

AN ENANTIOCONTROLLED ROUTE TO PROTOMYCINOLIDE IV
AND ITS PRESUMED BIOGENETIC PRECURSORS USING (S)-O-
BENZYLGLYCIDOL

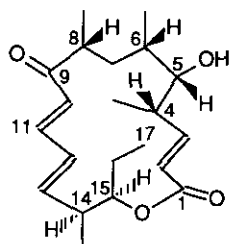
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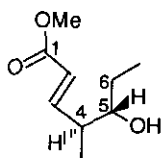
Abstract—— Starting with (S)-O-benzylglycidol (9) as only chiral building block, a formal synthesis of protomycinolide IV (1) and the first syntheses of its presumed biogenetic precursors methyl epimycinonate I (2), methyl mycinonate I (3), methyl mycinonate II (4), and decarboxymycinonic acid III (5), have been achieved *via* the eight-carbon unit (8) as a common intermediate.

1. INTRODUCTION

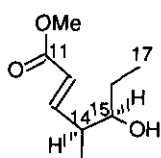
Protomycinolide IV (1) is a 16-membered macrolide produced by *Micromonospora griseorubida*.¹ Recently, four unsaturated carbonyl compounds, methyl epimycinonate I (2), methyl mycinonate I (3), methyl mycinonate II (4), and decarboxymycinonic acid III (5), presumed to be the biogenetic precursors of the macrolide (1), have been isolated from the same culture broth producing the macrolide² without determination of their configurations (**Figure 1**). We describe here the stereochemical determination of these presumed biogenetic intermediates (2)~(5) by enantiocontrolled synthesis and a formal synthesis of protomycinolide IV (1) *via* the common key intermediate (8) starting with a chiral building block (S)-O-benzylglycidol^{3,4} (9).



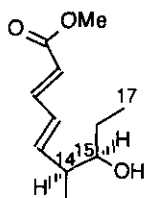
protomycinolide IV (1)



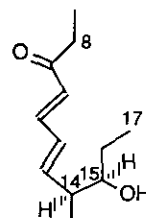
methyl epimycinonate I (2)



methyl mycinonate I (3)



methyl mycinonate II (4)



decarboxymycinonic acid III (5)

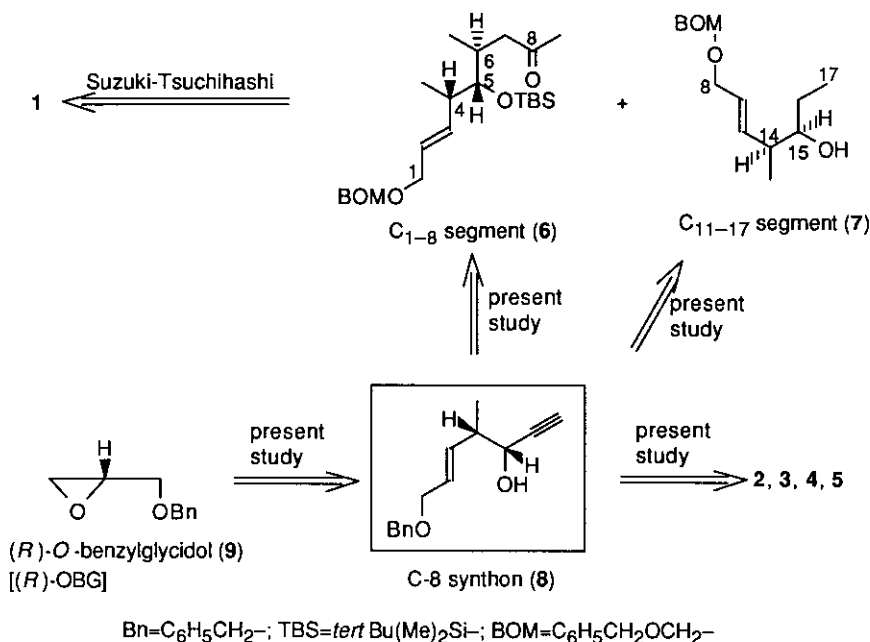
Figure 1

2. SYNTHETIC STRATEGY

Two total syntheses of protomycinolide IV (1), the first by Yamaguchi *et al.*,⁵ and the second by Suzuki *et al.*,⁶ have been reported to date.⁷ In the present synthesis,⁸ we intended to use the eight-carbon unit⁷ (8) available from (*S*)-*O*-benzylglycidol (9) as the common building block for the further construction of the known C₁₋₈ (6) and C₁₁₋₁₇ (7) segments of protomycinolide IV (1) as well as the first construction of four presumed biogenetic precursors,⁸ methyl epimycinonate I (2), methyl mycinonate I (3), methyl mycinonate II (4), and decarboxymycinonic acid III (5) (Scheme 1).

3. SYNTHESIS OF THE COMMON BUILDING BLOCK (8)

We have already reported the efficient synthesis⁹ of the (*S*)-(*Z*)-olefinic alcohol (12) starting from (*S*)-*O*-benzylglycidol (9) *via* the rearrangement of the terminal acetylene (10) to the internal acetylene (11). In the present synthesis 12 was first transformed into the propargyl ether (14) in two steps in a good overall yield employing a modified Williamson conditions using a complex of potassium fluoride and neutral alumina as catalyst.¹⁰ Treatment of 14 with *n*-butyllithium underwent a

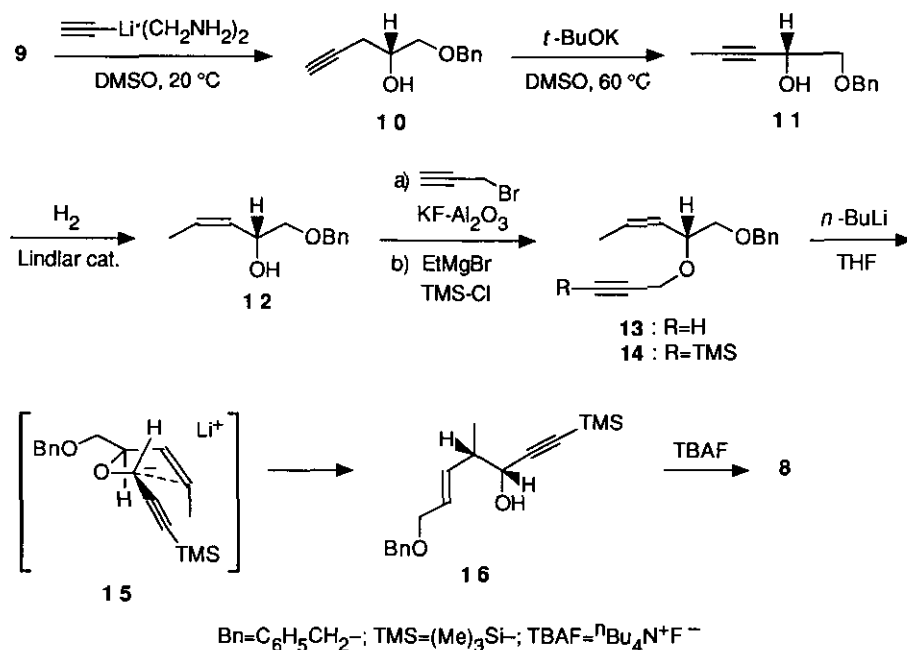


Scheme 1

facile diastereoselective [2,3]-Wittig rearrangement¹¹ to afford the *syn* product (16) exclusively in 73% yield presumably *via* the least hindered folded envelope transition state¹¹ (15). This was then treated with tetrabutylammonium fluoride to give the key common building block (8) in an excellent yield. Optical purity of 8 was determined to be $\geq 98\%$ ee by ¹H nmr (500 MHz) measurement of its MTPA esters (*R*- and *S*-) (Scheme 2).

