Synthetic Studies of Laurencin and Related Compounds. V.[1] Transformation of *cis*-2-Ethyl-8-formyl-3,4,7,8-dihydro-2*H*-oxocin-3-one 3-Ethylene Acetal into (±)-Laurencin

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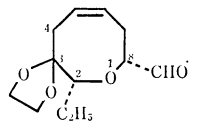
Transformation of the title starting material into (±)-laurencin, which implies synthesis of the natural product, is described. The structure and configuration of synthetic intermediates are defined on the basis of the spectral evidence.

In the preceding paper[1] we reported the synthesis of *cis*-2-ethyl-8-formyl-7,8-dihydro-2*H*-oxocin-3(4*H*)-one 3-ethylene acetal (**1**). The present paper describes transformation of the aldehyde (**1**) into (±)-laurencin (±-**2**),[2a] which constitutes the first synthesis[2b] of a representative member of a group of naturally occurring halogeno compounds with (a) medium-sized cyclic ether skeleton(s) as well as an enyne moiety.[3]



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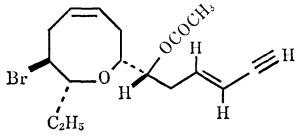

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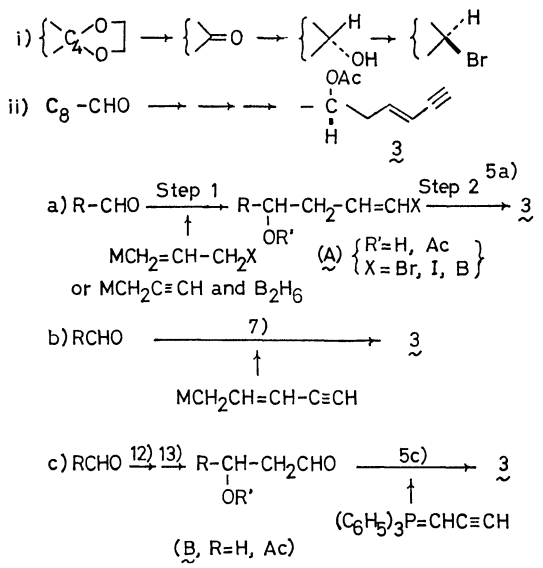
The transformation requires (i) conversion of the C_3-carbonyl group protected as the ethylene acetal in **1** into a bromine atom with the desired configuration (*trans* to the C_2-ethyl group), and (ii) that of the C_8-formyl into a 1-acetoxy-3-hexen-5-ynyl group (**3**). The former transformation (i) would probably proceed smoothly, apart from the yield, as had been illustrated in the synthesis of *t*-3-bromo-*r*-2,*c*-8-diethyl-3,4,7,8-tetrahydro-2*H*-oxocin[4] (**3**). On the other hand, many preparative methods for enyne units (–CH=CH–C≡CH) have recently been reported,[5] because the groups are characteristic of a number of natural products. A survey of literatures reveals that procedures applicable to the latter transformation (ii) are classified into three categories as shown in Scheme 1. The first route (iia) consists of at least two steps and involves groups of –CH(OR)CH_2CH=CHX (R=H or Ac, and X= Br, I, Cu, B, and so on) as the intermediates (**A**), which would be converted smoothly into the aimed group by various elegant methods[5a] (step 2). However, preparation of the intermediates (**A**), *e.g.*, by reaction of 3-halogeno-2-propenyl anions with the formyl group of **1** or by addition of 2-propynyl anion to the group followed by hydroboration, appeared to be considerably difficult owing to the possibility of allylic rearrangement or facile hydroboration to the *cis*-double bond in **1**.[6] This conceivable trouble led us to undertake syntheses by other routes.

The second route (iib) concerns the Grignard-type reaction of the formyl group with pentenynyl anions, obtained from 2-penten-4-ynyl halides and metals (Mg, Zn, and so on).[7] However, the reaction was reported to proceed with allylic rearrangement to give 2-ethynyl-1-hydroxy-3-butenyl groups, none of the products formed by expected addition of 2-penten-4-ynyl groups



Scheme 1. Possible routes from the aldehyde (**1**) into (±)-laurencin (±**2**).

being detected.[7] Nevertheless, in view of the fact that only a small amount of the starting aldehyde (**1**) is available, the route was very attractive in the sense of one-step synthesis of the aimed group, and the following model experiments were carried out. 2-Penten-4-yn-1-ol[8] (**4**) was converted into the pentenynyl phenyl sulfide (**5**) by reaction of the corresponding bromide[8] with sodium benzenethiolate, or into the 5-trimethylsilypentenynyl phenyl sulfide (**5a**) by bromination of 5-trimethylsilyl-2-penten-4-yn-1-ol[9] (**4a**) followed by reaction with sodium thiophenolate. Treatment of butanal with trimethylsilypentenynyl anions, prepared by reaction of **5a** with butyllithium (1 mol equiv) in tetrahydrofuran (THF) at −30 °C in the presence of 1,4-diazabicyclo[2.2.2]octane (Dabco),[10] at −50 °C for 1 h and subsequent removal of the trimethylsilyl group of the resultant addition products led to formation of a 1:5 (estimated by NMR) mixture of the expected alcohol, 5-phenylthio-6-nonen-8-yn-4-ol (**6**), and its rearranged isomer (**7**) in 26% yield from **5a**. On the other hand, the same treatment of butanal with pentenynyl anions, prepared from **5** and butyllithium (2 mol equiv) under almost the same conditions, produced a 1:1 mixture of **6** and **7** in 49% yield, from which *trans*-isomer (***t*-6**) and *cis*-isomer (***c*-7**) were isolated as the main products of the respec-

tive diastereoisomers. Compound ***t*-6** exhibited the following spectra as expected: UV, λ_{max} 217 nm (ε 16000); NMR, δ 2.96 (1H, d, 2 Hz, C≡C<u>H</u>), 5.32 and 6.10 (each 1H, do d, J=16 and 2 Hz, *trans*-C<u>H</u>=C<u>H</u>). The improved yield of **6** would be caused by *dianionic* character formed from the reactant (**5**). However, attempted selective reduction of the phenylthio group, *e.g.*, the Birch reduction, catalytic hydrogenation over Raney nickel, chemical treatment with aluminium amalgam or zinc and acetic acid, and so on, all failed; the reactions resulted in reduction of the triple bond or recovery of the starting material.

