Organic Chemistry

Synthesis of (*Z*)-trisubstituted olefins with all substituents different from methyl *via* α,β-disubstituted (*E*)-acroleins

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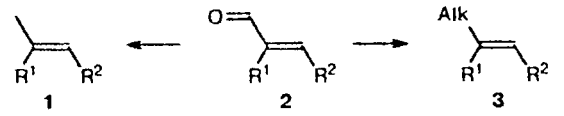
(*E*)-2,3-Disubstituted allyl bromides readily accessible in two steps from the corresponding enals react with dialkyl cuprates in a high regio- and stereoselective fashion to give (*Z*)-trisubstituted olefins with all substituents different from methyl. This reaction was used in the synthesis of benzyl 7-methyl-3-propyldeca-(2*Z*,6*Z*)-dienyl ether, a derivative of a component of the sex pheromone of the lesser apple worm *Laspeyresia pomonella* L.

Key words: (*Z*)-trisubstituted olefins, stereoselective synthesis, reaction of dialkyl cuprates with allyl bromides; insect pheromones.

Earlier, we described an effective and highly stereoselective method for constructing disubstituted (*Z*)-methylolefins (**1**)[1] based on higher thermodynamic stability of (*E*)-isomers of α,β-disubstituted acroleins (**2**).[2] The total synthesis of a large number of compounds of the polyprenol and dolichol series as well as their analogs was carried out using this method, which allowed us to study the structure—properties relationship for these important bioregulators.[3]



1 **2** **3**

In the present report, we consider the possibilities of using the "anchor effect" of (*E*)-acroleins **2**[2] for the highly stereoselective construction of (*Z*)-trisubstituted olefins (**3**) in which all substituents are different from methyl.

The transformation of (*E*)-enal (**4**)[4] into (*Z*)-olefins **3a,b** was studied as an example. As shown in Scheme 1, enal **4**, like its analogs synthesized earlier,[1] was transformed under the action of $NaBH_4$ into allylic alcohol (**5**) in a quantitative and stereospecific manner. The treatment of the latter with PBr_3 in the presence of pyridine affords the corresponding bromide (**6**) in high yield. The structures of compounds **5** and **6** were unambiguously determined from the ^1H and ^{13}C NMR spectra in which the signals of the CH_2X (X = OH, Br) and HC=C groups characteristic of (*E*)-isomers[5] were observed, while the corresponding signals for the (*Z*)-isomers are absent.

The transformation of bromide **6** into the target olefins **3a,b** was carried out using the cuprate method, which is known to be the most regio- and stereoselective

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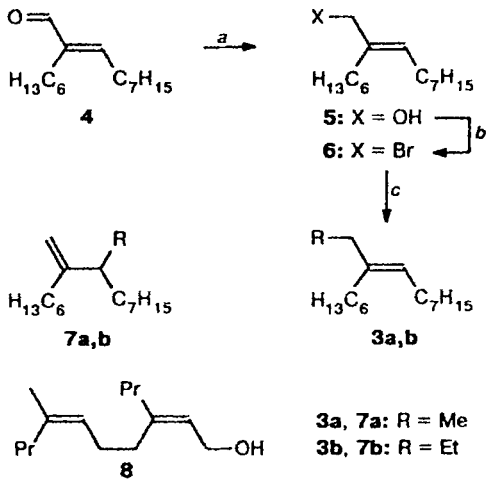
Scheme 1



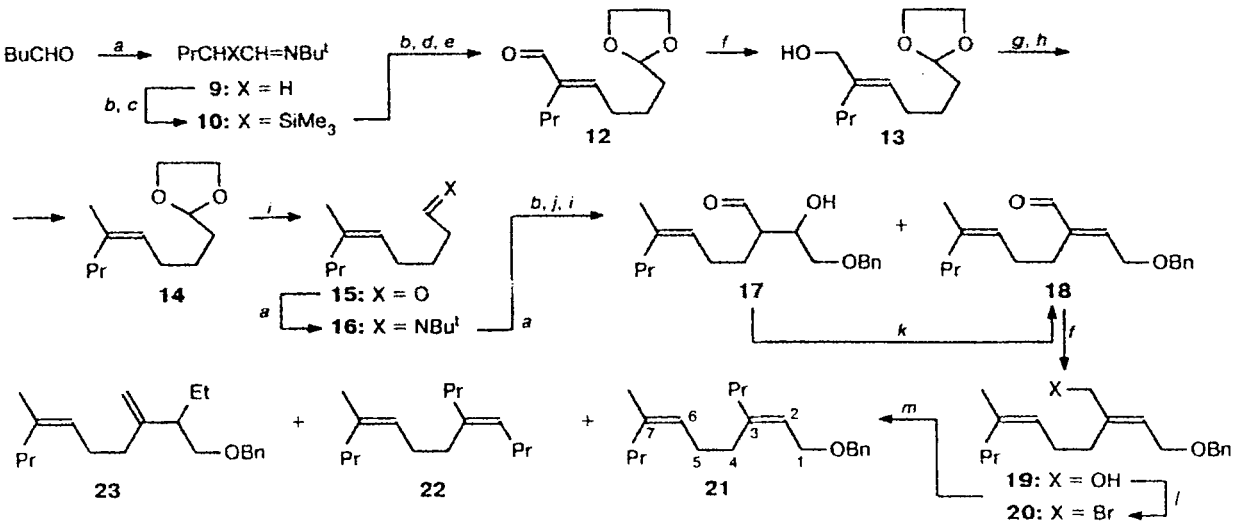
Reagents: *a*. $NaBH_4$; *b*. PBr_3/Py; *c*. R_2CuLi (R = Me, Et).

