(*Z*)-3-Alkylidene-4,5-dihydro-4-hydroxy-5-methyl-2-(3*H*)-furanones by Regio- and Diastereoselective Ene Reaction of Singlet Oxygen (Schenk Reaktion) with γ-Hydroxy Vinylstannanes: An Enantioselective Synthesis of Dihydromahubanolide B

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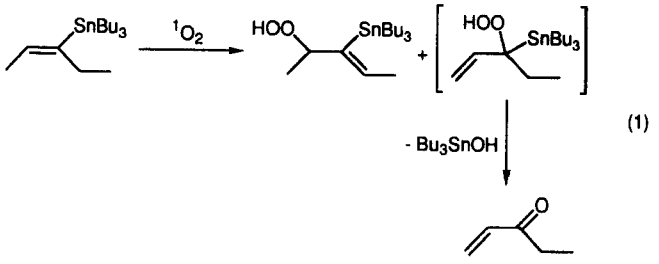
Received 26 November 1993

(*Z*)-3-Alkylidene-4,5-dihydro-4-hydroxy-5-methyl-2-(3*H*)-furanones **5** were prepared from appropriately substituted propargylic alcohols **1** by a sequence of hydromagnesation to γ-hydroxy vinylstannanes **2**, subsequent photooxygenation and reduction to stannyl diols **3**, iododestannylation to iodo diols **4**, and finally cyclization by palladium-catalyzed carbonylation (for **5a**) or $Ni(CO)_2(PPh_3)_2$ (for **5b,c**). The reaction sequence can be performed enantioselectively by starting with chiral propargylic alcohols. The current approach constitutes a convenient four-step synthesis of optically active lactones **5** from readily available starting materials and is applied herein to the preparation of the natural lactone dihydromahubanolide B.

3-Alkylidene-4,5-dihydro-4-hydroxy-5-methyl-2-(3*H*)-furanones **5** are a class of natural products isolated from plants of the *Lauraceae* family,[1] which are of interest in view of their biological activity[2] and have, therefore, been the goal of intensive synthetic efforts.

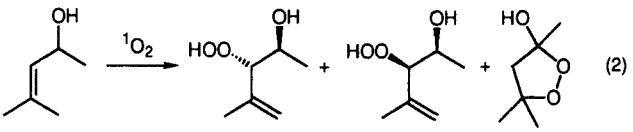
Although the skeleton of these compounds is comparative simple, the high density of functionalization makes the selective synthesis of such substrates rather problematic. Racemic mixtures were synthesized by a variety of methods,[3,4] often by starting from α-thio or α-seleno esters; however, most of these approaches cannot be used for enantioselective synthesis. Thus, optically active lactones **5** have been so far only accessible starting with material from the chiral pool (glucose, ribonolactone, L-tartrate, xylose, lactaldehyde),[5] which in most cases required multistep transformations to obtain the butyrolactone framework.

On the other hand, the ene reaction of $^1O_2$ with olefins is well-known to proceed rather unselectively with normal alkyl-substituted olefins.[6] Nevertheless, in the last few years, regioselective ene reactions of $^1O_2$ have been reported, which generally occur when electron-withdrawing groups[7] (CO_2Et, COR, CHO, SOPh) or organometallic groups (SiR_3,[8] SnR_3[9]) are attached to the double bond, with hydrogen abstraction geminal to the steering group (*gem* effect). Especially the organometallic substrates are highly interesting because they show remarkable regiocontrol without deactivating the double bond towards the ene reaction, as is normally the case for electron-withdrawing groups. In this context, the stannyl moiety[9] exhibits the additional benefit of high *Z* selectivity towards the newly formed double bond (Eq. 1). Consequently, the stannyl group constitutes a remarkable functionality in photooxygenations in that it exercises regio- and stereocontrol, can be readily introduced in the olefinic substrate, and extensively modified in the oxidized product.



(1)

Since it was recently shown that the singlet oxygen ene reaction of chiral allylic alcohols[10] and amines[11] proceeds regio- and diastereoselectively to yield *threo*-hydroperoxy alcohols and amines in high diastereomeric excess (Eq. 2), it was of synthetic interest to examine the photooxygenation of vinyl stannanes with a chiral allylic hydroxy functionality in the γ-position. Such substrates should undergo the ene reaction with $^1O_2$ highly regio- and diastereoselectively; in fact, double stereocontrol should apply in regard to the newly formed double bond through the allylic shift and the new oxyfunctionalized stereogenic center. These highly functionalized oxidation products should serve as valuable building blocks for further synthetic work. In the following we demonstrate that, indeed, the photooxygenation of γ-hydroxy vinylstannanes proceeds highly regio- and diastereoselectively to afford, after triphenylphosphine reduction, the desired stannyl diols **3**. This new method is illustrated in the convenient preparation of lactones **5**, e.g. the natural product dihydromahubanolide B.