R^1CH_2-CH=CH-C≡CR^2

4 R^1=OH, R^2=H

4a R^1=OH, R^2=$Si(CH_3)_3$

5 R^1=SC_6H_5, R^2=H

5a R^1=SC_6H_5, R^2=$Si(CH_3)_3$

C_3H_7-CH(OH)-CH(SC_6H_5)-CH=CH-C≡CH

6

C_3H_7-CH(OH)-CH(C≡CH)-CH=CH-SC_6H_5

7

The desired transformation was achieved by the final route (iic), a stepwise synthesis by a modification of the Corey procedure.[5c] Before proceeding with the title aldehyde (**1**), several preliminary model experiments were carried out. The route (iic) in Scheme 1 involves β-acetoxy aldehydes as the key intermediates (**B**). Reaction of 3-acetoxy-3-phenylpropanal[11] (**8**), one of the β-acetoxy aldehydes, with triphenyl(3-trimethylsilyl-2-propynylidene)phosphorane at −78 °C in THF proceeded smoothly *without elimination of acetic acid* to give a trimethylsilyl enyne compound (**9a**) in 58% yield, which on treatment with sodium hydroxide followed by acetylation afforded acetoxy *trans*-hexenyne (**9**) in 77% yield. The NMR spectrum was consistent with the structure: δ 2.80 (1H, d, J=2 Hz, C≡C<u>H</u>), 5.50 and 6.10 (each 1H, do d and do t, J=16, 2 and 16, 7, 7 Hz, *trans*-C<u>H</u>=C<u>H</u>). The route (iic) also requires extension of a formyl group to 1-acetoxy-3-oxopropyl group(s), β-acetoxy aldehyde(s) (**B**). Treatment of 3,4-dihydro-2*H*-pyran-2-carbaldehyde ("acrylaldehyde dimer") (**10**), which possesses an ether oxygen atom at β-position to the formyl group and hence is suitable for a model compound of the title aldehyde (**1**), with dimethylsulfinylmethanide in dimethyl sulfoxide (DMSO) or with dimethylsulfonium methanide in DMSO and THF,[12] produced a mixture of diastereoisomeric 2-(epoxyethyl)-dihydropyrans (**11**) in 34 or 17% yield, respectively. The low yields would result from instability of the "acrylaldehyde dimer." Hydrogenation of **11** over platinum gave 2-(epoxyethyl)tetrahydropyrans (**12**), which on further treatment with 2-lithio-1,3-dithiane in THF at −50——20 °C[11,13] followed by acetylation afforded β-acetoxy aldehyde trimethylene dithioacetals (**13**) in 62% yield from **11**. The 1,3-dithiane (**13**) was smoothly hydrolyzed with mercury(II) oxide and boron trifluoride etherate to give β-acetoxy aldehydes (**14**) in 83% yield, which in turn was converted by the same treatment as described above into the corresponding acetoxy hexenynes (**15**) in 48% yield. The NMR spectrum indicated the *trans*-configuration of the double bond in question: δ 5.52 and 6.20 (each 1H, do d and do t, J=16, 2, and 16, 7, 7 Hz). The successful result of these model experiments led us to apply these methods for construction of the relevant side chain of laurencin (**2**).

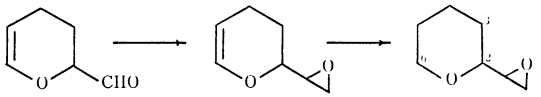
C_6H_5-CH(OAc)CH_2-CHO

8

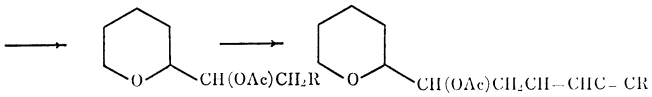
C_6H_5-CH(OAc)CH_2CH=CHC≡CR

9 R=H

9a R=$Si(CH_3)_3$



10 **11** **12**



13 R= 

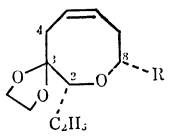
14 R=CHO

15 R=H

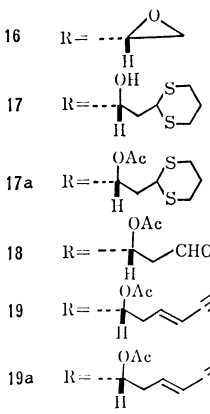
15a R=$Si(CH_3)_3$

Treatment of the title tetrahydrooxocincarbaldehyde (**1**) with dimethylsulfinylmethanide in DMSO at room temperature[12] afforded epoxyethyl hydrooxocin (**16**), mp 87—88 °C, showing a single spot by GLC and TLC, in 66% yield, as a sole isolable epoxide. In the NMR spectrum the epoxy protons appeared with the C_8-proton as two multiplets at δ 2.72 and 3.25. The epoxide (**16**), when treated with 2-lithio-1,3-dithiane in THF at −70——20 °C,[13] was converted into 2-(2-hydroxyalkyl)-1,3-dithiane (**17**), which was isolated as its acetate (**17a**), mp 161—162 °C, in 80% yield. Fortunately, the acetoxymethine proton was observed at δ 5.24 with almost the same splitting pattern (do t, J=9, 4, and 4 Hz) as that (δ 4.98, do t, J=8, 5, and 5 Hz) of laurencin[2a] (**2**), indicating that the relevant acetoxymethine carbon atom possesses the same relative configuration as the corresponding carbon in the natural product (**2**). Treatment of the dithiane (**17a**) with mercury(II) oxide and boron trifluoride etherate in 15% aqueous THF at room temperature[11] effected only hydrolysis of the 1,3-dithiano-2-yl group to yield β-acetoxy aldehyde (**18**), which was immediately submitted to the Wittig reaction with triphenyl(3-trimethylsilyl-2-propynylidene)phosphorane, prepared from triphenyl(3-trimethylsiliyl-2-propynyl)-phosphonium bromide and butyllithium (1 mol equiv) in THF.[5c] The reaction took place without elimination of acetic acid as expected to give acetoxy *trans*-trimethylsilylhexenyne (**19a**), which was converted readily into acetoxy *trans*-hexenyne (**19**), oil, in 94% yield, by treatment with ammonium fluoride in *N*,*N*-dimethylformamide (DMF) at room temperature.[5c,14] In good accord with the assigned structure and configuration, compound **19** exhibited parent and fragmentation peaks at *m*/*e* 334 and 274 in the mass spect-

rum and also absorption maxima at 223 and 230 nm (ε 13000 and 10500) and at 3300, 2110, 1740, 1645, 1247, 1160, 1105, 1027, and 960 cm^{-1} in the UV and IR spectra, respectively. The NMR spectrum confirmed the structure: δ 0.98 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.03 (3H, s, $OCOC\underline{H}_3$), 2.80 (1H, d, J=2 Hz, $C{\equiv}C\underline{H}$), 2.50 and 3.50 (6H and 2H, each m, $3C\underline{H}_2CH{=}CH$, and 2H at C_2 and C_8), 3.93 (4H, m, $OC\underline{H}_2C\underline{H}_2O$), 5.01 [1H, do t, J=9, 4, and 4 Hz, $C\underline{H}(OAc)$], 5.50 and 6.14 (each 1H, do d and do t, J=15, 2, and 15, 8, 8 Hz, *trans*-$C\underline{H}{=}C\underline{H}$), and 5.78 (2H, m, *cis*-$C\underline{H}{=}C\underline{H}$). A series of the reactions from the aldehyde (**1**) to the acetoxy hexenyne (**19**) *via* the epoxide (**16**) implies synthesis of the C_8-side chain (**3**) of laurencin (**2**).



