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Synthesis of D-glucose 3- and 6-[2-(perfluoroalkyl)ethyl phosphates]: a new type of anionic surfactant for biomedical use

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ABSTRACT

D-Glucose 3- and 6-[sodium 2-(perfluoro-hexyl or -octyl)ethyl phosphates] have been synthezised by condensation of 1,2,3,4,-tetra-*O*-acetyl-β-D-glucopyranose and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose with 2-(perfluoroalkyl)ethylphosphoroditriazolides followed by *O*-deacetylation or deacetalation. The structures of the compounds were established on the basis of ^{1}H-, ^{19}F-, ^{31}P-, and ^{13}C-NMR data. These salts display strong surface activities and appear to have good biocompatibility.

INTRODUCTION

The approval[1] by the Food and Drug Administration of the first human-injectable fluorocarbon-based emulsion (Fluosol®)[2] has stimulated efforts to improve injectable oxygen-carrying preparations[3]. Fluosol, which is approved solely for the oxygenation of the myocardium during percutaneous transluminal coronary angioplasty[4], has poor stability and a low fluorocarbon content, and hence low efficacy. Moreover, Pluronic F68®, a polyoxyethylene polyoxypropylene block copolymer used as the surfactant in the formulation of Fluosol, or some impurity it may contain, is held to be responsible for some transitory side effects[5]. Major progress has been made with the development of stable, concentrated (up to 100% w/v) fluorocarbon emulsions with egg-yolk phospholipids as the sole surfactant[6]. However, this surfactant allows only limited flexibility in determining the characteristics of the emulsions. Improvement of the control over these characteristics could allow injectable fluorocarbon emulsions to be adapted to each specific therapeutic need[7], as a substitute for blood in "transfusion", whenever oxygen is

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needed, including during surgery, ischemia, for organ preservation, for radio- and chemo-therapy of cancer, for diagnosis, in biomedical research, etc.

Such progress will depend on the availability of new biocompatible surfactants and/or cosurfactants more specifically suited to the emulsification of fluorocarbons. In this context, several new families of neutral perfluoroalkylated surfactants derived from sugars and polyols[8–13] were synthesized, most of which stabilize fluorocarbon emulsions when used[14] with Pluronic F-68. 6-*O*-[3-(Perfluorooctyl)propanoyl]-α,α-trehalose also displays good emulsifying properties when used as the sole surfactant[15]. However, none of these compounds was efficient as a cosurfactant with egg-yolk phospholipids. Perfluoroalkylated phosphocholines showed good emulsifying properties, both alone and in conjunction with egg-yolk phospholipids[16], but they have high acute toxicity. Consequently, in the hope of obtaining products with more acceptable properties, surfactants comprising phosphodiesters of glucose and of 2-(perfluoroalkyl)ethanols have been synthesized and are now reported. Since the surfactants must remain unchanged during the high-pressure emulsification and sterilization procedures, derivatives of D-glucose 3- and 6-phosphate were selected rather than those of the more-labile D-glucose 1-phosphate[17]. A hydrocarbon analogue was also prepared in order to evaluate the impact of the perfluoroalkylated chain on the emulsion stabilization properties and biological acceptance of the surfactants.

RESULTS AND DISCUSSION

Numerous methods, including the phosphodiester[18], phosphotriester[19], H-phosphonate[20], phosphite[21], phosphoramidite[22], and cyclic enediol pyrophosphate[23] approaches, can yield phosphodiesters. These syntheses involve nucleophilic substitution of a hydroxyl group at the phosphorus centre and require the protection of all but one of the hydroxyl groups of the carbohydrate. An alternative approach, namely, nucleophilic displacement of alkyl halides by a phosphate anion has been used to prepare mixed phospho-diesters[24] and -triesters[25–27]. This latter approach does not require protection of the hydroxyl groups in the sugar derivative but it is practical only for preparing esters of D-glucose 6-phosphate, the only commercially available, non-anomeric aldose phosphate.

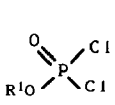
Despite growing activity on phosphodiester-bridged saccharide structures[28], the few available examples of phosphodiesters of carbohydrates and aliphatic alcohols involve glucose and galactose derivatives with the phosphate group on the anomeric[29] or 6-position[26,30]. A synthesis of D-glucose 6-(hexadecyl phosphate), by condensation of acetylated D-glucopyranose 6-phosphate with hexadecanol in the presence of trichloroacetonitrile as the phosphate-activating reagent, has been reported[26]. This strategy is limited, however, by the lack of easy access to aldose phosphates. The phosphotriester strategy adopted for the preparation of D-galactose 6-(tetradecyl phosphate)[30] requires a phosphate protective group, and hence an additional step for its removal. Phosphodiesters of 2,2,2-trichloroethanol and

various protected glucoses have been used also as intermediates in a phosphotriester strategy[31] designed for the isolation of phosphodiesters in which only sugar moieties are linked.

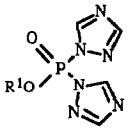
The phosphodiester approach was used first with phosphorylation of the perfluoroalkylated alcohol, then of the protected sugar derivative. Thus, the perfluoroalkylated alcohol was converted into the phosphorodichloridate by reaction with phosphorus oxychloride. Chlorination of the alcohol can be suppressed[16] by carrying out the condensation in ether, the major difficulty being to limit the reaction to the monoesterification stage. The best results were obtained by dropwise addition of 1 equiv of a ~0.5 M solution of the alcohol in dry ether (containing 2 equiv of triethylamine to scavenge the hydrogen chloride) to a slight excess of a cooled ~0.6 M solution of phosphorus oxychloride in ether. ^{31}P-NMR spectroscopy of the crude mixture, after removal of the excess of phosphorus oxychloride, revealed <5% of the diester and the absence of triester. The 2-(perfluorohexyl)ethyl (**1a**), 2-(perfluoro-octyl)ethyl (**1b**), and decyl (**1c**) phosphorodichloridates, obtained in yields of ~95% yield, were used in the coupling reaction without further purification.

