Chemistry of Natural Compounds and Bioorganic Chemistry

Synthesis of dolichyl phosphates with a fluorescent label in the γ-isoprene unit of the chain

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Stereoselective synthesis of the dolichyl phosphate derivatives WT_3C_2S—OP and $WT_2C_{6,7}S$—OP* containing the 1-naphtylamino group in the γ-isoprene unit of the chain was performed. The synthetic scheme includes directed aldol condensation to construct (*E*)-α,β-disubstituted acroleins, their reductive amination with 1-aminonaphthalene, and phosphorylation of the resulting amino alcohols.

Key words: dolichyl phosphates, stereodirected aldol condensation, reductive amination of α,β-disubstituted acroleins, phosphorylation, fluorescent label.

The important role of dolichyl phosphate (Dol—P) and its derivatives in the biosynthesis of carbohydrate chains of glycoproteins accounts for the enhanced interest aroused in recent years in the molecular mechanisms of interaction of these compounds with components of biological membranes and enzymes participating in the assembly of carbohydrate chains. The use of fluorescence methods appears promising in this respect. The first syntheses of Dol—P derivatives containing fluorophoric groups in the ω-unit of the polyisoprene chain were described recently.[1]

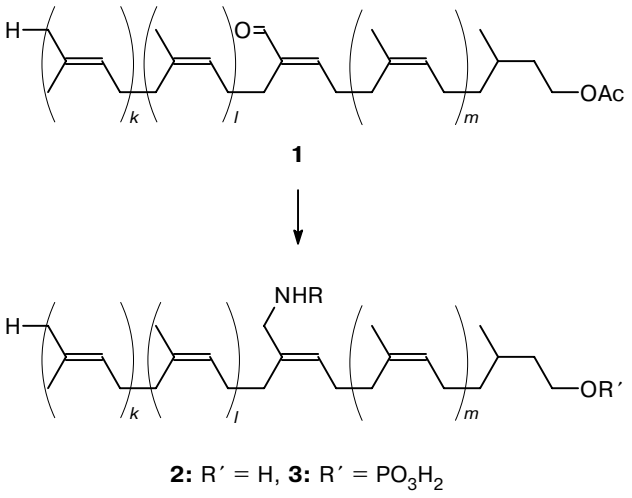
The use of (*E*)-α,β-disubstituted acroleins of type **1**, which are known intermediates in the total synthesis of dolichols, is expedient for the introduction of a fluorescent label into internal units of the polyisoprene chain of Dol—P.[2,3] Indeed, there are strong grounds to believe that reductive amination of aldehydes **1** with fluorescing amines and subsequent phosphorylation of the resulting amino alcohols of type **2** could be used to prepare the target Dol—P derivatives (**3**) containing a fluorescent label in an internal unit of the chain (Scheme 1). The position of the label would be determined by the structure of (*E*)-acrolein **1**.

* In accordance with the abbreviations accepted in the chemistry of polyprenols and dolichols, W means terminal, T means internal (*E*), and C means internal (*Z*) isoprene units; S is the dihydroisoprene unit.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2100—2106, December, 2000.

1066-5285/00/4912-2065 $25.00

Scheme 1



The present study* is devoted to the synthesis of Dol—P derivatives containing a fluorescent label in the methyl group of the γ-isoprene unit of the chain, namely, 11′-(1-naphthylamino) derivatives of dolichyl phosphate WT_3C_2S—OH (**3a**) and a mixture of dolichyl phosphates **3b**, obtained from the polyprenols of birch wood.[5] The choice of the 1-naphthylamine residue as the fluorophore was due to the encouraging results obtained in the first biophysical assays of Dol—P derivatives containing this group in the ω-unit of the polyisoprene chain.[1]

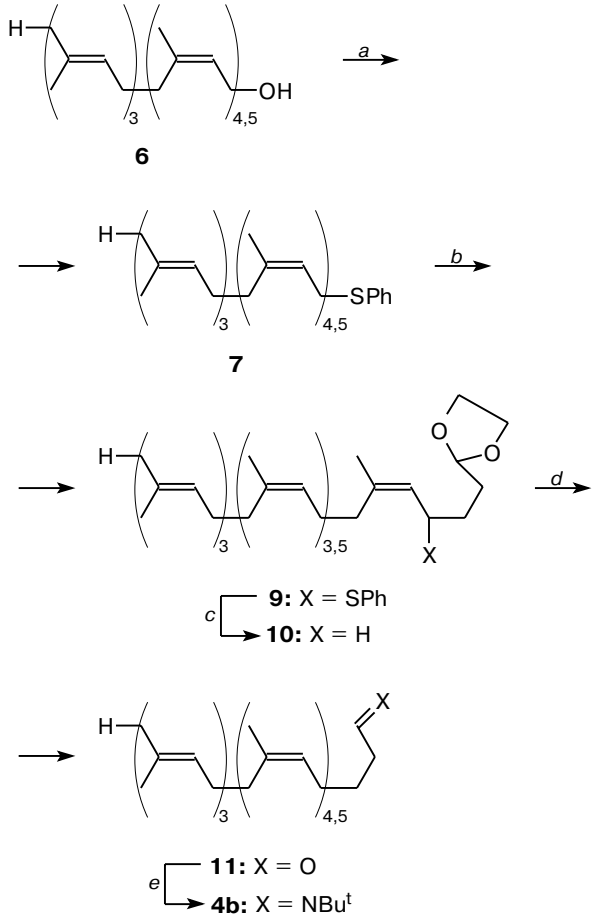
In accordance with the chosen methodology, the starting compounds used for the synthesis of racemic dolichyl phosphates **3a,b** were aldimines **4a,b** and racemic acetoxy aldehyde **5**, which was easily prepared from 2,3-dihydro-6(*Z*)-farnesyl acetate[1] (Schemes 2 and 3). Aldimine **4a** was synthesized as described previously[2,3] from the commercially available 6(*E*),10(*E*)-geranyllinalool. Aldimine **4b** was prepared from a mixture of polyprenols (**6**) isolated from birch wood. According to HPLC, this mixture contains polyprenols WT_2C_4—OH, WT_2C_5—OH, WT_2C_6—OH, and WT_2C_7—OH in 1 : 1 : 0.13 : 0.02 ratio. (Below this mixture is referred to as $WT_2C_{4,5}$—OH.)

Successive treatment of polyprenols **6** (Scheme 2) with BuLi and TsCl in an Et_2O—HMPA mixture (~2.5 : 1) at 0 °C yielded the corresponding tosylates, which were converted without isolation into phenyl sulfides **7** upon treatment with PhSLi. Alkylation of these products with 3-bromopropanal ethylene acetal (**8**) gave rise to 4-phenylthio acetals **9**, whose reductive desulfurization yielded acetals **10**. Hydrolysis of acetals afforded aldehydes **11**, which were converted into *tert*-butylimines **4b** in an overall yield of 39%.

Imines **4a,b** were deprotonated with LDA and condensed with aldehyde **5** (Scheme 3); subsequent treatment of the reaction products with 3.5% HCl resulted in a mixture of acetoxy (*E*)-acroleins (**1a,b**) and hydroxy (*E*)-acroleins (**12a,b**), which were separated by flash chromatography. The contents of (*Z*)-isomers in **1a,b** and **12a,b** did not exceed 3%, as indicated by the integral intensities of the signals of the CHO-group protons for (*E*)- and (*Z*)-isomers in the ^{1}H NMR spectra (δ 9.35 and 10.0, respectively). Upon acetylation under standard conditions, acroleins **12a,b** were quantitatively converted into acetates **1a,b** in overall yields of 40 and 21%.

