SYNTHESIS OF MODIFIED HEXAPRENOL WC_5OH FROM GLUTARALDEHYDE DERIVATIVES

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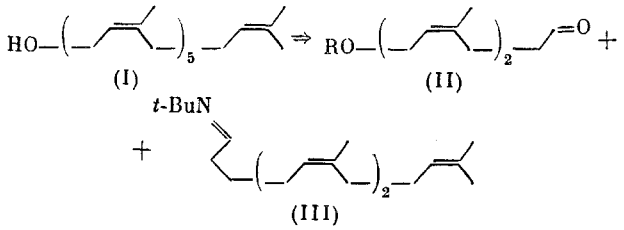
A new procedure was developed for building linear Z-isoprenoids from glutaraldehyde derivatives as nonisoprenoid precursors, and is illustrated by the synthesis of hexaprenol WC_5OH.

In continuation of our studies on the synthesis of polyprenols and their modified analogs [1, 2], we discuss in the present article the preparation of a fully cisoid hexaprenol WC_5OH (I), which is distinguished from other natural derivatives of this class of low-molecular-weight bioregulators by the absence of a transoid ω-sesqui- or ω-diterpenoid section in the chain, typical for these compounds. In accordance with our previously developed "block" scheme for building this type of molecule [2-5], the most obvious path for achieving this task should consist in the controlled aldol condensation of an aldehyde of the trisnor-Z,Z-farnesol series (II) with a trishomo-Z,Z-farnesal imine (III) (Scheme 1):

Scheme 1



These starting compounds can be obtained, and (II, R = OBn) has actually been obtained [5], from the fairly difficultly available Z,Z-farnesol. The below-described synthesis of modified hexaprenol (I) is based on the use of acetaldehyde and acrolein as nonisoprenoid precursors of the block-synthone (II), followed by the use of the above-indicated cross-condensation during the building of each new isoprene unit. Thus, the high stereoselectivity of the process is determined by the thermodynamic preference of the E-acroleins formed as a result of the condensation [6] and the stereospecificity of the reductive transformation of the latter into the corresponding Z-olefins according to [7].

In accordance with this approach (Scheme 2), acetaldehyde tert-butylimine (IV), deprotonated by lithium diisopropyl amide (LDA), was alkylated by bromoacetal (V), which is readily obtainable from acrolein, to give smoothly the imino-acetal (VI). Treatment of the lithium derivative of the latter with Me_3SiCl leads to the α-trimethylsilyl (TMS) derivative (VII), while a mild acid hydrolysis of (VI) gives the aldehydo-acetal (VIII). The structure of the previously unknown, variously protected glutaraldehyde derivatives (VI)-(VIII) was established spectrally and confirmed by their subsequent transformations under controlled aldol condensation conditions (see Scheme 2 on following page). The aldehydo-acetal (VIII) was used subsequently for the propagation of the "tail" [8], while the imino-acetals (VI) and (VII) for the elongation of the "head" sections of the constructed Z-isoprenoid chain. Thus, the block-synthone (XIVb) belonging to series (II) was prepared starting from the latter and the readily available benzyloxyacetaldehyde (IX) (see Scheme 3 on following page).

The condensation of aldimine (VI) deprotonated by LDA with aldehyde (IX) under the previously established conditions [4, 5] produces a mixture (~2:3) of the expected E-acrolein (Xa) with a substantially more polar product in a yield of ~50%. Absorption bands are observed in the IR spectrum of the latter for the OH and CHO groups (3600 and 1720 cm^{-1}, re-

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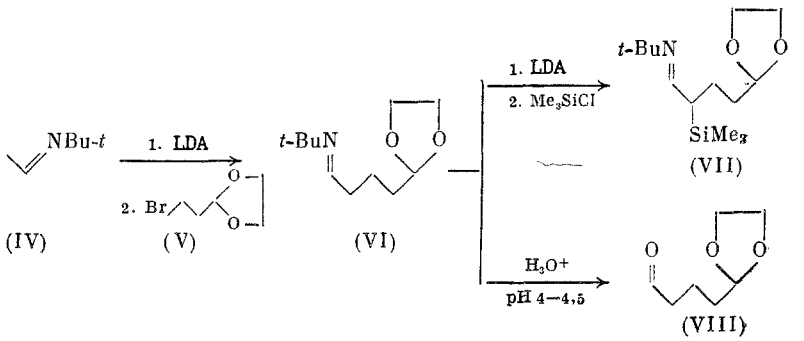
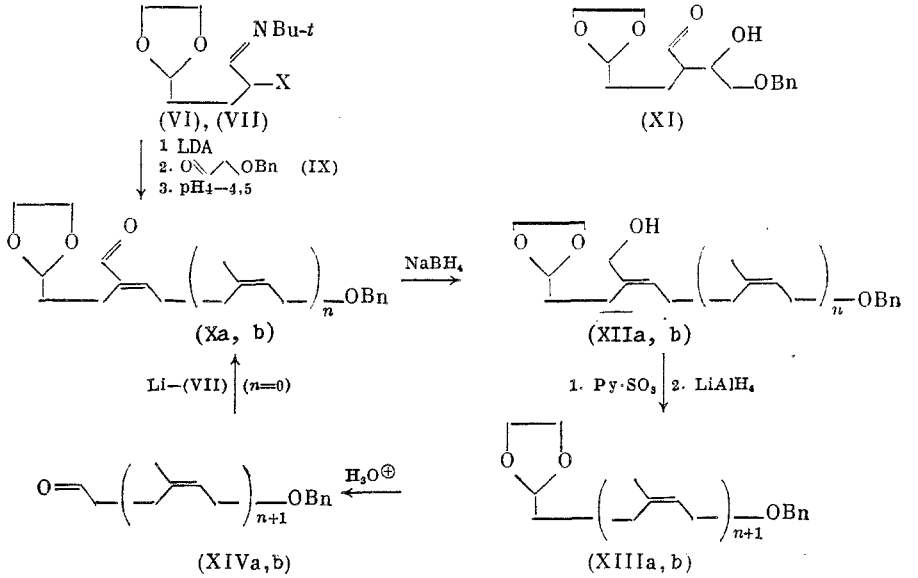
Scheme 2