Since (perfluoroalkyl)alkyl phosphorodichloridates have been used to prepare (perfluoroalkyl)alkyl phosphocholines[16], the condensation of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose with **1a** was explored. However, formation of the triester **5a** could not be avoided. Typically, when 1 equiv of the sugar derivative and 2 equiv of triethylamine in chloroform were allowed to react with **1a**, 55% of **5a** was obtained after chromatography together with a 95:5 mixture (^{31}P-NMR data) of the desired diester **3a** and of the 1-*O*-deacetylated phosphodiester **4a** obtained after treatment of appropriate chromatography fractions with triethylammonium hydrogencarbonate. Pure **3a** (26%) was readily separated from this mixture, but the isolation of **4a** required chromatography. Lowering the reaction temperature to 0° and slow addition of the sugar derivative did not significantly modify the result (45% yield of **5a**). Slow addition of a solution of the glucose derivative in pyridine at room temperature to an equimolar amount of **1a** in tetrahydrofuran reduced the yield of **5a** to 21%, but that (27%) of the diester was still not satisfactory, and, again, a 95:5 mixture of **3a** and **4a** was obtained. The formation of triester has been reported often when phosphorodichloridates were used as phosphorylating reagents[32–34], and an undesirably large excess of the phosphorodichloridate[34] is necessary in order to reduce the proportion. Although unexpected, the formation of **4a** can be explained by the presence of a base in the medium, since acylated aldoses can be selectively 1-*O*-deacylated by organic or inorganic bases[35,36]

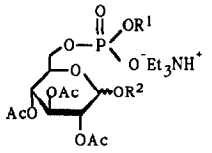
The use of phosphoroditriazolides[37] has been proposed as a convenient alternative in order to avoid symmetrical phosphorylation. Phosphoroditriazolide is a bifunctional phosphorylating agent[37,38], but it is also essentially monofunctional when present in excess[33,34,37,39,40]. Indeed, condensation of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (0.5 equiv in pyridine) with crude 2-(perfluorohexyl)ethyl phosphoroditriazolide **2a** (1 equiv), prepared[41] in situ from 1*H*-1,2,4-triazole in tetrahy-



1a,b,c

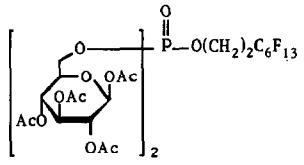


2a,b,c

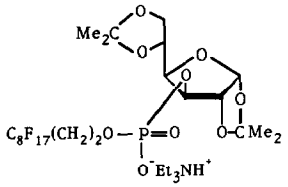


3a,b,c R^2 = β-OAc

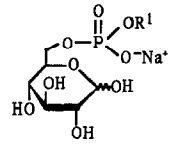
4a,b,c R^2 = α,β-OH



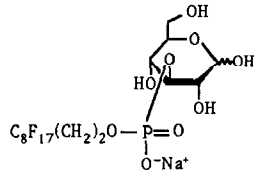
5a



6b



7a,b,c



8b

a R^1 = $(CH_2)_2C_6F_{13}$

b R^1 = $(CH_2)_2C_8F_{17}$

c R^1 = $(CH_2)_9CH_3$

Fig. 1.

drofuran and triethylamine, gave only traces (TLC) of triester **5a**. After conversion into the triethylammonium salt, the crude product was found (^{31}P-NMR data) to be a 95:5 mixture of **3a** and **4a**, from which **3a** (65%) was isolated readily. However, when the amount of the incoming sugar derivative was increased to 0.8 equiv, in an attempt to increase the yield, formation of triester **5a** (30%) was again observed together with a lowered yield of **3a** (30%). Consequently, the phosphodiester **3b** (64%) was prepared from 0.5 equiv of the glucose derivative and 1 equiv of **2b**.

One of the major drawbacks of the phosphodiester procedure, i.e., purification of a salt on silica gel, is overcome in this approach but only for the perfluoroalkylated compounds. Indeed, the mixture of **3c** and **4c** obtained by the reaction of the decyl phosphoroditriazolide **2c** with the glucose derivative could not be purified by simple trituration and was *O*-deacetylated.

Reaction of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (0.5 equiv) with **2b**, under the conditions described above, was incomplete and 50% of the unreacted sugar derivative was recovered by chromatography together with 50% of the expected phosphodiester **6b**, isolated as the triethylammonium salt. This limited

conversion reflects the lower reactivity of HO-3 in the sugar derivative compared to that of HO-6 in 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose.

The various phosphorylated products were characterized by ^{13}C-NMR spectroscopy. Assignment of the ^{13}C resonances of the sugar moiety was achieved on the basis of differences in chemical shifts relative to those for the non-phosphorylated compounds[42,43], taking into account the effects of phosphate substitution[44], namely, a significant downfield shift for the resonance of the carbon atom to which the phosphate is linked, with $^2J_{C,P}$ typically 5 ± 0.5 Hz, and usually marginal upfield shifts for the resonances of the neighbouring carbons, with $^3J_{C,P}$ values varying over a wide range according to the conformation around the phosphorus bridge[45].

In the ^{13}C-NMR spectra of **3a** and **3b**, the downfield shift (2.4–2.5 ppm) for the resonance of C-6 and the couplings ($^3J_{C\text{-}5,P}$ 8.3–8.5, $^2J_{C\text{-}6,P}$ 4.6–4.9 Hz) confirmed O-6 as the site of phosphorylation. The presence of the perfluoroalkylated chain was indicated by the characteristic couplings for the carbons α (dt, $^2J_{C,F}$ 21.2–21.6, $^3J_{C,P}$ 7.0–7.1 Hz) and β (q-like, $^3J_{C,F} = {}^2J_{C,P} = 5.2$–5.5 Hz) to the perfluoroalkylated chain.

The structure of **4a** was established by the ^{1}H- and ^{13}C-NMR data. The resonances of the perfluoroalkylated chain were identified on the basis of the magnitudes of the $J_{C,P}$ and $J_{C,F}$ values. Furthermore, the ^{13}C signal at δ 64.1 specific for C-6 of the sugar moiety, appearing as a doublet ($J_{C,P}$ 5.2 Hz), indicates that the phosphate group was located at position 6. The remainder of the ^{13}C-NMR spectrum contained two sets of resonances, the intensities of which were in the ratio 8:2 corresponding to the α and β anomers, and confirmed the loss of the AcO-1 from **3a**. The ^{1}H-NMR spectrum contained a characteristic signal (d, $J_{1\alpha,2\alpha}$ 2.8 Hz) for H-1α at δ 5.37. This large upfield shift with respect to **3a** (δ 5.61 for H-1β) also confirmed the loss of AcO-1. Since the H-1α resonance was identified unambiguously, those of H-2α,3α,4α could be assigned by ^{1}H{^{1}H}-decoupling techniques, and the signals of C-2α,3α,4α were assigned through selective ^{13}C{^{1}H}-decoupling techniques. The signal of C-5α was assigned by the characteristic magnitude (8.5 Hz) of $^3J_{C,P}$. Except for that of the resonance for C-6, which bears the phosphate group, the chemical shifts of the resonances for the sugar moiety of **4a**(α) corresponded well with those of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose[43]. The C-1β,5β,6β resonances were assigned on the basis of chemical shifts or coupling constants, and those of C-2β,3β,4β by comparison with data for 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose[43].

