_2CH_2); –122.35 to –124.12 m, 6 F (CF_2); –126.62 m, 2 F (C**F**$_2$CF$_3$). For $C_{15}H_{17}F_{13}O_4$ (508.3) calculated: 35.4% C, 3.4% H, 48.6% F; found: 35.7% C, 3.5% H, 48.2% F.

2,2-Dimethyl-4-(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-heptadecafluoro-4-hydroxy-2-oxatridecyl)-1,3-dioxolane (**7**), yield 24.3 g (80%), b.p. 114–116 °C/2.7 Pa. ^{1}H NMR ($CDCl_3$), 2 diastereoisomers, A (52 rel.%), B (48 rel.%): 1.35 s, 6 H (CH_3); 1.41 s, 6 H (CH_3); 2.27 m, 2 H (CH_2CF_2); 2.31 m, 2 H (CH_2CF_2); 3.34 bs, 1 H (OH); 3.46 dd, 1 H(a), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 2.5 (CH_2O); 3.49 dd, 1 H(a), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 2.5 (CH_2O); 3.55 m, 2 H (OC**H**$_2$CHO); 3.57 m, 2 H (OC**H**$_2$CHO); 3.60 dd, 1 H(b), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 1.0 (CH_2O); 3.62 dd, 1 H(b), $^2J_{HH}$ = 6.5, $^3J_{HH}$ = 1.0 (CH_2O); 3.70 dd, 1 H(a), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 4.5 (CH_2OC); 3.72 dd, 1 H(a), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 4.5 (CH_2OC); 4.03 dd, 1 H(b), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 1.6 (CH_2OC); 4.05 dd, 1 H(b), $^2J_{HH}$ = 6.4, $^3J_{HH}$ = 1.6 (CH_2OC); 4.26 m, 2 H (CHO). ^{13}C NMR ($CDCl_3$): 25.04 s, 2 C (CH_3); 26.39 s, 2 C (CH_3); 34.30 t, 1 C, $^2J_{CF}$ = 21 (C**H**$_2$CF$_2$); 34.36 t, 1 C, $^2J_{CF}$ = 21 (C**H**$_2$CF$_2$); 64.05 t, 1 C, $^3J_{CF}$ = 3 (CHOH); 66.04 s, 1 C (C**H**$_2$OC); 66.07 s, 1 C (C**H**$_2$OC); 72.19 s, 1 C (OC**H**$_2$CHO); 72.34 s, 1 C (OC**H**$_2$CHO); 74.56 s, 1 C (CH_2O); 74.62 s, 1 C (CH_2O); 74.93 s, 1 C (CHO); 74.99 s, 1 C (CHO); 109.52 s, 1 C (CO_2); 109.56 s, 1 C (CO_2); 105–125 m, 8 C (CF_2 and CF_3). ^{19}F NMR ($CDCl_3$): –81.56 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –113.45 m, 2 F (CF_2CH_2); –122.35 to –125.13 m, 10 F (CF_2); –126.71 m, 2 F (C**F**$_2$CF$_3$). For $C_{17}H_{17}F_{17}O_4$ (608.3) calculated: 33.6% C, 2.8% H, 53.1% F; found: 33.5% C, 2.9% H, 53.2% F.

2,2,5-Trimethyl-5-(6,6,7,7,8,8,9,9,9-nonafluoro-4-hydroxy-2-oxanonyl)-1,3-dioxane (**12**), yield 17.9 g (82%), b.p. 102–105 °C/10.4 Pa. ^{1}H NMR (DMSO-d_6): 0.80 s, 3 H (CH_3); 1.29 s, 6 H (CH_3CO); 1.35 s, 6 H (CH_3CO); 2.21 m, 2 H (CH_2CF_2); 2.38 m, 2 H (CH_2CF_2); 3.32 dd, 2 H, $^2J_{HH}$ =10, $^3J_{HH}$ = 6.5 and 5 (CH_2O); 3.42 s, 2 H (CCH_2O); 3.43 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 6.5 and 5 (CH_2O); 3.49 d, 4 H, $^2J_{HH}$ = 12 (CCH_2O); 3.59 d, 4 H, $^2J_{HH}$ = 12 (CCH_2O); 4.08 m, 1 H (CH); 5.19 d, 1 H, $^3J_{HH}$ = 6 (OH). ^{13}C NMR (DMSO-d_6): 17.59 s, 1 C (CH_3); 21.31 s, 2 C (CH_3CO); 25.87 s, 2 C (CH_3CO); 33.89 s, 1 C (C); 34.21 t, 1 C, $^2J_{CF}$ = 21 (C**H**$_2$CF$_2$); 62.80 s, 1 C (CHO); 65.43 s, 2 C (C**C**H$_2$O); 73.52 s, 1 C (C**C**H$_2$O); 74.50 s, 1 C (CH_2O); 97.17 s, 1 C (CO_2); 105–125 m, 4 C (CF_2 and CF_3). ^{19}F NMR (DMSO-d_6): –80.65 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –111.22 dm, 2 F, $^2J_{FF}$ = 271 (CF_2CH_2); –121.50 m, 2 F (CF_2); –125.85 m, 2 F (C**F**$_2$CF$_3$). For $C_{15}H_{21}F_9O_4$ (436.3) calculated: 41.3% C, 4.9% H, 39.2% F; found: 41.5% C, 4.9% H, 39.7% F.

