37. Synthesis of Highly Fluorinated Di-*O*-alk(en)yl-glycerophospholipids and Evaluation of Their Biological Tolerance

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The syntheses of various fluorocarbon/fluorocarbon and fluorocarbon/hydrocarbon *rac*-1,2- and 1,3-di-*O*-alk(en)ylglycerophosphocholines and *rac*-1,2-di-*O*-alkylglycerophosphoethanolamines (see *Fig. 2*), which may be used as components for drug-carrier and delivery systems, are described together with some results concerning their biological tolerance. They were obtained by phosphorylation of perfluoroalkylated *rac*-di-*O*-alk(en)ylglycerols using $POCl_3$, then condensation with choline tosylate or *N*-Boc-ethanolamine (2-[(*tert*-butoxy)carbonylamino]ethanol) followed by Boc-deprotection (*Schemes 6–8*). The fluorocarbon/fluorocarbon 1,2-di-*O*-alkylglycerols were prepared by *O*-alkylation of *rac*-1-*O*-benzylglycerol using perfluoroalkylated mesylates, then hydrogenolysis for benzyl deprotection (*Scheme 1*). The two different hydrophobic chains in the mixed fluorocarbon/fluorocarbon and fluorocarbon/hydrocarbon 1,2-di-*O*-alk(en)ylglycerols were introduced starting from 1,2-*O*-isopropylidene- then *O*-trityl-protected glycerols or from 1,3-*O*-benzylidene-glycerol (*Schemes 3* and *4*). The perfluoroalkylated *O*-alkenylglycerols were obtained by *O*-alkylation of a glycerol derivative using an ω-unsaturated alkenyl reagent, the perfluoroalkyl segment being connected onto the double bond in a subsequent step (*Schemes 1* and *3*). The perfluoroalkylated symmetrical and mixed 1,3-di-*O*-alkylglycerols were synthesized by displacement of the Cl-atom in epichlorohydrin by perfluoroalkylated alcohols, then catalytic ($SnCl_4$) opening of the oxirane ring of the resulting alkyl glycidyl ethers in neat alcohols (*Scheme 5*). When injected intravenously into mice, acute maximum tolerated doses higher than 1500 and 2000 mg/kg body weight were observed for the fluorinated glycerophosphocholines, indicating a very promising *in vivo* tolerance.

1. Introduction. – Vesicles formed from phospholipids (liposomes) provide valuable chemical models for the study of biological membrane functions [1] as well as challenging *in vivo* delivery systems for enhancing the efficacy of various biologically active materials [2] [3]. Liposomes can reduce the toxicity of various antitumor agents, facilitate intracellular drug delivery, increase the tumoricidal activity of macrophages, and enhance the immune response and thus serve as artificial vaccines [2]. Recently, much effort has been focused on liposomes with increased residence in the bloodstream [3] [4]. Progress in this field allowed specific drug targeting to cells and organs [2–4].

The elaboration of liposomal systems with new or significantly improved properties implies the development of components that are substantially different from those currently utilized. Highly fluorinated amphiphiles (*Fig. 1*) are such components: they offer some of the specific features that make up the uniqueness of fluorinated material, *e.g.* their hydrophobic *and* lipophobic character.

A series of analogs of phosphatidylcholines (*Fig. 1*) having two perfluoroalkylated acyl chains, *i.e.*, bis-*O*-(perfluoroacyl)glycerol derivatives, have been synthesized in our laboratory [5]. These fluorinated phospholipids form liposomes [6] [7], their fluorinated tails creating inside the liposomal membrane a highly hydrophobic and lipophobic

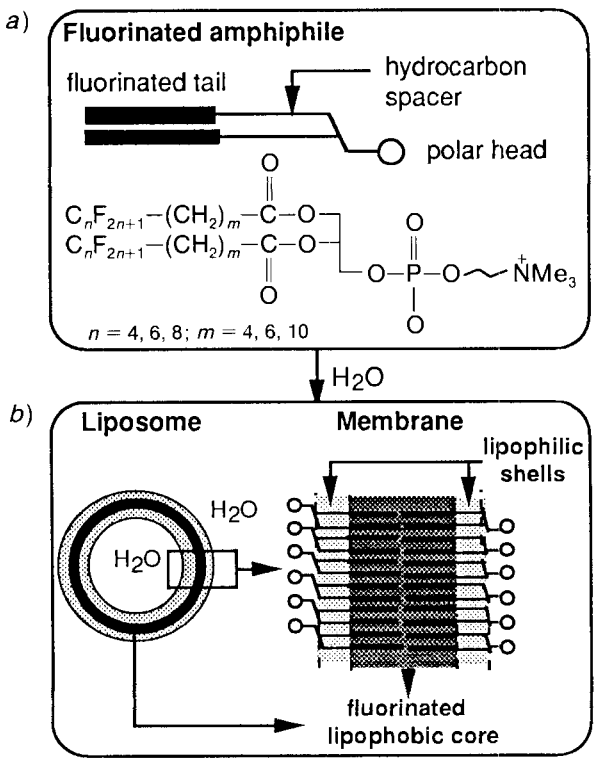


Fig. 1. a) *Concept of fluorinated amphiphile and molecular structure of fluorinated phosphatidylcholines.* b) *Structure of their corresponding membrane and liposome upon dispersion in water*

fluorocarbon layer (*Fig. 1*). This layer was shown to lower the membrane permeability and the release of encapsulated material [8], increase the stability of the liposomes in biological media [8], and prolonge their blood circulation [9]. Moreover, the preliminary assessments of the biological tolerance of these fluorinated phosphatidylcholines indicated a very low acute toxicity [5] [6a] which is a prerequisite when their use as *in vivo* drug-delivery devices is intended. To extend the range of fluorinated phospholipids, we have now explored the synthesis of 1,2-bis-*O*- and 1,3-bis-*O*-(perfluoroalkyl)glycerophospholipids (*Fig. 2*). Their ether moieties are intended to confer higher chemical and biological stability (in highly acidic media and more particularly towards the action of phospholipases) to these fluorinated phospholipids and to the liposomes that they will form.

We report in this paper the synthesis of various fluorocarbon/fluorocarbon and mixed fluorocarbon/hydrocarbon 1,2-di-*O*-alk(en)yl (**I**, **II**, and **IV**) and 1,3-di-*O*-alkyl glycerophospholipids (**III**; see *Fig. 2*) together with some results concerning their biological tolerance (hemolytic activity and acute toxicity in mice). Their molecular structures follow a modular design which allows incremental structural variations aimed at the establishment of structure/properties relationships. This design involves two hydrophobic chains, one (**IIB′** and **IIIB**) or both (**IA**, **IA′**, **IIA**, **IIIA**, and **IV**) of which end in a highly fluorinated tail, in combination with saturated (**IA**, **IIA**, **IIB′**, **III**, and **IV**) and/or

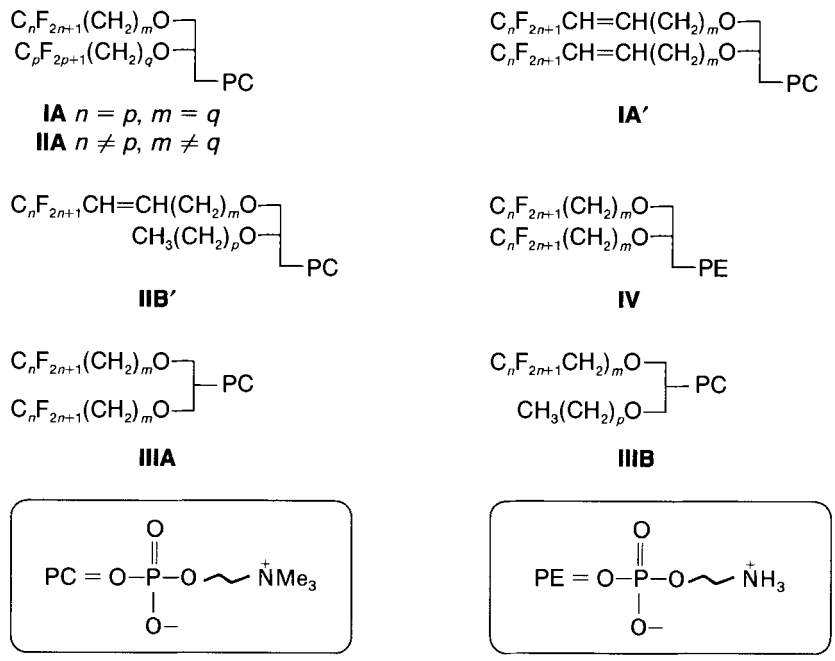


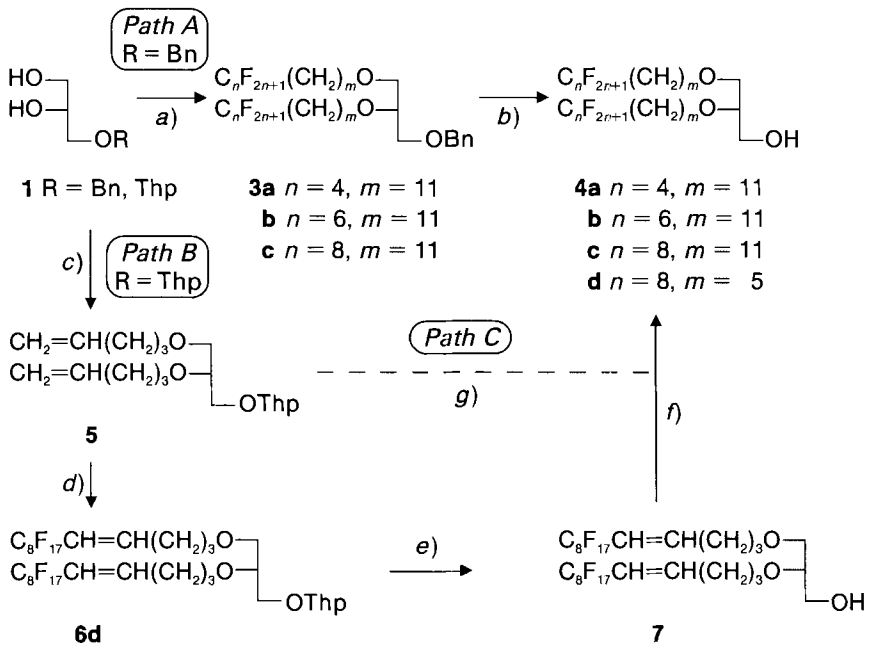
Fig. 2. *Molecular structure of the fluorocarbon/fluorocarbon and mixed fluorocarbon/hydrocarbon* rac-*1,2- and* rac-*1,3-di-O-alk(en)ylglycerophosphocholines* **I–III** *and -phosphoethanolamines* **IV**

unsaturated (**IA'** and **IIB'**) aliphatic chains connected through glycerol to phosphocholine (see **I–III**) or phosphoethanolamine (see **IV**) polar head groups. These structural features are expected to influence the hydrophobic-lipophobic/lipophilic/hydrophilic balance, and consequently the physico-chemical (stability, fluidity/rigidity, permeability) and biological (stability in biological fluids, interactions with bio compounds, *in vivo* fate) properties of the membranes and liposomes that these amphiphiles will form. The mixed fluorocarbon/hydrocarbon derivatives **IIB'** and **IIIB** were mainly designed in view of improving the miscibility of the fluorinated phospholipids with their hydrocarbon analogs [10]. Compounds **IA'** and **IIB'** were chosen for their double bonds which are known to affect substantially the physico-chemical properties of the membrane. The fluorinated phosphoethanolamines **IV** were selected for the primary-amine function they provide allowing the covalent conjugation of ligands (proteins, biotin, sugars, immunoglobulins, *etc.*) with the liposome's surface and thus favoring cell and organ targeting.

2. Results and Discussion. – 2.1. *Syntheses.* 2.1.1. *General.* The synthesis of di-*O*-alkylglycerophospholipids is well-documented in the literature and usually requires the preparation of the di-*O*-alkylglycerol precursors, the remaining OH group being phosphorylated in a final step [11]. These di-*O*-alkylglycerols were obtained from suitably protected glycerol derivatives. Their synthesis involved different strategies depending on the chemical structure of the di-*O*-alkylglycerol targets (1,2- or 1,3-isomers in which both chains are either identical or different).

2.1.2. *Fluorinated* rac-*1,2-Di-*O*-alk(en)ylglycerols.* The synthetic paths to the fluorinated *rac*-1,2-di-*O*-alkylglycerols **4** and *rac*-1,2-*O*-alkenylglycerol **7** in which both hydrophobic chains are identical are depicted in *Scheme 1*. These two series of compounds differ in the presence of a double bond in **7** between the perfluoroalkyl tail and the hydrocarbon spacer.

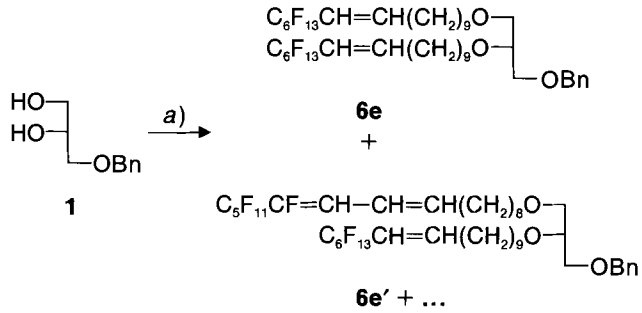
Scheme 1. *Synthesis of the Fluorocarbon/Fluorocarbon* rac-*1,2-Di-*O*-alkylglycerols* **4** *and* rac-*1,2-Di-*O*-alkenylglycerol* **7**



a) 1) NaH/THF; 2) $C_nF_{2n+1}(CH_2)_mX$ (X = OTs, OMs; **2a–c**) or 1) phase-transfer catalysis with **2a–c** (65–80%). *b*) H_2, Pd/C, EtOH/AcOH, 1.5 atm (*ca.* 100%). *c*) 1) NaH/THF; 2) $CH_2=CH(CH_2)_3OTs$ (**2d**) (60%). *d*) $C_8F_{17}I/CuCl/H_2N(CH_2)_2OH/t$-BuOH (75%). *e*) PPTS (95%). *f*) H_2, Pd/C, EtOH/AcOH, 40 atm (*ca.* 100%). *g*) 1) $C_nF_{2n+1}I$/AIBN; 2) Zn/HCl/EtOH.

The most straightforward synthesis of the 'saturated' compounds **4a–c** was performed by alkylation under phase-transfer-catalysis conditions of *rac*-1-*O*-benzylglycerol (**1**, R = Bn) using perfluoroalkyl tosylates or mesylates **2a–c** (→ **3a–c**; yields 65–80%) followed by hydrogenolysis for the removal of the benzyl protecting group which was rapid and almost quantitative when performed in the presence of AcOH (*Path A*). However, the alkylation step consumed a large quantity of the fluorinated reagents **2** as the conversion into the corresponding alcohols $C_nF_{2n+1}(CH_2)_mOH$ and ethers $C_nF_{2n+1}(CH_2)_mO(CH_2)_mC_nF_{2n+1}$ could not be avoided. Alternatively, the alkylation was also performed by reacting the dianion of **1** (R = Bn) with perfluoroalkyl tosylates or halides. In these cases, yields were lower (40%), and a competing elimination reaction (giving $C_nF_{2n+1}(CH_2)_{m-2}CH=CH_2$) was observed and was predominant when perfluoroalkyl bromides or iodides were used.

Scheme 2. *Alkylation of 1-O-Benzylglycerol* (**1**, R = Bn) *Using a Perfluoroalkenyl Mesylate*



a) 1) NaH/THF; 2) $C_6F_{13}CH{=}CH(CH_2)_9OMs$ (**2e**) or 1) phase-transfer catalysis with **2e**.

A similar direct strategy to prepare the fluorinated di-*O*-alkenylglycerols of type **7** starting from *rac*-1-*O*-benzylglycerol (**1**, R = Bn) and a perfluoroalkenyl mesylate such as **2e** was unsuccessful (*Scheme 2*). The alkylation of **1** (R = Bn) *via* its dianion or under phase-transfer catalysis resulted in an inextricable mixture of compounds. As shown by ^{1}H-, ^{13}C-, and ^{19}F-NMR, this mixture consisted of the desired derivative **6e** and of compounds having a CF=CH–CH=CH sequence in one (*e.g.* **6e'**) and/or in both hydrophobic chains, as a result of a 1,4-HF elimination initiated by the presence of acidic allylic protons.

