Synthesis of alkyl (α-phenylthioalkenyl) ketones containing a (*Z*)-trisubstituted olefinic fragment

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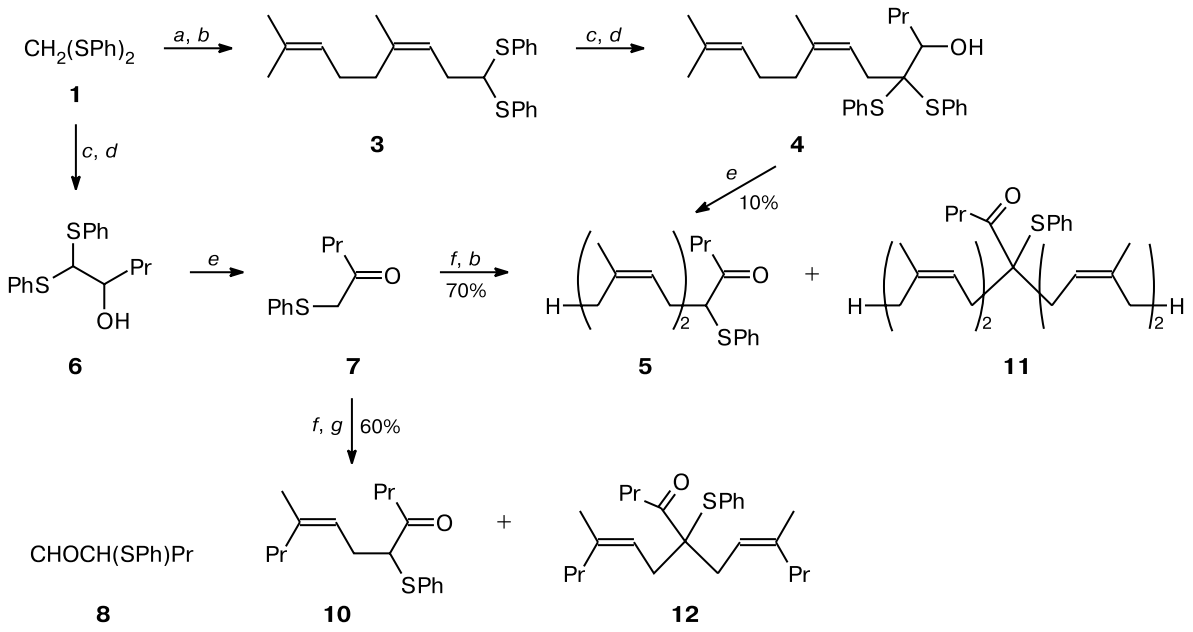
Warren's method, which has been proposed for the synthesis of α-phenylthiodialkyl ketones, appeared to be inefficient for the preparation of their alkenyl alkyl analogs. The latter were prepared in good yields by alkenylation of alkyl phenylthiomethyl ketones with alkenyl bromides.

Key words: alkyl (α-phenylthioalkenyl) ketones, (*Z*)-8-methyl-5-phenylthioundec-7-en-4-one, (*Z*)-8,12-dimethyl-5-phenylthiotrideca-7,11-dien-4-one; 1-phenylthiopentan-2-one, thioacetals, sulfides.

Earlier,[1,2] we have demonstrated that condensation of anions of alkyl trialkylsilylacetates with methyl α-phenylthioalkyl or -alkenyl ketones proceeds with (*Z*)-stereoselectivity of ~90%. This fact was used, in particular, in the total synthesis of the sex pheromone of bean beetle.[3] The stereochemistry of this reaction with ketones containing the alkyl substituent other than methyl remained unknown. Elucidation of this question requires the development of convenient and reliable procedures for the synthesis of such ketones.

The present study was aimed at solving this problem with the use of ketones containing the PhS group in the

Scheme 1



Reagents and conditions: *a*. BuLi; *b*. Br (**2**); *c*. BuLi/TMEDA; *d*. PrCHO; *e*. TsOH/PhH, 80 °C; *f*. NaH/THF; *g*. Pr Br (**9**).

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 3, pp. 635—639, March, 2004.

1066-5285/04/5303-0665

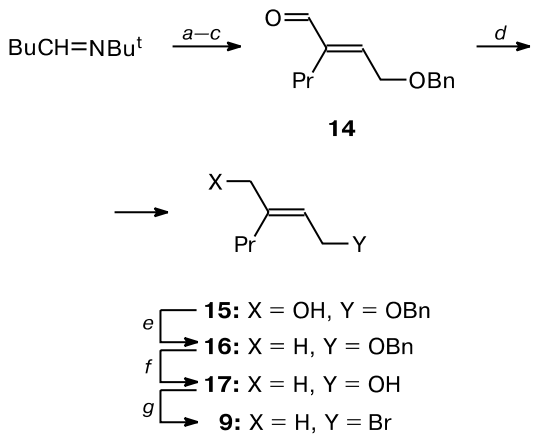
homoallylic position with respect to the (*Z*)-double bond. The method,[4] which works well with simplest ketones,[4,5] appeared to be inefficient for the preparation of the desired compounds. For example, alkenylation of di(phenylthio)methane (**1**) with neryl bromide (**2**) (Scheme 1) affords dithioacetal **3** in good yield. The latter is smoothly transformed into alcohol **4** by condensation with butanal. However, thermolysis of **4** in the presence of TsOH[3,4] is accompanied by strong resinification, and the yield of the target ketone **5** is no higher than 10%.

