Bull. Chem. Soc. Jpn., ***69***, *2071—2078 (1996)*

Synthesis of 2-Geranyl- and 2-Farnesyl-Substituted Geranylgeraniols and Their Phosphates

Hajime Nagano* and Kaori Kudo

Department of Chemistry, Faculty of Science, Ochanomizu University, Otsuka, Bunkyo-ku, Tokyo 112

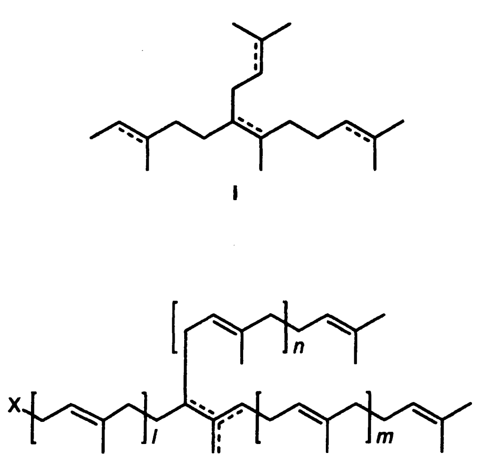
(Received February 8, 1996)

Allylation of the lithiated cyclohexylimine of (2*E*,6*E*,10*E*)-geranylgeranial with (2*E*)-geranyl bromide followed by acid-catalyzed hydrolysis gave (2*E*)-α-, (2*Z*)-α-, and γ-geranyl-substituted geranylgeranials. Farnesyl-substituted geranylgeranials were also prepared. (2*Z*)-α-Geranyl- and (2*Z*)-α-farnesyl-substituted geranylgeranials were photoisomerized to the corresponding (2*E*)-isomers, respectively. The branched polyprenyl alcohols, obtained by the reduction of these aldehydes, were transformed to geranyl- and farnesyl-substituted geranylgeranyl phosphates.

Highly branched isoprenoid hydrocarbons, such as **I**, which are distributed widely and abundantly in sediments,[1] have been postulated by Ourisson and Nakatani to be derived from the corresponding polyprenylated polyprenyl phosphates **II** comprising biomembranes in early evolution,[2,3] although these phosphates and alcohols **III** have been isolated neither from sediments nor from present-day microbial sources (Chart 1).[4] The availability of synthetic samples of these highly branched polyprenoids would greatly facilitate the search for such primitive microorganisms which may still exist on earth,[5] and the testing of this interesting speculation by evaluating the physicochemical properties of phosphates **II** in water.[3] We now report the synthesis of 2-geranyl- and 2-farnesyl-substituted geranylgeraniols **III** ($l=0$, $m=2$, $n=1$ and 2, Δ^2) and their phosphates **II** together with their isomers.

Results and Discussion

The introduction of (2*E*)-geranyl or (2*E*,6*E*)-farnesyl chain into (2*E*,6*E*,10*E*)-geranylgeraniol was performed through the allylation of cyclohexylimine **2** derived from (2*E*,6*E*,10*E*)-geranylgeranial (**1**) following a reported method.[6] In the reaction α-substitution was expected to proceed predominantly as described in the literature, although the geometry of the newly formed tetrasubstituted carbon–carbon double bond was not previsional. Cyclohexylimine **2** was prepared from aldehyde **1** and cyclohexylamine in the presence of potassium carbonate in quantitative yield. Imine **2** was lithiated with lithium diisopropylamide in HMPT/THF, and then treated with (2*E*)-geranyl bromide (**3a**).[7] The crude product was hydrolyzed with buffered aqueous acetic acid to give a mixture of geranyl-substituted geranylgeranials **4a**—**6a** (Scheme 1). Flash column chromatography on silica gel of the crude product gave (2*Z*)-α-substituted geranylgeranial **5a** [24% yield; $\delta=1.96$ (s, 3-Me), 2.96 (d, $J=6.8$ Hz, 1′-CH_2), and 10.04 (s, CH=O)] and an inseparable mixture of (2*E*)-α- and γ-substituted geranylgeranials **4a** and **6a** (16% combined yield). The major product **5a** was isomerized to the desired aldehyde **4a** as follows. Photoisomerization of α, β-unsaturated aldehyde **5a** was conducted under irradiation with a UV lamp (254 nm) for 90 h to give an equilibrium mixture of **4a** and **5a**, which was then chromatographed on silica gel to give **4a** [$\delta=2.19$ (s, 3-Me), 2.99 (d, $J=6.8$ Hz, 1′-CH_2) and 10.13 (s, CH=O)] and **5a** in 20 and 39% yields, respectively. The geometry of aldehydes **4a** and **5a** was assigned based on the chemical shifts of 3-Me in their ^{1}H NMR spectra; 3-Me *cis* to formyl group resonates at lower field.[8] The reduction of aldehydes **4a** and **5a** with sodium borohydride gave alcohols **7a** and **8a** in 50 and 67% yields, respectively.

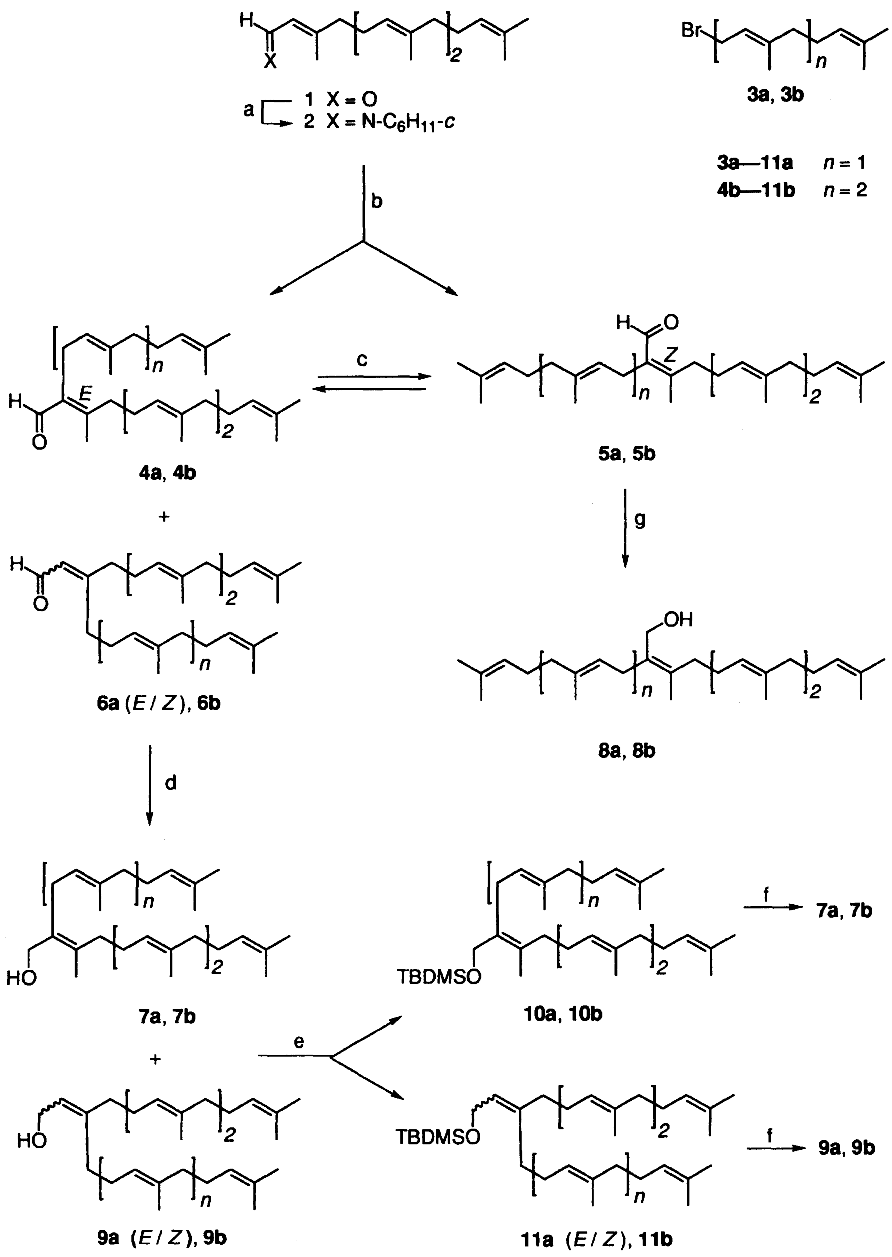


I

II X = OPO_3^{2-} $l+m=2$
III X = OH $n=0, 1, 2$

Chart 1. Chemical formulae I—III.