1 R=CHO



16 R=

17 R=

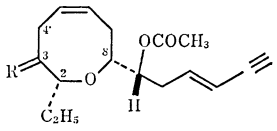
17a R=

18 R=

19 R=

19a R=

The final stage of laurencin synthesis consists in introduction of a bromine atom at C_3 with the *trans*-configuration to the ethyl group at C_2. Deacetalization of the tetrahydrooxocinone ethylene acetal (**19**) with *p*-toluenesulfonic acid in aqueous acetone under reflux proceeded smoothly to give ketone (**20**), oil, in 74% yield, which displayed a new absorption maximum at 1720 cm^{-1} and also a one-proton double doublet (J=11 and 8 Hz) at δ 3.86 due to one of the two C_4-protons.[1,4] Reduction of the ketone (**20**) with sodium borohydride in methanol at 0 °C[1,4] produced a mixture of alcohols, from which a major alcohol (**21**), oil, with three *cis*-oriented substituents at C_2, C_3, and C_8 of the hydrooxocin ring, and a minor alcohol (**22**), oil, a C_3-epimer of **21**, could be isolated in 50 and 30% yields, respectively. The configurations of the hydroxyl groups at C_4 in the respective compounds (**21** and **22**) were deduced by analogy of the NMR data with those of the corresponding diethyltetrahydrooxocins[4] and related compounds;[1] namely, the hydroxymethine proton in question of the former (**21**) appeared as a broad signal with half-width of 20 Hz at δ 3.64, while the corresponding proton of the latter (**22**) was observed as a clear double triplet with J= 9, 3, and 3 Hz at δ 3.72.[1,4] Contrary to the expectation that the bromination would take place easily, the major alcohol (**21**), when treated with triphenylphosphine and tetrabromomethane in dichloromethane at room temperature,[4,15] gave a complex mixture. However, an aimed bromo compound, mp 45—47 °C, could be isolated after careful chromatography in 14% yield along with the starting material (**21**, 20%). The bromo compound exhibited the following spectra: MS, *m/e* 356, 354 (M^+), 296, and 294; IR, ν_{max} 3285, 2100, 1735, 1230, 1168, 1080, 1035, and 950 cm^{-1}; NMR, δ 0.98 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.03 (3H, s, $OCOC\underline{H}_3$), 2.83 (1H, d, J=2 Hz, $C{\equiv}C\underline{H}$), 4.07 (1H, do t, J=9, 3, and 3 Hz, $C\underline{H}Br$), 4.98 [1H, do t, J=8, 5, and 5 Hz, $C\underline{H}(OAc)$], 5.52 and 6.15 (each 1H, do d and do t, J=15, 2, and 15, 7, 7 Hz, *trans*-$C\underline{H}{=}C\underline{H}$), and 5.90 (2H, m, *cis*-$C\underline{H}{=}C\underline{H}$). These spectra were completely identical with those of natural laurencin (**2**), indicating completion of the synthesis of (±)-laurencin. The overall yield amounted to 1.1% from the tetrahydrooxocincarbaldehyde.



19 R=OCH_2CH_2O
20 R=O
21 R=···OH, —H
22 R=—OH, ···H
±2 R=—Br, ···H

Experimental

All the mps and bps were uncorrected. The homogeneity of each compound was always checked by TLC over silica gel (Wakogel B-5) and/or GLC (Hitachi K-53) over 10% SE-30. Column chromatography was carried out over silicic acid (Merck, Kieselgel 60, 70—230 mesh) and/or alumina (Merck, Standard, Active I and II—III). The UV, IR, and NMR (100 MHz) spectra were measured in ethanol, in liquid state, and in chloroform-*d*, respectively, unless otherwise stated. The abbreviations "s, d, t, sex, m, br, do, and sh," in the NMR and IR spectra denote "singlet, doublet, triplet, sextet, multiplet, broad, double, and shoulder," respectively.

*2-Penten-4-ynyl Phenyl Sulfides (**5**) and Their Trimethylsilyl Derivatives (**5a**).* *a)*: Into a suspension of sodium thiophenolate in THF, prepared from sodium hydride (96 mg) and benzenethiol (424 mg) in THF (5 ml), was added a 1:1 mixture of *cis*- and *trans*-2-penten-4-ynyl bromides[8] (290 mg) in THF (1 ml) at 0 °C under stirring. The mixture was stirred at room temperature for 2 h, then mixed with water (10 ml) and extracted with ether (3×10 ml). The ether solution was washed with water, 5% aq potassium hydroxide and water, dried over sodium sulfate (or magnesium sulfate) and evaporated to leave yellow oil (466 mg). The oil was purified by chromatography over silica gel (20 g) with benzene and hexane (1:4) to give *cis*- and *trans*-pentenynyl phenyl sulfides (**c-5**, 62 mg, and **t-5**, 86 mg) with the mixture (82 mg), bp 85—90 °C/2 Torr: **c-5**, MS, *m/e* 174 (M^+), 109, 77, and 65; IR, ν_{max} 3280, 2090, 1687, and 775 cm^{-1}: NMR, δ 3.13 (1H, d, J=2 Hz, $C{\equiv}C\underline{H}$), 3.79 (2H, d, J=8 Hz, $C\underline{H}_2$), 5.50 and 6.00 (each 1H, do d and do t, J=10, 2, and 10, 8, 8 Hz, *cis*-$C\underline{H}{=}C\underline{H}$), and 7.30 (5H, m, $C_6\underline{H}_5$): **t-5**, MS, *m/e* 174, 109, 77, and 65;

IR, ν_{max} 3286, 2096, 1687, and 954 cm^{-1}; NMR, δ 2.84 (1H, d, J=2 Hz), 3.55 (2H, d, J=7 Hz), 5.48 and 6.22 (each 1H, do d and do t, J=15, 2 and 15, 7, 7 Hz), and 7.30 (5H, m).

b): Into an ice-cooled solution of 5-trimethylsilyl-2-penten-4-yn-1-ol alcohol[9] (**4a**) in ether (3 ml) containing pyridine (0.2 ml) was added dropwise phosphorus tribromide (1.9 g) in ether (3 ml) during a period of 15 min. The mixture was stirred at room temperature for 75 min and then mixed with ether (50 ml). The whole solution was washed with water, 5% aq sodium hydrogen carbonate and saturated brine, dried over magnesium sulfate, evaporated and then distilled to yield the corresponding bromides (2.0 g, *cis*:*trans*=1 : 2), which were used for the next reaction without further purification.

