SYNTHESIS OF RACEMIC OCTAPRENOL ωtttcccsOH AND NONAPRENOL ωtttccccsOH

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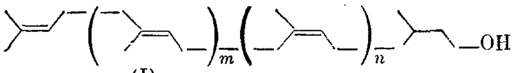
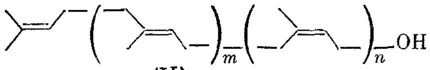
Dolichols of the polyprenol group (I; $m = 2$, $n > 10$) containing a saturated α-isoprene unit are of exceptional importance in the biosynthesis of carbohydrate-containing biopolymers [1]. Because of the limited availability of dolichols in natural sources, the full or partial synthesis of these and related compounds (to investigate their biochemical properties) is of current interest.



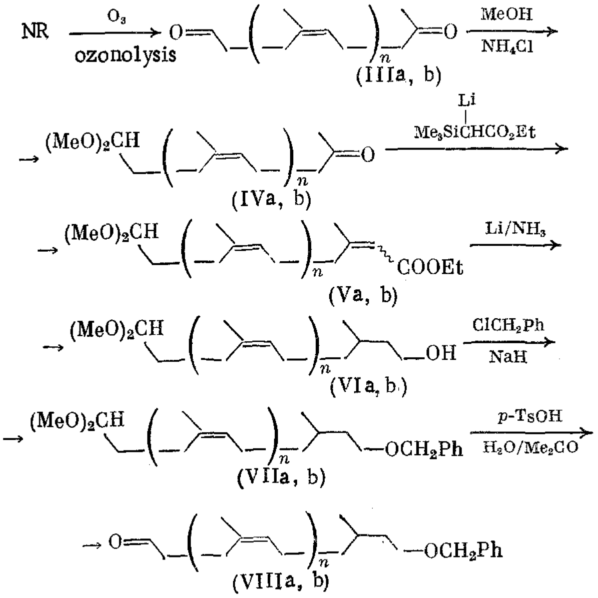
(I)



(II)

The partial synthesis of dolichols as the isoprenol mixture (I; $m = 2$, $n = 12$-18), starting from the polyprenol mixture (II; $m = 2$, $n = 12$-18), has been described in the literature, mostly patent [2-4]. The possibility of obtaining individual dolichols (I) through selective hydration of the α-isoprene unit of the appropriate polyprenols (II) has also been examined [5]. In the present communication we describe the synthesis of octaprenol ωtttcccsOH (Ia; $m = n = 3$) and nonaprenol ωtttccccsOH (Ib; $m = 3$, $n = 4$) by means of controlled aldol condensation, described earlier in the synthesis of cis-trisubstituted olefins, including prenols (II) [6-8].

The previously unknown isoprenoid aldehyde blocks (VIIIa,b), necessary intermediates in the synthesis, were obtained in five stages from ketoaldehydes (IIIa,b), which were obtained from selective ozonolysis of natural rubber (NR) [9].



$n = 2$ (a), 3 (b).

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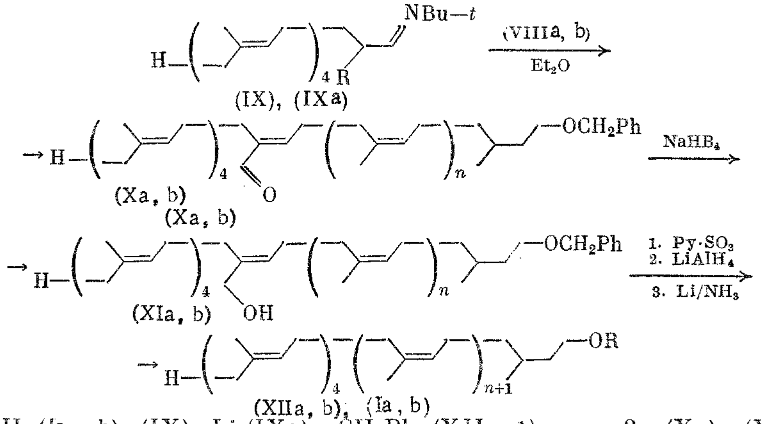
Selective reaction of ketoaldehyde (IIIa) with MeOH in the presence of NH_4Cl at ~25°C gave a quantitative yield of ketoacetal (IVa) [10], whose condensation with the Li derivative of ethyltrimethylsilyl acetate at −78°C yielded ester (Va). The latter was obtained as a mixture of isomers in the proportion 2Z/2E ~ 3:2, as can be seen from a comparison in the PMR spectrum of the integral intensities of isolated CH_2–C^3 signals at δ 1.87 (Z isomer) and 2.16 ppm (E isomer) [11]. Ester (Va) was reduced (Li/NH_3, method of Chatty et al. [12]) to carbinol (VIa), which was converted in the usual manner to benzyloxyacetal (VIIa), whose hydrolysis with p-TsOH in aqueous acetone afforded aldehyde (VIIIa). Similarly, ketoaldehyde (IIIb) was converted to benzyloxyaldehyde (VIIIb) in an overall yield of ~35% through intermediate stages involving ketoacetal (IVb), ester (Vb), carbinol (VIb), and benzyloxyacetal (VIIb). It should be noted that olefination of ketoacetal (IVb) also resulted in the formation of an ester mixture (Vb) with a marked selectivity for the Z isomer (2Z/2E ~ 3:2).

