Copper-catalysed coupling of undec-10-enylmagnesium bromide with ω-functionalised halogenoalkanes as a key reaction for the synthesis of novel bipolar phospholipids with different head groups and chain length

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The Grignard reagent from 11-bromoundec-1-ene undergoes copper-catalysed coupling with ω-functionalised halogenoalkanes of different chain length to provide long-chain ω-substituted alkenes. The reaction conditions for this have been studied to optimise the products yields, especially those for the preparation of the C_{32} unit. Functionalised alkenes are suitable building blocks for the direct synthesis of bipolar phospholipids with different head groups.

Introduction

Archaebacteria are organisms which can exist under extreme environmental conditions (*e.g.* anaerobic, acidic or high temperature). The structures of the membrane lipids[1] of the archaebacteria are quite different from those of other bacteria and eukaryotes (Fig. 1). Great attention has been paid to these lipid membranes, especially in the biotechnological field and material sciences,[2–4] because of their high stability. Since the isolation of pure lipid components remains a problem, the synthesis of model compounds is still of interest in order to study their biophysical properties. A further reason for interest in even simply structured bolaamphiphiles is a recent report on the structural elucidation and synthesis of irlbacholin, a 1,22-bisphosphocholin.[5]

In the context of our work on the physicochemical behaviour of phospholipids, we are interested in bipolar lipids with different head groups, since they can induce membrane curvature.[6]

Results and discussion

The aim of the present work was to find a method for the preparation of long hydrocarbon chains with different polar terminii.[7] In previous work on the synthesis of bolaamphiphiles the compounds carrying different head groups were merely by-products in the synthesis of symmetric bola compounds. Since they came from unchanged mono-substituted material[8,9] that had to be isolated from the reaction mixture in a time-consuming process with a poor chance of good yields, a direct synthesis was necessary to obtain satisfactory amounts of the desired material. First, we had to find a method for the preparation of long hydrocarbon chains. The copper-catalysed reaction of Grignard reagents with halides,[10] described as effective for the preparation of fatty acids,[11] was the most promising. We started from 11-bromoundec-1-ene **1**, which can be easily prepared from the commerically available undec-10-en-1-ol,[12] and coupled the corresponding Grignard reagent with 5-bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)pentane[13] **2a** and 11-bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)undecane[13] **2b** using Li_2CuCl_4 as a catalyst; the yields were 83% for **3a** and 81% for **3b**, respectively (Table 1). The by-products, namely unchanged 11-bromoundec-1-ene and docosa-1,21-diene, could be easily separated in this case by simple column chromatography.

More problems were attendant on the preparation of the C_{32} unit **3d**. Starting with 11-bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)undecane **2b** we coupled the corresponding Grignard reagent with 1,10-dibromodecane **5** to produce **4a**; the product yields were much lower than for **3a**,**b** and the number of by-products increased. In other words, product separation from unchanged **2b** was complicated. These two compounds differ only in ten methylene units and have closely similar chromato-

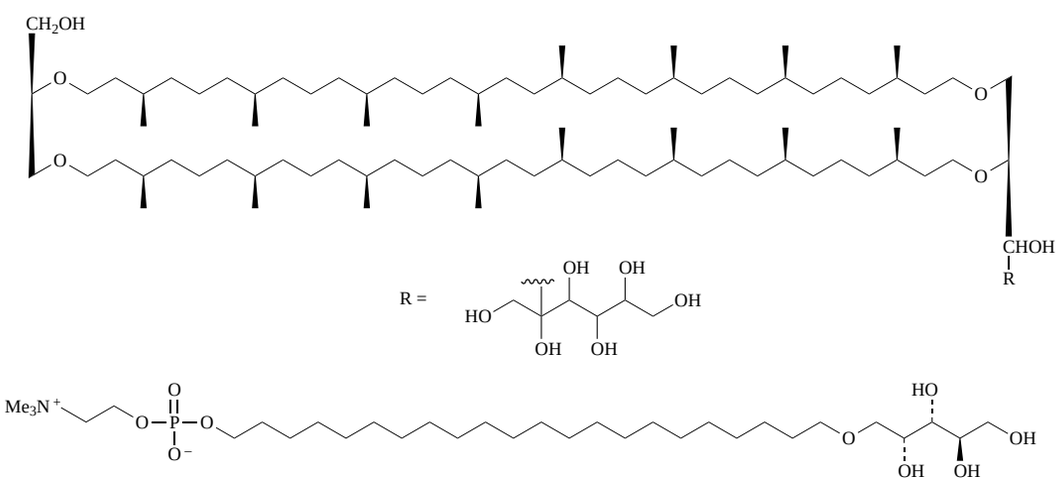
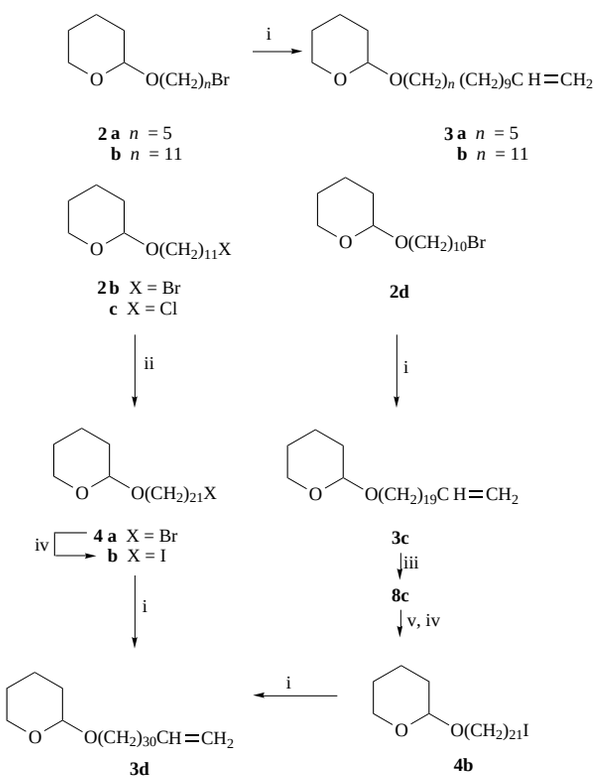


Fig. 1 Typical archaebacterial lipid structure and model lipid

Table 1 Compounds **3** and **4a** prepared

Grignard reaction				Coupling reaction				
Halide (g, mmol)	Mg (g, mmol)	Solvent	(ml)	Halide (g, mmol)	Catalyst (ml) 0.1 M in THF	THF (ml)	Product (g)	Yield (%)
1 (23.2, 100)	(4.86, 200)	Et_2O	120	**2a** (22.58, 90)	Li_2CuCl_4 (5)	200	**3a** (24.2)	83
1 (23.2, 100)	(4.86, 200)	Et_2O	120	**2b** (30.14, 90)	Li_2CuCl_4 (5)	200	**3b** (29.79)	81
1 (2.32, 10)	(0.48, 20)	Et_2O	10	**4a** (4.27, 9)	Li_2CuCl_4 (0.5)	20	**3d** (1.18)	24
1 (2.32, 10)	(0.48, 20)	Et_2O	10	**4a** (4.27, 9)	Li_2CuCl_3 (0.5)	20	**3d** (0.88)	18
1 (2.32, 10)	(0.48, 20)	Et_2O	10	**4b** (4.69, 9)	Li_2CuCl_4 (0.5)	20	**3d** (3.64)	74
1 (2.32, 10)	(0.48, 20)	Et_2O	10	**4b** (4.69, 9)	Li_2CuCl_3 (0.5)	20	**3d** (3.45)	70
1 (2.32, 10)	(0.48, 20)	Et_2O	10	**2d** (2.88, 9)	Li_2CuCl_4 (0.5)	20	**3c** (2.97)	84
2b (3.34, 10)	(0.48, 20)	Et_2O	10	**5** (2.95, 9)	Li_2CuCl_4 (0.5)	20	**4a** (1.05)	24
2c (2.95, 10)	(0.72, 30)	THF	8	**5** (2.95, 9)	Li_2CuCl_4 (0.5)	20	**4a** (1.11)	26