Into a suspension of sodium benzenethiolate, prepared from sodium hydride (72 mg) and thiophenol (330 mg) in THF (7 ml), was added the bromide mixture (300 mg) in THF (1 ml). The mixture was stirred at room temperature for 2 h and then worked up as described in (a) to leave oil (396 mg), which was purified by chromatography over silica gel (20 g, hexane) to give *cis*- and *trans*-isomers (***c*-5a**, 77 mg and ***t*-5a**, 177 mg) with the mixture (28 mg), bp 98—100 °C/2 Torr: ***c*-5a**, MS, *m/e* 246 (M^+), 173, 137, 109, 73, and 59; IR, ν_{max} 2146, 1690, 1250, and 760 cm^{-1}; NMR, δ 0.22 [9H, s, $Si(CH_3)_3$], 3.80 (2H, d, J=8 Hz, CH_2), 5.52 and 5.94 (each 1H, do d and do t, J=10, 2 and 10, 8, 8 Hz, *cis*-CH=CH), and 7.20 (5H, m, C_6H_5): ***t*-5a**, MS, *m/e* 246, 173, 137, 109, 73, and 59; IR, ν_{max} 2136, 1685, 1240, and 953 cm^{-1}; NMR, δ 0.18 (9H, s), 3.55 (2H, d, J=7 Hz), 5.54 and 6.18 (each 1H, J=16, 2, and 16, 7, 7 Hz), and 7.26 (5H, m).

*5-Phenylthio-6-nonen-8-yn-4-ols (**6**) and 1-Phenylthio-3-ethynyl-1-hepten-4-ols (**7**).* *a)* Into a solution of 1:1 mixture of ***c*-5** and ***t*-5** (870 mg, 5 mmol) in THF (50 ml) containg Dabco (560 mg, 5 mmol) was added butyllithium (12 mmol) in a 15% hexane solution (6.7 ml) at −30 °C under stirring. The mixture was further stirred for 1 h at −30—−20 °C, and cooled to −50 °C. Butanal (0.45 ml, excess) was added to the cooled solution and stirred at −50—−30 °C for 30 min and then at −30—−20 °C for 30 min. The reaction mixture was poured into water (200 ml) and extracted with ether (3×100 ml). The ether solution was washed with water and saturated brine, dried and evaporated to leave oil (1.2 g), which was purified by chromatography over silica gel (40 g, benzene) to give a 1:1 mixture (452 mg) of **6** and **7** with the starting material (**5**, 220 mg). A part (60 mg) of the mixture was further separated by preparative TLC (Wakogel B-5F, benzene) to yield a *trans*-isomer (***t*-6**, 25 mg) and a *cis*-isomer (***c*-7**, 5 mg) in pure state: ***t*-6**, MS, *m/e* 246 (M^+); UV, λ_{max} 217 nm (ε 16000); IR, ν_{max} 3400, 3280, 2090, 1600, and 958 cm^{-1}; NMR, δ 0.92 (3H, br s, CH_3), 1.52 (4H, m, CH_2CH_2), 2.54 (1H, s, OH), 2.86 (1H, d, J=2 Hz, C≡CH), 3.6 (2H, br m, CH(OH) and $CH(SC_6H_5)$], 5.32 and 6.10 (each 1H, do d, J=16, 2, and 16, 10 Hz, *trans*-CH=CH), and 7.30 (5H, m, SC_6H_5): ***c*-7**, MS, *m/e*, 246; UV, λ_{max} 266 nm (ε 10000); IR, ν_{max} 3420, 3096, 2114, and 1678 cm^{-1}; NMR, δ 0.94 (3H, br s), 2.56 (4H, m), 2.20 (1H, J=2 Hz), 3.66 (2H, br m), 5.80 and 6.30 (each 1H, do d and d, J=10, 10, and 10 Hz, *cis*-CH=CH), and 7.35 (5H, m).

b): Into a solution of a 1:2 mixture of ***c*-5a** and ***t*-5a** (492 mg, 2 mmol) in THF (20 ml) containing Dabco (224 mg, 2 mmol) was added butyllithium (2.4 mmol) in 15% hexane (1.36 ml) at −30 °C. The solution was stirred for 1 h at −30—−20 °C and cooled to −50 °C. Butanal (0.45 ml, excess) in THF (0.5 ml) was added to the cooled solution and stirred as described in (a). The reaction mixture was worked up as usual to leave oil (827 mg), which was purified by chromatography over silica gel (30 mg, benzene) to give acetylene compounds (307 mg). A part (80 mg) of the mixture in methanol (2.5 ml) was treated with 5 M aq sodium hydroxide (0.13 ml) at room temperature (25 °C) for 5 min. The reaction mixture was neutralized by addition of 2 M hydrochloric acid, evaporated and extracted with ether (2×50 ml). The ether solution was worked up as usual to leave oil (51 mg), which was separated by preparative TLC over silica gel with benzene and ethyl acetate (9 : 1) to yield a 1 : 5 mixture (by NMR) of **6** and **7** (30 mg) and **5** (10 mg). The mixture was not further purified.

*trans-1-Pheny-3-hexen-5-yn-1-yl Acetate (**9**) and Its 6-Trimethylsilyl Derivative (**9a**).* Into a suspension of triphenyl(3-trimethylsilyl-2-propynyl)phosphonium bromide[5c] (305 mg, 0.67 mmol) in THF (5 ml) cooled at −78 °C was added butyllithium (0.78 mmol) in 15% hexane (0.5 ml) under stirring. The mixture was stirred at −45—−40 °C for 30 min and cooled to −78 °C. 3-Oxo-1-phenylpropyl acetate[11] (**8**, 87 mg, 0.45 mmol) in THF (0.8 ml) was added to the cooled mixture and stirred at ice-bath temperature for 1 h. On addition of hexane (20 ml) the reaction mixture formed precipitates, which were removed by filtration. The procedure was repeated three times to give brown oil (150 mg), which was separated by chromatography (1.5 g, benzene) to yield **9a** (78 mg), oil; MS, *m/e* 280 (M^+) and 226; IR, ν_{max} 2150, 1748, 1245, 1233, 1085, 1025, and 955 cm^{-1}; NMR, δ 0.16 [9H, s, $Si(CH_3)_3$], 2.04 (3H, s, $OCOCH_3$), 2.62 (2H, br t, J=7 Hz, CH_2), 5.52 and 6.02 (each 1H, br d and do t, J=7 and 16, 7, 7 Hz, *trans*-CH=CH), 5.74 (1H, t, J=7 Hz, CH(OAc)], and 7.26 (5H, s, C_6H_5). The sample was rechromatographed for analysis. Found: C, 71.11; H, 7.71%. Calcd for $C_{17}H_{22}O_2Si$: C, 71.28; H, 7.74%.