Scheme 3



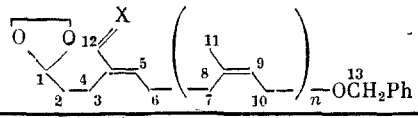
X = H (VI), $SiMe_3$(VII); n = 0 (Xa)—(XIVa), 1 (Xb)—(XIVb).

spectively), which conforms with the structure of the hydroxy-aldehyde (XI). There are, in particular, CHO signals in the ^1H and ^{13}C NMR spectra confirming this structure, doubled because of the diastereoisomerism, at δ ~ 9.7 and 204 ppm, respectively, and also the multiplet signals of HCCHO at 2.5-2.9 ppm with an overall intensity of 1H, together with the HCCHO signals at δ ~ 54 ppm. Since under these conditions enabling the retention of the acetal protection required at the subsequent stages (pH 4.0-4.5, ~20°C), the hydroxy-aldehyde (XI) does not split into (Xa), the overall yield of the latter does exceed 20%, cf. [8].

Better results were obtained when, instead of (VI), its α-TMS derivative (VII) was used for the cross-combination under consideration, which gave the disubstituted E-acrolein (Xa) with stereochemical purity of >95% in a yield of >50%. The stereochemical purity was found by comparison in the PMR spectrum of (Xa) of the integral intensity of singlet signals of the CHO group for the Z-isomer as the main compound and an admixed Z-isomer, δ ~ 9.42 and 10.10 ppm, respectively, see [6, 9], and was additionally confirmed by the ^{13}C NMR spectral data for these compounds (Table 1). As in related cases [4, 5], the stereospecific reductive transformation of the preparatively obtainable (Xa) into acetal (XIIIa) was carried out via the allyl alcohol (XIIa) stage, without isolation of the intermediate O-sulfate. The Z-prenolog of (IX), the known aldehyde (XIVa), was readily obtained by hydrolysis of (XIIIa). The structure of the previously unknown compounds (XIIa), (XIIIa) was confirmed spectrally.

The controlled cross-condensation of (XIVa) with α-TMS-imine (VII) under the above conditions led to E-acrolein (Xb) with an admixture of ~15% of its Z-isomer (NMR data), the content of which decreased to 2-3%, when a freshly prepared sample was held in a $CHCl_3$ solu-

TABLE 1. ^{13}C NMR Spectra of Compounds (Xa, b), (XIIIa, b)[a] ($CDCl_3$, δ, ppm)



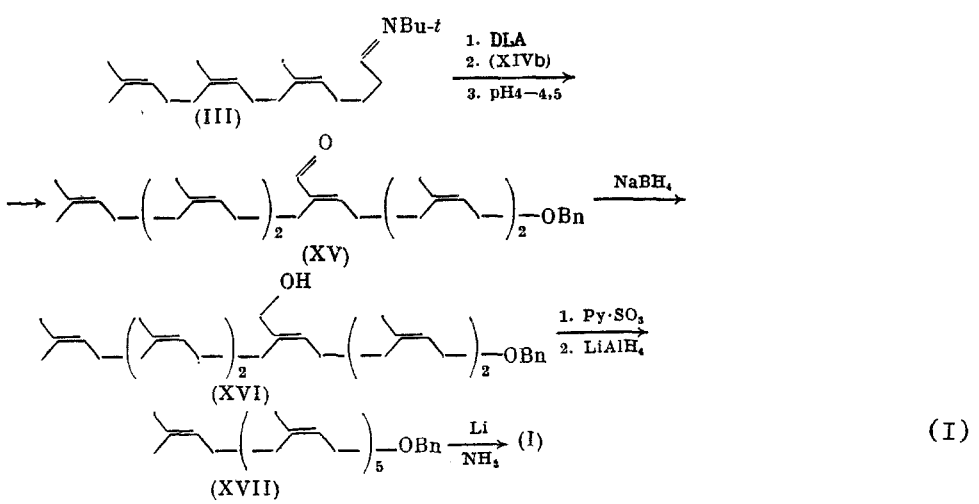
Atom	X=O		X=H, OH		X=H, H	
	(Xa), n=0	(Xb), n=1	(XIIa), n=0	(XIIb), n=1	(XIIIa), n=0	(XIIIb), n=1
C^1	103,49	103,54	104,03	104,12	104,16	104,11
C^2	31,90	32,28	32,58	32,57	32,34	32,33
C^3	18,77	18,35	22,66	22,33	26,54	26,26
C^4	142,90	142,80	142,44	139,88	139,83	134,68
C^5	149,61	153,59 [b]	123,20	122,13	122,41	124,68
C^6	66,40	24,85 [b]	66,54	25,79	66,49	26,02
C^7	–	30,57	–	31,97	–	32,20
C^8	–	138,14	–	138,76	–	140,09
C^9	–	122,92	–	122,13	–	121,98
C^{10}	–	65,84	–	66,80	–	66,33
C^{11}	–	22,96 [b]	–	23,37	–	23,08 [b]
C^{12}	193,70	194,25	66,19	66,27	23,38	23,34 [b]
C^{13}	72,91	71,96	72,57	72,11	72,28	71,92

a) Signals of ethylenedioxy and phenyl groups are also present in the spectra.
b) The marked signals may switch positions.

tion at -20°C in an Ar atmosphere for ~24 h. Repetition with (Xb) of the reductive operations indicated for (Xa) gave trisnor-Z,Z-farnesyl block-synthone (XIVb) via the intermediate stages of formation of allyl alcohol (XIIb) and acetal (XIIIb) with virtually the same effectiveness. The structure of these previously unknown compounds was confirmed spectrally.

