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Synthesis of double-tailed (perfluoroalkyl)alkyl phosphosugars: new components for drug-carrying and -targeting systems

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Abstract

Double-tailed D-glycose 3- and 6-[sodium (perfluoroalkyl)alkyl phosphates] were synthesized via the hydrogen phosphonate approach. Stable double-tailed (perfluoroalkyl)alkyl hydrogenphosphonates, prepared from double-tailed (perfluoroalkyl)alkanols and PCl_3–imidazole, reacted with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose or with 1,2:5,6 -di-*O*-isopropylidene-α-D-glucofuranose in the presence of Me_3CCOCl as the condensing agent to give, after oxidation with aqueous iodine, the corresponding *O*-protected glycose phosphate diesters. *O*-Deisopropylidenation of the latter by aqueous trifluoroacetic acid afforded the target compound in 70% yield, based on the protected glycosides. Condensation of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose or -mannopyranose with double-tailed (perfluoroalkyl)alkyl hydrogenphosphonates or 10-eicosyl hydrogenphosphonate, via the coupling and oxidation steps described above, afforded per-*O*-acetylglycose phosphodiesters. *O*-Deacetylation with MeONa–MeOH was achieved in 65% yield based on the protected sugar. All the compounds were characterized by ^{19}F, ^{1}H, ^{13}C, and ^{31}P NMR data. Preliminary biocompatibility assays indicate a reduction of hemolytic activity when fluorinated chains are present and maximum tolerated doses of ca. 125 mg/kg body weight in mice.

1. Introduction

Liposomes and other types of vesicles are being evaluated as a means of encapsulating, carrying, and targeting drugs [1]. The objectives are to deliver

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nonpermeating drugs into cells, allow targeting and delivery of drugs to desired tissues, reduce premature drug loss or breakdown in biological fluids, reduce toxicity, and enhance therapeutic efficacy [2].

In spite of having a lipid composition close to that of cell membranes, intravenously injected phospholipid-based liposomes are readily recognized as foreign particles by the reticuloendothelial system and are rapidly removed from the bloodstream. This characteristic can be used for the treatment of certain parasitic infections in macrophages and for intracellular delivery of macrophage activating substances [3].

An appropriate choice of the lipid composition, size, and surface charge of the liposomes can influence their fate and behavior in vivo. For example, the addition of small amounts of a negatively charged glycolipid in a solid-phase neutral phospholipid induces a reduction of the clearance rate [4]. Also, small unilamellar vesicles exhibit longer blood residence times than larger multilamellar vesicles of the same composition [5].

Liposomes made from natural phospholipids are, however, not very stable. They tend to aggregate, fuse, and eventually precipitate. Stabilization of their membrane usually requires a large compositional heterogeneity [6].

Synthetic double-tailed amphiphiles usually also assemble spontaneously in water to form bilayer type structures [7]. This has led to extensive research on biomembrane models and vesicles. Synthetic bilayer membranes often possess physicochemical characteristics similar to those of biolipid bilayer membranes. For instance, bilayers of dialkylated amphiphiles undergo gel-to-liquid crystal phase transitions in a manner similar to those of lecithin bilayers [8]. Structural variety and easy access make synthetic bilayers attractive for the production of vesicles with versatile properties, robust enough to be freeze-dried for long-term storage and stable in vivo.

A few amphiphiles with perfluoroalkylated tails have been reported to readily form bilayer membranes [9–11]. The perfluoroalkyl chain was found to enhance the amphiphile's surface activity and their tendency to form vesicles. Even short, single perfluoroalkylated tail compounds were found to form stable vesicles and other supramolecular assemblies while their hydrogenated analogues did not [12]. Perfluoroalkylated vesicles behave rather differently from vesicles obtained from hydrogenated analogues. They were shown in particular to offer an enhanced barrier against permeation of ions and small molecules, whether hydrophilic and lipophilic. This results from the formation of an impermeable film within the bilayer membrane [10,13].

In the present paper, we describe a new bilayer-forming class of anionic perfluoroalkylated amphiphiles. They consist of the glycose *n*-(sodium saturated-alkyl phosphates) **5(a–h)**. Their hydrophobic part is an unsymmetrical double-chain (one being fluorinated, the other not) and the polar head is an ionic glycose phosphate ester. The sugar moiety can be chosen to allow specific in vivo recognition and targeting. A hydrocarbon analogue, **5i**, has been synthesized to evaluate the impact of the perfluoroalkylated chain on the surfactant's aggregation

behavior. This project is part of an effort of our laboratory to develop new components for drug delivery systems [14].

2. Results and discussion

The most important step in the synthesis of oligonucleotides is the formation of the phosphodiester linkage. Two strategies can be considered for this purpose; nucleophilic substitution by an alcohol on an appropriate phosphorus center, or nucleophilic substitution of alkyl halides by a phosphate anion. Phosphodiesters of carbohydrates are accessible by various phosphorylation methods after appropriate protection of the sugar. These methods include the phosphodiester [15], phosphoramidite [16], phosphotriester [17], cyclic enediol phosphate [18], phosphoroditriazolide [19], and other methods [20].

The phosphodiester strategy consists in the condensation of an *O*-protected glycose phosphate with an alcohol in the presence of an activating agent such as dicyclohexylcarbodiimide [17,20], mesitylenesulfonyl chloride [15,17], triisopropylbenzenesulfonyl chloride [15,17], or trichloroacetonitrile [21]. This latter activating agent was utilized by Neumann et al. for the synthesis of a (hexadecyl) (glucose) phosphodiester [22] but it is restricted by access to aldose phosphates. Phosphoramidite chemistry, used for example by van Boom and co-workers to prepare fucosyl → P → 6-mannose [23], gave high yields but involves the use of chloro(2-cyanoethoxy)diisopropylaminophosphine [$(NCCH_2CH_2O)(Cl)PN(CHMe_2)_2$] which is an unstable intermediate. The phosphotriester approach, adopted by Ogawa for the preparation of bridged phosphate derivatives [24], was efficient for the condensation step but the removal of the protecting groups (trichloroethyl, chlorophenyl, methyl) led to poor overall yields. In the cyclic enediol phosphoryl method [18], investigated by Ramirez, the synthetic sequence was based on an oxyphosphorane whose access is difficult. Recently, we reported the synthesis of D-glucose 6- and 3-perfluoroalkylated phosphate derivatives via a phosphoroditriazolide [25], but this intermediate is unstable and the condensation with the secondary hydroxyl group of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose was incomplete.

The hydrogenphosphonate approach recently proposed for the preparation of oligonucleotides [26] and glycose phosphosugars [27] linked by primary or secondary hydroxyl groups attracted our attention for the synthesis of carbohydrate phosphodiesters. This method is known to give high yields and is easy to implement. Moreover, all the intermediates formed are stable in air at room temperature and there is no need to protect the phosphorus center. The synthetic sequence is the following: synthesis of a hydrogenphosphonate monoester via an iminophosphine, condensation of this hydrogenphosphonate monoester with a conveniently protected glycoside, then conversion under mild oxidative conditions into the phosphodiester, followed by deprotection of the sugar.

First, we chose to form the hydrogenphosphonate monoester by phosphorylation of 1-(perfluorooctyl)-3-dodecanol [28] with tris(imidazolyl)phosphine (prepared in situ from PCl_3, imidazole, and triethylamine in toluene) followed by

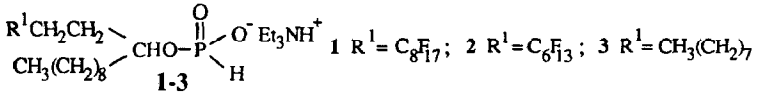
hydrolysis at pH 8. Purification by filtration on a silica gel column gave 1-(perfluorooctyl)-3-dodecyl triethylammonium hydrogenphosphonate (**1**) as an oil in 71% yield. The NMR data establish unambiguously the formation of the hydrogenphosphonate bond. The ^{31}P NMR spectrum decoupled from ^{1}H displays one single signal at δ 3.53 ppm and, in the absence of decoupling, a doublet of doublets due to the $^{1}J_{H,P}$ (628.5 Hz) and $^{3}J_{POCH}$ (10.3 Hz) couplings. The structure was further confirmed by ^{1}H NMR and by the characteristic ν(P–H) value at 2500 cm^{-1} in the IR spectrum. In the ^{13}C NMR spectrum, the expected $^{13}C-^{31}P$ couplings for the α carbon ($^{2}J_{C,P}$ 5.4 Hz) and for one β carbon ($^{3}J_{C,P}$ 3 Hz) are also observed; however, the resonance of the second β carbon is broadened by the additional $^{3}J_{C,F}$ coupling. The perfluorohexyl homologue **2**, and its hydrogenated counterpart, 10-eicosyl triethylammonium hydrogenphosphonate (**3**), synthesized by the same procedure, exhibit NMR data similar to those of compound **1** (Scheme 1).

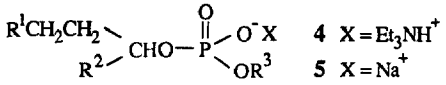
The second step of the synthesis involves a coupling reagent [29] such as pivaloyl chloride (PVCl, Me_3CCOCl), 2-chloro-5,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinane (NPCl), or bis(2-oxo-3-oxazolidinyl)phosphinic chloride (OXP). Of these three reagents, we chose PVCl which is the cheapest, the most commonly used in the synthesis of oligonucleotides, and allows fast coupling without side reactions. The others are also efficient, but OXP has a low solubility in organic solvents and NPCl is more expensive than pivaloyl chloride.

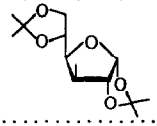
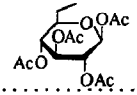
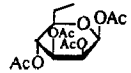
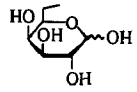
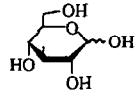
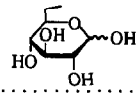
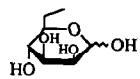
All of the *O*-protected sugars used are commercially available except for 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose which was prepared according to Reynolds et al. [30] from D-mannose by tritylation, acetylation, and detritylation using acetic acid saturated with hydrogen bromide.

Kinetic studies [31] have shown that, in the oxidation step, abstraction of the proton from hydrogenphosphonate diesters was the rate limiting step and also that the P–H bond's reactivity depended upon the other substituents present. A first attempt to oxidize these hydrogenphosphonate diesters without triethylamine afforded the target compounds in only 30% yield. This yield was improved to 60% by adding Et_3N to the oxidizing medium. We have determined that oxidation by an aqueous iodine solution, followed by addition of Et_3N, gave higher yields than the reverse sequence, whatever the carbohydrate employed.