Condensation of aldehyde blocks (VIIIa,b) with the Li derivative (IXa) of isoprenoid aldimine (IX) at −70°C [7] led to the disubstituted E-acroleins (Xa,b) with a stereochemical purity of >95%, as determined from PMR data (cf. [13]). Subsequent reduction of (Xa,b) to carbinols (XIa,b) and then to benzyl ethers (XIIa,b) was carried out with full preservation of the C=C configuration, as described in [6-8] for the synthesis of heptaprenol (II) (m = n = 3). Finally, debenzylation of (XIIa,b) with Li in NH_3 afforded the desired racemic prenols (Ia,b).



R = H (Ia, b), (IX), Li (IXa), CH_2Ph (XIIa, b); n = 2, (Xa)—(XIIa), 3 (Xb)—(XIIb).

The structure of compounds (I), (V)-(VIII), and (X)-(XII) was confirmed by elemental analysis of the key compounds and by the available spectral methods. The observed ^1H NMR (see Experimental) and ^{13}C NMR (Tables 1 and 2) spectral parameters are in good accord with those obtained for related structures [11, 13-15]. Moreover, analysis of the ^{13}C NMR spectra further confirms the effect of functionalization of the central isoprene unit on the magnitude of the chemical shifts of neighboring and distant centers, as noted by us earlier [7, 8, 14]. Thus in the spectra of E-acroleins (Xa,b) methylene atoms C^{12} and C^{16} resonate at δ ~ 30 and 24 ppm, respectively, whereas in the reduced products (Ia,b) and (XIIa,b) the signal of these atoms is found at δ ~ 32 ppm. This effect is also manifested in the PMR spectra of compounds (Xa,b) as a downfield shift (by ~0.4 ppm) of the methylene group in the γ position relative to the formyl group (in β- and δ-methylene groups the shift is ~0.2 ppm), compared to the same signals in spectra of the reduced products.

EXPERIMENTAL

IR spectra were obtained in CCl_4 on a UR-20 instrument; UV spectra were obtained in alcohol on a Specord UV-VIS spectrometer. PMR spectra were measured in $CDCl_3$* (relative to TMS) on Varian DA-60, Tesla BS-497 (100 MHz), and Bruker WM-250 spectrometers. ^{13}C NMR spectra were taken in $CDCl_3$ on a Bruker WM-250 spectrometer with a working frequency of 62.89 MHz. The parameters for compounds (Va,b), (VIa), (VIIa), and (VIIIa,b) are given in Table 1; those for compounds (Ia,b), X(a,b), and (XIIa) are shown in Table 2. Mass spectra were obtained at 70 eV on a Varian MAT-CH-6 spectrometer. R_f values are given for a fixed SiO_2 (Silufol) layer in the system hexane–ether (1:1).* Preparative chromatography was carried out in a flash variant on silica gel L (40-100 mμ; Chemapol).

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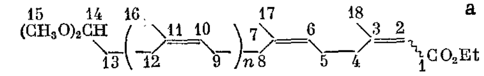
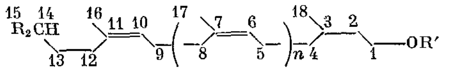
*Unless noted otherwise.

TABLE 1. ^{13}C NMR Spectra of Compounds (Va,b), (VIa), (VIIa), and (VIIIa,b)

C-atom No.	 [a]					
	(Va)	(Vb)[b]	(VIa)	(VIIa)[c]	(VIIIa)[d]	(VIIIb)[c,d]
1	166,2(*Z*) 166,8(*E*)	166,2(Z) 166,8(*E*)	60,8	68,8	68,7	68,7
2	116,3	116,4	39,8	36,8	36,8	36,8
3	159,8	159,7	29,2	29,7	29,7	29,7
4	32,1(Z) 41,2(*E*)	32,1(Z) 41,2(*E*)	37,4	37,5	37,5	37,5
5	26,8	26,5	25,2	25,3	25,3	25,3
6	124,5	124,5	125,4	125,7	125,9	125,4(125,6)
7	135,6	135,3	134,2 *	134,7 *	134,4	134,8
8	33,6	33,6	32,0	32,1	32,0	32,0
9	26,3	26,3	26,2	26,3	26,3	26,4
10	125,5	125,2	125,4	125,5	126,5	126,5
11	134,4	134,5	134,6 *	134,4 *	132,9	133,0
12	32,1	32,1	32,0	32,1	24,3	24,3
13	30,8	30,8	30,7	30,8	42,3	42,3
14	104,2	104,3	104,1	104,3	201,8	202,0
15	52,5	52,6	52,4	52,6	—	—
16	23,2	23,2	23,2	23,2	22,9	23,0
17	23,3	23,3	23,1	23,3	23,3	23,4
18	23,3(Z) 18,8(*E*)	23,3(Z) 18,8(*E*)	19,4	19,6	19,6	19,6

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[a] The spectra of (Va,b) also contain signals of the $CO_2C_2H_5$ group.