one for the alkylation of allyl halides. Indeed, the treatment of bromide **6** with an excess of Me_2CuLi in ether at −50 °C gives 7-ethylpentadec-(7*Z*)-ene (**3a**) in 88.5% yield, and its interaction with Et_2CuLi under the same conditions leads to 7-propylpentadec-(7*Z*)-ene (**3b**) in which the admixture of regioisomers (**7a,b**) amounts to 3.5 and 7.5%, respectively. This was concluded from HPLC and ^1H NMR spectroscopic data, in particular, from a comparison of the integral intensities of the signals of the HC=C and H_2C=C protons in the ^1H NMR spectrum (δ 5.1 and 4.8, respectively). The configuration of **3a,b** was determined from the NOE spectra using the NOESY procedure, which allowed us to reveal the steric proximity of HC(8) to the protons of the $\underline{CH_2}CH_2$ (**3a,b**) and $CH_3\underline{CH_2}$ (**3b**) groups of the substituent at C(7).

An attempt to use the above approach in the synthesis of natural compounds can be illustrated by the preparation of a derivative of 7-methyl-3-propyldeca-(2*Z*,6*Z*)-dien-1-ol (**8**), which is a component of the sex pheromone of the lesser apple worm *Laspeyresia pomonella* L.[6]

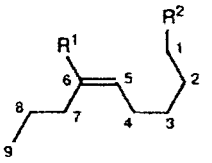
As shown in Scheme 2, the C(3)—C(10) fragment in **21** was constructed from *N-tert*-butylpentanimine (**9**) and glutaraldehyde monoethylene acetal (**11**).[7] Cross condensation of an α-trimethylsilyl (TMS) derivative (**10**) of imine **9** with aldehyde **11** under conditions elaborated for the synthesis of polyprenols leads to 2-propylhept-2-enedial 7-ethylene acetal (**12**) in ~80% yield. The latter contains <3% of the (*Z*)-isomer, which follows from a comparison of the integral intensities of the proton signals of the CHO group for (*E*)- and (*Z*)-isomers (δ 9.35 and 10.0, respectively) in the ^1H NMR spectrum of the sample obtained.[8] The reduction of enal **12** with $NaBH_4$ leads stereospecifically to hydroxyacetal **13** in quantitative yield, which was transformed by treatment of the corresponding sulfate with $LiAlH_4$ into acetal **14**. The (Z)-configuration of the latter was confirmed by ^1H and ^{13}C NMR spectroscopic data, which correlate well with the results obtained earlier.[4,5] The hydrolysis of acetal **14** leads to aldehyde **15**, whose *N-tert*-butylimine (**16**) was cross-coupled with

Scheme 2



Reagents: *a*. Bu^tNH_2; *b*. LDA; *c*. Me_3SiCl; *d*. $OCH(CH_2)_3CH(OCH_2)_2$ (**11**); *e*. H_3O^+(pH 4—4.5); *f*. $NaBH_4$; *g*. Py·SO_3; *h*. $LiAlH_4$; *i*. H_3O^+; *j*. $OCHCH_2OBn$; *k*. 3% HCl—THF (1 : 1, v/v); *l*. PBr_3/Py; *m*. Et_2CuLi.

Table 1. ^{13}C NMR spectra (δ) of compounds **12**—**15**



R^1, R^2	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)	C(11,12)
$R^1 = \overset{10}{C}HO$, $R^2 = (\overset{11,12}{C}H_2O)_2$ (**12**)	103.8	33.1	22.8	28.4	156.4	143.8	25.8	21.7	14.0	198.9	64.6
$R^1 = \overset{10}{C}H_2OH$, $R^2 = (\overset{11,12}{C}H_2O)_2$ (**13**)	104.3	33.2	23.9	27.1	125.9	139.5	30.0	21.6	14.1	66.6	64.6
$R^1 = \overset{10}{C}H_3$, $R^2 = (\overset{11,12}{C}H_2O)_2$ (**14**)	104.5	33.5*	24.4	27.5	125.0	135.3	33.8*	21.1	14.0	23.4	64.7
$R^1 = \overset{10}{C}H_3$, $R^2 = O$ (**15**)	202.6	43.3	22.3	26.9	123.8	136.5	33.65	21.0	13.8	23.2	—

Note. Assignments were made with consideration of the data obtained earlier.[5,8]
*These signals may be interchanged.