Condensation in situ of the hydrogenphosphonate **1** with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose in the presence of pivaloyl chloride, followed by oxidation with a freshly prepared solution of iodine in aqueous pyridine in the presence of Et_3N as a catalyst, afforded 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose 6-[triethylammonium 1-(perfluorooctyl)-3-dodecyl phosphate] (**4a**) isolated in 72% yield. The *O*-protected glycose (perfluoroalkyl)alkyl triethylammonium phosphates **4(b–h)** and their hydrocarbon analogue **4i** were synthesized by the same procedure (Scheme 1). It is noticeable that there was no alkaline hydrolysis of the phosphate diesters. However, it was shown and characterized by ^{13}C NMR that some chromatographic fractions were contaminated, e.g., for **4e** and **4h**, by traces of the 1-*O*-deacetylated compound; this had been previously observed in the preparation of (perfluoroalkyl)ethyl analogues [25].





Compound	R^1	R^2	R^3
4a	C_8F_{17}	$CH_3(CH_2)_8$	
4b	C_6F_{13}		
4c	C_8F_{17}	$CH_3(CH_2)_8$	
4d	C_6F_{13}		
4e	C_8F_{17}	$CH_3(CH_2)_8$	
4f	C_6F_{13}		
4g	C_8F_{17}	$CH_3(CH_2)_8$	
4h	C_6F_{13}		
4i	$CH_3(CH_2)_6$	$CH_3(CH_2)_9$	
5a	C_8F_{17}	$CH_3(CH_2)_8$	
5b	C_6F_{13}		
5c	C_8F_{17}	$CH_3(CH_2)_8$	
5d	C_6F_{13}		
5e	C_8F_{17}	$CH_3(CH_2)_8$	
5f	C_6F_{13}		
5g	C_8F_{17}	$CH_3(CH_2)_8$	
5h	C_6F_{13}		
5i	$CH_3(CH_2)_6$	$CH_3(CH_2)_9$	

Scheme 1. Structures of the compounds synthesized.

The structures of the *O*-protected glycose phosphodiester derivatives were unambiguously established by ^{13}C, ^{1}H, and ^{31}P NMR spectroscopy [32]. The position of the phosphate group can be conclusively determinated by the expected $^{31}P-^{13}C$ coupling constants [33]. The ^{13}C chemical shifts of the glycose phosphates were assigned by comparison with the nonphosphorylated saccharides [32]. Upon

phosphorylation, the phosphorylated carbon exhibits a deshielding of 2.5 ± 0.5 ppm; no appreciable change in chemical shift is observed for the neighboring carbon atoms; and values of 3-bond $^{31}P-^{13}C$ couplings (1–10 Hz) are sensitive to the dihedral angle between these bonds [34].

The location of the phosphate diester linkage is indicated by the C-6 and C-5 signals of the sugar in the ^{13}C NMR spectra of **4(a, b, e–i)** and by the C-2, C-3, and C-4 signals for **4(c, d)**. These signals are doublets; C-6 and C-3 signals are shifted downfield by 2–3 ppm; the $^{13}C-^{31}P$ couplings are indicated in Table 1. The C-1 to C-4 resonances for **4(a, b, e–i)** and those for C-1, C-5, and C-6 of **4(c, d)** underwent little change upon phosphorylation and their assignment was established by comparison with the nonphosphorylated *O*-protected sugar. The C-5 doublets of 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose 6-[triethylammonium 1-(perfluorohexyl)-3-dodecyl phosphate] (**4h**) and 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose 6-[triethylammonium 10-eicosyl phosphate] (**4i**) are not resolved because they are obscured by the C–H signals of the aliphatic chain.

Studies of nucleotides have shown that 3-bond P–C couplings are dependent on

Table 1
^{13}C and ^{31}P NMR chemical shifts (ppm) and C–P coupling constants (Hz) of the phosphodiester derivatives **4a–i** in $CDCl_3$ (except for **4c** in CD_2Cl_2) at 200 MHz and 25°C

Compound 4	C-1′	C-2′	C-3′ ($^2J_{C,P}$) [a]	C-4′ ($^3J_{C,P}$) [a]	C-5′ ($^3J_{C,P}$)	C-6′ ($^2J_{C,P}$)	^{31}P
a	96.3	70.8 [b]	70.7 [b]	70.6 [b]	67.3 d (8.8)	64.4 d (5.2)	−0.38 −0.42
b	96.3	70.9 [b]	70.7 [b]	70.7 [b]	67.4 d (9.2)	64.1 d (5.3)	0.20 0.14
c	106.3	85.2	78.9 d (5.4)	81.9 d (8.2)	74.2 74.1	67.7 bs	−0.08 −0.17
d	105.0	83.9	~ 77.2 [c]	80.8 d (8.0)	73.0 72.9	66.6 66.5	−0.21 −0.30
e	91.8	70.6 2 s	73.1 2 s	68.54 68.47	74.3 d (8.4)	63.77 63.67 dd ~ t (5.0)	−0.36 −0.39
f	91.6	70.4	73.06 73.03	68.4 68.3	74.1 d (8.5)	63.6 63.5 dd ~ t (5.2)	−0.33 −0.37
g	90.5	68.4	70.85 70.90	66.3 2 s	74.65 74.70 2 d (6.3)	64.5 bd (3.5)	−0.23 −0.32
h	90.4	68.3	70.8	66.1	74.8 [d] d not resolved	64.3 dd (1.8)	−0.30 [e]
i	90.3	68.3	70.7	66.2	74.9 [d] d not resolved	64.1 d (5.1)	0.23 [e]

[a] Coupling constants observed only for the 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose 3-[triethylammonium 1-(perfluoroalkyl)-3-dodecyl phosphates] **4(c,d)**. [b] May be reversed. [c] Overlapped by $CDCl_3$ signal. [d] Overlapped by POCH signal. [e] Diastereoisomers not resolved.

the dihedral angle between the $^{31}P-O-C$ and $O-C-^{13}C$ planes. Values of the coupling constants are given by the Karplus relationship [32] $^3J_{C,P} = 6.4 \cos^2\psi_{C,P} - 1.3 \cos 2\psi_{C,P} + 1.2$ where ψ is the $^{13}CCOP$ dihedral angle. In the ^{13}C NMR spectrum of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose 3-[triethylammonium 1-(perfluorooctyl)-3-dodecyl phosphate] (**4c**), $^3J_{C\text{-}2,P}$ equals zero, indicating that the phosphorus atom has a gauche orientation with respect to C-2 ($\psi_{C,P} = 90°$), and the value of $^3J_{C\text{-}4,P}$ (8.2 Hz) gives a trans orientation with a dihedral angle $\psi_{C,P}$ of 162°.

Where the ^{31}P NMR spectra are concerned, a peculiar result is observed. Thus, although the phosphorus atom of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose 6-[triethylammonium 1-(perfluorohexyl)-3-dodecyl phosphate] (**4f**) (with two chiral substituents) is not asymmetrical because of the possible mesomeric form, its ^{31}P NMR spectrum exhibits two resonances of equal intensity at ca. −0.37 and −0.33 ppm, characteristic of diastereoisomers in a 1:1 ratio. Heating this sample from 20 to 80°C caused rapid conversion of these two signals into a singlet at ca. −0.25 ppm. This phenomenon was attributed to a blocked configuration due to the bulky groups present, resulting in a diastereoisomeric mixture. This is supported by the fact that the energy associated with the rise in temperature allows the change from the diastereoisomeric to the mesomeric form. It is in agreement with a splitting (in two) of the C-3 and C-4 signals and with a doublet of doublet for the C-6 signal in the ^{13}C NMR spectrum of compound **4f**. Analogous patterns of signals were obtained for the other glycose perfluoroalkylated phosphodiester derivatives **4** (Table 1).

Several *O*-deisopropylidenation methods are known, such as the use of iodine in methanol [35] or an acidic ion-exchange resin [36], but the major drawback of the former is the methoxylation of the anomeric position, while the latter results in incomplete removal of the protecting groups. Complete and mild deprotection of **4(a, b)** and **4(c, d)** was achieved by aqueous trifluoroacetic acid (90% v/v) within 15 min [37], with no cleavage of glycose phosphate observed. Successive neutralization by Amberlite IR-120 cation-exchange resin (H^+ form), neutralization by 0.2 M NaOH, lyophilization, and trituration with ether gave **5(a–d)** in the 70% yield range based on the *O*-protected sugar (Scheme 1).

The acetyl groups of the glucopyranose **4(e, f)** and mannopyranose **4(g–i)** derivatives were rapidly removed (15 min) by methanolic 1% sodium methoxide. Compounds **5(e–i)** were isolated by the same treatment as above in the 65% yield range based on the *O*-protected saccharides (Scheme 1). The ^1H and ^{13}C NMR spectra show that, during this step, the phosphate group does not undergo acid-catalyzed migration from O-4 to O-6 via a cyclic phosphate, or alkaline hydrolysis [38] of the phosphate esters. The deprotection generates a mixture of the α and β anomers of **5(a–i)**: $\alpha/\beta \sim 60:40$ for the glucose and galactose derivatives and $\sim 80:20$ for the derivatives based on mannose.

Preliminary biocompatibility tests, including hemolysis and acute toxicity in mice, are collected in Table 2. Hemolytic activity was determinated on human red-blood cells suspended in an isotonic 0.9% NaCl solution according to the method described in ref. 39. The hemolysis threshold dose for fluorinated compounds **5(a–c)** and **5(g, h)** was at 0.01 g/L while it was 10^{-4} g/L for the totally

Table 2
In vivo acute toxicity (intravenous injection in mice)

Compound 5	Dose injected (mg/kg body wt)	Concn. (g/L)	Survival ratio
a	125	5	10/10
c	125	5	9/10
f	25	1	9/10
g	125	5	10/10

hydrogenated product **5i**. This illustrates again the beneficial contribution of the perfluoroalkyl chain in reducing hemolysis [40]. Acute toxicity estimations in mice gave an intravenous maximum tolerated dose (MTD) of ca. 125 mg/kg body weight (tail vein) for **5(a, c, h)** and of ca. 25 mg/kg body weight for **5f** (Table 2). The biocompatibility evaluations for **5e** and **5f** and for the hydrocarbon counterpart **5i** were hindered by their lower dispersibility in water.

Compounds **5(a–d)**, **5(g–h)** were shown to give stable liposomal structures (negatively stained electron microscopy) and display encapsulation properties for carboxyfluorescein [11].

3. Experimental

NMR spectra were recorded on a Bruker AC 200 spectrometer. Chemical shifts are given in ppm relative to Me_4Si, to external aq 85% H_3PO_4 (^{31}P), and to internal $CFCl_3$ (^{19}F); the deuterium signal of the solvent was used as a heteronuclear reference (^1H and ^{13}C). IR spectra were recorded with a Bruker IFS 45 spectrometer, on KBr discs for crystalline samples and on films for liquids. Optical rotations were measured with a Perkin–Elmer 141 polarimeter (1-dm cell). Elemental analyses were performed by the Service Central de Microanalyse du CNRS. TLC used precoated Silica Gel F_{254} plates (Merck), detections being performed by charring with 50% MeOH–H_2SO_4. Chromatographic separations were carried out on Silica Gel 60 (70–230 mesh; Merck).