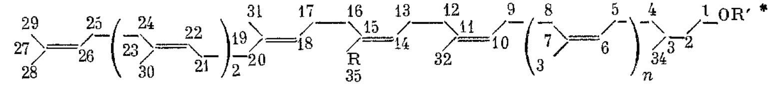
[b] In the spectrum of (Vb) the signals of atoms 9-12 have a double intensity.

[c] The spectra of (VIIa) and (VIIIa,b) also contain signals of the $CH_2C_6H_5$ group.

[d] In the spectrum of (VIIIb) the signals of atoms 5-8 have a double intensity.

Note. Signals marked by an asterisk (*) may be transposed.

TABLE 2. ^{13}C NMR Spectra of Compounds (Ia,b), (Xa, b), and (XIIa)



C-atom No.	(Xa) †	(Xb) †	(XIIa) †	(Ia)	(Ib) ‡	(Xa) †	(Xb) $^{2}_{3}$	(XII) †	(Ia)	(Ib) ‡	C-atom No.
1	68,95	68,9	68,8	61,4	61,3	135,0^{c}	135,0^{c}	135,0^{c}	135,3^{c}	135,2	19
2	37,7^{a}	37,7^{a}	37,6^{a}	40,2	40,1	39,9	39,9	39,8^{e}	39,9	39,8	20
3	29,95	29,9	29,8	29,8	29,7	27,2^{d}	26,8^{b}	26,8^{d}	26,8^{d}	26,9^{d}	21
4	37,0^{a}	36,9^{a}	36,9^{a}	37,7	37,6	124,5^{b}	124,5	125,2^{b}	125,2^{b}	125,2^{b}	22
5	25,5	25,4	25,4	25,4	25,4	134,6^{c}	134,8^{c}	134,9^{c}	135,3^{c}	135,4	23
6	124,4^{b}	124,4^{b}	124,3^{b}	124,5^{b}	124,3^{b}	39,9	39,9	40,1^{e}	39,9	39,8	24
7	136,2^{c}	136,2^{c}	135,4^{c}	135,1^{c}	135,0^{c}	26,6^{d}	27,2	26,8^{c}	26,8^{d}	26,8^{d}	25
8	32,2	32,2	32,1	32,2	32,2	124,7^{b}	125,8^{b}	125,7^{b}	125,3	125,5^{b}	26
9	26,9^{d}	26,6	26,6^{d}	26,6^{d}	26,5	133,6^{c}	131,2	131,2	131,2	131,2	27
10	124,5^{b}	124,4^{b}	126,8	126,7	124,4^{b}	25,6	25,7	25,7	25,7	25,6	28
11	135,1^{c}	135,0^{c}	135,2^{c}	135,2^{c}	135,2^{c}	17,6	17,7	17,7	17,7	17,7	29
12	32,2	32,3	30,9	30,8	32,3	16,1	16,1	16,1	16,1	16,0	30
13	26,8^{d}	26,7^{d}	27,6	27,5	26,6^{d}	16,1	16,1	16,1	16,1	16,0	31
14	124,6^{b}	125,1^{b}	153,9	154,0	124,6^{b}	23,2^{e}	23,2^{e}	23,5	23,4	23,4	32
15	135,1^{c}	135,2^{c}	143,8	143,7	135,2^{c}	23,4^{e}	23,4^{e}	23,5	23,4	23,4	33
16	32,4	32,1	24,5	24,45	32,3	19,7	19,7	19,7	19,7	19,6	34
17	26,9^{d}	26,8^{d}	27,0^{d}	26,7	26,8^{d}	194,8	194,35	23,5	23,4	23,4	35
18	125,2^{b}	125,2^{b}	123,5	123,5	125,1^{b}						

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*The signals of atoms 21-24 and 30 have a double intensity in all compounds.

†The spectra of (Xa,b) and (XII) also contain signals of the $CH_2C_6H_5$ group.

‡In the spectra of (Ib) and (Xb) the signals of atoms 5-8 and 33 have a double intensity.

Note. Signals marked with the letters a-f may be transposed.