O-benzylglycolaldehyde to give a mixture of aldol (**17**) and (*E*)-enal (**18**) in the ratio ~1 : 3.4, which was separated by chromatography. A solution of **17** was refluxed in a mixture of THF with 3% HCl to give an additional amount of product **18**, whose overall yield was 35%.

A freshly prepared sample of enal **18** contains ~8% of (2*Z*)-isomer, whose amount decreases to ~2% (^1H NMR data) after the solution of **18** in chloroform has been kept at ~20 °C for two weeks. It was the latter specimen that was used for the completion of the synthesis. With this aim, (*E*)-enal **18** was reduced with $NaBH_4$ into (*E*)-alcohol **19**, which was transformed with PBr_3 and pyridine into bromide **20**. The structures of compounds **19** and **20** were unambiguously confirmed by ^1H and ^{13}C NMR spectroscopy with account of the data obtained earlier.[5] The reaction of bromide **20** with Et_2CuLi differs from a similar reaction of bromide **6**. The target ether **21** was obtained in ~7% yield, while the main reaction product, according to NMR data, was unexpectedly diene **22**. The pathways of its formation will be discussed elsewhere.

The structure of benzyl ether **21** was unambiguously determined by NMR spectroscopy. In particular, the signals of the $H_2C{=}C$ group were not observed in its ^1H NMR spectrum, which suggests the absence of an admixture of regioisomer **23**. The NOE spectrum (NOESY procedure) reveals a steric proximity of the vinylic proton at C(2) to the $\underline{CH_2}CH_2$ protons of the propyl substituent at C(3), which is possible only in the (2*Z*)-configuration.

Experimental

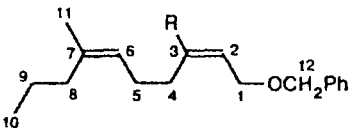
UV spectra of ethanolic solutions were obtained on a Specord UV-VIS spectrometer. IR spectra were recorded on a Perkin—Elmer 577 spectrometer (in a thin film). ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AC-200 spectrometer (50.3 MHz for ^{13}C) relative to tetramethylsilane. The spectroscopic data of compounds **12**—**15** are listed in Table 1, and those of compounds **18**—**21**, in Table 2. 2D-NOE spectra were recorded on a Bruker DRX-500 spectrometer (500.13 MHz) with a phase-sensitive NOESY pulse sequence (spectral width for F1 and F2 4500 Hz, pause between runs 1.3 s, mixing time 0.7 s, number of repetitions for each run 16, number of points for F2 2048, and number of runs 256). Mass spectra were obtained on a Varian MAT 311a spectrometer (EI, 70 eV; for $m/z < 200$, only peaks with a relative intensity >10% are given). Preparative flash-chromatography was carried out on silica gel L 40—100 μm (Chemapol). TLC was carried out on Silufol plates (Kavalier) in (*A*) ether—hexane (1 : 3) or (*B*) ether—hexane (1 : 1) systems. Analytical and preparative HPLC were performed on Armofer Sil-10 columns (150×4, 10 μm) with a PIDK-102 detector, the eluent rate being 6 mL min^{-1}.

The main solvents were purified as follows: ether and THF were kept over KOH, distilled successively over metallic Na and $LiAlH_4$, then refluxed with Na-benzophenone ketyl under Ar until a stable blue color formed, and distilled directly into a reaction vessel. Hexane and benzene were distilled over metallic Na.

2-Hexyldec-(2*E*)-en-1-ol (5) was obtained by reduction of aldehyde **4** [4] with $NaBH_4$ according to a standard procedure, yield 96%, R_f 0.31 (*B*). ^1H NMR, δ: 0.9 (t, 6 H, Me, J = 6.5 Hz); 1.3 (m, 18 H, CH_2); 2.05 (m, 4 H, $CH_2C{=}C$); 4.0 (s, 2 H, $C\underline{H_2}OH$); 5.38 (t, 1 H, HC(3), J = 7 Hz).

2-Hexyldec-(2*E*)-enyl bromide (6). To a solution of alcohol **5** (0.96 g, 4 mmol) and pyridine (0.14 g, 1.17 mmol) in 10 mL of hexane protected from light and stirred at −15 to −10 °C, a solution of PBr_3 (5.4 g, 2 mmol) in 5 mL of ether was added dropwise, and the mixture was stirred at this temperature for 1.5 h. Then the reaction mixture was heated to −5 °C, and water (5 mL) and ether (10 mL) were carefully added. The resulting mixture was stirred at ~0 °C for 15 min, the organic layer was separated, and the aqueous layer was extracted with ether. Conventional workup of the combined organic extracts gave an oily reaction product (1.1 g), which was