Solvents were dried and distilled according to standard procedures and stored over 4A molecular sieves. All reactions, except deisopropylidenation, were performed under anhyd N_2. Imidazole, 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (from Aldrich), 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (from Sigma), and 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose [30] were dried by repeated evaporations with anhyd pyridine. Phosphorus trichloride and pivaloyl chloride (from Aldrich) were redistilled before use.

13,13,14,14,15,15,16,16,17,17,18,18,19,19,20,20,20-Heptadecafluoro-10-eicosyl triethylammonium hydrogenphosphonate (4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-1-nonylundecyl triethylammonium hydrogenphosphonate; **1**).—PCl_3 (1.51 mL, 17.31 mmol) followed by Et_3N (8.6 mL, 61.70 mmol) were added dropwise at

0°C to a stirred solution of imidazole (3.86 g, 56.70 mmol) in anhyd toluene (40 mL). After 15 min of stirring, a solution of 1-(perfluorooctyl)-3-dodecanol (2.74 g, 4.53 mmol) in anhyd toluene (150 mL) was added dropwise (60 min) at 0°C. All the perfluoroalkylated alcohol was consumed after 90 min (TLC monitoring, 9:1 $CHCl_3$–MeOH). The mixture was then warmed up to room temperature, quenched with M TEAB (20 mL), and concentrated. Dichloromethane (300 mL) was added, the organic layer was washed with water (1 × 250 mL) and M TEAB (30 mL), filtered on phase separation paper, and concentrated, and the residue was purified on a silica gel column (9:1 CH_2Cl_2–MeOH). Appropriate fractions were treated again with M TEAB and then concentrated, to give **1** as an oil (2.48 g, 71%); IR: ν_{max} 3400 (N–H), 2930-2860 (CH), 2500 (P–H), 1235–1140 (CF), 1205 (P=O), 1060 cm^{-1} (P–O–C); NMR data ($CDCl_3$): ^{19}F, δ −81.5 (CF_3), −115.0 (CF_2CH_2), −122.6 to −124.0 (10 F), −126.8 (CF_2CF_3); ^1H, δ 0.68 (t, 3 H, $^3J_{H,H}$ 6.5 Hz, CH_3), 1.21–1.11 [m, 21 H, $(CH_2)_6CH_3$, NCH_2CH_3], 1.48–1.41 (m, 4 H, $CH_2CH_2C_8F_{17}$, $CHCH_2CH_2$), 1.80–1.60 (m, 2 H, $CHCH_2$), 2.25–1.95 (m, 2 H, $CH_2CH_2C_8F_{17}$), 2.94 (q, 6 H, $^3J_{H,H}$ 7.1 Hz, NCH_2CH_3), 4.12 (m, 1 H, CH), 6.73 (d, 1 H, $^1J_{H,P}$ 628.5 Hz, PH), 12.42 (bs, 1 H, NH^+); ^{13}C, δ 73.6 (d, $^2J_{C,P}$ 5.4 Hz, CH), 45.4 (NCH_2CH_3), 35.7 (d, $^3J_{C,P}$ 3.0 Hz, C-9), 31.7 (C-3), 29.4 and 29.1 (2 s, C-4–C-7), 27.0 (t, $^2J_{C,F}$ 22 Hz, $CH_2C_8F_{17}$), 26.0 (bs, $CH_2CH_2C_8F_{17}$), 25.2 (C-8), 22.4 (C-2), 13.7 (CH_3), 8.2 (NCH_2CH_3); ^{31}P, δ 3.53 (dd, $^1J_{P,H}$ 628.5, $^3J_{P,H}$ 10.3 Hz); Anal. Calcd for $C_{26}H_{41}F_{17}NO_3P$ (769.6): C, 40.58; H, 5.37; N, 1.82; P, 4.02. Found: C, 40.07; H, 5.78; N, 1.47; P, 4.06.

1,1,1,2,2,3,3,4,4,5,5,6,6-Tridecafluoro-9-octadecyl triethylammonium hydrogenphosphonate [1-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-octyl)decyl triethylammonium hydrogenphosphonate; **2**].—When processed as described for compound **1**, PCl_3 (3.74 mL, 42.9 mmol) and 1-(perfluorohexyl)-3-dodecanol (5.66 g, 11.22 mmol) yielded **2** as an oil (5.79 g, 77%); IR: ν_{max} 3400 (N–H), 2930–2860 (CH), 2490 (P–H), 1235–1145 (CF), 1205 (P=O), 1060 cm^{-1} (P–O–C); NMR data ($CDCl_3$): ^{19}F, δ −81.4 (CF_3), −115.0 (CF_2CH_2), −122.5 to −123.9 (6 F), −126.7 (CF_2CF_3); ^1H, δ 0.85 (t, 3 H, $^3J_{H,H}$ 6.4 Hz, CH_3), 1.33–1.23 [m, 21 H, $(CH_2)_6$, NCH_2CH_3], 1.68–1.37 (m, 4 H, $CH_2CH_2C_6F_{13}$, $CHCH_2CH_2$), 1.91–1.72 (m, 2 H, $CHCH_2$), 2.42–2.09 (m, 2 H, $CH_2C_6F_{13}$), 3.04 (q, 6 H, $^3J_{H,H}$ 7.2 Hz, NCH_2CH_3), 4.23 (m, 1 H, CH), 6.87 (d, 1 H, $^1J_{H,P}$ 622.6 Hz, PH), 12.70 (bs, 1 H, NH^+); ^{13}C, δ 73.5 (d, $^2J_{C,P}$ 5.4 Hz, CH), 45.4 (NCH_2CH_3), 35.9 (d, $^3J_{C,P}$ 2.8 Hz, C-10), 31.9 (C-16), 29.5 and 29.3 (2 s, C-12–C-15), 27.1 (t, $^2J_{C,F}$ 22.1 Hz, $CH_2C_6F_{13}$), 26.3 (bs, CH_2CH_2-C_6F_{13}), 25.5 (C-11), 22.7 (C-17), 14.1 (CH_3), 8.5 (NCH_2CH_3); ^{31}P, δ 4.01 (dd, $^1J_{P,H}$ 622.6, $^3J_{P,H}$ 10.4 Hz); Anal. Calcd for $C_{24}H_{41}F_{13}NO_3P \cdot H_2O$ (687.6): C, 41.92; H, 6.30; N, 2.04; P, 4.50. Found: C, 41.77; H, 6.07; N, 1.95; P, 4.85.

10-Eicosyl triethylammonium hydrogenphosphonate (*1-nonylundecyl triethylammonium hydrogenphosphonate*; **3**).—The procedure described above, applied to PCl_3 (2.8 mL, 32.1 mmol) and 10-eicosanol (2.5 g, 8.4 mmol), yielded **3** as an oil (2.98 g, 77%); IR: ν_{max} 3400 (N–H), 2920–2855 (CH), 2620 (P–H), 1200 (P=O), 1040 cm^{-1} (P–O–C); NMR data ($CDCl_3$): ^1H, δ 0.82 (t, 6 H, $^3J_{H,H}$ 6.2 Hz, CH_3), 1.35–1.10 [m, 39 H, $(CH_2)_7CH_3$, $(CH_2)_8CH_3$, NCH_2CH_3], 1.55–1.40 (m, 4 H, CH_2CHCH_2), 3.02 (q, 6 H, $^3J_{H,H}$ 7.3 Hz, NCH_2CH_3), 4.10 (m, 1 H, CH), 6.83 (d, 1

H, $^{1}J_{H,P}$ 624.8 Hz, PH), 12.65 (bs, 1 H, NH^{+}); ^{13}C, δ 75.4 (d, $^{2}J_{C,P}$ 5.6 Hz, CH), 45.3 (NCH_2CH_3), 35.7 (d, $^{3}J_{C,P}$ 3.8 Hz, C-9, C-11), 31.9 (C-3, C-18), 29.7, 29.6, and 29.3 (3 s, C-4–C-7 and C-13–C-17), 25.3 (C-8, C-12), 22.6 (C-2, C-19), 14.1 (CH_3), 8.5 (NCH_2CH_3); ^{31}P, δ 4.18 (dd, $^{1}J_{P,H}$ 624.8, $^{3}J_{P,H}$ 10.3 Hz); Anal. Calcd for $C_{26}H_{58}NO_3P$ (463.7): C, 67.34; H, 12.61; N, 3.02; P, 6.68. Found:C, 63.59; H, 11.85; N, 2.59; P, 6.85.

1,2:3,4-Di-O-isopropylidene-α-D-galactopyranose 6-(triethylammonium 13,13,14,14,15,15,16,16,17,17,18,18,19,19,20,20,20-heptadecafluoro-10-eicosyl phosphate) (**4a**). —A mixture of the hydrogenphosphonate **1** (2.4 g, 3.12 mmol) and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (0.81 g, 3.12 mmol) was dried by evaporation of anhyd pyridine and dissolved in the same solvent (30 mL). Pivaloyl chloride (1.53 mL, 13.3 mmol) was then added. After 15 min, the condensation being complete (TLC monitoring, 9:1 $CHCl_3$–MeOH), iodine (1.58 g, 6.23 mmol) in 98:2 pyridine–water (8.7 mL) followed by Et_3N (15 equiv) were added. After 4 h of stirring, the brown solution obtained was co-evaporated with 70:30 $CHCl_3$–toluene to remove traces of pyridine. Dichloromethane (200 mL) was then added and the organic layer was successively washed with M $Na_2S_2O_3$, water, and M TEAB (50 mL). After filtration on phase separation paper and concentration, the residue was purified on a silica gel column (elution with 9:1 CH_2Cl_2–MeOH). Treatment of the appropriate fractions with M TEAB gave, after concentration, a brown oil. This oil was subjected to decoloration on activated charcoal to give **4a** as a yellow oil (2.31 g, 72%); IR: ν_{max} 3375 (N–H), 2930–2860 (CH), 1235–1135 (CF), 1205 (P=O), 1060 cm^{-1} (P–O–C); NMR data ($CDCl_3$): ^{19}F, δ −81.5 (CF_3), −115.0 (CF_2CH_2), −122.6 to −123.8 (10 F), −126.8 (CF_2CF_3); ^{1}H, δ 0.82 (t, 3 H, $^{3}J_{H,H}$ 6.4 Hz, CH_3), 1.25–1.00 [m, 24 H, $(CH_2)_6CH_3$, NCH_2CH_3, CCH_3], 1.29, 1.36, and 1.46 (3 s, 9 H, CCH_3), 2.00–1.61 [m, 6 H, $CH_2CH_2C_8F_{17}$, $CHCH_2CH_2$-$(CH_2)_6$], 2.45–2.08 (m, 2 H, $CH_2C_8F_{17}$), 3.02 (q, 6 H, $^{3}J_{H,H}$ 6.8 Hz, NCH_2CH_3), 4.05–3.90 (m, 3 H, H-5, H-6), 4.35–4.15 (m, 3 H, H-2, H-4, CH), 4.53 (dd, 1 H, $^{3}J_{3,4}$ 2.3, $^{3}J_{3,2}$ 7.9 Hz, H-3), 5.44 (d, 1 H, $^{3}J_{1,2}$ 5.0 Hz, H-1), 12.34 (bs, 1 H, NH^{+}); ^{13}C, 109.2 and 108.5 (2 s, quaternary C), 96.3 (C-1′), 75.1 (d, $^{2}J_{C,P}$ 5.9 Hz, CH), 70.8[a] (C-2′), 70.7[a] (C-3′), 70.6[a] (C-4′), 67.3 (d, $^{3}J_{C,P}$ 8.8 Hz, C-5′), 64.4 (d, $^{2}J_{C,P}$ 5.2 Hz, C-6′), 45.4 (NCH_2CH_3), 35.2 (bs, C-9), 31.9 (C-3), 29.8, 29.6, and 29.3 (3 s, C-4–C-7), 26.8 (t, $^{2}J_{C,F}$ 22.8 Hz, $CH_2C_8F_{17}$), 26.0 and 25.9 (2 s, CCH_3), 25.5 (bs, $CH_2CH_2C_8F_{17}$), 25.1 and 24.9 (2 s, CCH_3), 24.3 (C-8), 22.7 (C-2), 14.0 (CH_3), 8.4 (NCH_2CH_3); ^{31}P, δ −0.42 and −0.38; Anal. Calcd for $C_{38}H_{59}F_{17}NO_9P$ (1027.8): C, 44.41; H, 5.79; N, 1.36; P, 3.01. Found: C, 44.07; H, 5.79; N, 1.26; P, 3.56.