The known aldehyde [(XIVb)≡(II) at R = Bn] thus prepared from the acetaldehyde (IV) and acrolein (V) derivatives was readily converted by the above-discussed sequence of reactions, first by condensation with imine (III) [8] into disubstituted E-acrolein (XV), and then into allyl alcohol (XVI) and, further, into the benzyl ether (XVII) and, lastly, by treatment of the latter with Li in NH_3 into the desired hexaprenol (I), with an overall yield of ~1% by 14 above-considered stages starting from (IV) (Scheme 4).

Scheme 4

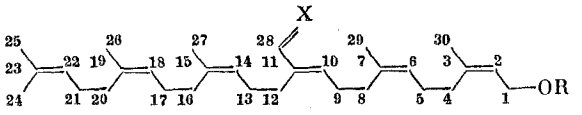


(I)

The structure of the intermediate compounds (XV)-(XVII) and the desired end product hexaprenol WC_5OH (I) was confirmed spectrally, in particular by means of their carbon spectra (Table 2), which were interpreted on the basis of data available for related objects [4-6, 9, 10].

The thus-described approach opens new possibilities for a highly stereoselective synthesis of linear Z-terpenoid structures with the participation of glutaraldehyde derivatives

TABLE 2. ^{13}C NMR Spectra of Compounds (I), (XV)-(XVII)[a] ($CDCl_3$, δ, ppm)



Atom	31 R=CH₂Ph			R=H	Atom	31 R=CH₂Ph			R=H
	X=O (XV)	X=H, OH (XVI)	X=H, H (I)	X=H, H (XVII)		X=O (XV)	X=H, OH (XVI)	X=H, H (XVII)	X=H, H (I)
C^1	66,13	66,26	66,47	59,05	C^{17}	26,45	26,60 [b]	26,71 [b]	26,46
C^2	122,06	121,87	122,00	124,55 [b]	C^{18}	124,77 [b]	124,88 [c]	125,88 [c]	125,07 [b]
C^3	138,52	138,35	135,59	140,00	C^{19}	135,65 [c]	135,45 [d]	135,60 [d]	135,36
C^4	32,14	32,40	32,55	32,28	C^{20}	31,76 [d]	31,91 [e]	32,00	32,28
C^5	26,22	26,40 [b]	26,45 [b]	26,46	C^{21}	26,65	26,82 [b]	26,71 [b]	26,46
C^6	124,10 [b]	124,28 [c]	125,08 [c]	124,56 [b]	C^{22}	124,20 [b]	124,88 [c]	124,68	125,07 [b]
C^7	135,79 [c]	135,13 [d]	135,30 [d]	135,36	C^{23}	131,50	131,50	131,50	135,36
C^8	30,38	31,77 [e]	32,25 [e]	32,28	C^{24}	17,39	17,58	17,65	17,70
C^9	27,16	25,96 [b]	26,45 [b]	26,46	C^{25}	25,50	25,66	25,76	25,76
C^{10}	153,99	126,24	125,08 [c]	124,56 [b]	C^{26}	23,28 [e]	23,31 [f]	23,46	23,47
C^{11}	143,16	138,92	135,30 [d]	135,36	C^{27}	23,21 [e]	23,36 [f]	23,46	23,47
C^{12}	24,05	28,37	32,25 [e]	32,28	C^{28}	194,58	66,81	23,46	23,47
C^{13}	26,45	26,60 [b]	26,45 [b]	26,46	C^{29}	22,95 [e]	23,46 [f]	23,46	23,47
C^{14}	125,8	124,87 [c]	125,08 [c]	125,07 [b]	C^{30}	23,30 [e]	23,36 [f]	23,46	23,47
C^{15}	135,04 [c]	135,20 [d]	135,60 [d]	135,36	C^{31}	71,92	71,96	72,15	–
C^{16}	31,92 [d]	32,15 [e]	32,25 [e]	32,28					

a) Signals of the phenyl group are also present in the spectra.
b-f) Signals marked in this column by the same letters may switch positions.

as nonisoprenoid starting materials. In particular, aldehydes (XIVa, b) can be readily transformed into nerol and Z,Z-farnesol, respectively, by olefinization according to Wittig; see [11].

EXPERIMENTAL

The IR spectra were obtained on a Perkin–Elmer 577 spectrophotometer in a thin layer or (for alcohols) in a CCl_4 solution, the UV spectra of alcoholic solutions on a Specord UV-VIS spectrophotometer at 70 eV, and the ^1H NMR spectra in $CDCl_3$ relative to TMS on a Bruker-250 spectrophotometer. The mass spectra were measured on a Varian MAT CH-6 spectrometer. The ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer with a working frequency of 75.5 Hz, and for compounds (Xa, b), (XIIa, b), (XIIIa, b) are given in Table 1, and for compounds (I), (XV)-(XVII), in Table 2. The preparative chromatography in a flash variant was carried out on silica gel L (40-100 mμ) from the firm Chemapol; TLC was carried out on Silufol plates from the firm Kavalier (CSSR) in a hexane–ether (4:1) system. All the experiments were carried out in an Ar atmosphere using freshly distilled solvents.