Compound **9a** (43 mg) in methanol (1.5 ml) was stirred with 5 M sodium hydroxide (0.75 ml) at room temperature for 10 min. The mixture was acidified with 2 M hydrochloric acid, extracted with hexane repeatedly. The hexane solution was worked up as usual to give crude alcohol (25 mg). The alcohol (22 mg) was treated with acetic anhydride (0.2 ml) and pyridine 0.5 ml to give crude acetate, which was purified by preparative TLC (benzene) to yield **9** (22 mg), oil, in pure state: MS, *m/e* 154 (M^+−CH_3COOH); IR, ν_{max} 3300, 2100, 1748, 1230, and 958 cm^{-1}; NMR, δ 2.08 (3H, s, $OCOCH_3$), 2.66 (2H, t, J=7 Hz, CH_2), 2.80 (1H, d, J=1.5 Hz, C≡CH), 5.50 and 6.10 (each 1H, br d and do t, J=16 and 16, 7, 7 Hz, *trans*-CH=CH), 5.77 [1H, t, J=7 Hz, CH(OAc)], and 7.28 (5H, s, C_6H_5). Found: C, 78.47; H, 6.50%. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.58%.

*2-(Epoxyethyl)-3,4-dihydropyranes (**11**).* *a)*: A suspension of sodium hydride (0.06 mol) (50% mineral oil dispersion, 2.9 g) and trimethyloxosulfonium iodide (13.2 g, 0.06 mol) in dry DMSO (60 ml) was stirred at room temperature under sitrring for 10 min, when evolution of hydrogen stopped. A solution of 3,4-dihydro-2*H*-pyran-2-carbaldehyde (**10**, 5.6 g, 0.05 mol) in DMSO (5 ml) was added to the aforementioned dimethylsufinylmethanide solution during a period of 5 min and then stirred at room temperature for 1.5 h. The reaction mixture was mixed with water (130 ml) and extracted with ether (4×100 ml). The ether solution was washed with water and saturated brine, dried, evaporated and distilled to give **11** (2.16 g), bp 68—70 °C/15 Torr; MS, *m/e* 126 (M^+), 83, and 43; IR, ν_{max} 1646, 1237, and 1070 cm^{-1}; NMR, δ 2.00 (4H, br, m, 4H at C_3

and C_4), 2.80 and 3.25 (2H and 1H, each m, 3H in epoxyethyl), 3.65 (1H, m, H at C_2), 4.70 and 6.35 (each 1H, m, CH=CH). Found: C, 66.15; H, 7.99%. Calcd for $C_6H_8O_2$: C, 66.65; H, 7.99%.

b): Into a solution of sodium methylsulfinylmethanide, prepared by treatment of DMSO (60 ml) with sodium hydride (0.06 mol) (50% mineral oil dispersion, 2.9 g) at 80 °C for 1 h, was added THF (60 ml) and then a solution of trimethylsulfonium iodide (12.4 g, 0.06 mol) in DMSO at 0 °C during a period of 5 min under stirring. To the resultant dimethylsulfonium methanide solution was added **10** (5.6 g, 0.05 mol) in DMSO (5 ml), and the whole solution was stirred at room temperature for 1 h. The reaction mixture was poured into water and extracted with ether (4×200 ml). The ether solution was worked up as usual to give **11** (1.04 g), bp 64—68 °C/15 Torr. The NMR spectrum showed complex signals similar to those of **11** obtained in (a), indicating both the samples (**11**) to be a mixture of diastereoisomers. In the following experiments were used the sample (**11**) obtained in the section (a).

*2-(Epoxyethyl)-3,4,5,6-tetrahydropyrans (**12**).* Compounds **11** (2.1 g) were hydrogenated over platinum (60 mg as $PtO_2 \cdot H_2O$) for 14.5 h, when 430 ml (1.02 mol equiv) of hydrogen had been consumed. After removal of the catalyst, the solution was evaporated and distilled to give oil (**12**, 1.7 g), bp 70—74 °C, showing a single spot on TLC; MS, *m/e* 128 (M^+) and 85; IR, ν_{max} 1255, 1110, 1094, and 1050 cm^{-1}; NMR, δ 1.60 (6H, br m, 6H at C_3, C_4 and C_5), 2.80 and 2.95 (2H and 1H, each m, 3H at C_2 and C_6). Found: C, 65.22; H, 9.64%. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44%.

*3-Oxo-1-(2-tetrahydropyranyl)propyl Acetate (**14**) and Its 1,3-Trimethylene Dithioacetal (**13**).* *a)*: To a solution of 2-lithio-1,3-dithiane in THF, prepared from 1,3-dithiane (1.41 g, 11.7 mmol) and butyllithium (14 mmol) in THF (45 ml) at −30——20 °C for 2 h, was added **12** (1.5 g, 11.7 mmol) in THF (2 ml) under cooling at −60 °C. The mixture was stirred at −50——30 °C for 1 h, at −30——20 °C for 1 h, and then at −20 °C for 16 h, and mixed with ether (150 ml). The ether solution was worked up as usual to leave amorphous residue (3.1 g), which was purified by chromatography over silica gel (90 g, benzene) to yield white solid (2.2 g). A part (54 mg) was further purified by preparative TLC to give solid substance (43 mg), showing a single spot on TLC. The solid (43 mg) was converted under usual conditions into the acetate (**13**), oil; MS, *m/e* 290 (M^+), 230, 119, and 85; IR, ν_{max} 1742, 1240, and 1090 cm^{-1}; NMR, δ 1.50 (6H, m, 6H at C_3, C_4, and C_5), 2.20 (2H, m, $SCH_2CH_2CH_2S$), 2.11 (3H, s, $OCOCH_3$), 2.85 (4H, m, $SCH_2CH_2CH_2S$), 3.42 and 4.00 (each 2H, m, 3H at C_2 and C_6, and SCHS), and 5.18 [1H, m, CH(OAc)].

