Glutaraldehyde Derivatives as Building Blocks for Stereoselective (*Z*)-C_5 Elongation of a Regular Isoprenoid Chain

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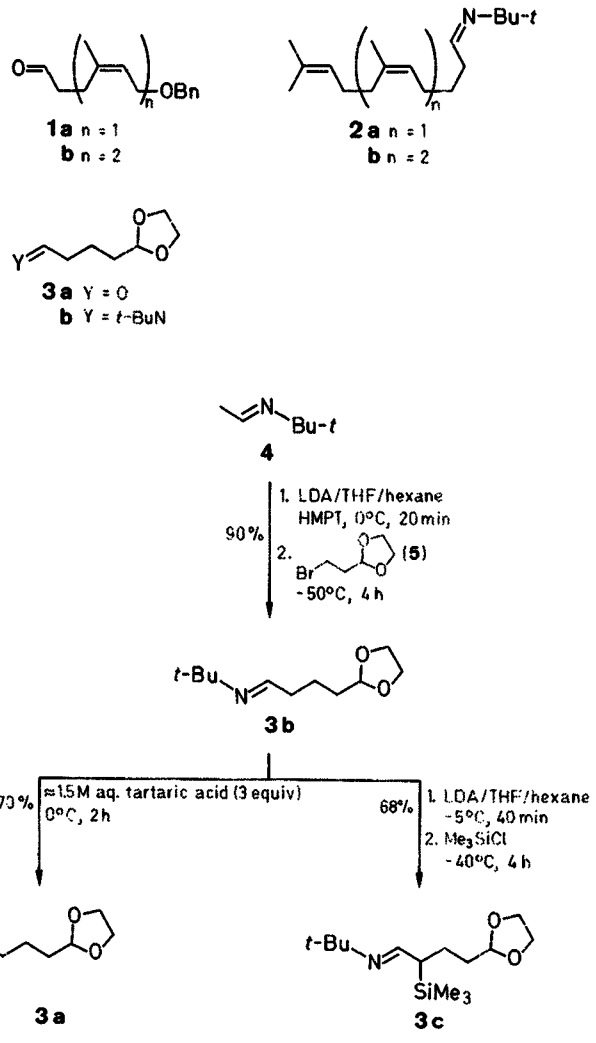
5,5-Ethylenedioxypentanal and its *tert*-butylimine may serve as versatile non-isoprenoid synthons for the construction of a regular *cisoid* terpenoid chain using the controlled crossed aldol condensation methodology.

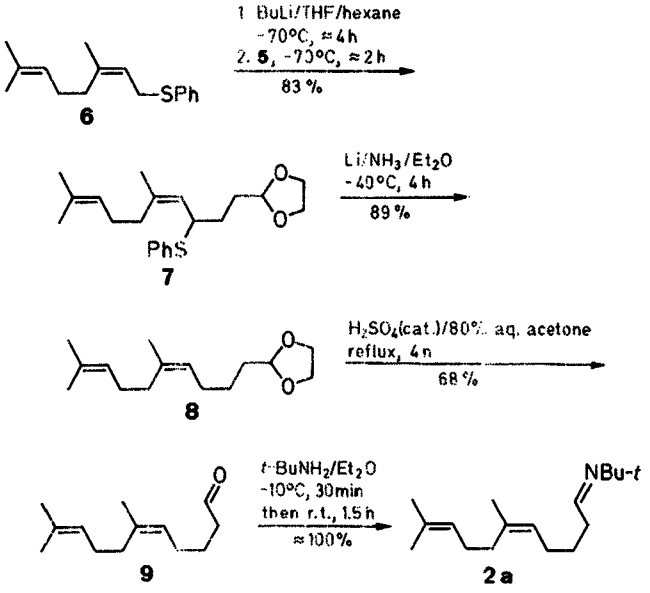
One of effective approaches to the construction of linear isoprenoid molecules containing inner (*Z*)-C_5 units consists of the controlled crossed aldol condensation of trisnorprenal derivatives of type **1** with trishomoprenal imines such as **2**.[1-5] Here we report the use of the same methodology for highly stereoselective *cis*-C_5 homologation of a terpenoid chain using readily available glutaraldehyde derivatives **3**. The versatility of such building blocks for the elongation of both the "tail" and the "head" moieties of terpenoid molecules is illustrated below the conversion of aldehyde **1a** and imine **2a** into respective prenologues **1b** and **2b** (Bn = CH_2Ph).