5,5-Ethylenedioxypentan-1-al tert-Butylamine (VI), 2-Trimethylsilyl-5,5-ethylenedioxypentan-1-al tert-Butylimine (VII), and 5,5-Ethylenedioxypentan-1-al (VIII). A solution of 9.9 g (100 moles) of (IV) [12] in 20 ml of THF was added in the course of 20 min with stirring at −5 to 0°C to a solution of LDA [freshly prepared at −15 to 0°C from 73.3 ml of 1.5 M solution of BuLi (110 mmoles) in hexane and 11.1 g (110 mmoles) of diisopropylamine] in 30 ml of THF and 17.9 g (100 mmoles) of HMPA. After 40 min, the reaction mixture was cooled to −70°C, treated for 20 min with a solution of 17.2 g (95 mmoles) of (V) [13] in 30 ml of THF, and stirred for 10 min. The temperature was then raised to −50°C, the mixture was held at this temperature for 4 h, and then decomposed with 50 ml of ice water at −5 to 0°C. The aqueous layer was separated and extracted with ether. The standard treatment of the extract gave 18.45 g (98%) of pure (according to the PMR data) imino-acetal (VI), bp 78°C (1 mm).* IR spectrum (ν, cm^{-1}): 2960, 2930, 2870, 2760, 1730, 1670, 1480, 1460, 1410, 1360, 1220, 1140, 1040, 945, 880, 735, 640. PMR spectrum (δ, ppm, J, Hz): 1.10 s (9H, CMe_3), 1.61 m (4H, CH_2), 2.20 d.t. (2H, $CH_2C{=}N$, J = 5 and 5.3), 3.85 m (4H, CH_2O), 4.82 t (1H, OCHO, J = 5), 7.55 t (1H, HC=N, J = 5). Found, %: C 66.11, H 10.47, N 7.32. $C_{11}H_{21}NO_2$. Calculated, %: C 66.29, H 10.62, N 7.03.

The thus-obtained reaction mixture was decomposed at −5 to 0°C by a solution of 31.5 g (210 mmoles) of tartaric acid and 0.22 liter of water, and stirred at this temperature for 2 h. The aqueous layer was separated, extracted with ether and the residue, after the standard treatment of the extract, was distilled under vacuum. Yield 9.1 g (70%) of (VIII) in the form of a colorless oil; bp 63°C (1 mm), $n_D^{19.5}$ 1.4469. IR spectrum (ν, cm^{-1}): 3020, 2960, 2890, 2725, 2670, 2620, 1720, 1480, 1440, 1410, 1360, 1340, 1310, 1270, 1240, 1140, 1070, 1040, 1020, 970, 950, 890, 790, 700. PMR spectrum (δ, ppm, J, Hz): 1.70 m (4H, CH_2), 2.45 d.t (2H, $CH_2C{=}O$, J = 1.8 and 6.6), 3.85 m (4H, CH_2O), 4.82 t (1H, OCHO, J = 4.8), 9.72 t (1H, CHO, J = 1.8). ^{13}C NMR spectrum (δ, ppm): 16.2 (C^3), 32.6 (C^4), 43.35 (C^2), 64.6 (CH_2O), 103.7 (C^5), 201.95 (C^1). Mass spectrum, m/z: 144 (M^+), 115, 73, 71, 29. Found, %: C 58.35, H 8.29. $C_7H_{12}O_3$. Calculated, %: C 58.32, H 8.39. Mol. wt. 144.2.

As described above, a solution of 16.5 g (83 mmoles) of (VI) in 20 ml THF was added in the course of 40 min to a solution of LDA (90 mmoles) in 60 ml of hexane and 30 ml of THF, stirred at −5°C. After 40 min, the reaction mixture was treated at −70°C for 10 min with a solution of 9.22 g (85 mmoles) of Me_3SiCl in 15 ml of THF, and allowed to stand for 4 h at −40°C. The temperature was raised in the course of 1.5 h to −5°C, and the mixture was decomposed with ice water. After 10 min, the aqueous layer was separated and extracted with ether. The standard treatment of the combined extracts and distillation of the crude product under vacuum gave 15.3 g (68%) of (VII) in the form of a colorless oil; bp 100.5°C (1 mm). IR spectrum (ν, cm^{-1}): 3380, 2960, 2930, 2870, 2750, 1650, 1620, 1470, 1455, 1405, 1360, 1250, 1225, 1135, 1035, 940, 885, 840, 750, 690, 615. PMR spectrum (δ, ppm, J, Hz): −0.02 s (9H, $SiMe_3$), 1.12 s (9H, CMe_3), 1.63 m (4H, CH_2), 1.84 m (1H, CHSi), 3.85 m (4H, CH_2O), 4.80 t (1H, OCHO, J = 4.5), 7.40 d (1H, HC=N, J = 6.2).

*The yield of the distilled product does not exceed 60%, and, therefore, it was further used without distillation, after being held in vacuo for 5 h at -20°C and 1 mm Hg, which did not affect the effectiveness of transformations with its participation.