Into a suspension of mercury(II) oxide (0.6 g) and boron trifluoride etherate (0.35 ml) in 15% aq THF (4 ml) was added **13** (0.20 g, 6.9 mmol) in THF (0.2 ml) under stirring during a period of 15 min. The mixture was stirred at room temperature for 1 h. On addition of ether (10 ml) to the mixture, precipitates were separated and removed by filtration. The filtrate was washed with 10% aq sodium carbonate and saturated brine, dried and evaporated to give oil [crude **14** (0.115 g)], which was used for the next reaction without further purification: IR, ν_{max} 2760, 1746, 1240, 1095, and 1045 cm^{-1}; NMR, δ 2.08 (3H, s, $OCOCH_3$), 2.76 (2H, m, CH_2CHO), 5.30 [1H, do t, J=3, 6 and 6 Hz, CH(OAc)], 9.66 (1H, t, J=1.5 Hz, CHO).

*1-(2-Tetrahydropyranyl)-3-hexen-5-ynyl Acetate (**15**) and Its Trimethylsilyl Derivative (**15a**).* *a)*: Into a suspension of triphenyl(3-trimethylsilyl-2-propynyl)phoshonium bromide (0.34 g, 0.75 mmol) in THF (5 ml) cooled at −70 °C was added butyllithium (0.78 mmol) (15% hexane solution, 0.5 ml) under stirring. The mixture was stirred at −40——30 °C for 30 min and again cooled to −70 °C. Aldehyde **14** (0.11 g, 0.55 mmol) in THF (0.5 ml) was added to the cooled mixture, stirred at the temperature for 5 min and then at ice-bath temperature for 1 h. On addition of hexane (20 ml), precipitates were formed and removed by filtration. The procedure was repeated three times to yield oil (0.145 g), which was purified by chromatography over silica gel (4.5 g, benzene) to give **15a** (0.124 g), colorless oil; MS, *m/e* 294 (M^+), 234, and 85; IR, ν_{max} 2170, 1748, 1248, 1235, 1090, 1050, 1040, and 960 cm^{-1}; NMR, δ 0.16 [9H, s, $Si(CH_3)_3$], 2.04 (3H, s, $OCOCH_3$), 2.44 (2H, t, J=7 Hz, CH_2CH=CH), 4.80 [1H, m, CH(OAc)], 5.52 and 6.10 (each 1H, br d and do t, J=16 and 16, 7, 7 Hz, *trans*-CH=CH). Found: C, 64.92; H, 8.82%; Calcd for $C_{16}H_{28}O_3S$: C, 65.26; H, 8.90%.

b): A solution of **15a** (60 mg, 0.2 mmol) in methanol (2 ml) was stirred with 5 M aq sodium hydroxide (1 ml) at room temperature for 5 min. The solution was made acidic by addition of 2 M hydrochloric acid and extracted with hexane (4×2 ml). The hexane solution was worked up as usual to give alcohol (35 mg), oil. The oil was acetylated under usual conditions and purified by preparative TLC over silica gel to give **15** (39 mg), oil; MS, *m/e* 222 (M^+) and 162; IR, ν_{max} 3300, 2100, 1748, 1240, 1100, 1050, and 960 cm^{-1}; NMR, δ 1.52 (6H, m, $CH_2CH_2CH_2$), 2.03 (3H, s, $OCOCH_3$), 2.48 (2H, t, J=7 Hz, CH_2CH=CH), 2.82 (1H, d, J=2 Hz, C≡CH), 3.35 and 4.00 (2H and 1H, each m, CH_2OCH), 4.86 [1H, do t, J=12, 6, and 6 Hz, CH(OAc)], 5.52 and 6.20 (each 1H, do d and do t, J=16, 2 and 16, 7, 7 Hz, *trans*-CH=CH). Found: C, 69.97; H, 8.02%. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16%.

*cis-2-Ethyl-8-epoxyethyl-3,4,7,8-dihydro-2H-oxocin-3-one 3-Ethylene Acetal (**16**).* A suspension of sodium hydride (3.12 mmol) (50% mineral oil dispersion, 0.15 ml) and trimethyloxosulfonium iodide (690 mg, 3.12 mmol) in DMSO (15 ml) was stirred at room temperature under nitrogen. A solution of **1** (593 mg, 2.6 mmol) in DMSO (5 ml) was added dropwise to the dimethylsulfinylmethanide solution and stirred at room temperature for 1 h. The reaction mixture was mixed with water (50 ml) and extracted with ether (3×20 ml) and then with ethyl acetate (2×20 ml). All the organic solutions were combined, washed with water (3×20 ml) and saturated brine, dried and evaporated to leave oil (555 mg), which was purified by chromatography over silica gel (12 g, benzene:ethyl acetate=9:1) to give **16** (418 mg), white solid. A part (145 mg) was crystallized and recrystallized from hexane and ether for analysis to give a pure sample (128 mg), mp 87—88 °C; MS, 240 (M^+) and 211; IR (Nujol), ν_{max} 1648, 1380, 1252, 1162, 1107, and 1080; NMR, δ 1.00 (3H, t, J=7 Hz, CH_2CH_3), 1.44 (2H, m, CH_2CH_3), 2.72 and 3.25 (2H and 1H, each m, 3H in epoxyethyl), 2.94 (1H, do d, J=13 and 8.5 Hz, H at C_4), 3.60 (1H, do d, J=7 and 6 Hz, H at C_2), 4.00 (4H, m, OCH_2CH_2O), and 5.82 (2H, m, *cis*-CH=CH). Found: C, 64.98; H, 8.39%. Calcd for $C_{13}H_{20}O_4$: C, 64.86; H, 8.31%.

*cis-2-Ethyl-8-[1-hydroxy-2-(1,3-dithian-2-yl)ethyl]-3,4,7,8-tetrahydro-2H-oxocin-3-one 3-Ethylene Acetal (**17**) and Its Acetate (**17a**).* To a solution of 2-lithio-1,3-dithiane in THF, prepared from 1,3-dithiane (418 mg, 3.48 mmol) and butyllithium (4.2 mmol) (15% hexane solution, 2.8 ml) at −30——20 °C for 2 h under stirring, was added dropwise **16** (418 mg, 1.74 mmol) in THF (3 ml) at −70 °C. The mix-

ture was stirred at −20 °C for 14 h, and shaken with ether (50 ml) and saturated brine (20 ml). After separation of the ether solution, the aqueous solution was extracted with chloroform (3×20 ml). All the ether and chloroform solutions were combined, washed with saturated brine, dried and evaporated to leave oil (822 mg), which was purified by chromatography over silica gel (30 g, benzene) to give **17** (564 mg), viscous oil. The oil was treated with acetic anhydride (5.6 ml) and pyridine (12 ml) at room temperature overnight and then worked up as usual to give **17a** (557 mg), mp 145—150 °C. A part (66 mg) of the sample was recrystallized from benzene and hexane for analysis to yield **17a** (45 mg), mp 161—162 °C, in pure state; MS, *m/e* 402 (M^+), 373, and 342; IR (Nujol), ν_{max} 1740, 1640, 1230, 1125, 1110, and 1090 cm^{-1}; NMR, δ 1.00 (3H, t, J=7 Hz, CH_2CH_3), 1.38 (2H, m, CH_2CH_3), 2.03 (3H, s, $OCOCH_3$), 3.50 (2H, m, 2H at C_2 and C_8), 3.90 (5H, m, OCH_2CH_2O and SCHS), 5.24 [1H, do t, J=9, 4 and 4 Hz, CH(OAc)], and 5.74 (2H, m, *cis*-CH=CH). Found: C, 56.79; H, 7.51%. Calcd for $C_{19}H_{30}O_5S_2$: C, 56.69; H, 7.51%.