2,2,5-Trimethyl-5-(6,6,7,7,8,8,9,9,10,10,11,11,11-tridecafluoro-4-hydroxy-2-oxaundecyl)-1,3-dioxane (**13**), yield 21.5 g (80%), b.p. 101–103 °C/2.7 Pa, m.p. 37–39 °C. ^{1}H NMR (DMSO-d_6): 0.80 s, 3 H (CH_3); 1.29 s, 6 H (CH_3CO); 1.35 s, 6 H (CH_3CO); 2.21 m, 2 H (CH_2CF_2); 2.38 m, 2 H (CH_2CF_2); 3.32 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 6.5 and 5 (CH_2O); 3.42 s, 2 H (CCH_2O); 3.43 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 6.5 and 5 (CH_2O); 3.49 d, 4 H, $^2J_{HH}$ = 12 (CCH_2O); 3.59 d, 4 H, $^2J_{HH}$ = 12 (CCH_2O); 4.08 m, 1 H (CH); 5.19 d, 1 H, $^3J_{HH}$ = 6 (OH). ^{13}C NMR (DMSO-d_6): 17.59 s, 1 C (CH_3); 21.31 s, 2 C (CH_3CO); 25.87 s, 2 C (CH_3CO); 33.89 s, 1 C (C); 34.21 t, 1 C, $^2J_{CF}$ = 21 (CH_2CF_2); 62.80 s, 1 C (CHO); 65.43 s, 2 C (CCH_2O); 73.52 s, 1 C (CCH_2O); 74.50 s, 1 C (CH_2O); 97.17 s, 1 C (CO_2); 105–125 m, 6 C (CF_2 and CF_3). ^{19}F NMR (DMSO-d_6): –80.77 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –111.35 dm, 2 F, $^2J_{FF}$ = 271 (CF_2CH_2); –121.50 to –123.52 m, 6 F (CF_2); –125.98 m, 2 F (CF_2CF_3). For $C_{17}H_{21}F_{13}O_4$ (536.3) calculated: 38.1% C, 4.0% H, 46.0% F; found: 38.2% C, 4.1% H, 46.1% F.

2,2,5-Trimethyl-5-(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-heptadecafluoro-4-hydroxy-2-oxatridecyl)-1,3-dioxane (**14**), yield 24.5 g (77%), b.p. 106–108 °C/0.66 Pa, m.p. 47–49 °C. ^{1}H NMR (DMSO-d_6): 0.80 s, 3 H (CH_3); 1.29 s, 6 H (CH_3CO); 1.35 s, 6 H (CH_3CO); 2.21 m, 2 H (CH_2CF_2); 2.38 m, 2 H (CH_2CF_2); 3.32 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 6.5 and 5 (CH_2O); 3.42 s, 2 H (CCH_2O); 3.43 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 6.5 and 5 (CH_2O); 3.49 d, 4 H, $^2J_{HH}$ = 12 (CCH_2O); 3.59 d, 4 H, $^2J_{HH}$ = 12 (CCH_2O); 4.08 m, 1 H (CH); 5.19 d, 1 H, $^3J_{HH}$ = 6 (OH). ^{13}C NMR (DMSO-d_6): 17.59 s, 1 C (CH_3); 21.31 s, 2 C (CH_3CO); 25.87 s, 2 C (CH_3CO); 33.89 s, 1 C (C); 34.21 t, 1 C, $^2J_{CF}$ = 21 (CH_2CF_2); 62.80 s, 1 C (CHO); 65.43 s, 2 C (CCH_2O); 73.52 s, 1 C (CCH_2O); 74.50 s, 1 C (CH_2O); 97.17 s, 1 C (CO_2); 105–125 m, 8 C (CF_2 and CF_3). ^{19}F NMR (DMSO-d_6): –80.90 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –113.27 dm, 2 F, $^2J_{FF}$ = 271 (CF_2CH_2); –121.50 to –124.25 m, 10 F (CF_2); –126.11 m, 2 F (CF_2CF_3). For $C_{19}H_{21}F_{17}O_4$ (636.3) calculated: 35.9% C, 3.3% H, 50.8% F; found: 35.9% C, 3.4% H, 51.1% F.