6-Benzyloxy-4-formylhex-4E-en-1-al Ethyleneacetal (Xa). A solution of 13.0 g (48 mmoles) of (VII) in 15 ml of ether was added in the course of 15 min to a solution of LDA (48 mmoles) in 45 ml of hexane and 225 ml of ether, stirred at −15°C. The reaction mixture was allowed to stand for 40 min at −10°C, and then was treated for 20 min at −70°C with a solution of 6.0 g (40 mmoles) of (IX) [14] in 10 ml of ether, and stirred at this temperature for 2.5 h. The temperature was then raised to −10°C for 1.5 h and the mixture was decomposed at −70°C by a solution of 2.88 g (48 mmoles) of AcOH in 10 ml of ether and poured into a cold (5°C) solution of 12.1 g (96 mmoles) of $(COOH)_2 \cdot 2H_2O$ in 0.2 liter of H_2O. After stirring at 20°C for ~1.5 h, the aqueous layer was separated and extracted with ether. The standard treatment of the combined extracts gave 12.2 g of an oily product, which was chromatographed on 240 g of SiO_2. Gradient elution from hexane to ether (up to 30% of the latter) gave 5.52 g (52%) of (Xa); bp (bath) 160°C (1 mm). IR spectrum (ν, cm^{-1}): 3100, 3080, 3040, 2960, 2890, 2830, 2720, 1700, 1600, 1500, 1460, 1410, 1390, 1360, 1350, 1210, 1140, 1110, 1080, 1030, 950, 910, 820, 740, 700. UV spectrum: λ_{max} 210 nm (log ε 3.93), 229 nm (log ε 3.92). PMR spectrum (δ, ppm, J, Hz): 1.70 m (2H, HC^2), 2.35 m (2H, HC^3), 3.86 m (4H, CH_2O), 4.40 d (2H, CH_2OBn, J = 6.5), 4.58 s (2H, CH_2Ph), 4.80 t (1H, OCHO, J = 4.8), 6.62 t (1H, HC=C, J = 6.5), 7.3 m (5H, Ph), 9.42 s (1H, CHO). Mass spectrum, m/z: 276 (M^+), 275, 184, 169, 107, 99, 92, 91, 86, 79, 77, 73, 65, 45, 28. Found, %: C 69.75, H 7.29. $C_{16}H_{20}O_4$. Calculated, %: C 69.55, H 7.29; mol. wt. 276.3.

In a similar manner, from 6.17 g (30.1 mmoles) of (VI), 3.75 g (25 mmoles) of (IX) and 36 mmoles of LDA in a mixture of 20 ml of hexane and 170 ml of ether, 7.6 g of an oily product was obtained, which was chromatographed on 200 g of SiO_2. Gradient elution from hexane to ether gave 1.4 g (20%) of (Xa) and 2.2 g (30%) of (XI); R_f 0.14. IR spectrum (ν, cm^{-1}): 3600, 3090, 3070, 3040, 2960, 2930, 2880, 2770, 2720, 1720, 1500, 1460, 1410, 1390, 1360, 1230, 1210, 1150, 1120, 1040, 1030, 950, 910, 820, 700. PMR spectrum (δ, ppm): 1.75 m (4H, CH_2), 2.52 m and 2.90 m (1H, CHC=O), 3.55 m (2H, CH_2OBn), 3.9 m (5H, CH_2O, CHOH), 4.52 s, 4.53 s (2H, CH_2Ph), 4.85 m (1H, OCHO), 7.3 m (5H, Ph), 9.72 m (1H, CHO). ^{13}C NMR (δ, ppm): 20.28 (C^3), 31.66 (C^2), 54.42 (C^4), 64.86 (CH_2O), 70.90 (C^6), 72.36 (C^5), 73.54 (CH_2Ph), 104.03 (C^1), 127.72, 127.80, 128.31, 128.45, 137.85 (Ph), 203.83 (CHO).

10-Benzyloxy-8-methyl-4-formyldeca-4E,8Z-dien-1-al Ethyleneacetal (Xb). As described for (Xa), from 13.0 g (48 mmoles) of (VII), 8.88 g (40 mmoles) of (XIVa) (see below) and 48 mmoles of LDA in a mixture of 45 ml of hexane and 250 ml of ether, 8.6 g of (Xb) was obtained containing ~15% of the Z isomer, in the form of colorless oil. The solution of the latter in 90 ml of $CHCl_3$ was allowed to stand for ~24 h at ~20°C in an Ar atmosphere, and evacuated. Yield 8.6 g (63%) of (Xb) with admixture of <3% of the Z isomer (PMR); bp (bath): 178-180°C (0.018 mm). IR spectrum (ν, cm^{-1}): 3090, 3070, 3040, 2980, 2940, 2890, 2860, 2720, 1690, 1640, 1500, 1460, 1405, 1380, 1360, 1310, 1260, 1210, 1140, 1070, 1030, 940, 905, 880, 810, 735, 700. UV spectrum: λ_{max} 230 nm (log ε 4.21). PMR spectrum (δ, ppm, J, Hz); 1.68 s (3H, CH_3), 1.7 m (2H, CH_2), 2.35 m (6H, CH_2C=C), 3.9 m (4H, CH_2O), 4.01 d (2H, CH_2OBn, J = 6.7), 4.50 s (2H, CH_2Ph), 4.81 t (1H, OCHO, J = 4.5), 5.50 t (1H, HC^9, J = 6.7), 6.42 t (1H, HC^5, J = 6.7), 7.3 m (5H, Ph), 9.30 s (1H, CHO). Mass spectrum, m/z: 344 (M^+), 343, 315, 253, 237, 236, 235, 191, 175, 169, 161, 92, 91, 86, 73, 65, 45, 28. Found, %: C 73.01, H 8.13. $C_{21}H_{28}O_4$. Calculated, %: C 73.23, H 8.19; mol. wt. 344.4.