Note: prime-marked carbons (C′) refer to distinct chemical shifts for the sugar; [a] assignments may be reversed.

1,2:3,4-Di-O-isopropylidene-α-D-galactopyranose 6-(triethylammonium 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-9-octadecyl phosphate) (**4b**).—A mixture of the hydrogenphosphonate **2** (2.1 g, 3.14 mmol) was allowed to react with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (0.81 g, 3.11 mmol) according to the procedure described above, to yield **4b** as an oil (2.03 g, 70%); $[\alpha]_D$ −23° (*c* 0.85, $CHCl_3$); IR: ν_{max} 3375 (N–H), 2930–2855 (CH), 1235–1135 (CF), 1205 (P=O), 1065 cm^{-1} (P–O–C); NMR data ($CDCl_3$): ^{19}F, δ −81.3 (CF_3), −114.8 (CF_2CH_2), −122.4 to

−123.7 (6 F), −126.6 (CF_2CF_3); ^{1}H, δ 0.75 (t, 3 H, $^3J_{H,H}$ 6.0 Hz, CH_3), 1.23–1.10 [m, 24 H, $(CH_2)_6CH_3$, NCH_2CH_3, CCH_3], 1.25, 1.33, and 1.43 (3 s, 9 H, CCH_3), 1.95–1.55 [m, 6 H, $CH_2CH_2C_6F_{13}$, $CHCH_2CH_2(CH_2)_6$], 2.38–2.05 (m, 2 H, $CH_2C_6F_{13}$), 2.95 (q, 6 H, $^3J_{H,H}$ 7.1 Hz, NCH_2CH_3), 3.95 (m, 3 H, H-5, H-6), 4.30–4.15 (m, 3 H, H-2, H-4, CH), 4.53 (dd, 1 H, $^3J_{3,4}$ 2.2, $^3J_{3,2}$ 7.7 Hz, H-3), 5.45 (d, 1 H, $^3J_{1,2}$ 5.0 Hz, H-1), 12.65 (s, 1 H, NH^+); ^{13}C, δ 109.1 and 108.5 (2 s, quaternary C), 96.3 (C-1′), 74.6 (d, $^2J_{C,P}$ 6.0 Hz, CH), 70.9 (C-2′) [a], 70.7 (C-3′ and C-4′) [a], 67.4 (d, $^3J_{C,P}$ 9.2 Hz, C-5′), 64.1 (d, $^2J_{C,P}$ 5.3 Hz, C-6′), 45.4 (NCH_2CH_3), 35.4 (d, $^3J_{C,P}$ 3.4 Hz, C-10), 31.9 (C-16), 29.8, 29.64, 29.60, and 29.3 (4 s, C-12–C-15), 26.9 (t, $^2J_{C,F}$ 22.0 Hz, $CH_2C_6F_{13}$), 26.0 (bs, $CH_2CH_2C_6F_{13}$), 25.9, 25.5, 25.2, and 24.9 (4 s, CCH_3), 24.3 (C-11), 22.7 (C-17), 14.1 (CH_3), 8.4 (NCH_2CH_3); ^{31}P, δ 0.20 and 0.14; Anal. Calcd for $C_{36}H_{59}F_{13}NO_9P \cdot H_2O$ (945.8): C, 45.72; H, 6.50; N, 1.48; P, 3.27. Found: C, 45.86; H, 6.47; N, 1.34; P, 3.50.

Note: prime-marked carbons (C′) refer to distinct chemical shifts for the sugar; [a] assignments may be reversed.

*1,2:5,6-Di-*O*-isopropylidene-α-*D*-glucofuranose 3-(triethylammonium 13,13,14,14, 15,15,16,16,17,17,18,18,19,19,20,20,20-heptadecafluoro-10-eicosyl phosphate)* (**4c**).—The hydrogenphosphonate **1** (4 g, 5.2 mmol) was allowed to react with 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1.35 g, 5.19 mmol) according to the method described above, to yield **4c** as an oil (4.86 g, 91%); $[\alpha]_D$ −7° (*c* 0.54, $CHCl_3$); IR: ν_{max} 3445 (N–H), 2930–2855 (CH), 1215–1135 (CF), 1210 (P=O), 1075 cm^{-1} (P–O–C); NMR data ($CDCl_3$): ^{19}F, δ −81.3 (CF_3), −114.8 (CF_2CH_2), −122.3 to −123.7 (10 F), −126.6 (CF_2CF_3); ^{1}H, δ 0.85 (t, 3 H, $^3J_{H,H}$ 6.7 Hz, CH_3), 1.26–1.17 [m, 21 H, $(CH_2)_6CH_3$, NCH_2CH_3], 1.45, 1.39, 1.33, and 1.30 (4 s, 12 H, CCH_3), 2.05–1.60 [m, 6 H, $CH_2CH_2C_8F_{17}$, $CHCH_2CH_2(CH_2)_6$], 2.40–2.10 (m, 2 H, $CH_2C_8F_{17}$), 3.03 (q, 6 H, $^3J_{H,H}$ 7.0 Hz, NCH_2CH_3), 4.06 (d, 2 H, H-6), 4.31–4.15 (m, 2 H, H-4, CH), 4.42–4.35 (m, 1 H, H-5), 4.60 (dd, 1 H, $^3J_{3,4}$ 2.5, $^3J_{H,P}$ 4.9 Hz, H-3), 4.89 (d, 1 H, $^3J_{2,1}$ 3.6 Hz, H-2), 5.83 (d, 1 H, $^3J_{1,2}$ 3.6 Hz, H-1), 12.34 (bs, 1 H, NH^+); ^{13}C (CD_2Cl_2), δ 112.8 and 109.6 (2 s, quaternary C), 106.3 (C-1′), 85.2 (C-2′), 81.9 (d, $^3J_{C,P}$ 8.2 Hz, C-4′), 78.9 (d, $^2J_{C,P}$ 5.4 Hz, C-3′), 76.1 and 76.0 (2 d, $^2J_{C,P}$ 5.6 Hz, CH), 74.2 and 74.1 (2 s, C-5′), 67.7 (bs, C-6′), 46.8 (NCH_2CH_3), 36.7 (bs, C-9), 33.2 (C-3), 31.1, 31.0, and 30.7 (4 s, C-4–C-7), 28.1 (t, $^2J_{C,F}$ 22.2 Hz, $CH_2C_8F_{17}$), 27.8, 27.7, and 27.3 (3 s, CCH_3), 26.8 (bs, $CH_2CH_2C_8F_{17}$), 26.4 (C-8), 24.0 (C-2), 15.2 (CH_3), 9.6 (NCH_2CH_3); ^{31}P, δ −0.08 and −0.17; Anal. Calcd for $C_{38}H_{59}F_{17}NO_9P$ (1027.8): C, 44.41; H, 5.79; N, 1.36; P, 3.01. Found: C, 44.17; H, 5.67; N, 1.36; P, 2.84.

Note: prime-marked carbons (C′) refer to distinct chemical shifts for the sugar.

*1,2:5,6-Di-*O*-isopropylidene-α-*D*-glucofuranose 3-(triethylammonium 1,1,1,2,2,3, 3,4,4,5,5,6,6-tridecafluoro-9-octadecyl phosphate)* (**4d**).—According to the method described above, the hydrogenphosphonate **2** (4 g, 5.97 mmol) was allowed to react with 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1.54 g, 5.92 mmol), to yield **4d** as an oil (3.61 g, 66%); $[\alpha]_D$ −8° (*c* 0.48, $CHCl_3$); IR: ν_{max} 3435 (N–H), 2935–2855 (CH), 1215–1130 (CF), 1205 (P=O), 1070 cm^{-1} (P–O–C); NMR data ($CDCl_3$); ^{19}F, δ −81.3 (CF_3), −114.9 (CF_2CH_2), −122.5 to 123.8 (6 F), −126.6 (CF_2CF_3); ^{1}H, δ 0.83 (t, 3 H, $^3J_{H,H}$ 6.2 Hz, CH_3), 1.25–1.15 [m, 21 H, $(CH_2)_6CH_3$,

NCH_2CH_3], 1.49, 1.38, 1.31, and 1.29 (4 s, 12 H, CCH_3), 2.00–1.60 [m, 6 H, $CH_2CH_2C_6F_{13}$, $CHCH_2CH_2(CH_2)_6$], 2.30–2.10 (m, 2 H, $CH_2C_6F_{13}$), 3.08 (q, 6 H, $^3J_{H,H}$ 3.5 Hz, NCH_2CH_3), 4.05 (d, 2 H, H-6), 4.28–4.12 (m, 2 H, H-4, CH), 4.42–4.33 (m, 1 H, H-5), 4.62 (dd, 1 H, H-3), 4.87 (d, 1 H, $^3J_{2,1}$ 3.6 Hz, H-2), 5.85 (d, 1 H, H-1), 12.70 (bs, 1 H, NH^+); ^{13}C, 111.6 and 108.6 (2 s, quaternary C), 105.0 (C-1'), 83.9 (C-2'), 80.8 (d, $^3J_{C,P}$ 8.0 Hz, C-4'), ~77.2 ($CDCl_3$ overlapped, C'-3), 74.9 (dd, $^2J_{C,P}$ 3.9 Hz, C–H), 73.0 and 72.9 (2 s, C-5'), 66.6 and 66.5 (2 s, C-6'), 45.4 (NCH_2CH_3), 35.3 (bs, C-10), 31.9 (C-16), 29.8, 29.7, 29.6, and 29.3 (4 s, C-12–C-15), 27.3 (t, $^2J_{C,F}$ 22.0 Hz, $CH_2C_6F_{13}$), 26.3, 26.2, and 25.9 (3 s, CCH_3), 25.5 (bs, $CH_2CH_2C_6F_{13}$), 25.3 (C-11), 22.7 (C-17), 14.1 (CH_3), 8.5 (NCH_2CH_3); ^{31}P, δ −0.21 and −0.30; Anal. Calcd for $C_{36}H_{59}F_{13}NO_9P \cdot H_2O$ (945.8): C, 45.72; H, 6.50; N, 1.48; P, 3.27. Found: C, 45.71; H, 6.34; N, 1.32; P, 3.39.