A mixture of **4a** and **6a** was reduced with diisobutylaluminium hydride (DIBAL) to give allylic alcohols **7a** and **9a** (65% yield). An inseparable mixture of **7a** and **9a** was first silylated with *t*-butyldimethylsilyl chloride (TBDMSCl) and then submitted to flash column chromatography on silica gel to give silyl ethers **10a** (77% yield) and **11a** (17% yield). Compound **10a** was hydrolyzed with Bu_4NF to give alcohol

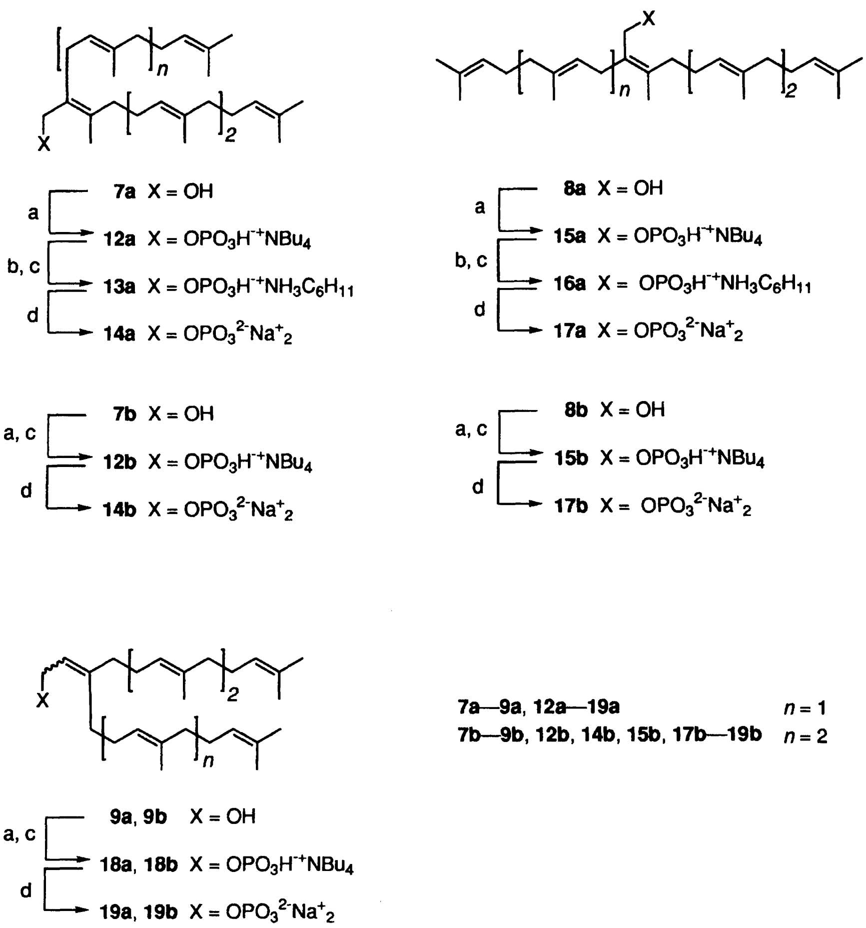


Scheme 1. (a) c-$C_6H_{11}NH_2$, K_2CO_3, benzene, 0 °C→room temp; (b) $LiN(i\text{-}Pr)_2$, HMPT, THF, then **3a** (−50 °C), or **3b** (−80 °C); (c) $h\nu$, hexane, N_2, room temp; (d) DIBAL, CH_2Cl_2, −50 °C; (e) TBDMSCl, imidazole, DMF, 30 °C; (f) n-Bu_4NF, THF, room temp; (g) $NaBH_4$, EtOH, room temp or (d).

7a in 93% yield. The hydrolysis of silyl ether **11a** gave alcohol **9a** as an inseparable mixture of (2*E*)- and (2*Z*)-isomers (2*E* : 2*Z* = ca. 1 : 1) in 90% yield. Although HPLC of the alcohol **9a** showed two slightly separated peaks (retention times 13.6 and 13.8 min), separation of the minor alcohol was discarded.

Farnesyl substituted geranylgeraniols were synthesized similarly using (2*E*,6*E*)-farnesyl bromide (**3b**)[7] instead of (2*E*)-geranyl bromide (**3a**). In the allylation of imine **2**, performed at −50 °C, α-farnesyl-substituted geranylgeranials **4b** and **5b** were yielded. Although γ-farnesyl-substituted geranylgeranial **6b** was not detected in the ^1H NMR spectrum of the reaction mixture, the spectra, which showed a signal at $\delta = 4.71$ (m, $CH{=}CH_2$), indicated that these aldehydes were contaminated by nucleophilic substitution products accompanied by an allylic rearrangement (S_N2' reaction). However, when allylation was performed at −80 °C, aldehydes **4b**—**6b** were obtained without contamination of the rearranged products (56% combined yield; **4b** : **5b** : **6b** = 1.7 : 5 : 1, determined by integration of CH=O signals in the ^1H NMR spectrum).

The photoisomerization of α,β-unsaturated aldehyde **5b**, followed by reduction with DIBAL, gave a mixture of allylic alcohols **7b** and **8b** (**7b** : **8b** = 1 : 1.1) in 33% overall yield. An inseparable mixture of **4b** and **6b** was first reduced with DIBAL and then treated with *t*-butyldimethylsilyl chloride to give silyl ethers **10b** and **11b**. The hydrolysis of **10b** and **11b** gave alcohol **7b** and **9b**, respectively.



Scheme 2. (a) Cl_3CCN, $(n\text{-}Bu_4N)H_2PO_4$, $CHCl_3$, room temp; (b) aq $c\text{-}C_6H_{11}NH_3Cl$, pH 9; (c) Sephadex LH-20 (eluent: MeOH); (d) CM-Sepharose FF (Na^+) (eluent: MeOH–$CHCl_3$, 2 : 1).

Although several methods for the conversion of polyprenols into polyprenyl monophosphates have been reported, the yields are low and the purification procedures are complicated. Recently, disodium farnesyl phosphate has been prepared from farnesol through tetrabutylammonium phosphate and bis (cyclohexylammonium) phosphate by combining methods reported by Danilov[9] and Julia.[10,11] We attempted to prepare disodium (2*E*)-2-geranyl-geranylgeranyl phosphate (**14a**) from alcohol **7a** using this method. Alcohol **7a** was phosphorylated with tetrabutylammonium dihydrogen phosphate and trichloroacetonitrile to give tetrabutylammonium phosphate **12a** (Scheme 2).[9] The phosphate **12a** was then converted to cyclohexylammonium phosphate **13a**. In the case of farnesol, bis(cyclohexylammonium) phosphate is yielded and purified by crystallization from water.[10] However, the crystallization of phosphate **13a** from water was not achieved because of its poor solubility in water. Phosphate **13a** was purified as follows. Cyclohexylammonium phosphate **13a**, possessing bulky hydrophobic chains, was extracted with hexane. The hexane solution was washed with water, and the extract was carefully purified by gel filtration using a Sephadex LH-20 column (eluent: MeOH) to give **13a** in 62% yield from alcohol **7a**.

Finally, compound **13a** was converted to disodium 2-geranyl-geranylgeranyl phosphate (**14a**) on an ion-exchange column of CM-Sepharose FF (Na^+) (MeOH–$CHCl_3$ = 2 : 1) in 86% yield.[10] Phosphate **14a** was characterized by ^1H, ^{13}C, and ^{31}P NMR and negative FAB-MS spectroscopies. Phosphate **17a** was prepared similarly from alcohol **8a** in 44% overall yield.

The phosphorylation of alcohol **7b** with tetrabutylammonium dihydrogen phosphate and trichloroacetonitrile, followed by purification by Sephadex LH-20,[12] gave tetrabutylammonium phosphate **12b** in 67% yield. Phosphate **12b** was then transformed to disodium (2*E*)-2-farnesyl-geranylgeranyl phosphate (**14b**) in 95% yield. Geranyl- and farnesyl-substituted geranylgeraniols **9a**, **8b**, and **9b** were also transformed to disodium phosphates **19a**, **17b**, and **19b** in 64, 71, and 55% overall yields, respectively. The two-step transformations of branched polyprenols to disodium phosphates were superior in yields.