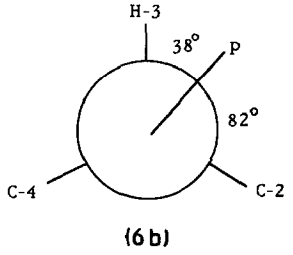
That **5a** was a triester with two sugar units was established by the elemental analysis and ^{1}H-NMR data. Integration of the well-separated resonances of the acetyl protons and protons α to the perfluoroalkylated chain gave a ratio 24:2. When compared to **3a**, an increase of ~0.2 ppm of the chemical shifts of the resonances for all the methylene protons coupled to phosphorus confirmed the phosphotriester linkage[26]. Furthermore, the ^{1}H-NMR spectrum contained two signals for H-1 of equal intensity at δ 5.67 (8.1 Hz) and 5.70 (8.1 Hz), and six

singlets for the acetyl resonances (four corresponding to three protons and two to six protons). These splittings indicate two diastereotopic glucose moieties. The ^{13}C-NMR spectrum also showed splittings for the resonances of C-3,4,6 and for one of the carbonyl carbons. The phosphotriester linkage was further established by an increase of chemical shifts of 1.9–2.1 and 2.9 ppm, with regard to the diester analogue, for the resonances of C-6 and the carbon β to the perfluoroalkylated chain, respectively.

Phosphorylation at O-3 was indicated by the expected $^{3}J_{3,P}$ value (7.4 Hz) in the ^{1}H-NMR spectrum of **6b**. Taking into account the above-mentioned phosphate-substitution effect, the ^{13}C resonances of the sugar moiety were assigned and showed the expected $^{3}J_{C\text{-}4,P}$ (8.3 Hz) and $^{2}J_{C\text{-}3,P}$ (5.5 Hz) values, and the absence of coupling between C-2 and P. A 2D ^{1}H–^{13}C correlated-shift NMR experiment confirmed the assignments. The magnitude of the coupling constants can be explained in terms of the conformation around the O–C-3 bond (see Fig. 1). The $^{3}J_{C,P}$ value is determined by a Karplus-type relationship[45]: a $^{3}J_{C\text{-}2,P}$ value of zero indicates a dihedral angle $\Psi_{P,C\text{-}2}$ of 90°, whereas a value of 8.3 Hz between C-4 and P requires these atoms to be *trans*. A computed $\Psi_{P,C\text{-}4}$ value of ~163° was obtained from eq (*1*)[46]. Application of eq (*2*)[47] for the dependence of $^{3}J_{H,P}$ on the dihedral angle $\Phi_{3,P}$ gave a value of ~38° and resulted in dihedral angles $\Psi_{P,C\text{-}4} \sim 158°$ and $\Psi_{P,C\text{-}2} \sim 82°$, which are in accord with the above data.

$$^{3}J_{C,P} = 6.4 \cos^{2}\Psi_{C,P} - 1.3 \cos \Psi_{C,P} + 1.2 \quad (1)$$

$$^{3}J_{H,P} = 18.1 \cos^{2}\Phi_{H,P} - 4.5 \cos \Phi_{H,P} \quad (2)$$



(6 b)

Fig. 1.

O-Deacetylation of **3a** and **3b** by brief treatment with methanolic sodium methoxide and ion exchange gave the sodium salts of **7a** and **7b** (~60% based on 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose). *O*-Deacetylation of the mixture of **3b** and **4b** also gave **7b** (75%). Likewise, the mixture of **3c** and **4c** gave **7c** (71% based on 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose).

The first attempts to deprotect **6b** with an acidic ion-exchange resin[48] in aqueous acetone or aqueous methanol resulted in incomplete reaction. Complete *O*-deisopropylidenation, without alteration of the phosphodiester linkage, was achieved readily by using aqueous trifluoroacetic acid[49] and gave 65% of **8b**

(sodium salt). The ^1H- and ^{13}C-NMR spectra showed that the phosphate group has not migrated and that **7a–7c** and **8b** were each 1:1 α,β-mixtures.

The present work shows that the D-glucose 6-phosphate derivatives could be prepared in high yields without column chromatography of the intermediates or of the end products.

Preliminary biocompatibility tests showed that **7a** had no hemolytic effect on human red blood cells suspended in an isotonic 0.9% NaCl solution even at concentrations as high as 100 g/L. Investigations on **7b** were limited by its lower solubility; however, a 30 g/L dispersion of **7b** in a 20 g/L solution of Pluronic F-68 in water displayed no hemolytic activity, whereas its hydrocarbon counterpart **7c** was significantly hemolytic at 5 g/L. These results confirm the absence of hemolytic effect of perfluoroalkylated chains[50]. Solutions of **7b** and **8b** (1 g/L) caused no significant inhibition of the rate of growth and viability of lymphoblastoid cells of the Namalva strain. Compound **7a** had an iv LD_{50} of 750 mg/kg in mice. Each compound displayed marked surface activities. Thus, 1 g/L solutions of **7a**, **7b**, and **8b** had lowered surface tension and water–perfluorodecalin interfacial tension (from 73 and 56 $mN \cdot m^{-1}$ to 19.7–27.5 and 5.1–5.6 $mN \cdot m^{-1}$, respectively).

EXPERIMENTAL

Silica Gel F_{254} (Merck) was used for TLC with detection by charring with H_2SO_4 or by reaction with Zinzadze's reagent[51] (phosphate-containing compounds). Triethylammonium salts were detected with the Dragendorff reagent[52]. Column chromatography was carried out on Silica Gel 60 (70–230 mesh; Merck). Optical rotations were measured with a Perkin–Elmer 141 polarimeter (1-dm cell). NMR spectra were recorded with a Bruker AC 200 spectrometer. Chemical shifts are given in ppm relative to that for Me_4Si, using the deuterium signal of the solvent as a heteronuclear reference (^1H and ^{13}C), to external aq 85% H_3PO_4 (^{31}P), and to internal $CFCl_3$ (^{19}F). Elemental analyses were performed by the Service Central de Microanalyse du C.N.R.S. Solvents were dried and distilled according to standard procedures and stored over molecular sieves (4A). All reactions, except deacetalation, were performed under anhyd Ar. Evaporations were conducted under reduced pressure at $< 40°$. 1,2,3,4-Tetra-*O*-acetyl-β-D-glucopyrano, 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, and 1*H*-1,2,4-triazole were commercial products and were dried by repeated concentrations with anhydrous pyridine. 2-(Perfluorohexyl)ethanol, 2-(perfluoro-octyl)ethanol, and phosphorus oxychloride were redistilled before use. Phosphorodichloridates **1a–c** were used within 2 days of preparation. Only one preparation each of **1a–c** is described, but all batches were prepared with similar yields.