A more successful synthesis of ketone **5** was accomplished using a reverse sequence of alkenylation steps. The first step of the synthesis involves condensation of dithioacetal **1** with butanal to form alcohol **6** (see Scheme 1), whose thermolysis according to Warren's method gives rise to ketone **7**.* Alkenylation of ketone **7** with neryl bromide (**2**) affords the target ketone **5** in 70% yield. Analogously, alkenylation of ketone **7** with bromide **9** gives ketone **10**. The preparation of ketones **5** and **10** by this method is accompanied by bis-alkenylation giving rise to dienic derivatives **11** and **12**, respectively, in 5—7% yields. These by-products are easily separated from the target reaction products by chromatography.

The structures of previously unknown compounds **5**—**8** and **10**—**12** were confirmed by elemental analysis and spectroscopic data, which are in good agreement with the earlier results.[1—3]

Bromide **9** required for the synthesis of ketone **10**, was prepared by the method, which we have developed earlier[6] for the construction of the (*Z*)-trisubstituted C=C bond.

Scheme 2



Reagents and conditions: *a*. LDA/THF/HMPA; *b*. $BnOCH_2CHO$ (**13**); *c*. H_3O^+; *d*. $NaBH_4$; *e*. 1) $Py \cdot SO_3$, 2) $LiAlH_4$/THF; *f*. Li/NH_3; *g*. PBr_3/Et_2O.

* Thermolysis of alcohol **6** was accompanied by the rearrangement giving rise to aldehyde **8** in ~8% yield. Under conditions of chromatography on SiO_2, alcohol **6** was partially decomposed to give ketone **7** in ~7% yield.

Scheme 2 demonstrates that condensation of pentanal *N-tert*-butylimine with benzyl ether of glycolaldehyde (**13**) afforded (*E*)-acrolein **14** in 80% yield with stereoselectivity of >98%. The stereochemistry of compound **14** was concluded from its ^1H NMR spectrum based on the integral intensity ratio of the signals for the protons of the CHO group in the (*E*) and (*Z*) isomers (δ 9.4 and 10.0, respectively).[7] The stereospecific transformation of acrolein **14** into bromide **9** was carried out using standard procedures through alcohol **15**, benzyl ether **16**, and alcohol **17**. The structures of previously unknown compounds **9** and **14**—**17** were confirmed by spectroscopic data, which agree well with the earlier results.[6,8]

Experimental

The IR spectra were measured on a Perkin—Elmer 577 spectrometer in a thin film or (for alcohols) in solutions in CCl_4. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200 spectrometer in $CDCl_3$ relative to Me_4Si as the internal standard. The electron-impact mass spectra were obtained on Varian MAT CH-6 or Varian MAT 311A spectrometers at 70 eV; *m/z* values of peaks with relative intensities higher than 10% are given; the exceptions are the molecular ion peaks. Preparative flash chromatography was carried out on silica gel 60 (Merck); TLC was performed on Silufol plates (Kavalier, Czech Republic) in benzene (*A*) or a diethyl ether—hexane system (1 : 1) (*B*).

The solvents were purified as follows. Diethyl ether and THF were kept over KOH, successively distilled from Na and $LiAlH_4$, refluxed under Ar with sodium benzophenone ketyl until the solution developed a steady blue color, and then distilled directly into a reaction vessel. Hexane and benzene were distilled from Na.

Solutions of LDA were prepared directly in a reaction vessel from equivalent amounts of diisopropylamine and a 1.3—1.5 *M* BuLi solution in hexane, which was prepared according to a standard procedure.

Experiments with the use of metallic lithium, BuLi, NaH, and LDA were carried out under argon using glassware which has been dried at 160 °C for 12 h followed by cooling under a stream of argon.

The standard workup of organic extracts implies their washing to pH ≈7, drying with $MgSO_4$, and vacuum evaporation of the solvent.

(*Z*)-4,8-Dimethylnona-3,7-dienal (homo-neral) diphenyl dithioacetal (3). A 1.25 *M* BuLi solution in hexane (11.2 mL, 14 mmol) was added to a solution of di(phenylthio)methane (3.25 g, 14 mmol) in THF (50 mL) at a temperature from 0 to −3 °C for 15 min. The reaction mixture was stirred at 0 °C for 30 min and cooled to −10 °C. Then a solution of neryl bromide (**2**) (Fluka) (3.79 g, 17.5 mmol) in THF (10 mL) was added to the reaction mixture for 20 min. The mixture was stirred at −10 °C for 15 min, warmed to ~20 °C over 20 min, stirred for 2 h, and treated with a mixture of ice water and *tert*-butyl methyl ether (TBME) (1 : 1, v/v; 50 mL). The aqueous solution was extracted with TBME (3×20 mL). After standard workup of the organic extracts, the residue was dried *in vacuo* (1 Torr) for 8 h to give acetal **3** (~100% yield) as a pale-yellow oil, which was used without additional purification. ^1H NMR, δ: 1.60 (s, 3 H,

cis-MeC(8)); 1.70 (s, 3 H, *trans*-MeC(8)); 1.76 (s, 3 H, MeC(4)); 2.05 (m, 4 H, CH_2C=C); 2.60 (dd, 2 H, C(2)H_2, $J_1 = J_2$ = 6.5 Hz); 4.40 (t, 1 H, C(1)H, J = 6.5 Hz); 5.06 (poorly resolved t, 1 H, C(7)H); 5.40 (t, 1 H, C(3)H, J = 6.5 Hz); 7.40 (m, 10 H, Ph).