The ^{19}F-NMR spectrum of the mixture exhibited, in addition to the expected signals for **6e** (same data as for **2e**, see *Exper. Part*), three new resonances located at −118.0 ($CF_2(\alpha)$), −123.6 ($CF_2(\beta)$), and −132.0 ppm (CF) consistent with a CF_2–CF_2–CF=CH sequence [11]. Its ^{13}C-NMR displayed, in agreement with a CF=CH–CH=CH sequence, a *d* (^1J(C,F) = 269 Hz) of *t*'s (^2J(C,F) = 29 Hz) at 145 ppm for CF^1), a *dt* (^3J(C,F) ≈ ^4J(C,F) ≈ 6 Hz) at 110.0 ppm, a *d* (^4J(C,F) = 5 Hz) at 139.9 ppm, and a *s* at 116.8 ppm for the ethylenic CH's in α,β, and γ to CF, respectively, in addition to the CH=CH resonances of **6e** (see data of **2e**). Moreover, **6e** accounted for less than 40% according to ^{19}F-NMR.

The *rac*-1,2-di-*O*-(perfluoroalkenyl)glycerol **7** was actually obtained using the strategy illustrated in *Scheme 1* (*Path B*). It implies first *O*-alkylation of *rac*-1-*O*-(tetrahydro-2*H*-pyran-2-yl)glycerol (**1**, R = Thp) using the ω-unsaturated alkenyl tosylate **2d** (→ **5**; 60%), followed by grafting the perfluoroalkyl segment onto the C=C bond of **5** and deprotection (Thp-protected glycerol was selected for the ease of its deprotection). The addition of a linear perfluoroalkyl iodide (R_FI) on a terminal CH_2=CH bond may be performed in high yields by various processes. One of the most attractive ways is the modified method of *Burton* and *Kehoe* [13a][2]) consisting of a one-pot two-step reaction, *i.e.*, radical addition of R_FI initiated by CuCl/2-aminoethanol and α,β-dehydroiodination in the presence of a base, which yields the perfluoroalkenyl derivative (mainly of (*E*)-configuration). When this method was applied to **5**, the addition of the R_F group to both its C=C bonds and subsequent HI elimination, led to **6d** and, after deprotection, to **7** in 70%

[1]) These ^{19}F- and ^{13}C-NMR data are consistent with those published for a compound having also a CF_2–CF=CH sequence [12].

[2]) Another attractive way would have been the two-step sequence developed by *Brace* [13b] which consists in the radical addition of perfluorooctyl iodide on **5** initiated by α,α'-azobisisobutyronitrile (= 2,2'-azobis[2-methylpropanenitrile]; AIBN) followed by HI elimination under the action of base.

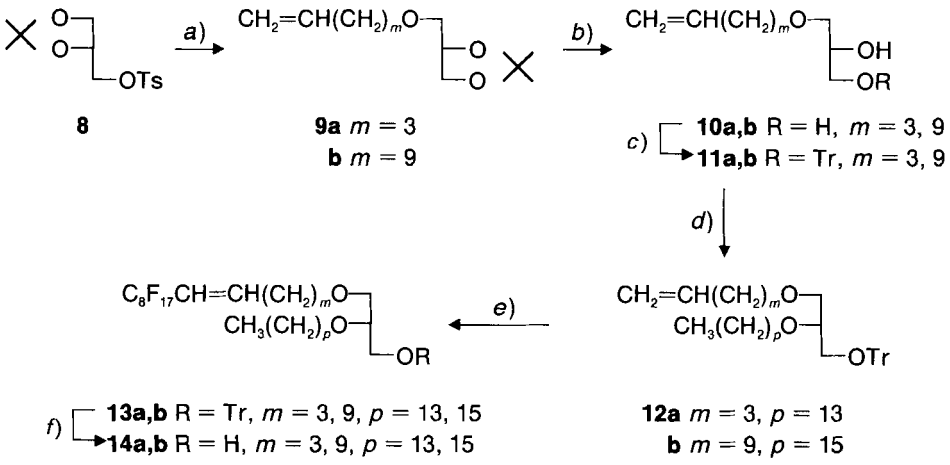
overall yield. Under these conditions, no HF elimination was observed. However, according to ^{19}F-NMR which showed more particularly the presence of two resonances for the CF_2 in α to the C=C bonds, the isolated compounds **6d** and **7** consisted each of a mixture of isomers differing in the configuration of their two C=C bonds. The most abundant one was the (*E,E*)-isomer (at least 80%). These products were contaminated by compound(s) (less than 10%) which possess(es) a CF_2–CH_2–CH=CH sequence in one and/or in both hydrophobic chains, as a result of a β,γ-HI elimination during the perfluoroalkylation step [13a]. This was evident from the ^{1}H-, ^{13}C-, and ^{19}F-NMR spectra of **7** (*dt* (^3J(H,H) = 7 Hz, ^3J(H,F) = 18 Hz) at 2.7 ppm and *t* (^2J(C,F) = 23 Hz) at 34.7 ppm for CH_2 and CF_2 at −115.8 ppm). This was further confirmed by the almost quantitative conversion of this mixture of double-bond isomers into their common saturated derivative **4d** by high-pressure hydrogenolysis.

Although a mixture of alkenyl isomers was obtained, the reaction sequence illustrated in *Scheme 1, Path B*, remains the best way for the synthesis of fluorinated di-*O*-alkenylglycerol derivatives such as **7**. One of its advantages lies also in the alkylation step which is not performed with expensive fluorinated material. Another advantage of this strategy is its versatility as the same synthon **5** can be used for the preparation of various unsaturated 1,2-di-*O*-substituted glycerols of type **7**, and even of saturated ones such as **4** (*vide supra*), differing in the length of their perfluoroalkyl tails. The alternative route to **4** starting from **5** which consists in the radical addition of a perfluoroalkyl iodide (R_FI) followed by reduction of the C–I bond in the R_FCH_2CHI intermediate, as exemplified in *Scheme 1, Path C*, was *a priori* excluded, as it was shown that this route is not very efficient when two intramolecular C=C bonds are concerned [14].

The more demanding synthetic routes to the mixed fluorocarbon/hydrocarbon (see **14**) and fluorocarbon/fluorocarbon (see **19**) *rac*-1,2-di-*O*-alk(en)ylglycerols are depicted in *Schemes 3* and *4*, respectively. Appropriate protecting groups were required in these cases so as to allow the selective and stepwise 1- and 2-*O*-alkylation of glycerol.

The synthesis of the mixed fluorocarbon/hydrocarbon 1,2-di-*O*-substituted glycerol derivatives **14** was performed using 1,2-*O*-isopropylidene- and *O*-trityl-protected glycerol intermediates (*Scheme 3*). The *O*-alkylation of the secondary OH group of glycerol being more difficult to achieve than that of its primary OH groups, we connected the hydrocarbon chain to glycerol in the 2-position using the commercially available long-chain aliphatic halides. The fluorocarbon chain was introduced in position 1 of glycerol using the two-step sequence mentioned above (*Scheme 1, Path B*). Compounds **9** were obtained in rather good yields (65–90%) by reacting an ω-unsaturated alkoxide with 1,2-*O*-isopropylidene-protected tosylate **8**. Hydrolysis of the isopropylidene group (→ **10**), tritylation (→ **11**), and subsequent alkylation under phase-transfer conditions using a long-chain alkyl iodide or bromide afforded compounds **12** in 40–50% yields. The latter reaction took very long, due to the low reactivity of the OH group and to the steric hindrance by the trityl group in **11**. Activation of the OH group in **11** *via* its thallium alkoxide derivative and further reaction with an alkyl bromide [15] or *via* its 4-nitrobenzenesulfonate and then reaction with a long-chain alkoxide [16] did not give better results in our case. The fluorinated tail was then introduced in **12** using the above described method, giving **13** ($(Z/E) \leq 10\%$ according to ^{19}F-NMR). Formation of **13** was also accompanied by that of the isomer having the CF_2–CH_2–CH=CH sequence ($\leq 5\%$). Detritylation of **13** yielding **14** was best performed using BF_3/MeOH [17]. Under these

Scheme 3. *Synthesis of the Mixed Fluorocarbon/Hydrocarbon* rac-*1*-O-*Alkenyl*-*2*-O-*alkylglycerols* **14**

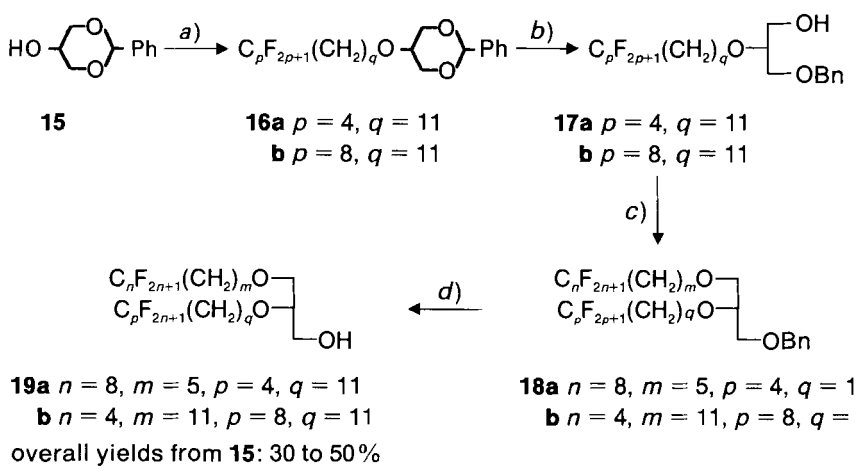


a) $CH_2{=}CH(CH_2)_mONa$ (65–90%). *b*) HCl. *c*) TrCl/Py (70–85% from **9**). *d*) Phase-transfer catalysis with $CH_3(CH_2)_pX$, X = Br, I (40–50%). *e*) $C_8F_{17}I/CuCl/H_2N(CH_2)_2OH/t$-BuOH. *f*) BF_3/MeOH (70–85% from **12**).

conditions, detritylation was more rapid and occurred in higher yields than with HBr in AcOH or HCl in MeOH. Starting from tosylate **8**, this six-step sequence afforded the mixed fluorocarbon/hydrocarbon 1,2-di-*O*-substituted glycerol derivatives **14** in 10–30% overall yields.

The preparation of the mixed fluorocarbon/fluorocarbon 1,2-di-*O*-substituted glycerol derivatives **19** (*Scheme 4*) was performed starting from *cis*-1,3-*O*-benzylideneglyc-

Scheme 4. *Synthesis of the Mixed Fluorocarbon/Fluorocarbon* rac-*1,2-Di*-O-*alkylglycerols* **19**



a) 1) NaH/THF; 2) $C_pF_{2p+1}(CH_2)_qOMs$; (**2a'** or **2c**, resp.) (70–75%). *b*) BH_3/THF (70–85%). *c*) 1) NaH/THF; 2) **2f** or **2a'** or 1) phase-transfer catalysis with **2f** or **2a'** (65–75%). *d*) H_2, Pd/C, EtOH/AcOH, 1.5 atm (*ca.* 100%).

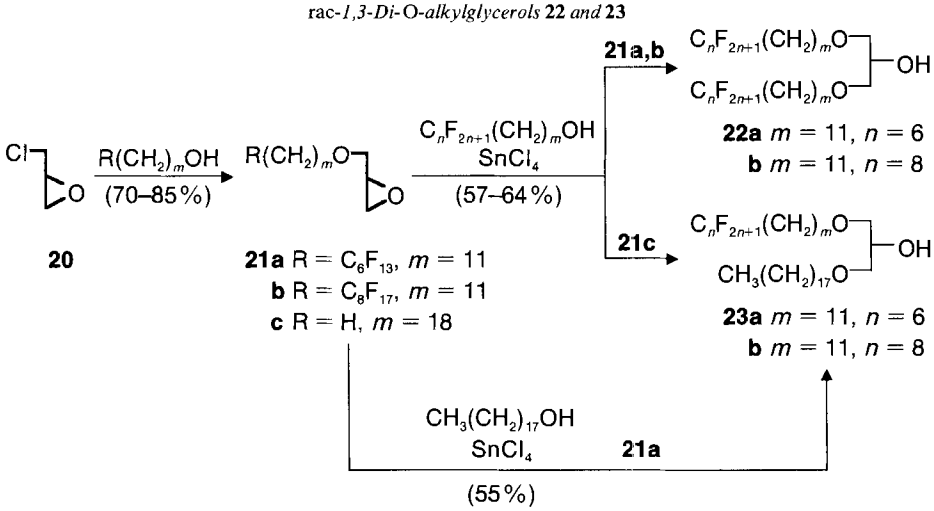
erol (**15**) [18]. In this strained cyclo-protected glycerol, the secondary OH function was shown to be more accessible and easier to alkylate than in acyclic protected analogs [19]. It is, therefore, a convenient precursor for introducing an expensive fluorinated chain. Furthermore, ring-opening using appropriate reagents will result in the formation of a glycerol derivative containing a free primary OH group, ready for a subsequent alkylation step while the other one is protected by the benzyl group. Alkylation of **15** (*via* its anion) was realized using perfluoroalkyl methanesulfonates **2** (see *Scheme 1*), and yields of **16** as high as 70–75% were attained. The reductive cleavage of the 1,3-*O*-benzylidene protecting group in **16** with the BH_3/THF complex [19] gave the benzyl-protected derivatives **17** in 70–85% yields. Alkylation of the remaining free OH group using the appropriate perfluoroalkylated methanesulfonate **2**, then benzyl deprotection by hydrogenolysis afforded the mixed fluorocarbon/fluorocarbon 1,2-di-*O*-substituted glycerol derivatives **19** in 30–45% overall yields starting from 1,3-*O*-benzylideneglycerol (**15**).

The 1,3-*O*-benzylideneglycerol approach to mixed fluorinated 1,2-di-*O*-alkylglycerols thus appears to be a more attractive method than the 1,2-*O*-isopropylidene and *O*-trityl route (30–45% *vs.* 10–30% yields). Its major drawback lies in the synthesis and purification of 1,3-*O*-benzylideneglycerol (**15**): the *cis*- and *trans*-isomer of **15** are obtained in poorly reproducible yields ($\leq$ 40%), and the competing formation of the 1,2-*O*-benzylideneglycerol isomers, which cannot be avoided, complicates its purification [18].

2.1.3. *Fluorinated 1,3-Di-*O*-alkylglycerols.* The synthetic routes to the fluorocarbon/fluorocarbon and mixed fluorocarbon/hydrocarbon 1,3-di-*O*-alkylglycerols **22** and **23** are depicted in *Scheme 5*. They were prepared from epichlorohydrin (**20**) in a two-step sequence which involves a nucleophilic substitution followed by opening of the epoxide ring. In this very flexible sequence, both hydrophobic chains are introduced stepwise, and it is, therefore, possible to prepare a large variety of compounds.

The nucleophilic substitution of the Cl-atom in **20** was performed under phase-transfer conditions using either a perfluoroalkylated alcohol or octadecanol, and the corre-

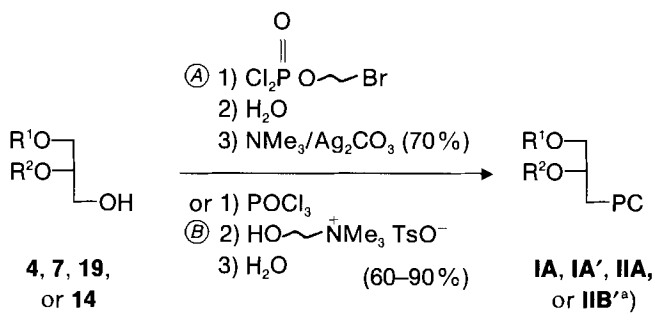
Scheme 5. *Synthesis of the Fluorocarbon/Fluorocarbon and Mixed Fluorocarbon/Hydrocarbon* rac-*1,3-Di-*O*-alkylglycerols* **22** *and* **23**



sponding long-chain glycidyl ethers **21a–c** were obtained in 70–80% yield. The opening of the oxirane ring in these glycidyl ethers was realized in neat perfluoroalkylated alcohols (and in octadecanol in the case of **21a**) in the presence of $SnCl_4$ as catalyst, giving the fluorocarbon/fluorocarbon and mixed fluorocarbon/hydrocarbon 1,3-di-*O*-alkylglycerols **22a,b** and **23a,b**, respectively, in 55% yield. Yields in 1,3-di-*O*-substituted compounds could not be improved: on oxirane opening using the regioselective BF_3/Et_2O catalytic system which was reported as being very efficient [20], the yields never exceeded 30% in our case. For the synthesis of **22** in which both fluorocarbon chains are identical, the one-step procedure which consists in reacting epichlorohydrin (**20**) with 2 equiv. of alkoxide was not very successful (yields $\leq$ 10%) [21].