4. SYNTHESIS OF THE PRESUMED BIOGENETIC PRECURSORS⁸

(i) Synthesis of the 'C₁₋₆' Precursor Methyl Epimycinonate I (2) — In order to discriminate the olefinic and the acetylenic bond, 8 was first treated with *N*-bromosuccinimide (NBS) in the presence of sodium hydrogen carbonate to give the bromo ether (17) as a mixture of diastereomers. Catalytic hydrogenation of the acetylenic bond of 17 followed by treating the resulting saturated product (18) with zinc powder in the presence of hydrochloric acid regenerated the olefinic bond to

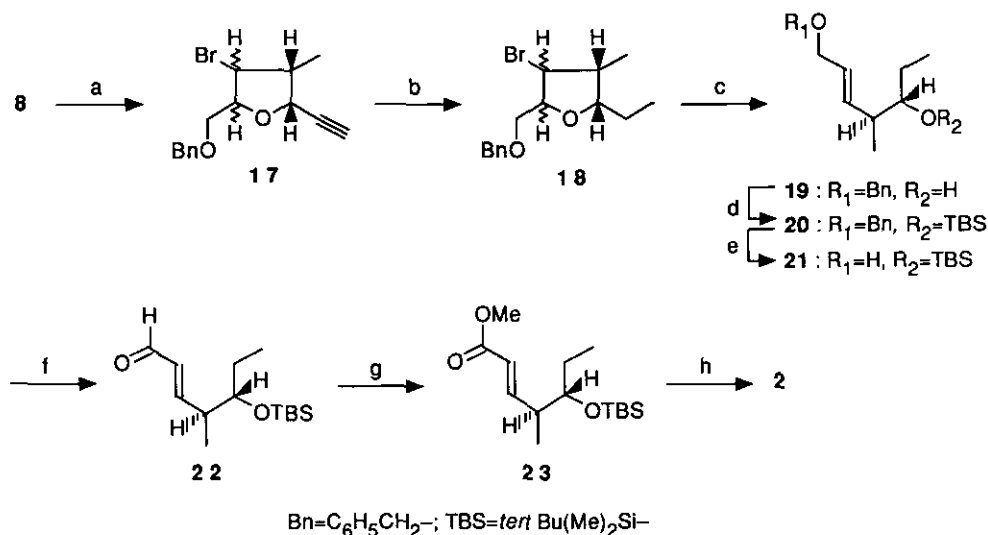


Scheme 2

give **19** in a satisfactory overall yield. Sequential protection of the secondary alcohol and debenzoylation yielded the primary alcohol (**21**) which gave the unsaturated ester (**23**) *via* the aldehyde (**22**) by employing Corey's procedure.¹² Deprotection of **23** with hydrochloric acid afforded the secondary alcohol (**2**) whose physical and spectral data were identical with those of natural methyl epimycinonate I (**2**) corresponding to the C₁₋₆ moiety of protomycinolide IV (**1**) (Scheme 3).

(ii) Synthesis of the 'C₁₁₋₁₇' Precursor Methyl Mycinonate I (**3**), the 'C₉₋₁₇' Precursor Methyl Mycinonate II (**4**), and the 'C₈₋₁₇' Precursor Decarboxymycinonic acid III (**5**) –

— On the other hand, the secondary hydroxy center of **8** was first inverted by employing the Mitsunobu reaction¹³ to give the epimeric alcohol (**25**) having the C₁₄ and C₁₅ stereocenters *via* the benzoate (**24**). Employing exactly the same approach as that for the epimeric counterpart (**8**), **25** could be transformed into the α,β-unsaturated ester (**3**), *via* the aldehyde (**31**), whose physical and spectral data were identical with those of natural methyl mycinonate I (**3**) corresponding to the C₁₁₋₁₇



Scheme 3

Reagents and conditions: a, NBS, THF; b, H_2 , PtO_2 ; c, Zn, MeOH; d, TBS-Cl, imidazole; e, Li, liq. NH_3 ; f, MnO_2 ; g, MnO_2 , NaCN, MeOH; h, conc. HCl (cat.), MeOH.

moiety of protomycinolide IV (1). The Horner-Emmons condensation of aldehyde (31) followed by deprotection of the resulting 33 afforded the diene (4) whose physical and spectral data were identical with those of natural methyl mycinonate II (4) corresponding to the C_{9-17} moiety of protomycinolide IV (1).

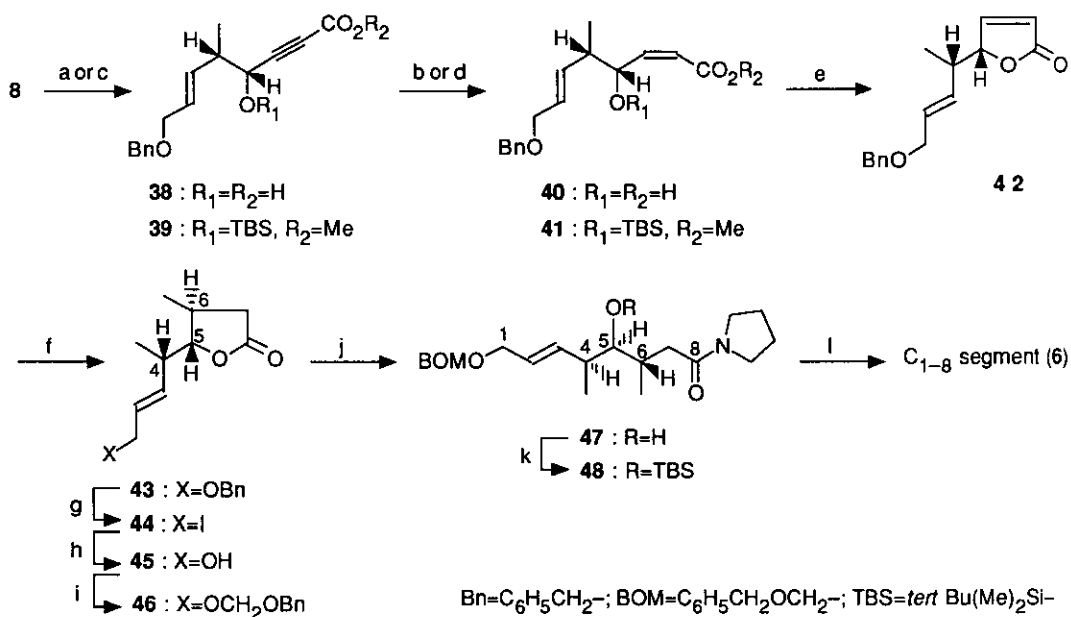
The protected diene intermediate (33) was further transformed into the dienone (5), *via* the intermediates, (34), (35), (36), and (37), whose physical and spectral data were identical with those of natural decarboxymycinonic acid III (5) corresponding to the C_{8-17} moiety of protomycinolide IV (1) (Scheme 4).

Since the biogenesis of protomycinolide IV (1) as well as other related natural macrolides has not been clarified,¹⁴ the present stereochemical determination and synthesis of the presumed biogenetic intermediates (2) ~ (5) are noteworthy.

5. SYNTHESIS OF THE C_{1-8} SEGMENT OF PROTOMYCINOLIDE IV⁷

To introduce the C_6 -methyl group having the requisite stereochemistry 8 was first transformed into the butenolide (42). Thus, 8 was treated with butyllithium followed by carbon dioxide to give the acid (38) which on partial reduction followed

alcohol (**45**) in 68% overall yield. After protecting **45** by benzyloxymethyl (BOM) group,¹⁶ the resulting ether (**46**) was exposed to the complex prepared from pyrrolidine and trimethylaluminum¹⁷ to give the amide alcohol (**47**) whose secondary hydroxy group was protected by *tert*-butyldimethylsilyl (TBS) group. Finally, the amide (**48**) was reacted with methyllithium to afford the C₁₋₈ segment (**6**) of the Suzuki-Tsuchihashi synthesis^{6,18} in 46% overall yield from **47** (Scheme 5).



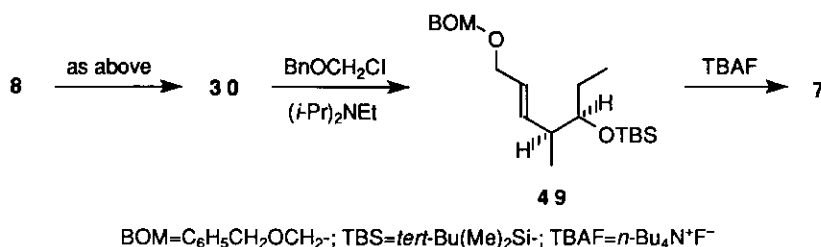
Scheme 5

Reagents and conditions: a, *n*-BuLi, then CO₂; b, H₂, Lindlar catalyst, then reflux, benzene (for **38** via **40**); c, (i) TBS-Cl, imidazole, (ii) *n*-BuLi, then ClCO₂Me; d, H₂, Lindlar catalyst; e, conc. HCl (cat.), MeOH (for **41**); f, Me₂CuLi; g, TMS-Cl, NaI; h, aq. NaHCO₃; i, BOM-Cl, (*i*-Pr)₂NEt; j, Et₂AlN(CH₂)₄; k, TBS-Cl, imidazole; l, MeLi.