Table 2. ^{13}C NMR spectra (δ) of compounds **18—21**



R	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)	C(11)	C(12)	C(13)	C(14)	C(15)
R = $\overset{13}{C}HO$ (**18**)	66.5	149.6	143.3	24.8	26.5	123.8	136.3	33.6	21.1	13.9	23.3	72.9	193.6	—	—
R = $\overset{13}{C}H_2OH$ (**19**)	66.1	121.9	143.0	28.6	26.9	124.1	138.1	33.6	21.0	13.9	23.2	72.3	66.1	—	—
R = $\overset{13}{C}H_2Br$ (**20**)	66.2	127.0	139.2	29.1	26.4	123.7	138.0	33.8	21.1	13.9	23.3	72.4	38.0	—	—
R = $\overset{13}{C}H_2\overset{14}{C}H_2\overset{15}{C}H_3$ (**21**)	67.0	121.7	144.6	31.5[a]	27.4	125.0	139.0	34.2[a]	21.4[b]	14.4[c]	23.8	72.5	39.4	21.6[b]	14.5[c]

Note. Assignments were made with consideration of the data obtained earlier;[5,8] the signals of the Ph group were also observed in the spectra.

[a,b,c] These signals may be interchanged.

chromatographed on SiO_2 (30 g) with hexane as the eluent to give bromide **6** (0.85 g, 70%), R_f 0.9 (*A*). IR, ν/cm^{-1}: 3040, 2960, 2930, 2880, 2860, 1650, 1470, 1460, 1440, 1380, 1210, 650. ^1H NMR, δ: 0.9 (m, 6 H, Me); 1.30 (m, 18 H, CH_2); 2.07 (q, 2 H, $H_2C(4)$, J = 7.2 Hz); 2.20 (t, 2 H, $H_2C(2')$, J = 7.4 Hz); 4.01 (s, 2 H, CH_2Br); 5.61 (t, 1 H, HC(3), J = 7.2 Hz). ^{13}C NMR, δ: 14.0 (Me); 22.6; 28.1; 28.2; 29.2*; 31.7; 31.8; 39.85 (CH_2); 29.3* (CH_2Br); 132.5 (C(3)); 136.2 (C(2)).

7-Ethylpentadec-(7*Z*)-ene (3a) and 7-propylpentadec-(7*Z*)-ene (3b). To a suspension of CuI (2.13 g, 11.2 mmol) in 10 mL of ether vigorously stirred under an argon atmosphere at −20 °C, a freshly prepared 0.7 *M* solution of MeLi (35 mL, 24.5 mmol) was added dropwise. The reaction mixture was stirred for 5 min and cooled to −50 °C, and a solution of bromide **6** (0.68 g, 2.24 mmol) in 3 mL of ether was added dropwise. The resulting solution was stirred at the indicated temperature for 1 h, heated to −20 °C over 3 h, and then transferred into a mixture of 3% HCl (10 mL) and ether (25 mL) cooled to 0 °C. Stirring was continued at −20 °C for 30 min, the organic layer was separated, and the aqueous layer was extracted with ether. Conventional workup of the combined organic extracts and evaporation of the solvent gave (*Z*)-olefin **3a** (0.47 g, 88.5%) contaminated with 3.5% of isomer **7a** (^1H NMR and HPLC data) was obtained. The individual product **3a** was isolated by HPLC. Found (%): C, 85.17; H, 14.24. $C_{17}H_{34}$. Calculated: C, 85.62; H, 14.38. ^1H NMR, δ: 0.9 (t, 6 H, Me, J = 6.3 Hz); 1.0 (t, 3 H, Me, J = 7.4 Hz); 1.3 (m, 18 H, CH_2); 2.02 (m, 6 H, H_2CC=C); 5.04 (t, 1 H, HC(8), J = 7 Hz). ^{13}C NMR, δ: 13.0; 14.1 (Me); 22.7; 27.7; 28.5; 29.3; 29.4; 29.5; 29.6; 30.2; 31.9 (CH_2); 123.5 (C(8)); 141.0 (C(7)).

Analogously, (*Z*)-olefin **3b** contaminated with 7.5% of isomer **7b** was obtained from bromide **6** (0.72 g, 2.37 mmol) and Et_2CuLi (11.85 mmol) in 85% yield. The individual product **3b** was isolated by HPLC. ^1H NMR, δ: 0.9 (m, 9 H, Me); 1.3 (m, 20 H, CH_2); 2.0 (m, 6 H, H_2CC=C); 5.08 (t, 1 H, HC(8), J = 7 Hz). ^{13}C NMR, δ: 14.1; 14.3; 14.4 (Me); 21.5; 21.8; 22.9; 27.9; 28.1; 28.4; 29.5; 29.6; 29.7; 30.4; 32.1; 39.3 (CH_2); 125.2 (C(8)); 139.1 (C(7)).

* These signals may be interchanged.