cis-*8-(1-Acetoxy-3-oxopropyl)-2-ethyl-3,4,7,8-tetrahydro-2H-oxocin-3-one 3-Ethylene Acetal (**18**).* To a vigorously stirred mixture of mercury(II) oxide (387 mg, 1.79 mmol) and boron trifluoride etherate (0.22 ml, 1.79 mmol) in 15% aq THF (2.4 ml) was added **17a** (240 mg, 0.597 mmol) in THF (2 ml) at room temperature during a period of 10 min. The mixture was stirred for 15 min at room temperature and mixed with ether (10 ml). After removal of precipitates by filtration, the reaction mixture (filtrate) was washed with saturated aq sodium carbonate and then with saturated brine, dried and evaporated to leave oily substance (**20**, 111 mg), which was used for the next reaction without further purification; NMR, 2.08 (3H, s, $OCOCH_3$), 4.00 (4H, m, OCH_2CH_2O), 5.54 [1H, do t, J=8, 4, and 4 Hz, CH(OAc)], 5.86 (2H, m, *cis*-CH=CH), and 9.78 (1H, t, J=2 Hz, CHO).

cis-*8-(1-Acetoxy-6-trimethylsilyl-3-hexen-5-ynyl)-2-ethyl-3,4,7,8-tetrahydro-2H-oxocin-3-one 3-Ethylene Acetal (**19a**).* Into a suspension of triphenyl (3-trimethylsilyl-2-propynyl)phosphonium bromide (242 mg, 0.534 mmol) in THF (2 ml) cooled at −78 °C was added butyllithium (0.543 mmol) (15% hexane solution, 0.33 ml). The mixture was stirred at −40 °C for 30 min and again cooled to −78 °C. A solution of **18** (111 mg, 0.356 mmol) in THF (1.5 ml) was added to the cooled mixture, and the whole mixture was stirred at ice-bath temperature for 1 h. After addition of ether, precipitates were formed and removed by filtration. The filtrate was evaporated to leave oil, which was separated by preparative TLC over silica gel (benzene:ethyl acetate=10:1) to give **19a** (99 mg), oil, showing a single spot on TLC; MS, *m/e* 406 (M^+), 391, 363, and 346; UV, λ_{max} 227 nm (ε 16600), 236 (22700), and 246 (17000); IR, ν_{max} 2160, 1740, 1248, and 960 cm^{-1}; NMR, δ 0.15 [9H, s, $Si(CH_3)_3$], 2.05 (3H, s, $OCOCH_3$), 3.50 (2H, m, 2H at C_2 and C_8), 3.94 (4H, m, OCH_2CH_2O), 5.02 [1H, do t, J=9, 4, and 4 Hz, CH(OAc)], 5.45 and 6.08 (1H, br d and do t, J=15 and 15, 7, 7 Hz, *trans*-CH=CH), and 5.80 (2H, m, *cis*-CH=CH). Found: C, 64.55; H. 8.49%. Calcd for $C_{22}H_{24}O_5Si$: C, 64.98; H, 8.43%.

cis-*8-(1-Acetoxy-3-hexen-5-ynyl)-2-ethyl-3,4,7,8-tetrahydro-2H-oxocin-3-one 3-Ethylene Acetal (**19**).* A solution of **19a** (166 mg, 0.419 mmol) in DMF (17 ml) was treated with ammonium fluoride (1.7 g, excess) at room temperature under stirring. The reaction mixture was treated with water (40 ml) and extracted with ether (3×50 ml). The combined ether solution was worked up as usual to leave oil (190 mg), which was purified by preparative TLC (benzene:ethyl acetate=10:1) to give **19a** (130 mg), oil, showing a single spot on TLC; MS, UV, IR, and NMR, in the text. Found: C, 68.13; H, 7.87%. Calcd for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84%.

cis-*8-(1-Acetoxy-3-hexen-5-ynyl)-2-ethyl-3,4,7,8-tetrahydro-2H-oxocin-3-one (**20**).* A solution of **19** (120 mg, 0.359 mmol) in acetone (50 ml) and water (8 ml) was heated with *p*-toluenesulfonic acid (90 mg, 0.474 mmol) under reflux for 24 h. After being cooled, the reaction mixture was treated with water (50 ml) and extracted with ethyl acetate (3×300 ml). The acetate solution was washed with 5% aq sodium hydrogencarbonate and saturated brine, dried and evaporated to leave oil (144 mg), which was purified by preparative TLC (benzene:ethyl acetate=10:1) to give **20** (31 mg), oil, and the starting acetal (**19**, 68 mg); MS, *m/e* 290 (M^+) and 230; UV, λ_{max} 322 nm (ε 194), 310 (279), 300 (300), 293 (323), 230 (sh) (11400), and 224 (14000); IR, ν_{max} 3310, 2110, 1740, 1720, 1236, and 960 cm^{-1}; NMR, δ 0.96 (3H, t, J=8 Hz, CH_2CH_3), 2.06 (3H, s, $OCOCH_3$), 2.81 (1H, d, J=2 Hz, C≡CH), 3.44 (1H, m, H at C_8), 3.72 (1H, t, J=7 Hz, H at C_2), 3.86 (1H, do d, J=11 and 8 Hz, H at C_4), 5.00 [1H, do t, J=8, 5, and 5 Hz, CH(OAc)], 5.52 and 6.14 (each 1H, do d and do t, J=15, 2, and 15, 7, 7 Hz, *trans*-CH=CH), and 5.64 (2H, m, *cis*-CH=CH). Found: C, 69.98; H, 7.91%. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64%.