14,14-Dimethoxy-3,7,11-trimethyltetradeca-2E/Z,6Z,10Z-trienoic Acid (Va) and 18,18-Dimethoxy-3,7,11,15-tetramethyloctadeca-2E/Z,6Z,10Z,14Z-tetraenoic Acid (Vb) Ethyl Esters. A 12-ml portion of 1.3 M n-BuLi in hexane (15.6 mmoles) was added at −20°C, with mixing, to 1.47 g (14.4 mmoles) of $i\text{-}Pr_2NH$ in 150 ml THF in an Ar atmosphere. The mixture was kept at −20°C for 40 min, treated at −78°C with 2.4 g (14.7 mmoles) ethyltrimethylsilyl acetate, allowed to stand for 1.5 h, and then treated at −78°C with 3.2 g (11.4 mmoles) of (IVa) [10] in 10 ml THF. After 1.3 h, the mixture was heated to ~25°C for 3 h, allowed to stand for another 30 min, separated out with 2.8 g $NaHSO_4 \cdot 2H_2O$, and filtered; then the precipitate was washed with ether. Standard processing of the pooled filtrate afforded 4.2 g of a light yellow, oily product, which was chromatographed on 95 g of SiO_2. Gradient elution from hexane to ether (up to 5% of the latter) yielded 3.4 g (85%) of an isomeric mixture of (Va) (2Z/2E ~ 3:2), R_f = 0.49. IR spectrum (ν, cm^{-1}): 860, 1065, 1130, 1150, 1220, 1380, 1450, 1650, 1715, 2830-3010; PMR spectrum (δ, ppm): 1.25 t and 1.27 t (3H, J = 7 Hz, $C\underline{H}_3CH_2$), 1.60 m (2H, H_2C^{13}), 1.69 s (6H, $2CH_3$), 1.87 d (1.8H, J = 1.5 Hz, Z-isomer $CH_3{-}C^3$), 2.0 m (6H, $3CH_3$), 2.15 m (4H, H_2C^5; E-isomer H_2C^4 and $CH_3{-}C^3$), 2.62 t (1.2H, J = 8 Hz, Z-isomer H_2C^4), 3.30 s (6H, $2CH_3O$), 4.13 q and 4.15 q (2H, J = 7 Hz, CH_2O), 4.32 t (1H, J = 6 Hz, HC^{14}), 5.13 m (2H, 2HC=C), 5.65 br. s (1H, HC^2); mass spectrum (m/z: 321 $[M - OCH_3]^+$ 290 $[M - 2OCH_3]^+$, 278, 262, 193, 161, 125, 93, 81, 68.

In a similar manner, 4.25 g (89%) of an isomeric mixture of (Vb) (2Z/2E ~ 3:2) was obtained from 2.4 g (14.7 mmoles) ethyltrimethylsilyl acetate and 4.0 g (11.4 mmoles) ketoacetal (IVb) [10]. bp = 194-195°C (0.05 mm); R_f = 0.65; IR spectrum (ν, cm^{-1}): 860, 1065, 1130, 1150, 1220, 1380, 1450, 1650, 1715, 2830-3010, UV spectrum: λ_{max} 230 nm (ε 21,900); PMR spectrum (δ ppm): 1.25 t and 1.27 t (3H, J = 7 Hz, $C\underline{H}_3CH_2$), 1.7 m (11H, H_2C^{17}, $3CH_3$), 1.87 d (1.8H, J = 1.5 Hz, Z-isomer CH_3C^3), 2.0 m (10H, $5CH_2$), 2.16 m (4H, H_2C^5; E-isomer H_2C^4 and $CH_3{-}C^3$), 2.62 t (1.2H, J = 8 Hz, Z-isomer H_2C^4), 3.31 s (6H, $2CH_3O$), 4.13 q and 4.15 q (2H, J = 7 Hz, CH_2O), 4.33 t (1H, J = 6 Hz, HC^{18}), 5.13 m (3H, 3HC=C), 5.65 br. s (1H, HC^2); mass spectrum (m/z): 420 M^+, 419, 389, 388, 358, 357, 356, 330, 261, 229, 193, 161, 149, 135, 124, 69. Found, %: C 74.52, H 10.65. $C_{26}H_{44}O_4$. Calculated, %: C 74.24, H 10.56. Mol. wt. 420.60.