(*Z*)-8,12-Dimethyl-5,5-di(phenylthio)trideca-7,11-dien-4-ol (4). A 1.3 *M* BuLi solution in hexane (15 mL, 20 mmol) was added dropwise to a stirred solution of dithioacetal **3** (4.75 g, 12.9 mmol) and TMEDA (2.45 mL, 15.6 mmol) in THF (120 mL) at −5 °C for 20 min. The solution was warmed to 0 °C and stirred for 30 min. Then a solution of butanal (1.1 g, 14 mmol) in THF (3 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 10 min, warmed to ~20 °C over 10 min, stirred for 1 h, and poured into ice water (100 mL). After 15 min, the aqueous layer was separated and extracted with TBME (5×50 mL). After standard workup of the organic extracts, the residue (5.15 g) was chromatographed on SiO_2 (100 g). Gradient elution (hexane→benzene, 2 : 3) afforded alcohol **4** in a yield of 3.32 g (60%) as a colorless oil, R_f 0.50 (*A*). ^{1}H NMR, δ: 0.95 (t, 3 H, Me, J = 7.1 Hz); 1.35 (m, 2 H, C(2)H_2); 1.55 (s, 3 H, *cis*-MeC(12)); 1.65 (s, 3 H, *trans*-MeC(12)); 1.73 (s, 3 H, MeC(8)); 1.90 (m, 6 H, C(3)H_2, C(9)H_2, C(10)H_2); 2.20—2.60 (2 H, C(6)H_2, AB portion of ABX system, δ_A 2.29, δ_B 2.49, J_{AB} = 9.9 Hz, $J_{AX} = J_{BX}$ = 6.0 Hz); 2.65 (d, 1 H, OH, J = 5.5 Hz); 3.73 (m, 1 H, CHOH); 4.97 (dt, 1 H, C(11)H, J_1 = 1.14 Hz, J_2 = 5.6 Hz); 5.55 (t, 1 H, C(7)H, X portion of ABX system, $J_{AX} = J_{BX}$ = 6.0 Hz); 7.50 (m, 10 H, Ph). ^{13}C NMR, δ: 13.9 (Me); 17.4 (*cis*-MeC(12)); 19.9 (C(2)); 23.5 (MeC(8)),; 25.5 (*trans*-MeC(12)); 25.9, 32.2, 34.3 (C(3), C(6), C(9), C(10)); 74.0 (C(5)); 75.6 (C(4)); 119.6 (C(7)); 123.8 (C(11)); 131.4 (C(12)); 137.3 (C(8)).*

Thermolysis of compound 4. Toluene-*p*-sulfonic acid monohydrate (0.53 g) was added in one portion with stirring under argon to a boiling solution of alcohol **4** (3.18 g, ~7 mmol) in anhydrous benzene (160 mL). The reaction mixture was stirred for 15 min, cooled to ~5 °C, and poured into a stirred saturated aqueous Na_2CO_3 solution at ~20 °C. The benzene layer was separated. After standard workup of this layer, a brown viscous oil was obtained in a yield of 2.31 g. According to the ^{1}H NMR spectroscopic data, the oil contained no more than 10% of ketone **5**.

1,1-Di(phenylthio)pentan-2-ol (6). A 1.3 *M* BuLi solution in hexane (57 mL, 74 mmol) was added to a stirred solution of **1** (14.46 g, 63.33 mmol) in THF (250 mL) at 0 °C for 30 min. After 15 min, a solution of butanal (4.49 g, 62.33 mmol) in THF (10 mL) was added at the same temperature. The reaction mixture was stirred at 0 °C for 10 min and then at ~20 °C for 40 min, after which the mixture was transferred into a cooled mixture of water and TBME (1 : 1, v/v; 200 mL). The mixture was stirred for 15 min. The aqueous layer was separated and extracted with TBME (3×100 mL). After standard workup of the combined organic extracts, the reaction product (17.05 g) was divided into three equal portions. Each portion was chromatographed on SiO_2 (100 g). Gradient elution (hexane→benzene) afforded alcohol **6** in a yield of 11.08 g (58.5%) and ketone **7** in a yield of 1.35 g (~7%) (see below). Alcohol **6**, R_f 0.26 (*A*). IR, ν/cm^{-1}: 3540, 3080, 3060, 3040, 3020, 3010, 2965, 2940, 2880, 1585, 1485, 1470, 1445, 1385, 1340, 1310, 1290, 1210, 1160, 1125, 1095, 1075, 1033, 1010, 935, 920, 910, 860, 730, 700, 688, 500. ^{1}H NMR, δ: 0.92 (t, 3 H, Me, J = 7.2 Hz); 1.45 (m, 2 H, C(4)H_2); 1.75 (m, 2 H, C(3)H_2); 2.73 (d, 1 H, OH, J = 4.7 Hz); 3.84 (m, 1 H, C(2)H); 4.50 (d, 1 H, C(1)H, J = 3.9 Hz); 7.40 (m, 10 H, Ph). ^{13}C NMR, δ: 13.9 (Me); 19.1 (C(4)); 35.6 (C(3)); 66.8 (C(1)); 72.2 (C(2)). MS, m/z (I_{rel} (%)): 304 [M]$^+$ (2), 195 (61), 135 (13), 123 (29), 121 (18), 111 (14.5), 110 (22), 109 (26.5), 85 (74), 79 (11), 78 (14), 77 (33.5), 71 (26), 67 (31.5), 66 (12), 65 (28), 58 (12), 57 (67), 55 (14), 51 (19), 45 (52), 43 (100), 41 (39).