***N*-*tert*-Butylpentanimine (9) and its α-TMS derivative (10).** To a solution of *tert*-butylamine (4.4 g, 60 mmol) in 50 mL of ether stirred at −5 °C, a solution of pentanal (5.26 g, 61 mmol) in 10 mL of ether was added slowly, the mixture was stirred at −20 °C for 2 h, then melted KOH (1 g) was added, and stirring was continued for 20 min. The ethereal layer was separated off and dried with K_2CO_3. The ether was removed, and the residue was distilled *in vacuo*. Aldimine **9** (6.98 g, 82%) was obtained, b.p. 59—61 °C (28 Torr), n_D^{21} 1.4243. Found (%): C, 76.54; H, 13.62. $C_9H_{19}N$. Calculated (%): C, 76.51; H, 13.56. ^1H NMR, δ: 0.92 (t, 3 H, Me, J = 7 Hz); 1.13 (s, 9 H, Me_3C); 1.4 (m, 4 H, CH_2); 2.22 (q, 2 H, $H_2C(2)$, J = 5.4 Hz); 7.57 (t, 1 H, HC=N, J = 5.4 Hz). ^{13}C NMR, δ: 14.05 (Me); 22.4; 28.6 (C(3,4)); 29.8 ($\underline{Me}_3C$); 36.1 (C(2)); 56.5 ($\underline{C}Me_3$); 158.4 (C(1)).

To a solution of Pr_2^iNLi (LDA) (20.6 mmol) in a mixture of hexane (13 mL) and THF (25 mL) stirred under an argon atmosphere at −10 to −15 °C, a solution of aldimine **9** (3.5 mL, 18.8 mmol) in 8 mL of THF was added dropwise. The reaction mixture was stirred at −0 °C for 40 min, then cooled to −78 °C, and a solution of Me_3SiCl (2.52 mL, 20 mmol) in 5 mL of THF was added dropwise. The resulting solution was stirred for 3.5 h, heated to −5 °C, poured into a mixture of 20 mL of water and 100 mL of ether, and stirred for 10 min. The aqueous layer was separated and extracted with ether. Conventional workup of the combined organic extracts and evaporation of the solvents gave compound **10** (3.44 g, 86%), b.p. 76—80 °C (10 Torr), n_D^{23} 1.4326. ^1H NMR, δ: 0.02 (s, 9 H, Me_3Si); 0.83 (t, 3 H, Me, J = 7.5 Hz); 1.09 (s, 9 H, Me_3C); 1.3—1.7 (m, 4 H, CH_2); 1.82 (m, 1 H, HC(2)); 7.40 (d, 1 H, HC=N, J = 8.3 Hz). ^{13}C NMR, δ: −2.7 (Me_3Si); 14.0 (Me); 23.6, 29.6 (C(3,4)); 29.8 ($\underline{Me}_3C$); 37.4 (C(2)); 56.4 ($\underline{C}Me_3$); 160.4 (C(1)).

2-Propylhept-(2*E*)-enedial 7-ethylene acetal (12). To a solution of LDA (48 mmol) in 200 mL of an ether—hexane (6.5 : 1) mixture stirred under an argon atmosphere at −50 °C, a solution of imine **10** (8.3 g, 39 mmol) in 30 mL of ether was added dropwise over 15 min. The reaction mixture was stirred at −50 °C for 1 h, heated to −15 °C over 40 min, and stirred for 15 min. Then it was cooled again to −78 °C, and a solution of monoacetal **11** (4.6 g, 32 mmol) in 10 mL of ether was

added dropwise. Stirring was continued at −78 °C for 2.5 h, and a solution of AcOH (1.91 g, 32 mmol) in 10 mL of ether was added dropwise. The resulting solution was heated to 0 °C over 4 h and poured into a solution of $(COOH)_2 \cdot H_2O$ (11.1 g) in 170 mL of a water—ether (1 : 1) mixture stirred at 5 °C. The layers were separated after 1.5 h. The aqueous layer was extracted with ether. Conventional workup of the combined organic extracts and evaporation of the solvents gave a residue (6.2 g), which was chromatographed on SiO_2 (100 g) with gradient elution (hexane→hexane : ether (85 : 15)) to give product **12** (5.44 g, 80%), b.p. 115 °C (bath) (3 Torr), $n_D^{21.5}$ 1.4810. Found (%): C, 67.81; H, 9.51. $C_{12}H_{20}O_3$. Calculated (%): C, 67.90, H, 9.50. UV, λ_{max}/nm (ε): 231 (12100), 312 (500). IR, ν/cm^{-1}: 2960, 2930, 2880, 2820, 2720, 1685, 1635, 1455, 1435, 1405, 1370, 1210, 1170, 1140, 1110, 1080, 1070, 1055, 1035, 950, 910, 880, 750. ^{1}H NMR, δ: 0.80 (t, 3 H, Me, J = 7.2 Hz), 1.25 and 1.55 (both m, 2 H and 4 H, CH_2); 2.10 (t, 2 H, $H_2C(2')$, J = 7 Hz); 2.30 (q, 2 H, $H_2C(4)$, J = 7 Hz); 3.80 (m, 4 H, CH_2O); 4.70 (t, 1 H, OCHO, J = 5.5 Hz); 6.32 (t, 1 H, HC(3), J = 7 Hz); 9.22 (s, 0.95 H, CHO of (*E*)-isomer); 10.0 (s, 0.05 H, CHO of (*Z*)-isomer).