Scheme 1 *Reagents and conditions:* i, 11-bromoundec-1-ene **1**, Mg, ether, then THF, Li_2CuCl_4, 3 h, 0 °C; ii, Mg, ether, then THF, Li_2CuCl_4, 1,10-dibromodecane **5**, 3 h, 0 °C; iii, 9-BBN, THF, H_2O_2, NaOH, 6 h, RT; iv, LiI, acetone, reflux, 5 h; v, MesCl, pyridine, RT, 16 h

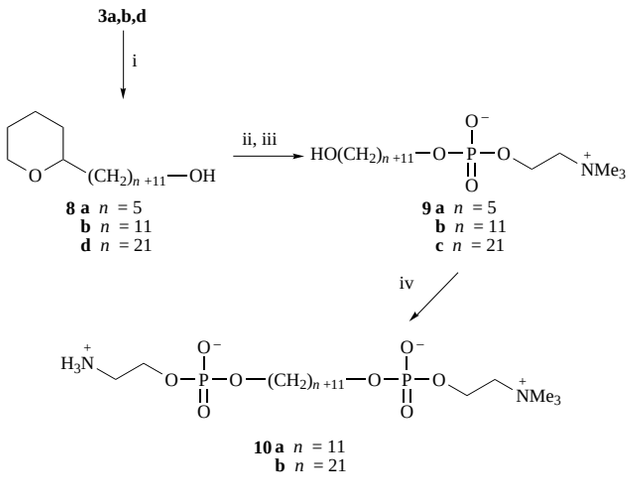
graphic properties. The other by-products resulted from the reaction of the Grignard reagent with unchanged **2b** [1,22-bis(tetrahydro-2*H*-pyran-2-yloxy)docosane] on the one hand and the coupling product [1,32-bis(tetrahydro-2*H*-pyran-2-yloxy)dotriacontane] on the other. They make up to 25% of the total material and were easy to separate. When the 11-chloro-analogue **2c** was used instead of **2b** the amount of by-products was reduced, especially of 1,22-bis(tetrahydro-2*H*-pyran-2-yloxy)docosane, although removal of unchanged **2c** remained a problem. The next step was the coupling of 21-bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)henicosane **4a** with the corresponding Grignard reagent of 11-bromoundecene **1** with Li_2CuCl_4 as a catalyst to give **3d** (24%). After a reaction time of 24 h most of the Grignard reagent remained unchanged, the main by-product of the reaction after hydrolysis being undec-1-ene. Use of the copper(I) salt Li_2CuCl_3[14] had no significant influence on the yield in the coupling of long hydrocarbon chains.

Much better results were obtained for the coupling of 21-iodo-1-(tetrahydro-2*H*-pyran-2-yloxy)henicosane **4b** with the Grignard reagent of 11-bromoundec-1-ene **1**. In this the 21-bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)henicosane **4a** was converted into the iodide **4b** by reaction with lithium iodide in acetone. The yields of **3d** were much higher, even with Li_2CuCl_3 as catalyst (Table 1).

An alternative synthesis of **4b** was developed in order to avoid the purification problems associated with the preparation of **4a**. The corresponding Grignard reagent of 11-bromoundec-1-ene **1** was coupled with 10-bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)decane **2d**,[13] to give an alkene **3c** which was converted into the primary alcohol **8c** by hydroboration with 9-BBN in THF; **8c** was then converted into the methanesulfonate. After reaction with lithium iodide in acetone the iodide **4b** was obtained in high yield and purity. Compound **4b** was coupled with the Grignard reagent of 11-bromoundec-1-ene **1** in the usual manner and led to **3d** in good yields (Table 1).

The described ω-(tetrahydro-2*H*-pyran-2-yloxy)alkenes with a chain length of 16, 22 and 32 carbon atoms were now suitable as basic structures for different types of unsymmetric bola compounds.

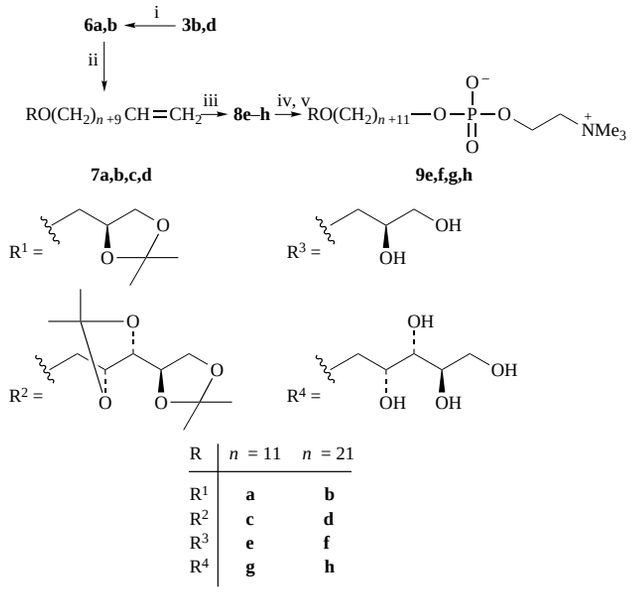
Initially, the alkenes **3a**,**b**,**d** were converted into the primary alcohols **8a**,**b**,**d** as described above. Each alcohol was then phosphorylated by reaction with 2-bromoethylphosphoric acid dichloride (IUPAC name: 2-bromoethyl dichlorophosphinate).[15] Quaternation of the resulting phosphoric acid diesters with trimethylamine led to *O*-protected ω-hydroxyalkylphosphocholines. An alternative route was the use of 2-chloro-2-oxo-1,3,2-dioxaphospholane in combination with lithium bromide[16] instead of 2-bromoethylphosphoric acid dichloride. This method, although having an additional step, provides good yields and has proved to be suitable for phosphorylation of long-chain compounds. In order to avoid cleavage of the (tetrahydro-2*H*-pyran-2-yl) ether group the pH of the reaction media was adjusted to 8 in both types of phosphorylation with triethylamine. Deprotection following standard methods[17] led to ω-hydroxyalkylcholines **9a**–**c**. These compounds are able to serve as model compounds for physicochemical investigation although they, too, are suitable for further phosphorylation. We have also prepared bola compounds **10a** and **10b** with a choline head group on one side and a kephaline on the other from **9b** and **9c** respectively.