6. SYNTHESIS OF THE C₁₁₋₁₇ SEGMENT OF PROTOMYCINOLIDE IV

Synthesis of the C₁₁₋₁₇ segment of protomycinolide IV (**1**) has virtually been accomplished in the synthesis of the C₁₁₋₁₇ biogenetic precursor (**3**). In order to connect **8** with the known Suzuki-Tsuchihashi intermediate⁶ (**7**), the primary alcohol

(30) used in the synthesis of the C₁₁₋₁₇ precursor (3) was alkylated with benzyloxymethyl chloride followed by removal of the protecting group of the secondary hydroxy group of the bis-ether product (49) to give rise to 7^{6,18} in 75% overall yield (Scheme 6).



Scheme 6

7. CONCLUSION

In conclusion a formal total synthesis of protomycinolide IV (1) and the first enantiocontrolled syntheses of its presumed biogenetic precursors, methyl epimycinonate I (2), methyl mycinonate I (3), methyl mycinonate II (4), and decarboxymycinonic acid III (5), have been achieved starting from a single chiral building block (*S*)-*O*-benzyglycidol (9) *via* the eight-carbon unit (8) as a common intermediate.

EXPERIMENTAL SECTION

Optical rotations were measured with a JASCO-DIP-370 digital polarimeter. IR spectra were measured with a JASCO-IR-700 spectrophotometer. ¹H Nmr spectra were recorded on JEOL-JNM-FX90A (90 MHz) and JEOL-JNM-GX500 (500 MHz) spectrometers. Mass spectra were measured with a JEOL JMS-DX303 instrument. Reactions were carried out under argon.

(R)-(Z)-1-Benzyloxy-2-propargyloxy-3-pentene (13)

Method A: To a stirred mixture of (*R*)-(-)-alcohol (12) (1.0 g, 5.2 mmol), tetra-*n*-butylammonium hydrogen sulfate (88 mg), and 60% (w/v) aqueous NaOH (20 ml)

was added propargyl bromide (3.1 g, 26.0 mmol) at 0 °C and the stirring was continued for 26 h at room temperature. The mixture was diluted with water and ether and the organic layer was separated. The organic layer was washed with brine, dried over MgSO_4 , and evaporated under reduced pressure to leave an oil which was purified on a silica gel column (50 g) using Et_2O -hexane (1:50 v/v) as eluent to give the ether (**13**) (0.92g, 77%) as a colorless oil

Method B: A suspension of (*R*)-(-)-alcohol (**12**) (21.7 g, 112.8 mmol), propargyl bromide (53.7 g, 451.3 mmol), and $\text{KF}\cdot\text{Al}_2\text{O}_3$ (2:3 w/w) (144.3 g) in acetonitrile (500 ml) was stirred at room temperature for 14 h. After filtration, the mixture was evaporated under reduced pressure to leave the residue which was purified on a silica gel column (1000 g) using Et_2O -hexane (1:15 v/v) as eluent to give the ether (**13**) (18.2 g, 70%) as a colorless oil; bp 130 °C/0.2 Torr (Kugelrohr); $[\alpha]_{\text{D}}^{25} -85.38^\circ$ (*c* 1.04, CHCl_3). Ir (film) ν_{max} : 2110 cm^{-1} ; ^1H nmr (CDCl_3) δ : 7.33 (s, 5H), 6.02-5.12 (m, 2H), 4.60 (s, 2H), 4.88-4.50 (m, 1H), 4.19 (t, $J=2.5$ Hz, 2H), 1.73 (dd, $J=6.8, 1.7$ Hz, 3H); ms (*m/z*): 189 ($\text{M}^+-\text{CH}_3\text{CH}=\text{CH}-$), 91 (100%). Anal. Calcd for $\text{C}_{15}\text{H}_{18}\text{O}_2$: C 78.23, H 7.88. Found: C 77.58, H 7.90.

(*R*)-(Z)-1-Benzoyloxy-2-(3'-trimethylsilylpropargyloxy)-3-pentene (14) — To a stirred solution of the ether (**13**) (10.0 g, 43.5 mmol) in THF (150 ml) was added EtMgBr (1.3 M in THF) (40 ml, 52 mmol) at 0 °C and after 3 h trimethylsilyl chloride (14.2 g, 130.4 mmol) was added at the same temperature and after 3 min an excess of saturated aqueous NH_4Cl was added to the mixture. The mixture was extracted with ether and the extract was washed with saturated aqueous NaHCO_3 , brine, dried over MgSO_4 , and evaporated under reduced pressure to leave a residue which was purified on a silica gel column (250 g) using Et_2O -hexane (1:30 v/v) as eluent to give the silylated product (**14**) (12.2 g, 93%) as a colorless oil; bp 130 °C/0.2 Torr (Kugelrohr); $[\alpha]_{\text{D}}^{27} -80.74^\circ$ (*c* 1.02, CHCl_3). Ir (film) ν_{max} : 2180 cm^{-1} ; ^1H nmr (CDCl_3) δ : 7.34 (s, 5H), 6.01-5.12 (m, 2H), 4.60 (s, 2H), 4.79-4.90 (m, 1H), 4.18 (d, $J=2.9$ Hz, 2H), 3.73-3.53 (m, 2H), 1.71 (dd, $J=7.1, 1.4$ Hz, 3H), 0.18 (br s, 9H); ms (*m/z*): 302

(M⁺), 91 (100%). Exact Mass Calcd for C₁₈H₂₆O₂Si: 302.1703. Found: 302.1711. *Anal.* Calcd for C₁₈H₂₆O₂Si: C 71.47, H 8.66. Found: C 71.44, H 8.72.

(3*R*,4*S*)-(E)-7-Benzoyloxy-4-methyl-1-trimethylsilylhept-5-en-1-yn-3-ol (16) — To a stirred solution of the ether (14) (100 mg, 0.33 mmol) in THF (2 ml) was added *n*-BuLi (1 M in hexane, 0.60 ml, 0.6 mmol) at -70 °C and the stirring was continued for 4 h. After addition of saturated aqueous NH₄Cl (3 ml) at the same temperature, the mixture was extracted with ether. The extract was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (5 g) using Et₂O-hexane (1:7 v/v) as eluent to give the alcohol (16) (73.4 mg, 73%) as a colorless oil; [α]_D²⁴ +18.91° (c 0.62, CHCl₃). Ir (film) ν_{max}: 3400, 2170 cm⁻¹; ¹H nmr (CDCl₃) δ: 7.33 (s, 5H), 5.82-5.67 (m, 2H), 4.52 (s, 2H), 4.24 (dd, *J*=7.4, 6.8 Hz, 1H), 4.08-3.94 (m, 2H), 2.67-2.28 (m, 1H), 1.86 (d, *J*=7.4 Hz, 1H, exchangeable with D₂O), 1.12 (d, *J*=6.8 Hz, 3H), 0.17 (br s, 9H); ms (m/z): 301 (M⁺-1), 91 (100%). *Anal.* Calcd for C₁₈H₂₈O₂Si: C 71.47, H 8.66. Found: C 71.29, H 8.73.

(3*R*,4*S*)-(E)-7-Benzoyloxy-4-methylhept-5-en-1-yn-3-ol (8) — A mixture of the silylacetylene (16) (1.77 g, 5.86 mmol) and tetra-*n*-butylammonium fluoride (1 M in THF) (17.6 ml, 17.6 mmol) in THF (20 ml) was stirred at room temperature for 8 min. After evaporation of the solvent under reduced pressure, the residue was purified on a silica gel column (30 g) using Et₂O-hexane (1:7 v/v) as eluent to give the acetylene (8) (1.29 g, 96%) as a colorless oil; bp 130 °C/0.2 Torr (Kugelrohr); [α]_D²⁵ +18.15° (c 1.15, CHCl₃). Ir (film) ν_{max}: 3500, 2100 cm⁻¹; ¹H nmr (CDCl₃) δ: 7.30 (s, 5H), 5.82-5.68 (m, 2H), 4.15 (s, 2H), 4.26 (dd, *J*=5.1, 2.3 Hz, 1H), 4.08-3.92 (m, 2H), 2.45 (d, *J*=2.3 Hz, 1H), 2.70-2.30 (m, 1H), 2.10-1.82 (br s, 1H, exchangeable with D₂O), 1.12 (d, *J*=7.1 Hz, 3H); ms (m/z): 230 (M⁺), 91 (100%). Exact Mass Calcd for C₁₅H₁₈O₂: 230.1307. Found: 230.1293.