Scheme A

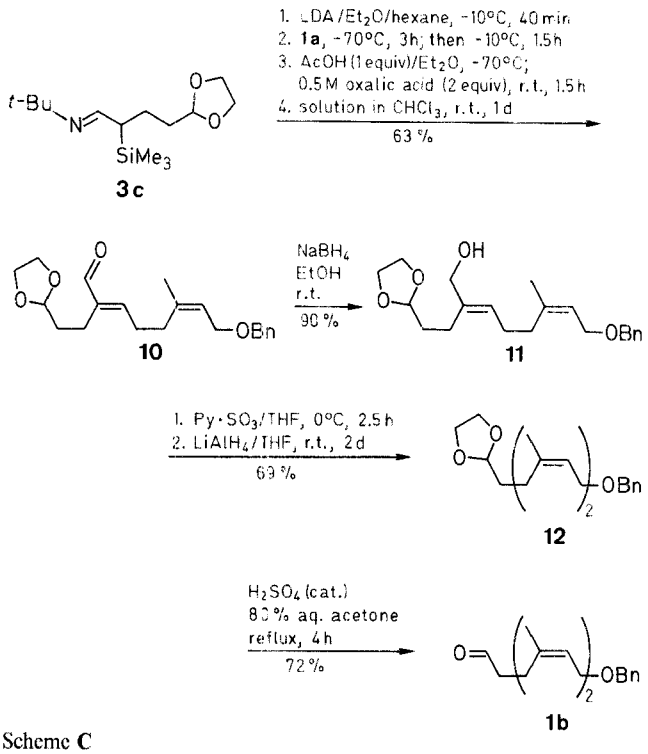
Both of these two transformations were previously unknown. The protected glutaraldehyde derivatives **3a–c** were prepared by deprotonated acetaldehyde *N-tert*-butylimine[6] (**4**) with lithium diisopropylamide (LDA) and hexamethylphosphoric triamide (HMPT) followed by alkylation with 3-bromopropanal ethylene acetal[7] (**5**) to give imine **3b** which was selectively hydrolyzed to aldehyde **3a**. Further, imine **3b** was readily transformed into its unstable trimethylsilyl derivative **3c** according to a previously reported procedure[8] (Scheme A).

The previously unknown aldimine **2a** used in the second transformation (**2a** → **2b**) was obtained by a four-step sequence (Scheme B) recently developed by us for the synthesis of all-(*E*)-farnesyl and all-(*E*)-geranylgeranyl analogs of **2**:[2,3] alkylation of neryl phenyl sulfide[9] (**6**) with **5** followed by reductive desulfurization of the intermediate **7** to the acetal **8** smoothly gave aldehyde **9**, which was converted into imine **2a** (≈ 50% overall yield from **6**). The structure of **2a** was confirmed by spectral (IR, ^{1}H-NMR) data.



Scheme B

The Peterson-type reaction of the silylated aldimine **3c** with the known nerol derivative **1a**[10] under the action of LDA proceeds smoothly to give, after mild acidic work-up and chromatography of the reaction mixture on silica gel, the (4*E*)-4-formyldecadienalmonoacetal **10** in 63% yield and in a stereochemical purity of ≈ 85% (Scheme C).



Scheme C

The purity of **10** was estimated by comparison in its ^{1}H-NMR spectrum of the integral intensities corresponding to aldehyde proton signals of the main (4*E*)-**10** and minor (4*Z*)-**10** isomers at $\delta = 9.3$ and 10.1, respectively (cf. Ref. 11). It was found that the portion of the former isomer is increased up to 95–97% on storage of a freshly prepared sample of **10** as its ca. 10% (*v*/*v*) chloroform solution under argon at room temperature for 1 day.

The transformation of formyldecadienal monoacetal **10** into the methyl derivative **12** was performed according to Corey[12] in 62% overall yield by the treatment of **10** with sodium borohydride in aqueous ethanol followed by lithium aluminum hydride reduction of the *O*-sulfate derivative of allylic alcohol without its isolation. Hydrolytic cleavage of the acetal **12** completes the preparation of **1b**, the known oxidative product of (*Z*,*Z*)-farnesyl benzyl ether.[2]

Starting with the aldimine **2a** and glutaraldehyde monoacetal **3a** (*Z*,*Z*)-trishomofarnesal derivative **2b** was then obtained (Scheme **D**). Thus, silylation of **2a** and Peterson-type condensation of the unstable intermediate **2c**, without its isolation, with **3a** furnished, after mild acidic treatment of the reaction mixture and equilibration of the crude product in chloroform solution, the (5*E*)-6-formylpentadecatrienal monoacetal **13** in 45% isolated yield with a stereochemical purity of > 95%, according to the above ^{1}H-NMR criteria. Successive hydride reduction of **13** to the hydroxymethyl derivative **14**, its further conversion into the triene acetal **15**, and hydrolytic cleavage of the latter gave (*Z*,*Z*)-trishomofarnesal **(16)** was followed by smooth transformation to the aldimine **2b** under the action of excess *tert*-butylamine.