3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-octyl phosphorodichloridate (**1a**). — A solution of 2-(perfluorohexyl)ethanol (30.6 g, 84.1 mmol) and triethylamine (17.0 g, 168.3 mmol) in anhydrous ether (160 mL) was added during 45 min to a stirred solution of phosphorus oxychloride (15.4 g, 100.7 mmol) in anhydrous ether (160

mL) maintained between −5 and 0°. The stirred mixture was then warmed up to room temperature, stirring was continued for 1 h, the precipitated triethylammonium hydrochloride was removed, the filtrate was concentrated to dryness under reduced pressure, and the residue was dried overnight (10^{-2} mmHg) in order to ensure removal of phosphorus oxychloride. The resulting yellow waxy **1a** (38.7 g, 96%) was used without further purification. ^{31}P-NMR data ($CDCl_3$): δ 8.29.

3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecyl phosphorodichloridate (**1b**). — The above process was applied to 2-(perfluoro-octyl)ethanol (37.6 g, 81.0 mmol), triethylamine (16.4 g, 162.1 mmol), and phosphorus oxychloride (14.9 g, 97.4 mmol) to yield **1b** (45.9 g, 97%) as a yellow powder. ^{31}P-NMR data ($CDCl_3$): δ 8.18.

Decyl phosphorodichloridate (**1c**). — Reaction of 1-decanol (12.6 g, 79.6 mmol), triethylamine (16.1 g, 159.1 mmol), and phosphorus oxychloride (14.6 g, 95.2 mmol), as described for **1a**, gave **1c** (21.2 g, 97%) as a red liquid. ^{31}P-NMR data ($CDCl_3$): δ 7.52.

*Phosphorylation of 1,2,3,4-tetra-*O*-acetyl-β-*D*-glucopyranose by* **1a**. — (*a*) A solution of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (3.00 g, 8.6 mmol) and triethylamine (1.74 g, 17.2 mmol) in anhyd $CHCl_3$ (25 mL) was added at room temperature during 40 min to a stirred solution of **1a** (4.14 g, 8.6 mmol) in $CHCl_3$ (20 mL). Stirring was continued for 6 h and the reaction was monitored by TLC ($CHCl_3$–MeOH, 4:1). The reaction was quenched with water (1 mL), and the mixture was stirred for 1 h, then concentrated. Column chromatography of the residue, first with 2:1 EtOAc–hexane, yielded solid **5a** (2.6 g, 55%). Elution with 4:1 $CHCl_3$–MeOH then gave a solid that was added to M triethylammonium hydrogencarbonate buffer (20 mL) and extracted with $CHCl_3$ (3 × 20 mL). The combined extracts were washed with 0.5 M buffer (2 × 20 mL) and water (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The resulting 95:5 mixture (2.9 g) of **3a** and **4a** (^{31}P-NMR data) was triturated with ether to yield **3a** (2.0 g, 26%) as a white powder. Compound **4a** was isolated by column chromatography ($CHCl_3$–MeOH–M buffer, 75:23:2) of the material in the mother liquor.

(*b*) A solution of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (4.60 g, 13.2 mmol) in anhydrous pyridine (100 mL) was added at room temperature during 50 min to a solution of **1a** (6.35 g, 13.2 mmol) in anhydrous tetrahydrofuran (100 mL). The mixture was stirred for 5 h, then worked-up as in (*a*) to give **5a** (1.5 g, 21%) and a 95:5 mixture (4.6 g) of **3a** and **4a**, trituration of which with ether afforded **3a** (3.1 g, 27%).

*1,2,3,4-Tetra-*O*-acetyl-β-D-glucopyranose (6-triethylammonium 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-octyl phosphate)* (**3a**). — Obtained as described above, **3a** had $[\alpha]_D$ + 13° (*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{1}H, δ 1.25 (t, 9 H, $^3J_{H,H}$ 7.2 Hz, 3 CH_2CH_3), 1.92, 1.95, 1.96, and 1.99 (4 s, each 3 H, 3 Ac), 2.42 (tt, 2 H, $^3J_{H,H}$ 7.0, $^3J_{H,F}$ 19.0 Hz, $CH_2C_6F_{13}$), 2.99 (q, 6 H, 3 CH_2CH_3), 3.77–3.94 (m, 3 H, H-5,6,6), 4.07 (dt ~ q, 2 H, $^3J_{H,H} = {}^3J_{H,P} = 7.0$ Hz, $CH_2CH_2C_6F_{13}$), 4.97–5.22 (m, 3 H, H-2,3,4), 5.64 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 12.00 (s, 1 H, NH^+); ^{19}F, δ −81.3 (3 F,

CF_3), −114.0 (2 F, CF_2CH_2), −122.4, −123.4, and −124.1 [6 F, $(CF_2)_3CF_2CH_2$], −126.6 (2 F, CF_2CF_3); ^{13}C, δ 169.9, 169.3, 169.1, 168.6 (4 C, 5 $COCH_3$), 91.5 (C-1), 73.9 (d, $^3J_{C,P}$ 8.3 Hz, C-5), 72.9 (C-3), 70.2 (C-2), 68.1 (C-4), 63.4 (d, $^2J_{C,P}$ 4.6 Hz, C-6), 57.3 (dt ~ q, $^2J_{C,P} = {}^3J_{C,F} = 5.5$ Hz, $CH_2CH_2C_6F_{13}$), 45.4 (3 C, 3 CH_2CH_3), 32.1 (dt, $^3J_{C,P}$ 7.0, $^2J_{C,F}$ 21.6 Hz, $CH_2C_6F_{13}$), 20.4 (4 C, 4 $COCH_3$), 8.3 (3 C, 3 CH_2CH_3); ^{31}P, δ −0.18.

Anal. Calcd for $C_{28}H_{39}F_{13}NO_{13}P$ (875.6): C, 38.41; H, 4.49; F, 28.21; N, 1.60; P, 3.54. Found: C, 38.18; H, 4.28; F, 27.62; N, 1.46; P, 3.46.