Branched polyprenyl phosphates **14a**, **14b**, **17a**, **17b**, **19a**, and **19b** were thus prepared in satisfactory yields.[13]

Experimental

IR spectra were taken on a JASCO A-3 spectrometer for thin-layer films on sodium chloride plates. ^1H NMR spectra were recorded on a JEOL GSX-270 (270 MHz) or GSX-400 (400 MHz) spectrometer with $CDCl_3$ as the solvent and tetramethylsilane as an internal standard. ^{13}C NMR spectra were recorded on the instruments operating at 67.9 or 100.5 MHz with $CDCl_3$ as the solvent and internal standard ($\delta = 77.05$). ^{31}P NMR spectra with complete proton decoupling were recorded on the JEOL GSX-270 spectrometer operating at 109.4 MHz in $CDCl_3$ (external standard: phosphoric acid in D_2O). Mass spectra (EI, 70 eV) were obtained on a JEOL DX-300 mass spectrometer. Negative FAB mass spectra were recorded on a JEOL SX-102 mass spectrometer. Accurate mass measurements were recorded on these mass spectrometers. HPLC was performed on a JASCO TRIROTAR-IV apparatus with RID-300 RI detector using a Finepak Sil column (4.6×250 mm; solvent, hexane–ethyl acetate 20 : 1 v/v; flow rate 2 $cm^3\,min^{-1}$). Precoated Merck Kieselgel 60 F_{254} and Wakogel C-300 were used for thin layer chromatography (TLC) and flash column chromatography, respectively. Sephadex LH-20 and CM-Sepharose FF were purchased from Pharmacia.

***N*-[(2*E*,6*E*,10*E*)-3,7,11,15-Tetramethyl-2,6,10,14-hexadecatetraenylidene]cyclohexylamine (2).** To a solution of (2*E*,6*E*,10*E*)-geranylgeranial (**1**) (4.5 g, 15 mmol) in benzene (1.5 cm^3) cooled to 0 °C were added cyclohexylamine (3.2 g, 33 mmol) and K_2CO_3 (0.65 g, 4.7 mmol). The solution was first stirred at 0 °C for 1 h, and then at room temperature for 2 h. After filtration, the solvent was evaporated to give imine **2** (5.7 g, 99% yield) as an orange oil; IR 1648 cm^{-1}; ^{1}H NMR $\delta = 8.24$ (1H, d, $J = 9.3$ Hz, 1-H), 6.01 (1H, d, $J = 9.3$ Hz, 2-H), 5.10 (3H, m, 3×CH=), 2.98 (1H, m, CH–N), 2.14 (3H, s, Me), 2.14—1.22 (22H, m, 6×CH_2CH= and 10×H on cyclohexane ring), 1.91 (3H, d, $J = 1.2$ Hz, Me), 1.68 (3H, d, $J = 1.0$ Hz, Me), and 1.59 (6H, s, 2×Me).

Preparation of Geranyl-Substituted Geranylgeranials 4a, 5a, and 6a. To a solution of lithium diisopropylamide [prepared from diisopropylamine (6.0 cm^3) and *n*-BuLi (1.6 mol dm^{-3}; 29 cm^3)] and HMPT (8.0 cm^3) in THF (57 cm^3) cooled to 0 °C was added a solution of imine **2** (5.7 g, 15 mmol) in THF (2.0 cm^3). The resulting brown-yellow solution was first stirred at 0 °C for 10 min, and then at −50 °C for 30 min. After a solution of (2*E*)-geranyl bromide (**3a**)[7] (9.9 g, 46 mmol) in THF (2.0 cm^3) was added, the mixture was stirred at −50 °C for 4 h. After evaporation of the solvent, the residue was extracted with diethyl ether and the ethereal solution was washed successively with water and saturated brine, and then dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated to give an orange oil (14 g).

The crude product dissolved in diethyl ether was hydrolyzed with buffered aqueous acetic acid [pH 4.5, 20 cm^3, prepared from acetic acid (13 cm^3), water (13 cm^3), and sodium acetate (5.4 g)] for 1 h at room temperature. The solution was first diluted with diethyl ether and then washed successively with water and saturated brine, and finally dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated to give an orange oil (11 g), which was chromatographed on silica gel (230 g; hexane–AcOEt, 200 : 1 and then 20 : 1) to give an oil (4.6 g). The oil was then submitted to flash column chromatography on silica gel (200 g; hexane–benzene, 1 : 1) to give (2*Z*)-2-geranyl-geranylgeranial (**5a**) (an oil; 1.5 g, 24% yield) and an inseparable mixture of (2*E*)-2-geranyl-geranylgeranial (**4a**) and *γ*-geranyl-substituted geranylgeranial **6a** (an oil; 1.0 g, 16% yield). TLC (benzene): $R_f = 0.46$ for **5a** and 0.37 for **4a** and **6a**.

(2*Z*,6*E*,10*E*)-2-[(2*E*)-3,7-Dimethyl-2,6-octadienyl]-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraenal (5a): IR 1670 cm^{-1}; ^{1}H NMR $\delta = 10.04$ (1H, s, 1-H), 5.10 (4H, m, 4×CH=), 4.86 (1H, tq, $J = 6.7$ and 1.2 Hz, 2′-H), 2.96 (2H, d, $J = 6.6$ Hz, 1′-H), 2.60 (2H, t, $J = 7.6$ Hz, 4-H), 2.22 (2H, q, $J = 7.6$ Hz, 5-H), 2.06—1.96 (12H, m, 6×CH_2CH=), 1.96 (3H, s, 3-Me), 1.68 (6H, s, 2×Me), 1.66 (3H, d, $J = 1.2$ Hz, Me), 1.60 (6H, s, 2×Me), and 1.58 (6H, s, 2×Me); ^{13}C NMR $\delta = 190.16$, 158.47, 137.01, 136.73, 135.21, 135.05, 131.18, 124.32, 124.23, 123.95, 122.22, 121.64, 39.73, 33.05, 27.82, 26.84, 26.73, 26.60, 25.75, 24.38, 21.70, 17.74, 16.19, and 16.07; MS *m*/*z* 424 (M^+; relative intensity 0.9%), 406 ($M^+ - H_2O$; 12), 123 (81), 109 (59), 81 (56), and 69 (100). Found: *m*/*z* 406.3568 ($M^+ - H_2O$). Calcd for $C_{30}H_{46}$: ($M - H_2O$), 406.3600.

Photoisomerization of (2*Z*)-2-Geranyl-geranylgeranial (5a) to (2*E*)-2-Geranyl-geranylgeranial (4a). A solution of aldehyde **5a** (86 mg, 0.20 mmol) in hexane (4.5 cm^3) placed in a quartz cell was irradiated with a UV lamp (254 nm) at room temperature for 90 h under nitrogen to give an equilibrium mixture of **4a** and **5a**. Flash column chromatography (silica gel, 30 g; hexane–benzene, 1 : 1) of the mixture gave **4a** (18 mg, 20% yield) and **5a** (34 mg, 39% yield). **4a**: IR 1670 cm^{-1}; ^{1}H NMR $\delta = 10.13$ (1H, s, CH=O), 5.10 (4H, m, 4×CH=), 4.89 (1H, tq, $J = 6.8$ and 1.2 Hz, 2′-H), 2.99 (2H, d, $J = 6.8$ Hz, 1′-H), 2.70—1.83 (16H, m, 8×CH_2CH=), 2.19 (3H, s, 3-Me), 1.68 (6H, s, 2×Me), 1.66 (3H, s, Me), 1.62 (3H, s, Me), 1.60 (6H, s, 2×Me), and 1.58 (3H, s, Me); ^{13}C NMR $\delta = 191.31$, 158.41, 136.40, 136.27, 135.15, 131.30, 124.33, 124.28, 123.99, 122.93, 122.25, 39.68, 37.06, 29.69, 26.76, 26.64, 26.56, 26.12, 25.68, 24.09, 17.65, 17.36, 16.15, and 16.00; MS *m*/*z* 424 (M^+; 2%), 406 ($M^+ - H_2O$; 2), 137 (29), 81 (37), and 69 (100).

(2*Z*,6*E*,10*E*)-2-[(2*E*)-3,7-Dimethyl-2,6-octadienyl]-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraen-1-ol (8a). Aldehyde **5a** (152 mg, 0.36 mmol) was reduced with sodium borohydride (122 mg, 3.2 mmol) in ethanol (1.5 cm^3). The crude product was purified by flash column chromatography on silica gel (16 g; benzene) to give (2*Z*)-2-geranyl-geranylgeraniol (**8a**) (104 mg, 67% yield) as an oil; HPLC: $R_t = 7.56$ min (purity 90%); IR 3330 and 995 cm^{-1}; ^{1}H NMR $\delta = 5.13$—5.04 (5H, m, 5×CH=), 4.06 (2H, s, 1-H), 2.86 (2H, d, $J = 7.1$ Hz, 1′-H), 2.20—1.88 (16H, m, 8×CH_2CH=), 1.72 (3H, s, 3-Me), 1.68 (9H, s, 3×Me), and 1.60 (12H, s, 4×Me); ^{13}C NMR $\delta = 135.92$, 135.73, 135.03, 133.69, 132.38, 131.47, 131.25, 124.39, 124.21, 124.11, 123.78, 122.69, 61.95, 39.75, 39.71, 34.27, 29.76, 27.07, 26.75, 26.61, 25.68, 18.46, 17.66, 16.04, 16.01, and 15.98; MS *m*/*z* 408 ($M^+ - H_2O$, 3%), 81 (27), and 69 (100).