(2*R*,3*S*,4*RS*,5*RS*)-5-Benzoyloxymethyl-4-bromo-2-ethynyl-3-methyltetrahydrofuran (17) — To a stirred solution of the eneyne (8) (20 mg, 0.09 mmol) in THF (1 ml) was added *N*-bromosuccinimide (23 mg, 0.13 mmol) at room temperature. After

stirring at the same temperature for 3 h, the mixture was diluted with Et₂O and the mixture was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (3 g) using Et₂O-hexane (1:15 v/v) as eluent to give the bromo ether (**46**) (21 mg, 78%) as a colorless oil. Ir (film) $\nu_{\max}$: 2120 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.38 (s, 5H), 4.76 (dd, $J=8.0, 2.3$ Hz, 1H), 4.64 (s, 2H), 4.31-4.09 (m, 1H), 3.90 (d, $J=9.1$ Hz, 1H), 3.79-3.61 (m, 2H), 2.81-2.32 (m, 1H), 2.52 (d, $J=2.3$ Hz, 1H), 1.22 (d, $J=7.1$ Hz, 2H); ms (m/z): 310, 308 (M⁺), 91 (100%). Exact Mass Calcd for C₁₅H₁₇O₂Br: 310.0392; 308.0411. Found: 310.0382; 308.0411.

(2*S*,3*S*,4*R*,5*R*)-5-Benzoyloxymethyl-4-bromo-2-ethyl-3-methyltetrahydrofuran (18)

—— A suspension of the bromoacetylene (**17**) (333.7 mg, 1.01 mmol) and PtO₂ (17 mg) in hexane (3 ml) was hydrogenated under atmospheric pressure of hydrogen at room temperature for 40 min. The suspension was filtered and evaporated under reduced pressure to leave an oil which was purified on a silica gel column (3.0 g) to give the saturated product (**18**) as separable isomers (**18a**) and (**18b**) both as colorless oil.

18a (200.6 mg, 60%): Ir (film) $\nu_{\max}$: 1090 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.33 (s, 5H), 4.60 (s, 2H), 4.28-3.45 (m, 5H), 2.48 (sext, $J=6.9$ Hz, 1H), 1.44 (q, $J=7.1$ Hz, 2H), 1.01 (d, $J=7.1$ Hz, 3H), 0.96 (t, $J=7.1$ Hz, 3H); ms (m/z): 316, 314 (M⁺), 91 (100%).

18b (67.2 mg, 20%): Ir (film) $\nu_{\max}$: 1090 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.33 (s, 5H), 4.60 (s, 2H), 4.28-3.45 (m, 5H), 2.48 (sext, $J=6.9$ Hz, 1H), 1.44 (q, $J=7.1$ Hz, 2H), 1.11-0.83 (m, 3H), 1.01 (d, $J=7.1$ Hz, 3H); ms (m/z): 316, 314 (M⁺), 91 (100%).

(3*S*,4*S*)-(E)-7-Benzoyloxy-4-methylhept-5-en-3-ol (19) —— A suspension of the bromo ether (**18**) (155.4 mg, 0.50 mmol) and zinc dust (164 mg, 2.5 mmol) in MeOH (5 ml) was refluxed for 3 h. After filtration, the filtrate was evaporated under reduced pressure. The residue was taken up into Et₂O and was filtered using Celite pad. The filtrate was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (3 g) using Et₂O-hexane (1:4 v/v) as eluent to give the enol (**19**) (102.3

mg, 87%) as a colorless oil; $[\alpha]_D^{26} -24.55^\circ$ (c 1.01, CHCl_3). Ir (film) ν_{max} : 2450 cm^{-1} ; ^1H nmr (CDCl_3) δ : 7.35 (s, 5H), 5.78-5.59 (m, 2H), 4.51 (s, 2H), 4.00 (d, $J=4.3$ Hz, 2H), 3.53-3.22 (m, 1H), 2.52-2.04 (s, 1H), 1.78-1.22 (m, 2H, 1H exchangeable with D_2O), 1.03 (d, $J=7.1$ Hz, 3H), 0.96 (t, $J=8.0$ Hz, 3H); ms (m/z): 234 (M^+), 91 (100%). Exact Mass Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_2$ (M^+): 234.1619. Found: 234.1620.

(4*S*,5*S*)-(E)-1-Benzoyloxy-5-*tert*-butyldimethylsilyloxy-4-methyl-2-heptene (20) —

A mixture of the enol (19) (576.4 mg, 2.51 mmol), *tert*-butyldimethylsilyl chloride (755.4 mg, 5.01 mmol), and imidazole (767.7 mg, 11.3 mg) in DMF (5 ml) was stirred at room temperature for 11 h. The mixture was diluted with Et_2O and was washed with saturated aqueous NaHCO_3 , brine, dried over MgSO_4 , and evaporated under reduced pressure. The residue was purified on a silica gel column (30 g) using Et_2O -hexane (1:50 v/v) as eluent to give the silyl ether (20) (827 mg, 95%) as a colorless oil; $[\alpha]_D^{30} -25.05^\circ$ (c 1.01, CHCl_3). Ir (film) ν_{max} : 1255, 1105, 780, 840, 700 cm^{-1} ; ^1H nmr (CDCl_3) δ : 7.33 (s, 5H), 5.90-5.38 (m, 2H), 4.50 (s, 2H), 3.99 (d, $J=4.9$ Hz, 2H), 3.46 (q, $J=5.4$ Hz, 1H), 2.34 (m, 1H), 1.62-1.24 (m, 2H), 0.97 (d, $J=7.1$ Hz, 3H), 0.89 (s, 9H), 0.86 (t, $J=7.8$ Hz, 3H), 0.04 (s, 6H); ms (m/z): 319 ($\text{M}^+-\text{C}_2\text{H}_5$), 173 (100%). Exact Mass Calcd for $\text{C}_{19}\text{H}_{31}\text{O}_2\text{Si}$ ($\text{M}^+-\text{C}_2\text{H}_5$): 319.2093. Found: 319.2115.

(4*S*,5*S*)-(E)-5-*tert*-Butyldimethylsilyloxy-4-methyl-2-hepten-1-ol (21) — To a stirred solution of the benzyl ether (20) (755.9 mg, 2.17 mmol) in THF (25 ml) and liquid NH_3 (25 ml) was added lithium (152 mg, 21.7 mmol) portionwise. After having faded blue color, MeOH (5 ml) was added to the mixture and NH_3 was evaporated at atmospheric pressure. The residue was diluted with dichloromethane and the solution was washed with brine, dried over MgSO_4 , and evaporated under reduced pressure. The residue was purified on a silica gel column (20 g) using Et_2O -hexane (1:4 v/v) to give the primary alcohol (21) (543.7 mg, 97%) as a colorless oil; $[\alpha]_D^{25} -29.47^\circ$ (c 1.02, CHCl_3). Ir (film) ν_{max} : 3125 cm^{-1} ; ^1H nmr (CDCl_3) δ : 5.89-5.42 (m, 2H), 4.10 (br d, $J=4.2$ Hz, 2H), 3.46 (q, $J=5.4$ Hz, 1H), 2.32 (m, 1H), 1.62-1.20 (m, 3H, 1H exchangeable with D_2O), 0.97 (d, $J=6.8$ Hz, 3H), 0.89 (t, $J=7.8$ Hz, 3H), 0.03 (s,

6H); ms (m/z): 257 ($M^+ + 1$), 133 (100%). Exact Mass Calcd for $C_{14}H_{29}O_2Si$ ($M^+ - 1$): 257.1936. Found: 257.1942.

