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[3,3]SIGMATROPIC RING EXPANSION OF CYCLIC THIONOCARBONATES. 9.[1] TOTAL SYNTHESIS OF (±)-YELLOW SCALE PHEROMONE *VIA* 10-MEMBERED THIOLCARBONATE[2]

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Abstract: (±)-Yellow scale pheromone **1** has been synthesized *via* the route illustrated in Scheme 1. The [3,3]sigmatropic ring expansion of 8-membered thionocarbonate **4** exclusively produced the (*Z*)-10-membered thiolcarbonate **3**, which was transformed *via* three steps to the intermediate **2** with all the necessary carbon atoms for the pheromone. Reductive removal of the SCO moiety in **2** followed by acetylation gave **1**.

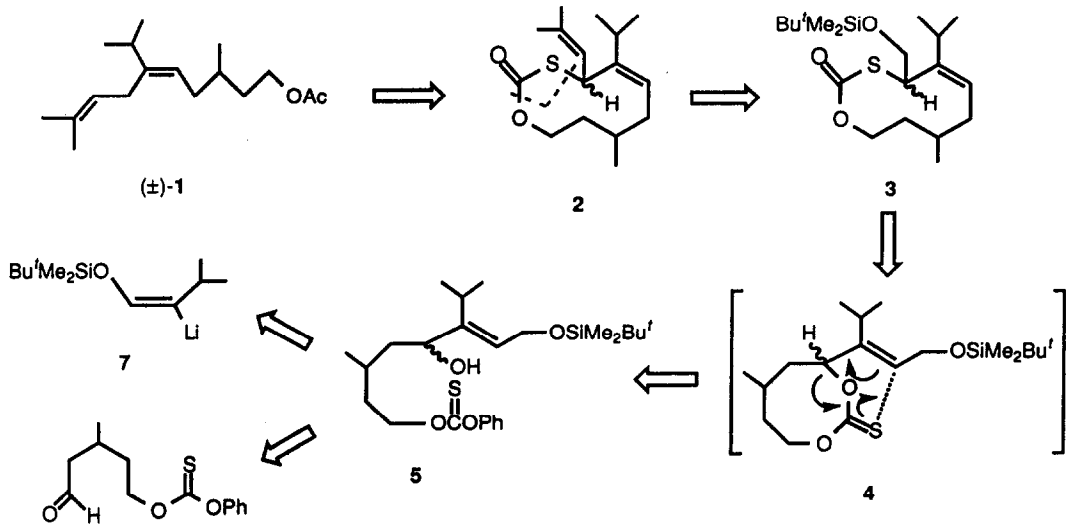
Sex pheromone has recently aroused interest in that it offers the possibility of species-specific control of populations. The yellow scale, *Aonidiella citrina* (Coquillett), is nearly a worldwide pest of citrus crops and it attacks a number of plants in addition to important ornamentals.[3]

The pheromone, (*E*)-6-isopropyl-3,9-dimethyl-5,8-decadienyl acetate **1**, was first isolated by Gieselmann and co-workers.[4] Mori and Kuwahara[5] have developed the synthetic routes to both *R*-(+) and *S*-(-) enantiomers of **1** from (+)-methyl citronellate in 1982. The compound with an (*S*)-configuration is the correct enantiomer.

The yellow scale pheromone has been synthesized by several groups.[5, 6] The major difficulty in the preparation of this compound is stereoselective synthesis of the (*E*)-5 double bond bearing isopropyl group. All published routes depend on the known methods for the synthesis of trisubstituted alkenes. We recently reported[1, 7] the highly stereoselective synthesis of (*Z*)- or (*E*)-double bond in 10-membered thiolcarbonates[8] by controlling chairlike-boatlike transition state[9] in the [3,3]sigmatropic rearrangement of 8-membered thionocarbonates.[10] Moreover, treatment of the 10-membered thiolcarbonates with lithium in liquid ammonia afforded (*Z*)-trisubstituted or tetrasubstituted olefins in high yields.[1, 7] This reductive desulfurization has stimulated interest in the stereoselective synthesis of naturally occurring (*Z*)-alkenol sex pheromones.[11] We report herein a unique and stereoselective synthesis of (±)-yellow scale pheromone **1**. This demonstrates the synthetic utility of the present method.

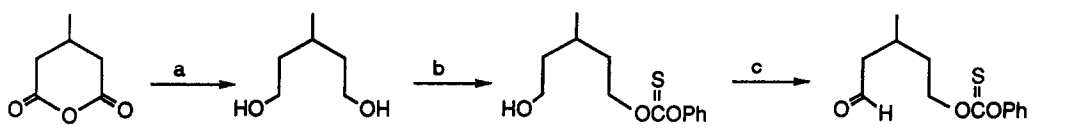
Our synthetic strategy is to employ a formation of 10-membered thiolcarbonate **3** *via* the [3,3]sigmatropic ring expansion of the 8-membered thionocarbonate **4**, illustrated in *Scheme 1*. The silylether moiety of the intermediate **3** allows a conversion into 10-membered thiolcarbonate **2** with all the necessary carbon atoms for the pheromone. Reductive desulfurization of **2** followed by acetylation may afford (±)-yellow scale pheromone **1**. The diol monothionocarbonate **5** is prepared from vinyllithium **7** and aldehyde **6**. The key problems seem to be the stereoselective introduction of a (*Z*)-trisubstituted double bond in the 10-membered ring and removal of the SCO moiety in **2** with retention of the stereochemistry.

The aldehyde **6** was easily prepared from 3-methylglutaric anhydride according to our previous procedure[8c] (see *Scheme 2*). (*E*)-Vinyltin **10**[12] was obtained *via* stannylation of methyl 4-methyl-2-pentynoate using Piers procedure[13] (*Scheme 3*). The methyl ester moiety of **10** was converted into a *tert*-