Reduction of Aldehydes 4a and 6a. To a solution of the mixture of aldehydes **4a** and **6a** (981 mg, 2.3 mmol) in CH_2Cl_2 (7.0 cm^3) cooled to −50 °C was added a solution of diisobutylaluminium hydride (DIBAL) in hexane (0.98 mol dm^{-3}; 4.6 cm^3, 4.5 mmol). After the solution was stirred for 30 min, an additional DIBAL solution (9.2 cm^3, 9.0 mmol) was added and the mixture was stirred for 1 h. An aqueous NaOH solution (10%; 5 cm^3) was added. The reaction mixture was warmed to room temperature and diluted with diethyl ether. The organic layer was washed with a 10% aqueous NaOH solution, and the combined basic aqueous layers were extracted twice with diethyl ether. The combined ethereal layer was washed successively with water (until neutral) and saturated brine, and then dried over anhydrous Na_2SO_4. The solvent was evaporated and the crude product was purified by flash column chromatography on silica gel (50 g; hexane–AcOEt, 50 : 1) to give a mixture of alcohols **7a** and **9a** (661 mg, 65% yield) as an oil.

(6*E*,9*E*,13*E*,17*E*)-9-[(*t*-Butyldimethylsiloxy)methyl]-2,6,10,14,18,22-hexamethyl-2,6,9,13,17,21-tricosahexaene (10a) and (6*E*,10*E*,17*E*)-14-[2-(*t*-Butyldimethylsiloxy)ethylidene]-2,6,10,18,22-pentamethyl-2,6,10,17,21-tricosapentaene (11a). To a solution of the mixture of **7a** and **9a** (661 mg, 1.5 mmol) in *N*,*N*-dimethylformamide (5.0 cm^3) were added *t*-butyldimethylsilyl chloride (467 mg, 3.1 mmol) and imidazole (634 mg, 9.3 mmol). The mixture was stirred at 30 °C for 30 min and then extracted with pentane. The extract was washed successively with water and saturated brine, and then dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated to give a mixture of *t*-butyldimethylsilyl ethers as an oil. Flash column chromatography of the mixture (silica gel, 70 g; hexane–benzene, 30 : 1 and then benzene) gave **10a** (an oil; 645 mg, 77% yield) and **11a** (an oil; 139 mg, 17% yield). TLC (hexane–benzene 10 : 1): $R_{\mathrm{f}}=0.44$ for **10a** and 0.27 for **11a**.

10a: IR 1258, 1060, 840, and 775 cm^{-1}; ^{1}H NMR $\delta=5.21$—5.02 (5H, m, 5×CH=), 4.14 (2H, s, O–CH$_2$), 2.88 (2H, d, $J=6.8$ Hz, 8-H), 2.16—1.94 (16H, m, 8×CH_2CH=), 1.73 (3H, s, Me), 1.70 (3H, s, Me), 1.69 (3H, s, Me), 1.68 (3H, s, Me), 1.62 (12H, s, 4×Me), 0.92 (9H, s, SiBu^t), and 0.08 (6H, s, Si(Me)$_2$); ^{13}C NMR $\delta=135.05$, 134.84, 134.57, 132.13, 131.40, 131.12, 131.10, 124.44, 124.41, 124.24, 123.54, 61.80, 39.81, 39.74, 34.83, 28.18, 26.76, 26.62, 26.00, 25.67, 18.38, 18.02, 17.64, 16.08, 15.97, and −5.23.

11a (2*E*/2*Z* Mixture): IR 1254, 1102, 1055, 833, and 773 cm^{-1}; ^{1}H NMR $\delta=5.31$ (1H, t, $J=6.1$ Hz, O–CH$_2$CH=), 5.10 (5H, m, 5×CH=), 4.21 (2H, d, $J=6.1$ Hz, O–CH$_2$), 2.16—1.92 (20H, m, 10×CH_2CH=), 1.68 (6H, s, 2×Me), 1.60 (15H, s, 5×Me), 0.90 (9H, s, SiBu^t), and 0.07 (6H, s, Si(Me)$_2$); ^{13}C NMR $\delta=140.76$, 140.73, 135.37, 135.34, 135.05, 134.87, 134.81, 131.20, 131.14, 131.11, 124.89, 124.39, 124.30, 124.23, 124.17, 124.07, 123.85, 60.08, 39.71, 36.77, 30.85, 27.08, 26.75, 26.68, 26.62, 26.59, 26.51, 26.00, 25.66, 18.37, 17.64, 15.99, 15.97, and −5.06.

(2*E*,6*E*,10*E*)-2-[(2*E*)-3,7-Dimethyl-2,6-octadienyl]-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraen-1-ol (7a). To a solution of **10a** (163 mg, 0.30 mmol) in THF (4.0 cm^3) was added tetrabutylammonium fluoride (297 mg, 0.94 mmol); the solution was stirred at room temperature for 3 h. After the addition of a drop of water, the solvent was evaporated, and the residue was extracted with diethyl ether. The ethereal layer was washed successively with water and saturated brine, and then dried over anhydrous Na$_2$SO$_4$. After filtration the solvent was evaporated, and the residue was chromatographed on silica gel (10 g; hexane–AcOEt, 20 : 1) to give (2*E*)-2-geranyl-geranylgeraniol (**7a**) (119 mg, 93% yield) as an oil; HPLC: $R_{\mathrm{t}}=12.2$ min (purity 96%); IR 3300 and 990 cm^{-1}; ^{1}H NMR $\delta=5.20$—5.02 (5H, m, 5×CH=), 4.09 (2H, s, 1-H), 2.88 (2H, d, $J=7.1$ Hz, 1′-H), 2.14—1.88 (16H, m, 8×CH_2CH=), 1.77 (3H, s, 3-Me), 1.68 (9H, s, 3×Me), 1.61 (3H, s, Me), and 1.60 (9H, s, 3×Me); ^{13}C NMR $\delta=135.82$, 135.32, 134.94, 133.86, 131.87, 131.50, 131.20, 124.36, 124.14, 123.94, 123.06, 62.41, 39.74, 39.69, 34.68, 29.37, 26.79, 26.72, 26.56, 25.66, 18.08, 17.64, 16.02, and 15.95; MS *m*/*z* 408 (M$^+-$H$_2$O; 9%), 81 (38), and 69 (100). Found: *m*/*z* 408.3735 (M$^+-$H$_2$O). Calcd for $\mathrm{C_{30}H_{48}}$: (M−H$_2$O), 408.3756.

(6*E*,10*E*)-3-[(3*E*)-4,8-Dimethyl-3,7-nonadienyl]-7,11,15-trimethyl-2,6,10,14-hexadecatetraen-1-ol (2*E*/2*Z* Mixture) (9a). Compound **11a** (115 mg, 0.21 mmol) was desilylated as described above and alcohol **9a** was obtained as an oil (81 mg, 90% yield); HPLC: $R_{\mathrm{t}}=13.6$ and 13.8 min, diastereomer ratio 48 : 52, purity >99%; IR 3320 and 1000 cm^{-1}; ^{1}H NMR $\delta=5.43$ (1H, t, $J=7.1$ Hz, 2-H), 5.10 (5H, m, 5×CH=), 4.13 (2H, d, $J=7.1$ Hz, 1-H), 2.18—1.87 (20H, m, 10×CH_2CH=), 1.67 (6H, s, 2×Me), and 1.60 (15H, s, 5×Me); ^{13}C NMR $\delta=143.33$, 135.82, 135.77, 135.26, 134.95, 134.87, 131.30, 131.21, 131.14, 124.33, 124.26, 124.17, 124.13, 124.03, 123.85, 123.81, 123.61, 59.00, 39.62, 36.67, 30.48, 27.01, 26.98, 26.69, 26.65, 26.56, 26.51, 25.61, 17.59, 15.95, and 15.92; MS *m*/*z* 408 (M$^+-$H$_2$O; 4%), 81 (37), and 69 (100).

Preparation of Farnesyl-Substituted Geranylgeranials 4b, 5b, and 6b. To a solution of the anion of imine **2** in THF (2.0 cm^3), prepared from **2** (950 mg, 2.6 mmol), as described for **4a**—**6a**, and cooled to −80 °C, was added a solution of farnesyl bromide (**3b**)[7] (1.1 g, 3.9 mmol) in THF (2.0 cm^3). The mixture was stirred at −80 °C for 3 h and the product was chromatographed on silica gel (100 g; hexane–benzene, 1 : 1 and then benzene) to give farnesyl-substituted geranylgeranials (873 mg). The mixture was chromatographed on silica gel (50 g; hexane–benzene 1 : 1) to give aldehyde **5b** (an oil; 417 mg, 33% yield) and a mixture of aldehydes **4b**, **5b**, and **6b** (**4b** : **5b** : **6b** = 3.4 : 1 : 2; 290 mg, 23% yield). TLC (benzene): $R_{\mathrm{f}}=0.47$ for **5b** and 0.34 for **4b** and **6b**.