(4*S*,5*S*)-(E)-5-*tert*-Butyldimethylsilyloxy-4-methylhept-2-en-1-ol (22) — A suspension of the enol (21) (107.8 mg, 0.42 mmol) and MnO_2 (1.08 g) in CH_2Cl_2 (3 ml) was stirred at room temperature for 4.5 h. After filtration using Celite pad, the filtrate was evaporated under reduced pressure and the residue was purified on a silica gel column (5 g) using Et_2O -hexane (1:100 v/v) as eluent to give the aldehyde (22) (83.7 mg, 78%) as a colorless oil; $[\alpha]_D^{29} -63.20^\circ$ (c 1.0, $CHCl_3$). Ir (film) ν_{max} : 1692 cm^{-1} ; 1H nmr ($CDCl_3$) δ : 9.52 (d, $J=7.8$ Hz, 1H), 6.95 (dd, $J=15.9, 6.6$ Hz, 1H), 6.11 (ddd, $J=15.9, 7.8, 1.5$ Hz, 1H), 3.61 (td, $J=6.6, 4.9$ Hz, 1H), 2.62 (m, 1H), 1.66-1.21 (m, 2H), 1.07 (d, $J=6.8$ Hz, 3H), 0.90 (s, 9H), 0.88 (t, $J=7.6$ Hz, 3H), 0.06 (s, 3H), 0.05 (s, 3H); ms (m/z): 256 (M^+), 73 (100%). Exact Mass Calcd for $C_{14}H_{28}O_2Si$: 256.1859. Found: 256.1882.

Methyl (4*S*,5*S*)-(E)-5-*tert*-Butyldimethylsilyloxy-4-methyl-2-heptenoate (23) — A suspension of the aldehyde (22) (295.7 mg), MnO_2 (3.24 g) and NaCN (283.1 mg, 5.78 mmol) in MeOH (10 ml) containing acetic acid (0.10 ml, 1.73 mmol) was stirred at room temperature for 17 h. After filtration using Celite pad, the filtrate was washed with saturated aqueous $NaHCO_3$, brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified on a silica gel column (8 g) using Et_2O -hexane (1:100 v/v) as eluent to give the ester (23) (274 mg, 76%) as a colorless oil; $[\alpha]_D^{25} -42.46^\circ$ (c 1.01, $CHCl_3$). Ir (film) ν_{max} : 1728, 1659 cm^{-1} ; 1H nmr ($CDCl_3$) δ : 7.01 (dd, $J=15.9, 7.6$ Hz, 1H), 5.80 (dd, $J=15.9, 1.5$ Hz, 1H), 3.73 (s, 3H), 3.54 (q, $J=5.4$ Hz, 1H), 2.48 (m, 1H), 1.62-1.28 (m, 2H), 1.02 (d, $J=6.8$ Hz, 3H), 0.89 (s, 9H), 0.86 (t, $J=7.8$ Hz, 3H), 0.04 (s, 6H); ms (m/z): 285 ($M^+ - 1$), 73 (100%). Exact Mass Calcd for $C_{15}H_{29}O_3Si$ ($M^+ - 1$): 285.1886. Found: 185.1862.

Methyl (4*S*,5*S*)-(E)-5-Hydroxy-4-methyl-2-heptenoate (Methyl Epimycinonate I) (2) — To a stirred solution of the silyl ether (23) (197.2 mg, 0.69 mmol) in MeOH (3 ml) was added 35% hydrochloric acid (3 drops) at room temperature and the stirring was continued for 12 h at the same temperature. After evaporation of the solvent

under reduced pressure, the residue taken up into Et₂O was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (5 g) using Et₂O-hexane (1:4 v/v) as eluent to give the 'C₁₋₆' precursor (2) (112.0 mg, 94%) as a colorless oil; [α]_D²⁶ -43.78° (*c* 1.01, MeOH) [lit.,^{2b} [α]_D²⁵ -45.9° (*c* 1.01, MeOH)]. Ir (film) $\nu_{\max}$: 3460, 1725, 1710, 1660 cm⁻¹; ¹H nmr (CDCl₃) δ : 6.95 (dd, *J*=15.9, 7.9 Hz, 1H), 5.87 (dd, *J*=15.9, 1.2 Hz, 1H), 3.74 (s, 3H), 3.49 (ddd, *J*=9.1, 4.9, 3.7 Hz, 1H), 2.44 (sext, d, *J*=6.7, 1.2 Hz, 1H), 1.63-1.46 (m, 1H, exchangeable with D₂O), 1.56 (m, *J*=7.3, 3.7 Hz, 1H), 1.40 (hept, *J*=7.3 Hz, 1H), 1.09 (d, *J*=7.3 Hz, 3H); ms (*m/z*): 141 (M⁺-OMe), 114 (100%). Exact Mass Calcd for C₈H₁₃O₂ (M⁺-OMe): 141.0915. Found: 141.0925. The spectral data were identical with those of the natural origin² (2).

(3*S*,4*S*)-(E)-3-Benzoyloxy-7-benzoyloxy-4-methylhept-5-en-1-yne (24) — To a stirred solution of the eneyne (8) (49.3 mg, 0.21 mmol) in THF (2 ml) was added benzoic acid (34.0 mg, 0.28 mmol), triphenylphosphine (84.0 mg, 0.32 mmol), and diisopropyl azodicarboxylate (64.9 mg, 0.32 mmol) at 0 °C and the mixture was stirred for 35 min at the same temperature. After evaporation of the solvent under reduced pressure, the residue was purified on a silica gel column (15 g) using Et₂O-hexane (1:50 v/v ~ 1:15 v/v) as eluent to give the benzoate (24) (5.34 mg, 75%) as a colorless oil; bp 182 °C/0.04 Torr (Kugelrohr); [α]_D²⁵ -31.74° (*c* 1.01, CHCl₃). Ir (film) $\nu_{\max}$: 3290, 2130, 1720 cm⁻¹; ¹H nmr (CDCl₃) δ : 8.16-7.95 (m, 2H), 7.70-7.38 (m, 3H), 7.30 (s, 5H), 5.84-5.68 (m, 2H), 5.54 (dd, *J*=6.1, 2.2 Hz, 1H), 4.47 (s, 2H), 4.00 (m, 2H), 2.78 (m, 1H), 2.49 (d, *J*=2.2 Hz, 1H), 1.25 (d, *J*=6.8 Hz, 3H); ms (*m/z*): 334 (M⁺), 91 (100%). Exact Mass Calcd for C₂₂H₂₂O₃: 334.1568. Found: 334.1535. Anal. Calcd for C₂₂H₂₂O₃: C 79.01, H 6.63. Found: C 79.21, H 6.73.

(3*S*,4*S*)-(E)-7-Benzoyloxy-4-methylhept-5-en-1-yn-3-ol (25) — To a stirred solution of the benzoate (24) (2.78 g, 8.31 mmol) in MeOH (20 ml) was added K₂CO₃ (1.72 g, 12.5 mmol) at room temperature and the stirring was continued for 1 h at the same temperature. After evaporation of the solvent, the residue taken into Et₂O was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and

evaporated under reduced pressure. The residue was purified on a silica gel column (80 g) using Et₂O-hexane (1:4 v/v) as eluent to give the alcohol (**25**) (1.86 g, 97%) as a colorless oil; bp 162 °C/0.3 Torr (Kugelrohr); [α]_D²⁵ -15.38° (c 1.01, CHCl₃). Ir (film) $\nu_{\max}$: 3380, 3280, 2120 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.33 (s, 5H), 5.82-5.65 (m, 2H), 4.52 (s, 2H), 4.22 (dd, *J*=5.9, 2.2 Hz, 1H), 4.02 (m, 2H), 2.50 (m, 1H), 2.47 (d, *J*=2.2 Hz, 1H), 1.98 (br d, *J*=5.9 Hz, 1H, exchangeable with D₂O), 1.15 (d, *J*=6.8 Hz, 3H); ms (*m/z*): 230 (M⁺), 91 (100%). Exact Mass Calcd for C₁₅H₁₈O₂: 230.1307. Found: 230.1338. *Anal.* Calcd for C₁₅H₁₈O₂: C 78.23, H 7.88. Found: C 78.22, H 8.03.