The attempts to convert acrolein **1a** into aldimine by the reaction with 1-naphthylamine in Et_2O or in THF in the presence of molecular sieves 4 Å for 8 h at ~20 °C, or even for 20 h in boiling THF were unsuccessful. The attempts to perform reductive amination of **1a** by a mixture of 1-naphthylamine with $NaBH(OAc)_3$ by a known procedure[6] or with $ZnBH_4$ on SiO_2 by a known procedure[7] also failed.

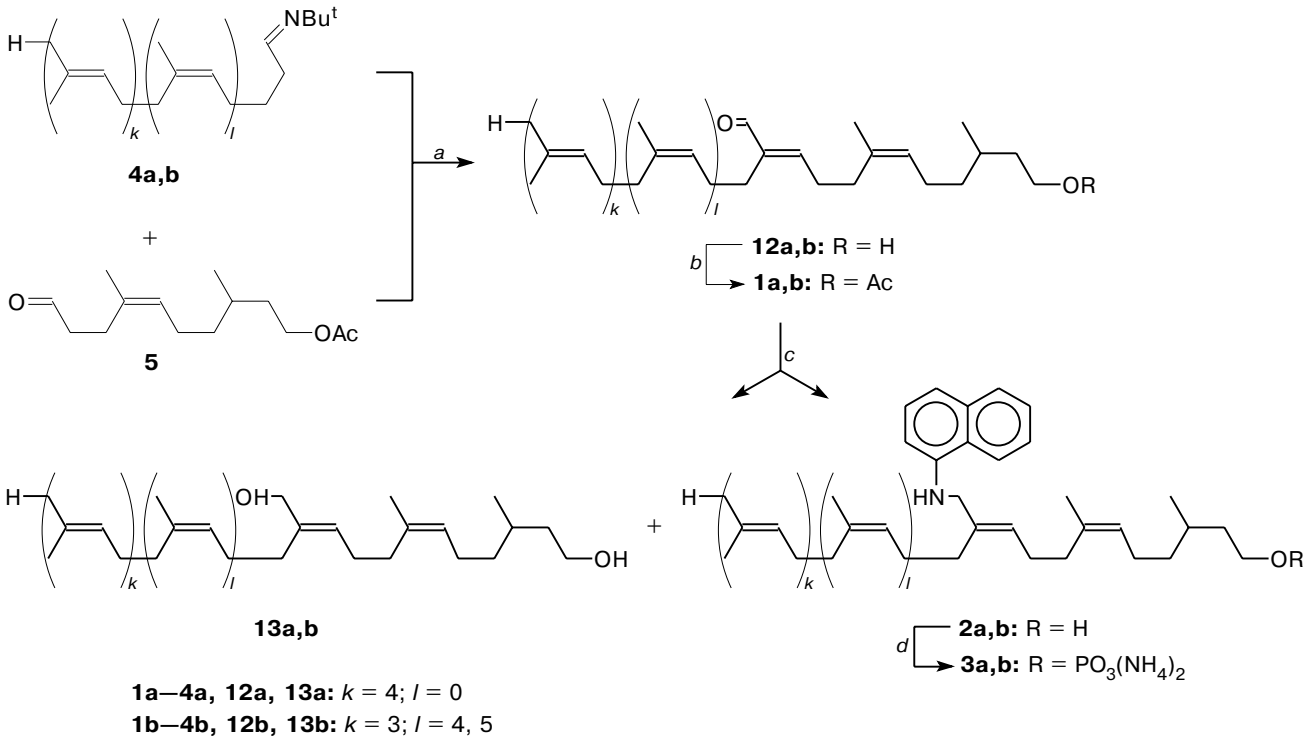
Scheme 2



Reagents and conditions: (*a*) BuLi/hexane—Et_2O—HMPA, 0 °C, then TsCl/HMPA, 0 °C, then PhSLi/HMPA, 0 °C→20 °C; (*b*) BuLi/THF, −70 °C, then $BrCH_2CH_2CH(OCH_2)_2$ (**8**), −70 °C; (*c*) Li/NH_3, −40 °C; (*d*) H_3O^+; (*e*) Bu^tNH_2, molecular sieves 4Å/Et_2O, ~20 °C.

* For preliminary communication, see Ref. 4.

Scheme 3



Reagents and conditions: (*a*) LDA/Et_2O—hexane (1 : 1), −70 °C → −20 °C, 2.5 h, then ~20 °C, 16 h, then 3.5% HCl, 3 h; (*b*) Ac_2O/Py/DMAP; (*c*) 1-naphthylamine, $NaBH_3CN$, AcOH/MeOH for **1a** or AcOH/MeOH—Et_2O for **1b**, then NaOH; (*d*) $(Bu_4N)H_2PO_4$, CCl_3CN/CH_2Cl_2, 20 °C, 48 h.

The use of $NaBH_3CN$ as the reducing agent in this reaction carried out under the conditions recommended previously[8] gave amino alcohol **2a** and diol **13a** in 38 and ~10% yields, respectively. The reductive amination of acrolein **1b**, poorly soluble in MeOH, in an Et_2O—MeOH mixture (1 : 2) yielded amino alcohol **2b** (~20%) and diol **13b** (32%).

The structures of previously unknown compounds **1a,b**, **2a,b**, **4b**, **7**, **9**—**11**, **12a,b**, and **13a,b** were confirmed by the data from IR and ^1H NMR and ^{13}C NMR spectroscopy, which are in good agreement with the results obtained previously for related structures[2,3,9] and with a calculation based on increments.

In the analysis of the ^1H NMR spectra of amino alcohols **2a,b**, it was found that the signals of the protons at the N and C(10) atoms appeared as two resonance bands with close chemical shifts, whose total intensity corresponded to one proton. Doubling of resonance signals can also be seen in the ^{13}C NMR spectra of compounds **2a,b** for some atoms of the naphthalene unit, *viz.*, C(1), C(2), C(4), C(5), and C(6), and for the C(11′) atom of the polyprenol residue. These findings may imply hindered rotation around the C—N bond in amino alcohols **2a,b**. It should be noted that this effect is less pronounced for amino alcohols **2b**, in which the 1-aminonaphthalene substituent is located near the (*Z*)-isoprene ring.

Phosphorylation of compounds **2a,b** was performed by a method that had been previously used successfully for the synthesis of several polyprenyl and dolichyl phosphates[10,11] and is based on treatment with $(Bu_4N)H_2PO_4/CCl_3CN$. In the case of amino alcohols **2a,b**, a much larger excess of the phosphorylating reagent and longer reaction times were required (*cf.* Ref. 1). The ammonium salts of phosphates **3a,b** were isolated using a procedure similar to a procedure reported previously,[1] namely, distribution of the reaction products between *n*-butyl alcohol and water, conversion of the phosphates present in the organic phase into the ammonium salts by treatment with NH_4OH and an excess of a cation-exchange resin, anion-exchange chromatrography on DEAE cellulose (AcO^-) using a solution of $AcONH_4$ in MeOH as the eluent, and removal of excess $AcONH_4$ by precipitation with toluene. The products **3a,b** thus obtained were homogeneous compounds according to TLC; they rapidly decomposed on storage in the solid state but were stable in solutions. For storage and characterization of the products, we used solutions in a heptane—propan-2-ol mixture; the concentration of the compounds was determined from the content of the inorganic phosphate after incineration by $HClO_4$.