The assigned structures of all new compounds prepared were consistent with their microanalytical and spectral data.

In summary, glutaraldehyde derivatives **3** can be regarded as versatile building blocks for the highly stereoselective *cis*-C_5 homologation of linear terpenoid aldehydes by means of controlled crossed aldol condensations.

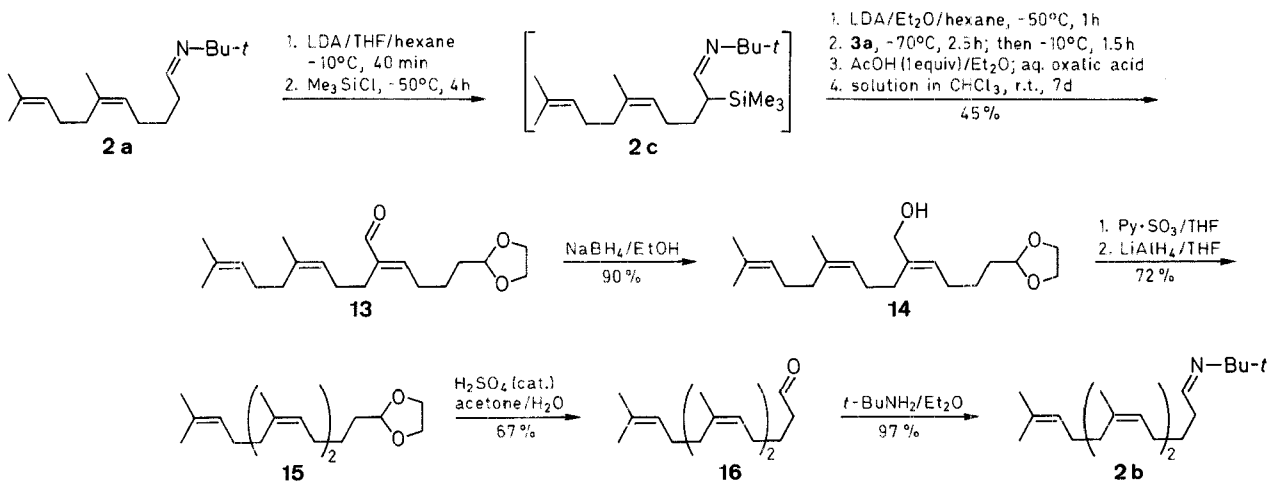
IR spectra were recorded on a Perkin-Elmer 577 spectrophotometer in Nujol (**11** and **14** were measured in CCl_4 solution), and UV spectra on a Perkin Elmer UV-VIS 552 spectrometer in EtOH. ^{1}H-NMR spectra were measured with a Bruker WM 250 spectrometer at 250 MHz.

All experiments were carried out under argon atmosphere and with freshly distilled and dried solvents.

5,5-Ethylenedioxypentanal (3a):

5,5-Ethylenedioxypentanal tert-Butylimine **(3b)**: A solution of acetaldehyde *tert*-butylimine (**4**;[6] 9.9 g, 100 mmol) in THF (20 mL) is added dropwise (40 min) to a stirred solution of LDA (110 mmol) in hexane (70 mL), THF (30 mL), and HMPT (17.6 mL, 100 mmol) at 0 °C. The mixture is stirred for 20 min and cooled at − 70 °C. A solution of 3-bromopropanal ethylene acetal[7] (**5**; 16.3 g, 90 mmol) in THF (20 mL) is then added during 20 min, and after 10 min the temperature is raised to − 50 °C and stirring is continued for 4 h. The reaction mixture is then treated at − 5 °C with ice-cold H_2O (50 mL). The aqueous phase is separated and extracted with Et_2O (3 × 70 mL). The combined organic layer is washed with sat. aq. NaCl (2 × 40 mL) and dried (Na_2SO_4). The solvent is removed *in vacuo*, and the residue is kept at 25 °C and 1 Torr for 6 h to give the imine **3b** as a colorless oil (Table); yield: 18.43 g (90%).