Perfluoroalkylated Triols **8**–**10** and **15**–**17**. General Procedure

In the equipment as in the above procedures, a mixture of fluoroalkylated compound **5**–**7** or **12**–**14** (25 mmol), methanol (16 g, 0.5 mol) and concentrated hydrochloric acid (0.5 g) was refluxed for 2 h while stirring (complete conversion of the starting compounds, check by TLC). After evaporation of methanol, the residual water together with acid was removed by azeotropic fractional distillation with added toluene, which was distilled off.

8,8,9,9,10,10,11,11,11-Nonafluoro-4-oxaundecane-1,2,6-triol (**8**), yield 8.2 g (89%), m.p. 56–58 °C ($CHCl_3$–petroleum ether, 1 : 3). ^{1}H NMR (DMSO-d_6), 2 diastereoisomers, A (50 rel.%), B (50 rel.%): 2.22 m, 2 H (CH_2CF_2); 2.38 m, 2 H (CH_2CF_2); 3.36 m, 2 H (CH_2OH); 3.38 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 4.5 (OCH_2CH); 3.39 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 5 (CH_2O); 3.45 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 4.5 (OCH_2CH); 3.46 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 5 (CH_2O); 3.59 qi, 1 H, $^3J_{HH}$ = 5 ($CHCH_2OH$); 4.03 m, 1 H (CHOH); 4.29 bs, 1 H (CH_2OH); 4.45 bs, 1 H ($CH(OH)CH_2OH$); 4.99 bs, 1 H (CHOH). ^{19}F NMR (DMSO-d_6): –80.26 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –110.73 dm, 2 F, $^2J_{FF}$ = 271 (CF_2CH_2); –121.25 m, 2 F (CF_2); –125.45 m, 2 F (CF_2CF_3). For $C_{10}H_{13}F_9O_4$ (368.2) calculated: 32.6% C, 3.6% H, 46.4% F; found: 32.4% C, 3.8% H, 45.2% F.

8,8,9,9,10,10,11,11,12,12, 13,13,13-Tridecafluoro-4-oxatridecane-1,2,6-triol (**9**), yield 10.1 g (86%), m.p. 70–72 °C ($CHCl_3$–petroleum ether, 1 : 3). ^{1}H NMR (DMSO-d_6), 2 diastereoisomers, A (50 rel.%), B (50 rel.%): 2.22 m, 2 H (CH_2CF_2); 2.38 m, 2 H (CH_2CF_2); 3.36 m, 2 H (CH_2OH); 3.38 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 4.5 (OCH_2CH); 3.39 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 5 (CH_2O); 3.45 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 4.5 (OCH_2CH); 3.46 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 5

(CH_2O); 3.59 qi, 1 H, $^3J_{HH}$ = 5 (C**H**CH_2OH); 4.03 m, 1 H (C**H**OH); 4.29 bs, 1 H (CH_2O**H**); 4.45 bs, 1 H (CH(O**H**)CH_2OH); 4.99 bs, 1 H (CHO**H**). ^{19}F NMR (DMSO-d_6): –80.41 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –110.85 dm, 2 F, $^2J_{FF}$ = 271 (CF_2CH_2); –121.25 to –123.05 m, 6 F (CF_2); –125.59 m, 2 F (C**F**$_2CF_3$). For $C_{12}H_{13}F_{13}O_4$ (468.2) calculated: 30.8% C, 2.8% H, 52.7% F; found: 30.6% C, 2.9% H, 52.2% F.