The structure of phosphates **3a,b** was confirmed by physicochemical data. UV spectra correspond to those expected for the 1-aminonaphthalene chromophore. As

expected, phosphates **3a,b** exhibit intense fluorescence with the excitation maximum at 340 nm and the emission maximum at 410 nm in a solution in an *n*-hexane—propan-2-ol mixture (~4 : 1). The ^{31}P NMR spectra of compounds **3a,b** contain only one signal at about δ 2—3, corresponding to phosphoric monoester. The ^{1}H and ^{13}C NMR spectra of phosphates **3a,b** are similar to the spectra of amino alcohols **2a,b**; the observed differences are in the chemical shifts of H(1) and C(1), which are typical of polyprenyl phosphates compared with polyprenols.[11] In the mass spectra of compound **3a**, recorded with electrospray ionization (ESI), the main signals correspond to the molecular ion of the corresponding acid (*m/z* 716 for the negative-ion spectrum and 718 for the positive-ion spectrum).

Experimental

UV spectra were recorded on a Specord UV-Vis spectrometer, IR spectra were measured on a Perkin—Elmer 577 spectrometer in solutions in CCl_4 or $CDCl_3$. ^{1}H and ^{13}C NMR spectra were run in $CDCl_3$ with respect to Me_4Si on Bruker AC-200 and Bruker DRX-500 spectrometers (^{1}H, 200 and 500 MHz; ^{13}C, 50.3 and 125.8 MHz, respectively); ^{31}P NMR spectra were measured with respect to 85% H_3PO_4 (external standard, Bruker DRX-500 instrument, operating frequency for phosphorus 202.5 MHz). EI mass spectra were obtained on a Varian MAT 311A spectrometer at 70 eV (for $m/z < 200$, peaks with relative intensity of >10% are given). Preparative flash chromatography was performed on silica gel L 40—100 μm (Chemapol, Czechia), TLC was carried out on Silufol plates (Kavalier, Czechia) in the following systems: benzene (*A*), hexane—Bu^{t}OMe (2 : 1) (*B*), hexane—Bu^{t}OMe (1 : 1) (*C*), hexane—Bu^{t}OMe (2 : 3) (*D*) or on Silica Gel 60 (Merck, Germany) plates (5×2 cm) in the $CHCl_3$—MeOH—H_2O solvent system (60 : 25 : 4) (*E*). Fluorescence of compounds on the plates was detected under a UV lamp; unsaturated compounds were visualized by $KMnO_4$ or iodine vapor, phosphates were detected using the Vaskovsky spray reagent[12] with subsequent heating of the plates. Analytical and preparative HPLC were carried out on Silasorb C-8 columns (250×24 mm, 10 μm) using an acetonitrile—acetone (4 : 1) mixture as the eluent and a refractometric detector; the eluent flow rate was 7 mL min^{-1}. Column anion-exchange chromatography of the phosphates was carried out on DE-52 DEAE cellulose (Whatman, UK). Colorimetric determination of the phosphates was done using a reagent described previously[13] after heating of the sample for 15 min at 200 °C with 57% perchloric acid.

The sample of birch polyprenols **6** was kindly provided by A. V. Kuchin (Komi Scientific Center, Ural Branch of the RAS). Components of the mixture were identified by HPLC under the conditions mentioned above with comparison with authentic samples of individual polyprenols.

Experiments with the use of BuLi were carried out under argon using glassware heated at 160 °C for 12 h and cooled in an argon flow.

The main solvents were purified as follows: diethyl ether and THF were kept over KOH, distilled successively from Na and from $LiAlH_4$, refluxed under argon with benzophenone Na ketyl until a persistent blue color appeared, and distilled directly into the reaction vessels. Hexane and benzene were distilled from Na. HMPA (Fluka) was distilled *in vacuo*.

The usual workup of organic extracts involves washing until the pH of the wash water was ~5, drying with $MgSO_4$, and concentration *in vacuo*.

Phenyl polyprenyl sulfide (7). A 1.36 *M* solution of BuLi (12 mL, 16.3 mmol) in hexane was added dropwise at 0 °C to a stirred solution of a mixture of polyprenols **6** (5.83 g, ~11 mmol) in 40 mL of HMPA and 170 mL of diethyl ether, the mixture was stirred for 10 min, and a solution of TsCl (2.67 g, 14 mmol) in 30 mL of HMPA was added dropwise at the same temperature. The mixture was stirred for 2 h at 0 °C and a solution of PhSLi, prepared from Li (0.11 g) and PhSH (1.56 g) in 35 mL of HMPA by a standard procedure, was added dropwise at the same temperature. The mixture was warmed to ~20 °C, stirred for an additional 2 h, and poured into a vigorously stirred mixture of 150 mL of ice water and 150 mL of Bu^{t}OMe. The resulting mixture was stirred for 15 min and the layers were separated. The aqueous layer was extracted with Bu^{t}OMe. The usual workup of the combined extracts gave 7.0 g of a mixture of products, which was chromatographed on 150 g of SiO_2. Gradient elution (hexane → benzene) gave sulfide **7**. After drying *in vacuo* to a constant mass (1.5 Torr, 6 h), the yield was 4.73 g (73%), R_f 0.72 (*A*), 0.66 (*B*). IR, ν/cm^{-1}: 3080, 3060, 3040, 2965, 2925, 2860, 2730 (w), 2380 (br.), 1665, 1585, 1480, 1450, 1440, 1380, 1095, 1030, 845, 745, 700. ^{1}H NMR, δ: 1.66 (s, 9 H, *cis*-Me); 1.73 (s, 13.5 H, *trans*-Me); 1.75 (s, 3 H, MeC(3)); 2.07 (m, 26 H, CH_2); 3.60 (d, 2 H, $H_2C(1)$, J = 7.5 Hz); 5.16 (m, 6.5 H, HC=C); 5.38 (t, 1 H, HC(2), J = 7.5 Hz); 7.3 (m, 5 H, Ph). ^{13}C NMR, δ: 16.0 (*cis*-Me); 17.7 (*cis*-Me of ω-units); 23.4 (*trans*-Me); 25.7 (*trans*-Me of ω-units); 26.3, 26.4, 26.6, 26.7 ($\underline{C}H_2CH$=C); 31.6, 31.8, 32.0, 32.2 ($H_2\underline{C}C$(Me)=C of (*Z*)-units); 39.7 ($H_2\underline{C}C$(Me)=C of (*E*)-units); 124.1, 124.2, 124.4, 124.6, 124.9, 125.8 (H$\underline{C}$=C); 131.2 (Me$\underline{C}$=C of ω-units); 134.9, 135.1, 135.2, 135.3, 135.6 (Me$\underline{C}$=C); 139.9 (C(3)).