5,5-Ethylenedioxypentanal **(3a)**: The above reaction mixture is treated at 5 °C, instead of ice-cold H_2O, with a solution of tartaric acid (29.25 g, 0.21 mol) in H_2O (0.2 L) and is vigorously stirred at 0 °C for 2 h. The aqueous phase is then separated and extracted with Et_2O (5 × 100 mL). The combined organic layer is washed with sat. aq. NaCl (3 × 70 mL)



Scheme D

Table. Physical Data of New Compounds Prepared

Product	Yield[a] (%)	bp (°C) Torr	Molecular Formula[b]	IR ν(cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
2a	~100		$C_{17}H_{31}N$ (249.4)	2970, 2930, 2860, 2725, 1730, 1670, 1450, 1380, 1360, 1215, 1140, 1110, 1070, 980, 835, 740, 690	1.15 (s, 9H, *t*-Bu); 1.50 (m, 2H, CH_2); 1.57 (s, 3H, *cis*-CH_3); 1.67 (s, 6H, *trans*-CH_3); 2.00 (m, 6H, CH_2C=C); 2.22 (m, 2H, CH_2C=N); 5.10 (m, 2H, HC=C); 7.59 (t, 1H, J = 5.0, CH=N)
2b	97		$C_{22}H_{39}N$ (317.5)	2960, 2920, 2860, 2720, 1730, 1665, 1560, 1450, 1380, 1230, 1215, 1110, 1070, 985, 835, 740	1.16 (s, 9H, *t*-Bu); 1.53 (m, 2H, CH_2); 1.60 (s, 3H, *cis*-CH_3); 1.68 (s, 9H, *trans*-CH_3); 2.02 (m, 10H, CH_2C=C); 2.22 (m, 2H, CH_2C=N); 5.11 (m, 3H, HC=C); 7.58 (t, 1H, J = 5.0, CH=N)
3a	70	63/1	$C_7H_{12}O_3$ (144.2)	3020, 2960, 2890, 2725, 2670, 2620, 1720, 1480, 1440, 1410, 1360, 1340, 1310, 1270, 1240, 1140, 1070, 1040, 1020, 970, 950, 890, 790, 700	1.70 (m, 4H, CH_2); 2.45 (dt, 2H, J_d = 1.8, J_t = 6.6, CH_2C=O); 3.85 (m, 4H, CH_2O); 4.82 (t, 1H, J = 4.8, OCHO); 9.72 (t, 1H, J = 1.8, CHO)
3b	90	78/1	$C_{11}H_{21}NO_2$ (199.3)	2960, 2930, 2870, 2760, 1730, 1670, 1480, 1460, 1410, 1360, 1220, 1140, 1040, 945, 880, 735, 640	1.10 (s, 9H, *t*-Bu); 1.61 (m, 4H, CH_2); 2.20 (dt, 2H, J_d = 5.0, J_t = 5.3, CH_2C=N); 3.85 (m, 4H, CH_2O); 4.82 (t, 1H, J = 5.0, OCHO); 7.55 (t, 1H, J = 5.0, HC=N)
3c	68	100.5/1	$C_{14}H_{29}NO_2Si$ (271.5)	3380, 2960, 2930, 2870, 2750, 1650, 1620, 1470, 1455, 1405, 1360, 1250, 1225, 1135, 1035, 940, 885, 840, 750, 690, 615	−0.02 (s, 9H, $SiMe_3$); 1.12 (s, 9H, *t*-Bu); 1.63 (m, 4H, CH_2); 1.84 (m, 1H, CHSi); 3.85 (m, 4H, CH_2O); 4.80 (t, 1H, J = 4.5, OCHO); 7.40 (d, 1H, J = 6.2, HC=N)
7	83	142–143/ 0.03[c]	$C_{21}H_{30}O_2S$ (346.5)	3030, 2960, 2930, 2880, 1660, 1585, 1480, 1450, 1440, 1410, 1380, 1300, 1260, 1230, 1215, 1140, 1090, 1025, 940, 885, 750, 690	1.58 (s, 3H, *cis*-CH_3); 1.61 (m, 2H, CH_2); 1.69 (s, 6H, *trans*-CH_3); 1.8 (m, 6H, CH_2); 3.9 (m, 5H, CH_2O, CHS); 4.83 (t, 1H, J = 4.3, OCHO); 5.02 (m, 2H, HC=C); 7.35 (m, 5H$_{arom}$)
8	89	110.5/2	$C_{15}H_{26}O_2$ (238.4)	2965, 2935, 2890, 2870, 1680, 1460, 1410, 1380, 1140, 1050, 950, 830, 790	1.46 (m, 2H, CH_2); 1.60 (s, 3H, *cis*-CH_3); 1.64 (m, 2H, CH_2); 1.68 (s, 6H, *trans*-CH_3); 2.03 (m, 6H, CH_2C=C); 3.9 (m, 4H, CH_2O); 4.83 (t, 1H, J = 4.7, OCHO); 5.10 (t, 2H, J = 6.5, HC=C)