r-*2*,c-*8-(1-Acetoxy-3-hexen-5-ynyl)-3,4,7,8-tetrahydro-2H-oxocin-3-ol and Its 3-Epimer (**22**).* Compound **20** (36 mg, 0.12 mmol) was treated with $NaBH_4$ (18 mg) in methanol (3 ml) at 0 °C for 20 min. The reaction mixture was made acidic with 2 M hydrochloric acid, concentrated and extracted with ethyl acetate (5×3 ml). The acetate solution was worked up as usual to leave oil (52 mg), showing two spots on TLC, which was separated by preparative TLC (benzene:ethyl acetate=4:1) to yield **22** (11 mg), oil, and **21** (18 mg), oil, as less and more polar fractions: **21**, MS, *m/e* 292 (M^+), 274, and 232; IR, ν_{max} 3440, 3300, 2120, 1740, 1645, 1235, 1130, 1075, 1048, 1030, and 960 cm^{-1}; NMR, δ 0.92 (3H, t, J=7 Hz, CH_2CH_3), 1.86 (1H, br s, OH), 2.05 (3H, s, $OCOCH_3$), 2.82 (1H, d, J=2 Hz, C≡CH), 3.40 (2H, m, 2H at C_2 and C_8), 3.64 [1H, br, W_H=20 Hz, CH(OH)], 4.98 [1H, do t, J=8, 5, and 5 Hz, CH(OAc)], 5.52 and 6.16 (each 1H, do d and do t, J=16, 2, and 16, 7, 7 Hz, *trans*-CH=CH), and 5.74 (2H, m, *cis*-CH=CH): **22**, MS, *m/e* 292 (M^+), 274, and 232; IR, ν_{max} 3440, 3300, 2110, 1740, 1235, 1120, 1090, 1070, 1050, 1025, and 960 cm^{-1}; NMR, δ 0.98 (3H, t, J=7.5 Hz, CH_2CH_3), 2.05 (3H, s, $OCOCH_3$), 2.80 (1H, d, J=2 Hz, C≡CH), 3.10 and 3.44 (each 1H, m, 2H at C_2 and C_8), 3.72 [1H, do t, J=9, 3, and 3 Hz, CH(OH)], 4.98 [1H, do t, J=8, 5, and 5 Hz, CH(OAc)], 5.52 and 6.16 (each, 1H, do d and do t, J=15, 2, and 15, 7, 7 Hz, *trans*-CH=CH), and 5.58 (2H, m, *cis*-CH=CH).

r-*2*,c-*8-(1-Acetoxy-3-hexen-5-ynyl)*-t-*3-bromo-3,4,7,8-tetrahydro-2H-oxocin Acetate [(±)-2].* Into a solution of **21** (15 mg, 0.05 mmol) and tetrabromomethane (125 mg, 0.375 mmol) in dichloromethane (4 ml) was added dropwise triphenylphosphine (65 mg, 0.25 mmol) in dichloromethane (6 ml, dried through Molecular Sieves 4A) at room temperature under stirring during a period of 3 h, and the whole solution was stirred at room temperature for 12 h. The reaction mixture was evaporated to leave resinous material, which was purified by preparative TLC (benzene) to yield (±)-**2** (2 mg), which crystallized spontaneously and had mp 45—47 °C, with the starting alcohol (**21**, 3 mg). The spectral data (described in the text) were com-

pletely identical with natural laurencin (MS, UV, IR, NMR, and TLC).

References

1) Part IV, T. Masamune, H. Matsue, and H. Murase, *Bull. Chem. Soc. Jpn.*, **52**, 127 (1979).

2) a) T. Irie, M. Suzuki, and T. Masamune, *Tetrahedron*, **24**, 4193 (1968); *Tetrahedron Lett.*, **1965**, 1091; b) For a preliminary communication of the present paper, see; A. Murai, H. Murase, H. Matsue, and T. Masamune, *Tetrahedron Lett.*, **1977**, 2507.

3) For a recent review, see, D. J. Faulkner, *Tetrahedron*, **33**, 1421 (1977). *Cf.*, Ref. 3 in the preceding paper.

4) T. Masamune, S. Numata, H. Matsue, A. Matsuyuki, T. Sato, and H. Murase, *Bull. Chem. Soc. Jpn.*, **48**, 2294 (1975).

5) a) A. O. King, N. Okukado, and E. Negishi, *J. Chem. Soc., Chem. Commun.*, **1977**, 683; E. Negishi and A. Abramovitch, *Tetrahedron Lett.*, **1977**, 411; E. Negishi, R. M. Williams, A. Lew, and T. Yoshida, *J. Organomet. Chem.*, **92**, C4, (1975); J. F. Normant, A. Commercon, and J. Villieras, *Tetrahedron Lett.*, **1975**, 1465; E. Negishi, G. Lew, and T. Yoshida, *J. Chem. Soc., Chem. Commun.*, **1973**, 874; b) A. B. Holmes, R. A. Raphael, and N. K. Wellard, *Tetrahedron Lett.*, **1976**, 1539, J. M. Laborits, C. A. Henrick, and V. L. Corbin, *Tetrahedron Lett.*, **1975**, 4209; These procedures appear not to be applicable to the present transformation. c) E. J. Corey and R. A. Ruden, *Tetrahedron Lett.*, **1973**, 1495.

6) *Cf.* H. C. Brown and A. W. Moerikofer, *J. Am. Chem. Soc.*, **85**, 2063 (1963); **83**, 3417 (1961). G. M. L. Cragg, "Organoboranes in Organic Synthesis," M. Dekker, New York (1973), p. 73.

7) L. Migniac, Ph. Migniac, and Ch. Prevost, *Bull. Soc. Chim. Fr.*, **1965**, 3560.

8) H. B. Henbest, E. R. H. Jones, and I. M. S. Walls, *J. Chem. Soc.*, **1950**, 3650.

9) J. S. Cochrane and J. R. Hanson, *J. Chem. Soc., Perkin Trans. 1*, **1972**, 361.

10) *Cf.*, P. M. Atlani, J. F. Biellmann, S. Dube, and J. J. Vicens, *Tetrahedron Lett.*, **1974**, 2665.

11) E. Vedejs and P. L. Fuchs, *J. Org. Chem.* **36**, 366 (1971).

12) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).

13) D. Seebach and E. J. Corey, *J. Org. Chem.*, **40**, 231 (1975); E. J. Corey and D. Crouse, *ibid.*, **33**, 298 (1968); D. Seebach, N. R. Jones, and E. J. Corey, *ibid.*, **33**, 300 (1968).

14) J. Drouin, F. Leyendecker, and J. M. Conia, *Tetrahedron Lett.*, **1975**, 4053.

15) R. K. Boekman, Jr., and B. Genam, *Tetrahedron Lett.*, **1974**, 913; A. K. Bose and B. Lal, *ibid.*, **1973**, 3937; J. Hooz and S. S. Gilani, *Can. J. Chem.* **46**, 86 (1968).