4-(Phenylthio)trishomopolyprenal ethylene acetal (9). Tetrahydrofuran (140 mL) was added to a solution of sulfide **7** (4.73 g, 7.63 mmol) in 10 mL of THF dried for 2 days over molecular sieves 4 Å under argon. The mixture was cooled with stirring to −70 °C and a 1.36 *M* solution of BuLi (11 mL, ~15 mmol) in hexane was added over a period of 30 min. The mixture was stirred for 4 h at −70 °C and a solution of bromide **8**[14] (3.26 g, 18 mmol) was added over a period of 20 min at the same temperature. The reaction mixture was stirred for 2 h, allowed to stand for 12 h at −20 °C, and poured into a vigorously stirred mixture of 150 mL of water and 150 mL of Bu^{t}OMe. The resulting mixture was stirred for 10 min, the organic layer was separated, and the aqueous layer was extracted with Bu^{t}OMe. The usual workup of the combined organic extracts gave 7.5 g of a mixture of products, from which excess bromide **8** was distilled off *in vacuo* (1 Torr), and the residue was chromatographed on 100 g of SiO_2. Gradient elution (hexane → benzene) yielded acetal **9**, which was dried to a constant mass *in vacuo* (1 Torr, 5 h), yield 3.21 g (~60%), R_f 0.44 (*A*). IR, ν/cm^{-1}: 3040, 2960, 2930, 2860, 2740, 1665, 1580, 1480, 1450, 1440, 1380, 1130, 1095, 1040, 1030, 845, 710, 685. ^{1}H NMR, δ: 1.58 (s, 9 H, *cis*-Me); 1.70 (s, 16.5 H, *trans*-Me); 1.85 (m, 4 H, $H_2C(2)$, $H_2C(3)$); 2.03 (m, 26 H, CH_2); 3.85 (m, 5 H, CH_2O, HC(4)); 4.85 (t, 1 H, HC(1), J = 4.5 Hz); 5.12 (m, 7.5 H, HC=C); 7.35 (m, 5 H, Ph). ^{13}C NMR, δ: 15.9 (*cis*-Me); 17.6 (*cis*-Me of ω-units); 23.1, 23.3, 23.4 (*trans*-Me); 25.6 (*trans*-Me of ω-units); 26.0, 26.4, 26.6, 26.7, 27.0 ($\underline{C}H_2CH$=C); 29.75 (C(3)); 31.6, 31.9, 32.1, 32.2, 32.3 ($H_2\underline{C}C$(Me)=C of (*Z*)-units); 39.7 ($H_2\underline{C}C$(Me)=C of (*E*)-units); 46.7 (C(4)); 64.8 (CH_2O); 104.2 (C(1)); 124.1, 124.2, 124.3, 124.9, 127.1, 133.6 (H$\underline{C}$=C); 131.15 (Me$\underline{C}$=C of ω-units); 134.65, 135.1, 135.2, 135.4 (Me$\underline{C}$=C); 138.3(C(6)).

Trishomopolyprenal ethylene acetal (10). A solution of compound **9** (3.11 g, 4.32 mmol) in 5 mL of diethyl ether was added dropwise at −50 °C to a stirred solution of Li (250 mg) in 70 mL of liquid NH_3, the mixture was stirred for 5 h at −40 °C, then NH_4Cl was added until the solution decolorized, and NH_3 was evaporated. Water (40 mL) and Bu^{t}OMe (40 mL) were added to the residue, the mixture was stirred for 10 min, the organic layer was separated, and the aqueous layer was extracted with Bu^{t}OMe. The usual workup of the combined organic extracts gave 3.06 g of a mixture of products, which was chromatographed on 100 g of SiO_2. Gradient elution (hexane → benzene) gave 2.36 g (~90%) of acetal **10**, R_f 0.50 (*A*). IR, ν/cm^{-1}: 3040, 2965, 2930, 2860, 2360 (br), 1450, 1440, 1380, 1140, 1040, 945, 840. ^{1}H NMR, δ: 1.50 (m, 2 H, $H_2C(3)$); 1.60 (s, 9 H, *cis*-Me); 1.65 (m, 2 H, $H_2C(2)$); 1.69 (s, 16.5 H, *trans*-Me); 2.08 (m, 28 H, CH_2); 3.90 (m, 4 H, CH_2O); 4.86 (t, 1 H, HC(1), J = 5 Hz); 5.15 (m, 7.5 H, HC=C). ^{13}C NMR, δ: 15.9 (*cis*-Me); 17.6 (*cis*-Me of ω-units); 23.35 (*trans*-Me); 25.6 (*trans*-Me of ω-units); 24.3, 26.4, 26.6, 26.7, 27.55 (CH_2); 31.9, 32.2 ($H_2\underline{C}C(Me)$=C of (*Z*)-units); 33.5 (C(2)); 39.7 ($H_2\underline{C}C(Me)$=C of (*E*)-units); 64.75 (CH_2O); 104.6 (C(1)); 124.1, 124.2, 124.4, 124.9, 125.0, 128.25 (H$\underline{C}$=C); 131.1 (Me$\underline{C}$=C of ω-units); 134.8, 135.1, 135.2, 135.4 (Me$\underline{C}$=C).

Trishomopolyprenal (11). A solution of 0.07 mL of concentrated H_2SO_4 in 15 mL of water was added to a solution of acetal **10** (2.32 g, 3.8 mmol) in 120 mL of acetone stirred under argon, and the mixture was refluxed for 5 h. The reaction mixture was cooled and neutralized with Na_2CO_3, acetone was evaporated *in vacuo*, and the aqueous residue was extracted with Bu^{t}OMe. The usual workup of the combined organic extracts gave 2.16 g (~100%) of an oily aldehyde **11** containing ~5% acetal **10** (^{1}H NMR data). This mixture was used in the synthesis of imine **4b** without further purification. Aldehyde **11**, R_f 0.51 (*A*). IR, ν/cm^{-1}: 3040, 2980, 2930, 2860, 2720, 1730, 1660, 1450, 1400, 1380, 1120, 1090, 1040, 840, 690. ^{1}H NMR, δ: 1.58 (s, 9 H, *cis*-Me); 1.63 (m, 2 H, $H_2C(3)$); 1.69 (s, 16.5 H, *trans*-Me); 2.08 (m, 28 H, CH_2); 2.42 (td, 2 H, $H_2C(2)$, J_1 = 7.5 Hz, J_2 = 1.5 Hz); 5.13 (m, 7.5 H, HC=C); 9.75 (t, 1 H, CHO, J = 1.5 Hz). ^{13}C NMR, δ: 15.9 (*cis*-Me); 17.6 (*cis*-Me of ω-units); 22.4 (C(3)); 23.4 (*trans*-Me); 25.6 (*trans*-Me of ω-units); 26.2, 26.4, 26.6, 26.7, 27.0 ($\underline{C}H_2CH$=C); 31.9, 32.1 ($H_2\underline{C}C(Me)$=C of (*Z*)-units); 39.7 ($H_2\underline{C}C(Me)$=C of (*E*)-units); 43.35 (C(2)); 124.1, 124.2, 124.3, 124.95 (H$\underline{C}$=C); 131.1 (Me$\underline{C}$=C of ω-units); 134.8, 135.05, 135.1, 135.2, 136.3 (Me$\underline{C}$=C); 202.4 (C(1)).