1-Phenylthiopentan-2-one (7) and 2-phenylthiopentanal (8). Toluene-*p*-sulfonic acid monohydrate (3.23 g) was added in one portion to a stirred solution of alcohol **6** (5.2 g, 17.1 mmol) in benzene (400 mL) at 80 °C. The reaction mixture was stirred for 15 min, cooled to ~20 °C for 3 min, and poured into a saturated aqueous Na_2CO_3 solution (150 mL). The mixture was stirred for 15 min. Then the layers were separated. After standard workup of the benzene layer, a mixture of the reaction products was obtained in a yield of 4.62 g as a pale-yellow oil. Chromatography on SiO_2 (100 g) using gradient elution (hexane→benzene) afforded ketone **7** in a yield of 1.83 g (55%), aldehyde **8** in a yield of 0.26 g (~8%), and the starting alcohol **6** in a yield of 0.68 g (~12%).

Ketone **7**, pale-yellow crystals, m.p. 25—27 °C, b.p. 108—110 °C (1 Torr). Found (%): C, 68.41; H, 7.27; S, 16.35. $C_{11}H_{14}OS$. Calculated (%): C, 68.00; H, 7.26; S, 16.50. IR, ν/cm^{-1}: 3080, 3060, 3020, 2965, 2940, 2905, 2880, 1710, 1585, 1485, 1465, 1440, 1405, 1380, 1370, 1305, 1275, 1190, 1160, 1130, 1090, 1075, 1055, 1045, 1030, 1005, 915, 750, 495, 480. ^{1}H NMR, δ: 0.89 (t, 3 H, Me, J = 7.4 Hz); 1.60 (tq, 2 H, C(4)H_2, $J_1 = J_2$ = 7.4 Hz); 2.57 (t, 2 H, C(3)H_2, J = 7.4 Hz); 3.67 (s, 2 H, C(1)H_2); 7.40 (m, 5 H, Ph). ^{13}C NMR, δ: 13.5 (Me); 17.1 (C(4)); 42.4 (C(3)); 43.8 (C(1)); 205.6 (C(2)). MS, m/z (I_{rel} (%)): 195 (18), 194 [M]$^+$ (66), 125 (17), 124 (79), 123 (90), 109 (14), 108 (31.5), 78 (11), 77 (28), 72 (10), 71 (100), 69 (12), 65 (19).

Aldehyde **8**, b.p. 111—113 °C (1 Torr). Found (%): C, 67.93; H, 7.51; S, 15.89. $C_{11}H_{14}OS$. Calculated (%): C, 68.00; H, 7.26; S, 16.50. IR, ν/cm^{-1}: 3060, 2960, 2940, 2880, 2820, 2720, 1720, 1585, 1480, 1470, 1460, 1440, 1380, 1310, 1185, 1160, 1125, 1095, 1075, 1030, 1005, 985, 850, 750, 700, 500, 380. ^{1}H NMR, δ: 0.97 (t, 3 H, Me, J = 7.15 Hz); 1.65 (m, 4 H, CH_2); 3.55 (dt, 1 H, C(2)H_2, J_1 = 4.25 Hz, J_2 = 7.2 Hz); 7.40 (m, 5 H, Ph); 9.38 (d, 1 H, CHO, J = 4.25 Hz). ^{13}C NMR, δ: 13.65 (Me); 20.1 (C(4)); 29.7 (C(3)); 56.4 (C(2)); 195.2 (C(1)). MS, m/z (I_{rel} (%)): 196 (4.5), 195 (11), 194 [M]$^+$ (63), 167 (14), 166 (30), 165 (77.5), 135 (12), 125 (23), 124 (41), 123 (100), 111 (16), 110 (45), 109 (61), 91 (16), 87 (21), 77 (29), 69 (17), 66 (20), 65 (45), 55 (80), 51 (24).

(*Z*)-8,12-Dimethyl-5-phenylthiotrideca-7,11-dien-4-one (5) and (7*Z*,2′*Z*)-8,12-dimethyl-5-(3,7-dimethylocta-2,6-dienyl)-5-phenylthiotrideca-7,11-dien-4-one (11). A solution of ketone **7** (2.32 g, ~12 mmol) in THF (3 mL) was added to a stirred suspension of NaH (0.56 g of a 50% emulsion in mineral oil was washed three times with hexane) in THF (75 mL) at ~20 °C for 7 min. After completion of the vigorous reaction, the mixture was stirred at ~20 °C for 1 h and cooled to 10 °C. Then a solution of neryl bromide (Fluka) (2.6 g, 11.8 mmol) in THF (5 mL) was added over 20 min. The reaction mixture was stirred at ~20 °C for 2 h, kept for 16 h, transferred to a mixture of a saturated aqueous NH_4Cl solution and TBME (1 : 1, v/v;

* The ^{13}C NMR spectra of compounds **4—8** and **10—16** have also signals of the Ph group.

100 mL), and stirred for 10 min. The layers were separated. The aqueous layer was extracted with TBME (3×20 mL). After standard workup of the organic extracts, the residue (5.47 g) was chromatographed on SiO_2 (100 g). Gradient elution (hexane→benzene, 7 : 3) afforded ketone **5** in a yield of 2.78 g (70%), ketone **11** in a yield of 0.34 g (7.3%), and the starting ketone **7** in a yield of 0.12 g (~5%).