6-Benzyloxy-4-hydroxymethylhex-4E-en-1-al Ethyleneacetal (XIIa). A 0.98-g portion (25.6 mmoles) of $NaBH_4$ was added in the course of 20 min to a solution of 5.52 g (20 mmoles) of (Xa) in 0.2 liter of EtOH stirred at 0°C. The reaction mixture was allowed to stand for 1.5 h at ~20°C, and was then decomposed with 0.9 g (15 mmoles) of AcOH at 0°C. The subsequent standard treatment gave 5.7 g of a crude product, which was chromatographed on 100 g of SiO_2. Gradient elution from hexane to ether (up to 30% of the latter) gave 5.2 g (90%) of (XIIa) in the form of colorless oil; bp (bath) 168-170°C (1 mm). IR spectrum (ν, cm^{-1}: 3620, 3090, 3060, 3030, 2950, 2930, 2880, 1500, 1460, 1410, 1380, 1360. 1210, 1140, 1120, 1070, 1030, 950, 900, 810, 740, 700. PMR spectrum (δ, ppm, J, Hz): 1.8 m (2H, HC^2), 2.25 m (2H, HC^3), 3.9 m (4H, CH_2O), 4.08 s (2H, CH_2OH), 4.14 d (2H, CH_2OBn, J = 6.5), 4.55 s (2H, CH_2Ph), 4.85 t (1H, OCHO, J = 4.8), 5.72 t (1H, HC^5, J = 6.5), 7.3 m (5H, Ph). Mass spectrum, m/z: 278 (M^+), 277, 260, 247, 216, 203, 190, 186, 173, 171, 169, 168, 125, 108, 107, 99, 91, 86, 79, 73, 57, 55, 45, 28, 18. Found, %: C 69.20, H 7.98. $C_{16}H_{22}O_4$. Calculated, %: C 69.02, H 7.97; mol. wt. 278.35.

10-Benzyloxy-8-methyl-4-hydroxymethyldeca-4E,8Z-dien-1-al Ethyleneacetal (XIIb). As described for (XIIa), 7.8 g (90%) of (XIIb) was obtained from 8.6 g (25 mmoles) of (Xb), in the form of a colorless oil, bp (bath) 165-170° (0.018 mm). IR spectrum (ν, cm^{-1}): 3650, 3050, 2970, 2940, 2870, 1460, 1410, 1360, 1210, 1140, 1070, 1030, 950, 900, 740, 700. PMR spec-

trum (δ, ppm, J, Hz); 1.75 m (2H, HC^2), 1.76 s (3H, CH_3), 2.15 m (6H, $CH_2C{=}C$), 3.9 m (4H, CH_2O), 3.98 d (2H, CH_2OBn, J = 6), 4.00 s (2H, CH_2OH), 4.50 s (2H, CH_2Ph), 4.83 t (1H, OCHO, J = 5), 5.37 t (1H, HC^9, J = 6), 5.43 t (1H, HC^5, J = 6.7), 7.3 m (5H, Ph). Mass spectrum, m/z: 346 (M^+), 328, 315, 255, 238, 237, 220, 211, 195, 193, 176, 175, 174, 170, 169, 165, 159, 158, 147, 145, 143, 135, 134, 127, 121, 119, 109, 108, 107, 105, 101, 91, 86, 81, 73, 67, 57, 45, 28, 18. Found, %: C 73.02, H 9.09. $C_{21}H_{30}O_4$. Calculated, %: C 72.80, H 8.73; mol. wt. 346.5.

6-Benzoyloxy-4-methylhex-4Z-en-1-al Ethyleneacetal (XIIIa). A 10.56-g portion (66 mmoles) of pyridine sulfotrioxide [15] was added in the course of 40 min to a solution of 12.5 g (45 mmoles) of (XIIa) in 0.6 liter of THF, stirred at 0°C. The reaction mixture was allowed to stand for 2 h at 0°C and was then treated for 1.5 h at −30°C with a 1 M solution of $LiAlH_4$ in THF (360 ml, 360 mmoles). After stirring at 20°C for 4 days, the reaction mixture was treated as described in [4, 5] to give 10.96 g of an oily product, which was chromatographed on 250 g of SiO_2. Gradient elution from hexane to ether (up to 20% of the latter) gave 7.9 g (67%) of (XIIIa), bp 145-147°C (1 mm). IR spectrum (ν, cm^{-1}): 3100, 3080, 3040, 2980, 2940, 2880, 2800, 1670, 1500, 1455, 1410, 1380, 1360, 1210, 1140, 1120, 1070, 1030, 950, 900, 810, 740, 700. PMR spectrum (δ, ppm, J, Hz); 1.78 s (3H, CH_3), 2.20 m (4H, CH_2), 3.90 m (4H, CH_2O), 4.05 d (2H, CH_2OBn, J = 7.5), 4.52 s (2H, CH_2Ph), 4.83 t (1H, OCHO, J = 4.5), 5.47 t (1H, HC=C, J = 7.5), 7.3 m (5H, Ph). Found, %: C 73.69, H 8.48. $C_{16}H_{22}O_3$. Calculated, %: C 73.25, H 8.45.

10-Benzyloxy-4,8-dimethyldeca-4Z,8Z-dien-1-al Ethyleneacetal (XIIIb). As described for (XIIIa), 5.1 g (69%) of (XIIIb) was obtained from 7.8 g (22.5 mmoles) of (XIIb), 5.28 g (33 mmoles) of pyridine sulfotrioxide, and 180 ml of a 1 M solution (180 mmoles) of $LiAlH_4$; bp (bath) 148-150°C (0.018 mm). IR spectrum (ν, cm^{-1}): 3040, 2970, 2950, 2870, 1670, 1460, 1410, 1380, 1360, 1140, 1100, 1070, 1030, 950, 900, 740, 700. PMR spectrum (δ, ppm, J, Hz); 1.70 s (3H, CH_3), 1.75 m (2H, CH_2), 1.77 s (3H, CH_3), 2.10 m (6H, $CH_2C{=}C$), 3.9 m (4H, CH_2O), 4.05 d (2H, CH_2OBn, J = 7), 4.50 s (2H, CH_2Ph), 4.83 t (1H, OCHO, J = 4.8), 5.13 t (1H, HC^5, J = 7), 5.43 t (1H, HC^9, J = 7), 7.3 m (5H, Ph). Mass spectrum, m/z: 330 (M^+), 239, 231, 222, 209, 207, 195, 193, 177, 160, 159, 153, 149, 147, 145, 142, 134, 127, 121, 119, 111, 107, 105, 99, 95, 93, 91, 87, 86, 81, 80, 79, 77, 73, 69, 67, 65, 55, 45, 28. Found, %: C 76.12, H 9.07. $C_{21}H_{30}O_3$. Calculated, %: C 76.33, H 9.09; mol. wt. 330.5.