Scheme 2 *Reagents and conditions:* i, 9-BBN, THF, H_2O_2, NaOH, 6 h, RT; ii, *either* (a) $Cl_2P(O)OCH_2CH_2Br$, $CHCl_3$, triethylamine, 24 h, RT, then $CHCl_3$–CH_3CN, trimethylamine, RT, 24 h; *or* (b) 2-chloro-2-oxo-1,3,2-dioxaphospholane, $CHCl_3$, triethylamine, then LiBr, acetone then trimethylamine $CHCl_3$–CH_3CN; iii, pyridinium toluene-*p*-sulfonate, MeOH, 40 °C, 2 h; iv, *either* (a) $Cl_2P(O)OCH_2CH_2Br$, $CHCl_3$, triethylamine, 24 h, RT, then $CHCl_3$–CH_3CN, ammonia, $CHCl_3$–CH_3CN–isopropyl alcohol 50 °C, 16 h; *or* (b) 2-chloro-2-oxo-1,3,2-dioxaphospholane, $CHCl_3$, triethylamine, then LiBr, acetone then ammonia $CHCl_3$–CH_3CN–isopropyl alcohol, 50 °C, 16 h

In order to introduce both chiral head groups and more hydroxy functions, the hydroxy groups of **9b**,**c** were substituted by *sn*-glycerol or an open-chain polyol residue. In doing so the ω-(tetrahydro-2*H*-pyran-2-yl) ethers **3b**,**d** were transformed into bromides **6a** and **6b** by reaction with triphenylphosphine dibromide.[18] The alkylations of **6a** and **6b** with 1,2-*O*-isopropylidene-*sn*-glycerol **11** and 2,3:4,5-di-*O*-isopropylidene-D-arabitol **13** provided good yields of **7a**–**d** when toluene was used as solvent. The synthesis of the protected polyol fragment started from D-glucono-1,5-lactone which was converted into methyl 3,4:5,6-di-*O*-isopropylidene-D-gluconate according to the method of Regeling *et al.*[19] Because of the difficulties in purification, the product was converted into the crystalline acetate,[19] which was purified by simple crystallisation. In contrast to Regeling, this acetate was reduced with lithium aluminium hydride to give 3,4:5,6-di-*O*-isopropylideneglucitol **12** making the method more convenient. Oxidative cleavage of the diol followed by reduction of the 2,3:4,5-di-*O*-isopropylidenealdehydro-D-arabinose with sodium borohydride led to **13**.

Hydroboration of **7a**–**d** gave **8e**–**h**, phosphorylation and deprotection of which resulted in the bola compounds **9e**–**h**. The bipolar phospholipids with different polar headgroups are new compounds, that offer manifold possibilities in membrane research biotechnology and material science.



Scheme 3 *Reagents and conditions:* i, PPh_3, CH_2Cl_2, Br_2, RT, 16 h; ii, 1,2-*O*-isopropylidene-*sn*-glycerol **11**, 2,3:4,5-di-*O*-isopropylidene-D-arabitol **13**, KOBu^t, THF; iii, 9-BBN, THF, H_2O_2, NaOH, 6 h, RT; iv, *either* (a) $Cl_2P(O)OCH_2CH_2Br$, $CHCl_3$, triethylamine, 24 h, RT, then $CHCl_3$–CH_3CN, trimethylamine, RT, 24 h; *or* (b) 2-chloro-2-oxo-1,3,2-dioxaphospholane, $CHCl_3$, triethylamine, then LiBr, acetone then trimethylamine $CHCl_3$–CH_3CN; v, pyridinium toluene-*p*-sulfonate, MeOH, 40 °C, 2 h

Experimental

Material and methods

The purity of all compounds was checked by TLC (Merck). The following eluents were applied: (A) = heptane, (B) = heptane–$CHCl_3$ (4:6), (C) = $CHCl_3$–Et_2O (8:2), (D) = $CHCl_3$–MeOH–ammonia (65:35:5), (E) = $CHCl_3$–MeOH–ammonia (50:50:10). The chromatograms were developed by means of Bromothymol Blue[20] for non-phosphorus-containing compounds and Molybdenum Blue[21] for phosphorus-containing compounds. Silica gel (Merck; 0.032–0.060 mm) was used for column chromatography. The NMR spectra were recorded on a Bruker AC 500 spectrometer using $SiMe_4$ as internal standard. Mass spectrometric data were obtained with a Finnigan mass spectrometer model MAT SSQ 710 C. All solvents used were purified and dried. 1,12-Dibromododecane **5**, undec-10-en-1-ol, 10-bromodecan-1-ol, 11-bromoundecan-1-ol and 2-chloro-2-oxo-1,3,2-dioxaphospholane were supplied by the Aldrich Co., 1,2-*O*-isopropylidene-*sn*-glycerol **11** was supplied by Lancaster. Bromoethylphosphoric acid dichloride was prepared according to the literature.[15]

5-Bromopentan-1-ol

This compound was prepared from 5-bromopentanoic acid according to the literature[22] and used without further characterisation; bp 98–100 °C/4 mmHg (lit.,[23] bp 117 °C/20 mmHg).

11-Bromoundec-1-ene 1

This compound was prepared from undec-10-en-1-ol according to the literature;[12] bp 100–102 °C/1 mmHg (lit.,[12] bp 95–98 °C/0.5 mmHg).

5-Bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)pentane 2a

This compound was prepared from 5-bromopentan-1-ol according to the literature;[13] bp 68–71 °C/0.008 mmHg.

11-Bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)undecane 2b

This compound was prepared from 11-bromoundecan-1-ol according to the literature.[13] In order to bring it to the high state of purity necessary for its use in preparing Grignard reagents or in coupling reactions the crude product was passed through a silica gel column with $CHCl_3$ as eluent; R_F 0.6 (B).

11-Chloro-1-(tetrahydro-2*H*-pyran-2-yloxy)undecane 2c

Following the procedure of Hooz and Giliani[24] 11-(tetrahydro-2*H*-pyran-2-yloxy)undecan-1-ol **8i** 2.72 g (0.01 mol) was allowed to react with tributylphosphine (2.02 g, 0.01 mol) in CCl_4 (10 ml). The mixture was washed twice with water (50 ml) and then evaporated. The residue was passed through a silica gel column eluting with a heptane–$CHCl_3$ gradient to give a clear liquid (2.75 g, 95%), R_F 0.6 (B) (Found: C, 66.01; H, 10.81; Cl, 12.21. $C_{16}H_{31}O_2Cl$ requires C, 66.07; H, 10.74; Cl, 12.19%); *m*/*z* (ESI-MS) 291.5 (M + H).

10-Bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)decane 2d

This compound was prepared from 10-bromodecan-1-ol according to the literature.[13] The product was subjected to further treatment as for **2b**.

1-(Tetrahydro-2*H*-pyran-2-yloxy)hexadec-15-ene 3a, 1-(tetrahydro-2*H*-pyran-2-yloxy)docos-21-ene 3b, 1-(tetrahydro-2*H*-pyran-2-yloxy)henicos-20-ene 3c and 1-(tetrahydro-2*H*-pyran-2-yloxy)dotriaconta-31-ene 3d.

The corresponding Grignard reagent for this compound was prepared from 11-bromoundec-1-ene in Et_2O and the mixture refluxed for 2 h. After removal of the ether the Grignard reagent was dissolved in absolute THF and the solution was added dropwise to an ice-cooled solution of the ω-bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)alkane **2a**,**b**,**d** or **4a,b** in THF with Li_2CuCl_4 as catalyst. After the mixture had been stirred for 3 h at 0 °C, it was warmed to room temperature within 30 min and hydrolysed with aqueous NH_4Cl. The organic phase was separated and the aqueous phase was extracted with $CHCl_3$ (×3). The combined organic phases were washed with aqueous $NaHCO_3$ and water, dried (Na_2SO_4) and evaporated. Crystallisation of the product from light petroleum was passed through a silica gel column eluted with a heptane–diethyl ether gradient (Table 1).