2.1.4. *Fluorinated Di-*O*-alk(en)ylglycerophospholipids.* The importance of phospholipids in biological processes has stimulated numerous studies concerning their chemistry, and various routes [11] were, therefore, devised for their synthesis. Most of them imply the preparation of cyclic phosphates of di-*O*-alkyl- or di-*O*-acylglycerols and subsequent

Scheme 6. *Synthesis of the Fluorocarbon* rac-*1,2-Di-*O*-alk(en)yl- and* rac-*1-*O*-Alkenyl-2-*O*-alkylglycero-3-phosphocholines* **I** *and* **II**



H_2/Pd, C (40 atm) (100%)

4a–d ⟶ IAa–d

$R^1 = R^2 = C_nF_{2n+1}(CH_2)_m$

a $n = 4$, $m = 11$
b $n = 6$, $m = 11$
c $n = 8$, $m = 11$
d $n = 8$, $m = 5$

7 ⟶ IA′d

$R^1 = R^2 = C_nF_{2n+1}CH{=}CH(CH_2)_m$

d $n = 8$, $m = 3$

19a,b ⟶ IIAa,b

$R^1 = C_nF_{2n+1}(CH_2)_m$, $R^2{=}C_pF_{2p+1}(CH_2)_q$

a $n = 8$, $m = 5$, $p = 4$, $q = 11$
b $n = 4$, $m = 11$, $p = 8$, $q = 11$

14a,b ⟶ IIB′a,b

$R^1 = C_nF_{2n+1}CH{=}CH(CH_2)_m$, $R^2 = CH_3(CH_2)_p$

a $n = 8$, $m = 3$, $p = 13$
b $n = 8$, $m = 9$, $p = 15$

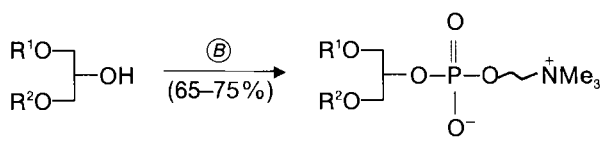
[a]) For the general formulae of **IA**, **IA′**, **IIA**, and **IIB′**, see *Fig. 2*.

ring opening of these cyclic intermediates in the presence of an amine or a hydracid. These methods have some drawbacks including the preparation of cyclic intermediates and the formation of by-products and subsequent problematic purifications during the ring-opening reaction by amines [11]. Recently, means of overcoming some of these problems have been devised [22] [23].

The preparation of the fluorinated phosphatidylcholines displayed in *Fig. 1* (60% yields) was achieved using an alternative and more versatile route which consists in the direct phosphorylation of fluorinated di-*O*-acylglycerols by 2-bromoethyl phosphorodichloridate and then direct amination with trimethylamine (*Method A*, *Scheme 6*) [5]. When this method was applied to the fluorinated di-*O*-alkyl analog **4a**, yields in **IAa** as high as 70% were obtained.

Another simple and efficient route was also applied for preparing fluorocarbon single-chain phosphocholine derivatives (55–73% yields) [24]. It consists in a three-step one-pot sequence (*Method B*, *Scheme 6*), *i.e.*, direct phosphorylation of the perfluoroalkylated alcohol by $POCl_3$ and then condensation with choline tosylate, a method which was also reported to afford di-*O*-alkylglycerophosphocholines in yields ranging from 70 to 85% [20]. This approach when applied to the fluorocarbon 1,2-di-*O*-alk(en)ylglycerol derivatives **4**, **7**, **14**, and **19** (*Scheme 6*) gave the corresponding 3-phosphocholines **IA**, **IA′**, **IIB′**, and **IIA** in 60–90% yield. This method was very efficient as the fluorocarbon 1,3-di-*O*-alkylglycero-2-phosphocholines **IIIA** and **IIIB** were also obtained in good yields (65–75%) in spite of the lower reactivity of the secondary OH group in the 1,3-di-*O*-substituted glycerols **22** and **23** (*Scheme 7*). It is noticeable that the fluorocar-

Scheme 7. *Synthesis of the Fluorocarbon* rac-*1,3-Di-*O*-alkyl-glycero-2-phosphocholines* **III**



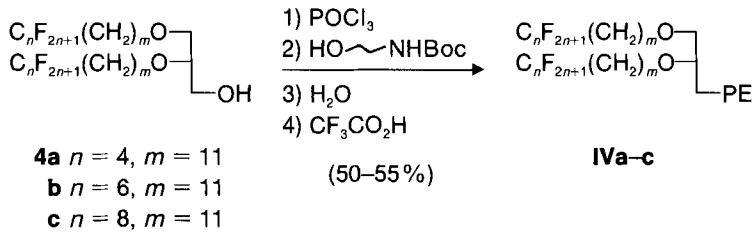
22 or **23** **IIIA** or **IIIB**

22a,b ⟶ **IIIAa,b**	**23a,b** ⟶ **IIIBa,b**
$R^1 = R^2 = C_nF_{2n+1}(CH_2)_m$	$R^1 = C_nF_{2n+1}(CH_2)_m$, $R^2 = CH_3(CH_2)_p$
a $n = 6$, $m = 11$	**a** $n = 6$, $m = 11$, $p = 17$
b $n = 8$, $m = 11$	**b** $n = 8$, $m = 11$, $p = 17$

bon 1,2-di-*O*-alkenylglycerol synthon **7** can be used for the synthesis not only of the alkenyl-phosphocholines **IA′d** but also of its saturated analog **IAd**, as shown by the quantitative high-pressure hydrogenolysis of **IA′d** into **IAd** (*Scheme 6*).

For the synthesis of the fluorocarbon *rac*-1,2-di-*O*-alkylglycero-3-phosphoethanolamines **IVa–c**, a similar approach (*Scheme 8*) was used, phosphorylation of the glycerol derivatives **4a–c** with $POCl_3$, condensation with *N*-Boc-ethanolamine (2-[(*tert*-butoxy)-carbonylamino]ethanol), hydrolysis, and then Boc-deprotection using CF_3COOH [11] giving the desired compounds in 50–55% yields.

Scheme 8. *Synthesis of the Fluorocarbon* rac-*1,2-Di-*O*-alkylglycero-3-phosphoethanolamines* **IV**



4a $n = 4$, $m = 11$
b $n = 6$, $m = 11$
c $n = 8$, $m = 11$

(50–55%)

IVa–c

2.2. *Biological Acceptance.* Biocompatibility is a major concern for drug-carrier components. It was, therefore, essential to check the *in vivo* and *in vitro* tolerance of these new fluorinated di-*O*-alkylglycerophospholipids. This section presents our results from hemolysis and acute-toxicity evaluations concerning a fluorocarbon/fluorocarbon (**IAa**) and a mixed alkenyl fluorocarbon/hydrocarbon glycerophosphocholine (**IIB'b**) which can be considered as being representative. The results of these preliminary toxicity tests are promising.

The tests for hemolytic activity were performed *in vitro* on human red blood cell suspensions [25]. It was found that 30 g/l concentrated liposomal dispersions of compound **IAa** had no detectable hemolytic effect. This result is in line with the low hemolytic activity which has been generally found for various series of fluorinated amphiphiles [26].

Concerning acute toxicity in mice, isotonic liposomal dispersions of **IAa** and **IIB'b** at various concentrations, when injected in the tail vein of mice (10 animals), allowed an estimation of their maximum tolerated dose (*MTD*) compatible with the survival of all injected animals. Acute *MTD* values higher than 1500 and 2000 mg/kg body weight were observed for **IAa** and **IIB'b**, respectively, indicating a very promising *in vivo* tolerance for these series of fluorinated di-*O*-alkylglycerophospholipids, as for their di-*O*-acyl analogs [5] [6a]. These two compounds are among the few perfluoroalkylated amphiphiles reported so far that were found to exhibit such high *MTD* values, confirming that the presence of highly fluorinated tail(s) does not affect acute toxicity [6a] [26].

In conclusion, the described syntheses provide easy and efficient routes to a wide range of perfluoroalkylated di-*O*-alk(en)ylglycerophospholipids. The perfluoroalkylated, chemically stable di-*O*-alk(en)ylglycerophosphocholines do form long-term, shelf-stable, and heat-sterilizable liposomes; further, their biological tolerance is most promising. These liposomes as drug-carrier and delivery systems show also much promise: their potential, which include studies concerning membrane permeability and stability (with respect to encapsulated carboxyfluorescein release) in biological fluids will be reported elsewhere. Thus, we found that the release of carboxyfluorescein from liposomes made from the perfluoroalkylated di-*O*-alkylglycerophosphocholines was much lower than from conventional di-*O*-acylglycerophospholipids, even when incubated in human serum.

The financial support of the *CNRS* and the technical assistance of the *Centre de la Transfusion Sanguine des Alpes-Maritimes* for the biological *in vivo* tests are gratefully acknowledged. The authors are indebted to Prof. *J. G. Riess* for permanent support of their research.

Experimental Part

1. *General.* Unless indicated otherwise, the reactions were performed under anh. N_2 using dry solvents and reagents. Anh. solvents were prepared by standard methods. The perfluoroalkylated alcohols were synthesized from perfluoroalkyl iodides (*Atochem*) and commercially available α,ω-alkenyl alcohols according to [5] [13], and [24]. Choline tosylate ((2-hydroxyethyl)trimethylammonium toluene-4-sulfonate) was prepared by neutralizing a commercial 50% aq. choline hydroxyde soln. (*Aldrich*) with toluene-4-sulfonic acid, dried then recrystallized from acetone, and stored under dry N_2. $POCl_3$ was distilled before use. Pyridinium toluene-4-sulfonate (PPTS) was prepared from pyridine and toluene-4-sulfonic acid monohydrate [27]. Toluene-4-sulfonyl chloride (TsCl; from *Aldrich*) was recrystallized from $CHCl_3$/pentan before use. The 1,2-*O*-isopropylideneglycerol was purchased from *Lancaster*. *rac*-1-*O*-Benzylglycerol (**1**, R = Bn) [5], 1,3-*O*-benzylideneglycerol (**15**) [28], and 2-bromoethyl phosphorodichloridate [5] were prepared according to published methods. *rac*-1-*O*-(tetrahydro-2*H*-pyran-2-yl)-glycerol (**1**, R = Thp) was synthesized by oxidation of tetrahydro-2*H*-pyran-2-yl allyl ether [28]. The purity of all new compounds was checked by thin-layer chromatography (TLC), NMR and/or elemental analysis. Column chromatography (CC): silica gel *60* (*Merck*, 70–230 mesh). TLC: precoated silica gel F_{254} plates (*Merck*), detection by UV and by charring with 50% $MeOH/H_2SO_4$ soln. and, for the phospholipids, with ninhydrin, *Dragendorff*'s and molybdenum-blue reagents (*Sigma*); R_f 0.35 ($CHCl_3$/MeOH/H_2O 65:35:4 (*v*/*v*)) and 0.75 ($CHCl_3$/MeOH/16N NH_3 60:30:6 (*v*/*v*)) for the phosphocholines **I**–**III** and phosphoethanolamines **IV**, resp. ^{1}H-, ^{13}C-, ^{19}F-, and $^{31}P\{^1H\}$-NMR Spectra: at 200, 50.3, 188.3, and 81 MHz, resp.; *Bruker-AC-200* spectrometer; chemical shifts δ in ppm rel. to the internal ref. Me_4Si or indirectly to $CHCl_3$ (δ 7.27) for ^{1}H, to internal ref. Me_4Si or indirectly to $CDCl_3$ (δ 76.9) for ^{13}C, to internal ref. $CFCl_3$ for ^{19}F, and to external ref. 75% H_3PO_4 soln. for ^{31}P; *J* in Hz; some ^{1}H-NMR spectra were recorded at 80 MHz with a *Bruker-CW-80* spectrometer. The elemental analyses were performed by the Service Central de Microanalyses of the CNRS.

2. *Starting Materials. 12,12,13,13,14,14,15,15,15-Nonafluoropentadecyl Toluene-4-sulfonate* (**2a**). At −15°, 12,12,13,13,14,14,15,15,15-nonafluoropentadecanol (18.0 g, 46.2 mmol), TsCl (10.5 g, 55.1 mmol), and dry pyridine (100 ml) were stirred for 5 h. After evaporation of pyridine, $CHCl_3$ was added and the soln. washed with H_2O, then dried, and evaporated. The residue was purified by CC (Et_2O): 22.2 g (88%) of **2a**. Colorless oil. TLC (CH_2Cl_2): R_f 0.84. ^{1}H-NMR ($CDCl_3$): 1.16–1.50 (br. *s*, $CF_2(CH_2)_2(CH_2)_7$); 1.51–1.80 (*m*, $CF_2CH_2CH_2$, CH_2CH_2O); 2.01 (*tt*, ^3J = 7.8, ^3J(H,F) = 18.8, CF_2CH_2); 2.47 (*s*, Me); 4.05 (*t*, ^3J = 6.5, CH_2OTs); 7.37 (*d*, ^3J = 8.0, 2 H_m); 7.82 (*d*, ^3J = 8.0, 2 H_o). ^{13}C-NMR ($CDCl_3$): 20.1 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 21.5 (*s*, Me); 28.7 (*s*, $CH_2(CH_2)_2O$); 28.8, 28.9, 29.0, 29.1, 29.2, 29.3, 29.4 (7*s*, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.8 (*t*, ^2J(C,F) = 22 Hz, CF_2CH_2); 70.6 (*s*, CH_2O); 127.9, 129.8 (2*s*, C_o, C_m); 133.4 (*s*, C_p); 144.6 (*s*, C_{ipso}). ^{19}F-NMR ($CDCl_3$): −81.5 (CF_3); −115.1 (CF_2CH_2); −125.0 ($CF_3CF_2CF_2$); −126.5 (CF_3CF_2).

12,12,13,13,14,14,15,15,15-Nonafluoropentadecyl Methanesulfonate (**2a′**). As described for **2a**, with 12,12,13,13,14,14,15,15,15-nonafluoropentadecanol (15.0 g, 38.5 mmol) and methanesulfonyl chloride (MsCl; 5.7 g, 49.7 mmol): **2a′** (16.6 g, 92%). White crystals. TLC (CH_2Cl_2): R_f 0.85. ^{1}H-NMR ($CDCl_3$): 1.14–1.42 (br. *s*, $CF_2(CH_2)_2(CH_2)_7$); 1.43–1.60 (*m*, $CF_2CH_2CH_2$); 1.80 (*quint.*, ^3J = 7.8, CH_2CH_2O); 2.00 (*tt*, ^3J = 7.8, ^3J(H,F) = 18.8, CF_2CH_2); 2.93 (*s*, Me); 4.15 (*t*, ^3J = 6.5, CH_2O). ^{13}C-NMR ($CDCl_3$): 20.1 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 25.4 (*s*, $CH_2(CH_2)_2O$); 29.0, 29.1, 29.2, 29.3, 29.4 (5*s*, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.8 (*t*, ^2J(C,F) = 23, CF_2CH_2); 37.4 (*s*, MeS); 70.1 (*s*, CH_2O). ^{19}F-NMR ($CDCl_3$): identical to that of **2a**.

12,12,13,13,14,14,15,15,16,16,17,17,17-Tridecafluoroheptadecyl Methanesulfonate (**2b**). As described for **2a**, with 12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecanol (21.0 g, 4.27 mmol) and MsCl (6.6 g, 57.6 mmol) in anh. pyridine (25 ml); **2b** (21.3 g, 88%). White crystals. TLC (CH_2Cl_2): R_f 0.85. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **2a′**. ^{19}F-NMR ($CDCl_3$): −81.3 (CF_3); −114.9 (CF_2CH_2); −122.4, −123.4, −124.1 (each 2F, $CF_3CF_2(CF_2)_3$); −126.6 (CF_3CF_2).

12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-Heptadecafluorononadecyl Methanesulfonate (**2c**). As described for **2a**, with 12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecanol (7.0 g, 11.8 mmol) and MsCl (1.8 g, 15.4 mmol): **2c** (7.2 g, 90%). White crystals. TLC (CH_2Cl_2): R_f 0.84. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **2a′**. ^{19}F-NMR ($CDCl_3$): −81.8 (CF_3); −115.3 (CF_2CH_2); −122.7, −123.6, −124.4 (6F, 2F, 2F, $CF_3CF_2(CF_2)_5$); −127.1 (CF_3CF_2).