8,8,9,9,10,10,11,11,12,12,13,13,14,14,15,15,15-Heptadecafluoro-4-oxapentadecane-1,2,6-triol (**10**), yield 12.5 g (88%), m.p. 83–85 °C ($CHCl_3$–petroleum ether, 1 : 3). ^{1}H NMR (DMSO-d_6), 2 diastereoisomers, A (50 rel.%), B (50 rel.%): 2.22 m, 2 H (CH_2CF_2); 2.38 m, 2 H (CH_2CF_2); 3.36 m, 2 H (C**H**$_2$OH); 3.38 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 4.5 (OC**H**$_2$CH); 3.39 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 5 (CH_2O); 3.45 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 4.5 (OC**H**$_2$CH); 3.46 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 5 (CH_2O); 3.59 qi, 1 H, $^3J_{HH}$ = 5 (C**H**CH_2OH); 4.03 m, 1 H (C**H**OH); 4.29 bs, 1 H (CH_2O**H**); 4.45 bs, 1 H (CH(O**H**)CH_2OH); 4.99 bs, 1 H (CHO**H**). ^{19}F NMR (DMSO-d_6): –80.55 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –112.21 dm, 2 F, $^2J_{FF}$ = 271 (CF_2CH_2); –121.25 to –124.13 m, 10 F (CF_2); –125.74 m, 2 F (C**F**$_2CF_3$). For $C_{14}H_{13}F_{17}O_4$ (568.2) calculated: 29.6% C, 2.3% H, 56.8% F; found: 30.0% C, 2.5% H, 55.2% F.

8,8,9,9,10,10,11,11,11-Nonafluoro-2-hydroxymethyl-2-methyl-4-oxaundecane-1,6-diol (**15**), yield 8.7 g (88%), m.p. 74–76 °C ($CHCl_3$–petroleum ether, 1 : 3). ^{1}H NMR (DMSO-d_6): 0.75 s, 3 H (CH_3); 2.22 m, 2 H (CH_2CF_2); 2.36 m, 2 H (CH_2CF_2); 3.24 m, 4 H (C**H**$_2$OH); 3.25 m, 2 H (CCH_2O); 3.28 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 7 and 5 (CH_2O); 3.39 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 7 and 5 (CH_2O); 4.02 m, 1 H (CHO); 4.33 t, 2 H, $^3J_{HH}$ = 5.5 (CH_2O**H**); 5.17 d, 1 H, $^3J_{HH}$ = 6 (CHO**H**). ^{19}F NMR (DMSO-d_6): –80.12 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –110.52 dm, 2 F, $^2J_{FF}$ = 270 (CF_2CH_2); –121.19 m, 2 F (CF_2); –125.25 m, 2 F (C**F**$_2CF_3$). For $C_{12}H_{17}F_9O_4$ (396.2) calculated: 36.4% C, 4.3% H, 43.2% F; found: 36.2% C, 4.3% H, 43.3% F.

8,8,9,9,10,10,11,11,12,12,13,13,13-Tridecafluoro-2-hydroxymethyl-2-methyl-4-oxatridecane-1,6-diol (**16**), yield 10.8 g (87%), m.p. 80–82 °C ($CHCl_3$–petroleum ether, 1 : 3). ^{1}H NMR (DMSO-d_6): 0.75 s, 3 H (CH_3); 2.22 m, 2 H (CH_2CF_2); 2.36 m, 2 H (CH_2CF_2); 3.24 m, 4 H (C**H**$_2$OH); 3.25 m, 2 H (CCH_2O); 3.28 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 7 and 5 (CH_2O); 3.39 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 7 and 5 (CH_2O); 4.02 m, 1 H (CHO); 4.33 t, 2 H, $^3J_{HH}$ = 5.5 (CH_2O**H**); 5.17 d, 1 H, $^3J_{HH}$ = 6 (CHO**H**). ^{19}F NMR (DMSO-d_6): –80.23 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –110.85 dm, 2 F, $^2J_{FF}$ = 270 (CF_2CH_2); –121.19 to –123.08 m, 6 F (CF_2); –125.41 m, 2 F (C**F**$_2CF_3$). For $C_{14}H_{17}F_{13}O_4$ (496.3) calculated: 33.9% C, 3.5% H, 49.8% F; found: 33.7% C, 3.4% H, 49.8% F.