1-(Tetrahydro-2*H*-pyran-2-yloxy)hexadec-15-ene 3a (from alkane 2a). This compound was a clear liquid, R_F 0.4 (B) (Found: C, 77.64; H, 12.51. $C_{21}H_{40}O_2$ requires C, 77.72; H, 12.42%); $\delta_H(CDCl_3)$ 1.23–1.38 (24 H, s, CH_2), 1.45–1.88 (6 H, m, C*H*$_2$CH$_2$O), 1.99–2.04 (2 H, m, C*H*$_2$CH=), 3.32–3.40 (1 H, m, HC*H*O), 3.45–3.51 (1 H, m, HC*H*O), 3.68–3.75 (1 H, m, HC*H*O), 3.83–3.89 (1 H, m, HC*H*O), 4.55–4.57 (1 H, t, OCHO), 4.89–4.99 (2 H, q, =CH_2) and 5.75–5.83 (1 H, m, CH=); *m/z* (ESI-MS) 325.1 (M + H) and 347.2 (M + Na).

1-(Tetrahydro-2*H*-pyran-2-yloxy)docos-21-ene 3b (from alkane 2b). This compound had mp 33 °C; R_F 0.5 (A) (Found: C, 79.44; H, 12.71. $C_{27}H_{52}O_2$ requires C, 79.35; H, 12.82%); $\delta_H(CDCl_3)$ 1.23–1.38 (36 H, s, CH_2), 1.45–1.88 (6 H, m, C*H*$_2$CH$_2$O), 1.99–2.04 (2 H, m, C*H*$_2$CH=), 3.32–3.40 (1 H, m, HC*H*O), 3.45–3.51 (1 H, m, HC*H*O), 3.68–3.75 (1 H, m, HC*H*O), 3.83–3.89 (1 H, m, HC*H*O), 4.55–4.57 (1 H, t, OCHO), 4.89–4.99 (2 H, q, =CH_2) and 5.75–5.83 (1 H, m, CH=); *m/z* (ESI-MS) 409.3 (M + H) and 432.4 (M + Na).

1-(Tetrahydro-2*H*-pyran-2-yloxy)henicos-20-ene 3c (from alkane 2d). This compound had mp 36 °C, R_F 0.6 (B) (Found: C, 79.23; H, 12.61. $C_{26}H_{50}O_2$ requires C, 79.12; H, 12.77%); $\delta_H(CDCl_3)$ 1.23–1.38 (34 H, s, CH_2), 1.45–1.88 (6 H, m, C*H*$_2$CH$_2$O), 1.99–2.04 (1 H, m, C*H*$_2$CH=), 3.32–3.40 (1 H, m, HC*H*O), 3.45–3.51 (1 H, m, HC*H*O), 3.68–3.75 (1 H, m, HC*H*O), 3.83–3.89 (1 H, m, HC*H*O), 4.55–4.57 (1 H, t, OCHO), 4.89–4.99 (1 H, q, =CH_2), 5.75–5.83 (1 H, m, CH=) *m/z* (ESI-MS) 395.1 (M + H) and 418.2 (M + Na).

1-(Tetrahydro-2*H*-pyran-2-yloxy)dotriaconta-31-ene 3d (from alkane 4a or 4b). This compound had mp 59–61 °C; R_F 0.6 (B) (Found: C, 80.71; H, 12.97. $C_{37}H_{72}O_2$ requires C, 80.95; H, 13.22%); $\delta_H(CDCl_3)$ 1.21–1.40 (58 H, s, CH_2), 1.44–1.82 (6 H, m, C*H*$_2$CH$_2$O), 2.00–2.06 (2 H, m, C*H*$_2$CH=), 3.34–3.40 (1 H, m, HC*H*O), 3.47–3.52 (1 H, m, HC*H*O), 3.68–3.74 (1 H, m, HC*H*O), 3.82–3.89 (1 H, m, HC*H*O), 4.54–4.58 (1 H, t, OC*H*O), 4.89–5.01 (2 H, q, =CH_2), 5.73–5.83 (1 H, m, CH=); *m/z* (ESI-MS) 571 (M + Na).

1-(Tetrahydro-2*H*-pyran-2-yloxy)undec-11-ene 3e

This compound was prepared from dec-10-en-1-ol according to the literature[13] and was used without further purification for the preparation of **8i**.

21-Bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)henicosane 4a

The corresponding Grignard reagent was prepared from 11-bromo-1-(tetrahydro-2*H*-pyran-2-yloxy)undecane **2b** in Et_2O (120 ml) and then refluxed for 2 h; for 11-chloro-1-(tetrahydro-2*H*-pyran-2-yloxy)undecane **2c** in THF (150 ml) and the mixture was refluxed for 5 h. After this each solution was added dropwise over 60 min to an ice-cooled solution of 1,10-dibromodecane **5**. Each mixture was then stirred for 3.5 h at room temperature. For further details see the procedure for **3**. The compound had mp 42 °C; R_F 0.5 (B) (Found: C, 65.54; H, 11.00. $C_{26}H_{51}O_2Br$ requires C, 65.66; H, 10.81%); $\delta_H(CDCl_3)$ 1.21–1.40 (36 H, s, CH_2), 1.44–1.82 (8 H, m, C*H*$_2$CH$_2$O, C*H*$_2$CH$_2$Br), 3.30–3.40 (3 H, m, HC*H*O, C*H*$_2$Br), 3.47–3.52 (1 H, m, HC*H*O), 3.68–3.74 (1 H, m, HC*H*O), 3.82–3.89 (1 H, m, HC*H*O), 4.54–4.58 (1 H, t, OC*H*O); *m/z* (ESI-MS) 497.4 (M + Na) and 499.4 (M + Na) (isotope).

21-Iodo-1-(tetrahydro-2*H*-pyran-2-yloxy)henicosane 4b

Method A. Compound **4a** (4.74 g, 0.01 mol) was dissolved in dry acetone (50 ml) and LiI (2.00 g, 0.015 mol) was added to the solution. The mixture was refluxed for 5 h and then stirred for 24 h at room temperature. After this it was concentrated, poured into ice-cooled water and extracted with heptane and $CHCl_3$ (×2). The combined organic phases were washed with brine, dried (Na_2SO_4) and evaporated. Chromatography of the residue on silica gel with a heptane–$CHCl_3$ gradient afforded **4b** (5.00 g, 96%) as a white waxy solid.

Method B. Methanesulfonyl chloride (1.14 g, 0.01 mol) was added to an ice-cooled solution of 21-(tetrahydro-2*H*-pyran-2-yloxy)henicosanol **8c** (4.12 g, 0.01 mol) in dry $CHCl_3$ (3 ml) and dry pyridine (5 ml). The mixture was stirred for 20 min at 5–10 °C and 16 h at room temperature. The precipitated C_5H_5NHCl was dissolved by addition of a little ice after which the mixture was poured into 1.5 M H_2SO_4 (200 ml) and extracted with diethyl ether. The extract was dried (Na_2SO_4) and evaporated to give an oily product which was dissolved in acetone (200 ml); for further treatment see method (A). The product (4.4 g, 85%) had R_F 0.5 (B); mp 46 °C (Found: C, 59.69; H, 9.73. $C_{26}H_{51}O_2I$ requires C, 59.76; H, 9.84%); $\delta_H(CDCl_3)$ 1.21–1.40 (36 H, s, CH_2), 1.44–1.82 (8 H, m, C*H*$_2$CH$_2$O, C*H*$_2$CH$_2$I), 3.28–3.40 (3 H, m, HC*H*O, C*H*$_2$I), 3.47–3.52 (1 H, m, HC*H*O), 3.68–3.74 (1 H, m, HC*H*O), 3.82–3.89 (1 H, m, HC*H*O) and 4.54–4.58 (1 H, t, OCHO); *m/z* (ESI-MS) 546 (M + Na).