(2*S*,3*S*,4*R*,5*R*)-5-Benzylloxymethyl-4-bromo-2-ethynyl-3-methyltetrahydrofuran

(26) — To a stirred suspension of the eneyne (**25**) (2.88 g, 12.5 mmol) and NaHCO₃ (10.5 g, 125 mmol) was added *N*-bromosuccinimide (2.67 g, 15 mmol) at room temperature and the stirring was continued for 1 h. The mixture was diluted with Et₂O and washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (150 g) using Et₂O-hexane (1:60~1:30 v/v) as eluent to give the bromo ether (**26**) (2.58 g, 66%) as a colorless oil. Ir (film) $\nu_{\max}$: 3200, 2140 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.33 (s, 5H), 4.68 (d, *J*=12.2 Hz, 1H), 4.52 (d, *J*=12.2 Hz, 1H), 4.37-4.14 (m, 2H), 3.90 (d, *J*=9.8 Hz, 1H), 3.77-3.63 (m, 2H), 2.79-2.32 (m, 1H), 2.54 (d, *J*=2.2 Hz, 1H), 1.22 (d, *J*=6.6 Hz, 3H); ms (*m/z*): 310, 308 (M⁺), 91 (100%). Exact Mass Calcd for C₁₅H₁₇O₂Br: 310.0391; 308.0411. Found: 310.0383; 308.0414.

(2*R*,3*S*,4*R*,5*R*)-5-Benzylloxymethyl-4-bromo-2-ethyl-3-methyltetrahydrofuran (**27**)

— A suspension of the bromoacetylene (**26**) (2.62 g, 8.5 mmol) and PtO₂ (79 mg) in hexane (10 ml) was hydrogenated under atmospheric pressure of hydrogen at room temperature for 2.5 h. The suspension was filtered and the filtrate was evaporated under reduced pressure to leave an oil which was purified on a silica gel column (80 g) using Et₂O-hexane (1:60 v/v) as eluent to give the saturated product (**27**) (2.12 g, 80%) as a colorless oil. Ir (film) $\nu_{\max}$: 1455, 1120, 1070, 740, 700 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.33 (s, 5H), 4.69 (d, *J*=12.2 Hz, 1H), 4.54 (d, *J*=12.2 Hz, 1H), 4.12 (ddd, *J*=8.8, 3.9, 2.7 Hz, 1H), 3.86 (d, *J*=9.8 Hz, 1H), 3.73-3.40 (m, 3H), 2.33-1.23 (m, 3H), 1.11 (d,

$J=6.6$ Hz, 3H), 0.98 (t, $J=7.6$ Hz, 3H); ms (m/z): 314, 312 (M^+), 112 (100%). Exact Mass Calcd for $C_{15}H_{21}O_2Br$: 314.0704; 312.0725. Found: 314.0688; 312.0706.

(3*R*,4*S*)-(E)-7-Benzoyloxy-4-methylhept-5-en-3-ol (28) — A suspension of the bromo ether (27) (2.08 g, 6.64 mmol) and zinc dust (2.17 g, 33.2 matom) in MeOH (5 ml) containing 35% hydrochloric acid (3 drops) was refluxed for 10 h. After filtration, the filtrate was evaporated under reduced pressure. The residue taken up into Et_2O , after filtration using Celite pad, was washed with saturated aqueous $NaHCO_3$, brine, and dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified on a silica gel column (80 g) using Et_2O -hexane (1:4 v/v) as eluent to give the enol (28) (1.53 g, 99%) as a colorless oil; $[\alpha]_D^{23} -12.62^\circ$ (c 1.01, $CHCl_3$). Ir (film) ν_{max} : 3450 cm^{-1} ; 1H nmr ($CDCl_3$) δ : 7.33 (s, 5H), 5.78-5.59 (m, 2H), 4.51 (s, 2H), 4.08-3.92 (m, 2H), 3.33 (m, 1H), 2.25 (m, 1H), 1.73-1.18 (m, 3H, 1H exchangeable with D_2O), 1.04 (d, $J=6.8$ Hz, 3H), 0.95 (t, $J=7.6$ Hz, 3H); ms (m/z): 234 (M^+), 68 (100%). Exact Mass Calcd for $C_{15}H_{22}O_2$ (M^+): 234.1620. Found: 234.1606.

(4*S*,5*R*)-(E)-1-Benzoyloxy-5-*tert*-butyldimethylsilyloxy-4-methyl-2-heptene (29) — A mixture of the enol (28) (1.23 g, 5.55 mmol), *tert*-butyldimethylsilyl chloride (1.67 g, 11.1 mmol), and imidazole (1.70 g, 24.97 mmol) in DMF (10 ml) was stirred at room temperature for 14 h. The mixture was diluted with Et_2O and was washed with saturated aqueous $NaHCO_3$, brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified on a silica gel column (80 g) using Et_2O -hexane (1:100 v/v) as eluent to give the silyl ether (29) (1.87 g, 97%) as a colorless oil; $[\alpha]_D^{23} -7.79^\circ$ (c 1.03, $CHCl_3$). Ir (film) ν_{max} : 1250, 1100, 835, 775, 735, 700 cm^{-1} ; 1H nmr ($CDCl_3$) δ : 7.33 (s, 5H), 5.88-5.35 (m, 2H), 4.50 (s, 2H), 3.99 (d, $J=4.6$ Hz, 2H), 3.46 (td, $J=6.1, 3.9$ Hz, 1H), 2.32 (m, 1H), 1.52-1.20 (m, 2H), 1.00 (d, $J=6.8$ Hz, 3H), 0.89 (s, 9H), 0.84 (t, $J=7.6$ Hz, 3H), 0.04 (s, 6H); ms (m/z): 319 ($M^+-C_2H_5$), 173 (100%). Exact Mass Calcd for $C_{19}H_{31}O_2Si$ ($M^+-C_2H_5$): 319.2093. Found: 319.2079.

(4*S*,5*R*)-(E)-5-*tert*-Butyldimethylsilyloxy-4-methyl-2-hepten-1-ol (30) — To a stirred solution of the benzyl ether (29) (1.83 g, 5.27 mmol) in THF (50 ml) and liquid NH_3 (50 ml) was added lithium (738 mg, 106.3 matom) portionwise. After

having faded blue color, MeOH (10 ml) was added to the mixture and NH_3 was evaporated at atmospheric pressure. The residue was diluted with dichloromethane and the solution was washed with brine, dried over MgSO_4 , and evaporated under reduced pressure. The residue was purified on a silica gel column (50 g) using Et_2O -hexane (1:4 v/v) as eluent to give the primary alcohol (30) (1.20 g, 89%) as a colorless oil; $[\alpha]_{\text{D}}^{24} -7.03^\circ$ (c 1.02, CHCl_3). Ir (film) ν_{max} : 3340 cm^{-1} ; ^1H nmr (CDCl_3) δ : 5.86-5.40 (m, 2H), 4.10 (br s, 2H), 3.45 (td, $J=6.1, 4.2$ Hz, 1H), 2.32 (m, 1H), 2.18-1.17 (m, 3H, 1H exchangeable with D_2O), 0.99 (d, $J=7.1$ Hz, 3H), 0.89 (s, 9H), 0.84 (t, $J=7.8$ Hz, 3H), 0.04 (s, 6H); ms (m/z): 229 ($\text{M}^+-\text{C}_2\text{H}_5$), 133 (100%). Exact Mass Calcd for $\text{C}_{12}\text{H}_{25}\text{O}_2\text{Si}$ ($\text{M}^+-\text{C}_2\text{H}_5$): 229.1624. Found: 229.1633.

(4*S*,5*R*)-(E)-5-tert-Butyldimethylsilyloxy-4-methylhept-2-en-1-al (31) — A suspension of the enol (30) (325.7 mg, 1.26 mmol) and MnO_2 (3.26 g) in CH_2Cl_2 (6 ml) was stirred at room temperature for 6 h. After filtration using Celite pad, the filtrate was evaporated under reduced pressure and the residue was purified on a silica gel column (5 g) using Et_2O -hexane (1:100 v/v) as eluent to give the aldehyde (31) (294.4 mg, 91%) as a colorless oil; $[\alpha]_{\text{D}}^{28} -10.05^\circ$ (c 1.01, CHCl_3). Ir (film) ν_{max} : 1692, 1630 cm^{-1} ; ^1H nmr (CDCl_3) δ : 9.51 (d, $J=7.8$ Hz, 1H), 6.89 (dd, $J=15.9, 7.8$ Hz, 1H), 6.10 (ddd, $J=15.9, 7.8, 1.0$ Hz, 1H), 3.57 (td, $J=6.1, 4.2$ Hz, 1H), 2.61 (m, 1H), 1.68-1.19 (m, 2H), 1.10 (d, $J=6.8$ Hz, 3H), 0.90 (s, 9H), 0.86 (t, $J=7.8$ Hz, 3H), 0.06 (s, 6H); ms (m/z): 256 (M^+), 78 (100%). Exact Mass Calcd for $\text{C}_{14}\text{H}_{28}\text{O}_2\text{Si}$: 256.1858. Found: 256.1869.