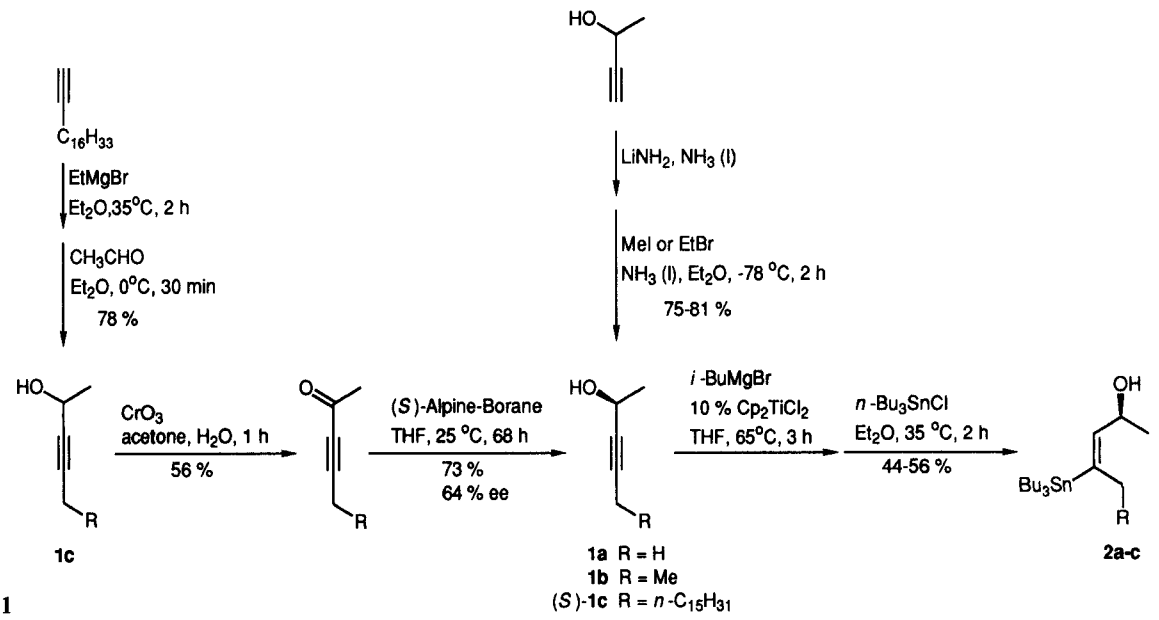


(2)

89 : 7 : 4

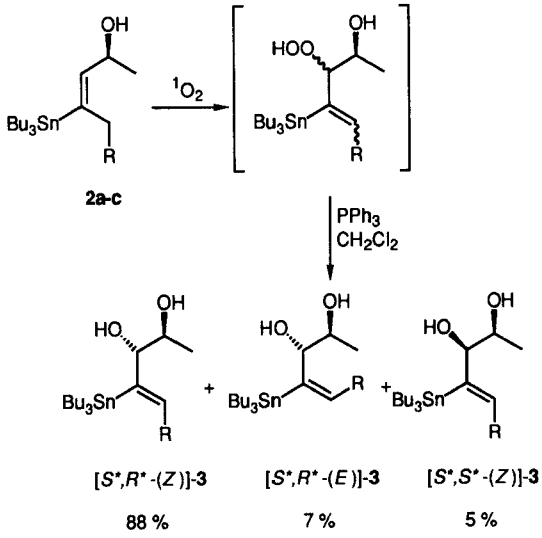
The propargylic alcohols **1** were prepared by monoalkylation of 1-butyn-3-ol[12] (Scheme 1) in 75–81% yield **(1a,b)** or by reaction of 1-octadecylmagnesium bromide with acetaldehyde in 78% yield **(1c)**. Enantiomerically enriched (*S*)-**1c** was synthesized by Jones oxidation[13] of racemic **1c** and subsequent (*S*)-alpine-borane reduction[14] (0.5 M solution) to yield (*S*)-**1c** in 73% chemical yield and 64% enantiomeric excess; the latter was confirmed by chiral HPLC analysis of the corresponding benzoate. Subsequent hydromagnesation[15] of **1a–c** and quenching with tributyltin chloride afforded the γ-hydroxy vinylstannanes **2a,b** and (*S*)-**2c** in 44–56% yield.

Photooxygenation [CH_2Cl_2, −15 °C, tetraphenylporphine (TPP) as sensitizer] of **2a,b** and (*S*)-**2c** occurred regio- and diastereoselectively and yielded after triphenylphosphine reduction of the intermediary hydroperoxides the stannylated diols **3** in high *threo*- and *Z* selectivity (Scheme 2). The regioisomeric ene products derived from abstraction of hydrogen geminal to the hydroxy functionality in the vinylstannane **2** were not observed. Thus, in the case of derivative **2a** a 93% yield of **3a** was obtained



Scheme 1

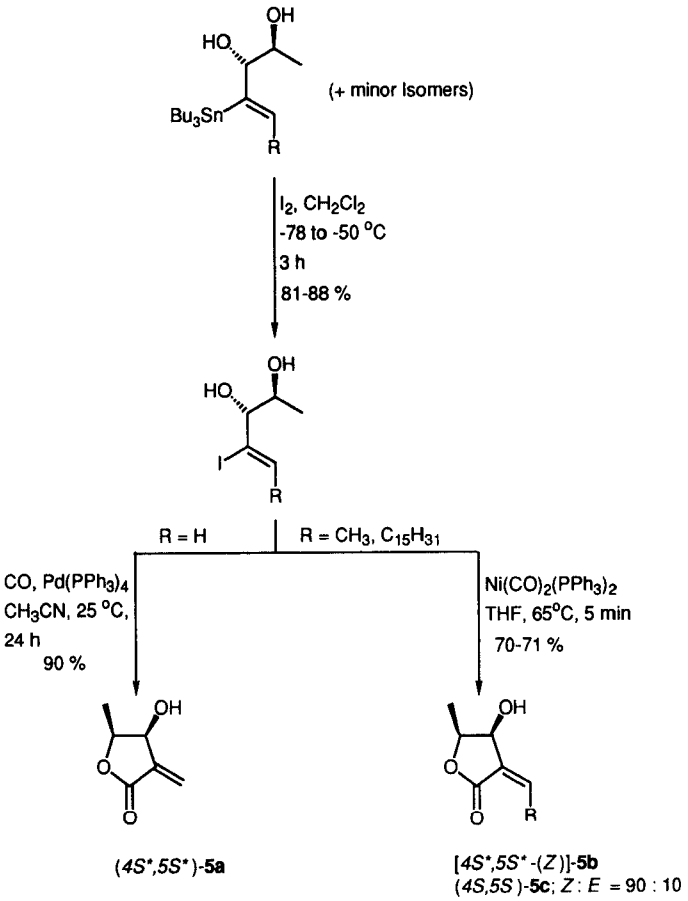
and a diastereomeric ratio of (2*S**,3*R**)-**3a**:(2*S**,3*S**)-**3a** = 95:5. In the photooxygenation of the substrates **2b** and (*S*)-**2c**, isomeric mixtures were obtained in 78 and 84% yields, in which the [2*S*,*,3*R**-(*Z*)]-isomer strongly predominated, i.e. [2*S**,3*R**-(*Z*)]-**3b,c**: [2*S**,3*R**-(*E*)]-**3b,c**:[2*S**,3*S**-(*Z*)]-**3b,c** = 88:7:5. These isomeric mixtures could not be separated by chromatographic means at this stage; however, iododestannylation afforded the hitherto unknown iodo diols **4** with complete retention of configuration, of which the major isomers were isolated in 81–88% yield in pure form by chromatography and recrystallization (Scheme 3).