Scheme 1

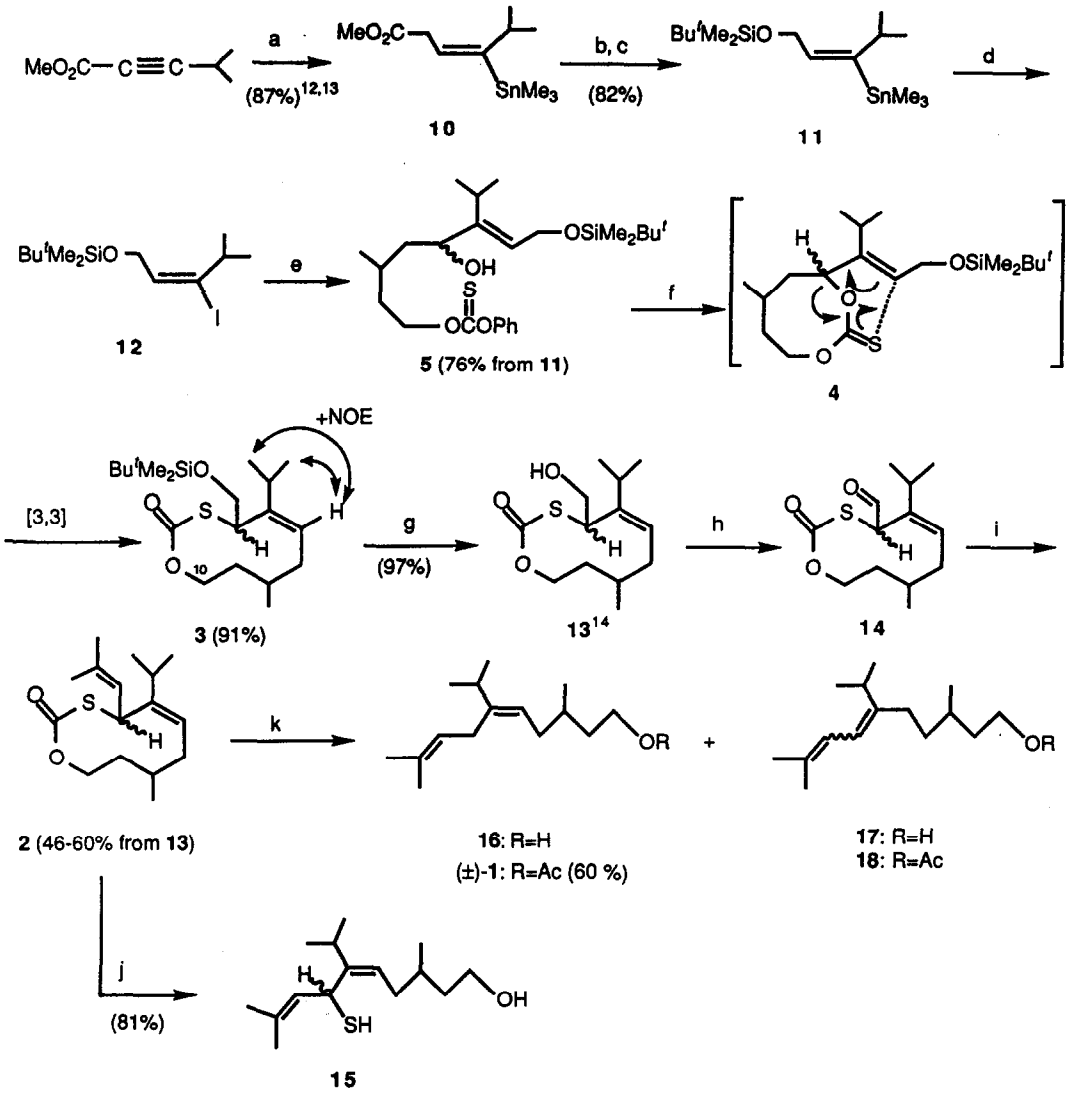
butyldimethylsilyl ether **11** by diisobutylaluminum hydride (DIBAL) reduction and silylation with *tert*-butyldimethylsilyl trifluoromethanesulfonate (Bu^{t}Me$_2$SiOTf). Next generation of vinyllithium **7** from compound **11** was investigated; however, reaction of **11** with MeLi or n-BuLi followed by addition of aldehyde **6** did not give the expected product **5**. Then, generation of **7** was investigated with vinyl iodide **12** prepared by treatment of **11** with iodine. After the reaction with *t*-BuLi in ether at -78 °C, addition of the aldehyde **6** gave a 1:1 mixture of diastereomeric diol monothionocarbonates **5** in 76% yield. Both diastereomers are utilized in the preparation of the yellow scale pheromone **1**, since a newly formed chiral center in **5** is



Reagents:
a) $LiAlH_4$ in THF b) ClC(S)OPh, Pyridine, 4-DMAP (cat.) in MeCN c) PCC in CH_2Cl_2

Scheme 2

not present in the final product. The diol monothionocarbonate **5** was here submitted to our methodology. A 1M hexane solution of lithium bis(trimethylsilyl)amide (1.1 eq.) was injected rapidly into a dry THF (10^{-2} M) solution of **5** at room temperature under N_2. The reaction went to completion instantly *via* the



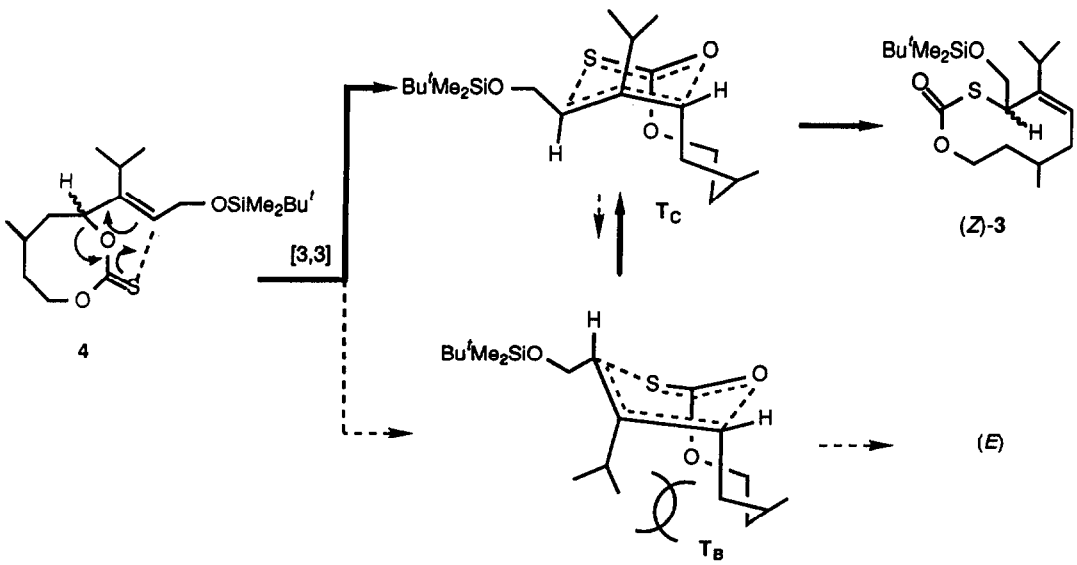
Reagents:

a) $Me_3SnCu\ SMe_2$ b) DIBAL c) Bu^tMe_2SiOTf, Pyridine d) I_2 e) *t*-BuLi, then **6** in Et_2O, -72 °C f) $(TMS)_2NLi$, THF, r.t. g) n-Bu_4NF, THF, 0 °C h) $(COCl)_2$ / DMSO, CH_2Cl_2, -78 °C, then Et_3N, -45 °C i) $Ph_3P{=}CMe_2$ Et_2O, r.t. j) 2N NaOH, MeOH, r.t. k) i: Li/liq. NH_3, -78 °C or LDBB-HMPA ii: Ac_2O, 4-DMAP, CH_2Cl_2, r.t.