Methyl (4*S*,5*R*)-(E)-5-tert-Butyldimethylsilyloxy-4-methyl-2-heptenoate (32) — A suspension of the aldehyde (31) (198.7 mg), MnO_2 (2.0 g), and NaCN (190.2 mg, 3.88 mmol) in MeOH (3 ml) containing acetic acid (0.04 ml, 1.17 mmol) was stirred at room temperature for 2 h. After filtration using Celite pad, the filtrate was washed with saturated aqueous NaHCO_3 , brine, dried over brine, and evaporated under reduced pressure. The residue was purified on a silica gel column (5 g) using Et_2O -hexane (1:100 v/v) as eluent to give the ester (32) (185.5 mg, 73%) as a colorless oil; $[\alpha]_{\text{D}}^{28} -16.27^\circ$ (c 1.02, CHCl_3). Ir (film) ν_{max} : 1730, 1655 cm^{-1} ; ^1H nmr (CDCl_3) δ : 6.98

(dd, $J=15.9$, 7.8 Hz, 1H), 5.80 (dd, $J=15.9$, 1.2 Hz, 1H), 3.73 (s, 3H), 3.53 (td, $J=5.9$, 4.6 Hz), 2.48 (m, 1H), 1.70-1.22 (m, 2H), 1.04 (d, $J=6.8$ Hz, 3H), 0.89 (s, 9H), 0.85 (t, $J=7.8$ Hz, 3H), 0.04 (s, 6H); ms (m/z): 285 (M^+-1), 73 (100%). Exact Mass Calcd for $C_{15}H_{29}O_3Si$ (M^+-1): 285.1886. Found: 285.1849.

Methyl (4*S*,5*R*)-(E)-5-Hydroxy-4-methyl-2-heptanoate (Methyl Mycinonate I) (3) —

— To a stirred solution of the silyl ether (32) (137.4 mg, 0.48 mmol) in MeOH (2 ml) was added 35% hydrochloric acid (3 drops) at room temperature and the stirring was continued for 4 h at the same temperature. After evaporation of the solvent under reduced pressure, the residue taken up into Et₂O was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (5 g) using Et₂O-hexane (1:4 v/v) as eluent to give the 'C₁₁₋₁₇' precursor (3) (78.4 mg, 95%) as a colorless oil; $[\alpha]_D^{24}$ -8.10° (c 0.94, MeOH) [lit.^{2b} $[\alpha]_D$ -8.1° (c 0.94, MeOH)]. Ir (film) $\nu_{\max}$: 3450, 1730, 1710, 1660 cm⁻¹; ¹H nmr (CDCl₃) δ : 6.98 (dd, $J=15.9$, 8.6 Hz, 1H), 5.88 (dd, $J=15.9$, 1.2 Hz, 1H), 3.74 (s, 3H), 3.47 (quint, $J=4.5$ Hz, 1H), 2.43 (m, $J=6.5$, 1.2 Hz, 1H), 1.65-1.50 (m, 1H, exchangeable with D₂O), 1.55 (m, $J=7.3$, 4.3 Hz, 1H), 1.43 (hept, $J=7.3$ Hz, 1H), 1.11 (d, $J=6.7$ Hz, 3H), 0.97 (t, $J=7.3$ Hz, 3H); ms (m/z): 155 (M^+-OH), 114 (100%). Exact Mass Calcd for $C_9H_{15}O_2$ (M^+-OH): 155.1072. Found: 155.1055. Spectral data were identical with those of the natural origin² (3).

Methyl (6*S*,7*R*)-(2*E*,4*E*)-7-*tert*-Butyldimethylsilyloxy-6-methylnona-2,4-dienoate (33) —

— To a stirred solution of methyl diisopropylphosphonoacetate (1.35 ml, 5.81 mmol) in THF (6 ml) and potassium *tert*-butoxide (495.5 mg) was added the aldehyde (31) (697.4 mg, 3.16 mmol) in THF (2 ml) at -30°C and the stirring was continued for 1 h at the same temperature. The mixture was treated with saturated aqueous NaHCO₃ (8 ml) and the mixture was extracted with Et₂O. The extract was washed with brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (25 g) using Et₂O-hexane (1:100 v/v) as eluent to give the ester (33) (551.1 mg, 79%) as a pale yellow oil; $[\alpha]_D^{26}$ -18.04° (c 1.02, CHCl₃). Ir (film) $\nu_{\max}$: 1727, 1645, 1620 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.45-7.12 (m,

1H), 6.65-6.24 (m, 2H), 5.79 (d, $J=15.4$ Hz, 1H), 3.74 (s, 3H), 3.49 (td, $J=5.9$, 3.9 Hz, 1H), 2.42 (m, 1H), 1.54-1.18 (m, 2H), 1.03 (d, $J=6.8$ Hz, 3H), 0.89 (s, 9H), 0.84 (t, $J=7.6$ Hz, 3H), 0.04 (s, 6H); ms (m/z): 311 (M^+-1), 73 (100%). Exact Mass Calcd for $C_{17}H_{31}O_3Si$ (M^+-1): 311.2043. Found: 311.2019.

Methyl (6*S*,7*R*)-(2*E*,4*E*)-7-Hydroxy-6-methylnonan-2,4-dienoate (Methyl Mycinonate II) (4) —

To a stirred solution of the silyl ether (33) (25.8 mg, 0.08 mmol) in MeOH (2 ml) was added 35% hydrochloric acid (2 drops) at room temperature and the stirring was continued for 5 h at the same temperature. After evaporation of the solvent under reduced pressure, the residue taken up into Et₂O was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (5 g) using Et₂O-hexane (1:4 v/v) as eluent to give the 'C₁₁₋₁₇' precursor (4) (16.0 mg, 98%) as a colorless oil; $[\alpha]_D^{24} -14.03^\circ$ (c 1.04, MeOH) [lit.,^{2b} $[\alpha]_D^{25} -5.2^\circ$ (c 1.00, MeOH)]. Ir (film) $\nu_{\max}$: 3450, 1720, 1705, 1640, 1620, cm⁻¹; ¹H nmr (CDCl₃) δ : 7.28 (dd, $J=15.3$, 10.4 Hz, 1H), 6.23 (dd, $J=15.3$, 10.4 Hz, 1H), 6.11 (dd, $J=15.3$, 7.9 Hz, 1H), 5.83 (d, $J=15.3$ Hz, 1H), 3.74 (s, 3H), 3.42 (ddd, $J=8.5$, 4.9, 4.3 Hz, 1H), 2.37 (sext, $J=7.3$ Hz, 1H), 1.64-1.50 (m, 1H, exchangeable with D₂O), 1.55 (m, $J=7.4$, 4.3 Hz, 1H), 1.41 (m, $J=7.3$, 4.3 Hz, 1H), 1.41 (hept, $J=7.3$ Hz, 1H), 1.09 (d, $J=6.7$ Hz, 3H), 0.96 (t, $J=7.3$ Hz, 3H); ms (m/z): 199 (M^+-1), 140 (100%). Spectral data were identical with those of the natural origin² (4).