9	68	91–92/1.5	$C_{13}H_{22}O$ (194.3)	2970, 2940, 2860, 2720, 1730, 1455, 1415, 1380, 1240, 1140, 1115, 1070, 985, 835, 670	1.52 (m, 2H, CH_2); 1.60 (s, 3H, *cis*-CH_3); 1.68 (s, 6H, *trans*-CH_3); 2.0 (m, 6H, CH_2C=C); 2.4 (dt, 2H, J_d = 2.0, J_t = 7.5, CH_2C=O); 5.07 (m, 2H, HC=C); 9.70 (t, 1H, J = 2.0, CHO)
10[d]	63	178–180/ 0.018[c]	$C_{21}H_{28}O_4$ (344.4)	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	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, J = 6.7, CH_2OBn); 4.50 (s, 2H, CH_2Ph); 4.81 (t, 1H, J = 4.5, OCHO); 5.50 (t, 1H, J = 6.7, H-7); 6.42 (t, 1H, J = 6.7, H-3); 7.3 (m, 5H$_{arom}$); 9.30 (s, 1H, CHO)
11	90	165–170/ 0.018[c]	$C_{21}H_{30}O_4$ (346.5)	3650, 3050, 2970, 2940, 2870, 1460, 1410, 1360, 1210, 1140, 1070, 1030, 950, 900, 740, 700	1.75 (m, 2H, CH_2); 1.76 (s, 3H, CH_3); 2.15 (m, 6H, CH_2C=C); 3.9 (m, 4H, CH_2O); 3.98 (d, 2H, J = 6.0, CH_2OBn); 4.00 (s, 2H, CH_2O); 4.50 (s, 2H, CH_2Ph); 4.83 (t, 1H, J = 5.0, OCHO); 5.37 (t, 1H, J = 6.0, H-9); 5.43 (t, 1H, J = 6.7, H-5); 7.3 (m, 5H$_{arom}$)
12	69	148–150/ 0.018[c]	$C_{21}H_{30}O_3$ (330.5)	3040, 2970, 2950, 2870, 1670, 1460, 1410, 1380, 1360, 1140, 1100, 1070, 1030, 950, 900, 740, 700	1.70 (s, 3H, CH_3); 1.75 (m, 2H, CH_2); 1.77 (s, 3H, CH_3); 2.10 (m, 6H, CH_2); 3.9 (m, 4H, CH_2O); 4.05 (d, 2H, J = 7.0, CH_2OBn); 4.50 (s, 2H, CH_2Ph); 4.83 (t, 1H, J = 4.8, OCHO); 5.13 (t, 1H, J = 7.0, H-5); 5.43 (t, 1H, J = 7.0, H-9); 7.3 (m, 5H$_{arom}$)
13[e]	45	153–154/ 0.02[c]	$C_{20}H_{32}O_3$ (320.4)	2960, 2920, 2870, 2710, 1690, 1640, 1450, 1410, 1380, 1135, 1045, 1030, 940, 830, 760, 710	1.59 (s, 3H, *cis*-CH_3); 1.63 (m, 4H, CH_2); 1.68 (s, 6H, *trans*-CH_3); 2.0 (m, 6H, CH_2C=C); 2.25 (t, 2H, J = 7.5, H-3); 2.40 (dt, 2H, J_d = J_t = 7.5, H-2'); 3.9 (m, 4H, CH_2O); 4.87 (t, 1H, J = 4.8, OCHO); 5.08 (t, 2H, J = 7.5, HC=C); 6.43 (t, 1H, J = 7.5, H-1'); 9.34 (s, 1H, CHO)
14	90	165–170/ 0.02[c]	$C_{20}H_{34}O_3$ (322.5)	3620, 2960, 2920, 2880, 2860, 1670, 1450, 1410, 1380, 1195, 1140, 1030, 945, 890, 840, 705	1.52 (m, 2H, CH_2); 1.61 (s, 3H, *cis*-CH_3); 1.65 (m, 2H, CH_2); 1.68 (s, 6H, *trans*-CH_3); 2.1 (m, 10H, CH_2C=C); 3.9 (m, 4H, CH_2O); 4.03 (s, 2H, CH_2O); 4.85 (t, 1H, J = 4.8, OCHO); 5.13 (m, 2H, HC=C); 5.43 (t, 1H, J = 6.8, H-5)
15	72	135–138/ 0.037[c]	$C_{20}H_{34}O_2$ (306.5)	2960, 2920, 2880, 2860, 1730, 1660, 1450, 1410, 1375, 1310, 1140, 1040, 940, 875, 835, 735, 710	1.46 (m, 2H, CH_2); 1.60 (s, 3H, *cis*-CH_3); 1.64 (m, 2H, CH_2); 1.68 (s, 9H, *trans*-CH_3); 2.16 (m, 10H, CH_2C=C); 3.9 (m, 4H, CH_2O); 4.83 (t, 1H, J = 4.5, OCHO); 5.1 (m, 3H, HC=C)
16	67	126–130/ 0.04[c]	$C_{18}H_{30}O$ (262.4)	2970, 2930, 2860, 2720, 1730, 1670, 1450, 1410, 1380, 1110, 1070, 835, 740	1.61 (s, 3H, *cis*-CH_3); 1.65 (m, 2H, CH_2); 1.68 (s, 9H, *trans*-CH_3); 2.0 (m, 10H, CH_2C=C); 2.41 (dt, 2H, J_d = 2.0, J_t = 7.5, CH_2C=O); 5.1 (m, 3H, HC=C); 9.75 (t, 1H, J = 2.0, CHO)