Scheme 2

For the conversion of the iodo diols **4** into the desired lactones **5**, the conditions reported by Stille[16] in the cyclization of simple α-methylenebutyrolactones were employed. Indeed, (2*S**,3*R**)-**4a** was cyclized smoothly with $Pd(PPh_3)_4$ (2.5%) under 1 atm of carbon monoxide in acetonitrile at 25°C within 24 h to yield 90% of the lactone (4*S**,5*S**)-**5a** (Scheme 3). This can be contrasted with the related bromo diol, which even at temperatures up to 70°C failed to cyclize under the above conditions,[16] and illustrates that the iodo diols **4** are considerably more reactive towards palladium-catalyzed cyclizations.

On application of these conditions, however, to the substrates [2*S**,3*R**-(*Z*)]-**4b** and [2*S*,3*R*-(*Z*)]-**4c**, no cycliza-



Scheme 3

tion occurred even at higher temperature (70 °C) and elevated CO pressures (10 atm). This may be due to the pronounced steric hindrance of the *Z* alkyl group in these substrates, which apparently retards the catalytic step of palladium insertion in the carbon–iodine bond. For these derivatives the stoichiometric reaction with $Ni(CO)_2(PPh_3)_2$ (1.2 equiv) proved to be successful.[17] Thus, **4b** was converted in THF within 5 min at 65 °C into the lactone **5b**, which was isolated in 71 % yield after column chromatography. The cyclization of [2*S**,3*R**-(*Z*)]-**4b** occurred with complete retention of the double bond geometry, i.e. exclusively [4*S**,5*S**-(*Z*)]-**5b** was obtained, which is the thermodynamically less stable isomer.

Under these conditions, substrate [2*S*,3*R*-(*Z*)]-**4c** gave a 90:10 isomeric mixture of [4*S*,5*S*-(*Z*)]-**5c**, which constitutes the naturally occurring dihydromahubanolide B (isolated from trunks of *Clinostemon mahuba*)[3] and [4*S*,5*S*-(*E*)]-**5c** (isodihydromahubanolide B). Unfortunately, presumably the increased steric strain in derivative **5c** led to some *Z*,*E* isomerization under the reaction conditions. HPLC analysis showed an enantiomeric excess (ee) of 76 % for lactone **5c**. Since the synthetic sequence was started with (*S*)-**1c** of 64 % ee, the reaction steps proceeded with complete retention of stereochemistry (the slight amplification in the optical purity occurred in the recrystallization step of **4c**). Thus, the present methodology enables the preparation of enantiomerically pure lactones **5** from the readily available chiral propargylic alcohols **1**. Since there are other methods for the preparation of propargylic alcohols in nearly 100 % ee,[18] this synthetic sequence allows the preparation of enantiomerically pure lactones of natural origin.

In summary, we have shown that the novel methodology described herein conveniently affords lactones **5** in four steps and good overall yield (25–32 %) from the readily available propargylic alcohols **1**. This synthetic sequence allows the enantioselective preparation of the thermodynamically less stable *Z* lactones, for which to date hardly any adequate syntheses are available.[4] Additionally, the present method tolerates extensive variations in the alkylidene as well as in the alkyl side chains. The key step in this sequence is the regio- and diastereoselective ene reaction of singlet oxygen with appropriate olefins, which demonstrates the synthetic value of photooxygenation in the preparation of highly oxyfunctionalized target molecules with several stereogenic centers.

All melting and boiling points are uncorrected. Solvents were purified according to standard procedures. CH_2Cl_2 for photooxygenations was purified by filtration over basic alumina (activity I). TLC was performed on Polygram Sil G UV (40 × 80 mm), Macherey & Nagel. Silica gel (32–64 μm) from Woelm was used for flash chromatography. Analytical HPLC was performed using a Waters 510 computer-monitored pump system, in which detections were made by means of a Waters 486 tunable absorbance detector at 254 nm. Area peaks were assessed by using the Millipore Maxima software system. As stationary phase, a Baker Chiracel OD column was used, with hexane/isopropyl alcohol mixtures as eluent. Optical rotations were determined on a Perkin-Elmer 241 MC Polarimeter. IR spectra were recorded on a Perkin-Elmer Model 1420 instrument. NMR spectra were recorded on a Bruker AC 200 spectrometer with $CDCl_3$ as internal standard [δ = 7.26 (^{1}H) and 77.0 (^{13}C)]. ^{1}H NMR resonances of the tributylstannyl groups of the alkenylstannanes at δ = 0.75–1.10 (m, 15 H) and 1.20–1.60 (m, 12 H) are not listed in the reported ^{1}H NMR data. The separate $J(^{117}SnH)$ and $J(^{119}SnH)$ values are reported when the satellite peaks were clearly distinct; otherwise the indicated J_{HSn} values represent approximate mean values of J (^{117}SnH) and J (^{119}SnH). Elemental analyses were obtained in house. Compounds **1c**, 3-eicosyn-2-one, **2a–c**, **3a–c**, **4a–c** and **5a,b** gave C, H ± 0.5 %. 1-Octadecyne was prepared from 1-octadecene by bromination/dehydrobromination[19]. 3-Pentyn-2-ol **(1a)** and 3-hexyn-2-ol **(1b)** were prepared by literature procedures.[12]