(2*Z*,6*E*,10*E*)-3,7,11,15,-Tetramethyl-2-[(2*E*,6*E*)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-2,6,10,14-hexadecatetraenal (5b): IR 1670 and 1625 cm^{-1}; ^{1}H NMR $\delta=10.04$ (1H, s, 1-H), 5.13—5.06 (5H, m, 5×CH=), 4.86 (1H, tq, $J=6.7$ and 1.2 Hz, 2′-H), 2.97 (2H, d, $J=6.7$ Hz, 1′-H), 2.60 (2H, t, $J=7.6$ Hz, 4-H), 2.22 (2H, q, $J=7.6$ Hz, 5-H), 2.10–1.78 (16H, m, 8×CH_2CH=), 1.96 (3H, s, 3-Me), 1.69 (3H, s, Me), 1.68 (6H, s, 2×Me), 1.59 (9H, s, 3×Me), and 1.58 (6H, d, $J=1.2$ Hz, 2×Me); ^{13}C NMR $\delta=190.34$, 158.62, 137.08, 136.78, 135.39, 135.13, 134.94, 131.25, 124.36, 124.13, 124.00, 122.27, 121.62, 39.69, 39.65, 32.97, 27.74, 26.75, 26.59, 26.51, 25.68, 24.27, 21.64, 17.66, 16.14, 16.08, and 15.98; MS *m*/*z* 492 (M$^+$; 0.2%), 474 (M$^+-$H$_2$O; 0.4), 149 (41), 81 (32), and 69 (100). Found: *m*/*z* 492.4312 (M$^+$). Calcd for $\mathrm{C_{35}H_{56}O}$: M, 492.4331.

Preparation of (2*E*,6*E*,10*E*)-3,7,11,15-Tetramethyl-2-[(2*E*,6*E*)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-2,6,10,14-hexadecatetraen-1-ol (7b). A solution of aldehyde **5b** (68 mg, 0.14 mmol) in hexane (5.5 cm^3) placed in a quartz cell was irradiated with a UV lamp (254 nm) at room temperature for 90 h under nitrogen to give an equilibrium mixture of **4b** and **5b** (65 mg, 0.13 mmol). To a solution of the mixture of **4b** and **5b** in CH$_2$Cl$_2$ (2.0 cm^3) cooled to −50 °C was added a solution of DIBAL in hexane (0.98 mol dm^{-3}; 0.20 cm^3, 0.20 mmol). Flash column chromatography on silica gel (50 g; benzene–hexane 3 : 1) of the crude product gave (2*E*)-alcohol **7b** (an oil, 11 mg, 16% yield) and (2*Z*)-alcohol **8b** (an oil, 12 mg, 17% yield). **7b**: HPLC: $R_{\mathrm{t}}=11.5$ min (purity 98%); IR 3320 and 990 cm^{-1}; ^{1}H NMR $\delta=5.21$—5.00 (6H, m, 6×CH=), 4.09 (2H, s, 1-H), 2.88 (2H, d, $J=7.1$ Hz, 1′-H), 2.16—1.82 (20H, m, 10×CH_2CH=), 1.77 (3H, s, 3-Me), 1.68 (9H, s, 3×Me), 1.61 (3H, s, Me), and 1.60 (12H, s, 4×Me); ^{13}C NMR $\delta=135.98$, 135.39, 135.17, 134.98, 133.95, 131.89, 131.27, 124.37, 124.17, 124.03, 123.95, 123.00, 62.49, 39.78, 39.71, 34.77, 29.39, 26.84, 26.74, 26.62, 26.56, 25.68, 18.11, 17.66, 16.11, and 15.99; MS *m*/*z* 476 (M$^+-$H$_2$O; 8%), 123 (35), 109 (43), 95 (41), 81 (54), and 69 (100). Found: *m*/*z* 476.4393 (M$^+-$H$_2$O). Calcd for $\mathrm{C_{35}H_{56}}$: M−H$_2$O, 476.4382.

(2*Z*,6*E*,10*E*)-3,7,11,15-Tetramethyl-2-[(2*E*,6*E*)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-2,6,10,14-hexadecatetraen-1-ol (8b). HPLC: $R_{\mathrm{t}}=7.25$ min (purity 94%); IR 3330 and 990 cm^{-1}; ^{1}H NMR $\delta=5.18$—5.00 (6H, broad s, 6×CH=), 4.06 (2H, s, 1-H), 2.86 (2H, d, $J=7.1$ Hz, 1′-H), 2.20—1.84 (20H, m, 10×CH_2CH=), 1.72 (3H, s, 3-Me), 1.68 (9H, s, 3×Me), and 1.60 (15H, s, 5×Me); ^{13}C NMR $\delta=135.90$, 135.77, 135.07, 135.01, 133.64, 132.38, 131.21, 124.37, 124.10, 124.05, 123.78, 122.61, 61.91, 39.75, 39.69, 34.25, 29.72, 27.05, 26.74, 26.58, 25.66, 18.44, 17.64, 16.08, and 15.98; MS *m*/*z* 494 (M$^+$; 0.2%), 476 (M$^+-$H$_2$O; 3), 149 (40), 81 (37), and 69 (100). Found: *m*/*z* 494.4496 (M$^+$). Calcd for $\mathrm{C_{35}H_{58}O}$: M, 494.4487.

(2*E*,6*E*,10*E*)-3,7,11,15-Tetramethyl-2-[(2*E*,6*E*)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-2,6,10,14-hexadecatetraen-1-ol (7b) and (6*E*,10*E*)-7,11,15-Trimethyl-3-[(3*E*,7*E*)-4,8,12-trimethyl-3,7,11-tridecatrienyl]-2,6,10,14-hexadecatetraen-1-ol (9b). A solution of aldehydes **4b**, **5b**, and **6b** (290 mg, 0.59 mmol) in CH$_2$Cl$_2$ (5.0 cm^3) was treated with DIBAL (0.95 mol dm^{-3} in hexane; 0.95 cm^3, 0.90 mmol) at −80 °C. The solution was stirred for 2 h. The crude product was purified by flash column chromatography on silica gel

(30 g; hexane–benzene 1 : 1) to give **8b** (an oil, 27 mg, 9% yield) and a mixture of **7b** and **9b** (an oil, 188 mg, 64% yield).

(6*E*,10*E*,13*E*,17*E*,21*E*)-13-[(*t*-Butyldimethylsiloxy) methyl]-2, 6,10,14,18,22,26-heptamethyl-2,6,10,13,17, 21,25-heptacosaheptaene (10b) and (6*E*,10*E*,17*E*,21*E*)-14-[2-(*t*-Butyldimethylsiloxy) ethylidene]-2,6,10,18,22,26-hexamethyl-2,6,10,17,21,25-heptacosahexaene (11b). A mixture of alcohols **7b** and **9b** (188 mg, 0.38 mmol) was silylated as described for **7a** and **8a**. The crude product was chromatographed on silica gel (50 g; hexane–benzene 30 : 1, 20 : 1, and then benzene) to give **10b** (an oil; 138 mg, 61% yield) and **11b** (an oil; 98 mg, 42% yield). TLC (hexane–benzene 3 : 1) : $R_f = 0.42$ for **10b** and 0.29 for **11b**.

10b: IR 1256, 1058, 834, and 772 cm^{-1}; ^{1}H NMR $\delta = 5.27$—5.00 (6H, m, 6×CH=), 4.13 (2H, s, O–CH$_2$), 2.87 (2H, d, $J = 6.8$ Hz, 12-H), 2.16—1.86 (20H, m, 10×C*H*$_2$CH=), 1.73 (3H, s, Me), 1.69 (6H, s, 2×Me), 1.68 (3H, s, Me), 1.61 (15H, s, 5×Me), 0.92 (9H, s, SiBu^t), and 0.07 (6H, s, Si(Me)$_2$); ^{13}C NMR $\delta = 135.11$, 134.91, 134.84, 134.69, 132.10, 131.47, 131.21, 124.40, 124.28, 124.24, 123.45, 61.80, 39.82, 39.72, 34.84, 28.15, 26.76, 26.69, 26.64, 26.00, 25.68, 18.40, 18.04, 17.66, 16.12, 15.98, and −5.21.