Note: prime-marked carbons (C') refer to distinct chemical shifts for the sugar.

1,2,3,4-Tetra-O-acetyl-β-D-glucopyranose 6-(triethylammonium 13,13,14,14,15,15, 16,16,17,17,18,18,19,19,20,20,20-heptadecafluoro-10-eicosyl phosphate) (**4e**).—Compound **4e** was obtained in 86% (2.49 g) overall yield from the hydrogenphosphonate **1** (2 g, 2.60 mmol) and 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (0.91 g, 2.61 mmol) by the procedure described above for the preparation of **4a**; $[\alpha]_D$ + 15° (*c* 0.47, $CHCl_3$); IR: ν_{max} 3480 (N–H), 2930–2860 (CH), 1760 (C=O), 1235–1135 (CF), 1210 (P=O), 1040 cm^{-1} (P–O–C); NMR data ($CDCl_3$): ^{19}F, δ −81.9 (CF_3), −115.3 (CF_2CH_2), −124.2 to −122.9 (10 F), −127.2 (CF_2CF_3); ^1H, δ 0.87 (t, 3 H, $^3J_{H,H}$ 6.1 Hz, CH_3), 1.60–1.25 [m, 23 H, $(CH_2)_7CH_3$, NCH_2CH_3], 2.05–1.65 [m, 4 H, $CH_2CH_2C_8F_{17}$, $CH_2(CH_2)_7CH_3$], 2.10–2.20 (4 s, 12 H, $COCH_3$), 2.50–2.30 (m, 2 H, $CH_2C_8F_{17}$), 3.20 (q, 6 H, $^3J_{H,H}$ 7.4 Hz, NCH_2CH_3), 4.15–3.94 (m, 3 H, H-5, H-6), 4.35 (m, 1 H, CH), 5.40–5.15 (m, 3 H, H-2, H-3, H-4), 5.85 (d, 1 H, $^3J_{1,2}$ 8.0 Hz, H-1), 12.75 (bs, 1 H, NH^+); ^{13}C, δ 170.2–168.8 [$C(O)CH_3$], 91.8 (C-1'), 74.7 (d, $^2J_{C,P}$ 6.1 Hz, CH), 74.3 (d, $^3J_{C,P}$ 8.4 Hz, C-5'), 73.1 (2 s, C-3'), 70.6 (2 s, C-2'), 68.54 and 68.47 (2 s, C-4'), 63.67 and 63.77 (dd ~ t, $^2J_{C,P}$ 5.0 Hz, C-6'), 45.5 (NCH_2CH_3), 35.4 (bs, $^3J_{C,P}$ ~3.0 Hz, C-9), 32.0 (C-3), 29.8, 29.7, and 29.4 (4 s, C-4–C-7), 26.9 (t, $^2J_{C,F}$ 22.5 Hz, $CH_2C_8F_{17}$), 25.6 (bs, $CH_2CH_2C_8F_{17}$), 25.2 (C-8), 22.7 (C-2), 20.7–20.6 [3 s, $C(O)CH_3$], 14.1 (CH_3), 8.5 (NCH_2CH_3); ^{31}P, δ −0.36 and −0.39; Anal. Calcd for $C_{40}H_{59}F_{17}NO_{13}P \cdot H_2O$ (1133.9): C, 42.37; H, 5.42; N, 1.23; P, 2.73. Found: C, 42.61; H, 5.35; N, 1.31; P, 2.83.

Note: prime-marked carbons (C') refer to distinct chemical shifts for the sugar.

1,2,3,4-Tetra-O-acetyl-β-D-glucopyranose 6-(triethylammonium 1,1,1,2,2,3,3,4,4, 5,5,6,6-tridecafluoro-9-octadecyl phosphate) (**4f**).—The hydrogenphosphonate **2** (2.8 g, 4.18 mmol) and 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (1.46 g, 4.19 mmol) were allowed to react in anhyd pyridine with pivaloyl chloride (2.06 mL, 17.93 mmol), Et_3N (15 equiv), and iodine (2.1 g, 8.27 mmol) in 98:2 pyridine–water (11.7 mL), according to the procedure described for compound **4a**, to give **4f** as a yellow oil (2.12 g, 50%); $[\alpha]_D$ +17° (*c* 0.45, $CHCl_3$); IR: ν_{max} 3475 (N–H), 2930–2860 (CH), 1755 (C=O), 1240–1140 (CF), 1215 (P=O), 1045 cm^{-1} (P–O–C); NMR data ($CDCl_3$): ^{19}F, δ −81.4 (CF_3), −115.0 (CF_2CH_2), −123.9 to −122.5 (6 F), −126.7 (CF_2CF_3); ^1H, δ 0.86 (t, 3 H, $^3J_{H,H}$ 6.1 Hz, CH_3), 1.33–1.24 [m, 23 H, $(CH_2)_7CH_3$, NCH_2CH_3], 1.88–1.40 [m, 4 H, $CH_2CH_2C_6F_{13}$, $CH_2(CH_2)_7CH_3$],

2.05–1.95 (4 s, 12 H, $COCH_3$), 2.47–2.10 (m, 2 H, $CH_2C_6F_{13}$), 3.02 (q, 6 H, $^3J_{H,H}$ 7.3 Hz, NCH_2CH_3), 4.05–3.80 (m, 3 H, H-5, H-6), 4.21 (m, 1 H, CH), 5.29–5.01 (m, 3 H, H-2, H-3, H-4), 5.70 (d, 1 H, $^3J_{1,2}$ 8.0 Hz, H-1), 12.70 (bs, 1 H, NH^+); ^{13}C, δ 170.1–168.8 [$C(O)CH_3$], 91.6 (C-1'), 74.5 (d, $^2J_{C,P}$ 5.2 Hz, CH), 74.1 (d, $^3J_{C,P}$ 8.5 Hz, C-5'), 73.06 and 73.03 (2 s, C-3'), 70.4 (bs, C-2'), 68.4 and 68.3 (2 s, C-4'), 63.6 and 63.5 (dd ~ t, $^2J_{C,P}$ 5.2 Hz, C-6'), 45.4 (NCH_2CH_3), 35.2 (bs, $^3J_{C,P}$ ~ 2.8 Hz, C-10), 31.9 (C-16), 29.7, 29.6, 29.5, and 29.3 (4 s, C-12–C-15), 26.7 (t, $^2J_{C,F}$ 21.6 Hz, $CH_2C_6F_{13}$), 25.4 (bs, $CH_2CH_2C_6F_{13}$), 25.1 (C-11), 22.6 (C-17), 20.5 and 20.6 [$C(O)CH_3$], 14.0 (CH_3), 8.4 (NCH_2CH_3); ^{31}P, δ −0.37 and −0.33; Anal. Calcd for $C_{38}H_{59}F_{13}NO_{13}P$ (1015.8): C, 44.93; H, 5.85; N, 1.38; P, 3.05. Found: C, 44.61; H, 5.86; N, 1.29; P, 3.08.

Note: prime-marked carbons (C') refer to distinct chemical shifts for the sugar.

1,2,3,4-Tetra-O-acetyl-β-D-mannopyranose 6-(triethylammonium 13,13,14,14,15,15,16,16,17,17,18,18,19,19,20,20,20-heptadecafluoro-10-eicosyl phosphate) (**4g**).—Compound **4g** was obtained in 73% (3.5 g) overall yield from the hydrogenphosphonate **1** (3.3 g, 4.3 mmol) and 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose (1.51 g, 4.3 mmol) by the same procedure as above; $[\alpha]_D$ +3° (*c* 0.45, $CHCl_3$); IR: ν_{max} 3345 (N–H), 2930–2860 (CH), 1755 (C=O), 1390–1140 (CF), 1215 (P=O), 1055 cm^{-1} (P–O–C); NMR data ($CDCl_3$): ^{19}F, δ −81.3 (CF_3), −114.8 (CF_2CH_2), −123.7 to −122.3 (10 F), −126.6 (CF_2CF_3); ^1H, δ 0.75 (t, 3 H, $^3J_{H,H}$ 6.2 Hz, CH_3), 1.25–1.00 [m, 25 H, $(CH_2)_8CH_3$, NCH_2CH_3], 2.20–1.30 (m, 16 H, $CH_2CH_2C_8F_{17}$, $COCH_3$), 2.90 (q, 6 H, $^3J_{H,H}$ 7.1 Hz, NCH_2CH_3), 3.77–3.70 (m, 1 H, H-5), 3.89–3.86 (m, 2 H, H-6), 4.11 (m, 1 H, CH), 5.18–4.96 (m, 2 H, H-3, H-4), 5.33 (dd, 1 H, $^3J_{2,3}$ 2.1, $^3J_{2,1}$ 1.1 Hz, H-2), 5.72 (d, 1 H, H-1), 12.60 (bs, 1 H, NH^+); ^{13}C, δ 170.4–168.4 [$C(O)CH_3$], 90.5 (C-1'), 75.0 (d, $^2J_{C,P}$ 8.1 Hz, C-5'), 74.70 and 74.65 (2 d, $^3J_{C,P}$ 5.5 Hz, CH), 70.90 and 70.85 (2 s, C-3'), 68.4 (C-2'), 66.3 (2 s, C-4'), 64.5 (bd, $^2J_{C,P}$ 3.5 Hz, C-6'), 45.5 (NCH_2CH_3), 35.4 (d, $^3J_{C,P}$ 3.8 Hz, C-9), 32.0 (C-3), 29.9, 29.8, 29.7, and 29.5 (4 s, C-4–C-7), 27.0 (t, $^2J_{C,F}$ 19.1 Hz, $CH_2C_8F_{17}$), 25.6 (bs, $CH_2CH_2C_8F_{17}$), 25.3 (C-8), 22.8 (C-2), 20.9–20.7 [$C(O)CH_3$], 14.2 (CH_3), 8.6 (NCH_2CH_3); ^{31}P, δ −0.23 and −0.32; Anal. Calcd for $C_{40}H_{59}F_{17}NO_{13}P$ (1115.9): C, 43.06; H, 5.33; N, 1.26; P, 2.78. Found: C, 42.88; H, 5.12; N, 1.20; P, 2.75.