Ketone **5**, b.p. 160 °C (0.1 Torr), R_f 0.23 (*A*). Found (%): C, 76.49; H, 9.23; S, 9.45. $C_{21}H_{30}OS$. Calculated (%): C, 76.30; H, 9.15; S, 9.70. IR, ν/cm^{-1}: 3080, 3060, 3040 3020, 2970, 2940, 2880, 1710, 1585, 1480, 1455, 1440, 1410, 1380, 1360, 1270, 1160, 1130, 1090, 1070, 1030, 1005, 840, 750, 700, 685, 500. ^{1}H NMR, δ: 0.91 (t, 3 H, Me, J = 7.4 Hz); 1.60 (m, 2 H, C(2)H$_2$); 1.62 (s, 3 H, *cis*-MeC(12)); 1.76 (s, 6 H, *trans*-MeC(12)); MeC(8)); 2.06 (m, 4 H, C(9)H$_2$, C(10)H$_2$); 2.52 (m, 4 H, C(3)H$_2$, C(6)H$_2$); 3.65 (dd, 1 H, C(5)H, J_1 = 7.07 Hz, J_2 = 7.2 Hz); 5.15 (m, 2 H, C(7)H, C(11)H); 7.35 (m, 5 H, Ph). ^{13}C NMR, δ: 13.6 (Me); 17.2 (C(2)); 17.5 (*cis*-MeC(12)); 23.3 (MeC(8)); 25.6 (*trans*-MeC(12)); 26.3, 29.0 (C(6), C(10)); 32.0 (C(9)); 41.8 (C(3)); 57.0 (C(5)); 120.6 (C(7)); 123.9 (C(11)); 131.6 (C(12)); 138.4 (C(8)); 206.8 (C(4)). MS, m/z (I_{rel} (%)): 331 (5.5), 330 [M]$^+$ (18), 221 (48), 194 (69), 163 (17), 150 (26), 148 (41), 137 (24), 135 (31), 123 (100), 121 (21), 109 (34), 108 (41), 106 (30), 104 (15), 95 (30.5), 93 (63), 91 (16), 82 (15), 81 (84), 80 (16), 79 (23), 77 (18), 71 (87.5), 70 (20), 69 (98.5), 67 (32).

Ketone **11**, R_f 0.40 (*A*). IR, ν/cm^{-1}: 3080, 3060, 3040, 2970, 2940, 2880, 2860, 2730, 1710, 1585, 1480, 1450, 1440, 1410, 1380, 1360, 1270, 1160, 1125, 1090, 1070, 1030, 1010, 835, 755, 700, 685, 500. ^{1}H NMR, δ: 0.98 (t, 3 H, Me, J = 7.4 Hz); 1.61 (s, 6 H, *cis*-MeC(12), *cis*-MeC(7′)); 1.62 (m, 2 H, C(2)H$_2$); 1.69 (s, 6 H, *trans*-MeC(12), *trans*-MeC(7′)); 1.72 (s, 6 H, MeC(8), MeC(3′)); 1.99 (m, 8 H, C(9)H$_2$, C(10)H$_2$, C(4′)H$_2$, C(5′)H$_2$); 2.45 (m, 4 H, C(6)H$_2$, C(1′)H$_2$); 2.76 (dd, 2 H, C(3)H$_2$, J_1 = 7.3 Hz, J_2 = 7.6 Hz); 5.13 (m, 4 H, C(7)H, C(11)H, C(2′)H, C(6′)H); 7.35 (m, 5 H, Ph). ^{13}C NMR, δ: 13.8 (Me); 17.5 (C(2), *cis*-MeC(12), *cis*-MeC(7′)); 23.5 (MeC(8), MeC(3′)); 25.5 (*trans*-MeC(12), *trans*-MeC(7′)); 26.2, 30.3 (C(6), C(10), C(1′), C(5′)); 32.3 (C(9), C(4′)); 38.7 (C(3)); 63.7 (C(5)); 119.0 (C(7), C(2′)); 124.0 (C(11), C(6′)); 131.4 (C(12), C(7′)); 138.2 (C(8), C(3′)); 207.5 (C(4)). MS, m/z (I_{rel} (%)): 467 (1.6), 466 [M]$^+$ (4), 395 (23), 357 (53), 273 (23), 259 (19.5), 189 (16), 177 (19), 163 (28), 161 (19.5), 150 (23), 148 (55), 146 (26), 137 (66), 135 (59), 123 (59), 122 (16), 121 (26.5), 119 (19.5), 110 (16), 109 (65), 108 (75), 106 (53), 104 (23), 95 (59), 93 (58), 91 (20), 83 (26), 82 (29), 81 (76), 79 (46), 77 (24), 72 (16), 71 (87.5), 70 (30), 69 (100), 67 (43), 66 (32), 65 (16), 56 (48).

(*Z*)-8-Methyl-5-phenylthioundec-7-en-4-one (10) and (7*Z*,2′*Z*)-8-methyl-5-(3-methylhex-2-enyl)-5-phenylthioundec-7-en-4-one (12). Analogously to the above-described synthesis of ketones **5** and **11**, ketone **10** (60% yield) and ketone **12** (5.4% yield) were prepared from ketone **7** and bromide **9** (see below).