22-Bromodocos-1-ene 6a and 32-bromodotriacont-1-ene 6b

A solution of triphenylphosphine dibromide was prepared by adding bromine (1.598 g, 0.01 mol) to a chilled, stirred solution of triphenylphosphine in CH_2Cl_2 (40 ml). The solution was maintained at 10 °C while **3b** (1.83 g, 0.0045 mol) or **3d** (2.46 g, 0.0045 mol) in CH_2Cl_2 (3 ml) was added. The solution was stirred at room temperature for 36 h, after which it was washed with water and dried. After evaporation the product was purified by means of column chromatography with heptane for elution.

22-Bromodocos-1-ene 6a. This compound (1.60 g, 95%) was a white waxy solid, R_F 0.7 (A); mp 32 °C (Found: C, 68.41; H, 10.61. $C_{22}H_{41}Br$ requires C, 68.55; H, 10.72%); *m/z* (ESI-MS) 387.0 (M + H) and 389.1 (isotope).

32-Bromodotriacont-1-ene 6b. This compound (2.20 g, 94%) was a white waxy solid, mp 30 °C; R_F 0.7 (A) (Found: C, 71.23; H, 11.71. $C_{32}H_{61}Br$ requires C, 73.11; H, 11.96%); *m/z* (ESI-MS) 526.9 (M + H) and 529.0 (isotope).

Alkylation of protected glycerol and arabitol derivatives: general procedure

The alcohols **11** and **13** were dissolved in absolute toluene to which solutions KOBu^t and catalytic amounts of $(Bu)_4NI$ were added. After the mixtures had been stirred for 30 min the bromide **6a** or **6b** was added in a little toluene. The mixtures were stirred under reflux for 36 h after which they were diluted with water. The organic phase was separated, dried (Na_2SO_4) and evaporated. The resulting crude product was purified by column chromatography on silica gel with a heptane–$CHCl_3$ gradient.

1,2-*O*-Isopropylidene-3-*O*-(docos-21-enyl)-*sn*-glycerol 7a. Compound **11** (1.32 g, 0.01 mol), **6a** (3.47 g), toluene (20 ml) and water (40 ml) gave a white waxy solid (3.28 g, 75%), mp

62 °C; R_F 0.2 (B) (Found: C, 76.67; H, 12.32. $C_{28}H_{54}O_3$ requires C, 76.65; H, 12.41%); $[\alpha]_D^{22}$ −0.849 (*c* 1, $CHCl_3$); δ_H($CDCl_3$) 1.20–1.29 (34 H, s, CH_2), 1.42 (3 H, s, CH_3), 1.45 (3 H, s, CH_3), 1.95–2.11 (2 H, m, C*H*$_2$CH=), 3.35–3.55 (4 H, m, CH_2O), 3.69–3.79 (1 H, m, HCO), 4.00–4.10 (1 H, m, HCO), 4.2–4.31 (1 H, m, HCO), 4.85–5.07 (2 H, m, =CH_2) and 5.70–5.91 (1 H, m, CH=); *m/z* (ESI-MS) 461.6 (M + Na).

1,2-*O*-Isopropylidene-3-*O*-(dotriacont-31-enyl)-*sn*-glycerol 7b. Compound **11** (1.32 g, 0.01 mol), **6b** (4.76 g, 0.009 mol) and toluene (30 ml) gave a white waxy solid (3.64 g, 70%), mp 54–56 °C; R_F 0.2 (B) (Found: C, 78.61; H, 12.71. $C_{38}H_{74}O_3$ requires C, 78.83; H, 12.88%); $[\alpha]_D^{22}$ −1.13 (*c* 1, $CHCl_3$); δ_H($CDCl_3$) 1.20–1.29 (54 H, s, CH_2), 1.42 (3 H, s, CH_3), 1.45 (3 H, s, CH_3), 1.5–1.69 (2 H, m, CH_2CH_2O), 1.95–2.11 (2 H, m, C*H*$_2$CH=), 3.35–3.55 (4 H, m, CH_2O), 3.69–3.79 (1 H, m, HCO), 4.00–4.10 (1 H, m, HCO), 4.2–4.31 (1 H, m, HCO), 4.85–5.07 (2 H, m, =CH_2) and 5.70–5.91 (1 H, m, CH=); *m/z* (ESI-MS) 601.9 (M + Na).

2,3 : 4,5-Di-*O*-isopropylidene-1-*O*-(docos-21-enyl)-D-arabitol 7c. Compound **13** (2.32 g, 0.01 mol), **6a** (3.47 g, 0.009 mol) and toluene (20 ml) gave a white waxy solid (3.48 g, 72%), mp 72 °C; R_F 0.2 (B) (Found: C, 73.45; H, 11.79. $C_{33}H_{62}O_5$ requires C, 73.56; H, 11.60%); $[\alpha]_D^{22}$ −0.804 (*c* 1, $CHCl_3$); δ_H($CDCl_3$) 1.15–1.45 (46 H, m, 4 s, CH_2, CH_3), 1.95–2.11 (2 H, m, C*H*$_2$CH=), 3.40–3.59 (3 H, m, HCO), 3.65–3.80 (2 H, m, HCO), 3.91–4.15 (4 H, m, HCO), 4.85–5.07 (2 H, m, =CH_2) and 5.70–5.91 (1 H, m, CH=); *m/z* (ESI-MS) 539.3 (M + H), 556.5 (M + NH_4), 561.5 (M + Na) and 577.5 (M + K).

2,3 : 4,5-Di-*O*-isopropylidene-1-*O*-(dotricont-31-enyl)-D-arabitol 7d. Compound **13** (2.32 g, 0.01 mol), **6b** (4.76 g, 0.009 mol) and toluene (40 ml) gave a white waxy solid (4.14 g, 68%), mp 59–61 °C; R_F 0.2 (B) (Found: C, 76.25; H, 11.99. $C_{43}H_{82}O_5$ requires C, 76.05; H, 12.17%); $[\alpha]_D^{22}$ −1.01 (*c* 1, $CHCl_3$); δ_H($CDCl_3$) 1.15–1.45 (66 H, m, 4 s, CH_2, CH_3), 1.95–2.11 (2 H, m, C*H*$_2$CH=), 3.40–3.59 (3 H, m, HCO), 3.65–3.80 (2 H, m, HCO), 3.91–4.15 (4 H, m, HCO), 4.85–5.07 (2 H, m, =CH_2) and 5.70–5.91 (1 H, m, CH=); *m/z* (ESI-MS) 702.1 (M + Na) and 719.0 (M + K).

Hydroboration of protected alkenes: general procedure

The alkenes **3** or **7** were separately dissolved in absolute THF and the solutions were stirred under argon. A solution of 9-BBN (0.5 M; 20 ml) was added dropwise over 20 min *via* a syringe to each solution which was then stirred for 6 h at 30 °C. After each mixture had been cooled to 20 °C EtOH (7 ml), aqueous NaOH (6 M; 2.12 ml) and H_2O_2 (30% in water; 4.25 ml) were added to it. The mixture was then stirred at 40 °C for 1 h. K_2CO_3 was added to saturate the aqueous phase and the organic phase was then separated, dried (K_2CO_3) and evaporated. The resulting crude product was purified by column chromatography on silica gel with a heptane–$CHCl_3$ gradient.