*2,3,4-Tri-*O*-acetyl-*D*-glucopyranose 6-(triethylammonium 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-octyl phosphate)* (**4a**). — NMR data ($CDCl_3$): α anomer: ^1H, δ 1.27 (t, 9 H, $^3J_{H,H}$ 7.3 Hz, 3 CH_2CH_3), 1.94, 1.97, and 2.00 (4 s, each 3 H, 3 Ac), 2.40 (tt, 2 H, $^3J_{H,H}$ 6.4, $^3J_{H,F}$ 18.8 Hz, $CH_2C_6F_{13}$), 3.04 (q, 6 H, 3 CH_2CH_3), 3.77–3.96 (m, 2 H, H-6,6), 4.10 (dt ~ q, 2 H, $^3J_{H,H} = {}^3J_{H,P} = 6.4$ Hz, $CH_2CH_2C_6F_{13}$), 4.18–4.27 (m, 1 H, H-5), 4.78 (dd, 1 H, $J_{1,2}$ 2.8, $J_{2,3}$ 9.7 Hz, H-2), 4.94 (dd ~ t, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4), 5.37 (d, 1 H, H-1), 5.49 (dd ~ t, 1 H, H-3), 11.61 (s, 1 H, NH^+); ^{19}F, δ −81.3 (3 F, CF_3), −114.0 (2 F, CF_2CH_2), −122.4, −123.4 and −124.1 [6 F, $(CF_2)_3CF_2CH_2$], −126.6 (2 F, CF_2CF_3); ^{13}C, δ 170.0 (Cα), 169.9 (2 C, Cαβ), 169.8 (Cβ), 169.6 (Cα), and 169.4 (Cβ) ($COCH_3$), 94.8 (C-1β), 89.5 (C-1α), 73.7 (C-2β), 72.7 (C-3β), 72.4 (d, $^3J_{C,P}$ 8.4 Hz, C-5β), 71.4 (C-2α), 70.5 (C-3α), 69.2 (C-4α), 68.9 (C-4β), 67.4 (d, $^3J_{C,P}$ 8.5 Hz, C-5α), 64.1 (d, 2 C, $^2J_{C,P}$ 5.2 Hz, C-6α,6β), 57.4 (dt ~ q, $^2J_{C,P} = {}^3J_{C,F} = 5.5$ Hz, $CH_2CH_2C_6F_{13}$, αβ), 45.5 (CH_2CH_3, αβ), 32.0 (dt, $^3J_{C,P}$ 3.6, $^2J_{C,F}$ 21.1 Hz, $CH_2C_6F_{13}$, αβ), 20.3–20.2 ($COCH_3$, αβ), 8.2 (CH_2CH_3, αβ); ^{31}P, δ −0.41.

*Bis(1,2,3,4-tetra-*O*-acetyl-β-*D*-glucopyranos-6-yl) 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-octyl phosphate* (**5a**). — Prepared as described above, **5a** had $[\alpha]_D$ + 15° (*c* 1.2, $CHCl_3$). NMR data ($CDCl_3$): ^1H, δ 1.90 (6 H), 1.92 (3 H), 1.93 (3 H), 1.95 (6 H), 2.03 (3 H), and 2.04 (3 H) (6 s, 8 Ac), 2.50 (tt, 2 H, $^3J_{H,H}$ 6.6, $^3J_{H,F}$ 19.0 Hz, $CH_2C_6F_{13}$), 3.76–3.85 (m, 2 H, 2 H-5), 3.93–4.17 (m, 4 H, 2 H-6,6), 4.28 (dt ~ q, 2 H, $^3J_{H,H} = {}^3J_{H,P} = 6.6$ Hz, $CH_2CH_2C_6F_{13}$), 4.96–5.29 (m, 6 H, 2 H-2,3,4), 5.67 and 5.70 (2 d, each 1 H, $J_{1,2}$ 8.1 Hz, 2 H-1); ^{19}F, δ −81.3 (3 F, CF_3), −113.9 (2 F, CF_2CH_2), −122.3, −123.4, and −123.9 [6 F, $(CF_2)_3CF_2CH_2$], −126.6 (2 F, CF_2CF_3); ^{13}C, δ 170.0 (2 C), 169.4 (2 C), 169.12 (1 C), 169.09 (1 C), and 168.9 (2 C) ($COCH_3$), 91.7 (2 C-1), 73.0 (d, $^3J_{C,P}$ 7.1 Hz, 2 C-5), 72.8 (C-3), 72.7 (C-3), 70.3 (2 C-2), 67.8 (C-4), 67.7 (C-4), 65.6 and 65.4 (2 d, each $^2J_{C,P}$ 5.1 Hz, 2 C-6), 60.1 (dt ~ q, $^2J_{C,P} = {}^3J_{C,F} = 4.8$ Hz, $CH_2CH_2C_6F_{13}$), 31.9 (dt, $^3J_{C,P}$ 7.4, $^2J_{C,F}$ 21.5 Hz, $CH_2C_6F_{13}$), 20.4–20.5 (8 C, $COCH_3$); ^{31}P, δ −1.40.

Anal. Calcd for $C_{36}H_{42}F_{13}O_{22}P$ (1104.7): C, 39.14; H, 3.83; F, 22.36; P, 2.80. Found: C, 39.35; H, 3.61; F, 21.07; P, 2.76.

*Phosphorylation of 1,2,3,4-tetra-*O*-acetyl-β-*D*-glucopryanose by* **2a**. — A solution of **1a** (13.00 g, 27.0 mmol) in anhydrous tetrahydrofuran (25 mL) was added to a solution of 1*H*-1,2,4-triazole (3.73 g, 54.0 mmol) and triethylamine (5.45 g, 54.0 mmol) in anhydrous tetrahydrofuran (160 mL) at 0°. The mixture was left at room temperature for 20 min, then filtered. To the resulting filtrate (**2a**) was added a

solution of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (4.70 g, 13.5 mmol) in anhydrous pyridine (100 mL) during 30 min. After 90 min, TLC ($CHCl_3$–MeOH, 4:1) showed that all of the sugar derivative has been consumed, and the reaction was quenched by water (2 mL). The mixture was kept for 1 h at room temperature, then concentrated under reduced pressure, and 7:3 $CHCl_3$–toluene was evaporated from the residue in order to remove traces of pyridine. In order to eliminate the 2-(perfluorohexyl)ethyl phosphate, the crude product was filtered through silica gel ($CHCl_3$–MeOH, 4:1). The appropriate fractions were combined, concentrated, and treated as described above, to give a 95:5 mixture (10.0 g) of **3a** and **4a** (^{31}P-NMR data). Trituration of this mixture with ether yielded **3a** (7.7 g, 65%).