3-Eicosyn-2-ol (1c):
To a solution of 0.350 mol of EtMgBr in 250 mL of Et_2O was added dropwise a solution of 64.7 g (0.258 mol) of 1-octadecyne[19] under an argon atmosphere. Stirring was continued for 30 min at 25 °C and 2 h at reflux, until evolution of ethane had ceased. At 0 °C, 22.0 g (0.500 mol, 28.2 mL) of acetaldehyde was added and the solution was stirred at this temperature for 30 min and at reflux for 2 h. After the reaction mixture was hydrolyzed with 25 mL of sat. aq NH_4Cl, water (200 mL) was added and the mixture was neutralized with 2 N HCl. The organic layer was separated, washed with sat. aq Na_2CO_3 (50 mL), and dried ($MgSO_4$). After removal of the solvent by rotoevaporation (50 °C at 20 Torr), the residue was recrystallized from 200 mL of pentane to yield 59.4 g (0.202 mol, 78 %) of a colorless amorphous solid, mp 37–40 °C. Further purification of a small sample by flash chromatography on silica gel (50 g; 5:1 pentane/Et_2O as eluent) afforded a colorless amorphous solid, mp 43–44 °C.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.87 (m, 3 H), 1.20–1.70 (m, 28 H), 1.42 (d, J = 6.5 Hz, 3 H), 1.76 (br s, 1 H), 2.18 (td, J = 7.0, 1.8 Hz, 2 H), 4.51 (m, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.1 (q), 18.6 (t), 22.7 (t), 24.7 (q), 28.6 (t), 28.8 (t), 29.1 (t), 29.4 (t), 29.5 (t), 29.6 (t), 29.7 (6 × t), 31.9 (t), 58.6 (d), 82.1 (s), 84.8 (s).

IR (CCl_4): ν = 3580, 2890, 2820, 2220, 1448, 1360, 1340, 1140, 1066 cm^{-1}.

3-Eicosyn-2-one:[13]
Alcohol **1c** (29.5 g, 100 mmol) was dissolved in 100 mL of acetone and cooled to 0 °C. Within 30 min, a solution of 11.0 g (110 mmol) of CrO_3 in 8 mL of conc. H_2SO_4 and 30 mL of water was added dropwise, and stirring was continued for a further 30 min. The reaction mixture was poured into 300 mL of water, extracted with Et_2O (3 × 100 mL), and the organic layer was washed with water, and dried ($MgSO_4$). The solvent was removed by rotoevaporation (20 °C at 20 Torr), the crude product dissolved in 100 mL of pentane and cooled to −20 °C. The precipitate was collected by filtration and dried in vacuo (0.01 Torr) to yield 16.3 g (55.7 mmol, 56 %) of a colorless amorphous solid, mp 25–27 °C.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.86 (m, 3 H), 1.24 (m, 26 H), 1.54 (m, 2 H), 2.30 (s, 3 H), 2.33 (t, J = 7.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.1 (q), 18.9 (q), 22.7 (t), 27.6 (t), 28.8 (t), 29.0 (t), 29.3 (t), 29.4 (t), 29.6 (t), 29.7 (6 × t), 31.9 (t), 32.7 (q), 81.3 (s), 94.2 (s), 184.9 (s).

IR (neat): ν = 2900, 2820, 2190, 1659, 1450, 1405, 1345, 1215, 1010, 950, 713 cm^{-1}.

(*S*)-3-Eicosyn-2-ol [(*S*)-1c]:[14]
Under an argon atmosphere 3-eicosyn-2-one (7.31 g, 25.0 mmol) was added to 100 mL of a 0.5 M solution of (*S*)-alpine-borane (Aldrich) at 25 °C and the reaction mixture was stirred for 68 h. Acetaldehyde (2.5 mL) was added and stirring was continued for 15 min. The solvent was evaporated (20 °C at 0.01 Torr) and the residue dissolved in 60 mL of Et_2O. After addition of 3.3 mL of ethanolamine at 0 °C and stirring for 15 min, the precipitate was removed by suction filtration. The filtrate was washed with brine (100 mL), dried ($MgSO_4$), and evaporated (40 °C at 0.01 Torr). The remaining solid was purified by flash chromatography on silica gel (150 g; 4:1 pentane/Et_2O as eluent) to yield 5.40 g (18.3 mmol, 73 %) of a colorless amorphous solid, mp 37.5–38.5 °C, $[\alpha]_D^{25}$ = −7.8° (c = 1.00, $CHCl_3$). The enantiomeric excess (ee) was determined to be 64 % by chiral HPLC (hexane as eluent) of the corresponding benzoate.

γ-Hydroxy Vinylstannanes 2a–c;[15] Typical Procedure:
To a solution of 2.1 equiv *i*-BuMgBr (about 1 M in Et_2O), diluted with the same volume of Et_2O and cooled to 0 °C, was added Cp_2TiCl_2 (10–15 mol%) and the mixture stirred at this temperature for 10 min. A solution of 1.0 equiv of the corresponding propargylic alcohol **1a–c** (10–70 mmol) in Et_2O was added within 15 min, stirred at r.t. for 15 min and at reflux for 3 h, until evolution of isobutane and isobutene had ceased. The solvent was removed (25 °C at 0.01 Torr) and the residue dissolved in dry THF (3 mL/mmol). Tributyltin chloride (1–1.5 equiv) was added at 0 °C within 15 min and the solution was stirred at 25 °C for 1 h and at 65 °C for 2 h. After addition of 10 mL of aq NH_4Cl, the solvent was removed (25 °C at 20 Torr) and the residue partitioned between water and pentane. The aqueous layer was extracted with pentane (2 × 100 mL), the combined organic layers were washed with water (50 mL) and brine (50 mL) and evaporated (25 °C at 20 Torr). Flash chromatography on silica gel afforded the pure products **2a–c**.

(*E*)-4-(Tributylstannyl)-3-penten-2-ol (2a):
According to the above general procedure, from 5.89 g (70.0 mmol) of **1a**, 144 mL of a 1.07 M solution of *i*-BuMgBr, 1.74 g (7.00 mmol) of Cp_2TiCl_2, and 25.1 g (77.0 mmol) of tributyltin chloride were obtained after silica gel flash chromatography (200 g; 100:0 to 3:1 pentane/Et_2O as eluent) 11.6 g (30.9 mmol, 44 %) of **2a** as a colorless oil.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.23 (d, J = 6.3 Hz, 3 H), 1.50 (s, 1 H), 1.89 (d, J = 1.8, J_{HSn} = 44.5/46.8 Hz, 3 H), 4.74 (m, 1 H), 5.56 (dq, J = 7.8, 1.8, J_{HSn} = 68.4 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 9.0 (t, J_{CSn} = 314/328 Hz), 13.7 (q), 19.4 (q), 23.3 (q), 27.3 (t, J_{CSn} = 54.9 Hz), 29.1 (t, J_{CSn} = 19.8 Hz), 63.6 (d), 140.3 (s), 144.6 (d).