Scheme 3

[3,3]sigmatropic ring expansion of 8-membered thionocarbonate **4**. The ordinary work-up and purification on silica gel exclusively gave the expected (*Z*)-10-membered thiolcarbonate **3** as a diastereomeric mixture in 91% yield. The remarkable ease of this reaction should be noted. The structure of **3** was examined by 300 MHz ^{1}H-NMR spectrum and all proton signals were assigned by the decoupling experiments. The (*Z*) geometry of **3** was determined by a positive ^{1}H-nuclear Overhauser effect (NOE) observed between two methyl groups in the isopropyl moiety and vinyl protons [δ 5.38 (0.5H, dd, *J*=12.5, 3.4 Hz), 5.50 (0.5H, dd, *J*=12.5, 3.4 Hz)]. The protons at C_{10} in **3** were characteristically observed at δ 3.71 (0.5 H, t, *J*=11.2 Hz), 3.96 (0.5H, t, *J*=11.2 Hz), 4.81 (0.5H, ddd, *J*=11.6, 5.1, 3.4 Hz) and 5.08 (0.5H, dt, *J*=11.6, 3.4 Hz), suggesting that this 10-membered ring is conformationally fixed at room temperature.

The stereochemistry of the rearrangement is predicted by the chair- and boatlike transition states (T_C and T_B) proposed from the previous studies.[1, 9] The exclusive formation of the (*Z*)-isomer **3** in the rearrangement of **4** may be accounted for by the conformational preference of a chairlike transition state (T_C) over the more congested boatlkie transition state (T_B) leading to the (*E*)-isomer (*Scheme 4*).



Scheme 4

Deprotection of the silyl ether **3** with tetrabutylammonium fluoride gave the alcohol **13**[14] in 97% yield. Careful Swern oxidation gave aldehyde **14**, which was subsequently treated with isopropylidene triphenylphosphorane to give **2** in 46~60% yield from **13**. The structure of **2** was clarified by conversion into an allylic thiol **15** by alkaline hydrolysis.[1, 8c]

The reductive desulfurization of **2** with retention of the double bond was not easy, but a great deal of effort was put into minimum formation of a migrated 6,8-dienic alcohol. Treatment of **2** with lithium in liquid ammonia in the presence of an *in situ* proton source afforded a dienic alcohol **16** with a migrated 6,8-dienic alcohol **17** (**16**:**17**=ca.2:1~4:1). On the other hand, reduction of **2** by lithium *p,p'*-di-*tert*-butylbiphenylide (LDBB)[15] in the presence of hexamethylphosphoric triamide (HMAP)[16] led to a 2.4:1 mixture of **16** and **17**.

Acetylation of the mixture followed by flash column chromatography finally gave (±)-yellow scale pheromone **1**. Spectroscopic data[17] for the synthetic material was identical in all respects with those reported for the isolated natural compound.[4]

We are presently investigating a more straightforward route to the key intermediate **2** as well as S-(-)-yellow scale pheromone synthesis by using the present method. Further synthetic applications of the [3,3]sigmatropic rearrangement of medium-membered thionocarbonates are also being investigated in our laboratories.

Experimental

General. The IR spectra were recorded on a Shimadzu IR-435, and MS on a Hitachi M-80 spectrometers. The ^{1}H- and ^{13}C-NMR spectra were taken with tetramethylsilane as an internal standard on a Varian Gemini-200 and XL-300 spectrometers in $CDCl_3$. VPC analyses were performed with a Shimadzu GC-4BMPF gas chromatography with a flame ionization detector. Unless otherwise noted, SiO_2 (Merck 9385) was used for column chromatography and all reactions were carried out under nitrogen stream. THF was distilled from sodium-benzophenone.

3-Methyl-1,5-pentanediol (8) A solution of 3-methylglutaric anhydride[18] (10.0 g, 78.05 mmol) in THF (60 ml) was added dropwise over 45 min to a suspension of $LiAlH_4$ (5.0 g, 131.75 mmol) in THF (120 ml). The suspension was refluxed for 4 h. After cooling with ice, the mixture was treated by successive dropwise addition of 5 ml of H_2O, 5 ml of 15% NaOH solution and 5 ml of H_2O. The resulting precipitate was filtered off with EtOAc through a Celite pad. The filtrate was washed with H_2O, dried over anhydrous Na_2SO_4 and then evaporated *in vacuo*. Distillation [76-80 °C / 0.08 mmHg (83-84 °C / 0.1 mmHg[19])] of residual material provided **8** (9.16 g, 100%) as a colorless oil.

O-(5-Hydroxy-3-methylpentyl) O-Phenyl Thionocarbonate (9) A solution of phenyl chlorothionoformate[18] (2.40 ml, 17.35 mmol) in acetonitrile (15 ml) was added slowly over 11 h to a solution of the diol **8** (1.70 g, 14.41 mmol) in acetonitrile (150 ml) in the presence of pyridine (1.40 ml, 17.35 mmol) and 4-DMAP (176 mg, 1.4 mmol) at 0 °C by a syringe pump technique. The reaction mixture was further stirred for 5 h at 0 °C. The solvent was evaporated off under reduced pressure to give an oil, which was subsequently diluted with EtOAc-hexane (2 : 1). The organic layer was washed with H_2O (x 2) and brine, dried over anhydrous Na_2SO_4 and then evaporated *in vacuo*. The residue was purified by column chromatography using EtOAc-hexane (7 : 3) for elution to give **9** (1.98 g, 54%) as an oil. IR (neat): 3350 (OH), 1200 cm^{-1} (C=S). ^{1}H-NMR: 0.97 (3H, d, *J*=6.8 Hz, CH_3), 1.34-1.96 (5H, br, 2 x $CHC\underline{H}_2$, CH), 3.69 (2H, td, *J*=6.8, 2.8 Hz, $C\underline{H}_2OH$), 4.56 (2H, td, *J*=6.8, 2.0 Hz, CH_2O), 7.04-7.45 (5H, m, ArH). MS *m/z*: 254 (M^+). HR-MS *m/z*: Calcd for $C_{13}H_{18}O_3S$ 254.0976, Found: 254.0988.