*Phosphorylation of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose by* **2b**. — A solution of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (13.8 g, 39.6 mmol) in anhydrous pyridine (300 mL) was added during 75 min at room temperature to a solution of **2b** in tetrahydrofuran, prepared, as described above for **2a**, from 1*H*-1,2,4-triazole (10.9 g, 158 mmol), **1b** (45.9 g, 79 mmol), and triethylamine (16 g, 158 mmol). After 90 min, water (5 mL) was added. Work-up as described above gave a 95:5 mixture (32 g) of **3b** and **4b**. Compound **3b** (24.9 g, 64%) was obtained as a white powder after trituration of the mixture with ether. Compound **4b** was not isolated.

*1,2,3,4-Tetra-*O*-acetyl-β-D-glucopyranose 6-(triethylammonium 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl phosphate)* (**3b**). — Prepared as described above, **3b** had $[\alpha]_D$ + 11° (*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{1}H, δ 1.22 (t, 9 H, $^3J_{H,H}$ 7.2 Hz, 3 CH_2CH_3), 1.89 (3 H), 1.92 (6 H), and 1.95 (3 H) (3 s, 4 Ac), 2.39 (tt, 2 H, $^3J_{H,H}$ 7.0, $^3J_{H,F}$ 19.1 Hz, $CH_2C_8F_{17}$), 2.96 (q, 6 H, 3 CH_2CH_3), 3.74–3.91 (m, 3 H, H-5,6,6), 4.03 (dt ~ q, 2 H, $^3J_{H,H} = {}^3J_{H,P}$ = 7.0 Hz, $CH_2CH_2C_8F_{17}$), 4.95–5.19 (m, 3 H, H-2,3,4), 5.61 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 12.32 (s, 1 H, NH^+); ^{19}F, δ −81.4 (3 F, CF_3), −113.9 (2 F, CF_2CH_2), −122.3, −123.2, and −124.0 [10 F, $(CF_2)_5CF_2CH_2$], −126.7 (2 F, CF_2CF_3); ^{13}C, δ 170.1, 169.4, 169.2, and 168.8 (4 C, 4 $COCH_3$), 91.6 (C-1), 74.0 (d, $^3J_{C,P}$ 8.5 Hz, C-5), 73.0 (C-3), 70.3 (C-2), 68.2 (C-4), 63.5 (d, $^2J_{C,P}$ 4.9 Hz, C-6), 57.4 (dt ~ q, $^2J_{C,P} = {}^3J_{C,F}$ = 5.2 Hz, $CH_2CH_2C_8F_{17}$), 45.4 (3 C, 3 CH_2CH_3), 32.2 (dt, $^3J_{C,P}$ 7.1, $^2J_{C,F}$ 21.2 Hz, $CH_2C_8F_{17}$), 20.4 (4 C, 4 $COCH_3$), 8.3 (3 C, 3 CH_2CH_3); ^{31}P, δ −0.11.

Anal. Calcd for $C_{30}H_{39}F_{17}NO_{13}P$ (975.6): C, 36.93; H, 4.03; F, 33.10; N, 1.44; P, 3.17. Found: C, 36.70; H, 4.04; F, 32.82; N, 1.21; P, 3.27.

*Phosphorylation of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose by* **2c**. — As described above, condensation of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (4.0 g, 11.5 mmol) with **2c**, prepared from **1c** (6.3 g, 22.9 mmol), gave a 95:5 mixture (6.5 g) of **3c** and **4c** which was not purified.

*Phosphorylation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose by* **2b**. — A solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (6.4 g, 24.6 mmol) in pyridine (180 mL) was added at room temperature during 1 h to **2b** prepared from 1*H*-1,2,4-triazole (6.9 g, 99.0 mmol), **1b** (28.8 g, 49.5 mmol), and triethylamine (10.0 g, 99.0 mmol). TLC ($CHCl_3$–MeOH, 4:1) showed the reaction to be incomplete after 2 days. The reaction was quenched by water (3 mL), the mixture was stirred

for 1 h at room temperature, then concentrated under reduced pressure, and 7:3 $CHCl_3$–toluene was evaporated from the residue. Column chromatography of the product gave unreacted sugar (3.2 g, 50%) by elution with ether. Elution with 4:1 $CHCl_3$–MeOH and treatment of the appropriate fractions with triethylammonium hydrogencarbonate yielded **6b** (10.9 g, ~ 100% based on consumed sugar) as a viscous product.

1,2:5,6-Di-O-isopropylidene-α-D-glucofuranose 3-(triethylammonium 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl phosphate) (**6b**). — Prepared as described above, **6b** had $[\alpha]_D$ −18° (*c* 1.2, $CHCl_3$). NMR data (CD_2Cl_2): ^1H, δ 1.27 (t, 9 H, $^3J_{H,H}$ 7.2 Hz, 3 CH_2CH_3), 1.23, 1.25, 1.35, and 1.42 (4 s, each 3 H, 4 CH_3), 2.46 (tt, 2 H, $^3J_{H,H}$ 6.4, $^3J_{H,F}$ 19.0 Hz, $CH_2C_8F_{17}$), 3.00 (q, 6 H, 3 CH_2CH_3), 3.90–4.19 (m, 5 H, $CH_2CH_2C_8F_{17}$ and H-4,6,6), 4.24–4.33 (m, 1 H, H-5), 4.47 (dd, 1 H, $J_{3,4}$ 2.8, $^3J_{H,P}$ 7.4 Hz, H-3), 4.80 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-2), 5.80 (d, 1 H, H-1), 12.00 (s, 1 H, NH^+); ^{19}F, δ −81.6 (3 F, CF_3), −114.2 (2 F, CF_2CH_2), −122.6, −123.5, and −124.4 [10 F, $(CF_2)_5CF_2CH_2$], −126.9 (2 F, CF_2CF_3); ^{13}C, δ 112.9 and 110.1 (2 C, quaternary C), 106.3 (C-1), 85.4 (C-2), 82.0 (d, $^3J_{C,P}$ 8.3 Hz, C-4), 78,9 (d, $^2J_{C,P}$ 5.5 Hz, C-3), 73.8 (C-5), 68.1 (C-6), 58.7 (dt ~ q, $^2J_{C,P} = {}^3J_{C,F} = 4.7$ Hz, $CH_2CH_2C_8F_{17}$), 47.0 (3 C, 3 CH_2CH_3), 33.7 (dt, $^3J_{C,P}$ 7.2, $^2J_{C,F}$ 20.9 Hz, $CH_2C_8F_{17}$), 27.8, 27.7, 27.2, and 26.2 (4 C, 4 CH_3), 9.8 (3 C, 3 CH_2CH_3); ^{31}P, δ −1.24.