16-(Tetrahydro-2*H*-pyran-2-yloxy)hexadecan-1-ol 8a. Compound **3a** (3.24 g, 0.01 mol) and THF (30 ml) gave a white waxy solid (3.20 g, 94%), mp 72–73 °C; R_F 0.5 (C) (Found: C, 73.51; H, 12.22. $C_{21}H_{42}O_3$ requires C, 73.63; H, 12.36%); δ_H($CDCl_3$) 1.21–1.40 (24 H, s, CH_2), 1.44–1.82 (8 H, m, C*H*$_2$CH$_2$O), 3.34–3.40 (1 H, m, HC*H*O), 3.47–3.52 (1 H, m, HC*H*O), 3.60–3.68 (2 H, t, C*H*$_2$OH), 3.68–3.74 (1 H, m, HC*H*O), 3.82–3.89 (1 H, m, HC*H*O) and 4.54–4.58 (1 H, t, OCHO); *m/z* (ESI-MS) 365 (M + Na).

22-(Tetrahydro-2*H*-pyran-2-yloxy)docosan-1-ol 8b. Compound **3b** (4.08 g, 0.01 mol) and THF (30 ml) gave a white waxy solid (3.90 g, 92%), mp 55–56 °C; R_F 0.5 (C) (Found: C, 75.81; H, 12.52. $C_{27}H_{54}O_3$ requires C, 76.00; H, 12.76%); δ_H($CDCl_3$) 1.21–1.40 (38 H, s, CH_2), 1.44–1.82 (8 H, m, C*H*$_2$CH$_2$O), 3.34–3.40 (1 H, m, HC*H*O), 3.47–3.52 (1 H, m, HC*H*O), 3.60–3.68 (2 H, t, C*H*$_2$OH), 3.68–3.74 (1 H, m, HC*H*O), 3.82–3.89 (1 H, m, HC*H*O) and 4.54–4.58 (1 H, t, OC*H*O); *m/z* (ESI-MS) 427.3 (M + H) and 449.1 (M + Na).

21-(Tetrahydro-2*H*-pyran-2-yloxy)henicosan-1-ol 8c. Compound **3c** (4.98 g, 0.01 mol) and THF (30 ml) gave a white waxy solid (3.92 g, 95%), mp 56 °C; R_F 0.5 (C) (Found: C, 75.71; H, 12.57. $C_{26}H_{52}O_3$ requires C, 75.67; H, 12.70%); δ_H($CDCl_3$) 1.21–1.40 (36 H, s, CH_2), 1.44–1.82 (8 H, m, C*H*$_2$CH$_2$O), 3.34–3.40 (1 H, m, HC*H*O), 3.47–3.52 (1 H, m, HC*H*O), 3.60–3.68 (2 H, t, C*H*$_2$OH), 3.68–3.74 (1 H, m, HC*H*O), 3.82–3.89 (1 H, m, HC*H*O) and 4.54–4.58 (1 H, t, OC*H*O); *m/z* (ESI-MS) 413.3 (M + H) and 435.1 (M + Na).

32-(Tetrahydro-2*H*-pyran-2-yloxy)dotriacontan-1-ol 8d. Compound **3d** (5.48 g, 0.01 mol) and THF (50 ml) gave a white waxy solid (4.64 g, 82%), mp 54–55 °C; R_F 0.6 (C) (Found: C, 78.25; H, 13.22. $C_{37}H_{74}O_3$ requires C, 78.38; H, 13.15%); δ_H($CDCl_3$) 1.21–1.40 (56 H, s, CH_2), 1.44–1.82 (8 H, m, C*H*$_2$CH$_2$O), 3.34–3.40 (1 H, m, HC*H*O), 3.47–3.52 (1 H, m, HC*H*O), 3.60–3.68 (2 H, t, C*H*$_2$OH), 3.68–3.74 (1 H, m, HC*H*O), 3.82–3.89 (1 H, m, HC*H*O) and 4.54–4.58 (1 H, t, OCHO); *m/z* (ESI-MS) 589.6 (M + Na).

1,2-*O*-Isopropylidene-3-*O*-(22-hydroxydocosanyl)-*sn*-glycerol 8e. Compound **7a** (4.38 g, 0.01 mol) and THF (30 ml) gave a white waxy solid (4.32 g, 87%), mp 78–79 °C; R_F 0.5 (C) (Found: C, 73.52; H, 12.41. $C_{28}H_{56}O_4$ requires C, 73.63; H, 12.36%); $[\alpha]_D^{22}$ −1.0 (*c* 1, $CHCl_3$); δ_H($CDCl_3$) 1.20–1.29 (42 H, m, 2 s, CH_2, CH_3), 1.50–1.79 (4 H, m, C*H*$_2$CH$_2$O), 3.35–3.85 (7 H, m, HCO, C*H*$_2$OH), 4.0–4.1 (1 H, m, CHO) and 4.19–4.31 (1 H, q, C*H*O); *m/z* (ESI-MS) 457.8 (M + H) and 496.9 (M + K).

1,2-*O*-Isopropylidene-3-*O*-(32-hydroxydotriacontan-1-yl)-*sn*-glycerol 8f. Compound **7b** (5.78 g, 0.01 mol) and THF (60 ml) gave a white waxy solid (4.94 g, 82%), mp 75–76 °C; R_F 0.6 (C) (Found: C, 76.32; H, 12.71. $C_{38}H_{76}O_4$ requires C, 76.45; H, 12.83%); $[\alpha]_D^{22}$ −0.9 (*c* 1, $CHCl_3$); δ_H($CDCl_3$) 1.20–1.29 (62 H, m, 2 s, CH_2, CH_3), 1.50–1.79 (4 H, m, C*H*$_2$CH$_2$O), 3.35–3.85 (7 H, m, *H*CO, C*H*$_2$OH), 4.0–4.1 (1 H, m, CHO) and 4.19–4.31 (1 H, q, C*H*O); *m/z* (ESI-MS) 597.8 (M + H) and 619.3 (M + Na).

3,4 : 5,6-Di-*O*-isopropylidene-1-*O*-(22-hydroxydocosan-1-yl)-D-arabitol 8g. Compound **7c** (5.38 g, 0.01 mol) and THF (30 ml) gave a white waxy solid (4.44 g, 80%), mp 78–81 °C; R_F 0.5 (C) (Found: C, 71.22; H, 11.61. $C_{33}H_{64}O_6$ requires C, 71.18; H, 11.58%); $[\alpha]_D^{22}$ −1.1 (*c* 1, $CHCl_3$); δ_H($CDCl_3$) 1.21–1.41 (48 H, m, 4 s, CH_2, CH_3), 1.45–1.65 (4 H, m, C*H*$_2$CH$_2$O), 3.35–3.75 (7 H, m, CHO, C*H*$_2$OH) and 3.85–4.15 (4 H, m, CHO); *m/z* (ESI-MS) 579.6 (M + Na).

3,4 : 5,6-Di-*O*-isopropylidene-1-*O*-(32-hydroxydotriacontan-1-yl)-D-arabitol 8h. Compound **7d** (6.78 g, 0.01 mol) and THF (60 ml) gave a white waxy solid (5.15 g, 74%), mp 77–78 °C; R_F 0.6 (C) (Found: C, 74.12; H, 12.21. $C_{43}H_{84}O_6$ requires C, 74.08; H, 12.14%); $[\alpha]_D^{22}$ −1.2 (*c* 1, $CHCl_3$); δ_H($CDCl_3$) 1.21–1.41 (68 H, m, 4 s, CH_2, CH_3), 1.45–1.65 (4 H, m, C*H*$_2$CH$_2$O), 3.35–3.75 (7 H, m, CHO, C*H*$_2$OH) and 3.85–4.15 (4 H, m, C*H*O); *m/z* (ESI-MS) 697.9 (M + H) and 720.3 (M + Na).

11-(Tetrahydro-2*H*-pyran-2-yloxy)undecan-1-ol 8i. Compound **3e** (2.56 g, 0.01 mol) gave a clear liquid (2.61 g, 96%), mp 78 °C; R_F 0.6 (C) (Found: C, 69.54; H, 11.67. $C_{16}H_{32}O_3$ requires C, 70.54; H, 11.84%).