(±)-14-Hydroxy-4,8,12-trimethyltetradeca-4Z,8Z-dien-1-al (VIa) and (±)-18-Hydroxy-4,8,12,16-tetramethyloctadeca-4Z,8Z,12Z-trienl-al (VIb) Dimentylacetals. Lithium (0.45 g; 65.0 mg-atom) was added at −40°C, with mixing, to 2.8 g (8.1 mmoles) of (Va) dissolved in 200 ml NH_3, 30 ml dioxane, and 20 ml ether in an Ar atmosphere. The reaction mixture was kept at −40°C for 1.5 h, separated out with excess EtOH, and the NH_3 evaporated. Processing of the residue by an standard procedure yielded 2.27 g of an oily product, which was chromatographed on 100 g SiO_2. Gradient elution from hexane to ether (up to 40% of the latter) afforded 1.5 g (60%) of product (VIa) (colorless oil; $R_f = 0.23$). IR spectrum (ν, cm^{-1}): 1060, 1130, 1380, 1450, 2820-3050, 3650; PMR spectrum (δ, ppm); 0.91 d (3H, J = 7 Hz, CH_3), 1.13 m and 1.31 m (4H, H_2C^{11}, H_2C^{13}), 1.6 m (3H, H_2C^2), HC^{12}), 1.68 s (6H, $2CH_3$), 2.1 m (8H, $4CH_3$), 2.37 s (1H, OH), 3.31 s (6H, $2CH_3O$), 3.67 m (2H, CH_2O), 4.37 t (1H, J = 6 Hz, HC^1), 5.1 m (2H, 2HC=C); mass spectrum (m/z): 294 ($M^+ - H_2O$), 281 ($M^+ - OCH_3$), 265, 249, 248, 222, 207, 179, 175, 161, 147, 125, 124, 69.

In a similar manner, 3.4 g (8.1 mmoles) of (Vb) afforded 1.84 g (60%) of product (VIb). bp = 178-180°C (0.06 mm); IR spectrum (ν, cm^{-1}): 1060, 1130, 1380, 1450, 2830-3080, 3640; PMR spectrum (δ, ppm): 0.91 d (3H, J = 7 Hz, CH_3), 1.13 m and 1.30 m (4H, H_2C^{15}, H_2C^{17}), 1.6 m (3H, HC^2, H_2C^{16}), 1.70 s (9H, $3CH_3$), 2.1 m (12H, $6CH_2$), 3.32 s (6H, $2CH_3O$), 3.68 m (2H, CH_2O), 4.34 t (1H, J = 6 Hz, HC^1), 5.1 m (3H, 3HC=C). Found, %: C 75.14, H 11.58. $C_{24}H_{44}O_3$. Calculated, %: C 75.71, H 11.65. Mol. wt. = 380.7.

(±)-14-Benzyloxy-4,8,12-trimethyltetradeca-4Z,8Z-dien-1-al (VIIa) and (±)-18-Benzyloxy-4,8,12,16-tetramethyloctadeca-4Z,8Z,12Z-trien-1-al (VIIb) Dimethylacetals. These compounds were obtained by the standard procedure in a yield of 70-72% after chromatography on Al_2O_3 (gradient elution from hexane to 8% ether).

For (VIIa), bp = 195°C (0.01 mm); IR spectrum (ν, cm^{-1}): 700, 740-820, 1060, 1080, 1190, 1365, 1380, 1455, 2820-3000, 3030; PMR spectrum (δ, ppm): 0.91 d (3H, J = 7 Hz, CH_3), 1.20 m and 1.45 m (4H, H_2C^{11}, H_2C^{13}), 1.60 m (3H, H_2C^2, HC^{12}), 1.68 s (6H, $2CH_3$), 2.0 m (8H, $4CH_2$), 3.32 s (6H, $2CH_3O$), 3.51 t (2H, J = 6 Hz, CH_2O), 4.36 t (1H, J = 6 Hz, HC^1), 4.52 s (2H, CH_2Ph), 5.1 m (2H, 2HC=C), 7.3 m (5H, C_6H_5); mass spectrum (m/z): 372 $[M - CH_3O]^+$, 371, 339, 338, 312, 279, 247, 229, 174, 161, 135, 125, 107, 91, 69. Found, %: C 77.20, H 10.25. $C_{26}H_{12}O_3$. Calculated, %: C 77.57. H 10.51.

For (VIIb), $R_f = 0.57$; PMR spectrum (CCl_4, δ, ppm): 0.82 d (3H, J = 6 Hz, CH_3), 1.20-1.59 m (7H, H_2C^2, H_2C^{15}, HC^{16}, H_2C^{17}), 1.62 s (9H, $3CH_3$), 2.0 m (12H, $6CH_2$), 3.15 s (6H, $2CH_3O$), 3.3 t (2H, J = 7 Hz, CH_2O), 4.15 t (1H, J = 6 Hz, HC^1), 4.35 s (2H, CH_2Ph), 5.0 m (3H, 3HC=C), 7.2 m (5H, C_6H_5).