Trishomopolyprenal *N*-*tert*-butylimine (4b). Molecular sieves 4 Å (2.2 g) and *tert*-butylamine (1 mL) were added to a solution of aldehyde **11** (2.16 g, 3.8 mmol) in 50 mL of diethyl ether and the mixture was stirred for 10 h. The molecular sieves were filtered off and thoroughly washed with diethyl ether. The filtrate was concentrated and the residue was dried *in vacuo* to a constant mass (1 Torr, 5 h) to give 2.36 g (~100%) of aldimine **4b** containing ~5% acetal **10** (^{1}H NMR data). The solution of the resulting imine **4b** in 5 mL of diethyl ether was kept for 2 days over molecular sieves 4 Å at 4 °C and used in the synthesis of **1b** without further purification. Aldimine **4b**, IR, ν/cm^{-1}: 3160, 3040, 2970, 2930, 2860, 2740, 2260, 2200, 1720, 1665, 1450, 1380, 1220, 1110, 1095, 1040, 930, 890, 850, 700, 660, 650. ^{1}H NMR, δ: 1.15 (s, 9 H, Me_3C); 1.60 (m, 2 H, $H_2C(3)$); 1.65 (s, 9 H, *cis*-Me); 1.72 (s, 16.5 H, *trans*-Me); 2.05 (m, 28 H, CH_2); 2.26 (m, 2 H, $H_2C(2)$); 5.11 (m, 7.5 H, HC=C); 7.60 (t, 1 H, HC(1), J = 5 Hz). ^{13}C NMR, δ: 16.0 (*cis*-Me); 17.7 (*cis*-Me of ω-units); 23.35 (*trans*-Me); 25.6 (*trans*-Me of ω-units); 26.3, 26.5, 26.6, 26.8, 27.3 ($\underline{C}H_2CH$=C and C(3)); 29.6 ($\underline{Me}_3C$); 31.9, 32.1 ($H_2\underline{C}C(Me)$=C of (*Z*)-units); 36.15 (C2)); 39.7 ($H_2\underline{C}C(Me)$=C of (*E*)-units); 56.5 ($Me_3\underline{C}$); 124.0, 124.1, 124.3, 124.7, 124.9, 125.0 (H$\underline{C}$=C); 131.2 (Me$\underline{C}$=C of ω-units); 134.9, 135.2, 135.3, 135.6 (Me$\underline{C}$=C); 199.1 (C(1)).

12-Acetoxy-6,10-dimethyl-2-(4,8,12,16-tetramethylheptadeca-3(*E*),7(*E*),11(*E*),15-tetraenyl)dodeca-2(*E*),6(*Z*)-dienal (1a) and 12-hydroxy-6,10-dimethyl-2-(4,8,12,16-tetramethylheptadeca-3(*E*),7(*E*),11(*E*),15-tetraenyl)dodeca-2(*E*),6(*Z*)-dienal (12a). A solution of imine **4a** [2,3] (4.21 g, 11 mmol) in 10 mL of diethyl ether was added dropwise at −10 °C over a period of 1 h to a stirred solution of LDA (12 mmol), freshly prepared from BuLi and Pr^i_2NH by a standard procedure, in 20 mL of a mixture of hexane and diethyl ether (1 : 1). The bright-yellow reaction mixture was warmed up to 0 °C, stirred for 40 min, and cooled to −70 °C. A solution of acetoxy aldehyde **5** [1] (2.09 g, 8.7 mmol) in 10 mL of diethyl ether was added dropwise, and the mixture was stirred for 2 h at −70 °C, warmed up to −20 °C over a period of 2.5 h, and allowed to stand for 16 h at 20 °C. The reaction mixture was poured into a vigorously stirred mixture of 50 mL of 3.5% HCl and 50 mL of Bu^{t}OMe, the resulting mixture was stirred for 3 h, the organic layer was separated, and the aqueous layer was extracted with Bu^{t}OMe. The usual workup of the combined organic extracts gave 5.18 g of a mixture of products as a yellow oil, which was chromatographed on 100 g of SiO_2. Gradient elution (hexane → benzene → Bu^{t}OMe) gave 0.45 g of acetoxy acrolein **1a**, 0.44 g of a mixture (~1 : 1) of **1a** with hydroxy acrolein **12a**, and 0.87 g of compound **12a**.

Pyridine (0.5 mL), Ac_2O (0.38 mL), and DMAP (30 mg) was added with stirring at 0 °C to a solution of the obtained mixture **1a**+**12a** and **12a** in 5 mL of diethyl ether, the mixture was stirred for 4 h at ~20 °C and poured into 5 mL of ice water, and the resulting mixture was stirred for 10 min and extracted with Bu^{t}OMe. The usual workup of the combined extracts gave 1.37 g of acetoxy acrolein **1a,** identical with the above-mentioned sample, according to spectral data. The total yield of **1a** is 1.82 g (~40%). Acetoxyacrolein **1a**, R_f 0.87 (*D*). IR, ν/cm^{-1}: 3025, 3005, 2975, 2935, 2860, 2740, 2720, 1735, 1680, 1640, 1450, 1380, 1370, 1260, 1240, 1215, 1150, 1110, 1060, 1035, 980, 900, 840. ^{1}H NMR, δ: 0.92 (d, 3 H, MeC(10), J = 6.5 Hz); 1.05—1.50 (m, 5 H, $H_2C(9)$, $H_2C(11)$, HC(10)); 1.62 (s, 12 H, *cis*-Me); 1.71 (s, 6 H, *trans*-Me); 2.0 (m, 16 H, CH_2C=C); 2.01 (s, 3 H, MeCO); 2.25 (m, 4 H, $H_2C(5)$, $H_2C(1')$); 2.45 (pseudo-q, 2 H, $H_2C(4)$, J_1 = J_2 = 7 Hz); 4.09 (td, 2 H, $H_2C(12)$, J_1 = 7 Hz, J_2 = 2.5 Hz); 5.12 (m, 5 H, HC=C); 6.43 (t, 1 H, HC(3), J = 7 Hz); 9.34 (s, 1 H, HC(1)). ^{13}C NMR, δ: 15.9 (*cis*-Me); 17.5 (*cis*-MeC(16′)); 19.3 ($\underline{Me}$C(10)); 20.9 ($\underline{Me}$CO); 23.1 ($\underline{Me}$C-6); 24.2 (C(1′)); 25.5 (*trans*-MeC(16′)); 25.2, 25.6, 26.0, 26.7, 27.0, 27.3 ($\underline{C}H_2CH$=C); 29.5 (C(10)); 30.6 (C(5)); 35.4 (C(9)); 37.1 (C(11)); 39.6 ($H_2\underline{C}C(Me)$=C of (*E*)-units); 62.8 (C(12)); 123.2, 124.2, 124.35, 126.6 (H$\underline{C}$=C); 131.1 (C(16′)); 133.2, 134.8, 134.9, 136.0 (Me$\underline{C}$=C); 143.3 (C(2)); 154.3 (C(3)); 171.0 ($\underline{C}$OMe); 194.9 (C(1)). MS (EI, 70 eV), *m/z*: 492 [M − AcOH]$^+$. Hydroxyacrolein **12a**, R_f 0.60 (*D*). IR, ν/cm^{-1}: 3620, 3480, 3030, 3005, 2970, 2930, 2860, 2730, 1720, 1680, 1640, 1450, 1380, 1265, 1255, 1240, 1145, 1115, 1080, 1060, 1000, 990, 900, 870, 850. ^{1}H NMR, δ: 0.92 (d, 3 H, MeC(10), J = 6.45 Hz); 1.05—1.55 (m, 5 H, $H_2C(9)$, $H_2C(11)$, HC(10)); 1.60 (s, 12 H, *cis*-Me); 1.69, 1.72 (both s, each 3 H, *trans*-Me); 2.02 (m, 16 H, CH_2C=C); 2.25 (m, 4 H, $H_2C(5)$, $H_2C(1')$); 2.46 (pseudo-q, 2 H, $H_2C(4)$, J_1 = J_2 = 7.5 Hz); 3.70 (td, 2 H, $H_2C(12)$, J_1 = 6.7 Hz, J_2 = 2.5 Hz); 5.12 (m, 5 H, HC=C); 6.45 (t, 1 H, HC(3), J = 7.5 Hz); 9.38 (s, 1 H, CHO). MS (EI, 70 eV), *m/z*: 510 [M]$^+$.