O-(4-Formyl-3-methylbutyl) O-Phenyl Thionocarbonate (6) The thionocarbonate **9** (1.099 g, 4.3 mmol) in CH_2Cl_2 (4 ml) was added to a suspension of PCC[18] (1.40 g, 6.5 mmol) in CH_2Cl_2 (3 ml) and the mixture was stirred at room temperature for 2 h. The mixture was diluted with ether and filtered through a Celite pad. The filtrate was concentrated *in vacuo* to give a crude oil, which was purified by column chromatography using EtOAc-hexane (9 : 1) for elution to give **6** (1.085 g, quant.) as a colorless oil. IR (neat): 1720 (CO), 1250-1080 (C=S) cm^{-1}. ^{1}H-NMR: 1.06 (3H, d, *J*=6.0 Hz, CH_3), 1.62-1.99 (2H, m, $CHC\underline{H}_2CH_2$), 2.19-2.58

(3H, m, CH_2CHO, CH), 4.56 (2H, t, *J*=6.0 Hz, CH_2O), 7.05-7.47 (5H, m, ArH), 9.76 (1H, s, CHO). MS *m/z*: 252 (M^+). HR-MS *m/z*: Calcd for $C_{13}H_{16}O_3S$ 252.0819, Found: 252.0829.

(*E*)-1-*tert*-Butyldimethylsiloxy-4-methyl-3-trimethylstannyl-2-pentene (11) A 1.5 M solution of DIBAL in toluene[18] (33 ml, 49.5 mmol) was added slowly to a solution of methyl ester **10**[13] (4.802 g, 16.5 mmol) in pentane (40 ml) at -40 ~ -50 °C, and the mixture was stirred for 10 min. The reaction was quenched by the addition of saturated NH_4Cl solution. The mixture was diluted with ether and anhydrous $MgSO_4$ was added. The resulting suspension was stirred for 5 min at room temperature, and then filtered through a Celite pad, and washed with ether. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (10% EtOAc in hexane) to give (*E*)-4-methyl-3-trimethylstannyl-2-penten-1-ol (3.567 g, 82%) as a colorless oil. IR (neat): 3300 cm^{-1} (OH). ^{1}H-NMR: 0.16 (9H, s, J_{Sn-H}=52.4 Hz, 3 x $SnCH_3$), 0.98 (6H, d, *J*=7.2 Hz, 2 x $CHCH_3$), 2.95 (1H, sept, *J*=7.2 Hz, $CHCH_3$), 4.27 (2H, d, *J*=5.6 Hz, CH_2O), 5.64 (1H, t, J=5.6 Hz, J_{Sn-H}=80 Hz, =CH). MS *m/z*: 249 (M^+-CH_3). *tert*-Butyldimethylsilyl trifluoromethanesulfonate[18] (0.64 ml, 2.79 mmol) was added dropwise to a solution of the above alcohol (700 mg, 2.66 mmol) in pyridine (3 ml) at 0 °C, and the mixture was stirred for 20 min. The reaction was quenched by the addition of H_2O and the mixture was diluted with EtOAc-hexane (1 : 1). The organic layer was washed with H_2O and brine, and dried over anhydrous Na_2SO_4. Evaporation of the solvent left a crude oil, which was purified by column chromatography using EtOAc-hexane (3 : 17) for elution to give **11** (1.003 g, quant) as a colorless oil. IR (neat): 1250, 1080 cm^{-1}. ^{1}H-NMR: 0.08 (6H, s, 2 x $SiCH_3$), 0.15 (9H, s, J_{Sn-H}=53.3 Hz, 3 x $SnCH_3$), 0.91 (9H, s, 3 x CH_3), 0.96 (6H, d, *J*=6.7 Hz, 2 x $CHCH_3$), 2.88 (1H, sept. *J*=6.7 Hz, $CHCH_3$), 4.31 (2H, d, *J*=5.4 Hz, CH_2O), 5.55 (1H, t, *J*=5.4 Hz, J_{Sn-H}=82.0 Hz, =CH). MS *m/z*: 363 (M^+-CH_3).

(*E*)-1-*tert*-Butyldimethylsiloxy-3-iodo-4-methyl-2-pentene (12) A solution of iodine (3.167 g, 12.48 mmol) in dry ether (20 ml) was added over 5 min to a cold (0 °C), stirred solution of **11** (4.276 g, 11.34 mmol) in the same solvent (35 ml). The reaction mixture was stirred for 20 min at room temperature and treated with saturated sodium bisulfate solution. A 10% KF solution was added and the mixture was stirred for additional 20 min at room temperature. The resulting turbidity was filtered off through a Celite pad, and washed with ether. The combined ether solution was washed with H_2O (x 2) and dried over anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure gave **12** (3.856 g, quant.) as a pale yellow oil. IR (neat): 1620 cm^{-1}. ^{1}H-NMR: 0.04 (6H, s, 2 x $SiCH_3$), 0.87 (9H, s, 3 x CCH_3), 0.92 (6H, d, *J*=6.4 Hz, 2 x $CHCH_3$), 2.13 (1H, sept, $CHCH_3$), 4.17 (2H, d, *J*=6.3 Hz, CH_2O), 6.26 (1H, t, *J*=6.3 Hz, =CH). MS *m/z*: 340 (M^+). HR-MS *m/z*: Calcd for $C_{12}H_{25}IOSi$ 340.0718, Found: 340.0719.

O-[(*E*)-8-*tert*-Butyldimethylsiloxy-5-hydroxy-6-isopropyl-3-methyl-6-octenyl] O-Phenyl Thionocarbonate (5) The dry flask was charged with **12** (970 mg, 2.85 mmol) and dry ether (5 ml). The solution was cooled to -78 °C and 1.7 M *tert*-BuLi in pentane[18] (2.7 ml, 4.56 mmol) was added. Stirring was continued at - 78 °C for 70 min. The aldehyde **6** (575 mg, 2.28 mmol) in ether (5 ml) was added at the same temperature and the resulting mixture was stirred for 1 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl and the mixture was diluted with ether. The ether solution was washed with H_2O and brine, dried over anhydrous $MgSO_4$, then evaporated under reduced pressure. The residue was purified by column chromatography (10% EtOAc in hexane) to give **5** (805 mg, 76%) as a pale yellow oil. IR (neat): 3440 (OH), 1190 (C=S) cm^{-1}. ^{1}H-NMR: 0.06 (6H, s, 2 x $SiCH_3$), 0.88 (9H, s, 3 x CCH_3), 1.06-1.13 (9H, m, 2 x

=CCHC<u>H</u>3, C<u>H</u>3CHCH2), 1.19-2.09 (5H, br m, 2 x CH2, CH3C<u>H</u>CH2), 2.64 (1H, sept. d, *J*=6.4, 1.5 Hz, =CHC<u>H</u>CH3), 4.18 (1H, br t, *J*=5.8 Hz, C<u>H</u>OH), 4.29 (2H, d, *J*=6.2 Hz, CH2OSi), 4.46-4.67 [2H, m, CH2OC(S)], 5.55 (0.5H, t, *J*=6.1 Hz, =CH), 5.57 (0.5H, t, *J*=6.1 Hz, =CH), 7.04-7.12 (2H, m, ArH), 7.21-7.46 (3H, m, ArH). MS *m/z*: 449 (M^+-OH). HR-MS *m/z*: Calcd for $C_{25}H_{41}O_3SSi$ 449.2543, Found: 449.2546 (M^+-OH).