Anal. Calcd for $C_{28}H_{39}F_{17}NO_9P$ (887.6): C, 37.89; H, 4.43; F, 36.39; N, 1.58; P, 3.49. Found: C, 37.61; H, 4.37; F, 34.77; N, 2.12; P, 3.40.

D-Glucose 6-(sodium 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-octyl phosphate) (**7a**). — Compound **3a** (5.4 g, 6.2 mmol) was stirred in methanolic 1% sodium methoxide (120 mL) for 15 min at room temperature. The pH of the solution was brought to 4 with Amberlite IR-120 (H^+) resin, the resin was collected and washed with MeOH, and the filtrate and washings were combined and concentrated to dryness. A solution of the residue in the minimum volume of 1:1 water–MeOH was passed through a column of Amberlite IR-120 (Na^+) resin (200 mL) by elution with water. Fractions corresponding (TLC; $CHCl_3$–MeOH–water, 60:35:6) to **7a** were combined and lyophilized. A solution of the solid residue in the minimum volume of MeOH was treated dropwise with ether to yield **7a** (3.7 g, 93%) as a white solid, $[\alpha]_D$ + 15° (*c* 1.2, water). NMR data (CD_3OD): ^1H, δ 2.57 (tt, 4 H, $^3J_{H,H}$ 6.9, $^3J_{H,F}$ 19.2 Hz, $CH_2C_6F_{13}$ αβ), 3.10–3.19 (m, 1 H, H-2β), 3.34–3.46 (m, 5 H, H-2α,3β,4α,4β,5β), 3.68 (dd ~ t, 1 H, $J_{2\alpha,3\alpha} = J_{3\alpha,4\alpha} = 9.4$ Hz, H-3α), 3.84–3.89 (m, 1 H, H-5α), 3.98–4.11 (m, 4 H, H-6α,β), 4.17 (dt ~ q, 4 H, $^3J_{H,H} = {}^3J_{H,P} = 6.9$ Hz, $CH_2CH_2C_6F_{13}$ αβ), 4.48 (d, 1 H, $J_{1\beta,2\beta}$ 7.7 Hz, H-1β), 5.10 (d, 1 H, $J_{1\alpha,2\alpha}$ 3.7 Hz, H-1α); ^{19}F, δ −80.8 (3 F, CF_3), −113.1 (2 F, CF_2CH_2), −121.4, −122.3, and −123.1 [6 F, $(CF_2)_3CF_2CH_2$], −125.8 (2 F, CF_2CF_3); ^{13}C, δ 98.2 (C-1β), 93.9 (C-1α), 77.6 (C-3β), 76.7 (d, $^3J_{C,P}$ 7.2 Hz, C-5β), 76.2 (C-2β), 74.5 (C-3α), 73.7 (C-2α), 72.0 (d, $^3J_{C,P}$ 7.5 Hz, C-5α), 71.2 (C-4α), 71.1 (C-4β), 65.9 (2 d, 2 C, $^2J_{C,P}$ 4.0 Hz, C-6α,6β), 58.6 (dt ~ q, 2 C, $^2J_{C,P} = {}^3J_{C,F} = 4.6$ Hz, $CH_2CH_2C_6F_{13}$ αβ), 33.1 (dt, 2 C, $^3J_{C,P}$ 7.2, $^2J_{C,F}$ 20.9 Hz, $CH_2C_6F_{13}$ αβ); ^{31}P, δ 2.09 and 2.06.

Anal. Calcd for $C_{14}H_{15}F_{13}NaO_9P \cdot H_2O$ (646.2): C, 26.02; H, 2.65; F, 38.22; Na, 3.56; P, 4.79. Found: C, 26.39; H, 2.71; F, 38.70; Na, 3.73; P, 4.80.

D-*Glucose 6-(sodium 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl phosphate)* (**7b**). — After processing as for **3a**, **3b** (24 g, 24.6 mmol) yielded the white solid **7b** (16.9 g, 92%), $[\alpha]_D$ + 12° (*c* 1.0, water). NMR data (CD_3OD): ^1H, δ 2.57 (tt, 4 H, $^3J_{H,H}$ 6.6, $^3J_{H,F}$ 19.0 Hz, $CH_2C_8F_{17}$ $\alpha\beta$), 3.10–3.18 (m, 1 H, H-2β), 3.32–3.46 (m, 5 H, H-2α,3β,4α,4β,5β), 3.68 (dd ~ t, 1 H, $J_{2\alpha,3\alpha} = J_{3\alpha,4\alpha} = 9.3$ Hz, H-3α), 3.83–3.89 (m, 1 H, H-5α), 3.98–4.10 (m, 4 H, H-6,6α,β), 4.17 (dt ~ q, 4 H, $^3J_{H,H} = {}^3J_{H,P} = 6.6$ Hz, $CH_2CH_2C_8F_{17}$ $\alpha\beta$), 4.47 (d, 1 H, $J_{1\beta,2\beta}$ 7.7 Hz, H-1β), 5.09 (d, 1 H, $J_{1\alpha,2\alpha}$ 3.7 Hz, H-1α); ^{19}F, δ −80.8 (3 F, CF_3), −113.1 (2 F, CF_2CH_2), −121.3, −122.2, and −123.1 [10 F, $(CF_2)_5$ CF_2CH_2], −125.8 (2 F, CF_2CF_3); ^{13}C, δ 98.2 (C-1β), 93.9 (C-1α), 77.7 (C-3β), 76.9 (d, $^3J_{C,P}$ 7.3 Hz, C-5β), 76.3 (C-2β), 74.6 (C-3α), 73.8 (C-2α), 72.1 (d, $^3J_{C,P}$ 7.6 Hz, C-5α), 71.3 (C-4α), 71.2 (C-4β), 65.9 (2 d, 2 C, $^2J_{C,P}$ 4.5 Hz, C-6α,6β), 58.6 (dt ~ q, 2 C, $^2J_{C,P} = {}^3J_{C,F} = 4.6$ Hz, $CH_2CH_2C_8F_{17}$ $\alpha\beta$), 33.2 (dt, 2 C, $^3J_{C,P}$ 7.6, $^2J_{C,F}$ 20.8 Hz, $CH_2C_8F_{17}$ $\alpha\beta$); ^{31}P, δ 2.13 and 2.17.