(±)-14-Benzyloxy-4,8,12-trimethyltetradeca-4Z,8Z-dien-1-al (VIIIa) and (±)-18-Benzyloxy-4,8,12,16-tetramethyloctadeca-4Z,8Z,12Z-trien-1-al (VIIIb). A solution containing 2.49 g (6.15 mmoles) (VIIa) and ~300 mg p-TsOH·H_2O in 60 ml of 66% aqueous acetone was boiled for 4 h, neutralized with Na_2CO_3, concentrated in vacuo, and the residue extracted with ether. Standard processing of the extract yielded 2.1 g (95%) of product (VIIIa), with a bp (bath) of 180°C (0.02 mm). IR spectrum (ν. cm^{-1}): 700, 740-820, 1030, 1100, 1205, 1365, 1730, 2720, 2820-2980, 3030, 3065, 3085; PMR spectrum (δ, ppm): 0.91 d (3H, J = 7 Hz, CH_3), 1.2 m and 1.45 m (4H, H_2C^{11}, H_2C^{13}), 1.64 m (1H, HC^{12}), 1.69 s (6H, $2CH_3$), 2.1 m (6H, $3CH_2$), 2.36 t (2H, J = 8 Hz, H_2C^3), 2.50 double t (2H, J = 1 and 8 Hz, H_2C^2), 3.52 t (2H, J = 7 Hz, CH_2O), 4.52 s (2H, CH_2Ph), 5.2 m (2H, 2HC=C), 7.3 m (5H, C_6H_5), 9.78 t (1H, J = 1 Hz, HC^1); mass spctrum (m/z): 357 M^+, 356, 265, 248, 247, 229, 161, 147, 135, 69. Found, %: C 80.70, H 9.96. $C_{24}H_{36}O_2$. Calculated, %: C 80.84, H 10.11. Mol. wt. = 356.6.

In a similar manner, 2.9 g (6.1 mmoles) of (VIIb) afforded 2.2 g (84%) of product (VIIIb), a colorless oil with a bp (bath) of 200°C (0.01 mm). IR spectrum (ν, cm^{-1}): 700, 740-820, 1030, 1100, 1204, 1365, 1375, 1450, 1728, 2720, 2820-2960, 3030, 3065, 3090; PMR spectrum (CCl_4, δ, ppm): 0.82 d (3H, J = 6 Hz, CH_3), 1.25 m (4H, $2CH_2$), 1.60 m (10H, HC^{16}, $3CH_3$), 2.0 m (12H, $6CH_2$), 2.30 m (2H, H_2C^2), 3.38 t (2H, J = 6 Hz, CH_2O), 4.33 s (2H, CH_2Ph), 5.0 m (3H, 3HC=C), 7.2 m (5H, C_6H_5), 9.55 br. s (1H, HC^1); mass spectrum (m/z): 425 M^+, 424, 406, 380, 333, 315, 313, 298, 233, 221, 204, 161, 135, 69. Found, %: C 81.82, H 10.37. $C_{29}H_{44}O_2$. Calculated, %: C 82.08, H 10.37. Mol. wt. = 424.6.

(±)-1-Benzyloxy-15-formyl-3,7,11,19,23,27,31-heptamethylditriaconta-6Z,10Z,14E,18E,22E,26E,30-heptaene (Xa) and (±)-1-Benzyloxy-19-formyl-3,7,11,15,23,27,31,35-octamethylhexatriaconta-6Z,10Z,14Z,18E,22E,26E,30E,34-octaene (Xb). An aldimine (IX) solution, prepared according to [7] from 2.97 g (9 mmoles) 3-geranylgeranylproionaldehyde in 5 ml ether, was added (−20°C, Ar atmosphere) during a 20-min interval, with mixing, to i-Pr_2NLi, obtained from

1.2 ml (8.5 mmoles) $i\text{-}Pr_2NH$ in 4 ml ether and 7.3 ml 1.16 M $n\text{-}BuLi$ in hexane (8.5 mmoles). The mixture was kept at 0°C for 2 h, treated (−70°C, 15 min) with 2.06 g (5.8 mmoles) of (VIIIa) in 8 ml ether, and kept at −70°C for 2.5 h. It was then heated for 2 h to ~25°C and left to stand overnight. The reaction mixture was dissolved in 40 ml ether, treated at 0°C with 2.3 g $(CO_2H)_2 \cdot 2H_2O$ in 45 ml H_2O, and mixed for 1.5 h at ~25°C. Subsequent processing in the usual manner yielded 4.0 g of an oily product, which was chromatographed on 90 g SiO_2. Gradient elution from hexane to ether (up to 5% of the latter) afforded 0.3 g [8% with respect to (VIIIa)] of product (Xa), a colorless oil with a R_f of 0.43 (hexane:ether, 6:1). IR spectrum (ν, cm^{-1}): 700, 740-830, 1040, 1100, 1360, 1450, 1640, 1690, 2720, 2800-3050; UV spectrum: λ_{max} 237 nm (ε 12,000); PMR spectrum (δ, ppm): 0.91 d (3H, J = 7 Hz, CH_3), 1.3 m (4H, H_2C^2, H_2C^4), 1.60 s (4H, HC^3, $CH_3{-}C^{19}$), 1.65 s (9H, 3 cis-CH_3), 1.71 s (6H, 2 trans-CH_3), 1.73 s (3H, $CH_3{-}C^{11}$), 2.0 m (20H, $10CH_2$), 2.27 m (4H, H_2C^{16}, H_2C^{12}), 2.45 double t (2H, $J_1 = J_2 =$ 7 Hz, H_2C^{13}), 3.52 t (2H, J = 6 Hz, CH_2O), 4.50 s (2H, CH_2Ph), 5.15 m (5H, $5HC{=}C$), 5.25 t (1H, J = 6.5 Hz, HC^{18}), 6.45 t (1H, J = 7 Hz, HC^{14}), 7.3 m (5H, C_6H_5), 9.37 s (1H, CHO); mass spectrum (m/z): 669 M^+, 668, 650, 625, 599, 577, 559, 490, 423, 355, 337, 271, 204, 135, 68.