ω-Hydroxyalkylphosphocholines 9

Phosphorylation. *Method A*.—2-Bromoethylphosphoric acid dichloride (0.002 mol) was dissolved in $CHCl_3$ (10 ml) and the solution maintained at 0 °C while triethylamine (0.0035 mol) in $CHCl_3$ (5 ml) was added dropwise. A solution of each of the alcohols **8a**,**b**,**d**–**h** (0.001 mol) in $CHCl_3$ (15 ml) was added to the solution which was then stirred at room temperature for 24 h with exclusion of moisture. Ice (1 : 1 v/v) and triethylamine (0.002 mol) were added to the mixture which was then stirred until the ice had melted. The organic layer was then removed and evaporated and the residual oil was taken up in THF (0.9 ml) and water (0.12 ml). This mixture was stirred for 2 h, whilst being maintained at pH 8 by the addition of triethylamine. After that diisopropyl ether (2.0 ml), water (2.0 ml) and MeOH (1.6 ml) were added to the mixture. The organic layer was separated, evaporated and the residue dissolved in $CHCl_3$–MeCN

(1:1, v/v; 20.0 ml) and ethanolic trimethylamine (33%; 2.5 ml). This mixture, in an air-tight vessel, was stirred for 48 h and then evaporated. The residual oil was used without further purification.

Method B.—A solution of each of the alcohols **8a**,**b**,**d**–**h** (0.001 mol) dissolved in dry $CHCl_3$ (2.0 ml) was treated with trimethylamine (0.002 mol). After cooling of the mixture to 0 °C it was stirred and treated with 2-chloro-2-oxo-1,3,2-dioxophospholane (0.002 mol). The mixture was stirred for 2 h at room temperature after which precipitated triethylammonium chloride was filtered off and the filtrate concentrated under reduced pressure. The residual solid was dissolved in ethyl methyl ketone (20.0 ml) and lithium bromide (0.70 g, 0.004 mol) was added to the solution. After dissolution of the lithium bromide the reaction mixture was refluxed for 6 h and then evaporated. The residual oil was dissolved in diisopropyl ether (16.0 ml) and methanol (4.0 ml) and the solution washed with aqueous formic acid (0.1%; 16.0 ml). The organic layer was washed again with 0.1 M aqueous sodium acetate (16.0 ml), dried and evaporated. The residual oil was used for quaternation as described in method A.

Cleavage of the isopropylidene- and THP-groups: general procedure. The crude protected cholines were dissolved in $CHCl_3$–MeOH–water (5 ml) and a catalytic amount of pyridinium toluene-*p*-sulfonate was added to the solution. The mixture was stirred at 40 °C until starting material was no longer detectable after which it was evaporated. The residual oil was passed through a silica gel column with $CHCl_3$–MeOH–NH_3 (65:35:5) or $CHCl_3$–MeOH–NH_3 (45:45:10) as eluent. After the column chromatography the products were dissolved in a little $CHCl_3$–MeOH to which acetone was then added to give a white precipitate. This was dried *in vacuo* over phosphorus pentoxide at 63 °C.

16-*Hydroxyhexadecanyl* 2-(*trimethylammonio*)*ethyl phosphate* **9a**.—Compound **8a** (0.342 g, 0.001 mol) gave a white powder (0.334 g, 79%; method A: or 0.317 g, 75%; method B), mp 192 °C; R_F 0.2 (D) (Found: P, 6.92. $C_{21}H_{46}O_5NP{\cdot}H_2O$ requires P, 7.01%); δ_H(CD_3OD, 500 MHz) 1.26–1.38 (24 H, s, CH_2), 1.52–1.63 (4 H, m, C$H_2$$CH_2O$), 3.20 [9 H, s, $N^+(CH_3)_3$], 3.49–3.61 (4 H, m, CH_2N^+, CH_2OH), 3.80–3.85 (2 H, m, CH_2OP) and 4.16–4.20 (2 H, m, CH_2OP); *m/z* (ESI-MS) 424.4 (M + H) and 446.5 (M + Na).

22-*Hydroxydocosanyl* 2-(*trimethylammonio*)*ethyl phosphate* **9b**.—Compound **8b** (0.426 g, 0.001 mol) gave a white powder (0.370, 73%; method A: or 0.381, 75%; method B), mp 175 °C; R_F 0.2 (D) (Found: P, 5.72. $C_{27}H_{58}O_5NP{\cdot}H_2O$ requires P, 5.89%); δ_H(CD_3OD, 500 MHz) 1.27–1.38 (36 H, s, CH_2), 1.51–1.63 (4 H, m, C$H_2$$CH_2O$), 3.21 [9 H, s, $N^+(CH_3)_3$], 3.48–3.62 (4 H, m, CH_2N^+, CH_2OH), 3.80–3.85 (2 H, m, CH_2OP) and 4.16–4.23 (2 H, m, CH_2OP); *m/z* (ESI-MS) 508.3 (M + H) and 531 (M + Na).

32-*Hydroxydotriacontanyl* 2-(*trimethylammonio*)*ethyl phosphate* **9c**.—Compound **8d** (0.566 g, 0.001 mol) gave a white powder (0.424 g, 75%; method A: 0.475 g, 84%; method B), mp 135–137 °C; R_F 0.3 (D) (Found: P, 4.53. $C_{37}H_{78}O_5NP{\cdot}H_2O$ requires P, 4.65%); δ_H(CD_3OD, 500 MHz) 1.27–1.38 (56 H, s, CH_2), 1.53–1.64 (4 H, m, C$H_2$$CH_2O$), 3.23–3.24 [9 H, s, $N^+(CH_3)_3$], 3.49–3.61 (4 H, m, CH_2N^+, CH_2OH), 3.81–3.86 (2 H, m, CH_2OP) and 4.14–4.21 (2 H, m, CH_2OP); *m/z* (ESI-MS) 649.2 (M + H) and 671.1 (M + Na).

22-(sn-3-*Glyceryl*)*docosanyl* 2-(*trimethylammonio*)*ethyl phosphate* **9e**.—Compound **8e** (0.456 g, 0.001 mol) gave a white powder (0.441 g, 76%; method A: 0.418 g, 0.72%; method B), mp 149–151 °C; R_F 0.5 (E) (Found: P, 4.93. $C_{30}H_{64}O_7NP{\cdot}H_2O$ requires P, 5.16%); $[\alpha]_D^{22}$ −0.8 (*c* 1, CH_3OH); δ_H(CD_3OD, 500 MHz) 1.24–1.26 (36 H, s, CH_2), 1.50–1.65 (4 H, m, C$H_2$$CH_2O$), 3.21–3.23 [9 H, s, $N^+(CH_3)_3$], 3.39–3.57 (6 H, m, CH_2O), 3.59–3.61 (2 H, CH_2N^+), 3.74 (1 H, m, CHO), 3.84–3.87 (2 H, m, CH_2OP) and 4.22–4.25 (2 H, m, CH_2OP); *m/z* (ESI-MS) 604.5 (M + Na).