Ketone **10**, b.p. 135—137 °C (0.09 Torr), R_f 0.52 (*A*). Found (%): C, 74.23; H, 9.03; S, 10.86. $C_{18}H_{26}OS$. Calculated (%): C, 74.43; H, 9.02; S, 11.04. IR, ν/cm^{-1}: 3065, 2960, 2944, 2936, 2888, 2872, 1708, 1604, 1585, 1544, 1460, 1448, 1440, 1392, 1376, 1240, 1120, 1104, 1088, 1036, 1024, 1016, 1000, 976, 916, 856, 744, 716, 692. ^{1}H NMR, δ: 0.89 (t, 6 H, Me, J = 7.4 Hz); 1.40 and 1.58 (both m, 2 H each, CH$_2$); 1.69 (s, 3 H, MeC(8)); 1.99 (m, 2 H, C(9)H$_2$); 2.50 (m, 2 H, C(6)H$_2$); 2.53 (t, 2 H, C(3)H$_2$, J = 7.3 Hz); 3.63 (dd, 1 H, C(5)H, J_1 = J_2 = 7.5 Hz); 5.14 (t, 1 H, C(7)H, J = 6.4 Hz); 7.4 (m, 5 H, Ph). ^{13}C NMR, δ: 13.7, 14.0 (Me); 17.3, 21.1 (C(2), C(10)); 23.4 (MeC(8)); 29.2 (C(6)); 34.0 (C(9)); 42.0 (C(3)); 57.2 (C(5)); 120.5 (C(7)); 138.8 (C(8)); 207.0 (C(4)). MS, m/z (I_{rel} (%)): 291 (0.8), 290 [M]$^+$ (7), 219 (31), 196 (12), 195 (30), 194 (76), 182 (39.5), 181 (81), 165 (13), 149 (18), 137 (38), 135 (24), 125 (15), 124 (16), 123 (47.5), 122 (10), 115 (10), 110 (25), 109 (59), 108 (100), 106 (15), 99 (14), 97(29), 95 (27.5), 91 (22), 81 (39), 79 (35), 77 (29.5), 72 (10), 71 (58), 69 (37.5), 68 (18), 67 (52.5), 66 (31), 65 (32), 59 (10), 58 (45), 56 (10), 55 (71), 53 (26), 51 (24.5), 46 (32), 45 (48), 44 (91), 43 (27), 41 (52), 40 (70), 39 (42).

Ketone **12**, R_f 0.61 (*A*). Found (%): C, 77.67; H, 9.89; S, 8.14. $C_{25}H_{39}OS$. Calculated (%): C, 77.46; H, 10.14; S, 8.27. IR, ν/cm^{-1}: 3064, 3032, 2960, 2944, 2936, 2888, 2872, 2760, 2728, 2344, 1700, 1676, 1664, 1604, 1584, 1552, 1440, 1392, 1376, 1320, 1304, 1208, 1128, 1104, 1088, 1040, 1024, 1016, 1000, 928, 896, 856, 784, 768, 748, 716, 700. ^{1}H NMR, δ: 0.89 (t, 6 H, C(11)H$_3$, C(6′)H$_3$, J = 7.4 Hz); 0.97 (t, 3 H, C(1)H$_3$, J = 7.5 Hz); 1.37 (m, 4 H, C(10)H$_2$, C(5′)H$_2$); 1.65 (m, 2 H, C(2)H$_2$); 1.69 (s, 6 H, MeC(8), MeC(3′)); 1.93 (t, 4 H, C(9)H$_2$, C(4′)H$_2$), J = 7.7 Hz); 2.43 (dd, 4 H, C(6)H$_2$, C(1′)H$_2$, J_1 = J_2 = 6.4 Hz); 2.74 (t, 2 H, C(3)H$_2$, J = 7.5 Hz); 5.14 (t, 2 H, C(7)H, C(2′)H), J = 6.4 Hz); 7.35 (m, 5 H, Ph). ^{13}C NMR, δ: 14.1 (Me); 17.7, 21.0 (C(2), C(10), C(5′)); 23.7 (MeC(8), MeC(3′)); 30.4 (C(6)); C(1′)); 34.4 (C(9), C(4′)); 39.0 (C(3)); 64.1 (C(5)); 119.0 (C(7), C(2′)); 138.7 (C(8), C(3′)); 208.0 (C(4)). MS, m/z (I_{rel} (%)): 387 (1), 386 [M]$^+$ (1), 316 (20), 315 (42), 291 (17), 290 (18), 289 (14), 278 (26), 277 (51.5), 233 (30), 221 (15), 220 (37), 219 (57), 207 (11), 206 (24), 205 (45), 194 (16), 193 (18), 191 (20), 181 (30.5), 179 (27), 165 (29), 163 (25), 151 (17), 149 (33), 147 (14.5), 137 (27), 135 (47), 134 (10), 124 (12), 123 (54), 121 (36.5), 119 (11), 110 (20), 109 (48), 108 (66.5), 107 (13), 106 (28), 104 (24), 99 (11), 98 (33), 97(79), 95 (30), 94 (11), 93 (32), 92 (12), 91 (34), 84 (11), 83 (27), 81 (35), 80 (16), 79 (37.5), 78 (20.5), 77 (33.5), 72 (29), 71 (82), 69 (56), 68 (15), 67 (42), 66 (28), 65 (31), 63 (13), 58 (37), 57 (41), 56 (28), 55 (100), 53 (34), 52 (12), 51 (28), 50 (15), 46 (26), 45 (54), 44 (95), 42 (32), 41 (53), 40 (38), 39 (35), 37 (13).