Pent-4-enyl Toluene-4-sulfonate (**2d**). As described for **2a**, with pent-4-en-1-ol (12.6 g, 150 mmol) and toluene-4-sulfonyl chloride (27.9 g, 150 mmol): 30.9 g (88%) of **2d**. Oil which crystallized at r.t. TLC (CH_2Cl_2): R_f 0.84, ^{1}H-NMR (80 MHz, CCl_4): 1.50–1.80 (*m*, $(CH_2)_2CH_2O$); 2.16 (*dt*, both ^3J = 8.0, CH_2=$CHCH_2$); 2.40 (*s*, Me); 4.03 (*t*, ^3J = 6.0, CH_2OTs); 4.72–5.12 (*m*, CH_2=CH); 5.45–6.00 (*m*, CH_2=CH); 7.33 (*d*, ^3J = 8.0, 2 H_m); 7.82 (*d*, ^3J = 8.0, 2 H_o).

12,12,13,13,14,14,15,15,16,16,17,17,17-Tridecafluoroheptadec-10-enyl Methanesulfonate (**2e**). As described for **2a**, with 12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadec-10-enol (7.1 g, 14.5 mmol) and MsCl (2.2 g, 19.3 mmol): **2e** (7.7 g, 93%). White powder. TLC (CH_2Cl_2): R_f 0.84. ^{1}H-NMR ($CDCl_3$): 1.15–1.50 (br. *s*, CH=CHCH$_2$(CH_2)$_6$); 1.70 (*quint.*, ^3J = 7.3, CH_2CH$_2$O); 2.03–2.22 (*m*, CH=CHCH_2); 2.92 (*s*, Me); 4.15 (*t*, ^3J = 7.3, CH$_2$O); 5.40–5.68 (*m*, CF$_2$CH); 6.22–6.43 (*m*, CF$_2$CH=C*H*). ^{13}C-NMR ($CDCl_3$): 25.4 (*s*, CH_2(CH$_2$)$_2$O); 27.9, 28.8, 28.9, 29.1, 29.2 (5*s*, CHCH$_2$(CH_2)$_5$, CH_2CH$_2$O); 32.0 (*s*, CHCH_2); 37.3 (*s*, Me); 70.1 (*s*, CH$_2$O); 116.9 (*t*, ^2J(C,F) = 23, CF$_2$CH); 143.3 (*t*, ^3J(C,F) = 9, CF$_2$CH=*C*H). ^{19}F-NMR ($CDCl_3$): −81.7 (CF$_3$); −111.9 (CF$_2$CH=); −122.3, −123.6, −124.2 (each 2F, (CF$_2$)$_3$); −126.9 (CF$_3$CF_2).

6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-Heptadecafluorotridecyl Methanesulfonate (**2f**). As described for **2a**, with 6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-heptadecafluorotridecanol (10.0 g, 19.7 mmol) and MsCl (3.4 g, 29.7 mmol): **2f** (10.9 g, 95%). White powder. TLC (CH_2Cl_2): R_f 0.84. ^{1}H-NMR ($CDCl_3$); 1.40–1.70 (*m*, CF$_2$CH$_2$(CH_2)$_2$); 1.75 (*quint.*, ^3J = 7, CH_2CH$_2$O); 1.98 (*tt*, ^3J = 7.8, ^3J(H,F) = 18.8, CF$_2$CH$_2$); 2.94 (*s*, Me); 4.18 (*t*, ^3J = 6.2, CH$_2$O). ^{13}C-NMR ($CDCl_3$): 20.1 (*t*, ^3J(C,F) = 4, CF$_2$CH$_2$CH_2); 25.1, 28.9 (2*s*, CF$_2$(CH$_2$)$_2$(CH_2)$_2$); 30.7 (*t*, ^2J(C,F) = 23, CF$_2$CH_2); 37.4 (*s*, MeS); 69.3 (*s*, CH$_2$O). ^{19}F-NMR ($CDCl_3$): identical to that of **2c**.

rac-*2,3-(Isopropylidenedioxy)propyl Toluene-4-sulfonate* (**8**). As described for **2a** with *rac*-2,3-(isopropylidenedioxy)propanol (11.6 g, 87.9 mmol) and TsCl (20.0 g, 105 mmol): 22.7 g (90%) of **9**. White crystals. ^{1}H-NMR (CCl_4): 1.26, 1.29 (2*s*, Me$_2$C); 2.43 (*s*, *Me*C$_6$H$_4$); 3.63–4.39 (*m*, 2 CH$_2$O, CHO); 7.39 (*d*, ^3J = 8.0, 2 H$_m$); 7.82 (*d*, ^3J = 8.0, 2 H$_o$); data identical to those reported in [29].

3. *Fluorocarbon/Fluorocarbon Derivatives* **4** *and* **7**. 3.1. rac-*2,3-Bis(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)propanol* (**4a**). *Method 1* (liquid-liquid phase-transfer catalysis): A soln. of 12N KOH (20 ml) and Bu$_4$N(HSO$_4$) (6.0 g, 17.7 mmol) and a soln. of **2a** (6.0 g, 11.0 mmol) and **1** (R = PhCH$_2$; 1.0 g, 5.5 mmol) in 35 ml of Et$_2$O were heated for 3 days under reflux. The aq. phase was extracted with Et$_2$O and the combined org. phase washed, dried, and evaporated. CC (petroleum ether/Et$_2$O) afforded 3.3 g (65%) of **3a** as a white powder.

Method 2: A mixture of NaH (0.43 g, 17.9 mmol) and **1** (R = PhCH$_2$; 1.5 g, 8.2 mmol) in anh. THF (100 ml) was stirred at r.t. for 4 h and at 65° for 45 min. Then, a soln. of **2a** (11.0 g, 20.2 mmol) in THF (10 ml) was added and the mixture refluxed for 3 days. The crude product was then purified by CC (petroleum ether/Et$_2$O): 5.7 g (65%) of rac-*1-[2,3-bis(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)propyloxy]benzene* (**3a**). TLC (petroleum ether/Et$_2$O 9:1): R_f 0.38. ^{1}H-NMR ($CDCl_3$): 1.18–1.35 (br. *s*, 2 CF$_2$(CH$_2$)$_2$(CH_2)$_7$); 1.37–1.70 (*m*, 2 CF$_2$CH$_2$CH_2, 2 CH_2CH$_2$O); 2.02 (*tt*, ^3J = 7.5, ^3J(H,F) = 19.0, 2 CF$_2$CH$_2$); 3.35–3.65 (*m*, 4 CH$_2$O, CHO): 4.58 (*s*, PhCH_2); 7.28–7.38 (*m*, Ph). ^{13}C-NMR ($CDCl_3$): 20.1 (*t*, ^3J(C,F) = 4, CF$_2$CH$_2$CH_2); 26.1 (*s*, CH_2(CH$_2$)$_2$O); 29.1, 29.2, 29.4, 29.5, 29.6, 29.7, 30.1 (7*s*, CF$_2$(CH$_2$)$_2$(CH_2)$_6$, CH_2CH$_2$O); 30.9 (*t*, ^2J(C,F) = 22, CF$_2$CH_2); 70.4, 70.6, 70.8 (3 *s*, CH_2OCH$_2$, CH_2OCH); 71.7 (*s*, CH_2OBn); 73.4 (*s*, PhCH_2O); 78.0 (*s*, CHO); 127.5, 127.6, 128.3, 138.5 (4 *s*, Ph). ^{19}F-NMR ($CDCl_3$): identical to that of **2a**.

Hydrogenolysis of **3a** (6.7 g, 7.2 mmol) in 50 ml of EtOH and 0.7 ml of AcOH with 0.85 g of 10% Pd/C under H$_2$ (1.5 atm) gave **4a** (6.0 g, 100%). White powder. TLC ($CHCl_3$): R_f 0.32. ^{1}H-NMR ($CDCl_3$): 1.15–1.38 (br. *s*, 2 CF$_2$(CH$_2$)$_2$(CH_2)$_7$); 1.40–1.62 (*m*, 2 CF$_2$CH$_2$CH_2, 2 CH_2CH$_2$O); 2.00 (*tt*, ^3J = 7.5, ^3J(HF) = 19.0, CF$_2$CH$_2$); 2.29 (*m*, OH); 3.30–3.70 (*m*, 4 CH$_2$O, CHO); ^{13}C-NMR ($CDCl_3$): 20.1 (*t*, ^3J(CF) = 4, CF$_2$CH$_2$CH_2); 26.1 (*s*, CH_2(CH$_2$)$_2$O); 29.1, 29.2, 29.3, 29.4, 29.5, 29.6, 29.7, 30.1 (8*s*, CF$_2$(CH$_2$)$_2$(CH_2)$_6$, CH_2CH$_2$O); 30.8 (*t*, ^2J(CF) = 22, CF$_2$CH_2); 63.1 (*s*, CH$_2$OH); 70.4, 71.0, 71.9 (3*s*, CH$_2$O); 78.3 (*s*, CHO). ^{19}F-NMR ($CDCl_3$): identical to that of **2a**.

3.2. rac-*2,3-Bis(12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecyloxy)propan-1-ol* (**4b**). *Method 1*, with **2b** (5.1 g, 9.0 mmol), **1** (R = PhCH$_2$; 0.76 g, 4.1 mmol), and Bu$_4$N(HSO$_4$) (0.6 g, 1.7 mmol): 2.7 g (58%) of **3b** as a white powder and 970 mg of its corresponding monoether. The same procedure when applied to this monoether in toluene at 80° gave a further crop of **3b**. Total yield of rac-*1-[2,3-bis(12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecyloxy)propyloxy]benzene* (**3b**) 78%. TLC (petroleum ether/Et$_2$O 8:2) R_f 0.64. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **3a**. ^{19}F-NMR ($CDCl_3$): identical to that of **2b**.

Hydrogenolysis of **3b** gave **4b** (100%). White powder. TLC ($CHCl_3$): R_f 0.32. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **4a**. ^{19}F-NMR ($CDCl_3$): identical to that of **2b**.

3.3. rac-*2,3-Bis(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecyloxy)propan-1-ol* (**4c**). *Method 1*, with **2c** (6.4 g, 9.6 mmol), **1** (R = PhCH$_2$; 0.74 g, 4.0 mmol), and Bu$_4$N(HSO$_4$) (0.6 g, 1.7 mmol): 3.5 g (65%) of rac-*1-[2,3-bis(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecyloxy)-propyloxy]benzene* (**3c**). White powder. TLC (petroleum ether/Et$_2$O 9:1): R_f 0.38. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **3a**. ^{19}F-NMR ($CDCl_3$): identical to that of **2c**.

Hydrogenolysis of **3c** as described for **4a** afforded **4c** (100%). White powder. TLC ($CHCl_3$): R_f 0.30. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **4a**, ^{19}F-NMR ($CDCl_3$): identical to that of **2c**.

3.4. rac-*2,3-Bis(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-heptadecafluorotridec-4-enyloxy)propan-1-ol* (**7**). *Method 2*, with **1** (R = Thp; 10.5 g, 59.5 mmol), NaH (3.1 g, 127 mmol) and **2d** (28.6 g, 119 mmol) gave after CC (hexane/acetone), 11.2 g (60%) of rac-*2-[2,3-bis(pent-4-enyloxy)propyloxy]tetrahydro-2*H-*pyran* (**5**) as a colorless oil. ^{1}H-NMR ($CDCl_3$): 1.22–1.90 (*m*, 2 $(CH_2)_3$, 2 CH_2=CHCH_2CH_2); 1.90–2.32 (*m*, 2 CH_2=CHCH_2); 3.17–4.00 (*m*, 5 CH_2O, CHO); 4.63 (*m*, OCHO); 4.82–5.23 (*m*, 2 CH_2=CH); 5.57–6.15 (*m*, 2 CH_2=C*H*).

A soln. of **5** (11.2 g, 35.9 mmol), perfluorooctyl iodide (65.1 g, 119 mmol), 2-aminoethanol (14.4 ml), and CuCl (1.1 g) in *t*-BuOH (80 ml) was then stirred under reflux during 9 days. After extraction with CH_2Cl_2, the combined org. phase was washed, dried, and evaporated and the residue purified by CC (hexane/CH_2Cl_2): 30.7 g (75%) of rac-*2-[2,3-bis(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-heptadecafluorotridec-4-enyloxy)propyloxy]tetrahydro-2*H-*pyran* (**6d**). Yellow oil. TLC ($CHCl_3$): R_f 0.30. ^{1}H-NMR ($CDCl_3$): 1.20–2.10 (*m*, 2 CH=CHCH_2CH_2, $(CH_2)_3$); 2.10–2.64 (*m*, 2 CH=CHCH_2); 3.33–4.06 (*m*, 5 CH_2O, CHO); 4.67 (br. *s*, OCHO); 5.40–6.00 (*m*, 2 C*H*=CH); 6.27–6.77 (*m*, 2 CH=C*H*).

For 6 h, **6d** (30.6 g, 3.4 mmol) in 200 ml of EtOH was then allowed to react with PPTS (0.9 g, 3.4 mmol) at 55°. Evaporation and CC(CH_2Cl_2) of the residue afforded 26.8 g (95%) of **7**. Colorless oil. TLC (Et_2O/hexane 1:1): R_f 0.23. ^{1}H-NMR ($CDCl_3$): 1.60–1.87 (*m*, 4 H, CH_2CH_2O); 2.15–2.50 (*m*, 2 CH=CHCH_2, CH_2O*H*); 3.30–3.70 (*m*, 4 CH_2O, CHO); 5.28–5.78 (*m*, 2 CF_2C*H*=CH); 6.22–6.45 (*m*, 2 CF_2CH=C*H*). ^{13}C-NMR ($CDCl_3$): 25.6 (*cis*), 28.1, 28.5, 28.7 (4*s*, CH=CHCH_2CH_2); 62.7 (*s*, CH_2OH); 69.1, 70.3, 70.8 (3*s*, CH_2O); 79.0 (*s*, CHO), 117.6 (*t*, ^2J(C,F) = 23, CF_2C*H*=); 142.5 (*t*, ^3J(C,F) = 9, CF_2CH=C*H*, *trans*); 144.7 (*t*, ^3J(C,F) = 5, CF_2CH=C*H*, *cis*). ^{19}F-NMR ($CDCl_3$): −81.8 (CF_3); −107.5 (0.2 F, CF_2CH, *cis*): −112.2 (1.8 F, CF_2CH, *trans*); −122.3, −122.8, −123.6, −124.2 (2F, 4F, 2F, 2F, $CF_3CF_2(CF_2)_5$); −127.0 (CF_3CF_2).

The heptadecafluorotridec-3-enyloxy isomer(s) of **7** amounted to less than 10% (by NMR). ^{1}H-NMR ($CDCl_3$): 2.70 (*dt*, ^3J(H,F) = 18, ^3J = 7, CF_2CH_2); 5.94–6.15 (*m*, CH=CH). ^{13}C-NMR ($CDCl_3$): 29.0, 29.4, 32.8, 33.2 (4*s*, CH_2); 34.7 (*t*, ^2J(C,F) = 23, CF_2CH_2); 62.8, 69.3, 70.6 (3*s*, CH_2O); 135.0, 135.1 (2*s*, CH=). ^{19}F-NMR ($CDCl_3$): 114.2 (CF_2CH_2).

3.5. rac-*2,3-Bis(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-heptadecafluorotridecycloxy)propan-1-ol* (**4d**). A mixture of **7** (10.1 g, 9.5 mmol) and 10% Pd/C (1.1 g) in EtOH (40 ml) was stirred for 84 h in an autoclave under a H_2 pressure of 40 atm. The mixture was then filtered off over *Celite*, evaporated, and chromatographed (Et_2O/hexane): **4d** (9.6 g, 95%). White powder. TLC (Et_2O/hexane 1:1): R_f 0.23. ^{1}H-NMR ($CDCl_3$): 1.26–1.45 (*m*, 2 $CF_2(CH_2)_2$CH_2); 1.46–1.66 (*m*, 2 CF_2CH_2CH_2, 2 CH_2CH_2O); 1.97 (*tt*, ^3J = 7.5, ^3J(H,F) = 18.2, 2 CF_2CH_2); 225 (br. *s*, CH_2O*H*); 3.30–3.72 (*m*, 4 CH_2O, CHO). ^{13}C-NMR ($CDCl_3$): 19.9 (*t*, ^3J(C,F) = 4, CF_2CH_2CH_2); 25.7 (*s*, $CF_2(CH_2)_2$CH_2); 29.2, 29.6, (2*s*, CH_2CH_2O); 30.7 (*t*, ^2J(CF) = 23, CF_2CH_2); 62.7 (*s*, CH_2OH); 69.8, 70.9, 71.2 (3*s*, CH_2O); 78.6 (*s*, CHO). ^{19}F-NMR ($CDCl_3$): identical to that of **2c**.