32-(sn-3-*Glyceryl*)*dotriacontanyl* 2-(*trimethylammonio*)*ethyl phosphate* **9f**.—Compound **8f** (0.596 g, 0.001 mol) gave a white powder (0.462 g, 64%; method A: 0.584 g, 81%; method B); R_F 0.5 (E); mp 136–138 °C (Found: P, 4.01. $C_{40}H_{84}O_5NP{\cdot}H_2O$ requires P, 4.19%); $[\alpha]_D^{22}$ −0.7 (*c* 1, CH_3OH); δ_H(CD_3OD, 500 MHz) 1.23–1.25 (56 H, s, CH_2), 1.51–1.65 (4 H, m, C$H_2$$CH_2O$), 3.20–3.22 [9 H, s, $N^+(CH_3)_3$], 3.40–3.57 (6 H, m, CH_2O), 3.59–3.61 (2 H, CH_2N^+), 3.74 (1 H, m, CHO), 3.83–3.87 (2 H, m, CH_2OP) and 4.22–4.25 (2 H, m, CH_2OP); *m/z* (ESI-MS) 723.4 (M + H) and 745.1 (M + Na).

22-(D-1-*Arabityl*)*docosanyl* 2-(*trimethylammonio*)*ethyl phosphate* **9g**.—Compound **8g** (0.556 g, 0.001 mol) gave a white powder (0.449 g, 70%; method A: 0.481 g, 75%; method B), mp 102–104 °C; R_F 0.5 (E) (Found: P, 4.58. $C_{32}H_{68}O_9NP{\cdot}H_2O$ requires P, 4.69%); $[\alpha]_D^{22}$ −0.9 (*c* 1, CH_3OH); δ_H(CD_3OD, 500 MHz) 1.21–1.32 (36 H, s, CH_2), 1.52–1.67 (4 H, m, C$H_2$$CH_2O$), 3.19–3.21 [9 H, s, $N^+(CH_3)_3$], 3.45–3.59 (4 H, 2 m, CH_2O), 3.59–3.62 (2 H, m, CH_2N^+), 3.69 (1 H, m, CHO), 3.78 (1 H, m, CHO), 3.82–3.86 (2 H, m, CH_2OP), 3.99–4.00 (1 H, m, CHO) and 4.19–4.21 (2 H, m, CH_2OP); *m/z* (ESI-MS) 642.9 (M + H) and 665.9 (M + Na).

32-(D-1-*Arabityl*)*dotriacontanyl* 2-(*trimethylammonio*)*ethyl phosphate* **9h**.—Compound **8h** (0.697 g, 0.001 mol) gave a white powder (0.499 g, 64%; method A: 0.531 g, 68%; method B), mp 98–99 °C; R_F 0.6 (E) (Found: P, 3.79. $C_{42}H_{88}O_9NP{\cdot}H_2O$ requires P, 3.87%); $[\alpha]_D^{22}$ −0.7 (*c* 1, CH_3OH); δ_H(CD_3OD, 500 MHz) 1.21–1.32 (56 H, s, CH_2), 1.53–1.66 (4 H, m, C$H_2$$CH_2O$), 3.20–3.22 [9 H, s, $N^+(CH_3)_3$], 3.46–3.60 (4 H, 2 m, CH_2O), 3.59–3.61 (2 H, m, CH_2N^+), 3.69 (1 H, m, CHO), 3.78 (1 H, m, CHO), 3.82–3.86 (2 H, m, CH_2OP), 3.99–4.00 (1 H, m, CHO) and 4.19–4.21 (2 H, m, CH_2OP); *m/z* (ESI-MS) 782.9 (M + H) and 805.9 (M + Na).

1,ω-Bisphosphorylated alkanes

The bromoethyl esters of **9b** or **9c** were prepared as described above. The crude intermediate was then dissolved in $CHCl_3$–MeCN–isopropyl alcohol (1:1:1, v/v/v; 20 ml) and 25% aqueous ammonia (3.0 ml) was added. The mixture was stirred in an air-tight vessel at 50 °C for 16 h after which it was evaporated. The crude product was passed through a silica gel column and eluted with $CHCl_3$–MeOH–NH_3 (50:50:10). After column chromatography the product was dissolved in a little $CHCl_3$–MeOH to which acetone was added. The resulting white precipitate was dried over phosphorus pentoxide *in vacuo* at 63 °C.

22-(2-*ammonioethoxyphosphinatooxy*)*docosanyl* 2-(*trimethylammonio*)*ethyl phosphate* **10a**.—Compound **9b** (0.507 g, 0.001 mol) gave a white powder (0.466 g, 74%; method A: 0.454 g, 72%; method B), mp 147–149 °C; R_F 0.7 (E) (Found: P, 8.99. $C_{29}H_{64}O_8N_2P_2{\cdot}2H_2O$ requires P, 9.29%); δ_H(CD_3OD, 500 MHz) 1.21–1.31 (36 H, s, CH_2), 1.60–1.68 (4 H, m, C$H_2$$CH_2OP$), 3.10–3.15 (2 H, m, C$H_2N^+$, kephalin), 3.19–3.21 [9 H, s, $N^+(CH_3)_3$], 3.59–3.61 (2 H, CH_2N^+, choline), 3.80–3.87 (4 H, m, CH_2OP), 3.95–4.05 (2 H, m, CH_2OP, kephalin) and 4.19–4.21 (2 H, m, CH_2OP, choline); *m/z* (ESI-MS) 632.0 (M + H).

32-(2-*ammonioethoxyphosphinatooxy*)*dotriacontanyl* 2-(*trimethylammonio*)*ethyl phosphate* **10b**.—Compound **9c** (0.649 g, 0.001 mol) gave a white powder (0.531 g, 69%; method A: 0.551 g, 72%; method B), mp 132–135 °C; R_F 0.7 (E) (Found: P, 7.69. $C_{39}H_{84}O_8N_2P_2{\cdot}2H_2O$ requires P, 7.86%); δ_H(CD_3OD, 500 MHz) 1.21–1.31 (56 H, s, CH_2), 1.61–1.67 (4 H, m, C$H_2$$CH_2OP$), 3.09–3.14 (2 H, m, CH_2N^+, kephalin), 3.20–3.22 [9 H, s, $N^+(CH_3)_3$], 3.58–3.61 (2 H, CH_2N^+, choline), 3.81–3.86 (4 H, m, CH_2OP), 3.94–4.03 (2 H, m, CH_2OP, kephalin) and 4.18–4.20 (2 H, m, CH_2OP, choline); *m/z* (ESI-MS) 772.3 (M + H) and 795.3 (M + Na).

3,4:5,6-Di-*O*-isopropylidene-D-glucitol 12. Methyl 3,4:5,6-di-*O*-isopropylidene-2-*O*-acetylgluconate[19] (3.26 g, 0.01 mol) was dissolved in dry ether (25 ml) and this solution was added dropwise to a stirred and cooled suspension of $LiAlH_4$ (0.72 g, 0.02 mol) in ether (5 ml). After being heated under reflux for 5 h

the mixture was diluted with water (30 ml) and the organic layer was separated, dried and evaporated. Further treatment was as described in ref. 19.

2,3 : 4,5-Di-*O*-isopropylidene-D-arabitol 13. 2,3 : 4,5-Di-*O*-isopropylidene-aldehydo-D-arabinose (2.30 g, 0.01 mol) in methanol (30 ml) was treated with sodium borohydride (1.13 g, 0.03 mol) at 60–65 °C for 18 h. After this the mixture was cooled and treated with water. The mixture was concentrated *in vacuo* and the residue was partitioned between water (30 ml) and dichloromethane (70 ml). The organic layer was washed twice with 10% aqueous ammonium sulfate and water, dried and passed through a silica gel column eluting with a heptane–ether gradient to yield **13** as a syrup (2.03 g, 90%); R_F 0.3 (C) (Found: C, 56.75; H, 8.72. $C_{11}H_{20}O_5$ requires C, 56.88; H, 8.68%); *m/z* (ESI-MS) 233.5 (M + H) and 255.2 (M + Na).

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