Acetoxyacrolein (1b). Condensation of aldimine **4b** (2.35 g, 3.8 mmol) with aldehyde **5** (0.91 g, ~4 mmol) under the conditions described above gives 0.40 g of acetoxyacrolein **1b**

and 0.23 g of a *ca.* 3 : 1 mixture of **1b** and **12b**, which was converted into 0.24 g of compound **1b** as described above. Acetoxyacrolein **1b**, yield 21%, R_f 0.26 (*A*). UV (EtOH), λ/nm (ε): 212.8 (30600), 214.4 (31000), 236.2 (11400). IR, ν/cm^{-1}: 3040, 2970, 2920, 2860, 2740, 2720, 1740, 1690, 1680, 1640, 1450, 1380, 1370, 1335 (w), 1315 (w), 1240, 1135, 1090, 1060, 1040, 990, 975, 960, 900, 850. ^{1}H NMR, δ: 0.93 (d, 3 H, MeC(10), J = 6.5 Hz); 1.10—1.60 (m, 5 H, H_2C(9), H_2C(11), HC(10)); 1.59 (s, 9 H, *cis*-Me); 1.68 (s, 19.5 H, *trans*-Me); 2.0 (m, 33 H, CH_2C=C, MeCO); 2.20 (m, 4 H, H_2C(5), H_2C(1′)); 2.45 (pseudo-q, 2 H, H_2C(4), J_1 = J_2 = 7 Hz); 4.11 (td, 2 H, H_2C(12), J_1 = 7 Hz, J_2 = 2.5 Hz); 5.15 (m, 8.5 H, HC=C); 6.45 (t, 1 H, HC(3), J = 7 Hz); 9.35 (s, 0.97 H, HC(1) of (*E*)-isomer); 10.10 (s, 0.03 H, CHO of (*Z*)-isomer). ^{13}C NMR, δ: 15.9 (*cis*-Me); 17.6 (*cis*-Me of ω-units); 19.3 (MeC(10)); 20.9 (MeCO); 23.1 (MeC(6)); 23.4 (*trans*-Me); 24.4 (C(1′)); 25.6 (*trans*-Me of ω-units); 25.2, 26.3, 26.6, 26.7, 26.8, 27.0, 27.3 (CH_2CH=C); 29.4 (C(10)); 30.5, 31.9, 32.1 (H_2CC(Me)=C of (*Z*)-units); 35.3 (C(9)); 37.1 (C(11)); 39.7 (H_2CC(Me)=C of (*E*)-units); 62.8 (C(12)); 124.1, 124.15, 124.3, 124.4, 124.95, 126.6 (HC=C); 131.15 (MeC=C of ω-units); 133.2, 134.8, 135.1, 135.3 135.95 (MeC=C); 143.6 (C(2)); 154.45 (C(3)); 171.0 (COMe); 194.9 (C(1)).

3,7,15,19,23,27-Hexamethyl-11-(1-naphthylamino)methyloctacosa-6(*Z*),10(*E*),14(*E*),18(*E*),22(*E*),26-hexaen-1-ol (2a) and 11-hydroxymethyl-3,7,15,19,23,27-hexamethyloctacosa-6(*Z*),10(*E*),14(*E*),18(*E*),22(*E*),26-hexaen-1-ol (13a). Acetic acid (0.033 mL), acrolein **1a** (320 mg, 0.58 mmol), and $NaBH_3CN$ (Fluka) (59.8 mg, 0.95 mmol) were added successively to a solution of 1-naphthylamine (165.9 mg, 1.16 mmol) in 2 mL of anhydrous MeOH stirred under argon at ~20 °C. The mixture was stirred for 92 h, concentrated HCl was added dropwise to pH 2, the mixture was stirred for 10 min, NaOH (0.6 g) was added to pH 10, the mixture was stirred for an additional 15 min, and MeOH was evaporated *in vacuo*. Water (5 mL) was added to the residue and the product was extracted with Bu^{t}OMe. The usual workup of the combined extracts gave 0.36 g of a mixture of products as a red oil, which was chromatographed on 20 g of SiO_2. Gradient elution (hexane → benzene → Bu^{t}OMe) yielded 140 mg (37%) of amino alcohol **2a** and 20 mg (8%) of diol **13a**. Amino alcohol **2a**, R_f 0.45 (*C*). IR, ν/cm^{-1}: 3610, 3060, 2965, 2930, 2860, 2740 (w), 1585, 1530, 1480, 1460, 1450, 1410, 1380, 1280, 1250, 1120, 1060, 930, 850, 790, 780. ^{1}H NMR, δ*: 0.91 (d, 3 H, MeC(3), J = 6.6 Hz); 1.10—1.60 (m, 5 H, H_2C(2), H_2C(4)), HC(3)); 1.65 (s, 12 H, *cis*-Me); 1.72 (s, 6 H, *trans*-Me); 2.05 (m, 18 H, CH_2C=C); 2.27 (m, 4 H, H_2C(9), H_2C(12)); 3.20, 3.23 (both s, in total 1 H, NH); 3.63 (dt, 2 H, H_2C(1), J_1 = 1.5 Hz, J_2 = 7 Hz); 3.87 (br.s, 2 H, CH_2N); 5.14 (m, 5 H, HC=C); 5.45, 5.55 (both t, in total 1 H, HC(10), J_1 = 5 Hz, J_2 = 7 Hz). ^{13}C NMR, δ**: 16.0, 16.1 (*cis*-Me); 17.6 (*cis*-MeC(27)); 19.5 (MeC(3)); 23.4 (MeC(7)); 25.1, 25.3, 26.2, 26.6, 26.7, 27.2 (CH_2CH=C); 25.7 (*trans*-MeC(27)); 29.2, 29.4 (C(3), C(12)); 31.8 (C(8)); 37.4 (C(4)); 39.7 (CH_2C(Me)=C of (*E*)-units); 39.8 (C(2)); 47.5, 50.0 (C(11′)); 61.1 (C(1)); 123.8, 124.2, 124.4, 125.5, 125.55, 127.1 (HC=C); 131.2 (C(27)); 134.2, 134.6, 135.0, 135.4, 136.2 (MeC=C). Diol **13a**, R_f 0.17 (*C*). IR, ν/cm^{-1}: 3610, 3430, 3050, 2970, 2930, 2860, 2260, 1715 (w), 1660 (w), 1630 (w), 1585, 1530, 1480, 1465, 1450, 1410, 1380, 1280, 1255 (w), 1060, 930 (w), 850, 790, 780. ^{1}H NMR, δ: 0.91 (d, 3 H, MeC(3), J = 6.5 Hz); 1.05—1.65 (m, 5 H, H_2C(2), H_2C(4), HC(3)); 1.61 (s, 12 H, *cis*-Me); 1.70 (s, 6 H, *trans*-Me); 2.08 (m, 22 H, CH_2C=C); 3.66 (dt, 2 H, H_2C(1), J_1 = 3 Hz, J_2 = 6.5 Hz); 4.05 (s, 2 H, HOCH_2C(11)); 5.02 (m, 5 H, HC=C); 5.42 (t, 1 H, HC(10), J = 7 Hz).