(*Z*)-4-*tert*-Butyldimethylsiloxymethyl-5-isopropyl-8-methyl-7,8,9,10-tetrahydro-4*H*-1,3-oxathiecin-2-one (3) A 1 M solution of (TMS)2NLi in THF[18] (0.29 ml, 0.29 mmol) was injected rapidly to a solution of **5** (123 mg, 0.26 mmol) in THF (26 ml) with stirring at room temperature. The reaction mixture was quenched by the addition of H2O within 5 min, and diluted with hexane-EtOAc (2 : 1). The organic layer was washed with H2O (x 3) and brine, dried over anhydrous Na2SO4, and then evaporated under reduced pressure. The residual oil was purified by column chromatography (5% EtOAc in hexane) to give **3** (88 mg, 91%). IR (neat): 1675 cm^{-1} (CO). ^{1}H-NMR (300 MHz): 0.07 (6H, s, 2 x SiCH3), 0.89 (9H, s, 3 x CCH3), 1.00 (1.5H, d, *J*=6.9 Hz, CH2CHC<u>H</u>3), 1.02 and 1.08 (3H, each d, *J*=6.9 Hz, 2 x =CCHC<u>H</u>3), 1.10 and 1.16 (3H, each d, *J*=6.9 Hz, 2 x =CCHC<u>H</u>3), 1.11 (1.5H, d, *J*=6.9 Hz, CH2CHC<u>H</u>3), 1.40 (2H, br, C<u>H</u>2CH2O), 1.89 (0.5H, dt, *J*=14.3, 3.3 Hz, 1/2 x =CHC<u>H</u>2), 1.95 (0.5H, dt, *J*=14.2, 3.3 Hz, 1/2 x =CHC<u>H</u>2), 2.01 (1H, br, CH2C<u>H</u>CH3), 2.45 (0.5H, td, *J*=13.7, 5.1 Hz, 1/2 x =C<u>H</u>CH2), 2.48 (1H, quint, *J*=6.7 Hz, =CC<u>H</u>CH3), 2.92 (0.5H, td, *J*=13.7, 5.1 Hz, 1/2 x =C<u>H</u>CH2), 3.71 (0.5H, t, *J*=11.2 Hz, 1/2 x OC<u>H</u>2), 3.74 (1H, d, *J*=2.4 Hz, 1/2 x SiOC<u>H</u>2), 3.77 (1H, d, *J*=2.4 Hz, 1/2 x SiOC<u>H</u>2), 3.96 (0.5H, t, *J*=11.2 Hz, 1/2 x OC<u>H</u>2), 4.72 (1H, t, *J*=7.1 Hz, SCH), 4.81 (0.5H, ddd, *J*=11.6, 5.1, 3.4 Hz, 1/2 x OC<u>H</u>2), 5.08 (0.5H, dt, *J*=11.6, 3.4 Hz, 1/2 x OC<u>H</u>2), 5.38 (0.5H, dd, *J*=12.5, 3.4 Hz, =CH), 5.50 (0.5H, dd, *J*=12.5, 3.4 Hz, =CH). MS *m/z*: 373 (M^++1). HR-MS *m/z*: calcd for $C_{19}H_{37}O_3SSi$ 373.2231, Found: 373.2240 (M^++1). GLC (5% Silicon OV-17, 3 mm i.d. x 3 m at 170-270 °C (+10 °C/min), carrier gas, N2, 50 ml/min): t_R 13.6 min (100%).

(*Z*)-4-Hydroxymethyl-5-isopropyl-8-methyl-7,8,9,10-tetrahydro-4*H*-1,3-oxathiecin-2-one (13) A 1 M solution of tetrabutylammonium fluoride[18] (0.79 ml, 0.79 mmol) in THF was added dropwise to a solution of **3** (329 mg, 0.88 mmol) in THF (20 ml) at 0 °C and the mixture was stirred for 30 min at 0 °C. An additional tetrabutylammonium fluoride (0.09 ml, 0.09 mmol) in THF was added and the mixture was further stirred for 5 min. The reaction was quenched by the addition of H2O. The mixture was diluted with EtOAc-hexane (1 : 1) and the organic layer was washed with H2O and brine, dried over anhydrous Na2SO4, and then evaporated under reduced pressure. The residue was purified by column chromatography (20% EtOAc in hexane) to give **13** (220 mg, 97%) as a mixture of isomers **13a** and **13b** at C4. **13a**[14] (less polar): IR (neat): 3500 (OH), 1650 (CO) cm^{-1}. ^{1}H-NMR: 0.99 (3H, d, *J*=6.9 Hz, =CHCHC<u>H</u>3), 1.06 (3H, d, *J*=6.9 Hz, CH2CHC<u>H</u>3), 1.09 (3H, d, *J*=6.9 Hz, =CHCHC<u>H</u>3), 1.38 (1H, dt, *J*=15.3, 4.6 Hz, 1/2 x C<u>H</u>2CH2O), 1.71 (1H, ddt, *J*=15.3, 11.3, 3.4 Hz, 1/2 x C<u>H</u>2CH2O), 1.82-2.06 (1H, overlap, CH2C<u>H</u>CH3), 1.96 (1H, dt, *J*=14.3, 3.7 Hz, 1/2 x =CHC<u>H</u>2), 2.38 (1H, sept, *J*=6.9 Hz, =CC<u>H</u>CH3), 2.46 (1H, dt, *J*=14.3, 12.4 Hz, 1/2 x =CHC<u>H</u>2), 3.73 (2H, d, *J*=7.6 Hz, C<u>H</u>2OH), 3.96 [1H, td, *J*=11.3, 1.2 Hz, 1/2 x CH2OC(O)], 4.75-4.88 [1H, overlap, 1/2 x CH2OC(O)], 4.77 (1H, t, *J*=7.6 Hz, SCH), 5.45 (1H, dd, *J*=12.4, 3.7 Hz, =CH). **13b**[14] (polar): IR (neat): 3420 (OH), 1680 cm^{-1} (CO). ^{1}H-NMR: 1.02 (3H, d, *J*=6.9 Hz, =CCHC<u>H</u>3), 1.08 (3H, d, *J*=7.0 Hz, CH2CHC<u>H</u>3), 1.12 (3H, d, *J*=6.9 Hz, =CCHC<u>H</u>3), 1.22-1.53 (2H, m, C<u>H</u>2CH2O), 1.93 (1H, dt, *J*=13.8, 2.9 Hz, 1/2 x =CHC<u>H</u>2), 2.01 (1H, m, CH2C<u>H</u>CH3), 2.42 (1H, sept, *J*=6.9 Hz, =CC<u>H</u>CH3), 2.93 (1H, td, *J*=13.8, 3.7 Hz, 1/2 x =CHCH2), 3.65-3.86 (1H, overlap, 1/2 x CH2C<u>H</u>2O), 3.76 (2H, br d, *J*=8.0 Hz, C<u>H</u>2OH), 4.80 (1H, t, *J*=8.0 Hz, SCH), 5.08 (1H,