[a] Yield of isolated, pure product.
[b] Satisfactory microanalyses obtained (exception: unstable **2a,b** and **3c**): C ±0.22, H ±0.15, N ±0.3, S ±0.1.
[c] In bath.
[d] UV: λ_{max} = 230 nm, lg ε = 4.21.
[e] UV: λ_{max} = 234 nm, lg ε = 4.14.

and dried ($MgSO_4$). The solvent is removed *in vacuo*, and the residue (12.0 g) is distilled to give **3a** as a colorless liquid (Table); yield: 9.1 g (70%); n_D^{19} 1.4469.

5,5-Ethylenedioxy-2-trimethylsilylpentanal *tert*-Butylimine (3c):

A solution of **3b** (16.5 g, 83 mmol) in THF (20 mL) is added dropwise (40 min) to a stirred solution of LDA (90 mmol) in hexane (60 mL) and THF (30 mL) at −5 °C. The mixture is stirred for 40 min and cooled at −70 °C. A solution of trimethylsilyl chloride (9.22 g, 85 mmol) in THF (15 mL) is then added during 10 min, and after an additional 10 min, stirring is continued at −40 °C for 4 h. The reaction mixture is then treated at −5 °C with ice-cold H_2O (50 mL), and the aqueous phase is separated and extracted with Et_2O (3 × 70 mL). The combined organic layer is washed with sat. aq. NaCl (2 × 40 mL) and dried (Na_2SO_4). The solvent is removed *in vacuo*, and the residue (21.8 g) is distilled to give **3c** as a colorless oil (Table); yield: 15.3 g (68%).

(*Z*)-6,10-Dimethyl-5,9-undecadienal *tert*-Butylimine (2a):

(Z)-6,10-Dimethyl-4-phenylthio-5,9-undecadienal Ethylene Acetal **(7)**: To a stirred solution of neryl phenyl sulfide[9] (**6**; 16.97 g, 69 mmol) in THF (0.3 L) at −70 °C, 1.5 M BuLi in hexane (50 mL, 75 mmol) is added during 30 min. The reaction mixture is kept at −70 °C for 3.5, treated at this temperature with a solution of **5**[7] (19.9 g, 110 mmol) in THF (50 mL) for 20 min, stirred further for 1.5 h, and then quenched at −70 °C with MeOH/Et_2O (1:1, 20 mL). The mixture is poured with stirring into ice-cold H_2O/Et_2O (1:1, 0.2 L); the aqueous phase is separated and extracted with Et_2O (3 × 50 mL). The combined organic layer is washed with aq. NaCl (3 × 50 mL) and dried (Na_2SO_4). The solvent and excess of **5** are removed *in vacuo*, and the residue (22.7 g) is chromatographed on silica gel (250 g) using gradient elution from hexane to hexane/Et_2O (85:15) to give the sulfide **7** as a colorless oil (Table); yield: 19.22 g (83%).

(Z)-6,10-Dimethyl-5,9-undecadienal Ethylene Acetal **(8)**: To a stirred solution of Li (0.8 g, 114 mmol) in NH_3 (150 mL) at −50 °C, a solution of **7** (8.5 g, 24.5 mmol) in Et_2O (15 mL) is added during 10 min. The reaction mixture is kept at −40 °C for 4 h, then quenched with an excess of solid NH_4Cl. The NH_3 is evaporated, and the residue is treated with H_2O (50 mL) and extracted with Et_2O (5 × 25 mL). The extract is washed with sat. aq. NaCl (3 × 25 mL) and dried (Na_2SO_4). The solvent is removed *in vacuo*, and the residue (5.8 g) is chromatographed on silica gel (100 g) using gradient elution from hexane to hexane/Et_2O (9:1) to give the acetal **8** as a colorless oil (Table); yield: 5.2 g (89%).