6-Hydroxymethylnon-(5*E*)-enal ethylene acetal (13) was obtained by reduction of aldehyde **12** with $NaBH_4$ in EtOH according to a standard procedure, yield 99%, b.p. 126 °C (bath) (1 Torr). Found (%): C, 67.67; H, 9.80. $C_{12}H_{22}O_3$. Calculated (%): C, 67.57; H, 9.92. IR, ν/cm^{-1}: 3620, 2980, 2952, 2880, 1460, 1435, 1410, 1380, 1365, 1220, 1210, 1140, 1120, 1080, 1040, 1025, 950. ^{1}H NMR, δ: 0.85 (t, 3 H, Me, J = 7.3 Hz); 1.38 (m, 4 H, CH_2); 1.55 (m, 2 H, CH_2); 2.00 (m, 4 H, $H_2CC{=}C$); 3.80 (m, 4 H, CH_2O); 3.85 (br.s, 2 H, $\underline{CH_2}OH$); 4.72 (t, 1 H, OCHO, J = 4.6 Hz); 5.30 (t, 1 H, HC(5)) J = 6.4 Hz).

6-Methylnon-(5*Z*)-enal ethylene acetal (14). To a solution of hydroxy acetal **13** (5.8 g, 27 mmol) in 350 mL of THF stirred under an argon atmosphere at 0 °C, $Py \cdot SO_3$ (6 g, 39.6 mmol) was added over 30 min. The reaction mixture was stirred at ~0 °C for 2 h (monitored by TLC), cooled to −30 °C, and 187 mL of a 1.16 *M* solution of $LiAlH_4$ (217 mmol) in THF was added dropwise. The resulting solution was slowly heated to ~20 °C, stirred for 48 h, then cooled to 0 °C, and treated successively with water (18 mL), 15% NaOH (18 mL), and water (60 mL). The solution was filtered, and the precipitate was thoroughly washed with ether. Conventional workup of the combined organic extracts and evaporation of the solvents gave a light yellow oil (4.5 g), which was chromatographed on SiO_2 (200 g). Acetal **14** (3.9 g, 73%) was isolated by gradient elution (hexane→hexane : ether (97 : 3)), b.p. 80 °C (bath) (1 Torr), n_D^{22} 1.4600. Found (%): C, 72.87; H, 11.29. $C_{12}H_{22}O_2$. Calculated (%): C, 72.68; H, 11.18. IR, ν/cm^{-1}: 2960, 2860, 2760, 1665, 1450, 1410, 1380, 1210, 1140, 1040, 940, 885, 830, 740. ^{1}H NMR, δ: 0.85 (t, 3 H, Me, J = 7.5 Hz); 1.4 (m, 4 H, CH_2); 1.60 (m, 2 H, CH_2); 1.65 (s, 3 H, MeC(6)); 1.95 (m, 4 H, $H_2CC{=}C$); 3.85 (m, 4 H, CH_2O); 4.76 (t, 1 H, OCHO, J = 4.5 Hz); 5.08 (t, 1 H, HC(5)), J = 7 Hz).

6-Methylnon-(5*Z*)-enal (15) and its *N*-*tert*-butylimine (16). A solution of acetal **14** (5 g, 25.3 mmol) and 0.1 mL of conc. H_2SO_4 in 0.5 mL of 80% aqueous acetone was refluxed for 5 h (monitored by TLC), then cooled and neutralized with $NaHCO_3$. The acetone was removed *in vacuo*. The residue was extracted with ether. Conventional workup of the extract, evaporation of the ether, and distillation of the residue *in vacuo* gave aldehyde **15** (3.49 g, 90%), b.p. 38 °C (bath) (1 Torr). n_D^{21} 1.4608. Found (%): C, 77.81; H, 11.71. $C_{10}H_{18}O$. Calculated (%): C, 77.87; H, 11.76. IR, ν/cm^{-1}: 2960, 2940, 2880, 2820, 2720, 1730, 1470, 1460, 1450, 1410, 1380, 1190, 1080. ^{1}H NMR, δ: 0.90 (t, 3 H, Me, J = 7.3 Hz); 1.40 and 1.65 (both m, 2×2 H, CH_2); 1.68 (s, 3 H, MeC(6)); 2.00 (m, 4 H, $H_2CC{=}C$); 2.40 (dt, 2 H, $H_2C(2)$, J_1 = 6.6 Hz, J_2 = 1.5 Hz); 5.12 (t, 1 H, HC(5), J = 6 Hz); 9.75 (t, 1 H, CHO, J = 1.5 Hz).