dt, *J*=11.1, 2.9 Hz, 1/2 x $CH_2C\underline{H}_2O$), 5.60 (1H, dd, *J*=13.8, 3.7 Hz, =CH). MS of **13** *m/z*: 258 (M^+). HR-MS *m/z*: Calcd for $C_{13}H_{22}O_3S$ 258.1287, Found: 258.1282.

(Z)-4-Formyl-5-isopropyl-8-methyl-7,8,9,10-tetrahydro-4*H*-1,3-oxathiecin-2-one (14) A solution of DMSO (0.17 ml, 2.33 mmol) in CH_2Cl_2 (1 ml) was added to a solution of oxalyl chloride (0.15 ml, 1.74 mmol) in CH_2Cl_2 (5 ml) at -78 °C and the mixture was stirred for 15 min at -78 °C. A solution of **13** (30 mg, 0.12 mmol) in CH_2Cl_2 (1 ml) was added, and the mixture was stirred for 20 min at -78 °C. After stirring at -45 °C for 1 h, Et_3N (0.32 ml, 2.33 mmol) was added at this temperature and the mixture was stirred for 25 min at 0 °C. The reaction was quenched by the addition of H_2O and diluted with EtOAc-hexane (2 : 1). The organic layer was washed with H_2O (x 2) and brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to give **14** (30 mg, quant) as a white wax. IR ($CHCl_3$): 1720, 1690 (CO), 1140 (C-O-C) cm^{-1}. ^{1}H-NMR (the spectrum was not sufficiently well resolved for assignment of the total signals because of the mixture of diastereomers): 0.91-1.02 (18H, m), 1.15-1.54 (5H, m), 1.54-1.82 (2H, m), 1.82-2.30 (6H, m), 2.42 (2H, q, *J*=13 Hz), 2.70-3.01 (1H, br), 3.58-3.86 (1H, m), 3.95 (1H, t, *J*=13 Hz), 4.77-4.90 (1H, m), 4.95-5.12 (0.5H, br), 5.65 (1H, dd, *J*=13, 4 Hz), 5.76 (0.5H, dd, J=13, 4 Hz), 9.51 (1H, d, *J*=6 Hz). MS *m/z*: 256 (M^+). HR-MS *m/z*: Calcd for $C_{13}H_{20}O_3S$ 256.1132, Found: 256.1141.

(Z)-5-Isopropyl-8-methyl-4-(2-methyl-1-propenyl)-7,8,9,10-tetrahydro-4*H*-1,3-oxathiecin-2-one (2) A 1.6 M solution of n-BuLi in hexane (0.15 ml, 0.244 mmol) was added to a suspension of isopropyltriphenylphosphonium bromide[20] (94 mg, 0.244 mmol) in anhydrous ether (3 ml) at room temperature. After the suspension was stirred for 2 h in a sealed flask, a solution of **14** (83 mg, 0.244 mmol) in anhydrous ether (4 ml) was added to a resulting wine red solution. The mixture was stirred for 17 h at room temperature in a sealed flask. The resulting white precipitate was filtered off and washed with ether. The combined ether solution was evaporated under reduced pressure and the residue was purified by column chromatography using EtOAc-hexane (1 : 19) for elution to give **2** (55 mg, 60%) as a white wax. IR ($CHCl_3$): 1680 (CO), 1130 (C-O-C) cm^{-1}. ^{1}H-NMR (the spectrum was not sufficiently well resolved for assignments of the total signals because of the mixture of diastereomers): 0.99-1.12 (18H, m), 1.30-1.44 (3H, br), 1.72 (12H, s), 1.56-2.14 (5H, br), 2.40-2.65 (3H, m), 2.98 (1H, td, *J*=12.8, 4.3 Hz), 3.73 (1H, br t, *J*=12.8 Hz), 3.98 (1H, t, *J*=9.8 Hz), 4.83 (1H, ddd, *J*=11.6, 4.5, 2.8 Hz), 5.05-5.46 (7H, br). MS *m/z*: 282 (M^+). HR-MS *m/z*: Calcd for $C_{16}H_{26}O_2S$ 282.1651, Found: 282.1647.

(Z)-6-Isopropyl-3,9-dimethyl-7-mercapto-5,8-decadien-1-ol (15) A 2 N aqueous NaOH solution (0.5 ml) was added to a solution of **2** (9.5 mg, 0.034 mmol) in MeOH (1 ml) at room temperature. The reaction mixture was stirred for 0.5 h at room temperature and then slightly acidified with 10% HCl. The mixture was extracted with EtOAc-hexane (1 : 1), and the extract was washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent left a crude oil, which was purified by column chromatography using EtOAc-hexane (1 : 4) for elution to give **15** (7 mg, 81%) as a colorless oil. IR (neat): 3330 cm^{-1} (OH). ^{1}H-NMR: 0.89 and 0.90 (each 1.5H, each d, *J*=6.0 Hz, $CH_2CHC\underline{H}_3$), 1.00 and 1.10 (each 3H, each d, *J*=6.0 Hz, 2 x $=CCHC\underline{H}_3$), 1.50-1.60 (2H, br, $C\underline{H}_2CH_2O$), 1.66 and 1.70 (each 3H, each s, 3 x $=CCH_3$), 1.88-2.25 (3H, m, $=CHC\underline{H}_2$, $CH_2C\underline{H}CH_3$), 2.54 (1H, sept, *J*=7.0 Hz, $=CCHCH_3$), 3.68 (2H, br, CH_2O), 4.87 (1H, dd, *J*=9.0, 3.5 Hz, $C\underline{H}SH$), 5.18 (1H, t, *J*=7.0 Hz, $=C\underline{H}CH_2$), 5.38 (1H, br d, *J*=9.0 Hz, $=CHC\underline{H}$),. MS *m/z*: 256 (M^+). HR-MS *m/z*: Calcd for $C_{15}H_{28}OS$ 256.1859, Found: 256.1864.