8,8,9,9,10,10,11,11,12,12,13,13,14,14,15,15,15-Heptadecafluoro-2-hydroxymethyl-2-methyl-4-oxapentadecane-1,6-diol (**17**), yield 12.7 g (85%), m.p. 85–87 °C ($CHCl_3$–petroleum ether, 1 : 3). ^{1}H NMR (DMSO-d_6): 0.75 s, 3 H (CH_3); 2.22 m, 2 H (CH_2CF_2); 2.36 m, 2 H (CH_2CF_2); 3.24 m, 4 H (C**H**$_2$OH); 3.25 m, 2 H (CCH_2O); 3.28 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 7 and 5 (CH_2O); 3.39 dd, 2 H, $^2J_{HH}$ = 10, $^3J_{HH}$ = 7 and 5 (CH_2O); 4.02 m, 1 H (CHO); 4.33 t, 2 H, $^3J_{HH}$ = 5.5 (CH_2O**H**); 5.17 d, 1 H, $^3J_{HH}$ = 6 (CHO**H**). ^{19}F NMR (DMSO-d_6): –80.35 t, 3 F, $^3J_{FF}$ = 10 (CF_3); –112.37 dm, 2 F, $^2J_{FF}$ = 270 (CF_2CH_2); –121.19 to –124.32 m, 10 F (CF_2); –125.58 m, 2 F (C**F**$_2CF_3$). For $C_{16}H_{17}F_{17}O_4$ (596.3) calculated: 32.2% C, 2.9% H, 54.2% F; found: 32.1% C, 2.9% H, 54.3% F.

Fluoroalkylation of Propane-1,2-diol and Butane-1,3-diol with Epoxide **3** (Products **18** and **19**). General Procedure

In a round-bottomed flask (10 ml) equipped with a Dimroth reflux condenser connected with atmosphere through drying tube (KOH) and with magnetic spinbar, a mixture of pro-

pane-1,2-diol (2.0 g, 26.6 mmol) or butane-1,3-diol (2.4 g, 26.6 mmol), epoxide **3** (1.0 g, 2.66 mmol) and appropriate catalyst (0.44 mmol) was mixed at room temperature for 30 h (complete conversion of epoxide). The unreacted diol was distilled off in vacuum and the residue was separated by column chromatography (silica gel, 20 × 2.5 cm, acetone–petroleum ether, 1 : 4) to obtain product **18a** and **18b** or **19a** and **19b**. For regioselectivity of products and yields see Table I.

8,8,9,9,10,10,11,11,12,12,13,13,13-Tridecafluoro-4-oxatridecane-2,6-diol (**18a**) *and 7,7,8,8,9,9,10,10,11,11,12,12,12-tridecafluoro-2-methyl-3-oxadodecane-1,5-diol* (**18b**). NMR spectral data of **18a** (mixture of 2 diastereoisomers): ^{1}H NMR ($CDCl_3$): 1.03 d, 3 H, $^3J_{HH}$ = 6 (CH_3); 2.10–2.42 dm, 2 H (CH_2CF_2); 3.41 m, 4 H (CH_2O); 3.92 m, 1 H (OH); 4.12 bs, 1 H (OH); 4.22 dm, 2 H (CH). ^{13}C NMR ($CDCl_3$): 19.15 s, 1 C (CH_3); 35.08 t, 1 C, $^2J_{CF}$ = 21 ($\mathbf{C}H_2CF_2$); 65.00 s, 1 C (CHOH); 67.21 s, 1 C (CHOH); 75.48 s, 1 C (CH_2O); 75.62 s, 1 C (CH_2O); 77.56 s, 1 C (CH_2O); 107–124 m, 6 C (CF_2 and CF_3). ^{19}F NMR ($CDCl_3$): –81.54 tt, 3 F, $^3J_{FF}$ = 9.8, $^4J_{FF}$ = 2.5 (CF_3); –113.55 m, 2 F (CH_2CF_2); –122.29 to –124.09 m, 6 F (CF_2); –126.63 m, 2 F ($C\mathbf{F}_2CF_3$). NMR spectral data of **18b** (mixture of 2 diastereoisomers): ^{1}H NMR ($CDCl_3$): 1.07 d, 3 H, $^3J_{HH}$ = 6.5 (CH_3); 2.10 dm, 2 H (CH_2CF_2); 2.42 dm, 2 H (CH_2CF_2); 3.42 m, 4 H (CH_2O and CH_2OH); 3.59 dm, 1 H (OH); 4.12 bs, 1 H (OH); 4.18 dm, 2 H (CH); 4.26 dm, 2 H (CH). ^{13}C NMR ($CDCl_3$): 16.07 s, 1 C (CH_3); 16.25 s, 1 C (CH_3); 35.08 t, 1 C, $^2J_{CF}$ = 21 ($\mathbf{C}H_2CF_2$); 64.75 s, 1 C (CHO); 65.47 s, 1 C (CHO); 66.82 s, 1 C (CHOH); 66.84 s, 1 C (CHOH); 72.92 s, 1 C (CH_2OH); 73.56 s, 1 C (CH_2OH); 77.56 s, 1 C (CH_2O); 107–124 m, 6 C (CF_2 and CF_3). ^{19}F NMR ($CDCl_3$): –81.54 tt, 3 F, $^3J_{FF}$ = 9.8, $^4J_{FF}$ = 2.5 (CF_3); –113.55 m, 2 F (CH_2CF_2); –122.29 to –124.09 m, 6 F (CF_2); –126.63 m, 2 F ($C\mathbf{F}_2CF_3$). For $C_{12}H_{13}F_{13}O_3$ (452.2) calculated: 32.9% C, 2.9% H, 54.6% F; found: 32.9% C, 3.2% H, 54.8% F.