4. *Mixed Fluorocarbon/Hydrocarbon Derivatives* **14**. 4.1. rac-3-*(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-Heptadecafluorotridec-4-enyloxy)-2-(tetradecyloxy)propan-1-ol* (**14a**). *Method 2* (see *3.1*), with pent-4-en-1-ol (28.0 g, 32.6 mmol), NaH (0.9 g, 36.3 mmol), and **8** (10.3 g, 36.0 mmol), afforded, after distillation (92°/10 Torr) and CC (pentane/$CHCl_3$), 4.3 g (65%) of rac-*5-[2,3-(isopropylidenedioxy)propyloxy]pent-1-ene* (**9a**). Colorless oil. TLC ($CHCl_3$/hexane 1:1): R_f 0.64. ^{1}H-NMR (80 MHz, CCl_4): 1.29, 1.32 (2*s*, Me_2C); 1.65 (*quint.*, ^3J = 8.0, CH_2CH_2O); 2.16 (*dt*, ^3J = 8.0, 8.0, CH_2=CHCH_2); 3.17–4.39 (*m*, 3 CH_2O, CHO); 4.85–5.25 (*m*, CH_2=CH); 5.60–6.25 (*m*, CH_2=C*H*). To a soln. of **9a** (7.3 g, 36.5 mmol) in a MeOH/H_2O 9:1 (100 ml) were then added a few drops of 12N HCl. The mixture was stirred at reflux for 4 h and then evaporated, and the residue was purified by (Et_2O): 3-(pent-4-enyloxy)propane-1,2-diol (**10a**; 4.1 g, 70%). Colorless oil. TLC (Et_2O): R_f 0.65. ^{1}H-NMR (80 MHz, CCl_4): 1.65 (*quint.*, ^3J = 8.0, CH_2CH_2O); 2.16 (*dt*, ^3J = 8.0, 8.0, CH_2=CHCH_2); 3.25–4.00 (*m*, 3 CH_2O, CHO); 4.39 (br. *s*, 2 OH); 4.85–5.25 (*m*, CH_2=CH); 5.60–6.25 (*m*, CH_2=CH).

A soln. of **10a** (3.9 g, 24.4 mmol) and trityl chloride (TrCl; 7.5 g, 26.9 mmol) in dry pyridine (40 ml) was then heated under reflux for 24 h. The resulting mixture was poured in H_2O/ice and extracted with Et_2O. The combined org. phase was washed, dried, and evaporated and the residue purified by CC (pentane/$CHCl_3$): rac-*1-(pent-4-enyloxy)-3-(triphenylmethoxy)propan-2-ol* (**11a**; 8.2 g, 84%). Yellow oil. TLC ($CHCl_3$): R_f 0.33. ^{1}H-NMR (80 MHz, CCl_4): 1.65 (*quint.*, ^3J = 8.0, CH_2CH_2O); 2.16 (*dt*, ^3J = 8.0, 8.0, CH_2=CHCH_2); 2.34 (*d*, ^3J = 4, OH); 3.18–3.75 (*m*, 3 CH_2O); 3.75–4.20 (*m*, CHO); 4.85–5.25 (*m*, CH_2=CH); 5.60–6.25 (*m*, CH_2=C*H*); 7.25–7.90 (*m*, Ph_3C).

A soln. of **11a** (8.2 g, 20.4 mmol) and tetradecyl iodide (17.8 g, 55.0 mmol) in Et_2O was stirred with 12N KOH (100 ml) and $Bu_4N(HSO_4)$ (6.9 g, 20.3 mmol) under reflux for 8 days. Extraction with Et_2O and CC (Et_2O) gave 6.0 g (50%) of rac-*1,1′,1″-{[3-(pent-4-enyloxy)-2-(tetradecyloxy)propyloxy]methylidyne}tris[benzene]* (**12a**). Oil. TLC (CH_2Cl_2): R_f 0.75. ^{1}H-NMR (80 MHz, CCl_4): 0.78–2.41 (br. *s*, 3 $Me(CH_2)_{12}$, CH=CH(CH_2)$_2$); 3.03–3.76 (*m*, 4 CH_2O, CHO); 4.85–5.25 (*m*, CH_2=CH); 5.60–6.25 (*m*, CH_2=C*H*); 7.25–7.90 (*m*, Ph_3C).

The method described for **6d**, when applied to **12a** (6.0 g, 10.0 mmol), perfluorooctyl iodide (11.0 g, 20.2 mmol), CuCl (2.4 g, 23.7 mmol), 2-aminoethanol (3 ml), and *t*-BuOH (25 ml) gave, after CC (pentane/$CHCl_3$),

8.3 g (80%) of rac-*1,1',1''-{[3-(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-heptadecafluorotridec-4-enyloxy)-2-(tetradecyloxy)propyloxy]methylidyne}tris[benzene]* (**13a**). Colorless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 0.71–2.34 (br. *s*, 31 H, CH=CH(CH_2)$_2$, Me(CH_2)$_{12}$); 3.00–3.73 (*m*, 4 CH_2O, CHO); 5.20–5.90 (*m*, CF_2CH=CH); 6.10–6.80 (*m*, CF_2CH=C*H*); 7.25–7.90 (*m*, Ph_3C).

For detritylation, 5.9 g (5.8 mmol) of **13a** were added at 0° to a soln. of BF_3/MeOH (4.9 ml, 7.9 mmol) in dry CH_2Cl_2 (175 ml). After 2 h, the mixture was washed with ice-cold H_2O (3×). The org. layer was then dried and evaporated and the crude product purified by CC ($CHCl_3$): 3.1 g (70%) of **14a**. Colorless oil. TLC ($CHCl_3$): R_f 0.21. ^{1}H-NMR ($CDCl_3$): 0.86 (*t*, ^3J = 5.2, Me); 1.10–1.45 (br. *s*, Me(CH_2)$_{11}$); 1.50–1.65 (*m*, Me(CH_2)$_{11}CH_2$); 1.70 (*quint.*, ^3J = 8.0, CH=CHCH_2CH_2); 2.25–2.35 (*m*, CH=CHCH_2); 2.43 (br. *s*, OH); 3.36–3.77 (*m*, 3 CH_2O, CHO); 5.35–5.76 (*m*, CF_2CH=CH); 6.30–6.50 (*m*, CF_2CH=C*H*); ^{13}C-NMR ($CDCl_3$): 14.2 (*s*, Me); 22.9 (*s*, MeCH_2); 26.4 (*s*, $CH_2(CH_2)_2O$); 28.4, 29.0, 29.7, 29.8, 30.0, 30.4 (6*s*, CH_2CH_2O, CH=CH(CH_2)$_2$, $MeCH_2CH_2(CH_2)_8$); 32.2 (*s*, $MeCH_2CH_2$); 62.9 (*s*, CH_2OH); 70.5, 70.7, 71.0 (3*s*, CH_2O); 78.9 (*s*, CHO); 117.7 (*t*, ^2J(C,F) = 23, CF_2CH=CH); 142.6 (*t*, ^3J(C,F) = 9, CF_2CH=CH, *trans*); 145.0 (CF_2CH=CH, *cis*). ^{19}F-NMR ($CDCl_3$): identical to that of **7**.

4.2. rac-3-*(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-Heptadecafluorononadec-10-enyloxy)-2-(hexadecyloxy)propan-1-ol* (**14b**). As described for **9a**, with undec-10-en-1-ol (10.0 g, 59.0 mmol), NaH (1.4 g, 60.0 mmol), and **8** (17.0 g, 59.0 mmol). CC (Et_2O) gave *11-[2,3-(isopropylidenedioxy)propyloxy]undec-1-ene* (**9b**; 14.9 g, 90%). Colorless oil. TLC ($CHCl_3$/hexane): R_f 0.63. ^{1}H-NMR (80 MHz, CCl_4): 1.13–1.77 (*m*, 2 Me, CH_2=CH$CH_2(CH_2)_7$); 1.77–2.33 (*m*, CH_2=CHCH_2); 3.17–4.39 (*m*, 3 CH_2O, CHO); 4.85–5.25 (*m*, CH_2=CH); 5.60–6.25 (*m*, CH_2=C*H*)].

Deprotection of **9b** (14.7 g, 51.6 mmol) with HCl gave *3-(undec-10-enyloxy)propane-1,2-diol* (**10b**; 11.3 g, 90%). Colorless oil. TLC (Et_2O): R_f 0.48. ^{1}H-NMR (80 MHz, CCl_4): 1.06–1.81 (br. *s*, $(CH_2)_7$); 1.81–2.20 (*m*, CH_2=CHCH_2); 3.25–4.20 (*m*, 2 OH, 3 CH_2O, CHO); 4.85–5.25 (*m*, CH_2=CH); 5.60–6.25 (*m*, CH_2=C*H*).

Tritylation of **10b** (5.4 g, 22.0 mmol) using TrCl (7.9 g, 28.4 mmol) in dry pyridine (50 ml) afforded 7.5 g (70%) of *1-(triphenylmethoxy)-3-(undec-10-enyloxy)propan-2-ol* (**11b**). TLC (CH_2Cl_2): R_f 0.45. ^{1}H-NMR (80 MHz, CCl_4): 1.25–1.80 (br. *s*, $(CH_2)_7$); 1.80–2.30 (*m*, CH_2=CHCH_2); 2.60 (br. *s*, OH); 3.25–3.75 (*m*, 3 CH_2O); 3.80–4.25 (*m*, CHO); 4.85–5.25 (*m*, CH_2=CH); 5.60–6.25 (*m*, CH_2=C*H*); 7.25–7.90 (*m*, Ph_3C).

As described for **12a**, with **11b** (7.5 g, 15.4 mmol), 1-bromohexadecane (10.9 g, 35.7 mmol), $Bu_4N(HSO_4)$ (1.0 g, 2.9 mmol), and 12N KOH (20 ml). Extraction and CC (hexane/EtO) gave rac-*1,1',1''-{[3-(undec-10-enyloxy)-2-(hexadecyloxy)propyloxy]methylidyne}tris[benzene]* (**12b**; 4.6 g, 42%). Oil. TLC (CH_2Cl_2): R_f 0.76. ^{1}H-NMR (80 MHz, CCl_4): 1.25–2.00 (br. *s*, Me(CH_2)$_{14}$, $(CH_2)_7$); 2.00–2.40 (*m*, CH_2=CHCH_2); 3.25–3.80 (*m*, 4 CH_2O, CHO); 5.00–5.30 (*m*, CH_2=CH); 5.75–6.30 (*m*, CH_2=C*H*); 7.25–7.90 (*m*, Ph_3C).

Then **12b** (4.6 g, 6.5 mmol) was reacted with perfluorooctyl iodide (7.1 g, 13.0 mmol), CuCl (1.6 g, 16.5 mmol), and 2 amino-ethanol (3 ml) in *t*-BuOH (22 ml) to give, after CC (hexane/$CHCl_3$), 5.9 g (80%) of rac-*1,1',1''-{[3-(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadec-10-enyloxy)-2-(hexadecyloxy)propyloxy]methylidyne}tris[benzene]* (**13b**). Colorless oil. ^{1}H-NMR (80 MHz, CCl_4): 0.86–2.35 (br. *s*, $(CH_2)_8CH_2$, Me(CH_2)$_{14}$); 3.00–3.75 (*m*, 4 CH_2O, CHO); 5.30–5.80 (*m*, CF_2CH=CH); 6.30–6.55 (*m*, CF_2CH=C*H*); 7.25–7.90 (*m*, Ph_3C). ^{13}C-NMR ($CDCl_3$): 14.0 (*s*, Me); 22.8 (*s*, MeCH_2); 26.2, 26.3 (2*s*, $CH_2CH_2CH_2O$); 28.1, 29.1, 29.2, 29.4, 29.5, 29.6, 29.7, 29.8, 29.9, 30.3 (10*s*, CH_2CH_2O, Me(CH_2)$_2(CH_2)_{10}$, CH=CH(CH_2)$_6$); 32.1 (*s*, $MeCH_2CH_2$); 63.8 (*s*, CH_2OTr); 70.7, 71.2, 71.6 (3*s*, CH_2O); 78.6 (*s*, CHO); 86.6 (*s*, Ph_3C); 116.9 (*t*, ^2J(C,F) = 23, CF_2CH=CH); 126.9, 127.7, 128.8, 143.3 (4*s*, Ph); 143.2 (*t*, ^3J(C,F) = 9, CF_2CH=CH, *trans*); 144.0 (CF_2CH=CH, *cis*). ^{19}F-NMR (CDCl): identical to that of **7**.

Detritylation of **13b** (4.3 g, 3.8 mmol) with BF_3/MeOH (3.7 ml, 5.7 mmol) gave **14b** (2.9 g, 86%). White powder. TLC ($CHCl_3$): R_f 0.20. ^{1}H-NMR ($CDCl_3$): 0.85 (*t*, ^3J = 6.5, Me); 1.05–1.45 (br. *s*, $(CH_2)_6CH_2CH_2O$, Me(CH_2)$_{13}$); 1.45–1.70 (*m*, 2 CH_2CH_2O); 2.07–2.28 (*m*, 2 CH=CHCH_2); 2.48 (br. *s*, CH_2OH); 3.30–3.80 (*m*, 4 CH_2O, CHO); 5.40–5.74 (*m*, CF_2CH=CH); 6.35–6.50 (*m*, CF_2CH=C*H*). ^{13}C-NMR ($CDCl_3$): 13.8 (*s*, Me); 22.6 (*s*, Me_3CH_2); 26.0 (*s*, $CH_2CH_2CH_2O$); 27.9, 28.9, 29.2, 29.3, 29.6, 30.0 (6*s*, CH_2CH_2O, Me(CH_2)$_2(CH_2)_{10}$, CH=CH(CH_2)$_6$); 31.8 (*s*, $MeCH_2CH_2$); 62.8 (*s*, CH_2OH); 70.3, 70.7, 71.6 (3*s*, CH_2O); 78.3 (*s*, CHO); 116.7 (*t*, ^2J(C,F) = 23, CF_2CH=CH); 143.0 (*t*, ^3J(C,F) = 9, CF_2CH=CH, *trans*); 145.0 (CF_2CH=CH, *cis*), ^{19}F-NMR ($CDCl_3$): identical to that of **7**.

5. *Mixed Fluorocarbon/Fluorocarbon Derivatives* **19**. 5.1. rac-*3-(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-Heptadecafluorotridecyloxy)-2-(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)propan-1-ol* (**19a**). *Method 2* (see *3.1*), with **15** (3.0 g, 16.7 mmol), NaH (0.9 g, 37.0 mmol) dry THF (10 ml), and **2a'** (9.3 g, 20.0 mmol). CC ($CHCl_3$/hexane) gave 7.2 g (75%) of *5-(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)-2-phenyl-1,3-dioxane* (**16a**). White powder. TLC ($CHCl_3$/hexane (8:2): R_f 0.61. ^{1}H-NMR ($CDCl_3$): 1.20–1.50 (br. *s*, $CF_2(CH_2)_2CH_2)_7$); 1.51–1.80 (*m*, $CF_2CH_2CH_2$, CH_2CH_2O); 2.07 (*tt*, ^3J = 7.5, ^3J(H,F) = 19.0, CF_2CH_2); 3.30

(*tt*, $^3J \approx 1.4$, CH_2CHCH_2); 3.68 (*t*, $^3J = 6.6$, CH_2CH_2OCH); 4.05, 4.38 (*AB* of *ABX*, $^2J_{AB} = 12.4$, $^3J_{AX} = 1.6$, $^3J_{BX} = 1.3$, 2 CH_2CHO); 5.60 (*s*, PhC*H*); 7.31–7.49, 7.50–7.65 (2*m*, 3 H, 2 H, Ph). ^{13}C-NMR ($CDCl_3$): 20.1 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 26.2 (*s*, $CH_2CH_2CH_2O$); 29.1, 29.2, 29.4, 29.5, 29.6, 29.8 (6*s*, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.9 (*t*, ^2J(C,F) = 23, CF_2CH_2); 69.0, 69.1 (2*s*, CH_2O); 70.7 (*s*, CH_2OCH); 101.4 (*s*, PhCH); 126.2, 128.2, 128.8, 138.3 (4*s*, Ph). ^{19}F-NMR ($CDCl_3$): identical to that of **2a**.