Note: prime-marked carbons (C') refer to distinct chemical shifts for the sugar.

1,2,3,4-Tetra-O-acetyl-β-D-mannopyranose 6(triethylammonium 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-9-octadecyl phosphate) (**4h**).—Compound **4h** was obtained as an oil, in 66% (4.91 g) yield, from the hydrogenphosphonate **2** (4.9 g, 7.32 mmol) and 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose (2.55 g, 7.32 mmol) by the same procedure as above; $[\alpha]_D$ +5° (*c* 0.47, $CHCl_3$); IR: ν_{max} 3380 (N–H), 2930–2855 (CH), 1750 (C=O), 1220 (P=O), 1230–1145 (CF), 1050 cm^{-1} (P–O–C); NMR data ($CDCl_3$): ^{19}F, δ −81.4 (CF_3), −114.9 (CF_2CH_2), −122.5 to −123.8 (6 F), −126.7 (CF_2CF_3); ^1H, δ 0.85 (t, 3 H, $^3J_{H,H}$ 6.8 Hz, CH_3), 1.40–1.10 [m, 25 H, $(CH_2)_8CH_3$, NCH_2CH_3], 2.30–1.50 (m, 16 H, $CH_2CH_2C_6F_{13}$, $COCH_3$), 3.04 (q, 6 H, $^3J_{H,H}$ 7.4 Hz, NCH_2CH_3), 3.86–3.77 (m, 1 H, H-5), 3.98–3.90 (m, 2 H, H-6), 4.22 (m, 1 H, CH), 5.22–5.04 (m, 2 H, H-3, H-4), 5.44 (dd, 1 H, $^3J_{2,3}$ 2.8, $^3J_{2,1}$ 1.2 Hz, H-2), 5.83 (d, 1 H, H-1), 12.10 (bs, 1 H, NH^+); ^{13}C, δ 170.4–168.4 [$C(O)CH_3$], 90.4 (C-1'),

74.8 (m, CH, C-5′), 70.8 (C-3′), 68.3 (C-2′), 66.1 (C-4′), 64.3 (dd, $^2J_{C,P}$ 1.8 Hz, C-6′), 45.5 (NCH_2CH_3), 35.2 (bd, $^3J_{C,P}$ 2.8 Hz, C-10), 31.9 (C-16), 29.8, 29.7, and 29.4 (3 s, C-12–C-15), 26.7 (t, $^2J_{C,F}$ 20.5 Hz, $CH_2C_6F_{13}$), 25.5 (bs, $CH_2CH_2C_6F_{13}$), 25.2 (C-11), 22.7 (C-17), 20.8–20.6 [3 s, $C(O)CH_3$], 14.1 (CH_3), 8.5 (NCH_2CH_3); ^{31}P, δ −0.30; Anal. Calcd for $C_{38}H_{59}F_{13}NPO_{13}\cdot H_2O$ (1033.9): C, 44.15; H, 5.95; N, 1.35; P, 3.00. Found: C, 43.84; H, 5.97; N, 1.40; P, 3.02.

Note: prime-marked carbons (C′) refer to distinct chemical shifts for the sugar.

1,2,3,4-Tetra-O-acetyl-β-D-mannopyranose 6-(triethylammonium 10-eicosyl phosphate) (**4i**).—Compound **4i** was obtained in 60% (2.82 g) overall yield from the hydrogenphosphonate **3** (2.7 g, 5.8 mmol) and 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose (2.03 g, 5.8 mmol) by the same procedure; $[\alpha]_D$ +4° (*c* 0.43, $CHCl_3$); IR: ν_{max} 3375 (N–H), 2930–2855 (CH), 1755 (C=O), 1220 (P=O), 1050 cm^{-1} (P–O–C); NMR data ($CDCl_3$): ^1H, δ 0.83 (t, 6 H, $^3J_{H,H}$ 6.4 Hz, CH_3), 1.30–1.21 [m, 39 H, $(CH_2)_7CH_3$, $(CH_2)_8CH_3$, NCH_2CH_3], 1.55–1.40 [m, 4 H, $CH_2(CH_2)_8CH_3$, $CH_2(CH_2)_7CH_3$], 2.02–1.95 (3 s, 12 H, $COCH_3$), 3.00 (q, 6 H, $^3J_{H,H}$ 7.3 Hz, NCH_2CH_3), 3.88–3.75 (m, 1 H, H-5), 4.00–3.89 (m, 2 H, H-6), 4.12 (m, 1 H, CH), 5.20–5.04 (m, 2 H, H-3, H-4), 5.41 (dd, 1 H, $^3J_{2,3}$ 2.6 Hz, H-2), 5.81 (d, 1 H, $^3J_{1,2}$ 1.0 Hz, H-1), 12.68 (bs, 1 H, NH^+); ^{13}C, δ 166.1–166.0 [$C(O)CH_3$], 90.3 (C-1′), 74.9 (CH, C-5′), 70.7 (C-3′), 68.3 (C-2′), 66.2 (C-4′), 64.1 (d, $^2J_{C,P}$ 5.1 Hz, C-6′), 45.3 (NCH_2CH_3), 35.0 (d, $^3J_{C,P}$ 4.0 Hz, C-9, C-11), 31.9 (C-3, C-18), 29.9, 29.7, 29.6, and 29.3 (4 s, C-4–C-7), 25.0 (C-8, C-12), 22.6 (C-2, C-19), 20.8–20.5 [4 s, $C(O)CH_3$], 14.1 (CH_3), 8.5 (NCH_2CH_3); ^{31}P, δ 0.23; Anal. Calcd for $C_{40}H_{76}NO_{13}P$ (810.0): C, 59.31; H, 9.46; N, 1.73; P, 3.82. Found: C, 59.04; H, 9.66; N, 1.70; P, 3.76.

Note: prime-marked carbons (C′) refer to distinct chemical shifts for the sugar.

D-Galactose 6-(sodium 13,13,14,14,15,15,16,16,17,17,18,18,19,19,20,20,20-heptadecafluoro-10-eicosyl phosphate) (**5a**).—The phosphate **4a** (2.2 g, 2.14 mmol) was treated for 15 min with Amberlite IR-120 cation-exchange resin (H^+ form, 40 mL). The resin was removed by filtration and washed with MeOH. The filtrate was evaporated to dryness and the resulting yellow oil was stirred at room temperature in aq CF_3CO_2H (9:1 CF_3CO_2H–H_2O, 27.5 mL). After 15 min (TLC monitoring, 7:3 $CHCl_3$–MeOH), the solvent was evaporated and the viscous residue co-evaporated with hexane (3 × 50 mL). The resulting oil was dissolved in aqueous 1:1 MeOH and adjusted to pH 7 with 0.2 M NaOH. Concentration and precipitation in acetone led to a solid which was purified by trituration with ether to give a yellow powder. This powder was subjected to decoloration on activated charcoal (1.30 g, 70%); $[\alpha]_D$ +10° (*c* 0.60, MeOH); IR: ν_{max} 3350 (OH), 2925–2860 (CH), 1235–1150 (CF), 1215 (P=O), 1020 cm^{-1} (P–O–C); NMR data (CD_3OD): ^{19}F, δ −80.9 (CF_3), −113.9 (CF_2CH_2), −121.4 to −122.7 (10 F), −125.8 (CF_2CF_3); ^1H, δ (α anomer ~ 60%) 0.93 (t, 3 H, $^3J_{H,H}$ 6.3 Hz, CH_3), 1.34 [bs, 14 H, $(CH_2)_7CH_3$]), 2.10–1.55 [m, 4 H, $CH_2CH_2C_8F_{17}$, $CH_2(CH_2)_7CH_3$], 2.60–2.20 (m, 2 H, $CH_2C_8F_{17}$), 3.54–3.51 (m, H-2β), 4.25–3.87 (m, H-3,4,5,6α, H-2,3,4,5,6β), 4.31 (m, 1 H, CH-α,β), 4.45 (d, $^3J_{1\beta,2\beta}$ 6.2 Hz, H-1β), 5.19 (d, $^3J_{1\alpha,2\alpha}$ 3.1 Hz, H-1α); ^{13}C, δ 98.6 (C-1β), 94.2 (C-1α), 76.2 (d, $^2J_{C,P}$ 5.3 Hz, CH-α,β), 75.1 (d, $^3J_{C,P}$ 6.9 Hz, C-5β), 74.6 (C-3β), 73.7 (C-2β), 70.8 (C-4α), 70.4 (C-4β), 70.25 (d, $^3J_{C,P}$ 7.0 Hz,

C-5α), 70.1 (C-3α), 69.5 (C-2α), 64.7 (d, $^2J_{C,P}$ 5.0 Hz, C-6α), 64.5 (d, $^2J_{C,P}$ 4.7 Hz, C-6β), 36.3 (d, $^3J_{C,P}$, 5.5 Hz, C-9), 33.0 (C-3), 30.8, 30.7, and 30.4 (3 s, C-4–C-7), 27.9 (t, $^2J_{C,F}$ 22.4 Hz, $CH_2C_8F_{17}$), 26.7 (bs, $CH_2CH_2C_8F_{17}$), 26.0 (C-8), 23.7 (C-2), 14.4 (CH_3); ^{31}P, δ 1.57; Anal. Calcd for $C_{26}H_{35}F_{17}NaO_9P$ (868.5): C, 35.96; H, 4.06; Na, 2.65; P, 3.57. Found: C, 35.93; H, 4.09; Na, 2.52; P, 3.40.

D-*Galactose 6-(sodium 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-9-octadecyl phosphate*) (**5b**).—Compound **5b** (2.0 g) was obtained in 72% yield by the same procedure as described above for **5a**, by deacetalation of 3.35 g (3.61 mmol) of **4b**; $[\alpha]_D$ +12° (*c* 0.70, MeOH); IR ν_{max} 3340 (OH), 2925–2860 (CH), 1230–1150 (CF), 1205 (P=O), 1020 cm^{-1} (P–O–C); NMR data (CD_3OD): ^{19}F, δ −82.6 (CF_3), −115.7 (CF_2CH_2), −123.2 to −124.5 (6 F), −127.6 (CF_2CF_3); ^{1}H, δ (α anomer ~ 55%) 0.92 (t, 3 H, $^3J_{H,H}$ 6.2 Hz, CH_3), 1.31 [bs, 14 H, $(CH_2)_7CH_3$], 2.00–1.55 [m, 4 H, $CH_2CH_2C_6F_{13}$, $CH_2(CH_2)_7CH_3$], 2.50–2.15 (m, 2 H, $CH_2C_6F_{13}$), 3.50–3.45 (m, H-2β), 4.20–3.65 (m, H-3,4,5,6α, H-2,3,4,5,6β), 4.25 (m, 1 H, CH-α,β), 4.43 (d, $^3J_{1\beta,2\beta}$ 6.1 Hz, H-1β), 5.14 (d, $^3J_{1\alpha,2\alpha}$ 3.0 Hz, H-1α); ^{13}C, δ 99.1 (C-1β), 94.5 (C-1α), 76.0 (d, $^2J_{C,P}$ 5.6 Hz, CH-α,β), 74.9 (d, $^3J_{C,P}$ 6.9 Hz, C-5β), 74.4 (C-3β), 73.6 (C-2β), 70.7 (C-4α), 70.3 (C-4β), 70.1 (d, $^3J_{C,P}$ 7.0 Hz, C-5α), 69.9 (C-3α), 69.2 (C-2α), 64.6 (d, $^2J_{C,P}$ 5.0 Hz, C-6α), 64.2 (d, $^2J_{C,P}$ 4.7 Hz, C-6β), 36.1 (d, $^3J_{C,P}$ 5.5 Hz, C-10), 32.9 (C-16), 30.6, 30.5, and 30.2 (3 s, C-12–C-15), 27.8 (t, $^2J_{C,F}$ 21.8 Hz, $CH_2C_6F_{13}$), 26.5 (bs, $CH_2CH_2C_6F_{13}$), 25.9 (C-11), 23.5 (C-17), 12.7 (CH_3); ^{31}P, δ 1.91; Anal. Calcd for $C_{24}H_{35}F_{13}NaO_9P$ (768.5): C, 37.51; H, 4.59; Na, 2.99; P, 4.03. Found: C, 37.21; H, 4.85; Na, 3.50; P, 4.33.