A solution of aldehyde **15** (2.35 g, 15.2 mmol) in ether was treated with *tert*-butylamine (1.44 g, 19.7 mmol) as described above for compound **9**. Aldimine **16** (3.2 g, ~100%) was obtained in the individual state (according to NMR spectral data). It was dried *in vacuo* (1 Torr) for 12 h, then dissolved in ether, kept over 4A molecular sieves at ~5 °C for 12 h, and used further without additional purification. IR, ν/cm^{-1}: 2970, 2930, 2870, 2725, 1670, 1470, 1460, 1370, 1220, 830, 770, 750, 690. ^{1}H NMR, δ: 0.89 (t, 3 H, Me, J = 7.2 Hz); 1.18 (s, 9 H, Me_3C); 1.40 and 1.55 (both m, 2×2 H, CH_2); 1.67 (s, 3 H, MeC(6)); 2.0 (m, 4 H, $H_2CC{=}C$); 2.25 (m, 2 H, $H_2C(2)$); 5.10 (t, 1 H, HC(5), J = 6.2 Hz); 7.60 (t, 1 H, HC(1), J = 5.5 Hz).

2-(2-Benzyloxy-1-hydroxyethyl)-6-methylnon-(5*Z*)-enal (17) and 2-[2-(*E*)-benzyloxyethylidene]-6-methylnon-(5*Z*)-enal (18). To a solution of LDA (17 mmol) in 70 mL of an ether—hexane (~9 : 1) mixture stirred at −10 °C, a solution of imine **16** (3.15 g, 15 mmol) in 8 mL of ether was added dropwise over 10 min. The reaction mixture was stirred at 0 °C for 45 min and then cooled to −78 °C. A solution of *O*-benzylglycolaldehyde (1.8 g, 12 mmol) in 8 mL of ether was added dropwise, and the resulting solution was stirred at −78 °C for 2.5 h, heated slowly to ~4 °C, and left overnight. The cooled reaction mixture was poured into 200 mL of a mixture of ether with 3% HCl (1 : 1, v/v) and stirred for 2 h. The layers were separated. The aqueous layer was extracted with ether. Conventional workup of the combined extracts and evaporation of the ether gave a light yellow oil (2.5 g), which was chromatographed on SiO_2 (150 g). Product **18** (1.02 g) and hydroxyaldehyde **17** (0.3 g) were isolated by gradient elution (hexane→hexane : ether (85 : 15)). Refluxing a solution of **17** in 20 mL of a THF—3% HCl (1 : 1, v/v) mixture for 40 h followed by conventional workup of the reaction mixture gave an additional 0.18 g of product **18**, the overall yield of the latter being 35%. Aldol **17**, R_f 0.38 (*A*). ^{1}H NMR, δ: 0.9 (t, 3 H, Me, J = 7 Hz); 1.35 (m, 4 H, CH_2); 1.65 (s, 3 H, MeC(6)); 2.0 (m, 4 H, $CH_2C{=}C$); 2.4 (m, 1 H, HC(2)); 3.5 (m, 1 H, HC(2')); 4.55 (d, 2 H, $H_2C(2'')$, J = 7.2 Hz); 4.67 (s, 2 H, $\underline{CH_2}Ph$); 5.05 (t, 1 H, HC(5), J = 7 Hz); 7.35 (m, 5 H, Ph); 9.7 (d, 1 H, CHO, J = 6 Hz). Dienal **18**, b.p. 170 °C (1 Torr). Found (%): C, 79.47; H, 9.24. $C_{19}H_{26}O_2$. Calculated (%): C, 79.67; H, 9.15. UV, λ_{max}/nm (ε): 205 (13175), 228 (9740). IR, ν/cm^{-1}: 3090, 3070, 3040, 2980, 2940, 2890, 2860, 2720, 1735, 1690, 1500, 1460, 1405, 1380, 1360, 1310, 1260, 1210, 1140, 1070, 1030, 940, 905, 880, 810, 750, 700. ^{1}H NMR, δ: 0.88 (t, 3 H, Me, J = 7.0 Hz); 1.35 (m, 2 H, $CH_3C\underline{H_2}$); 1.65 (s, 3 H, MeC(6)); 2.0 (m, 4 H, $H_2C(4,7)$); 2.20 (t, 2 H, $H_2C(3)$, J = 7 Hz); 4.30 (d, 2 H, $H_2C(2'')$, J = 6.7 Hz); 4.55 (s, 2 H, $\underline{CH_2}Ph$); 5.05 (t, 1 H, HC(5), J = 7 Hz); 6.55 (t, 1 H, HC(2'), J = 6.7 Hz); 7.30 (m, 5 H, Ph); 9.40 (s, 0.96 H, CHO of (*E*)-isomer); 10.0 (s, 0.04 H, CHO of (*Z*)-isomer). MS, m/z (I_{rel} (%)): 286 $[M]^+$ (3), 203 (15), 178 (11), 135 (11), 109 (9.5), 107 (23), 97 (17), 92 (12), 91 (95), 81 (11), 79 (12), 69 (16), 56 (100), 44 (15), 42 (23), 33 (11), 29 (12), 28 (58).