Then, 1.0M BH_3/THF (10.4 ml) was added to an ice-cooled soln. of **16a** (4.0 g, 7.2 mmol) in dry THF (4 ml). The mixture was heated at 40–45° until all the starting material was consumed (*ca.* 60 h). After hydrolysis, the solvent was evaporated, the residue extracted with Et_2O, the soln. washed with H_2O and evaporated, and the residue submitted to CC (AcOEt/hexane): 3.4 g (85%) of rac-*3-(benzyloxy)-2-(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)propan-1-ol* (**17a**). Colorless oil. TLC (hexane/AcOEt 6:4: R_f 0.61). ^{1}H-NMR ($CDCl_3$): 1.12–1.40 (*m*, $CF_2(CH_2)_2(CH_2)_7$); 1.40–1.62 (*m*, $CF_2CH_2CH_2$, CH_2CH_2O); 2.00 (*tt*, $^3J = 7.8$, ^3J(H,F) = 18.8, CF_2CH_2); 2.32 (br. *s*, OH); 3.35–3.78 (*m*, 3 CH_2O, CHO); 4.50 (*s*, PhCH_2); 7.20–7.35 (*m*, Ph). ^{13}C-NMR ($CDCl_3$): 20.1 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 26.1 (*s*, $CH_2CH_2CH_2O$); 29.1, 29.2, 29.4, 29.5, 29.6, 30.1 (6*s*, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.9 (*t*, ^2J(C,F) = 22, CF_2CH_2); 62.8 (*s*, CH_2OH); 70.1, 70.4 (2*s*, CH_2O); 73.5 (*s*, PhCH_2); 78.7 (*s*, CHO); 127.6, 127.7, 128.4, 138.1 (4*s*, Ph). ^{19}F-NMR ($CDCl_3$): identical to that of **2a**.

Method 2 (see *3.1*) was applied to **17a** (1.8 g, 2.2 mmol), NaH (0.16 mg, 6.5 mmol), and **2f** (2.2 g, 6.5 mmol): rac-*1-[3-(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-heptadecafluorotridecyloxy)-2-(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)propyloxy]benzene* (**18a**; 2.0 g, 66%). Colorless oil, after CC (CH_2Cl_2/hexane) and recrystallization from pentane. TLC (CH_2Cl_2): R_f 0.76. ^{1}H-NMR ($CDCl_3$): 1.10–1.35 (*m*, $CF_2(CH_2)_2CH_2$, $CF_2(CH_2)_2(CH_2)_7$); 1.40–1.60 (*m*, 2 $CF_2CH_2CH_2$, 2 CH_2CH_2O); 2.00 (*tt*, $^3J = 7.8$, ^3J(H,F) = 18.8, 2 CF_2CH_2); 3.30–3.60 (*m*, 4 CH_2O, CHO); 4.50 (*s*, PhCH_2); 7.15–7.35 (*m*, Ph). ^{13}C-NMR ($CDCl_3$); 20.1 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 25.8, 26.1 (2*s*, $CH_2(CH_2)_2O$); 29.1, 29.2, 29.3, 29.4, 29.5, 29.6, 30.1 (7*s*, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.8, 30.9 (2*t*, ^2J(C,F) = 22, CF_2CH_2); 70.2, 70.6, 70.9, 71.1 (4*s*, CH_2O); 73.4 (*s*, PhCH_2O); 78.0 (*s*, CHO); 127.5, 127.6, 128.3, 138.5 (4*s*, Ph). ^{19}F-NMR ($CDCl_3$): −81.4, −81.7 (each 3F, CF_3); −115.2 (4F, CF_2CH_2); −122.4, −123.3, −124.1, −125.1 (6F, 2F, 2F, 2F, 2F, $CF_3CF_2(CF_2)_5$, and $CF_3CF_2CF_2$); −126.6 (4F, CF_3CF_2).

Hydrogenolysis of **18a** (1.9 g, 1.8 mmol) in EtOH/AcOH, as described for **4a**, afforded 1.8 g (*ca.* 100%) of **19a**. White powder. TLC ($CHCl_3$): R_f 0.37. ^{1}H-NMR ($CDCl_3$): 1.18–1.40 (*m*, $CF_2(CH_2)_2CH_2$, $CF_2(CH_2)_2(CH_2)_7$); 1.42–1.65 (*m*, 2 $CF_2CH_2CH_2$, 2 CH_2CH_2O); 3.35–3.75 (*m*, 2 CH_2O, CHO). ^{13}C-NMR ($CDCl_3$): 20.0 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 25.8, 26.1 (2*s*, $CH_2(CH_2)_2O$); 29.1, 29.2, 29.3, 29.4, 29.5, 29.6, 30.1 (7*s*, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.8, 30.9 (2*t*, ^2J(C,F) = 22, CF_2CH_2); 63.0 (*s*, CH_2OH); 70.4, 70.9, 71.3 (3*s*, CH_2O); 78.4 (*s*, CHO). ^{19}F-NMR ($CDCl_3$): identical to that of **18a**.

5.2. rac-*2-(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-Heptadecafluorononadecyloxy)-3-(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)propan-1-ol* (**19b**). As described for **17a**, with **15** (1.3 g, 7.2 mmol), NaH (0.34 g, 14.0 mmol), and **2c** (5.6 g, 8.4 mmol). CC ($CHCl_3$/hexane) gave 3.8 g (70%) of *5-(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecyloxy)-2-phenyl-1,3-dioxane* (**16b**). White powder. TLC ($CHCl_3$): R_f 0.68. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **16a**. ^{19}F-NMR ($CDCl_3$): identical to that of **2c**.

Then, **16b** (2.3 g, 3.0 mmol) was reacted with 1.0M BH_3/THF (9.0 ml). CC (CH_2Cl_2/hexane) gave 1.6 g (70%) of rac-*3-(benzyloxy)-2-(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecyloxy)propan-1-ol* (**17b**). White powder. TLC ($CHCl_3$): R_f 0.30. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **17a**. ^{19}F-NMR ($CDCl_3$): identical to that of **2c**.

Method 1 (see *3.1*) was applied to **17b** (1.5 g, 1.9 mmol), **2a'** (1.1 g, 2.3 mmol), and $Bu_4N(HSO_4)$ (1.0 g, 2.9 mmol). CC (petroleum ether/Et_2O) gave 1.7 g (75%) of *1-[2-(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecyloxy)-3-(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)propyloxy]benzene* (**18b**). White powder. TLC (CH_2Cl_2): R_f 0.63. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **3a**. ^{19}F-NMR ($CDCl_3$): identical to that of **18a**.

Finally, hydrogenolysis of **18b** (1.2 g, 1.1 mmol) afforded 1.0 g (98%) of **19b**. White powder. TLC ($CHCl_3$): R_f 0.39. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **4a**. ^{19}F-NMR ($CDCl_3$): identical to that of **18a**.

6. *Fluorocarbon/Fluorocarbon and Mixed Fluorocarbon/Hydrocarbon Derivatives* **22** *and* **23**. 6.1. *2-[(12,12,13,13,14,14,15,15,16,16,17,17,17-Tridecafluoroheptadecyloxy)methyl]oxirane* (**21a**). *Method 1* (see *3.1*), with epichlorohydrin (**20**; 5.1 g, 55.7 mmol), 12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecan-1-ol (5.5 g, 11.2 mmol), 25N NaOH (7.4 ml), and $Bu_4N(HSO_4)$ (0.16 g, 0.5 mmol). CC (Et_2O/hexane) gave 5.2 g (85%) of **21a**. Colorless oil which crystallized slowly at r.t. TLC (Et_2O/hexane 1:1): R_f 0.69. ^{1}H-NMR ($CDCl_3$): 1.15–1.50 (br. *s*, $CF_2(CH_2)(CH_2)_7$); 1.50–1.70 (*m*, $CF_2CH_2CH_2$, CH_2CH_2O); 2.05 (*tt*, $^3J = 7.5$, ^3J(H,F) = 18.8, CF_2CH_2);

2.60, 2.79 (*AB* of *ABX*, $^2J_{AB}$ = 5.0, $^3J_{AX}$ = 2.7, $^3J_{BX}$ = 4.1, CH_2 (oxiran)); 3.10–3.20 (*m*, CH); 3.35, 3.70 (*AB* of *ABX*, $^2J_{AB}$ = 11.4, $^3J_{AX}$ = 5.8, $^3J_{BX}$ = 3.1, $CHCH_2OCH_2$); 3.40–3.58 (*m*, OCH_2CH_2). ^{13}C-NMR ($CDCl_3$): 20.1 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 26.0 (*s*, $CH_2(CH_2)_2O$); 29.1, 29.2, 29.3, 29.4, 29.5, 29.7 (6*s*, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.9 (*t*, ^2J(C,F) = 22, CF_2CH_2); 44.2 (*s*, CH_2 (oxirane)); 50.8 (*s*, CH); 71.5, 71.7 (2*s*, $CH_2OCH_2CH_2$). ^{19}F-NMR ($CDCl_3$): identical to that of **2b**.

2-[(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-Heptadecafluorononadecyloxy)methyl]oxirane (**21b**). *Method 1* (see *3.1*), with **20** (8.5 g, 91.5 mmol), 12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecan-1-ol (9.0 g, 15.2 mmol), 25N NaOH (12 ml), and $Bu_4N(HSO_4)$ (0.2 g, 0.6 mmol). CC (Et_2O/hexane) gave 7.8 g (79%) of **21b**. White powder. TLC (Et_2O/hexane 1:1): R_f 0.69. ^{1}H-NMR and ^{13}C-NMR ($CDCl_3$): identical to those of **21a**. ^{19}F-NMR ($CDCl_3$): identical to that of **2c**.

2-[(Octadecyloxy)methyl]oxirane (**21c**). *Method 1* (see *3.1*), with **20** (37.0 g, 0.4 mol), octadecanol (21.6 g, 79.8 mmol), 25N NaOH (50 ml), and $Bu_4N(HSO_4)$ (1.1 g, 3.2 mmol). CC (Et_2O/hexane) gave **21c** (18.3 g, 70%). White powder. TLC (Et_2O/hexane 1:1): R_f 0.71. ^{1}H-NMR ($CDCl_3$): 0.77 (*t*, ^3J = 6.3, Me); 1.03–1.34 (*m*, $Me(CH_2)_{15}$); 1.40–1.58 (*m*, OCH_2CH_2); from 2.60 to 3.70 identical to signals of **21a**. ^{13}C-NMR ($CDCl_3$): 14.1 (*s*, Me); 22.7 (*s*, $MeCH_2$); 26.1 (*s*, $CH_2(CH_2)_2O$); 29.4, 29.5, 29.6, 29.7 (4*s*, $Me(CH_2)_2(CH_2)_{12}$, CH_2CH_2O); 31.9 (*s*, $MeCH_2CH_2$); 44.3 (*s*, CH_2 (oxirane)); 50.9 (*s*, CH); 71.5, 71.8 (2*s*, $CH_2OCH_2CH_2$).

6.2. *1,3-Bis(12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecyloxy)propan-2-ol* (**22a**). As described for **23a**, with **21a** (2.1 g, 3.9 mmol), 12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecan-1-ol (1.9 g, 3.9 mmol), and 0.13 ml of 0.1M $SnCl_4$: **22a** (2.6 g, 64%). White powder. TLC (Et_2O/hexane 1:1): R_f 0.64. ^{1}H-NMR ($CDCl_3$): 1.06–1.39 (br. *s*, 2 $CF_2(CH_2)_2(CH_2)_7$); 1.40–1.63 (*m*, 2 $CF_2CH_2CH_2$, 2 CH_2CH_2O); 1.98 (*tt*, ^3J = 7.8, ^3J(H,F) = 18.8, 2 CF_2CH_2); 2.51 (*d*, ^3J = 4.0, OH); 3.25–3.53 (*m*, 2 CH_2OCH_2); 3.80–3.94 (*m*, CH). ^{13}C-NMR ($CDCl_3$): 20.1 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 26.1 (*s*, $CH_2(CH_2)_2O$); 29.1, 29.2, 29.3, 29.4, 29.5, 29.6 (6*s*, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.9 (*t*, ^2J(C,F) = 22, CF_2CH_2); 69.5 (*s*, CHOH); 71.6, 71.9 (2*s*, CH_2O). ^{19}F-NMR ($CDCl_3$): identical to that of **2b**.

1,3-Bis(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecyloxy)propan-2-ol (**22b**). As described for **23a**, with **21b** (3.1 g, 4.8 mmol), 12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecan-1-ol (2.8 g, 4.8 mmol), and 0.10 ml of 0.1M $SnCl_4$: **22b** (3.4 g, 57%). White powder. TLC (Et_2O/hexane 1:1): R_f 0.62. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **22a**. ^{19}F-NMR ($CDCl_3$): identical to that of **2c**.

6.3. rac-*1-(Octadecyloxy)-3-(12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecyloxy)propan-2-ol* (**23a**). A mixture of **21c** (1.8 g, 5.5 mmol), 12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecan-1-ol (2.7 g, 5.5 mmol), and 0.18 ml of 0.1M $SnCl_4$ in $CHCl_2$ was stirred at 80° for 7 h. The mixture was then diluted with $CHCl_3$, washed with a sat. aq. $NaHCO_3$ soln. and H_2O, and evaporated. CC (Et_2O/hexane) of the residue and recrystallization from pentane gave **23a** (4.0 g, 54%). White powder. TLC (Et_2O/hexane 1:1): R_f 0.65. ^{1}H-NMR ($CDCl_3$): 0.80 (*t*, ^3J = 6.3, Me); 1.10–1.37 (*m*, $CF_2(CH_2)_2(CH_2)_7$, $Me(CH_2)_{15}$); 1.40–1.61 (*m*, $CF_2CH_2CH_2$, 2 CH_2CH_2O); 2.00 (*t*, ^3J = 7.5, ^3J(H,F) = 18.8, CF_2CH_2); 2.51 (*d*, ^3J = 3.8, OH); 3.30–3.50 (*m*, 2 CH_2OCH_2); 3.80–3.95 (*m*, CH). ^{13}C-NMR ($CDCl_3$): 14.1 (*s*, Me); 20.1 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 22.7 (*s*, $MeCH_2$); 26.1 (*s*, $CH_2(CH_2)_2O$); 29.1, 29.2, 29.3, 29.4,29.5, 29.6, 29.7 (7*s*, $CF_2(CH_2)_2(CH_2)_6$, $Me(CH_2)_2(CH_2)_{12}$, CH_2CH_2O); 30.9 (*t*, ^2J(C,F) = 23, CF_2CH_2); 31.9 (*s*, $MeCH_2CH_2$); 69.5 (*s*, CHOH); 71.6, 71.7, 71.9 (3*s*, CH_2O). ^{19}F-NMR ($CDCl_3$): identical to that of **2b**. Compound **23a** was also obtained from **21a** and octadecanol using this procedure.

rac-*1-(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-Heptadecafluorononadecyloxy)-3-(octadecyloxy)-propan-2-ol* (**23b**). As described for **23a**, with **21c** (3.0 g, 9.2 mmol), 12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecan-1-ol (5.4 g, 9.2 mmol) and 0.30 ml of 0.1M $SnCl_4$: 4.6 g (55%) of **23b**. White powder. TLC (Et_2O/hexane 1:1): R_f 0.64. ^{1}H- and ^{13}C-NMR ($CDCl_3$): identical to those of **23a**. ^{19}F-NMR ($CDCl_3$): identical to that of **2c**.