11′-(1-Naphthylamino)dolichol-10,11 (2b) and 11′-hydroxydolichol-10,11 (13b)* were prepared similarly to **2a** and **13a** by reductive amination of acrolein **1b** (380 mg, 0.48 mmol) on treatment with 1-naphthylamine and $NaBH_3CN$ in a Et_2O—MeOH mixture (1 : 2). Amino alcohol **2b**, yield ~20%, R_f 0.60 (*B*). IR, ν/cm^{-1}: 3620, 3030, 2965, 2935, 2920, 2860, 2735, 1720 (w), 1680 (w), 1665 (w), 1630 (w), 1585, 1520, 1460, 1450, 1410, 1380, 1280 (w), 1240 (w), 1090 (w), 1060 (w), 1045 (w), 855, 845, 840. ^{1}H NMR, δ: 0.90 (d, 3 H, MeC(3), J = 6.5 Hz); 0.95—1.55 (m, 5 H, H_2C(2), H_2C(4), HC(3)); 1.57 (s, 9 H, *cis*-Me); 1.65 (s, 19.5 H, *trans*-Me); 2.01 (m, 32 H, CH_2C=C); 2.20 (m, 4 H, H_2C(9), H_2C(12)); 3.21, 3.33 (both s, in total 1 H, NH); 3.70 (dt, 2 H, H_2C(1), J_1 = 1.5 Hz, J_2 = 7 Hz); 3.87 (s, 2 H, CH_2N); 5.13 (m, 8.5 H, HC=C); 5.41 and 5.53 (both t, in total 1 H, HC(10), J_1 = 5 Hz, J_2 = 7 Hz). ^{13}C NMR, δ: 16.0 (*cis*-Me); 17.7 (*cis*-Me of ω-units); 19.5 (MeC(3)); 23.4 (*trans*-Me); 25.7 (*trans*-Me of ω-units); 25.1, 26.2, 26.4, 26.6, 26.7, 27.0 (CH_2CH=C); 29.1 (C(3)); 29.6 (C(12)); 31.8, 31.9, 32.2 ((CH_2C(Me)=C of (*Z*)-units); 37.4 (C(4)); 39.7 (CH_2C(Me)=C of (*E*)-units); 39.8 (C(2)); 50.0 (CN); 61.0 (C(1)); 123.8, 124.1, 124.2, 124.3, 124.7, 124.9, 125.6, 125.7, 127.1, 128.8 (HC=C); 131.2 (MeC=C of ω-units); 134.2, 134.6, 135.15, 135.2, 135.3, 135.7, 136.0 (MeC=C). Diol **13b**, yield 32%, R_f 0.24 (*B*), 0.42 (*C*). IR, ν/cm^{-1}: 3615, 3350, 3020, 2960, 2920, 2860, 2730, 1720 (w), 1660 (w), 1450, 1380, 1360, 1340 (w), 1310 (w), 1130 (w), 1065, 1010, 895 (w), 850. ^{1}H NMR, δ: 0.92 (d, 3 H, MeC(3), J = 6.2 Hz); 1.0—1.60 (m, 5 H, H_2C(2), H_2C(4), HC(3)); 1.59 (s, 9 H, *cis*-Me); 1.70 (s, 19.5 H, *trans*-Me); 2.08 (m, 32 H, CH_2C=C); 3.65 (dt, 2 H, H_2C(1), J_1 = 2.5 Hz, J_2 = 7 Hz); 4.02 (s, 2 H, HOCH_2C(11)); 5.12 (m, 8.5 H, HC=C); 5.43 (t, 1 H, HC(10), J = 7 Hz). ^{13}C NMR, δ: 15.9 (*cis*-Me); 17.6 (*cis*-Me of ω-units); 19.5 (MeC(3)); 23.2, 23.4 (*trans*-Me); 25.7 (*trans*-Me of ω-units); 25.2, 25.8, 26.3, 26.6, 26.7, 26.8 (CH_2CH=C); 28.4 (C(12)); 29.0 (C(3)); 31.7, 31.9, 32.1 ((CH_2C(Me)=C of (*Z*)-units); 37.3 (C(4)); 39.7 (CH_2C(Me)=C of (*E*)-units and C(2)); 60.8 (C(1)); 66.8 (C(11′)); 124.1, 124.15, 124.3, 124.7, 124.9, 125.0, 125.8, 126.4 (HC=C); 131.2 (MeC=C of ω-units); 134.4, 134.8, 135.1, 135.2, 135.3, 135.5 (MeC=C); 138.7 (C(11)).

3,7,15,19,23,27-Hexamethyl-11-(1-naphthylamino)methyloctacosa-6(*Z*),10(*E*),14(*E*),18(*E*),22(*E*),26-hexaenyl phosphate, diammonium salt (3a). CCl_3CN (40.3 mg, 28 μL, 280 μmol) was added to a solution of amino alcohol **2a** (48.7 mg, 76.3 μmol) and $(Bu_4N)H_2PO_4$ (88.2 mg, 247 μmol) in 1.76 mL of CH_2Cl_2. After 48 h at 20 °C, the solvent was evaporated and the residue was dissolved in 4 mL of the upper (organic) phase of an equilibrated *n*-butyl alcohol—water mixture. The solution was washed with the lower phase of the same mixture (4×1 mL). Then MeOH (1.5 mL), a concentrated aqueous solution of NH_3 (75 μL), and Dowex 50W×8 (NH_4^+) cation-exchange resin (1 mL) were added and the mixture was stirred for 3 h. The ion-exchange resin was filtered off and washed (4×4 mL) with a toluene—MeOH mixture (3 : 1) and the combined solution was

* The spectra of **2a,b** and **3a,b** exhibit also signals for the naphthalene fragment, δ: 6.65 (d, 1 H, J = 6.7 Hz); 7.3—7.5 (m, 4 H); 7.8 (m, 2 H).

** The spectra of **2a,b** and **3a,b** exhibit also signals for the naphthalene fragment, δ: 104.0, 104.5 (C(2)); 116.8, 117.0 (C(4)); 119.7, 119.8 (C(6)); 123.3, 124.5 (C(7), C(8)); 125.7 (C(9)); 126.6 (C(10)); 128.6 (C(3)); 134.9, 135.0 (C(5)); 143.5, 143.7 (C(1)).