(Z)-6,10-dimethyl-5,9-undecadienal **(9)**:

A solution of **8** (5.2 g, 21.8 mmol) and conc. H_2SO_4 (0.1 mL) in 80% aq. acetone (0.5 L) is refluxed for 4 h, then neutralized with 10% aq. $NaHCO_3$, and concentrated *in vacuo*. The residue is extracted with Et_2O (5 × 80 mL). The extract is washed with sat. aq. NaCl (3 × 40 mL) and dried (Na_2SO_4). The solvent is removed, and the residue is distilled to give the aldehyde **9** as a colorless oil (Table); yield: 4.88 g (68%).

(Z)-6,10-Dimethyl-5,9-undecadienal tert-butylimine **(2a)**: To a stirred solution of **9** (2.72 g, 14 mmol) in Et_2O (70 mL) at −10 °C, a solution of *t*-$BuNH_2$ (5.4 g, 73 mmol) in Et_2O (10 mL) is added during 10 min. The reaction mixture is warmed to 25 °C, kept at this temperature for 1.5 hours, and after addition of dried KOH powder (1 g), is vigorously stirred for a further 20 min. The organic phase is separated and dried (K_2CO_3). The solvent is removed *in vacuo*, and the residue is kept at 25 °C and 1 Torr for 6 h to give the imine **2a** as a colorless oil (Table); yield: 3.38 g (~ 100%).

(4*Z*,8*Z*)-10-Benzyloxy-4,8-dimethyl-4,8-decadienal (1b):

(2E,6Z)-8-Benzyloxy-2-(3,3-ethylenedioxypropyl)-2,6-octadienal **(10)**: A solution of **3c** (13.0 g, 48 mmol) in Et_2O (15 mL) is added dropwise (15 min) to a stirred solution of LDA (52 mmol) in hexane (45 mL) and Et_2O (225 mL) at −10 °C. The mixture is stirred for 40 min and cooled at −70 °C. A solution of (*Z*)-6-benzyloxy-4-methyl-4-decanal[10] (**1a** 8.88 g, 40 mmol) in Et_2O (15 mL) is then added during 20 min, and after stirring for 2.5 h, the mixture is warmed to −10 °C and kept at that temperature for 1.5 h. The reaction mixture is then quenched at −70 °C with a solution of AcOH (2.88 g, 48 mmol) in Et_2O (10 mL) and poured into the vigorously stirred solution of oxalic acid dihydrate dissolved in dry $CHCl_3$ (90 mL). The solution is left at 25 °C under argon atmosphere for 1 day and then evaporated. The residue is kept at 25 °C and 1 Torr for 5 h to give the aldehyde **10** as a colorless oil (Table); yield: 8.68 g (63%).

(4E,8Z)-10-Benzyloxy-4-hydroxymethyl-8-methyl-4,8-decadienal Ethylene Acetal **(11)**: To a stirred solution of **10** (8.6 g, 25 mmol) in EtOH (0.2 L) at 0 °C $NaBH_4$ (1.22 g, 32 mmol) is added during 20 min. The reaction mixture is kept at 25 °C for 1.5 h, then quenched at 0 °C with AcOH (0.9 g, 15 mmol), stirred for 10 min, neutralized with sat. aq. $NaHCO_3$ and evaporated *in vacuo*. The residue is dissolved in Et_2O (50 mL), washed with sat. aq. NaCl (3 × 15 mL), dried (Na_2SO_4) and evaporated *in vacuo*. Chromatography of the crude product (8 g) on silica gel (250 g) using gradient elution from hexane to hexane/Et_2O (7:3) gives the alcohol **11** as a colorless oil (Table); yield: 7.8 g (90%).

(4Z,8Z)-10-Benzyloxy-4,8-dimethyl-4,8-decadienal Ethylene Acetal **(12)**: Sulfur trioxide–pyridine complex[13] (5.28 g, 33 mmol) is added during 20 min to a vigorously stirred solution of **11** (7.8 g, 22.5 mmol) in THF (0.3 L) at 0 °C. The mixture is maintained at this temperature for 2 h and then is treated dropwise (40 min) at −30 °C with a 1 M solution of $LiAlH_4$ in THF (180 mL, 180 mmol). The reaction mixture is stirred at 25 °C for 2 days, is then treated at 0–2 °C successively with H_2O (5 mL), 15% aq. NaOH (5 mL) and H_2O (15 mL). The solid formed is filtered and washed with Et_2O (150 mL). The aqueous phase is separated and extracted with Et_2O (2 × 10 mL). The combined organic layers are washed with sat. aq. NaCl (3 × 50 mL) and dried (Na_2SO_4). The solvent is removed *in vacuo* and the residue is dissolved in hexane (30 mL). The filtered hexane solution is evaporated *in vacuo* to give the oily product (6.2 g), which is chromatographed on silica gel (250 g). Gradient elution from hexane to hexane/Et_2O (4:1) leads to the acetal **12** as a colorless oil (Table); yield: 5.1 g (69%).