In a similar manner, aldimine (IX), prepared according to [7] from 2.97 g (9 mmoles) 3-geranylgeranylpropionaldehyde and 2.47 g (5.8 mmoles) aldehyde (VIIIb), afforded 0.22 g [5% with respect to (VIIIb)] of product (Xb), a colorless oil with a R_f of 0.67. IR spectrum (ν, cm^{-1}): 700, 740-815, 845, 1030, 1050, 1080, 1120, 1380, 1450, 1640, 1690, 2730, 2850-3100; PMR spectrum (CCl_4, δ, ppm): 0.85 d (3H, J = 6 Hz, CH_3), 1.2 m (4H, H_2C^2, H_2C^4), 1.52 br. s (13H, 4 cis-CH_3, HC^3), 1.60 br. s (12 H, 4 trans-CH_3), 2.0 m (30H, $15CH_2$), 3.38 t (2H, J = 6 Hz, CH_2O), 4.35 s (2H, CH_2Ph), 5.0 m (7H, $7HC{=}C$), 6.25 t (1H, J = 6 Hz, HC^{18}), 7.2 m (5H, C_6H_5), 9.25 s (1H, CHO); mass spectrum (m/z): 737 M^+, 736, 718, 693, 669, 645, 627, 557, 491, 423, 341, 337, 271, 204, 135, 69.

(±)-Benzyloxy-15-hydroxymethyl-3,7,11,19,23,27,31-heptamethylditriaconta-6Z,10Z,14E,18E,22E,26E,30-heptaene (XIa) and (±)-Benzyloxy-19-hydroxymethyl-3,7,11,15,23,27,31,35-octamethylhexatriaconta-6Z,10Z,14Z,18E,22E,26E,30E,34-octaene (XIb). A 50-mg (1.35 mmoles) portion of $NaBH_4$ was added, with mixing, to 0.3 g (0.45 mmole) of (Xa) in 15 ml EtOH at 0°C. The mixture was kept for about 20 min at 25°C, separated at 0°C with 0.1 ml AcOH, and evaporated to dryness. The residue was dissolved in H_2O and extracted with ether. Standard processing yielded 0.3 g of an oily product, which was chromatographed on 15 g SiO_2. Gradient elution from hexane to ether (up to 5% of the latter) afforded 0.23 g [75% with respect to (Xa)] of product (XIa), a colorless oil with a R_f of 0.48. IR spectrum (ν, cm^{-1}): 700, 740-820, 1030, 1100, 1380, 1455, 2860-2980, 3040, 3620; PMR spectrum (δ, ppm): 0.91 d (3H, J = 7 Hz, CH_3), 1.25 m (4H, $2CH_2$), 1.62 br. s (13H, HC^3, 4 cis-CH_3), 1.72 s (9H, 3 trans-CH_3), 2.1 m (26H, $13CH_2$), 3.51 t (2H, J = 6 Hz, CH_2O), 4.03 br. s (2H, $\underline{CH_2}OH$), 4.51 s (2H, CH_2Ph), 5.2 m (6H, $6HC{=}C$), 5.44 t (1H, J = 6 Hz, HC^{14}), 7.3 m (5H, C_6H_5).

In a similar manner, 0.17 g (0.23 mmole) of (Xb) afforded 0.13 g (76%) of product (XIb), a colorless oil with a R_f of 0.47. IR spectrum (ν, cm^{-1}): 700, 745-815, 840, 1035, 1075, 1105, 1380, 1455, 1660, 2860-2980, 3040, 3100, 3620; PMR spectrum (CCl_4, δ, ppm): 0.80 d (3H, J = 6 Hz, CH_3), 1.20 m (4H, $2HC_2$), 1.50 br. s (13H, HC^3, 4 cis-CH_3), 1.55 s (12H, 4 trans-CH_3), 2.1 m (30H, $15CH_2$), 3.4 t (2H, J = 6 Hz, CH_2O), 3.85 br. s (2H, $\underline{CH_2}OH$), 4.40 s (2H, CH_2Ph), 5.0 m (8H, $8HC{=}C$), 7.2 m (5H, C_6H_5).