11b: IR 1258, 1058, 836, and 774 cm^{-1}; ^{1}H NMR $\delta = 5.32$ (1H, t, $J = 6.4$ Hz, O–CH$_2$C*H*=), 5.12 (6H, m, 6×CH=), 4.22 (2H, d, $J = 6.4$ Hz, O–CH$_2$), 2.22—1.85 (24H, m, 12×C*H*$_2$CH=), 1.69 (6H, s, 2×Me), 1.61 (18H, s, 6×Me), 0.91 (9H, s, SiBu^t), and 0.08 (6H, s, Si(Me)$_2$); ^{13}C NMR $\delta = 140.80$, 135.44, 135.16, 134.94, 134.88, 131.20, 124.87, 124.40, 124.24, 124.18, 124.08, 123.85, 60.13, 39.72, 36.80, 30.88, 27.10, 26.76, 26.65, 26.62, 26.55, 26.02, 25.68, 17.66, 16.02, 15.99, and −5.03.

(6*E*,10*E*)-7,11,15-Trimethyl-3-[(3*E*,7*E*)-4,8,12-trimethyl-3,7, 11-tridecatrienyl]-2,6,10,14-hexadecatetraen-1-ol (9b). Desilylation of **11b** (78 mg, 0.13 mmol) as described above gave **9b** (64 mg, 100% yield) as an oil; HPLC: $R_t = 12.1$ min (purity 96%); IR 3317 and 1000 cm^{-1}; ^{1}H NMR $\delta = 5.43$ (1H, t, $J = 6.8$ Hz, 2-H), 5.20—5.00 (6H, m, 6×CH=), 4.13 (2H, d, $J = 6.8$ Hz, 1-H), 2.18—1.84 (24H, m, 12×C*H*$_2$CH=), 1.68 (6H, s, 2×Me), and 1.60 (18H, s, 6×Me); ^{13}C NMR $\delta = 143.51$, 135.92, 135.37, 135.03, 134.94, 131.22, 124.36, 124.16, 124.07, 123.84, 123.64, 59.10, 39.69, 36.71, 30.52, 27.04, 26.74, 26.62, 26.56, 25.67, 17.65, 16.02, and 15.98; MS *m*/*z* 476 (M$^+$ − H$_2$O; 4%), 149 (17), 81 (35), and 69 (100). Found: *m*/*z* 476.4337. Calcd for $C_{35}H_{56}$: M − H$_2$O, 476.4382.

Tetrabutylammonium (2*E*,6*E*,10*E*)-2-[(2*E*)-3, 7-Dimethyl-2, 6-octadienyl]-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraenyl Hydrogenphosphate (12a). To a solution of alcohol **7a** (112 mg, 0.26 mmol) and tetrabutylammonium dihydrogen phosphate (449 mg, 1.3 mmol) in CHCl$_3$ (1.0 cm^3) was added a solution of trichloroacetonitrile (0.16 cm^3, 1.6 mmol) in CHCl$_3$ (0.20 cm^3). The solution was stirred at room temperature for 30 min. After evaporation of the solvent, the residue was extracted with the upper phase of equilibrium butanol/water mixture (6 cm^3), and the solution was washed with the lower phase of the same mixture (15×3 cm^3). The butanol solution was coevaporated with heptane at room temperature to give crude **12a** (353 mg).

Cyclohexylammonium (2*E*,6*E*,10*E*)-2-[(2*E*)-3,7-Dimethyl-2, 6-octadienyl]-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraenyl Hydrogenphosphate (13a). A solution of the crude phosphate **12a** (353 mg) in aqueous cyclohexylammonium chloride [prepared from cyclohexylamine (3.0 cm^3) and 1 mol dm^{-3} hydrochloric acid (20 cm^3); pH 9] was stirred at room temperature for 17 h. The reaction mixture was extracted with hexane and the hexane layer was washed with water. The solvent was evaporated and the crude product was purified by gel filtration using a Sephadex LH-20 column (1.8 cm×24 cm; MeOH; twice) to give cyclohexylammonium phosphate **13a** (98 mg, 62% yield from **7a**) as a viscous oil; ^{1}H NMR $\delta = 8.42$ (3H, broad s, NH$_3$), 5.26—4.96 (5H, m, 5×CH=), 4.30 (2H, d, $J = 4.4$ Hz, 1-H), 2.92 (1H, s, N–CH), 2.83 (2H, d, $J = 6.1$ Hz, 1′-H), 2.26—1.83 (18H, m, 8×C*H*$_2$CH= and 2×H on cyclohexane ring), 1.82—1.00 (8H, 8×H on cyclohexane ring), 1.73 (3H, s, Me), 1.68 (3H, s, Me), 1.65 (6H, s, 2×Me), 1.60 (9H, s, 3×Me), and 1.58 (3H, s, Me); ^{13}C NMR $\delta = 135.08$, 134.90, 134.58, 131.18, 131.07, 124.43, 124.37, 124.31, 124.21, 123.08, 63.97, 49.90, 39.92, 39.71, 34.96, 30.75, 28.84, 26.87, 26.82, 26.74, 26.68, 25.66, 25.02, 24.59, 17.95, 17.64, 17.61, 16.02, 15.95, and 15.92; ^{31}P NMR $\delta = -0.62$ (s).

Disodium (2*E*,6*E*,10*E*)-2-[(2*E*)-3,7-Dimethyl-2,6-octadienyl]-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraenyl Phosphate (14a). Phosphate **13a** (86 mg, 0.14 mmol) was put on an ion-exchange column of CM-Sepharose FF (Na$^+$) (1.8 cm×27 cm) and was eluted with MeOH–CHCl$_3$ (2 : 1) to give disodium phosphate **14a** (67 mg, 86% yield) as a viscous oil; ^{1}H NMR $\delta = 5.32$—4.90 (5H, m, 5×CH=), 4.31 (2H, s, 1-H), 2.81 (2H, d, $J = 4.4$ Hz, 1′-H), 2.28—1.82 (16H, m, 8×C*H*$_2$CH=), 1.73 (3H, s, Me), 1.67 (3H, s, Me), 1.63 (6H, s, 2×Me), 1.59 (9H, s, 3×Me), and 1.55 (3H, s, Me); ^{13}C NMR $\delta = 135.75$, 135.13, 134.84, 131.17, 130.94, 124.47, 124.39, 124.27, 124.18, 123.06, 64.88, 39.81, 39.72, 35.00, 28.94, 26.75, 25.67, 25.64, 18.04, 17.64, 16.11, 15.95, and 15.92; ^{31}P NMR $\delta = 3.78$ (s); negative FAB-MS (glycerol) *m*/*z* 505 [M − (2×Na$^+$) + H$^+$; 100%]. Found: *m*/*z* 505.3461 [M − (2×Na$^+$) + H$^+$], Calcd for $C_{30}H_{50}O_4P$: [M − (2×Na$^+$) + H$^+$], 505.3446.

Cyclohexylammonium (2*Z*,6*E*,10*E*)-2-[(2*E*)-3,7-Dimethyl-2, 6-octadienyl]-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraenyl Hydrogenphosphate (16a). Alcohol **8a** (100 mg, 0.23 mmol) was transformed to **16a** as described for **13a**. Purification by gel filtration using a Sephadex LH-20 column (1.0 cm×62 cm; MeOH) gave **16a** (64 mg, 48% yield from **8a**) as a viscous oil; ^{1}H NMR $\delta = 8.45$ (3H, broad s, NH$_3$), 5.20—4.90 (5H, m, 5×CH=), 4.33 (2H, d, $J = 4.4$ Hz, 1-H), 2.90 (1H, s, N–CH), 2.82 (2H, d, $J = 5.9$ Hz, 1′-H), 2.30—1.82 (18H, m, 8×C*H*$_2$CH= and 2×H on cyclohexane ring), 1.80—1.00 (8H, m, 8×H on cyclohexane ring), 1.67 (6H, s, 2×Me), 1.66 (6H s, 2×Me), and 1.58 (12H, s, 4×Me).

Disodium (2*Z*,6*E*,10*E*)-2-[(2*E*)-3,7-Dimethyl-2,6-octadienyl]-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraenyl Phosphate (17a). Ion-exchange of phosphate **16a** (64 mg, 0.11 mmol) with CM-Sepharose FF (Na$^+$) [1.8 cm×30 cm; eluent: MeOH–CHCl$_3$ (2 : 1)] gave disodium phosphate **17a** (53 mg, 91% yield) as a viscous oil; ^{1}H NMR $\delta = 5.25$—5.00 (4H, m, 4×CH=), 4.95 (1H, br s, CH=), 4.32 (2H, s, 1-H), 2.80 (2H, d, $J = 4.4$ Hz, 1′-H), 2.38—1.78 (16H, m, 8×C*H*$_2$CH=), 1.67 (6H, s, 2×Me), 1.64 (6H, s, 2×Me), 1.59 (6H, s, 2×Me), and 1.57 (6H, s, 2×Me); ^{13}C NMR $\delta = 135.28$, 134.74, 131.11, 130.89, 129.63, 124.44, 124.36, 123.88, 122.63, 64.33, 39.88, 39.75, 33.85, 28.85, 27.59, 26.79, 25.66, 18.89, 17.64, 16.08, 15.97, and 15.91; ^{31}P NMR $\delta = 3.71$; negative FAB-MS (glycerol) *m*/*z* 505 [M − (2×Na$^+$) + H$^+$; 100%]. Found; *m*/*z* 505.3456 [M − (2×Na$^+$) + H$^+$]. Calcd for $C_{30}H_{50}O_4P$: [M − (2×Na$^+$) + H$^+$], 505.3446.