IR (neat): ν = 3580–3060, 2945, 2910, 2860, 2840, 1450, 1410, 1370, 1109, 1068, 1049, 688, 660 cm^{-1}.

(*E*)-4-(Tributylstannyl)-3-hexen-2-ol (2b):
By following the above general procedure, from 3.08 g (31.4 mmol) of **1b**, 64 mL of a 1.08 M solution of *i*-BuMgBr, 747 mg (3.00 mmol) of Cp_2TiCl_2, and 10.2 g (31.4 mmol) tributyltin chloride were obtained after silica gel flash chromatography (150 g; 3:1 pentane/Et_2O as eluent) 6.84 g (17.6 mmol, 56 %) of **2b** as a colorless liquid.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.96 (t, J = 7.5 Hz, 3 H), 1.23 (d, J = 6.3 Hz, 3 H), 1.48 (s, 1 H), 2.30 (m, 2 H), 4.72 (m, 1 H), 5.51 (dt, J = 8.0, 1.3, J_{HSn} = 69 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 9.6 (t), 13.7 (q), 15.4 (q), 23.7 (q), 26.5 (t), 27.4 (t), 29.1 (t), 63.5 (d), 143.7 (d), 147.8 (s).

IR (neat): ν = 3580–3050, 2960, 2920, 2860, 2840, 1460, 1375, 1115, 1060, 670 cm^{-1}.

(2*S*,3*E*)-4-(Tributylstannyl)-3-eicosen-2-ol (2c):
According to the above general procedure, from 2.95 g (10.0 mmol) of (*S*)-**1c**, 21 mL of a 1.05 M solution of *i*-BuMgBr, 374 mg (1.50 mmol) of Cp_2TiCl_2 and 4.88 g (15.0 mmol) tributyltin chloride were obtained after silica gel flash chromatography (50 g; 10:1 pentane/Et_2O as eluent) 2.99 g (5.11 mmol, 51 %) of a colorless oil, $[\alpha]_D^{25}$ = −9.9° (c = 1.00, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.70–1.10 (m, 3 H), 1.10–1.75 (m, 32 H), 2.28 (m, 2 H), 4.70 (m, 1 H), 5.53 (br d, J = 8.1, J_{HSn} = 68.3/71.5 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 9.7 (t), 13.7 (q), 14.1 (q), 17.5 (t), 22.7 (t), 23.6 (q), 26.8 (t), 27.4 (t), 27.8 (t), 29.1 (t), 29.4 (t), 29.5 (t), 29.7 (6 × t), 30.6 (t), 31.9 (t), 33.6 (t), 63.6 (d), 144.1 (d), 146.5 (s).

IR (neat): ν = 3600–3100, 2940, 2905, 2835, 1451, 1369, 1070, 1045 cm^{-1}.

Photooxygenation of γ-Hydroxy Vinylstannanes 2; Typical Procedure:
The stannylated alcohols **2a–c** (2.5–5.5 mmol) and 20 mg of TPP were dissolved in 70 mL of dry CH_2Cl_2, placed into a 100 mL Schlenk tube, equipped with a disposable pipette for passage of a slow stream of dried O_2 ($CaCl_2$, P_4O_{10}). The Schlenk tube was placed into a transparent Dewar vessel filled with EtOH, which was connected to a cryostat (HGW Lauda) and maintained at −15 °C. This apparatus, which was surrounded by an aluminum reflector to optimize the light intensity, was irradiated externally by two 150 W sodium lamps (Philips G/28/2/SON 150) **(2a, b)** or by two 250 W sodium lamps (Osram Vialox NAV E 250 W) **(2c)** until complete consumption of the starting material (TLC monitoring). PPh_3 (1.1 equiv) was added at 0 °C and the solution was stirred at this temperature for 30 min. After removal of the solvent (25 °C at 20 Torr), the crude product was purified by silica gel flash chromatography.

(2*S,3*R**)-4-(Tributylstannyl)-4-pentene-2,3-diol (3a):**
The photooxygenation of 2.00 g (5.33 mmol) **2a** for 1.5 h and reduction by 1.44 g (5.50 mmol) of PPh_3 gave 1.93 g (4.94 mmol, 93 %) of a colorless oil after silica gel flash chromatography (50 g; 3:1 pentane/Et_2O as eluent) as a diastereomeric mixture (2*S**,3*R**)-**3a**: (2*S**,3*S**)-**3a** = 95:5.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.13 (d, J = 6.3 Hz, 3 H), 2.38 (d, J = 3.2 Hz, 1 H), 2.43 (d, J = 3.5 Hz, 1 H), 3.59 (dqd, J = 7.0, 6.3, 3.5 Hz, 1 H), 3.91 (dd, J = 7.0, 3.2 Hz, 1 H), 5.34 (dd, J = 2.2, 1.0, J_{HSn} = 60.6 Hz, 1 H), 5.88 (dd, J = 2.3, 1.2, J_{HSn} = 128 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 10.1 (t), 13.7 (q), 18.8 (q), 27.4 (t), 29.0 (t), 70.0 (d), 84.5 (d), 127.5 (t), 155.6 (s).

IR (neat): ν = 3640–3080, 3030, 2950, 2920, 2860, 2840, 1453, 1370, 1120, 1069, 1030, 923, 665 cm^{-1}.

(2*S,3*R**,4*Z*)-4-(Tributylstannyl)-4-hexene-2,3-diol (3b):**
According to the above general procedure, from 1.00 g (2.97 mmol) **2b** were obtained after photooxygenation for 4 h, reduction by 0.700 g (2.67 mmol) of PPh_3, and silica gel flash chromatography (50 g; 3:1 pentane/Et_2O as eluent) 816 mg (2.01 mmol, 78 %) of **3b** as a colorless liquid, which consisted of a 88:7:5 mixture of (2*S**,3*R**,4*Z*), (2*S**,3*R**,4*E*), and (2*S**,3*S**,4*Z*), respectively.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.08 (d, J = 6.3 Hz, 3 H), 1.75 (d, J = 6.6 Hz, 3 H), 2.32 (br s, 1 H), 2.58 (br s, 1 H), 3.56 (dq, J = 7.8 Hz, 6.3 Hz, 1 H), 3.84 (d, J = 7.8 Hz, 1 H), 6.31 (qd, J = 6.7, 0.9, J_{HSn} = 119/124 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 11.0 (t), 13.6 (q), 18.9 (q), 19.4 (q), 27.4 (t), 29.2 (t), 70.4 (d), 85.4 (d), 138.1 (d), 145.7 (s).