7. *Fluorocarbon* rac-*1,2-Di-O-alk(en)ylglycero-3-phosphocholines* **I** *and* **II**. 7.1. rac-*2,3-Bis(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)propyl 2-(Trimethylammonio)ethyl Phosphate* (**IAa**). *Method A*: A soln. of **4a** (4.6 g, 5.5 mmol) and Et_3N (2 ml, 14.4 mmol) in dry Et_2O (50 ml) was added dropwise to a cooled soln. (0°) of 2-bromoethyl phosphodichloridate (1.9 g, 7.9 mmol) in dry Et_2O (50 ml). The mixture was first stirred at r.t. for 12 h, then heated for 4 h at reflux. At r.t., 20 ml of H_2O were added, and stirring was continued for 17 h. The mixture was decanted, the aq. phase extracted with $CHCl_3$, the org. phase evaporated, the crude residue dissolved in $CHCl_3$/MeCN 90:40, and gaseous Me_3N (10.0 g, 169 mmol) bubbled through this soln. The flask was closed and heated for 21 h at 50°. After cooling, the solvents were removed. The waxy residue was dissolved in $CHCl_3$/MeOH 2:1 and stirred for 3 h with Ag_2CO_3 (6.0 g, 21.8 mmol). The soln. was filtered over *Celite* and evaporated and the residue purified by CC ($CHCl_3$/MeOH) and recrystallization from a $CHCl_3$/acetone: 4.0 g (73%) of **IAa**. White

powder. ^{1}H-NMR ($CDCl_3/CD_3OD$): 1.00–1.25 (*m*, 2 $CF_2(CH_2)_2(CH_2)_7$); 1.26–1.50 (*m*, 2 $CF_2CH_2CH_2$, 2 CH_2CH_2O); 1.83 (*tt*, ^3J = 7.7, ^3J(H,F) = 18.8, CF_2CH_2); 3.00 (*s*, Me_3N^+); 3.16–3.50 (*m*, 2 CH_2OCH_2, CH_2OCH, CH_2N); 3.67 (*dd*, ^3J = 5.5, ^3J(H,P) = 5.5, $CHCH_2OP$); 3.94–4.10 (*m*, $POCH_2CH_2N$). ^{13}C-NMR ($CDCl_3/CD_3OD$): 20.0 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 25.9, 26.0 (2*s*, $CH_2(CH_2)_2O$); 28.9, 29.1, 29.2, 29.3, 29.4, 29.5, 29.6, 29.9 (8*s*, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.7 (*t*, ^2J(C,F) = 22, CF_2CH_2); 54.0 (*t*, ^1J(C,N) = 4, MeN); 58.8 (*d*, ^2J(C,P) = 5, $POCH_2CH_2N$); 65.0 (*d*, ^2J(C,P) = 6, $CHCH_2OP$); 66.5 (*dt*, ^1J(C,N) = 4, ^3J(C,P) = 8, CH_2N); 70.5, 70.6, 71.6 (3*s*, CH_2O); 78.0 (*d*, ^3J(C,P) = 8, $CHCH_2OP$). ^{19}F-NMR ($CDCl_3/CD_3OD$): identical to that of **2a**. ^{31}P-NMR ($CDCl_3/CD_3OD$): 0.22 (*s*). Anal. calc. for $C_{38}H_{62}F_{18}NO_6P \cdot H_2O$: C 44.75, H 6.32, N 1.37, P 3.04; found: C 44.73, H 6.47, N 1.20, P 2.97.

rac-*2,3-Bis(12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecyloxy)propyl 2-(Trimethylammonio)ethyl Phosphate* (**IAb**). *Method B*: A soln. of **4b** (1.3 g, 1.2 mmol) and Et_3N (0.34 ml, 2.4 mmol) in anh. THF (5 ml) was added dropwise to a THF (5 ml) soln. of $POCl_3$ (0.22 ml, 2.4 mmol) cooled to 0°. After stirring for 45 min at 0° and 5 h at r.t., the mixture was filtered under anh. N_2 to remove the precipitate of Et_3NHCl. Solvents and excess $POCl_3$ were evaporated under reduced pressure. After redissolution in dry $CHCl_3$ (5.1 ml), pyridine (0.8 ml), and choline tosylate (0.52 g, 1.9 mmol) were added. The mixture was stirred at r.t. for 4 h. After hydrolysis with 0.4 ml of H_2O (3 h), the solvents were evaporated. The crude product solubilized in $CHCl_3$/MeOH 1:1 was passed through a mixed-bed ion-exchange resin (*Serdolit MB-3*). CC (silica gel, $CHCl_3$/MeOH) gave 1.4 g (90%) of **IAb**. White powder. ^{1}H- and ^{13}C-NMR ($CDCl_3/CD_3OD$): identical to those of **IAa**. ^{19}F-NMR ($CDCl_3/CD_3OD$): identical to that of **2b**. ^{31}P-NMR ($CDCl_3/CD_3OD$): 0.26 (*s*). Anal. calc. for $C_{42}H_{62}F_{26}NO_6P \cdot 3\ H_2O$: C 40.17, H 5.45, N 1.11, P 2.46; found: C 40.86, H 5.59, N 1.07, P 2.38.

rac-*2,3-Bis(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecyloxy)propyl 2-(Trimethylammonio)ethyl Phosphate* (**IAc**). *Method B*, with **4c** (1.1 g, 0.9 mmol), Et_3N (0.23 ml, 1.6 mmol), $POCl_3$ (0.15 ml, 1.6 mmol), then choline tosylate (0.37 mg, 1.3 mmol), pyridine (0.6 ml), and H_2O (0.3 ml). Ion-exchange and CC ($CHCl_3$/MeOH) gave 0.87 g (72%) of **IAc**. White powder. ^{1}H- and ^{13}C-NMR ($CDCl_3/CD_3OD$): identical to those of **IAa**. ^{19}F-NMR ($CDCl_3/CD_3OD$): identical to that of **2c**. ^{31}P-NMR ($CDCl_3/CD_3OD$): 0.21 (*s*). Anal. calc. for $C_{46}H_{62}F_{34}NO_6P \cdot 3\ H_2O$: C 37.94, H 4.71, N 0.96, P 2.12; found: C 38.28, H 4.77, N 0.91, P 2.20.

rac-*2,3-Bis(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-heptadecafluorotridecyloxy)propyl 2-(Trimethylammonio)ethyl Phosphate* (**IAd**). Hydrogenolysis of **IA'd** (0.20 g, 0.16 mmol) with Pd/C (30 mg) in EtOH (10 ml) at r.t. in an autoclave under H_2 (40 atm) during 4 days led to 0.20 g (100%) of **IAd**. Alternatively, **IAd** was also obtained from **4d** using *Method B*. ^{1}H-NMR ($CDCl_3/CD_3OD$): 1.10–1.28 (*m*, 2 $CF_2(CH_2)_2CH_2$); 1.30–1.50 (*m*, 2 $CF_2CH_2CH_2$, 2 CH_2CH_2O); 1.80 (*tt*, ^3J = 7.7, ^3J(H,F) = 18.8, 2 CF_2CH_2); 3.00 (*s*, Me_3N^+); 3.15–3.52 (*m*, CH_2OCH_2, CH_2OCH, CH_2N); 3.62–3.81 (*m*, $CHCH_2OP$); 3.95–4.17 (*m*, $POCH_2CH_2N$). ^{13}C-NMR ($CDCl_3/CD_3OD$): 19.6 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 25.3, 25.4 (2*s*, $CF_2(CH_2)_2CH_2$); 29.2, 29.6 (2*s*, CH_2CH_2O); 30.8 (*t*, ^2J(C,F) = 22, CF_2CH_2); 53.7 (*t*, ^1J(C,N) = 6, MeN); 59.2 (br. *s*, $POCH_2CH_2N$); 65.4 (br. *s*, $CHCH_2OP$); 65.9 (br. *s*, CH_2N); 69.7, 70.1, 70.8 (3*s*, CH_2O); 77.7 (*d*, ^3J(C,P) = 8, $CHCH_2OP$). ^{19}F-NMR ($CDCl_3/CD_3OD$): identical to that of **2c**. ^{31}P-NMR ($CDCl_3/CD_3OD$): 0.24 (*s*). Anal. calc. for $C_{34}H_{38}F_{34}NO_6P \cdot 2\ H_2O$: C 32.16, H 3.33, N 1.10, P 2.44; found: C 31.94, H 3.40, N 1.19, P 2.42.

rac-*2,3-Bis(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-heptadecafluorotridec-4-enyloxy)propyl 2-(Trimethylammonio)ethyl Phosphate* (**IA'd**). *Method B*, with **7** (1.5 g, 1.4 mmol), $POCl_3$ (0.32 ml, 3.5 mmol), Et_3N (0.5 ml, 3.5 mmol), choline tosylate (0.58 g, 2.1 mmol), and 0.9 ml of pyridine. Hydrolysis, ion exchange, and CC ($CHCl_3$/MeOH) gave 1.1 g (64%) of **IA'd**, contaminated by its heptadecafluorotridec-3-enyloxy isomer(s) (see **7**). White powder. ^{1}H-NMR ($CDCl_3/CD_3OD$): 1.46–1.74 (*m*, 2 CH_2CH_2O); 2.02–2.38 (*m*, 2 $CH{=}CHCH_2$); 3.09 (*s*, Me_3N^+); 3.25–3.65 (*m*, CH_2OCH_2, CH_2OCH, CH_2N); 3.78 (*dd*, ^3J = 5.7, ^3J(H,P) = 5.7, $CHCH_2OP$); 4.00–4.20 (*m*, $POCH_2CH_2$); 5.25–5.65 (*m*, 2 CF_2CH); 6.16–6.44 (*m*, 2 $CF_2CH{=}CH$). ^{13}C-NMR ($CDCl_3/CD_2OD$): 25.2 (*cis*), 27.8, 28.2, 28.4 (4*s*, $CH{=}CHCH_2CH_2$); 54.1 (*t*, ^1J(C,N) = 4, MeN); 58.7 (*d*, ^2J(C,P) = 5, $POCH_2CH_2$); 64.8 (*d*, ^2J(C,P) = 6, $CHCH_2OP$); 66.4 (*m*, CH_2N); 69.0, 70.1, 70.7 (3*s*, CH_2OCH_2, CH_2OCH); 78.0 (*d*, ^3J(C,P) = 8, CHO); 117.0 (*t*, ^2J(C,F) = 23, CF_2CH); 142.5 (*t*, ^3J(C,F) = 9, $CF_2CH{=}CH$, *trans*); 145.0 (*t*, ^3J(C,F) = 5, $CF_2CH{=}CH$, *cis*). ^{19}F-NMR ($CDCl_3/CD_3OD$): identical to that of **7**. ^{31}P-NMR ($CDCl_3/CD_3OD$): 0.22 (*s*). Anal. calc. for $C_{34}H_{34}F_{34}NO_6P \cdot H_2O$: C 32.73, H 2.91, N 1.12, P 2.48; found: C 32.69, H 3.02, N 1.15, P 2.42.

7.2. rac-*3-(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-Heptadecafluorotridec-4-enyloxy)-2-(tetradecyloxy)-propyl 2-(Trimethylammonio)ethyl Phosphate* (**IIB'a**). *Method B* (see *7.1*), with **14a** (3.1 g, 4.0 mmol), $POCl_3$ (0.45 ml, 4.9 mmol), Et_3N (0.7 ml, 5.0 mmol) in dry Et_2O, choline tosylate (1.7 g, 6.0 mmol), and 2.6 ml of pyridine. Hydrolysis, ion exchange, CC ($CHCl_3$/MeOH), and recrystallization from acetone/MeCN gave 2.0 g (53%) of **IIB'a**. White powder. ^{1}H-NMR ($CDCl_3/CD_3OD$): 0.81 (*t*, ^3J = 6.1, Me); 1.07–1.39 (*m*, $Me(CH_2)_{11}$); 1.40–1.58 (*m*, CH_2CH_2OCH); 1.66 (*quint.*, ^3J = 6.3, $CH{=}CHCH_2CH_2$); 2.12–2.40 (*m*, $CH{=}CHCH_2$); 3.20 (*s*, Me_3N^+); 3.32–3.78 (*m*, CH_2OCH_2, CH_2OCH, CH_2N); 3.83 (*dd*, ^3J = 5.2, ^3J(H,P) = 5.2, $CHCH_2OP$); 4.11–4.30 (*m*, $POCH_2CH_2N$);

5.40–5.71 (*m*, CF_2CH=CH); 6.27–6.48 (*m*, CF_2CH=C*H*). ^{13}C-NMR ($CDCl_3/CD_3OD$): 13.9 (*s*, Me); 22.5 (*s*, $MeCH_2$); 25.9 (*s*, $CH_2(CH_2)_2O$); 27.9, 28.5, 29.2, 29.4, 29.5, 29.9 (6*s*, $Me(CH_2)_2(CH_2)_8$, CH_2CH_2O, CH=CH($CH_2)_2$); 31.8 ($MeCH_2CH_2$); 54.2 (*s*, MeN); 58.9 (*d*, ^2J(C,P) = 5, $POCH_2CH_2N$); 64.8 (*d*, ^2J(C,P) = 6, $CHCH_2OP$); 66.3 (*d*, ^3J(C,P) = 5, CH_2N); 70.2, 70.5 (2*s*, CH_2O); 77.8 (*d*, ^3J(C,P) = 8, $CHCH_2OP$); 117.0 (*t*, ^2J(C,F) = 23, CF_2CH=CH); 142.6 (*t*, ^3J(C,F) = 9, CF_2CH=CH, *trans*); 145 (CF_2CH=CH, *cis*). ^{19}F-NMR ($CDCl_3/CD_3OD$): identical to that of **7**. ^{31}P-NMR ($CDCl_3/CD_3OD$): 0.10 (*s*). Anal. calc. for $C_{35}H_{55}F_{17}NO_6P$: C 44.73, H 5.90, N 1.49, P 3.29; found: C 44.72, H 5.97, N 1.61, P 3.26.

rac-*3-(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-Heptadecafluorononadec-10-enyloxy)-2-(hexadecyloxy)propyl 2-(Trimethylammonio)ethyl Phosphate* (**IIB'b**). *Method B* (see *7.1*), with **14b** (2.4 g, 2.7 mmol), $POCl_3$ (0.3 ml, 3.3 mmol), Et_3N (0.5 ml, 3.6 mmol), choline tosylate (1.1 g, 4.1 mmol), and 1.4 ml of pyridine. Hydrolysis, ion exchange, and recrystallization from acetone/MeCN gave 2.1 g (73%) of **IIB'b**. White powder. ^{1}H-NMR ($CDCl_3/CD_3OD$): 0.70 (*t*, ^3J = 6.0, Me); 0.88–1.50 (*m*, CH=CH$CH_2(CH_2)_7$, $CH_3(CH_2)_{14}$); 1.90–2.22 (*m*, CH=CHCH_2); 3.07 (*s*, Me_3N^+); 3.18–3.57 (*m*, CH_2OCH_2, CH_2OCH, CH_2N); 3.62–3.82 (*m*, $CHCH_2OP$); 3.96–4.19 (*m*, $POCH_2CH_2N$); 5.28–5.56 (*m*, CF_2CH=CH); 6.10–6.43 (*m*, CF_2CH=C*H*). ^{13}C-NMR ($CDCl_3/CD_3OD$): 13.6 (*s*, Me); 22.4 ($MeCH_2$); 25.9 (*s*, $CH_2(CH_2)_2O$); 27.8, 28.3, 28.8, 28.9, 29.1, 29.3, 29.4, 29.5, 29.9 (9*s*, $Me(CH_2)_2(CH_2)_{10}$, CH_2CH_2O, CH=CH($CH_2)_6$); 31.7 ($MeCH_2CH_2$); 53.9 (*s*, MeN); 58.8 (*d*, ^2J(C,P) = 5, $POCH_2CH_2N$); 64.9 (*d*, ^2J(C,P) = 5, $CHCH_2OP$); 66.2 (*m*, CH_2N); 70.4, 71.5 (2*s*, CH_2O); 77.8 (*d*, ^3J(C,P) = 8, $CHCH_2OP$); 116.5 (*t*, ^2J(C,F) = 23, CF_2CH=CH); 143.1 (*t*, ^3J(C,F) = 9, CF_2CH=CH, *trans*); 145 (CF_2CH=CH, *cis*). ^{19}F-NMR ($CDCl_3/CD_3OD$): identical to that of **7**. ^{31}P-NMR ($CDCl_3/CD_3OD$): 0.28 (*s*). Anal. calc. for $C_{43}H_{71}F_{17}NO_6P \cdot H_2O$: C 48.31, H 6.88, N 1.31, P 2.89; found: C 48.14, H 6.98, N 1.25, P 2.84.