* The term "dolichol-*n*" accepted in the chemistry of dolichols designates compounds of this series containing (n − 1) isoprene units and one dihydroisoprene unit.

concentrated. The residue was dissolved in 50 mL of a $CHCl_3$—MeOH (2 : 1) mixture and the solution was applied on a column (1.1×15 cm) with DEAE cellulose (AcO^-) equilibrated with the same solvent mixture. The column was washed with this solvent mixture (40 mL) and MeOH (50 mL); compound **3a** was eluted with 200 mL of a 10 m*M* solution of $AcONH_4$ in MeOH. The fractions containing the target product (monitoring by TLC in system *E*) were concentrated, and 10 mL of toluene was added to the residue. The mixture was concentrated to ~3 mL, diluted to 15 mL with toluene, and allowed to stand for 18 h at 0 °C. The toluene solution was decanted and concentrated to dryness, and the residue was dissolved in 5 mL of a heptane—propan-2-ol mixture (4 : 1). According to a colorimetric experiment, the solution contained 13.6 μmol of phosphate, which corresponds to 18% yield of the product. Phosphate **3a**, R_f 0.45 (*E*). UV (heptane—propan-2-ol, 4 : 1): λ/nm (ε): 252 (18000), 335 (5500). ^{1}H NMR, δ: 0.92 (d, 3 H, MeC(3), J = 6.0 Hz); 1.10—1.50 (m, 5 H, $H_2C(2)$, $H_2C(4)$, HC(3)); 1.57—1.70 (m, 18 H, *cis*- and *trans*-Me); 1.96—2.12 (m, 18 H, $CH_2C{=}C$); 2.32 (m, 4 H, $H_2C(9)$, $H_2C(12)$); 3.21 and 3.25 (both s, in total, 1 H, NH); 3.86 (s, 2 H, CH_2N); 3.90 (m, 2 H, $H_2C(1)$); 5.11 (m, 5 H, HC=C); 5.52 (m, 1 H, HC(10)). ^{13}C NMR, δ: 16.0 (*cis*-Me); 17.6 (*cis*-MeC(27)); 19.2 (MeC(3)); 23.3 (MeC(7)); 25.2, 25.8, 26.3, 26.7, 26.8, 27.2 ($CH_2CH{=}C$); 25.7 (*trans*-MeC(27)); 29.2, 29.4 (C(3), C(12)); 31.8 (C(8)); 37.4 (C(4)); 39.7 ($CH_2C(Me){=}C$ of (*E*)-units, C(2)); 49.5, 50.3 (C(11′)); 64.0 (C(1)); 124.1, 124.2, 124.3, 125.5, 125.7, 126.0 (HC=C); 131.2 (C(27)); 134.27, 134.33, 135.7 (MeC=C). ESI mass spectra (recorded on an API III triple quadrupole mass spectrometer (PE-Sciex, Canada) from a solution in propan-2-ol containing 10 m*M* of $AcONH_4$), negative-ion spectrum, m/z (I_{rel} (%)): 750, $[M - H]^-$ (15), 716, $[M - 2\,NH_3 - H]^-$, (100); positive-ion spectrum, m/z (I_{rel} (%)): 752, $[M + H]^+$, (25), 718, $[M - 2\,NH_3 + H]^+$, (100).

11′-(1-Naphthylamino)dolichyl-10,11 phosphate diammonium salt (3b) was synthesized similarly to phosphate **3a** from dolichol derivative **2b** (36.7 mg, 41.3 μmol), $(Bu_4N)H_2PO_4$ (82 mg, 230 μmol), and CCl_3CN (35.4 mg, 253 μmol) in 2 mL of CH_2Cl_2. The solution of the product obtained after anion exchange chromatography and removal of $AcONH_4$ contained 13.0 μmol of phosphate, which corresponds to 28% yield. Phosphate **3b**, R_f 0.51 (*E*). UV (heptane—propan-2-ol, 4 : 1): λ/nm (ε): 252 (18500), 335 (5000). ^{1}H NMR (CD_3OD—$CDCl_3$, 1 : 2), δ: 0.91 (d, 3 H, MeC(3), J = 7.3 Hz); 1.00—1.50 (m, 5 H, $H_2C(2)$, $H_2C(4)$, HC(3)); 1.58 (s, 9 H, *cis*-Me); 1.66 (s, 19.5 H, *trans*-Me); 2.00 (m, 32 H, $CH_2C{=}C$); 2.12 (m, 4 H, $H_2C(9)$, $H_2C(12)$); 3.20, 3.31 (both s, in total 1 H, NH); 3.77 (s, 2 H, CH_2N); 3.85 (m, 2 H, $H_2C(1)$); 5.15 (m, 8.5 H, HC=C); 5.40 (br.t, 1 H, HC(10)). ^{13}C NMR (CD_3OD—$CDCl_3$), 1 : 2, δ: 16.0 (*cis*-Me); 17.9 (*cis*-Me of ω-units); 18.8 (MeC(3)); 22.9 (*trans*-Me); 25.8 (*trans*-Me of ω-units); 24.8, 26.0, 26.2, 26.3, 26.6 ($CH_2CH{=}C$); 28.6, 28.8, 29.2, 30.1 (C(9), C(12), C(13), C(3)); 31.6, 31.8 (($CH_2C(Me){=}C$ of (*Z*)-units); 37.1 (C(4)); 39.3 ($CH_2C(Me){=}C$ of (*E*)-units and C(2)); 50.8 (CN); 65.4 (C(1)); 123.8, 124.0, 124.6, 124.8, 126.7 (HC=C); 130.8 (MeC=C of ω-units); 135.1 (MeC=C). ^{31}P NMR (CD_3OD—$CDCl_3$), 1 : 2, δ: 2.25.

This work was supported by the State Foundation for Leading Scientific Schools (Projects Nos. 00-15-97347 and 00-15-97373) and the American Foundation for Scientific Research and Development (CRDF) (Grant RN1-404).

References

1. V. N. Shibaev, V. V. Veselovsky, A. V. Lozanova, S. D. Mal′tsev, L. L. Danilov, W. T. Forsee, J. Xing, H. C. Cheung, and M. J. Jedrzejas, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 189.
2. N. Ya. Grigorieva, O. A. Pinsker, V. N. Odinokov, G. A. Tolstikov, and A. M. Moiseenkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1987, 1546 [*Bull. Acad. Sci USSR, Div. Chem. Sci.*, 1987, **36**, 1426 (Engl. Transl.)].
3. N. Ya Grigorieva, O. A. Pinsker, E. D. Daeva, and A. M. Moiseenkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 2325 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1991, **40**, 2037 (Engl. Transl.)].
4. N. Y. Grigorieva, O. A. Pinsker, S. D. Maltsev, L. L. Danilov, V. N. Shibaev, and M. J. Jedrzejas, *Mendeleev Commun.*, 2000, 92.
5. A. R. Wellburn and F. W. Hemming, *Nature*, 1966, **212**, 1364.
6. A. F. Abdel-Magid, K. G. Carron, B. D. Harris, C. A. Maryanoff, and R. D. Shah, *J. Org. Chem.*, 1996, **61**, 3849.
7. B. C. Ranu, A. Majee, and A. Sarkar, *J. Org. Chem.*, 1998, **63**, 370.
8. A. Schepartz and R. Breslow, *J. Am. Chem. Soc.*, 1987, **109**, 1814.
9. A. S. Shashkov, N. Ya. Grigorieva, I. M. Avrutov, A. V. Semenovsky, V. N. Odinokov, V. K. Ignatyuk, and G. A. Tolstikov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1979, 388 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1979, **28**, 259 (Engl. Transl.)].
10. L. L. Danilov, T. N. Druzhinina, N. A. Kalinchuk, S. D. Mal′tsev, and V. N. Shibaev, *Chem. Phys. Lipids*, 1989, **51**, 191.
11. L. L. Danilov and V. N. Shibaev, in *Studies in Natural Products Chemistry*, Ed. Atta-ur-Rahman, Elsevier, Amsterdam, 1991, **8**, 63.
12. V. E. Vaskovsky, E. Y. Kostetsky, and J. M. Vasendin, *J. Chromatogr.*, 1975, **114**, 129.
13. L. L. Danilov, N. S. Utkina, and V. N. Shibaev, *Bioorgan. khimiya* [*Sov. J. Bioorg. Chem.*], 1980, **6**, 780 (in Russian).
14. G. Büchi and H. Wüest, *J. Org. Chem.*, 1966, **34**, 1122.

Received July 10, 2000