D-*Glucose 3-(sodium 13,13,14,14,15,15,16,16,17,17,18,18,19,19,20,20,20-heptadecafluoro-10-eicosyl phosphate*) (**5c**).—The phosphate **4c** (4.1 g, 3.99 mmol), when treated in the same way as for the preparation of **5a**, yielded **5c** as a solid (2.84 g, 82%); $[\alpha]_D$ +17° (*c* 0.81, MeOH); IR: ν_{max} 3325 (OH), 2930–2865 (CH), 1235–1140 (CF), 1215 (P=O), 1130 cm^{-1} (P–O–C); NMR data (CD_3OD): ^{19}F, δ −80.3 (CF_3), −113.6 (CF_2CH_2), −121.1 to −122.4 (10 F), −125.4 (CF_2CF_3); ^{1}H, δ (α anomer ~ 58%) 0.90 (t, 3 H, $^3J_{H,H}$ 6.4 Hz, CH_3), 1.50–1.35 [m, 14 H, $(CH_2)_7CH_3$], 2.10–1.55 [m, 4 H, $CH_2CH_2C_8F_{17}$, $CH_2(CH_2)_7CH_3$], 2.55–2.18 (m, 2 H, $CH_2C_8F_{17}$), 4.03–3.39 (m, 6 H, H-2,3,4,5,6α, H-2,3,4,5,6β), 4.34 (m, 1 H, CH-α,β), 4.58 (d, $^3J_{2\beta,1\beta}$ 7.8 Hz, H-1β), 5.22 (d, $^3J_{1\alpha,2\alpha}$, 3.6 Hz, H-1α); ^{13}C, δ 97.4 (C-1β), 93.2 (C-1α), 81.9 (d, $^2J_{C,P}$ 5.5 Hz, C-3β), 79.3 (d, $^2J_{C,P}$ 5.7 Hz, C-3α), 77.2 (C-5β), 76.5 and 76.4 (dd ~ t, $^2J_{C,P}$ ~ 5.5 Hz, CH-α,β), 75.2 (bs, C-2β), 72.5 (C-5α, C-2α), 71.0 (bs, C-4α), 70.8 (bs, C-4β), 62.4 and 62.3 (2 s, C-6α,β), 36.0 (m, C-9), 32.7 (C-3), 30.4, 30.3, and 30.1 (3 s, C-4–C-7), 27.6 (t, $^2J_{C,F}$ 21.6 Hz, $CH_2C_8F_{17}$), 26.2 (bs, $CH_2CH_2C_8F_{17}$), 25.7 (C-8), 23.4 (C-2), 14.3 (CH_3); ^{31}P, δ 0.87 and 0.84; Anal. Calcd for $C_{26}H_{35}F_{13}NaO_9P$ (868.5): C, 35.96; H, 4.06; Na, 2.65; P, 3.57. Found: C, 35.57; H, 4.21; Na, 2.83; P, 3.35.

D-*Glucose 3-(sodium 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-9-octadecyl phosphate*) (**5d**). —The process described above for preparing **5a**, when applied to 3.4 g (3.66 mmol) of phosphate **4d**, gave 2.11 g of **5d** (75%); $[\alpha]_D$ +17° (*c* 0.71, MeOH); IR: ν_{max} 3325 (OH), 2930–2865 (CH), 1235–1140 (CF), 1215 (P=O), 1125 cm^{-1} (P–O–C); NMR data (CD_3OD): ^{19}F, δ −82.6 (CF_3), −115.7 (CF_2CH_2), −123.1 to −124.5 (6 F), −127.6 (CF_2CF_3); ^{1}H, δ (α anomer ~ 57%) 0.85 (t, 3 H, $^3J_{H,H}$

6.5 Hz, CH_3), 1.50–1.30 [bs, 14 H, $(CH_2)_7$], 2.10–1.60 [m, 4 H, $CH_2CH_2C_6F_{13}$, $CH_2(CH_2)_7CH_3$], 2.60–2.15 (m, 2 H, $CH_2C_6F_{13}$), 4.00–3.40 (m, 6 H, H-2,3,4,5,6α, H-2,3,4,5,6β), 4.32 (m, 1 H, CH-α,β), 4.53 (d, $^3J_{1\beta,2\beta}$ 7.8 Hz, H-1β), 5.14 (d, $^3J_{1\alpha,2\alpha}$ 3.8 Hz, H-1α); ^{13}C, δ 97.6 (C-1β), 93.4 (C-1α), 82.6 (d, $^2J_{C,P}$ 6.5 Hz, C-3β), 79.7 (d, $^2J_{C,P}$ 4.7 Hz, C-3α), 77.6 (C-5β), 76.4 (d, $^2J_{C,P}$ 6.0 Hz, CH-α,β), 75.6 (bs, C-2β), 73.1 (d, $^2J_{C,P}$ 4.7 Hz, C-2α), 73.0 (C-5α), 71.3 (m, C-4α), 71.2 (m, C-4β), 62.6 and 62.5 (2 s, C-6α,β), 36.2 (m, C-10), 33.0 (C-16), 30.6, 30.5, and 30.3 (3 s, C-12–C-15), 28.1 (t, $^2J_{C,F}$ 22.0 Hz, $CH_2C_8F_{17}$), 26.5 (bs, $CH_2CH_2C_8F_{17}$), 25.9 (C-11), 23.6 (C-17), 14.3 (CH_3); ^{31}P, δ −0.63 and −1.02; Anal. Calcd for $C_{24}H_{35}F_{13}NaO_9P \cdot 2H_2O$ (804.5): C, 35.83; H, 4.89; Na, 2.86; P, 3.85. Found: C, 35.10; H, 4.24; Na, 3.25; P, 3.48.

D-*Glucose 6-(sodium 13,13,14,14,15,15,16,16,17,17,18,18,19,19,20,20,20-heptadecafluoro-10-eicosyl phosphate*) (**5e**).—The phosphate **4e** (2.4 g, 2.15 mmol) was stirred for 15 min in methanolic 1% NaOMe at room temperature, the reaction being monitored by TLC (7:3 $CHCl_3$–MeOH). The solution was adjusted to pH 4 with Amberlite IR-120 resin (H^+ form, 30 mL). The resin was removed by filtration and washed with MeOH, and the filtrate was concentrated. The resulting gum was dissolved in aq 1:1 MeOH and adjusted to pH 7 with 0.2 M NaOH. Concentration and precipitation in acetone led to a solid which was purified by trituration with ether to give a yellow powder. This powder, when subjected to decoloration on activated charcoal, gave **5e** (1.66 g, 89%); $[\alpha]_D$ +12° (*c* 0.40, MeOH); IR: ν_{max} 3470 (OH), 2930–2860 (CH), 1240–1145 (CF), 1205 (P=O), 1120 cm^{-1} (P–O–C); NMR data (CD_3OD): ^{19}F, δ −82.6 (CF_3), −115.6 (CF_2CH_2), −123.1 to −124.5 (10 F), −127.5 (CF_2CF_3); ^{1}H, δ (α anomer ~ 59%) 0.97 (t, 3 H, $^3J_{H,H}$ 6.2 Hz, CH_3), 1.52–1.25 [m, 14 H, $(CH_2)_7CH_3$], 2.08–1.55 [m, 4 H, $CH_2CH_2C_8F_{17}$, $CH_2(CH_2)_7CH_3$], 2.65–2.20 (m, 2 H, $CH_2C_8F_{17}$), 3.23 (t, $^3J_{2\beta,1\beta} = {}^3J_{2\beta,3\beta} \simeq 7.9$ Hz, H-2β), 3.59–3.42 (m, H-2α, H-3β, H-4α, 4β, H-5β), 3.76 (dd ~ t, $^3J_{3\alpha,2\alpha} = {}^3J_{3\alpha,4\alpha} \simeq 8.6$ Hz, H-3α), 3.98–3.85 (m, H-5α), 4.20–4.00 (m, 2 H, H-6α,6β), 4.40–4.28 (m, 1 H, CH-α,β), 4.51 (d, $^3J_{1\beta,2\beta}$ 7.7 Hz, H-1β), 5.16 (d, $^3J_{1\alpha,2\alpha}$ 3.7 Hz, H-1α); ^{13}C, δ 97.9 (C-1β), 93.6 (C-1α), 77.1 (C-3β), 76.7 (d, $^3J_{C,P}$ 6.7 Hz, C-5β), 76.0 (C-2β), 75.6 (dd ~ t, $^2J_{C,P}$ 5.5 Hz, CH-α,β), 74.0 (C-3α), 73.5 (C-2α), 71.8 (d, $^3J_{C,P}$ 7.5 Hz, C-5α), 70.9 (C-4α), 70.8 (C-4β), 65.3 (m, C-6α,6β), 35.9 (dd ~ t, $^3J_{C,P}$ ~ 4.2 Hz, C-9), 32.6 (C-3), 30.4, 30.3, and 30.0 (3 s, C-4–C-7), 27.6 (t, $^2J_{C,F}$ 21.8 Hz, $CH_2C_8F_{17}$), 26.2 (bs, $CH_2CH_2C_8F_{17}$), 25.6 (C-8), 23.3 (C-2), 14.0 (CH_3); ^{31}P, δ −1.67 and −1.73; Anal. Calcd for $C_{26}H_{35}F_{17}NaO_9P \cdot 2H_2O$ (904.5): C, 34.53; H, 4.35; Na, 2.54; P, 3.42. Found: C, 34.40; H, 4.08; Na, 2.85; P, 3.38.