(4Z,8Z)-10-Benzyloxy-4,8-dimethyl-4,8-decadienal **(1b)**: A solution of **12** (3.46 g, 10.5 mmol) in 80% aq. acetone (0.2 L) containing conc. H_2SO_4 (0.08 mL) is refluxed for 4 hours. Work-up as for **9** above and distillation of the crude product gives the aldehyde **1b**[2] as a colorless oil; yield: 2.17 g (72%).

(5*Z*,9*Z*)-6,10,14-trimethyl-5,9,13-pentadecatrienal *tert*-Butylimine (2b):

(Z)-2-(Z-5,5-Ethylenedioxypentylidene)-6,10-dimethyl-5,9-undecadienal **(13)**: A solution of **2a** (3.44 g, 13.8 mmol) in THF (8 mL) is added dropwise (10 min) to a stirred solution of LDA (16 mmol) in hexane (12 mL) and THF (40 mL) at −10 °C. The mixture is stirred for 40 min and cooled at −50 °C. A solution of trimethylsilyl chloride (1.5 g, 13.8 mmol) in THF (12 mL) is then added during 20 min and stirring is continued for 4 h. The reaction mixture is filtered, cooled to −70 °C and added dropwise (30 min) to a vigorously stirred solution of LDA (16 mmol) in hexane (12 mL) and Et_2O (60 mL) at −50 °C. The mixture is kept at this temperature for 40 min, warmed rapidly to −30 °C, stirred for an additional 15 min, then cooled to −70 °C, and treated during 10 min with a solution of **3a** (1.58 g, 11 mmol) in Et_2O (5 mL). After 2.5 h, the reaction mixture is warmed to −10 °C for 1.5 h, recooled to −70 °C, quenched at this temperature with a solution of AcOH (0.96 g, 16 mmol) in Et_2O (3 mL) and poured into the vigorously stirred solution of oxalic acid dihydrate (6.05 g, 48 mmol) in H_2O (0.1 L) at 5 °C. The mixture is then worked up as for **10** above to give, after chromatography of the crude product (ca. 3 g) on silica gel (100 g) using gradient elution from hexane to hexane/Et_2O (4:1) and storage at 25 °C of thus purified sample in $CHCl_3$ solution for 1 week, the aldehyde **13** as a colorless oil (Table); yield: 1.6 g (45%).

(5E,9Z)-6-Hydroxymethyl-10,14-dimethyl-5,9,13-pentadecatrienal Ethylene Acetal **(14)**: As described above for **11**, treatment of **13** (2.5 g, 7.8 mmol) with $NaBH_4$ (0.38 g, 10 mmol) in EtOH (70 mL), work-up of the reaction mixture, and chromatography of the crude product (2.4 g) on silica gel (80 g) using gradient elution from hexane to hexane/Et_2O (7:3) gives the alcohol **14** as a colorless oil (Table); yield: 2.25 g (90%).

(5Z,9Z)-6,10,14-Trimethyl-5,9,13-pentadecatrienal Ethylene Acetal **(15)**: As described above for **12**, successive treatment of **14** (5.45 g, 16.9 mmol) with sulfur trioxide–pyridine complex (4.48 g, 28.4 mmol) in THF (0.2 L) followed by 1 M solution of $LiAlH_4$ in THF (135 mL, 135 mmol), work-up of the reaction mixture, and chromatography of the crude product (4.2 g) on silica gel (150 g) using gradient elution from

elution from hexane to hexane/Et_2O (3:1) to give the aldehyde **16** as a colorless oil (Table); yield: 2.16 g (67%).

(5Z,9Z)-6,10,14-Trimethyl-5,9,13-pentadecatrienal tert-Butylimine (**2b**): As described above for **2a**, starting from **16** (1.82 g, 6.9 mmol) and *t*-$BuNH_2$ (3.8 g, 36.5 mmol) in Et_2O (40 mL), the imine **2b** is obtained as a colorless oil (Table); yield: 2.13 g (97%).

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