6-Benzyloxy-4-methylhex-4Z-en-1-al (XIVa). A solution of 10 g (38.15 mmoles) of (XIIIa) and 0.25 ml of 96% of H_2SO_4 in 0.8 liter of an H_2O–acetone (2:3) mixture was boiled for 4 h. The mixture was then neutralized at ~20°C with $NaHCO_3$, concentrated in vacuo, and the residue was extracted with ether. Following the standard treatment of the extract and the distillation of the oily product under vacuum, 6.49 g (78%) of (XIVa) was obtained; bp 147-148°C (2 mm). The physicochemical characteristics of the sample correspond to those described in the literature [16].

10-Benzyloxy-4,8-dimethyldeca-4Z,8Z-dien-1-al (XIVb). As described above for (XIVa), 2.16 g (72%) of XIVb was obtained from 3.46 (10.5 mmoles) of (XIIIb). The physicochemical characteristics of the sample fully correspond to those described previously in [5].

Benzyl Ether of 3,7,15,19,23-Pentamethyl-11-formyltetraeicosa-2Z,6Z,10E,14Z,18Z,22-hexaen-1-ol (XV). As described above for (Xa), by condensation at −70°C of 2.13 g (6.7 mmoles) of imine (III) [8], deprotonated by means of LDA, with 1.57 g (5.5 mmoles) of (XIVb) in 60 ml of a hexane–ether (1:4) mixture, 0.63 g (27%)* of (XV) was obtained with a stereochemical purity of >98% (PMR); bp (bath) 213-215°C (0.04 mm). IR spectrum (ν, cm^{-1}): 3360, 3100, 3080, 3040, 2975, 2940, 2860, 2720, 1690, 1640, 1500, 1455, 1405, 1380, 1370, 1315, 1260, 1205, 1180, 1115, 1090, 1070, 1030, 1010, 950, 840, 760, 700. UV spectrum: λ_{max} 238 nm (log ε 4.15). PMR spectrum (δ, ppm, J, Hz): 1.62 s (3H, cis-CH_3), 1.70 s (12H, trans-CH_3), 1.77 s (3H, CH_3C^3), 2.10 m (14H, $CH_2C{=}C$), 2.24 m (4H, HC^8, H^{12}), 2.43 m (2H, HC^9), 4.01 d (2H, CH_2OBn, J = 7.6), 4.51 s (2H, CH_2Ph), 5.13 m (4H, HC=C), 5.46 t (1H, HC^2, J = 7.6), 6.41 t (1H, HC^{10}, J = 7.6), 7.35 m (5H, Ph), 9.36 s (1H, CHO). Mass spectrum, m/z:** 531, 530 (M^+), 512, 439, 423, 422, 421, 405, 404, 394, 393, 379, 376, 354, 353, 301, 286, 285, 272, 271, 269, 267, 257, 255, 254, 253, 203, 175, 161, 159, 149, 147, 137, 136, 135, 134, 133, 123, 121, 119 , 109, 107, 105, 69. Found, %: C 83.17, H 10.28. $C_{37}H_{54}O_2$. Calculated, %: C 83.72, H 10.25; mol. wt. 530.8.

*The yield was not optimized.

**In the region with m/z 350-250, ions are listed whose intensity is higher than 10%, and in the region with m/z lower than 250, it is higher than 50% of the intensity of the ion with m/z 107 (100%).

Benzyl Ether of 3,7,15,19,23-Pentamethyl-11-hydroxymethyltetraeicosa-2Z,6Z,10E,14Z,18Z,22-hexen-1-ol (XVI). As described above for (XIIa), 0.45 g (96%) of (XVI) was obtained in the form of a colorless oil by reduction of 0.47 g (0.88 mmole) of (XV) with 40 mg (1.05 mmole) of $NaBH_4$ in 20 ml of EtOH; R_f 0.08; 0.4 (hexane:ether = 3:2). IR spectrum (ν, cm^{-1}): 3520, 3030, 2970, 2930, 2860, 2335, 1640, 1550, 1450, 1380, 1365, 1310, 1245, 1210, 1110, 1080, 1070, 1030, 1010, 950, 890, 840, 810, 795, 700. PMR spectrum (δ, ppm, J, Hz): 1.62 s (2H, cis-CH_3), 1.70 s (12H, trans-CH_3), 1.77 s (3H, CH_3C^3), 2.07 m (20H, $CH_2C{=}C$), 4.02 d (2H, CH_2OBn, J = 6), 4.04 s (2H, CH_2OH), 4.51 s (2H, CH_2Ph), 5.13 m (5H, $HC{=}C$), 5.40 t and 5.43 t (2H, HC^2, HC^{10}, $J_1 = J_2 = 6$), 7.3 m (5H, Ph). Mass spectrum, m/z:* 532 (M^+), 514, 450, 442, 441, 426, 425, 424, 423, 407, 406, 393, 381, 365, 364, 363, 356, 355, 274, 269, 257, 256, 255, 161, 159, 149, 147, 137, 135, 134, 133, 123, 121, 119, 107, 105, 103, 69.