9,9,10,10,11,11,12,12,13,13,14,14,14-Tridecafluoro-5-oxatetradecane-2,7-diol (**19a**) *and 8,8,9,9, 10,10,11,11,12,12,13,13,13-tridecafluoro-3-methyl-4-oxatridecane-1,6-diol* (**19b**). NMR spectral data of **19a** (mixture of 2 diastereoisomers): ^{1}H NMR ($CDCl_3$): 1.14 d, 3 H, $^3J_{HH}$ = 6 (CH_3); 1.66 m, 2 H (CH_2); 2.10 dm, 2 H (CH_2CF_2); 2.42 dm, 2 H (CH_2CF_2); 3.39 m, 4 H (CH_2O); 3.97 dm, 1 H (OH); 4.08 bs, 1 H (OH); 4.18 dm, 2 H (CH); 4.26 dm, 2 H (CH). ^{13}C NMR ($CDCl_3$): 23.92 s, 1 C (CH_3); 35.22 t, 1 C, $^2J_{CF}$ = 21 ($\mathbf{C}H_2CF_2$); 38.66 s, 1 C (CH_2); 64.67 s, 1 C (CHOH); 67.12 s, 1 C (CHOH); 67.27 s, 1 C (CHOH); 70.12 s, 1 C (CH_2O); 70.25 s, 1 C (CH_2O); 75.16 s, 1 C (CH_2O); 75.26 s, 1 C (CH_2O); 107–124 m, 6 C (CF_2 and CF_3). ^{19}F NMR ($CDCl_3$): –81.54 tt, 3 F, $^3J_{FF}$ = 9.8, $^4J_{FF}$ = 2.5 (CF_3); –113.55 m, 2 F (CH_2CF_2); –122.29 to –124.09 m, 6 F (CF_2); –126.63 m, 2 F ($C\mathbf{F}_2CF_3$). NMR spectral data of **19b** (mixture of 2 diastereoisomers): ^{1}H NMR ($CDCl_3$): 1.18 d, 3 H, $^3J_{HH}$ = 6.5 (CH_3); 1.68 m, 2 H (CH_2); 2.10 dm, 2 H (CH_2CF_2); 2.42 dm, 2 H (CH_2CF_2); 3.39 m, 4 H (CH_2O and $C\mathbf{H}_2OH$); 3.62 dm, 1 H (OH); 4.12 bs, 1 H (OH); 4.18 dm, 2 H (CH); 4.26 dm, 2 H (CH). ^{13}C NMR ($CDCl_3$): 20.04 s, 1 C (CH_3); 20.15 s, 1 C (CH_3); 35.22 t, 1 C, $^2J_{CF}$ = 21 ($\mathbf{C}H_2CF_2$); 39.22 s, 1 C (CH_2); 60.45 s, 1 C (CHO); 60.59 s, 1 C (CHO); 65.20 s, 1 C (CHOH); 65.39 s, 1 C (CHOH); 72.49 s, 1 C (CH_2OH); 73.08 s, 1 C (CH_2OH); 75.50 s, 1 C (CH_2O); 107–124 m, 6 C (CF_2 and CF_3). ^{19}F NMR ($CDCl_3$): –81.54 tt, 3 F, $^3J_{FF}$ = 9.8, $^4J_{FF}$ = 2.5 (CF_3); –113.55 m, 2 F (CH_2CF_2); –122.29 to –124.09 m, 6 F (CF_2); –126.63 m, 2 F ($C\mathbf{F}_2CF_3$). For $C_{13}H_{15}F_{13}O_3$ (466.2) calculated: 33.5% C, 3.2% H, 53.0% F; found: 33.4% C, 3.0% H, 53.6% F.

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