Anal. Calcd for $C_{16}H_{15}F_{17}NaO_9P \cdot H_2O$ (746.2): C, 25.75; H, 2.30; F, 43.28; Na, 3.08; P, 4.15. Found: C, 25.96; H, 2.15; F, 44.18; Na, 3.00; P, 4.19.

O-Deacetylation of the mixture (1.0 g) of **3b** and **4b**, as described above, gave **7b** (0.7 g, 76% based on 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose) (*Anal.* Found: C, 25.74; H, 2.26; F, 42.68; Na, 3.12; P, 3.95).

D-*Glucose 6-(sodium decyl phosphate)* (**7c**). — The same procedure as for **7a**, when applied to a mixture (6.5 g) of **3c** and **4c**, yielded **7c** (3.6 g, 71% based on 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose), $[\alpha]_D$ + 17° (*c* 1.1, water). NMR data: ^1H (CD_3OD), δ 0.93 (t, 6 H, $^3J_{H,H}$ 7.2 Hz, CH_3 $\alpha\beta$), 1.35 [bs, 28 H, $(CH_2)_7CH_3$ $\alpha\beta$], 1.65 (tt ~ quin, 4 H, $^3J_{H,H}$ 6.3 Hz, OCH_2CH_2 $\alpha\beta$), 3.12–3.28 (m, 1 H, H-2β), 3.34–3.48 (m, 5 H, H-2α,3β,4α,4β,5β), 3.57 (dd ~ t, 1 H, $J_{2\alpha,3\alpha} = J_{3\alpha,4\alpha} = 10.2$ Hz, H-3α), 3.68–3.78 (m, 1 H, H-5α), 3.90 (dt ~ q, 4 H, $^3J_{H,H} = {}^3J_{H,P} = 6.3$ Hz, OCH_2CH_2 $\alpha\beta$), 4.08–4.18 (m, 4 H, H-6,6α,β), 4.52 (d, 1 H, $J_{1\beta,2\beta}$ 7.7 Hz, H-1β), 5.15 (d, 1 H, $J_{1\alpha,2\alpha}$ 3.7 Hz, H-1α); ^{13}C (D_2O), δ 96.0 (C-1β), 92.1 (C-1α), 75.4 (C-3β), 74.9 (d, $^3J_{C,P}$ 6.8 Hz, C-5β), 74.2 (C-2β), 72.5 (C-3α), 71.6 (C-2α), 70.6 (d, $^3J_{C,P}$ 7.5 Hz, C-5α), 69.4 (C-4α), 69.1 (C-4β), 66.2 (m, 2 C, OCH_2CH_2 $\alpha\beta$), 64.3 (m, 2 C, C-6α,6β), 31.8 (2 C, $OCH_2CH_2CH_2$ $\alpha\beta$), 30.3 (d, 2 C, $^3J_{C,P}$ 7.4 Hz, OCH_2CH_2 $\alpha\beta$), 29.4 (4 C, 2 CH_2 $\alpha\beta$), 29.2 (4 C, 2 CH_2 $\alpha\beta$), 25.4 (2 C, CH_3 $\alpha\beta$), 22.5 (2 C, CH_2 $\alpha\beta$), 13.8 (2 C, CH_3 $\alpha\beta$); ^{31}P (D_2O), δ 1.63.

D-*Glucose 3-(sodium 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl phosphate)* (**8b**). — Compound **6b** (8.9 g, 10.0 mmol) was dissolved in aq 90% trifluoroacetic acid (100 mL) at room temperature. The solution was stirred for 30 min, then concentrated under reduced pressure, and toluene (3 × 20 mL) was evaporated from the residue, which was triturated with ether. The resulting solid was dissolved in the minimum volume of 1:1 water–MeOH and passed through a column of Amberlite IR-120 (Na^+) resin (400 mL) by elution with water. Lyophilisation of the appropriate fractions (TLC; $CHCl_3$–MeOH–water, 60:35:6) gave

solid **8b** (4.8 g, 65%), $[\alpha]_D + 14°$ (*c* 1.1, water). NMR data (CD_3OD): ^1H, δ 2.60 (tt, 4 H, $^3J_{H,H}$ 6.8 ,$^3J_{H,F}$ 19.7 Hz, $CH_2C_8F_{17}$ $\alpha\beta$), 3.46–4.02 (m, 12 H, H-2α,2β,3α,3β,4α,4β,5α,5β,6,6α,6,6β), 4.30 (dt ~ q, 4 H, $^3J_{H,H} = {}^3J_{H,P} = 6.8$ Hz, $CH_2CH_2C_8F_{17}$ $\alpha\beta$), 4.56 (d, 1 H, $J_{1\beta,2\beta}$ 7.8 Hz, H-1β), 5.18 (d, 1 H, $J_{1\alpha,2\alpha}$ 3.8 Hz, H-1α); ^{19}F, −80.8 (3 F, CF_3), −113.2 (2 F, CF_2CH_2), −121.4, −122.3, and −123.2 [10 F, $(CF_2)_5CF_2CH_2$], −125.8 (2 F, CF_2CF_3); ^{13}C, δ 98.0 (C-1β), 93.8 (C-1α), 82.6 (d, $^2J_{C,P}$ 6.2 Hz, C-3β), 80.1 (d, $^2J_{C,P}$ 5.9 Hz, C-3α), 77.7 (C-5β), 75.6 (d, $^3J_{C,P}$ 3.0 Hz, C-2β), 72.92 (d, $^3J_{C,P}$ 4.6 Hz, C-2α), 72.87 (C-5α), 71.1 (d, $^3J_{C,P}$ 2.9 Hz, C-4β), 71.0 (d, $^3J_{C,P}$ 3.7 Hz, C-4α), 62.6 (C-6β), 62.5 (C-6α), 59.0 (dt ~ q, 2 C, $^2J_{C,P} = {}^3J_{C,F} = 4.9$ Hz, $CH_2CH_2C_8F_{17}$ $\alpha\beta$), 33.2 (dt, 2 C, $^3J_{C,P}$ 7.9, $^2J_{C,F}$ 21.2 Hz, $CH_2C_8F_{17}$ $\alpha\beta$); ^{31}P, δ 2.82 and 2.66.

Anal. Calcd for $C_{16}H_{15}F_{17}NaO_9P \cdot H_2O$ (746.2): C, 25.75; H, 2.30; F, 43.28; Na, 3.08; P, 4.15. Found: C, 26.20; H, 2.05; F, 43.18; Na, 3.08; P, 4.13.

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