The Reductive Desulfurization of 2 with LDBB To an oven-dried flask with stirring bar were added THF (1.5 ml) and di-*tert*-butylbiphenyl[18] (266 mg, 1 mmol). The shiny lithium pieces (20 mg, 2.90 mmol) was quickly added to the solution. The mixture was cooled to 0 °C and vigorously stirred for 5 min. THF (4.5 ml) was added, and then the mixture was stirred for additional 1.5 h at 0 °C. When HMAP (3 ml) was added to the resulting dark green-blue solution, the color was turned to orange and then recovered to dark green-blue. The mixture was further stirred for 1 h and cooled to -78 °C. A solution of **2** (9.0 mg, 0.032 mmol) in THF (1 ml) was added to the mixture. The reaction was subsequently quenched with MeOH, and extracted with EtOAc-hexane (1 : 1) and H_2O. The organic phase was washed with H_2O (x 2) and brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure gave a crude oil, which was purified by column chromatography (20% EtOAc in hexane) to give a mixture of (*E*)-6-isopropyl-3,9-dimethyl-5,8-decadienol **16** and 6-isopropyl-3,9-dimethyl-6,8-decadienol **17** (**16** : **17**=2.4 : 1, determined from ^{1}H-NMR). Acetic anhydride (4 µl) and 4-DMAP (4 mg) were added to a solution of the mixture in CH_2Cl_2 (1 ml). The resulting solution was stirred overnight at room temperature. Workup gave a crude oil, which was purified by medium-pressure liquid chromatography [Waters associates Prep PAK-500/silica, 20% benzene in hexane] to yield (±)-(*E*)-6-isopropyl-3,9-dimethyl-5,8-decadienyl acetate **1** (5.1 mg, 60%) and (±)-6-isopropyl-3,9-dimethyl-6,8-decadienyl acetate **18** (2.0 mg, 23%) .

Compound **1:** colorless oil. ^{1}H-NMR in $CDCl_3$: 0.87 (3H, d, *J*=6.7 Hz, $CH_2CHC\underline{H}_3$), 0.97 (6H, d, *J*=6.7 Hz, 2 x =$CCHC\underline{H}_3$), 1.3-1.5 (2H, m, $C\underline{H}_2CH_2O$), 1.5 (1H, m, $CH_2C\underline{H}CH_3$), 1.64 and 1.67 (each 3H, each br s, 2 x =CCH_3), 1.76-2.05 (2H, m, =$CHC\underline{H}_2CH$), 2.03 (3H, s, CH_3CO), 2.20 (1H, sept, *J*=6.7 Hz, =$CC\underline{H}CH_3$), 2.67 (2H, br d, *J*=6.7 Hz, =$CHCH_2C$=), 4.08 (2H, td, *J*=7.3, 1.7 Hz, CH_2O), 4.95 [1H, br t, *J*=6.7 Hz, $(CH_3)_2C$=$C\underline{H}$], 5.11 [1H, t, *J*=6.7 Hz, $CH_2(CH)C$=$C\underline{H}$]. ^{1}H-NMR in C_6D_6: 0.86 (3H, d, *J*=6.5 Hz, $CH_2CHC\underline{H}_3$), 1.08 (6H, d, *J*=6.8 Hz, 2 x =$CCHC\underline{H}_3$), 1.20-1.46 (3H, m, $C\underline{H}_2CH_2O$, $CH_2C\underline{H}CH_3$), 1.63 and 1.68 (each 3H, each s, 2 x =CCH_3), 1.71 (3H, s, CH_3CO), 1.84-2.14 (2H, m, =$CHC\underline{H}_2CH$), 2.32 (1H, quint, *J*=6.8 Hz, =$CC\underline{H}CH_3$), 2.82 (2H, br d, *J*=7.0 Hz, =$CHC\underline{H}_2C$=), 4.10 (2H, td, *J*=6.3, 1.7 Hz, CH_2O), 5.19 [1H, t, *J*=7.0 Hz, $(CH_3)_2C$=$C\underline{H}$], 5.26 [1H, t, *J*=7.0 Hz, $CH_2(CH)C$=$C\underline{H}$]. The ^{1}H-NMR spectrum in C_6D_6 was identical with that of the natural pheromone.[4, 17] ^{13}C-NMR: 17.8, 19.5, 21.1, 22.0, 25.7, 28.4, 30.8, 34.5, 34.8, 35.2, 63.2, 120.4, 123.6, 130.9, 145.9, 171.3. MS m/z: 266 (M^+). HR-MS *m/z*: Calcd for $C_{17}H_{30}O_2$ 266.2244, Found: 266.2245.

Compound **18** :colorless oil. ^{1}H-NMR: 0.92 (3H, d, *J*=6.1 Hz, CH_3-C_3), 1.00 [6H, d, *J*=6.7 Hz, $(CH_3)_2CH$], 1.3-1.7 (4H, m, 2 x CH_2), 1.74 and 1.80 (each 3H, each s, $(CH_3)_2C$=), 1.9-2.1 (2H, br m, =CCH_2), 2.03 [3H, s, $CH_3C(O)O$], 2.95 [1H, sept, *J*=6.7 Hz, $(CH_3)_2C\underline{H}$], 4.10 (2H, t, *J*=7.2 Hz, CH_2O), 5.87 and 6.07 [each 1H, each d, *J*=11.6 Hz, -CH=CH-]. ^{13}C-NMR: 18.0, 19.5, 21.1, 21.3, 26.5, 29.1, 30.1, 35.5, 36.9, 63.1, 119.4, 120.4, 132.9, 145.2, 171.3. MS *m/z*: 266 (M^+). HR-MS *m/z*: Calcd for $C_{17}H_{30}O_2$ 266.2244, Found: 266.2242.