IR (neat): ν = 3640–3050, 2920, 2900, 2825, 2815, 1605, 1440, 1375, 1255, 1115, 1075, 1010, 865 cm^{-1}.

(2*S*,3*R*,4*Z*)-4-(Tributylstannyl)-4-eicosene-2,3-diol (3c):
According to the above general procedure, from 2.35 g (4.01 mmol) (*S*)-**2c** were obtained after photooxygenation for 5 h, reduction by 1.15 g (4.40 mmol) of PPh_3 and silica gel flash chromatography (50 g; 5:1 to 1:1 pentane/Et_2O as eluent) 2.03 g (3.38 mmol, 84 %) of **3c** as a colorless liquid, which consisted of a 88:7:5 mixture of (2*S*,3*R*,4*Z*), (2*S*,3*R*,4*E*), and (2*S*,3*S*,4*Z*), respectively, $[\alpha]_D^{25}$ = +0.7° (c = 1.00, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.75–1.05 (m, 3 H), 1.09 (d, J = 6.2 Hz, 3 H), 1.15–1.65 (m, 26 H), 2.02 (m, 2 H), 2.25 (br s, 1 H), 2.46 (br s, 1 H), 3.56 (dq, J = 7.8, 6.2, J_{HSn} = 58.9 Hz, 1 H), 3.84 (br d, J = 7.8 Hz, 1 H), 6.21 (td, J = 6.9, 0.7, J_{HSn} = 119/125 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 11.2 (t), 13.7 (q), 14.1 (q), 18.9 (q), 22.7 (t), 27.4 (t), 29.2 (t), 29.3 (t), 29.5 (t), 29.6 (t), 29.7 (7 × t), 30.0 (t), 31.9 (t), 34.5 (t), 70.4 (d), 85.5 (d), 144.1 (s), 144.4 (d).

IR (neat): ν = 3600–3050, 2920, 2880, 2815, 1592, 1441, 1359, 1059, 1002 cm^{-1}.

Iodo Diols 4; Typical Procedure:
To a solution of 3–9 mmol of dihydroxy vinylstannane **3** in 50 mL of CH_2Cl_2 was added dropwise a solution of I_2 (1.05 equiv) in 50 mL of CH_2Cl_2 under an argon atmosphere at −78 °C. Stirring was continued for 3 h, during which time the temperature was allowed to rise to −50 °C. After the addition of 1 mL of sat. aq Na_2SO_3, the reaction mixture was allowed to warm to r.t. and the solvent was removed by rotoevaporation (20 °C at 20 Torr). The residue was purified by silica gel flash chromatography (50 g; 1:1 pentane/Et_2O as eluent).

(2*S,3*R**)-4-Iodo-4-pentene-2,3-diol (4a):**
By following the above general procedure, from 3.70 g (9.46 mmol) **3a** was obtained after flash chromatography and recrystallization **4a** (1.89 g, 8.29 mmol, 88%) as colorless leaflets, mp 52–53 °C (pentane/Et_2O); (2*S**,3*R**)-**4a**:(2*S**,3*S**)-**4a** = 97:3.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.18 (d, J = 6.4 Hz, 3H), 2.30 (br s, 1H), 2.71 (br s, 1H), 3.43 (d, J = 6.1 Hz, 1H), 3.92 (qi, J = 6.3 Hz, 1H), 6.00 (d, J = 1.7 Hz, 1H), 6.49 (d, J = 1.7 Hz, 1H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 18.7 (q), 69.8 (d), 81.7 (d), 112.8 (s), 128.1 (t).

IR (CCl_4): ν = 3600–3440, 2965, 2920, 2855, 1605, 1320, 1300, 1142, 1115, 1062, 1042, 1029, 909 cm^{-1}.

(2*S,3*R**,4*Z*)-4-Iodo-4-hexene-2,3-diol (4b):**
According to the above general procedure, from 2.45 g (6.05 mmol) of **3b** was isolated after flash chromatography and recrystallization (2*S**,3*R**,4*Z*)-**4b** (1.21 g, 5.00 mmol, 83%) as colorless leaflets, mp 70–71 °C (pentane/Et_2O), R_f = 0.07. The minor isomers eluted slightly faster (R_f = 0.11) during the silica gel chromatography and remained in the mother liquor after recrystallization.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.11 (d, J = 6.3 Hz, 3H), 1.81 (d, J = 6.5 Hz, 3H), 2.63 (d, J = 2.6 Hz, 1H), 2.85 (d, J = 5.1 Hz, 1H), 3.44 (dd, J = 7.0, 5.0 Hz, 1H), 3.92 (dqd, J = 7.0, 6.3, 2.1 Hz, 1H), 6.11 (qd, J = 6.4, 0.7 Hz, 1H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 18.6 (q, 21.5 (q), 70.5 (d), 82.3 (d), 111.4 (s), 133.9 (d).

IR (CCl_4): ν = 3600–3050, 2945, 2880, 1652, 1620, 1615, 1378, 1360, 1248, 1216, 1109, 1087, 1069, 995, 632 cm^{-1}.