1-*O*-Benzyl-3-hydroxymethyl-7-methyldeca-(2*E*,6*Z*)-dien-1-ol (19) was obtained by reduction of aldehyde **18** with $NaBH_4$ in EtOH according to a standard procedure. Yield 94%, b.p. 120 °C (0.08 Torr), n_D^{20} 1.5228. Found (%): C, 79.26; H, 9.78. $C_{19}H_{28}O_2$. Calculated (%): C, 79.12; H, 9.78. IR, ν/cm^{-1}: 3620, 3050, 2970, 2940, 2870, 1460, 1410, 1360,

1210, 1140, 1070, 1030, 950, 900, 735, 698. ^{1}H NMR, δ: 0.90 (t, 3 H, Me, J = 7.0 Hz); 1.37 (m, 2 H, $H_2C(9)$); 1.68 (s, 3 H, MeC(7)); 2.0 (t, 2 H, $H_2C(8)$, J = 7 Hz); 2.12 (m, 4 H, $H_2C(4,5)$); 4.05 (s, 2 H, CH_2OH); 4.10 (d, 2 H, $H_2C(1)$, J = 6.8 Hz); 4.55 (s, 2 H, CH_2Ph); 5.11 (t, 1 H, HC(6), J = 7 Hz); 5.70 (t, 1 H, HC(2), J = 6.8 Hz); 7.30 (m, 5 H, Ph). MS, m/z (I_{rel} (%)): 288 $[M]^+$ (2.5), 270 (2.5), 258 (8.5), 257 (23), 197 (11), 180 (27), 162 (18), 151 (12), 149 (65), 137 (23), 135 (12.5), 133 (12), 123 (14), 121 (14), 120 (11.5), 119 (54), 113 (29), 110 (19), 109 (32), 108 (20), 107 (40), 105 (17), 97 (53), 96 (35), 95 (38), 93 (38), 92 (52), 91 (100), 87 (12), 83 (20), 81 (58), 80 (18), 79 (53), 77 (15), 71 (22), 69 (44), 68 (13), 67 (38), 65 (20), 58 (16), 57 (23), 56 (100), 54 (12).

1-*O*-Benzyl-3-bromomethyl-7-methylideca-(2*E*,6*Z*)-dien-1-ol (20). As described above for bromide **6**, bromide **20** (0.69 g, 73%) was obtained from alcohol **19** (0.78 g, 2.73 mmol), PBr_3 (0.3 g, 1.17 mmol), and pyridine (0.07 mL, 0.87 mmol) and purified by chromatography (Al_2O_3, hexane). R_f 0.89 (*A*). ^{1}H NMR, δ: 0.89 (t, 3 H, Me, J = 7 Hz); 1.40 (m, 2 H, $H_2C(9)$); 1.68 (s, 3 H, MeC(7)); 2.00 (t, 2 H, $H_2C(8)$, J = 6 Hz); 2.15 (t, 2 H, $H_2C(4)$, J = 6.3 Hz); 2.25 (m, 2 H, $H_2C(5)$); 4.03 (s, 2 H, CH_2Br); 4.08 (d, 2 H, $H_2C(1)$, J = 6.3 Hz); 4.50 (s, 2 H, CH_2Ph); 5.10 (t, 1 H, HC(6), J = 6.5 Hz); 5.82 (t, 1 H, HC(2), J = 6.3 Hz); 7.30 (m, 5 H, Ph).

1-*O*-Benzyl-7-methyl-3-propylideca-(2*Z*,6*Z*)-dien-1-ol (21). Reaction of bromide **20** (0.5 g, 1.42 mmol) with Et_2CuLi (7.1 mmol) under the conditions described above for bromide **6** yields a mixture of products (0.34 g) as a yellow oil from which diene **22** (0.12 g, 40%), ^{1}H NMR, δ: 0.80 (t, 9 H, Me, J = 7 Hz); 1.40 (m, 6 H, CH_2CH_3); 1.68 (s, 3 H, MeC(7)); 2.05 (m, 10 H, $H_2CC{=}C$); 5.18 (poorly resolved t, 2 H, HC=C), and 0.05 g of a mixture of product **21** and its isomer **23** in the ratio ~5 : 1 were isolated by gradient elution (hexane→hexane : ether (95 : 5)) on SiO_2 (50 g). Product **21** in the individual state was isolated from this mixture by HPLC, yield 0.03 g, R_f 0.84 (*A*). ^{1}H NMR (500 MHz), δ: 0.88 (t, 3 H, Me, J = 7.3 Hz); 0.92 (t, 3 H, Me, J = 7.3 Hz); 1.40 (m, 4 H, CH_2); 1.66 (s, 3 H, MeC(7)); 2.05 (m, 8 H, $H_2CC{=}C$); 4.05 (d, 2 H, $H_2C(1)$, J = 6.8 Hz); 4.50 (s, 2 H, CH_2Ph); 5.12 (poorly resolved t, 1 H, HC(6)); 5.42 (t, 1 H, HC(2), J = 6.8 Hz); 7.35 (m, 5 H, Ph).

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