Tetrabutylammonium (6*E*,10*E*)-3-[(3*E*)-4,8-Dimethyl-3,7-nonadienyl]-7,11,15-trimethyl-2,6,10,14-hexadecatetraenyl Hydrogenphosphate (2*E*/2*Z* Mixture) (18a). Alcohol **9a** (139 mg, 0.33 mmol) was transformed to phosphate **18a** as described for phosphate **12a**. The crude product was purified by gel filtration using a Sephadex LH-20 column (2.8 cm×22 cm; MeOH) to give tetrabutylammonium phosphate **18a** (169 mg, 70% yield) as a viscous oil; ^{1}H NMR $\delta = 8.84$ (1H, br s, P–OH), 5.34 (1H, t, $J = 6.1$ Hz, 2-H), 5.05 (5H, broad s, CH=), 4.46 (2H, t, $J = 5.6$ Hz, 1-H), 3.32 (8H, m, $4\times\mathrm{CH_2}$), 2.32—1.80 (20H, m, $10\times\mathrm{C}H_2\mathrm{CH}$=), 1.63 (6H, s, 2×Me), 1.55 (15H, s, 5×Me), 1.76—1.58 (8H, m, $4\times\mathrm{CH_2}$), 1.44 (8H, m, $4\times\mathrm{CH_2}$), and 0.93 (12H, t, J = 7.3 Hz, 4×Me); ^{13}C NMR δ = 139.68, 135.00, 134.88, 134.82, 134.80, 134.71, 131.14, 131.11, 131.07, 124.33, 124.26, 124.23, 124.16, 124.10, 124.05, 61.29, 61.23, 58.45, 39.61, 37.07, 30.91, 27.20, 26.88, 26.85, 26.65, 26.58, 25.57, 23.99, 19.58, 17.55, 15.94, 15.87, and 13.66; ^{31}P NMR δ = 1.91 (s).

Disodium (6*E*,10*E*)-3-[(3*E*)-4,8-Dimethyl-3,7-nonadienyl]-7,11,15-trimethyl-2,6,10,14-hexadecatetraenyl Phosphate (2*E*/2*Z* Mixture) (19a). Ion-exchange of phosphate **18a** (80 mg, 0.11 mmol) with CM-Sepharose FF (Na$^+$) (1.8 cm×25 cm) gave disodium phosphate **19a** (58 mg, 91% yield) as a viscous oil; ^{1}H NMR δ = 5.38 (1H, s, 2-H), 5.09 (5H, broad s, 5×CH=), 4.43 (2H, broad s, 1-H), 2.30–1.74 (20H, m, $10\times\mathrm{C}H_2\mathrm{CH}$=), 1.66 (6H, s, 2×Me), and 1.57 (15H, s, 5×Me); ^{13}C NMR δ = 143.98, 135.31, 135.17, 134.77, 131.12, 131.07, 124.46, 124.43, 124.34, 124.01, 121.12, 62.36, 39.75, 37.36, 31.57, 30.85, 27.38, 26.79, 25.66, 22.65, 17.64, 16.04, 15.99, 15.97, 15.94, and 14.11; ^{31}P NMR δ = 3.56 (s) and 3.42 (s); negative FAB-MS (glycerol) *m*/*z* 505 $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+$, 100%]. Found: *m*/*z* 505.3439 $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+]$. Calcd for $\mathrm{C_{30}H_{50}O_4P}$: $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+]$, 505.3447.

Tetrabutylammonium (2*E*,6*E*,10*E*)-3,7,11,15-Tetramethyl-2-[(2*E*,6*E*)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-2,6,10,14-hexadecatetraenyl Hydrogenphosphate (12b). Alcohol **7b** (90 mg, 0.18 mmol) was transformed to cyclohexylammonium phosphate **12b** as described for **18a**. Purification by gel filtration using a Sephadex LH-20 column (2.8 cm×34 cm; MeOH) gave **12b** (101 mg, 67% yield) as a viscous oil; ^{1}H NMR δ = 8.67 (1H, br s, OH), 5.15—4.90 (6H, m, 6×CH=), 4.32 (2H, d, J = 3.9 Hz, 1-H), 3.30 (8H, m, $4\times\mathrm{CH_2}$), 2.80 (2H, d, J = 7.2 Hz, 1′-H), 2.10—1.78 (20H, m, $10\times\mathrm{C}H_2\mathrm{CH}$=), 1.74—1.46 (8H, m, $4\times\mathrm{CH_2}$), 1.68 (3H, s, Me), 1.62 (6H, s, 2×Me), 1.59 (3H, s, Me), 1.54 (12H, s, 4×Me), 1.52 (3H, s, Me), 1.39 (8H, tq, J = 7.3 and 7.3 Hz, $4\times\mathrm{CH_2}$), and 0.91 (12H, t, J = 7.3 Hz, 4×Me); ^{13}C NMR δ = 134.80, 134.77, 134.58, 133.76, 132.81, 131.14, 131.08, 130.97, 130.82, 124.56, 124.46, 124.39, 124.33, 124.23, 123.74, 63.57, 63.49, 58.69, 39.92, 39.67, 34.96, 28.82, 26.87, 26.69, 26.65, 25.61, 24.06, 19.64, 18.10, 17.59, 16.41, 15.89, 15.87, and 13.71; ^{31}P NMR δ = 1.84 (s).

Disodium (2*E*,6*E*,10*E*)-3,7,11,15-Tetramethyl-2-[(2*E*,6*E*)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-2,6,10,14-hexadecatetraenyl Phosphate (14b). Ion-exchange of phosphate **12b** (101 mg, 0.12 mmol) with CM-Sepharose FF (Na$^+$) [2.8 cm×24 cm; eluent: MeOH–$\mathrm{CHCl_3}$ (2 : 1)] gave disodium phosphate **14b** (73 mg, 95% yield) as a viscous oil; ^{1}H NMR δ = 5.09 (5H, m, 5×CH=), 4.99 (1H, br s, CH=), 4.30 (2H, s, 1-H), 2.82 (2H, s, 1′-H), 2.30—1.82 (20H, m, $10\times\mathrm{C}H_2\mathrm{CH}$=), 1.74 (3H, s, 3-Me), 1.67 (3H, s, Me), 1.66 (6H, s, 2×Me), 1.58 (12H, s, 4×Me), and 1.56 (3H, s, Me); ^{13}C NMR δ = 135.70, 135.14, 134.81, 134.71, 131.14, 131.01, 129.28, 124.47, 124.41, 124.30, 124.18, 123.03, 64.85, 39.85, 39.80, 39.75, 35.03, 29.70, 26.85, 26.78, 25.67, 18.07, 17.64, 16.23, 15.98, and 15.95; ^{31}P NMR δ = 3.97 (s); negative FAB-MS (glycerol) *m*/*z* 573 $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+$, 53%] and 183 (100). Found: *m*/*z* 573.4081 $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+]$. Calcd for $\mathrm{C_{35}H_{58}O_4P}$: $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+]$, 573.4072.

Tetrabutylammonium (2*Z*,6*E*,10*E*)-3,7,11,15-Tetramethyl-2-[(2*E*, 6*E*)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-2,6,10,14-hexadecatetraenyl Hydrogenphosphate (15b). Alcohol **8b** (50 mg, 0.10 mmol) was transformed to tetrabutylammonium phosphate **15b** as described for **12a**. The crude product was purified by gel filtration using a Sephadex LH-20 column (2.8 cm×25 cm; MeOH) to give **15b** (58 mg, 71% yield) as a viscous oil; ^{1}H NMR δ = 6.05 (1H, br s, P–OH), 5.09 (6H, m, 6×CH=), 4.37 (2H, d, J = 4.6 Hz, 1-H), 3.33 (8H, m, $4\times\mathrm{CH_2}$), 2.83 (2H, d, J = 6.8 Hz, 1′-H), 2.32—1.84 (20H, m, $10\times\mathrm{C}H_2\mathrm{CH}$=), 1.80—1.50 (8H, m, $4\times\mathrm{CH_2}$), 1.66 (6H, s, 2×Me), 1.64 (3H, s, Me), 1.62 (3H, s, Me), 1.58 (12H, s, 4×Me), 1.56 (3H, s, Me), 1.43 (8H, tq, J = 7.3 and 7.3 Hz, $4\times\mathrm{CH_2}$), and 0.96 (12H, t, J = 7.3 Hz, 4×Me); ^{13}C NMR δ = 134.85, 134.75, 134.62, 133.83, 131.15, 124.49, 124.43, 124.39, 124.33, 123.38, 63.08, 63.02, 58.77, 39.94, 39.81, 39.71, 34.32, 28.90, 27.69, 26.89, 26.76, 25.66, 24.13, 19.70, 18.72, 17.64, 16.14, 16.01, 15.94, and 13.75; ^{31}P NMR δ = 1.73 (s).