(2*S*,3*R*,4*Z*)-4-Iodo-4-eicosene-2,3-diol (4c):
By following the above general procedure, from 1.91 g (3.17 mmol) **3c** was obtained after flash chromatography and recrystallization (2*S*,3*R*,4*Z*)-**4c** (2.57 mmol, 81%) as a colorless amorphous solid, mp 43–44 °C (pentane/Et_2O), $[\alpha]_D^{25}$ = +1.1° (c = 1.00, $CHCl_3$), R_f = 0.07. The minor isomers eluted faster during silica gel chromatography (R_f = 0.10) and could be removed completely.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.87 (m, 3H), 1.12 (d, J = 6.3 Hz, 3H), 1.20–1.55 (m, 26H), 2.18 (m, 2H), 2.38 (d, J = 2.6 Hz, 1H), 2.54 (d, J = 5.3 Hz, 1H), 3.41 (dd, J = 7.0, 5.3 Hz, 1H), 3.93 (qid, J = 6.4 Hz, 2.4 Hz, 1H), 6.02 (td, J = 6.8, 0.5 Hz, 1H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.1 (q), 18.5 (q), 22.7 (t), 28.0 (t), 29.2 (t), 29.3 (t), 29.4 (t), 29.5 (6 × t), 29.7 (t), 31.9 (t), 35.6 (t), 70.5 (d), 82.4 (d), 109.7 (s), 139.4 (d).

IR (CCl_4): ν = 3640–3500, 2890, 2820, 1450, 1350, 1250, 1113, 1095, 1060, 1000 cm^{-1}.

(4*S,5*S**)-4,5-Dihydro-4-hydroxy-5-methyl-3-methylene-2(3*H*)-furanone (5a):**
Under an argon atomsphere, 228 mg (1.00 mmol) of **4a**, 202 mg (2.00 mmol) of Et_3N and 30.0 mg (2.5 mol%) of $Pd(PPh_3)_4$ were dissolved in 15 mL of dry acetonitrile and the contents stirred under carbon monoxide (1 atm) at 25 °C for 24 h. Evaporation of the solvent (0 °C at 20 Torr) and silica gel flash chromatography (2 × 50 g; 1:1 CH_2Cl_2/Et_2O as eluent) of the residue yielded **5a** (115 mg, 0.900 mmol, 90%) as a colorless liquid.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.34 (d, J = 6.5 Hz, 3H), 3.85 (d, J = 5.8 Hz, 1H), 4.62 (qi, J = 6.4 Hz, 1H), 4.79 (m, 1H), 5.95 (d, J = 1.7 Hz, 1H), 6.32 (d, J = 2.0 Hz, 1H).

^{13}C NMR ($CDCl_3$, 200 MHz): δ = 14.1 (q), 69.1 (d), 79.0 (d), 126.5 (t), 138.4 (s), 169.7 (s).

IR (CCl_4): ν = 3600–3100, 3570, 2960, 2910, 1758, 1738, 1650, 1328, 1255, 1160, 1090, 1040, 942, 900 cm^{-1}.

(4*S,5*S**,*Z*)-3-Ethylidene-4,5-dihydro-4-hydroxy-5-methyl-2(3*H*)-furanone (5b):**
(2*S**,3*R**,*Z*)-**4b** (242 mg, 1.00 mmol), 959 mg (1.50 mmol) of $Ni(CO)_2(PPh_3)_2$ (Aldrich),[17] and 202 mg (2.00 mmol) of Et_3N were dissolved in 10 mL of dry THF under an argon atmosphere. The solution was heated to 65 °C until darkening occured (precipitation of nickel metal) and maintained at this temperature for 5 min. The solvent was removed at 0 °C/20 Torr and the residue was purified by flash chromatography on silica gel (2 × 50 g; 1:1 CH_2Cl_2/Et_2O as eluent) to yield 101 mg (0.710 mmol, 71%) of **5b** as a colorless liquid.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.38 (d, J = 6.4 Hz, 3H), 2.21 (dd, J = 7.3, 1.1 Hz, 3H), 2.45 (br s, 1H), 4.53 (qi, J = 6.4 Hz, 1H), 6.65 (dqi, J = 6.4, 1.2 Hz, 1H), 6.65 (qd, J = 7.3, 1.3 Hz, 1H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.0 (q), 14.3 (q), 71.1 (d), 78.2 (d), 130.1 (s), 144.5 (d), 169.2 (s).

IR (CCl_4): ν = 3630–3540, 2960, 2920, 2850, 1750, 1660, 1375, 1345, 1198, 1162, 1118, 1070, 1051, 955, 921 cm^{-1}.

(4*S*,5*S*,*Z*)-3-Hexadecylidene-4,5-dihydro-4-hydroxy-5-methyl-2-(3*H*)-furanone (Dihydromahubanolide B) (5c):[3]
According to the procedure for **5b**, from 438 mg (1.00 mol) of (2*S*,3*R*,*Z*)-**4c**, 767 mg (1.20 mmol) of $Ni(CO)_2(PPh_3)_2$, and 202 mg (2.00 mmol) of Et_3N was obtained after flash chromatography on silica gel (3 × 50 g; 1:1 pentane/Et_2O as eluent) **5c** (238 mg, 0.703 mmol, 70%) as a colorless amorphous solid, mp 59–60.5 °C, which consisted of a 90:10 mixture of (4*S*,5*S*,*Z*) (dihydromahubanolide B)[3] and (4*S*,5*S*,*E*) isomers (isodihydromahubanolide B).[3] These *E*,Z isomers could not be separated by recrystallization from hexane, $[\alpha]_D^{25}$ = −38.2° (c = 1.02, $CHCl_3$). HPLC analysis (Chiracel OD; hexane/*i*-PrOH, 97:3 as eluent) established an enantiomeric excess of 76%.

(4*S*,5*S*,*Z*)-**5c**:
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.88 (m, 3H), 1.20–1.60 (m, 26H), 1.39 (d, J = 6.4 Hz, 3H), 2.25 (d, J = 6.1 Hz, 1H), 2.72 (m, 2H), 4.54 (m, 1H), 4.64 (br t, J = 5.3 Hz, 1H), 6.56 (td, J = 7.7, 1.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.1 (2 × q), 22.7 (t), 27.9 (t), 28.8 (t), 29.3 (2 × t), 29.4 (t), 29.5 (t), 29.7 (5 × t), 29.8 (t), 31.7 (t), 71.3 (d), 78.0 (d), 129.2 (s), 149.8 (d), 168.9 (s).

IR (CCl_4): ν = 3620–3100, 3590, 2905, 2840, 1750, 1660, 1455, 1365, 1165, 1120, 1072, 1050 cm^{-1}.