Lithium-Liquid Ammonia Reduction of 2 A mixture of **2** (5.2 mg, 0.018 mmol) and acetic acid[21] (18 mg, 0.3 mmol) in THF (1 ml) was added to a stirred solution of Li (16 mg, 2.3 mmol) in liquid ammonia (7 ml) at -78 °C and isoprene (0.2 ml) was added immediately to the reaction mixture. The ammonia was evaporated off and the residue was extracted with EtOAc-hexane (2 : 1). The organic phase was washed with H_2O and brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography (EtOAc : hexane=1 : 9) to give a mixture (4.0 mg, quant.) of **16** and **17**

in a ratio of 84 : 16 (from ^{1}H-NMR). The mixture was separable by medium-pressure liquid chromatography [Waters Associates Prep PAK-500/silica, EtOAc : hexane=7 : 93].

16: Colorless oil. ^{1}H-NMR: 0.87 (3H, d, *J*=6.5 Hz, $CH_2CHC\underline{H}_3$), 0.96 (6H, d, *J*=6.8 Hz, 2 x $=CCHC\underline{H}_3$), 1.18-1.46 (3H, m, $C\underline{H}_2CH_2O$, $CH_2C\underline{H}CH_3$), 1.63 and 1.65 (each 3H, s, 2 x $=CCH_3$), 1.80-2.10 (3H, m, $=CHC\underline{H}_2CH$, OH), 2.21 (1H, sept, *J*=6.8 Hz, $=CC\underline{H}CH_3$), 2.68 (2H, br d, *J*=6.8 Hz, $=CHC\underline{H}_2C=$), 3.66 (2H, td, *J*=6.5, 2.6 Hz, CH_2O), 4.95 [1H, br t, *J*=6.8 Hz, $(CH_3)_2C=C\underline{H}$], 5.12 [1H, t, *J*=7.0 Hz, $CH_2(CH)C=C\underline{H}$]. MS *m/z*: 224 (M^+). Acetylation of **16** (3 mg, 0.013 mmol) afforded (±)-**1** (3.4 mg, quant).

17: Colorless oil. ^{1}H-NMR: 0.92 (3H, d, *J*=6.0 Hz, $CH_2CHC\underline{H}_3$), 1.00 (6H, d, *J*=7.0 Hz, 2 x $=CCHC\underline{H}_3$), 1.4-1.7 (4H, br m, $C\underline{H}_2CH_2O$, $CH_2C\underline{H}CH_3$, OH), 1.73 and 1.78 (each 3H, each s, 2 x $=CCH_3$), 1.9-2.1 (2H, br m, $=CCH_2$), 3.00 (1H, sept, J=7.0 Hz), 3.69 (1H, td, *J*=7.5, 2.5 Hz, $C\underline{H}_2OH$), 5.88 and 6.08 (each 1H, each d, *J*=12.5 Hz, =CH-CH=). MS *m/z*: 224 (M^+).

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REFERENCES AND NOTES

1. Part, 8: S. Harusawa, H. Osaki, H. Fujii, R. Yoneda, and T. Kurihara, *Tetrahedron*, **1992**, 48, 9433.
2. S. Harusawa, H. Osaki, S. Takemura, R. Yoneda, and T. Kurihara, *Tetrahedron Lett.*, **1992**, 33, 2543.
3. W.T. Johnson and H.H. Lyon, "Insects that feed on trees and shrubs," 2nd, Cornell University Press, **1988**, p378.
4. M.J. Gieselmann, D. S. Moreno, J. Fargerlund, H. Tashiro, and W.L. Roelofs, *J. Chem. Ecol.*, **1979**, 5, 27.
5. K. Mori and S. Kuwahara, *Tetrahedron*, **1982**, 38, 521.
6. a) R.J. Anderson and C.A. Henrick, *J. Chem. Ecol.*, **1979**, 5, 773.
   b) S. Masuda, S. Kuwahara, T. Suguro, and K. Mori, *Agric. Biol. Chem.*, **1981**, 45, 2515.
   c) T. Suguro, W.L. Roelofs, and K. Mori, *Agric. Biol. Chem.*, **1981**, 45, 2509.
   d) E. Alvarez, T. Cuvigny, C. Hervé du Penhoat, and M. Julia, *Tetrahedron*, **1988**, 44, 119.
   e) J.G. Millar, *Tetrahedron Lett.*, **1989**, 30, 4913.
   f) R. Baudouy, M.-R. Sancho, *Tetrahedron*, **1991**, 48, 10015.
7. S. Harusawa, H. Osaki, H. Fujii, R. Yoneda, and T. Kurihara, *Tetrahedron Lett.*, **1990**, 31, 5471.
8. a) S. Harusawa, T. Kurokawa, H. Fujii, R. Yoneda, and T. Kurihara, *Chem. Pharm. Bull.*, **1989**, 37, 2567.
   b) S. Harusawa, H. Ohishi, H. Osaki, S. Tomii, R. Yoneda, and T. Kurihara, *ibid.*, **1992**, 40, 2185.
   c) S. Harusawa, H. Osaki, T. Kurokawa, H. Fujii, R. Yoneda, and T. Kurihara, *ibid.*, **1991**, 39, 1659.
9. S. Harusawa, H. Osaki, R. Yoneda, T. Kurihara, and H.Ohishi, *Tetrahedron Lett.*, **1991**, 32, 1203.
10. S. Harusawa, S. Tomii, C. Takehisa, H. Ohishi, R. Yoneda, and T. Kurihara, *Chem. Pharm. Bull.*, **1992**, 40, 2279.
11. K. Mori, "The Total Synthesis of Natural Products," Vol. 4, John Wiley & Sons, New York, **1981**, p1.
12. The yield (87%) of **10** was improved in a large scale reaction (cf. reference 13).
13. E. Piers, J.M. Chong, and H.E. Morton, *Tetrahedron*, **1989**, 45, 363.
14. Both isomers **13a** (less polar) and **13b** (polar) at C_4 were isolated by column chromatography.
15. P.K. Freeman, L.L. Hutchinson, *J. Org. Chem.*, **1980**, 45, 1924; **1983**, 48, 4705.
16. HMPA was used in order to prevent the formation of side products.
17. The stereochemistry of **1** was also confirmed by NOE experiments. Positive NOEs were observed in the ^{1}H resonance signals corresponding to the C_5 vinyl proton (+ 3.2%) and C_7 methylene protons (+ 2.0%) when the methyl groups of isopropyl moiety were irradiated.
18. These are available from Aldrich Chemical Company.
19. A.J. Irwin and J.B. Jones, *J. Am. Chem. Soc.*, **1977**, 99, 556.
20. U.H.M. Fagerlund and D.R. Idler, *J. Am. Chem. Soc.*, **1957**, 79, 6473.
21. Migrated 6,8-dienic alcohol **17** was obtained as major product in the absence of acetic acid.