Disodium (2*Z*,6*E*,10*E*)-3,7,11,15-Tetramethyl-2-[(2*E*,6*E*)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-2,6,10,14-hexadecatetraenyl Phosphate (17b). Ion-exchange of phosphate **15b** (58 mg, 0.071 mmol) with CM-Sepharose FF (Na$^+$) [1.8 cm×26 cm; eluent: MeOH–$\mathrm{CHCl_3}$ (2 : 1)] gave disodium phosphate **17b** (44 mg, quantitative yield) as a viscous oil; ^{1}H NMR δ = 5.08 (5H, broad s, 5×CH=), 4.95 (1H, broad s, 2′-H), 4.31 (2H, s, 1-H), 2.79 (2H, s, 1′-H), 2.32—1.76 (20H, m, $10\times\mathrm{C}H_2\mathrm{CH}$=), 1.66 (12H, s, 4×Me), 1.58 (9H, s, 3×Me), and 1.57 (6H, s, 2×Me); ^{13}C NMR δ = 135.27, 134.72, 131.08, 129.76, 124.46, 124.36, 123.88, 122.51, 64.27, 39.87, 39.78, 33.86, 28.88, 27.61, 26.84, 25.67, 18.92, 17.64, 16.18, 15.99, and 15.95; ^{31}P NMR δ = 3.60 (s); negative FAB-MS (glycerol) *m*/*z* 573 $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+$; 100%]. Found: *m*/*z* 573.4080 $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+]$. Calcd for $\mathrm{C_{35}H_{58}O_4P}$: $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+]$, 573.4073.

Tetrabutylammonium (6*E*,10*E*)-7,11,15-Trimethyl-3-[(3*E*,7*E*)-4,8,12-trimethyl-3,7,11-tridecatrienyl]-2,6,10,14-hexadecatetraenyl Hydrogenphosphate (18b). Alcohol **9b** (49 mg, 0.10 mmol) was transformed to tetrabutylammonium phosphate **15b** as described for **12a**. The crude product was purified by gel filtration using a Sephadex LH-20 column (2.8 cm×23 cm; MeOH) to give **18b** (46 mg, 56% yield) as a viscous oil; ^{1}H NMR δ = 7.73 (1H, br s, P-OH), 5.36 (1H, t, J = 6.1 Hz, 2-H), 5.07 (6H, m, 6×CH=), 4.48 (2H, t, J = 5.6 Hz, 1-H), 3.33 (8H, m, $4\times\mathrm{CH_2}$–N), 2.32—1.82 (24H, m, $12\times\mathrm{C}H_2\mathrm{CH}$=), 1.65 (6H, s, 2×Me), 1.58 (18H, s, 6×Me), 1.75—1.52 (8H, m, $4\times\mathrm{CH_2}$), 1.44 (8H, tq, J = 7.3 and 7.3 Hz, $4\times\mathrm{CH_2}$), and 0.96 (12H, t, J = 7.3 Hz, 4×Me); ^{13}C NMR δ = 139.96, 135.10, 134.97, 134.87, 134.78, 131.18, 131.14, 124.40, 124.33, 124.30, 124.18, 124.10, 61.42, 61.36, 58.54, 39.68, 37.15, 30.98, 27.28, 26.94, 26.72, 26.66, 25.64, 24.04, 19.65, 17.62, 16.01, 15.94, and 13.73; ^{31}P NMR δ = 1.84 (s).

Disodium (6*E*,10*E*)-7,11,15-Trimethyl-3-[(3*E*,7*E*)-4,8,12-trimethyl-3,7,11-tridecatrienyl]-2,6,10,14-hexadecatetraenyl Phosphate (19b). Ion-exchange of phosphate **18b** (46 mg, 0.056 mmol) with CM-Sepharose FF (Na$^+$) (2.8 cm×25 cm) gave disodium phosphate **19b** (34 mg, 98% yield) as a viscous oil; ^{1}H NMR δ = 5.37 (1H, broad s, 2-H), 5.09 (6H, broad s, 6×CH=), 4.39 (2H, broad s, 1-H), 2.30—1.76 (24H, m, $12\times\mathrm{C}H_2\mathrm{CH}$=), 1.66 (6H, s, 2×Me), and 1.57 (18H, s, 6×Me); ^{13}C NMR δ = 143.59, 135.44, 135.18, 134.75, 131.10, 124.44, 124.33, 124.00, 121.65, 61.85, 39.84, 39.75, 37.43, 30.85, 27.48, 27.04, 26.89, 26.81, 25.67, 17.64, 16.05, and 15.94; ^{31}P NMR δ = 5.43 (s); negative FAB-MS (glycerol) *m*/*z* 573 $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+$; 100%]. Found: *m*/*z* 573.4080 $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+]$. Calcd for $\mathrm{C_{35}H_{58}O_4P}$: $[\mathrm{M}-(2\times\mathrm{Na}^+)+\mathrm{H}^+]$, 573.4073.

We thank Professors Guy Ourisson and Yoichi Nakatani (Université Louis Pasteur, Strasbourg, France) for valuable suggestions and Dr. Hiroshi Hirota (Fusetani Biofouling Project, JRDC) for measuring the FAB-MS spectra. We are also grateful to Kuraray Co., Ltd. for the gift of farnesol and geranylgeraniol.

References

1) J. K. Volkman, J. W. Farrington, R. B. Gagosian, and S. G. Wakeham, "Advances in Organic Geochemistry 1981," ed by M. Bjoroy, Wiley, Chichester (1983), pp. 228—240; J. N. Robson and S. J. Rowland, *Nature*, **324**, 561 (1986).

2) G. Ourisson and Y. Nakatani, *Chem. Biol.*, **1**, 11 (1994).

3) N. Plobeck, S. Eifler, A. Brisson, Y. Nakatani, and G. Ourisson, *Tetrahedron Lett.*, **33**, 5249 (1992); G. Pozzi, V. Birault, B. Werner, O. Dannenmuller, Y. Nakatani, G. Ourisson, and S. Terakawa, *Angew. Chem., Int. Ed. Engl.*, **35**, 177 (1996).

4) Recently highly branched isoprenoid alkenes have been isolated from diatomaceous algae. J. K. Volkman, S. M. Barrett, and G. A. Dunstan, *Org. Geochem.*, **21**, 407 (1994).

5) E. Lemmich, *Phytochemistry*, **18**, 1195 (1979); H. Nagano, M. Tori, M. Shiota, and J. de Pascual Teresa, *Bull. Chem. Soc. Jpn.*, **57**, 2971 (1984); M. Bruno, L. Lamartina, F. Lentini, C. Pascual, and G. Savona, *Tetrahedron Lett.*, **25**, 4287 (1984); L. Mangoni, D. Merola, P. Monaco, M. Parrilli, and L. Previtera, *Tetrahedron Lett.*, **25**, 2597 (1984).

6) G. R. Kieczykowski, R. H. Schlessinger, and R. B. Sulsky, *Tetrahedron Lett.*, **1976**, 597.

7) A. Castro and T. A. Spencer, *J. Org. Chem.*, **57**, 3496 (1992).

8) L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, **1960**, 2881.

9) L. L. Danilov, T. N. Druzhinina, N. A. Kalinchuk, S. D. Maltsev, and V. N. Shibaev, *Chem. Phys. Lipids*, **51**, 191 (1989).

10) M. Julia, H. Mestdagh, and C. Roland, *Tetrahedron*, **42**, 3841 (1986).

11) V. Birault, Ph.D. Thesis, Université Louis Pasteur, Strasbourg, France, 1995.

12) Recently Poulter has reported the purification of tetrabutylammonium phosphate of presqualene by Sephadex LH-20. D. H. Rogers, E. C. Yi, and C. D. Poulter, *J. Org. Chem.*, **60**, 941 (1995).

13) Phosphates **14a** and **14b** formed liposomes in water, but phosphate **17a** did not. Y. Nakatani, personal communication.