2(*E*)-(2-Benzyloxyethylidene)pentanal (14). A solution of pentanal *tert*-butylimine[9] (8.3 g, 39 mmol) in THF (30 mL) was added dropwise to a stirred solution of LDA (45 mmol) in a THF—hexane mixture (9 : 1, v/v; 280 mL) at −10 °C for 15 min. The reaction mixture was stirred at 0 °C for 40 min and cooled to −15 °C. Then HMPA (50 mL) was added. The reaction mixture was stirred for 15 min and cooled to −70 °C. Then a solution of benzyl ether of glycolaldehyde (**13**) (4.8 g, 32 mmol), which has been prepared as described earlier,[10] in THF (10 mL) was added dropwise. The reaction mixture was stirred at −70 °C for 2.5 h, warmed to 0 °C over 4 h, transferred into a stirred mixture TBME and 3% HCl at 0 °C, and stirred at ~20 °C for 3.5 h. The layers were separated. The aqueous layer was extracted with TBME. After standard workup of the combined organic extracts, the residue (5.2 g) was chromatographed on SiO_2 (100 g). Gradient elution (hexane→ethylacetate, 3 : 1) afforded enal **14** in a yield of 4.26 g (61%) as a colorless oil, b.p. 110 °C (1 Torr). Found (%): C, 77.16; H, 8.48. $C_{14}H_{18}O_2$. Calculated (%): C, 77.03; H, 8.31. IR, ν/cm′$^{-1}$: 3060—2860, 2740, 1690, 1640, 1500, 1470, 1450, 1380, 1340, 1320, 1230,

1180, 1090, 1080, 1030, 950, 910, 860, 700. ^{1}H NMR, δ: 0.90 (t, 3 H, Me, J = 7.0 Hz); 1.35 (m, 2 H, C(4)H_2); 2.20 (t, 2 H, C(3)H_2, J = 7.0 Hz); 4.37 (d, 2 H, C(2′)H_2, J = 6.0 Hz); 4.60 (s, 2 H, H_2CPh); 6.58 (t, 1 H, C(1′)H, J = 6.0 Hz); 7.35 (m, 5 H, Ph); 9.40 (s, 1 H, CHO). ^{13}C NMR, δ: 13.9 (Me); 21.7 (C(4)); 26.25 C(3)); 66.5 (C(2′)); 73.0 (CH_2Ph); 143.8 (C(2)); 149.9 (C(1′)); 194.5 (C(1)). MS, m/z (I_{rel} (%)): 218 $[M]^+$ (0.25), 108 (10), 107 (13.85), 105 (21), 92 (22), 91 (64), 78 (16), 77 (23), 71 (27).

2(*E*)-(2-Benzyloxyethylidene)pentan-1-ol (15) was prepared by reduction of enal **14** with $NaBH_4$ according to a standard procedure and purified by flash chromatography on SiO_2. The yield was 94%, b.p. 151 °C (1 Torr). Found (%): C, 76.17; H, 9.22. $C_{14}H_{20}O_2$. Calculated (%): C, 76.33; H, 9.15. IR, ν/cm^{-1}: 3600, 3550—3150, 3000—2860, 1670, 1600, 1490, 1470, 1450, 1380, 1360, 1320, 1230, 1120, 1070, 1030, 1000, 940, 850, 700. ^{1}H NMR, δ: 0.90 (t, 3 H, Me, J = 7.2 Hz); 1.40 (m, 2 H, C(4)H_2); 2.05 (m, 3 H, C(3)H_2, OH); 4.03 (s, 2 H, C(1)H_2); 4.08 (d, 2 H, C(2′)H_2, J = 6.3 Hz); 4.50 (s, 2 H, H_2CPh); 5.65 (t, 1 H, C(1′)H, J = 6.3 Hz); 7.30 (m, 5 H, Ph). ^{13}C NMR, δ: 14.2 (Me); 21.9 (C(4)); 30.4 C(3)); 66.0, 66.1 (C(1), C(2′)); 72.3 (CH_2Ph); 121.9 (C(1′)); 143.3 (C(2)).

(*Z*)-1-Benzyloxy-3-methylhex-2-ene (16). Pyridine-sulfur trioxide (Fluka) (11.13 g, 70 mmol) was added portionwise to a stirred solution of alcohol **15** (10.22 g, 46.455 mmol) in THF (160 mL) at 0 °C. The resulting suspension was stirred at 0 °C for 3 h (TLC control) and cooled to −10 °C. A 0.57 M $LiAlH_4$ solution in THF (480 mL, 273.6 mmol) was added dropwise over 2 h. The reaction mixture was stirred for 25 h and cooled to −10 °C. Then water (10.5 mL), a 15% NaOH solution (10.5 mL), and water (31.5 mL) were successively added with caution. The precipitate that formed was filtered off and thoroughly washed with TBME. After standard workup of the filtrate, the residue (10.48 g) was chromatographed on SiO_2 (150 g). Elution with hexane afforded benzyl ether **16** in a yield of 6.36 g (67%) as a colorless oil, b.p. 110—112 °C (2.5 Torr). Found (%): C, 81.99; H, 10.08. $C_{14}H_{20}O$. Calculated (%): C, 82.30; H, 9.86. IR, ν/cm^{-1}: 3090, 3070, 3040, 2970, 2940, 2880, 2860, 1670, 1500, 1470, 1460, 1380, 1370, 1355, 1210, 1140, 1100, 1080, 1035, 1020, 950, 910, 745, 705. ^{1}H NMR, δ: 0.94 (t, 3 H, Me, J = 7.3 Hz); 1.47 (m, 2 H, C(5)H_2); 1.80 (s, 3 H, MeC(3)); 2.09 (t, 2 H, C(4)H_2, J = 7.6 Hz); 4.08 (d, 2 H, C(1)H_2, J = 6.9 Hz); 4.56 (s, 2 H, H_2CPh); 5.50 (t, 1 H, C(2)H, J = 6.9 Hz); 7.40 (m, 5 H, Ph). ^{13}C NMR, δ: 13.9 (Me); 21.2 (C(5)); 23.5 (MeC(3)); 34.0 (C(4)); 66.3 (C(1)); 72.0 (CH_2Ph); 121.6 (C(2)); 140.8 (C(3)). MS, m/z (I_{rel} (%)): 204 $[M]^+$ (0.1), 161 (9.4), 113 (28), 112 (9.8), 107 (12), 105 (13), 98 (25), 97 (24), 96 (30), 95 (30), 92 (70), 91 (98), 81 (40), 79 (11), 77(17), 71 (22), 70 (22), 69 (100), 67 (14), 65 (27), 57 (16), 56 (14), 55 (72), 43 (58), 41 (44).