D-*Glucose 6-(sodium 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-9-octadecyl phosphate*) (**5f**).—The same procedure as above, when applied to the phosphate **4f** (2 g, 1.97 mmol), yielded **5f** (0.82 g, 54%); $[\alpha]_D$ +12° (*c* 0.60, MeOH); IR: ν_{max} 3470 (OH), 2930–2855 (CH), 1240–1145 (CF), 1200 (P=O), 1120 cm^{-1} (P–O–C); NMR data (CD_3OD): ^{19}F, δ −80.9 (CF_3), −113.9 (CF_2CH_2), −121.4 to −122.8 (6 F), −125.9 (CF_2CF_3); ^{1}H, δ (α-anomer ~ 58%) 0.94 (t, 3 H, $^3J_{H,H}$ 6.4 Hz, CH_3), 1.52–1.30 [m, 14 H, $(CH_2)_7CH_3$], 2.02–1.58 [m, 4 H, $CH_2CH_2C_6F_{13}$, $CH_2(CH_2)_7CH_3$], 2.60–2.21 (m, 2 H, $CH_2C_6F_{13}$), 3.20 (t, $^3J_{2\beta,1\beta} = {}^3J_{2\beta,3\beta} \simeq 8.3$ Hz,

H-2β), 3.54–3.34 (m, H-2α, H-3β, H-4α,4β, H-5β), 3.73 (dd ~ t, $^3J_{3\alpha,2\alpha} = {}^3J_{3\alpha,4\alpha}$ = 9.3 Hz, H-3α), 3.94–3.87 (m, H-5α), 4.15–4.06 (m, 2 H, H-6α,6β), 4.38–4.21 (m, 1 H, CH-α,β), 4.51 (d, $^3J_{1\beta,2\beta}$ 7.7 Hz, H-1β), 5.13 (d, $^3J_{1\alpha,2\alpha}$ 3.6 Hz, H-1α); ^{13}C, δ 98.2 (C-1β), 93.9 (C-1α), 77.5 (C-3β), 77.0 (d, $^3J_{C,P}$ 6.7 Hz, C-5β), 76.3 (C-2β), 76.0 (dd ~ t, $^2J_{C,P}$ ~ 4.0 Hz, CH-α,β), 74.3 (C-3α), 73.9 (C-2α), 72.1 (d, $^3J_{C,P}$ 7.2 Hz, C-5α), 71.2 (C-4α), 71.1 (C-4β), 65.8 (m, C-6α,6β), 36.3 (t, $^3J_{C,P}$ ~ 4.2 Hz, C-10), 33.0 (C-16), 30.8, 30.7 and 30.4 (3 s, C-12–C-15), 27.9 (t, $^2J_{C,F}$ 22.1 Hz, $CH_2C_6F_{13}$), 26.6 (bs, $CH_2CH_2C_6F_{13}$), 26.0 (C-11), 23.7 (C-17), 14.4 (CH_3); ^{31}P, δ 2.10 and 2.04; Anal. Calcd for $C_{24}H_{35}F_{13}NaO_9P$ (768.5): C, 37.51; H, 4.59; Na, 2.99; P, 4.03. Found: C, 36.87; H, 4.74; Na, 3.33; P, 3.92.

D-*Mannose 6-(sodium 13,13,14,14,15,15,16,16,17,17,18,18,19,19,20,20,20-heptadecafluoro-10-eicosyl phosphate*) (**5g**).—The phosphate **4g** (3.5 g, 3.14 mmol) was deacetylated as described for the synthesis of **5e**, to give **5g** (2.59 g, 95%) as a solid; $[\alpha]_D$ +4° (*c* 1.0, MeOH); IR: ν_{max} 3480 (OH), 2935–2850 (CH), 1225–1145 (CF), 1205 (P=O), 1120 cm^{-1} (P–O–C); NMR data (CD_3OD): ^{19}F, δ −81.0 (CF_3), −114.0 (CF_2CH_2), −122.8 to −121.5 (10 F), −125.9 (CF_2CF_3); ^{1}H, δ (α anomer ~ 84%) 0.91 (t, 3 H, $^3J_{H,H}$ 6.4 Hz, CH_3), 1.60–1.25 [m, 14 H, $(CH_2)_7CH_3$], 2.10–1.65 [m, 4 H, $CH_2CH_2C_8F_{17}$, $CH_2(CH_2)_7CH_3$], 2.65–2.15 (m, 2 H, $CH_2C_8F_{17}$), 3.33 (m, H-5α), 4.00–3.75 (m, H-3,4,6α), 4.11 (m, H-2α), 4.27 (m, 1 H, CH-α,β), 4.79 (bs, H-1β), 5.08 (bs, H-1α); ^{13}C, δ 95.8 (C-1α), 95.6 (C-1β), 77.1 (d, $^3J_{C,P}$ 5.0 Hz, C-5β), 75.9 (d, $^2J_{C,P}$ 6.1 Hz, CH-α,β), 74.8 (2 s, C-3β), 73.0 (d, $^3J_{C,P}$ 6.7 Hz, C-5α), 72.8 (C-2β), 72.7 (C-2α), 71.9 (C-3α), 68.4 (2 s, C-4α), 67.8 (2 s, C-4β), 66.1 (d, $^2J_{C,P}$ 5.5 Hz, C-6α), 65.8 (d, $^2J_{C,P}$ 5.1 Hz, C-6β), 36.1 (d, $^3J_{C,P}$ 3.8 Hz, C-9), 32.9 (C-3), 30.6, 30.5, and 30.3 (3 s, C-4–C-7), 28.8 (t, $^2J_{C,F}$ 21.4 Hz, $CH_2C_8F_{17}$), 26.5 (bs, $CH_2CH_2C_8F_{17}$), 25.9 (C-8), 23.6 (C-2), 14.3 (CH_3); ^{31}P, δ −0.25; Anal. Calcd for $C_{26}H_{35}F_{17}NaO_9P$ (868.5): C, 35.96; H, 4.06; Na, 2.65; P, 3.57. Found: C, 35.67; H, 4.22; Na, 2.79; P, 3.62.

D-*Mannose 6-(sodium 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-9-octadecyl phosphate*) (**5h**).—The phosphate **4h** (3.5 g, 3.45 mmol) was deacetylated as described for the synthesis of **5e**, to give **5h** (2.59 g, 98%) as a solid; $[\alpha]_D$ +4° (*c* 1.1, CH_3OH); IR: ν_{max} 3470 (OH), 2935–2855 (CH), 1240–1145 (CF), 1200 (P=O), 1120 cm^{-1} (P–O–C); NMR data (CD_3OD): ^{19}F, δ −80.9 (CF_3), −113.8 (CF_2CH_2), −121.4 to −122.7 (6 F), −125.8 (CF_2CF_3); ^{1}H, δ (α anomer ~ 78%) 0.94 (t, 3 H, $^3J_{H,H}$ 6.7 Hz, CH_3), 1.50–1.30 [m, 14 H, $(CH_2)_7CH_3$], 2.05–1.55 [m, 4 H, $CH_2CH_2C_6F_{13}$, $CH_2(CH_2)_7CH_3$], 2.60–2.20 (m, 2 H, $CH_2C_6F_{13}$), 3.35 (m, H-5α), 3.65–3.90 (m, H-3,4,6α), 4.12 (m, H-2α), 4.30 (m, 1 H, CH-α,β), 4.83 (bs, H-1β), 5.12 (bs, H-1α); ^{13}C, δ 95.9 (C-1α), 95.5 (C-1β), 77.1 (d, $^3J_{C,P}$ 5.1 Hz, C-5β), 76.0 (d, $^2J_{C,P}$ 6.1 Hz, CH-α,β), 74.8 (2 s, C-3β), 73.0 (d, $^3J_{C,P}$ 6.5 Hz, C-5α), 72.9 (C-2β), 72.7 (C-2α), 71.9 (C-3α), 68.3 (2 s, C-4α), 67.7 (2 s, C-4β), 66.1 (d, $^2J_{C,P}$ 5.6 Hz, C-6α), 65.8 (d, $^2J_{C,P}$ 6.5 Hz, C-6β), 36.2 (d, $^3J_{C,P}$ 2.7 Hz, C-10), 33.0 (C-16), 30.7, 30.6, and 30.4 (3 s, C-12–C-15), 27.9 (t, $^2J_{C,F}$ 21.2 Hz, $CH_2C_6F_{13}$), 26.6 (bs, $CH_2CH_2C_6F_{13}$), 26.0 (C-11), 23.6 (C-17), 14.3 (CH_3); ^{31}P, δ 1.98; Anal. Calcd for $C_{24}H_{35}F_{13}NaO_9P$ (768.5): C, 37.51; H, 4.59; Na, 2.99; P, 4.03. Found: C, 37.35; H, 4.56; Na, 2.89; P, 3.79.

D-*Mannose 6-(sodium 10-eicosyl phosphate*) (**5i**).—Deacetylation of **4i** (2.6 g, 3.21

mmol), formation of the sodium salt, and isolation were performed as described for **5e**, to yield **5i** as a white solid (1.55 g, 86%); $[\alpha]_D$ +5° (*c* 0.51, MeOH); IR: ν_{max} 3500 (OH), 2925–2855 (CH), 1200 (P=O), 1085 cm^{-1} (P–O–C); NMR data (CD_3OD): ^1H, δ (α anomer ~ 76%) 0.81 (t, 6 H, $^3J_{H,H}$ 6.1 Hz, CH_3), 1.25–1.00 [m, 30 H, $(CH_2)_7CH_3$, $(CH_2)_8CH_3$], 1.45–1.35 [m, 4 H, $CH_2(CH_2)_8CH_3$, $CH_2(CH_2)_7CH_3$], 4.10–3.35 (m, CH-α,β, H-2,3,4,5,6α), 4.84 (bs, H-1β), 5.13 (bs, H-1α); ^{13}C, δ 95.9 (C-1α), 95.6 (C-1β), 77.7 (d, $^2J_{C,P}$ 6.1 Hz, CH-α,β), 77.1 (d, $^3J_{C,P}$ 6.5 Hz, C-5β), 74.8 (C-3β), 73.1 (d, $^3J_{C,P}$ 6.4 Hz, C-5α), 73.0 (C-2β), 72.8 (C-2α), 71.8 (C-3α), 68.3 (C-4α), 67.7 (C-4β), 66.0 (d, $^2J_{C,P}$ 5.8 Hz, C-6α), 65.6 (d, $^2J_{C,P}$ 5.5 Hz, C-6β), 36.1 (d, $^3J_{C,P}$ 3.9 Hz, C-9, C-11), 33.1 (C-3, C-18), 31.0, 30.8 and 30.5 (3 s, C-4–C-7 and C-13–C17), 26.0 (C-8, C-12), 23.7 (C-2, C-19), 14.5 (CH_3); ^{31}P, δ 5.41 and 5.38; Anal. Calcd for $C_{26}H_{52}NaO_9P \cdot H_2O$ (580.7): C, 53.78; H, 9.37; Na, 3.96; P, 5.33. Found: C, 53.25; H, 9.29; Na, 4.25; P, 5.22.

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