(±)-3,7,11,15,19,23,27,31-Octamethylditriaconta-6Z,10Z,14Z,18E,22E,26E,30-heptaenol-1 (XIIa) and (±)-3,7,11,15,19,23,27,31,35-Nonamethylhexatriaconta-6Z,10Z,14Z,18Z,22E,26E,30E,34-octaenol-1 (XIIb) Benzyl Ethers. At 0°C in an Ar atmosphere, 0.11 g (0.69 mmole) $PySO_3$ was added, with mixing to 0.22 g (0.33 mmole) of (XIa) in 8 ml THF. The mixture was kept at 0°C for 1 h, treated with 0.12 g (3.12 mmoles) $LiAlH_4$, heated for 1 h to ~25°C, and mixed for an additional 48 h. Further processing (using the standard procedure) yielded 0.21 g of an oily product, which was chromatographed on 25 g SiO_2. Elution of the mixture in hexane–ether (98:2) afforded 0.11 g [52% with respect to (XIa)] of product (XIIa), a colorless oil with a R_f of 0.75. PMR spectrum (δ, ppm): 0.91 d (3H, J = 7 Hz, CH_3), 1.2 m and 1.4 m (4H, $2CH_2$), 1.62 br. s (13H, HC^3, 4 cis-CH_3), 1.71 s (12H, 4 trans-CH_3), 2.1 m (26H, $13CH_2$) 3.52 t (2H, J = 6 Hz, CH_2O), 4.51 s (2H, CH_2Ph), 5.2 m (7H, $7HC{=}C$), 7.3 m (5H, C_6H_5).

In a similar manner, 0.12 g (0.16 mmole) of (XIb) afforded 60 mg (53%) of product (XIIb), a colorless oil with a R_f of 0.72. PMR spectrum (CCl_4, δ, ppm): 0.80 d (3H, J = 6 Hz, CH_3), 1.20 m (4H, $2CH_2$), 1.52 br. s (13H, HC^3, 4 cis-CH_3), 1.60 s (15H, 5 trans-CH_3), 2.1 m (30H, $15CH_2$), 3.38 t (2H, J = 6.5 Hz, CH_2O), 4.38 s (2H, CH_2Ph), 5.0 m (8H, $8HC{=}C$), 7.2 m (5H, C_6H_5).

(±)-3,7,11,15,19,23,27,31-Octamethylditriaconta-6Z,10Z,14Z,18E,22E,26E,30-heptaenol-1, Octaprenol ωttttcccsOH (Ia), and (±)-3,7,11,15,19,23,27,31,35-Nonamethylhexatriaconta-6Z,10Z, 14Z,18Z,22E,26E,30E,34-octaenol-1, Nonaprenol ωtttccccsOH (Ib). At −35°C in an Ar atmosphere, 21 mg (3 mmoles) of Li was added, with mixing, to 50 mg (0.076 mmole) of (XIIa) in 20 ml NH_3. The mixture was separated out with NH_4Cl for 2.5 h and then processed in the usual manner. The oily product (50 mg) was chromatographed on 25 g SiO_2. Elution with hexane–ether (9:1) afforded 44 mg (90%) of product (Ia), a colorless oil with a R_f of 0.42. IR spectrum (ν, cm^{-1}): 850, 1065, 1380, 1450, 2850-2970, 3640; PMR spectrum (δ, ppm): 0.91 d (3H, J = 7 Hz, CH_3), 1.3 m (4H, $2CH_2$), 1.62 br. s (13H, HC^3, 4 cis-CH_3), 1.69 s (12H, 4 trans-CH_3), 2.1 m (26H, $13CH_2$), 3.67 m (2H, CH_2O), 5.1 m (7H, 7HC=C); mass spectrum (m/z): 565 M^+, 564, 563, 496, 428, 427, 409, 408.

In a similar manner, 60 mg (0.084 mmole) of (XIIb) afforded 30 mg (57%) of product (Ib), a colorless oil with a R_f of 0.52. IR spectrum (ν, cm^{-1}): 850, 1060, 1130, 1378, 1448, 1665, 2850-2970, 3030, 3690; PMR spectrum (δ, ppm): 0.91 d (3H, J = 7 Hz, CH_3), 1.3 m (4H, $2CH_2$), 1.60 br. s (13H, HC^3, 4 cis-CH_3), 1.69 s (15H, 5 trans-CH_3), 2.1 m (30H, $15CH_2$), 3.68 m (2H, CH_2O), 5.1 m (8H, 8HC=C); mass spectrum (m/z): 633 M^+, 632, 631, 564, 563, 496, 495, 428, 427, 426, 410, 409, 408.

CONCLUSIONS

A ten-stage synthesis of the dolichol-related racemic octaprenol ωtttcccsOH and nonaprenol ωtttccccsOH was carried out using controlled aldol condensation at the key stage.

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