Benzyl Ether of 3,7,11,15,19,23-hexamethyltetraeicosa-2Z,6Z,10Z,14Z,18Z,22-hexaen-1-ol (XVII). As described above for (XIIIa), 0.39 g (86%) of (XVII) was obtained in the form of a colorless oil by treatment of 0.45 g (0.84 mmole) of (XVI) in 15 ml of THF with 0.24 g (1.48 mmole) of pyridine sulfotrioxide, followed by reduction of the intermediate O-sulfate (without isolation) by 4.5 ml of a 1.53-M solution of $LiAlH_4$ (7 mmoles) in THF; R_f 0.86. IR spectrum (ν, cm^{-1}): 3030, 2960, 2920, 2860, 1665, 1490, 1450, 1380, 1360, 1310, 1240, 1200, 1110, 1080, 1070, 1030, 1000, 940, 905, 835, 725, 700. PMR spectrum (δ, ppm, J, Hz): 1.62 s (3H, cis-CH_3), 1.70 s (15H, trans-CH_3), 1.77 s (3H, $CH_3{-}C^3$), 2.05 m (20H, $CH_2C{=}C$), 4.03 d (2H, CH_2OBn, J = 7), 4.51 s (2H, CH_2Ph), 5.15 m (5H, $HC{=}C$), 5.43 t (1H, HC^2, J = 7), 7.35 m (5H, Ph). Mass spectrum, m/z: 517, 516 (M^+), 447, 446, 425, 408, 379, 365, 340, 339, 298, 297, 271, 257, 229, 217, 215, 203, 191, 189, 187, 177, 175, 163, 161, 159, 149, 147, 137, 135, 133, 123, 122, 121, 119, 109, 107, 105, 95, 94, 93, 92, 91, 81, 79, 69, 68, 67.

3,7,11,15,19,23-Hexamethyltetraeicosa-2Z,6Z,10Z,14Z,18Z,22-hexen-1-ol (Hexaprenol WC_5OH, I). A solution of 0.38 g (0.72 mmole) of (XVII) in 2 ml of ether was added in the course of 2 min to a solution of 26 mg (3.7 mg·at) of Li in 50 ml of NH_3 stirred at −40°C. The reaction mixture was held at this temperature for 3 h and then was decomposed by an excess of NH_4Cl. Subsequent standard treatment gave 0.24 g of a crude product, which was chromatographed on 10 g SiO_2. Gradient elution from hexane to ether (up to 20% of the latter) gave 0.19 g (73%) of (I) in the form of a colorless oil; bp (bath) 172°C (0.018 mm). IR spectrum (ν, cm^{-1}): 3610, 2960, 2930, 2860, 1660, 1450, 1380, 1240, 1040, 980, 840, 730. PMR spectrum (δ, ppm, J, Hz): 1.60 s (3H, cis-CH_3), 1.68 s (15H, trans-CH_3), 1.74 s (3H, $CH_3{-}C^3$), 2.07 m (20H, $CH_2C{=}C$), 4.07 d (2H, CH_2O, J = 7), 5.12 m (5H, $HC{=}C$), 5.43 t (1H, HC^2, J = 7). Mass spectrum, m/z: 427, 426 (M^+), 408, 339, 271, 204, 203, 191, 189, 187, 177, 175, 173, 163, 161, 159, 149, 147, 137, 135, 134, 133, 123, 122, 121, 119, 109, 107, 105, 95, 94, 93, 91, 83, 82, 81, 80, 79, 69, 68, 67. Found, %: C 84.73, H 11.90. $C_{30}H_{50}O$. Calculated, %: C 84.44, H 11.81; mol. wt. 426.7.

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SYNTHESIS OF Z,Z-TRISHOMOFARNESAL TERT-BUTYLIMINE

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A highly stereoselective method was developed for the preparation of Z,Z-trishomofarnesal tert-butylimine, a key block synthone required for the construction of polyprenols with a nonnatural configuration of the "head" end of the chain, using as a basis the controlled condensation of aldehydes with aldimines. It was shown that introduction into the condensation of aldehydes containing an acetal grouping at the ω-position results in the formation of considerable amounts of aldols. The use of α-trimethylsilyl derivatives of aldimines makes it possible to dispense with this process and to direct the reaction toward the desired E-acroleins.

The use of the "block" scheme we have proposed for constructing linear isoprenoids [1], as applied to fully cisoid analogs of polyprenols, for example to hexaprenol WC_5OH [2], required development of a reliable method of synthesis of the aldimine (I) indicated in the heading. The limited availability of Z,Z-farnesol, an obvious precursor of (I), prompted us to study the possibility of obtaining this block-synthone starting from the substantially more readily available nerol, using for the Z-C_5-propagation of the "tail" fragment of its chain the glutaraldehyde monoacetal, similarly as tert-butylimine of this aldehyde was used by us for the Z-C_5-elongation of the "head" end of the isoprene chain in the synthesis of the above-mentioned hexaprenol [2]. The results thereby obtained are presented in the present article.

The alkylation of neryl sulfide (II) with β-bromopropanal ethyleneacetal gives sulfide (III), the reductive desulfuration of the latter gives acetal (IV), the hydrolytic splitting of this gives aldehyde (V), and finally, treatment of (V) with t-$BuNH_2$ gives aldimine (VI) (Scheme 1). The cross-combination of (VI), deprotonated by means of lithium diisopropylamide (LDA), with glutaraldehyde monoacetal (VII) [2] gives a mixture of the expected E-acrolein (VIII) in a good yield with an approximately fivefold amount of much more polar product which is readily separated by chromatography. The presence of absorption bands of the OH (3600 cm^{-1}) and CHO groups (1720 cm^{-1}) in the latter's IR spectrum, conforms well with the structure of aldol (IX). Confirming this structure, there are in the ^1H and ^{13}C NMR spectra of this compound the CHO signals in particular at δ ~ 9.7 and 205 ppm, respectively, doubled because of diastereomerism, together with signals at 2.4 and 55 ppm, corresponding to the HCCHO fragment.

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