(*Z*)-3-Methylhex-2-en-1-ol (17). Metallic lithium (0.7 g, 100 mmol) was added portionwise to a stirred solution of compound **16** (5.17 g, 25.34 mmol) in liquid NH_3 (300 mL) at −50 °C. The reaction mixture was stirred at −40 °C for 3 h, NH_4Cl was added up to discoloration of the solution, and NH_3 was evaporated. The residue was treated with an H_2O—Et_2O mixture (1 : 1, v/v; 60 mL) and stirred for 15 min. The layers were separated. The aqueous layer was extracted with diethyl ether. After standard workup, the combined extracts were concentrated to ~5 mL, hexane (50 mL) was added, and the resulting solution was chromatographed on a column with SiO_2 (100 g). Gradient elution (hexane→benzene, 3 : 1) afforded a fraction containing alcohol **17**, which was noticeably volatile with diethyl ether and hexane. An aliquot of this fraction was concentrated to dryness to give alcohol **17** with 98% purity (^{1}H NMR spectroscopic data) as a colorless oil, R_f 0.10 (*A*), 0.40 (*B*). IR, ν/cm^{-1}: 3616, 3560, 3432, 3072, 3008, 2960, 2936, 2872, 1664, 1452, 1380, 1212, 1200, 1164, 1120, 1104, 1064, 984, 948, 900, 860, 820, 700, 664, 624. ^{1}H NMR, δ: 0.82 (t, 3 H, Me, J = 7.45 Hz); 1.28 (br.s, 1 H OH); 1.43 (m, 2 H, C(5)H_2); 1.75 (s, 3 H, Me(C(3)); 2.06 (t, 2 H, C(4)H_2, J = 7.6 Hz); 4.12 (d, 2 H, C(1)H_2, J = 7.1 Hz); 5.43 (t, 1 H, C(2)H, J = 7.1 Hz). ^{13}C NMR, δ: 14.3 (Me); 21.75 (C(5)); 23.8 (MeC(3)); 34.3 (C(4)); 59.35 (C(1)); 124.7 (C(2)); 140.2 (C(3)). MS, m/z (I_{rel} (%)): 115 (2), 114 $[M]^+$ (7), 113 (23.5), 108 (23), 107 (30), 99 (37), 97 (36.5), 96 (16), 95 (12), 91 (27), 87 (16.5), 86 (12), 83 (24.5), 81 (52), 79 (31), 77 (23), 73 (26), 71 (100), 70 (19), 69 (25), 67 (19.5), 65 (14), 60 (24), 57 (63), 56 (28), 55 (88), 54 (16), 53 (35), 51 (13).

The major portion of the fraction containing alcohol **17** was concentrated to ~7 mL under atmospheric pressure. According to the ^{1}H NMR spectroscopic data, the solution contained only trace amounts of benzene. A comparison of the integral intensities of the signals of MeC(3) (δ 1.75) with the signals of the Me group of hexane and diethyl ether (δ 0.82) demonstrated that the solution contained ~30% (~2 g, 17—18 mmol) of alcohol **17**. Diethyl ether (25 mL) was added to the resulting solution of alcohol **17**. The mixture was dried with 4 A molecular sieves and used without additional purification.

(*Z*)-3-Methylhex-2-enyl bromide (9). Pyridine (0.5 mL) was added with stirring to the solution of alcohol **17** (see above). The mixture was cooled to −15 °C and then a solution of freshly distilled PBr_3 (0.9 mL) in diethyl ether (7 mL) was added for 20 min. The reaction mixture, which was protected from light with an Al foil, was stirred at a temperature from −15 to −10 °C for 4 h and poured into ice water (20 mL). The mixture was stirred for 15 min and the layers were separated. The organic layer was washed with saturated $NaHCO_3$ and NaCl solutions, dried with Na_2SO_4, filtered, and dried with 4 A molecular sieves for 12 h. An aliquot of the resulting solution was concentrated to dryness to give bromide **9** with 95—97% purity (according to the ^{1}H NMR spectroscopic data). Bromide **9**, R_f 0.72 (*B*). ^{1}H NMR, δ: 0.92 (t, 3 H, Me, J = 7.5 Hz); 1.48 (m, 2 H, C(5)H_2); 1.78 (s, 3 H, Me(C(3)); 2.13 (t, 2 H, C(4)H_2, J = 7.6 Hz); 4.02 (d, 2 H, C(1)H_2, J = 7.1 Hz); 5.56 (t, 1 H, C(2)H, J = 7.1 Hz). The major portion of the solution of bromide **9** was used without additional purification for the preparation of ketone **10** (see above).

This study was financially supported by the President of the Russian Federation (the Federal Program for the Support of Leading Scientific Schools of the Russian Foundation, Grant NSh-1802.2003.3).

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Received December 17, 2003;
in revised form January 21, 2004