7.3. rac-*3-(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-Heptadecafluorotridecyloxy)-2-(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)propyl 2-(Trimethylammonio)ethyl Phosphate* (**IIAa**). *Method B* (see *7.1*), with **19a** (0.68 g, 0.7 mmol), $POCl_3$ (0.84 ml, 0.9 mmol), Et_3N (0.13 ml, 0.9 mmol), choline tosylate (0.31 g, 1.1 mmol), and pyridine (0.5 ml). Hydrolysis, ion exchange, CC (silica gel, $CHCl_3$/MeOH), and recrystallization from acetone/MeCN gave 0.60 g (75%) of **IIAa**. White powder. ^{1}H-NMR ($CDCl_3/CD_3OD$): 1.13–1.48 (*m*, $CF_2(CH_2)_2(CH_2)_7$, $CF_2(CH_2)_2CH_2$); 1.50–1.67 (*m*, 2 $CF_2CH_2CH_2$, 2 CH_2CH_2O); 1.82–2.17 (*m*, 2 CF_2CH_2); 3.25 (*s*, Me_3N^+); 3.33–3.65 (*m*, CH_2OCH_2, CH_2OCH, CH_2N); 3.84 (*dd*, ^3J = 7, ^3J(H,P) = 7, $CHCH_2OP$); 4.11–4.27 (*m*, $POCH_2CH_2N$). ^{13}C-NMR ($CDCl_3/CD_3OD$): 20.0 (br. *s*, $CF_2CH_2CH_2$); 25.7, 26.0 (2*s*, $CH_2CH_2CH_2O$); 29.0, 29.1, 29.2, 29.3, 29.5, 29.6, 30.0 (7*s*, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.7 (*t*, ^2J(C,F) = 21, CF_2CH_2); 54.3 (*s*, MeN); 58.8 (*d*, ^2J(C,P) = 6, $POCH_2CH_2N$); 64.9 (*d*, ^2J(C,P) = 7, $CHCH_2OP$); 66.4 (*m*, CH_2N); 70.6, 70.7, 71.1 (3*s*, CH_2O); 77.9 (*d*, ^3J(C,P) = 8, $CHCH_2OP$). ^{19}F-NMR ($CDCl_3/CD_3OD$): identical to that of **18a**. ^{31}P-NMR ($CDCl_3/CD_3OD$): 0.22 (*s*). Anal. calc. for $C_{36}H_{50}F_{26}NO_6P \cdot H_2O$: C 38.07, H 4.61, N 1.23, P 2.72; found: C 38.50, H 4.61, N 1.17, P 2.67.

rac-*2-(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-Heptadecafluorononadecyloxy)-3-(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)propyl 2-(Trimethylammonio)ethyl Phosphate* (**IIAb**). *Method B* (see *7.1*), with **19b** (0.80 g, 0.8 mmol), $POCl_3$ (0.14 ml, 1.5 mmol), Et_3N (0.2 ml, 1.5 mmol), choline tosylate (0.33 g, 1.2 mmol), and pyridine (0.5 ml). Hydrolysis, ion exchange, and CC ($CHCl_3$/MeOH) gave 0.72 g (78%) of **IIAb**. White powder. ^{1}H-NMR ($CDCl_3/CD_3OD$): identical to that of **IAa**. ^{13}C-NMR ($CDCl_3/CD_3OD$): identical to that of **IAa**, apart the *t* for CF_2CH_2 at 30.7 which is replaced by 2 *t* at 30.5 and 30.6 (^2J(C,F) = 22). ^{19}F-NMR ($CDCl_3/CD_3OD$): identical to that of **18a**. ^{31}P-NMR ($CDCl_3/CD_3OD$): −0.20 (*s*). Anal. calc. for $C_{42}H_{62}F_{26}NO_6P \cdot 2\,H_2O$: C 40.75, H 5.37, N 1.13, P 2.51; found: C 40.96, H 5.28, N 1.18, P 2.54.

8. *Fluorocarbon 1,3-Di-*O*-alkylglycero-2-phosphocholines* **III**. 8.1. rac-*2-(Octadecyloxy)-1-[(12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecyloxy)methyl]ethyl 2-(Trimethylammonio)ethyl Phosphate* (**IIIBa**). *Method B* (see *7.1*), with **23a** (1.8 g, 2.2 mmol), $POCl_3$ (0.46 ml, 5.0 mmol), Et_3N (0.7 ml, 5.0 mmol), choline tosylate (0.95 g, 3.5 mmol), and pyridine (1.5 ml). Hydrolysis, ion exchange, and CC ($CHCl_3$/MeOH) gave **IIIBa** (1.6 g, 74%). White powder. ^{1}H-NMR ($CDCl_3/CD_3OD$): 0.69 (*t*, ^3J = 6.1, Me); 0.94–1.25 (*m*, $Me(CH_2)_{15}$, $CF_2(CH_2)_2(CH_2)_7$); 1.26–1.53 (*m*, 2 $CF_2CH_2CH_2$, 2 CH_2CH_2O); 1.86 (*t*, ^3J = 7.5, ^3J(H,F) = 19.0, CF_2CH_2); 3.05 (*s*, Me_3N^+); 3.25 (*t*, ^3J = 6.7, 2 $CH_2CH_2OCH_2$); 3.40–3.61 (*m*, CH_2CHCH_2, CH_2N); 4.00–4.22 (*m*, CH, $POCH_2CH_2N$). ^{13}C-NMR ($CDCl_3/CD_3OD$): 13.7 (*s*, Me); 19.8 (*t*, ^3J(C,F) = 3, $CF_2CH_2CH_2$); 22.4 (*s*, $MeCH_2$); 25.8 (*s*, $CH_2CH_2CH_2O$); 28.6, 28.7, 28.8, 28.9, 29.0, 29.1 (6*s*, $Me(CH_2)_2(CH_2)_{12}$, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.3 (*t*, ^2J(C,F) = 23, CF_2CH_2); 31.4 (*s*, $MeCH_2CH_2$); 53.5 (*t*, ^1J(C,N) = 4, MeN); 58.4 (*d*, ^2J(C,P) = 5, $POCH_2CH_2N$); 66.2 (*dt*, ^1J(C,N) = 4, ^3J(C,P) = 7, CH_2N); 70.0 (*d*, ^3J(C,P) = 4, CH_2CHCH_2); 71.3 (*s*, CH_2OCH_2CH); 73.3 (*d*, ^2J(C,P) = 6, CHOP). ^{19}F-NMR ($CDCl_3/CD_3OD$): identical to that of **2b**. ^{31}P-NMR ($CDCl_3/CD_3OD$): −0.54 (*s*). Anal. calc. for $C_{43}H_{77}F_{13}NO_6P \cdot H_2O$: C 51.64, H 7.96, N 1.40, P 3.09; found: C 51.66, H 8.01, N 1.34, P 3.16.

rac-*2-(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-Heptadecafluorononadecyloxy)-1-[(octadecyloxy)-methyl]ethyl 2-(Trimethylammonio)ethyl Phosphate* (**IIIBb**). *Method B* (see *7.1*), with **23b** (1.0 g, 1.1 mmol), $POCl_3$ (0.19 ml, 2.1 mmol), Et_3N (0.3 ml, 2.1 mmol), choline tosylate (0.45 g, 1.6 mmol), and pyridine (0.7 ml). Hydrolysis, ion exchange, and CC ($CHCl_3$/MeOH) gave 0.87 g (73%) of **IIIBb**. White powder. ^{1}H- and ^{13}C-NMR ($CDCl_3$/CD_3OD): identical to those of **IIIBa**. ^{19}F-NMR ($CDCl_3$/CD_3OD): identical to that of **2c**. ^{31}P-NMR ($CDCl_3$/CD_3OD): 0.41 (*s*). Anal. calc. for $C_{45}H_{77}F_{17}NO_6P \cdot H_2O$: C 49.13, H 7.23, N 1.27, P 2.81; found: C 48.85, H 7.38, N 1.35, P 2.77.

8.2. *2-(12,12,13,13,14,14,15,15,16,16,17,17,17-Tridecafluoroheptadecyloxy)-1-[(12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecyloxy)methyl]ethyl 2-(Trimethylammonio)ethyl Phosphate* (**IIIAa**). *Method B* (see *7.1*), with **22a** (1.7 g, 1.67 mmol), $POCl_3$ (0.35 ml, 3.8 mmol), Et_3N (0.5 ml, 3.8 mmol), choline tosylate (0.7 g, 2.5 mmol), and pyridine (1.0 ml). Hydrolysis, ion exchange, CC ($CHCl_3$/MeOH), and recrystallization ($CHCl_3$/MeCN) gave 1.34 g (67%) of **IIIAa**. White powder. ^{1}H-NMR ($CDCl_3$/CD_3OD): 1.10–1.34 (*m*, 2 $CF_2(CH_2)_2(CH_2)_7$); 1.35–1.60 (*m*, 2 $CF_2CH_2CH_2$, 2 CH_2CH_2O); 1.94 (*t*, ^3J = 7.5, ^3J(H,F) = 19.0, CF_2CH_2); 3.10 (*s*, Me_3N^+); 3.33 (*t*, ^3J = 6.7, 2 CH_2OCH_2); 3.41–3.58 (*m*, CH_2CHCH_2, CH_2N); 4.09–4.31 (*m*, CH, $POCH_2CH_2N$). ^{13}C-NMR ($CDCl_3$/CD_3OD): 19.8 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 25.8 (*s*, $CH_2CH_2CH_2O$); 28.9, 29.0, 29.1, 29.3, 29.4, 29.5 (6*s*, $CF_2(CH_2)_2(CH_2)_6CH_2CH_2$); 30.6 (*t*, ^2J(C,F) = 22, CF_2CH_2); 54.1 (*t*, ^1J(C,N) = 3, MeN); 58.8 (*d*, ^2J(C,P) = 5, $POCH_2CH_2N$); 66.3 (*m*, CH_2N); 70.4 (*d*, ^3J(C,P) = 4, CH_2CHCH_2); 71.4 (*s*, CH_2OCH_2CH); 73.5 (*d*, ^2J(C,P) = 6, CHOP). ^{19}F-NMR ($CDCl_3$/CD_3OD): identical to that of **2b**. ^{31}P-NMR ($CDCl_3$/CD_3OD): −0.44 (*s*). Anal. calc. for $C_{42}H_{62}F_{26}NO_6P \cdot 2\ H_2O$: C 40.75, H 5.37, N 1.13, P 2.50; found: C 40.54, H 5.41, N 1.18, P 2.46.

2-(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-Heptadecafluorononadecyloxy)-1-[(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptadecafluorononadecyloxy)methyl]ethyl 2-(Trimethylammonio)ethyl Phosphate (**IIIAb**). *Method B* (see *7.1*), with **22b** (1.0 g, 0.8 mmol), $POCl_3$ (0.15 ml, 1.6 mmol), Et_3N (0.23 ml, 1.6 mmol), choline tosylate (0.33 g, 1.2 mmol), and pyridine (0.5 ml). Hydrolysis, ion exchange, and CC ($CHCl_3$/MeOH) gave 0.80 g (70%) of **IIIAb**. White powder. ^{1}H- and ^{13}C-NMR ($CDCl_3$/CD_3OD): identical to those of **IIIAa**. ^{19}F-NMR ($CDCl_3$/CD_3OD): identical to that of **2c**. ^{31}P-NMR ($CDCl_3$/CD_3OD): −0.44 (*s*). Anal. calc. for $C_{46}H_{62}F_{34}NO_6P \cdot 2\ H_2O$: C 38.48, H 4.62, N 0.97, P 2.15; found: C 38.55, H 4.83, N 1.09, P 2.14.

9. *Fluorocarbon* rac-*1,2-Di-O-alkylglycero-3-phosphoethanolamines* **IV**. rac-*2,3-Bis(12,12,13,13,14,14,15,15,15-nonafluoropentadecyloxy)propyl 2-Ammonioethyl Phosphate* (**IVa**). A soln. of **4a** (0.46 g, 0.6 mmol) and Et_3N (0.16 ml, 1.1 mmol) in 3 ml of anh. THF was added to a THF (3 ml) soln. of $POCl_3$ (0.10 ml, 1.1 mmol) cooled to 0°. After stirring for 45 min at 0° and 5 h at r.t., the mixture was filtered under anh. N_2 to remove the precipitate of Et_3NHCl. The solvents and excess of $POCl_3$ were evaporated. After redissolution in dry $CHCl_3$ (2.5 ml), pyridine (0.2 ml) and 2-[(*tert*-butoxy)carbonylamino]ethanol (0.13 g, 0.8 mmol) were added. The mixture was stirred at r.t. during 13 h and then evaporated. The hydrolysis was performed by solubilizing the residue in $CHCl_3$/pyridine/H_2O 1:1:0.1 followed by evaporation. This was repeated several times until completion (^{31}P-NMR monitoring). The crude product was then dissolved in 50 ml of CH_2Cl_2, and 5.4 ml of CF_3COOH were added for the deprotection (TLC monitoring) ($CHCl_3$/MeOH/16N NH_3 6:3:0.6). After completion (1 h), cyclohexane was added, and the solvents were evaporated. The residue was purified by CC (silica gel, $CHCl_3$/MeOH 9:1, then $CHCl_3$/MeOH/16N NH_3 9:1:0.1): 0.27 g (52%) of **IVa**. White powder. ^{1}H-NMR ($CDCl_3$/CD_3OD): 1.10–1.30 (br. *s*, 2 $CF_2(CH_2)_2(CH_2)_7$); 1.30–1.50 (*m*, 2 $CF_2CH_2CH_2$, 2 CH_2CH_2O); 1.92 (*tt*, ^3J = 7.8, ^3J(H,F) = 18.8, 2 CF_2CH_2); 2.95 (*m*, CH_2N); 3.22–3.55 (*m*, CH_2OCH_2, CH_2OCH); 3.75 (*dd*, ^3J = 5.6, ^3J(H,P) = 5.6, $CHCH_2OP$); 3.82–4.00 (*m*, $POCH_2CH_2N$). ^{13}C-NMR ($CDCl_3$/CD_3OD): 19.9 (*t*, ^3J(C,F) = 4, $CF_2CH_2CH_2$); 25.8, 25.9 (2*s*, $CH_2CH_2CH_2O$); 29.0, 29.1, 29.2, 29.3, 29.4, 29.5, 29.9 (7*s*, $CF_2(CH_2)_2(CH_2)_6$, CH_2CH_2O); 30.7 (*t*, ^2J(C,F) = 23, CF_2CH_2); 40.2 (*d*, ^3J(C,P) = 6, CH_2N); 61.5 (*d*, ^2J(C,P) = 5, $POCH_2CH_2N$); 65.2 (*d*, ^2J(C,P) = 5, $CHCH_2OP$); 70.1, 70.5, 71.7 (3*s*, CH_2OCH_2, CH_2OCH); 77.7 (*d*, ^3J(C,P) = 8, CH in CD_2Cl_2/CD_3OD). ^{19}F-NMR ($CDCl_3$/CD_3OD): identical to that of **2a**. ^{31}P-NMR ($CDCl_3$/CD_3OD): 1.42 (*s*). Anal. calc. for $C_{35}H_{56}F_{18}NO_6P$: C 43.80, H 5.88, N 1.46, P 3.23; found: C 44.05, H 5.77, N 1.43, P 3.31.

rac-*2,3-Bis(12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecyloxy)propyl 2-Ammonioethyl Phosphate* (**IVb**). As described for **IVa**, with **4b** (1.0 g, 1.0 mmol), $POCl_3$ (0.12 ml, 1.3 mmol), Et_3N (0.2 ml, 1.3 mmol), 2-[(*tert*-butoxy)carbonylamino]ethanol (0.28 g, 1.7 mmol), and 0.3 ml of pyridine. Hydrolysis, deprotection with CF_3COOH (10 ml), and CC gave 0.60 g (50%) of **IVb**. White powder. ^{1}H- and ^{13}C-NMR ($CDCl_3$/CD_3OD): identical to those of **IVa**. ^{19}F-NMR ($CDCl_3$/CD_3OD): identical to that of **2b**. ^{31}P-NMR ($CDCl_3$/CD_3OD): 1.62 (*s*). Anal. calc. for $C_{39}H_{56}F_{26}NO_6P \cdot H_2O$: C 39.77, H 4.96, N 1.19, P 2.63; found: C 40.08, H 5.13, N 1.33, P 2.56.

rac-*2,3-Bis(12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19,19-heptafluorononadecyloxy)propyl 2-Ammonioethyl Phosphate* (**IVc**). As described for **IVa**, with **4c** (0.81 g, 0.6 mmol), $POCl_3$ (0.12 ml, 1.2 mmol), Et_3N (0.2 ml,

1.3 mmol), 2-[(*tert*-butoxy)carbonylamino]ethanol (0.20 g, 1.2 mmol), and 0.3 ml of pyridine. Hydrolysis, deprotection with CF_3COOH (6.5 ml), and CC gave 0.50 g (55%) of **IVc**. White powder. ^1H- and ^{13}C-NMR ($CDCl_3$/CD_3OD): identical to those of **IVa**. ^{19}F-NMR ($CDCl_3$/CD_3OD): identical to that of **2c**. ^{31}P-NMR ($CDCl_3$/CD_3OD): 1.51 (*s*). Anal. calc. for $C_{43}H_{56}F_{34}NO_6P \cdot H_2O$: C 37.45, H 4.24, N 1.01, P 2.24; found: C 37.21, H 4.22, N 1.11, P 2.11.

10. *Biological Tests.* The biological tests were performed on liposomal dispersions of the phospholipid to be tested in 0.9% NaCl soln. These dispersions (average particle size *ca.* 100 nm, measured by light-scattering spectroscopy using a *Coulter-N4-MD* sub-micron particle analyzer) were prepared according to the general procedure described in [6a]. The hemolytic activity was evaluated on human red blood cells according to [25]. The *in vivo* test consisted of injecting 500 µl of the isotonic heat-sterilized liposomal dispersion into the tail vein of 10 *Dawley* mice of 20–25 g weight. Growth and any symptoms of intoxication of the animals were monitored over a period of one month and compared with those of a control group.

Supplementary Material. – ^1H-, ^{13}C-, and ^{19}F-NMR spectra are available upon request.

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