(4*S*,5*S*,*E*) **5c** (only separated signals):
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.45 (d, J = 6.6 Hz, 3H), 2.39 (m, 2H), 4.81 (m, 1H), 6.93 (td, J = 7.7, 1.5 Hz, 1H).

Financial support by the Deutsche Forschungsgemeinschaft (SFB 347: "Selektive Reaktionen Metall-aktivierter Moleküle") is gratefully acknowledged and P.K. thanks the Fonds der Chemischen Industrie for a doctoral fellowship (1992–94).

(1) Martinez, J.C.V.; Yoshida, M.; Gottlieb, O.R. *Phytochemistry* **1981**, *20*, 459.
Martinez, J.C.V.; Yoshida, M.; Gottlieb, O.R. *Tetrahedron Lett.* **1979**, *20*, 1021.
Niwa, M.; Iguchi, M.; Yamamura, S. *Chem. Lett.* **1977**, 581.
Takeda, K.; Sakurawi, K.; Ishii, H. *Tetrahedron* **1972**, *28*, 3757.
(2) Slob, A. *Phytochemistry* **1973**, *12*, 811.
Tschesche, R.; Kämmerer, F.-J.; Wulff, G. *Chem. Ber.* **1969**, *102*, 2057.
(3) Wells Rollinson, S.; Amos, R.A.; Katzenellenbogen, J.A. *J. Am. Chem. Soc.* **1981**, *103*, 4114.
(4) Wollenberg, R.H. *Tetrahedron Lett.* **1980**, *21*, 3139.
Kende, A.S.; Toder, B.H. *J. Org. Chem.* **1982**, *47*, 163.
Tanaka, K.; Terauchi, M.; Kaji, A. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3935.
Barbier, P.; Benezra, C. *J. Org. Chem.* **1983**, *48*, 2705.
Wakabayashi, S.; Ogawa, H.; Ueno, N.; Kunieda, N.; Mandai, T.; Nokami, J. *Chem. Lett.* **1987**, 875.
Burke, S.D.; Pacofsky, G.J.; Piscopio, A.D. *J. Org. Chem.* **1992**, *57*, 2228.

(5) Wood, W.W.; Watson, G.M. *J. Chem. Soc., Perkin Trans 1* **1990**, 3201.
Chen, S.-Y.; Joullié, M.M. *Tetrahedron Lett.* **1983**, *24*, 5027.
Tanaka, A.; Yamashita, K. *Chem. Lett.* **1981**, 319.
Papageorgiou, C.; Benezra, C. *J. Org. Chem.* **1985**, *50*, 157.
Nair, V.; Sinhababu, A.K. *J. Org. Chem.* **1980**, *45*, 1893.
Bernardi, A.; Beretta, M.G.; Colombo, L.; Gennari, C.; Poli, G.; Scolastico, C. *J. Org. Chem.* **1985**, *50*, 4442.
(6) Frimer, A.A.; Stephenson, L.M. In *Singlet Oxygen*; Frimer, A.A., Ed.; CRC Press: Boca Raton, 1985; Vol II, p 67.
(7) Ensley, H.E. In *Advances in Oxygenated Processes*: Baumstark, A.L., Ed.; JAI Press: Greenwich, 1990: Vol. 2, p 181.
Adam, W.; Griesbeck, A. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1070.
Orfanopoulos, M.; Foote, C.S. *Tetrahedron Lett.* **1985**, *26*, 5991.
Ensley, H.E.; Carr, R.V.C.; Martin, R.S.; Pierce, T.E. *J. Am. Chem. Soc.* **1980**, *102*, 2836.
Akasaka, T.; Misawa, Y.; Goto, M.; Ando, W. *Tetrahedron* **1989**, *45*, 6657.
(8) Fristad, W.E.; Bailey, T.R.; Paquette, L.A.; Gleiter, R.; Böhm, M.C. *J. Am. Chem. Soc.* **1979**, *101*, 4420.
Fristad, W.E.; Bailey, T.R.; Paquette, L.A. *J. Org. Chem.* **1980**, *45*, 3028.
Adam, W.; Richter, M. *Tetrahedron Lett.* **1992**, *33*, 3461.
(9) Adam, W.; Klug, P. *J. Org. Chem.* **1993**, *58*, 3416.
(10) Adam, W.; Nestler, B. *J. Am. Chem. Soc.* **1992**, *114*, 6549.
Adam, W.; Nestler, B. *J. Am. Chem. Soc.* **1993**, *115*, 5041.
(11) Adam, W.; Brünker, H.-G. *J. Am. Chem. Soc.* **1993**, *115*, 3008.
(12) D'Engenieres, M.D.; Miocque, M.; Gautier, J.-A. *Bull. Chim. Soc. Fr.* **1964**, 2477.
(13) Bowden, K.; Heilbron, I.M.; Jones, E.R.H.; Weedon, B.C.L. *J. Chem. Soc.* **1946**, 39.
(14) Midland, M.M.; Mc Dowell, D.C.; Hatch, R.L.; Tramontano, A. *J. Am. Chem. Soc.* **1980**, *102*, 867.
(15) Lautens, M.; Huboux, A.H. *Tetrahedron Lett.* **1990**, *31*, 3105.
(16) Martin, L.D.; Stille, J.K. *J. Org. Chem.* **1982**, *47*, 3630.
Cowell, A.; Stille, J.K. *J. Am. Chem. Soc.* **1980**, *102*, 4193.
(17) Trost, B.M.; Coppola, B.P. *J. Am. Chem. Soc.* **1982**, *104*, 6879.
(18) Brown, H.C.; Pai, G.G. *J. Org. Chem.* **1982**, *47*, 1606.
Vigneron, J.-P.; Bloy, V. *Tetrahedron Lett.* **1979**, *20*, 2683.
Giacomelli, G.; Lardicci, L.; Palla, F. *J. Org. Chem.* **1984**, *49*, 310.
Johnson, W.S.; Elliot, R.; Elliot, J.D. *J. Am. Chem. Soc.* **1983**, *105*, 2904.
(19) Dehmlow, E.V.; Lissel, M. *Liebigs Ann. Chem.* **1980**, 1.