(6*S*,7*R*)-(2*E*,4*E*)-7-*tert*-Butyldimethylsilyloxy-6-methylnonan-2,4-dien-1-ol (34) —

To a stirred solution of the ester (33) (217.9 mg, 0.70 mmol) in THF (4 ml) was added diisobutylaluminum hydride (0.76 M in toluene) (4.6 ml, 3.50 mmol) at 0 °C and the stirring was continued for 30 min at the same temperature. The mixture was treated with 30% NH₄OH and the mixture was diluted with Et₂O. The organic layer was separated, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (5 g) using Et₂O-hexane (1:10 v/v) as eluent to give the primary alcohol (34) (194.6 mg, 98%) as a colorless oil; $[\alpha]_D^{28} -9.82^\circ$ (c 1.02, CHCl₃). Ir (film) $\nu_{\max}$: 3330 cm⁻¹; ¹H nmr (CDCl₃) δ : 6.42-5.50 (m, 4H), 4.30-4.06 (m, 2H), 3.45 (td, $J=6.1$, 4.2 Hz, 1H), 2.34 (m, 1H), 1.60-1.17 (m, 3H, 1H

exchangeable with D₂O), 0.99 (d, $J=6.8$ Hz, 3H), 0.89 (s, 9H), 0.84 (t, $J=7.8$ Hz, 3H), 0.04 (s, 6H); ms (m/z): 283 (M^+-1), 73 (100%). Exact Mass Calcd for C₁₆H₃₁O₂Si (M^+-1): 283.2093. Found: 283.2082.

(6*S*,7*R*)-(2*E*,4*E*)-7-*tert*-Butyldimethylsilyloxy-6-methylnona-2,4-dien-1-al (35) ———

A suspension of the alcohol (34) (164.5 mg, 0.58 mmol) and MnO₂ (1.65 g) in CH₂Cl₂ (5 ml) was stirred at room temperature for 2 h. After filtration using Celite pad, the filtrate was evaporated under reduced pressure and the residue was purified on a silica gel column (5 g) using Et₂O-hexane (1:100 v/v) as eluent to give the aldehyde (35) (139.1 mg, 85%) as a colorless oil; $[\alpha]_D^{28}$ -14.73° (c 1.02, CHCl₃). Ir (film) $\nu_{\max}$: 1690, 1640, 1600 cm⁻¹; ¹H nmr (CDCl₃) δ : 9.55 (d, $J=7.8$ Hz, 1H), 7.23-6.94 (m, 1H), 6.38-6.20 (m, 2H), 6.08 (dd, $J=15.1, 7.8$ Hz, 1H), 3.52 (td, $J=6.1, 4.2$ Hz, 1H), 2.48 (m, 1H), 1.56-1.22 (m, 2H), 1.06 (d, $J=6.8$ Hz, 3H), 0.90 (s, 9H), 0.86 (t, $J=7.6$ Hz, 3H), 0.05 (s, 6H); ms (m/z): 281 (M^++1), 73 (100%). Exact Mass Calcd for C₁₆H₂₉O₂Si (M^++1): 281.1937. Found: 281.1937.

(2*RS*,8*S*,9*R*)-(4*E*,6*E*)-9-*tert*-Butyldimethylsilyloxy-8-methylundeca-4,6-dien-3-ol

(36) ——— To a stirred solution of the aldehyde (35) (102.3 mg, 0.36 mmol) in THF (3 ml) was added ethylmagnesium bromide (2.27 M in THF) (0.32 ml, 0.73 mmol) at -30°C . After 10 min saturated aqueous NH₄Cl was added to the mixture with stirring. The mixture was extracted with Et₂O and the extract was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (5 g) using Et₂O-hexane (1:10 v/v) as eluent to give the secondary alcohol (36) (104.2 mg, 92%) as a colorless oil. Ir (film) $\nu_{\max}$: 3340 cm⁻¹; ¹H nmr (CDCl₃) δ : 6.37-5.93 (m, 4H), 4.05 (br q, $J=6.7$ Hz, 1H), 3.45 (td, $J=6.1, 4.2$ Hz, 1H), 2.53-2.11 (m, 1H), 1.78-1.21 (m, 5H, 1H exchangeable with D₂O), 1.08-0.72 (m, 9H), 0.89 (s, 9H), 0.04 (s, 6H); ms (m/z): 283 ($M^+-\text{C}_2\text{H}_5$), 173 (100%). Exact Mass Calcd for C₁₆H₃₁O₂Si ($M^+-\text{C}_2\text{H}_5$): 283.2094. Found: 283.2097.

(8*S*,9*R*)-(4*E*,6*E*)-9-*tert*-Butyldimethylsilyloxy-8-methylundecan-4,6-dien-3-one (37)

——— A suspension of the secondary alcohol (36) (256.2 mg, 0.82 mmol) and MnO₂ (2.56 g) in CH₂Cl₂ (10 ml) was stirred at room temperature for 2 h. The mixture,

after filtration using Celite pad, was evaporated under reduced pressure and the residue was purified on a silica gel column (10 g) using Et₂O-hexane (1:100 v/v) as eluent to give the ketone (37) (221.2 mg, 87%) as a colorless oil; $[\alpha]_{\text{D}}^{25} -18.57^\circ$ (*c* 1.01, CHCl₃). Ir (film) ν_{max} : 1690, 1670, 1635, 1600 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.32-6.99 (m, 1H), 6.37-5.92 (m, 3H), 3.49 (td, *J*=6.1, 4.2 Hz, 1H), 2.66-2.18 (m, 1H), 2.58 (q, *J*=7.3 Hz, 2H), 1.54-0.68 (m, 11H), 0.89 (s, 9H), 0.04 (s, 6H); ms (*m/z*): 295 (M⁺-CH₃), 73 (100%). Exact Mass Calcd for C₁₇H₃₁O₂Si (M⁺-CH₃): 295.2094. Found: 295.2095.

(8*S*,9*R*)-(4*E*,6*E*)-9-Hydroxy-8-methylundecan-4,6-dien-3-one (Decarboxymycinonic Acid III) (5) — To a stirred solution of the silyl ether (37) (74.9 mg, 0.24 mmol) in MeOH (2 ml) was added 35% hydrochloric acid (3 drops) at room temperature and the stirring was continued for 3 h at the same temperature. After evaporation of the solvent under reduced pressure, the residue taken up into Et₂O was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (5 g) using Et₂O-hexane (1:4 v/v) as eluent to give the 'C₈₋₁₇' precursor (5) (43.3 mg, 91%) as a colorless oil; $[\alpha]_{\text{D}}^{27} -8.90^\circ$ (*c* 0.78, MeOH) [lit.,^{2b} $[\alpha]_{\text{D}}^{25} -6.3^\circ$ (*c* 0.86, MeOH)]. Ir (film) ν_{max} : 3450, 1685, 1660, 1630, 1595 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.15 (dd, *J*=15.9, 9.1 Hz, 1H), 6.24 (dd, *J*=15.3, 10.4 Hz, 1H), 6.15 (dd, *J*=15.3, 7.9 Hz, 1H), 6.12 (d, *J*=15.9 Hz, 1H), 3.43 (quint, *J*=4.3 Hz, 1H), 2.58 (q, *J*=7.3 Hz, 2H), 2.38 (sext, *J*=6.7 Hz, 1H), 1.66-1.50 (m, 1H, exchangeable with D₂O), 1.55 (m, d, *J*=7.3, 4.3 Hz, 1H), 1.42 (hept, *J*=7.3 Hz, 1H), 1.11 (t, *J*=7.3 Hz, 3H), 1.10 (d, *J*=6.7 Hz, 3H), 0.97 (t, *J*=7.3 Hz, 3H); ms (*m/z*): 197 (M⁺+1), 109 (100%). Exact Mass Calcd for C₁₂H₂₁O₂ (M⁺+1): 197.1542. Found: 197.1516. Spectral data were identical with those of the natural origin² (5).

(4*R*,5*S*)-(2*Z*,6*E*)-8-Benzoyloxy-4-hydroxy-5-methyl-2,6-octadienoic Acid Lactone (42) from the Eneyne (8) — To a stirred solution of the eneyne (8) (100 mg, 0.44 mmol) in THF (3 ml) was treated with *n*-butyllithium (1.57 M in hexane) (0.67 ml, 1.04 mmol) at -30 °C for 15 min, then CO₂ was introduced for 40 min at the same temperature. The mixture was treated with brine (5 ml) and the aqueous layer was

separated. After washing with Et₂O, the aqueous layer was made acidic by addition of 35% hydrochloric acid and was extracted with Et₂O. The extract was dried over MgSO₄ and evaporated under reduced pressure to give the crude acid (**38**) (96.2 mg) which was used for the next reaction without purification.

The crude acid (**38**) (96.2 mg) was hydrogenated in ethyl acetate (1 ml) under atmospheric pressure in the presence of Lindlar catalyst (5 mg) at room temperature for 16 h to give the crude (*Z*)-olefinic acid (**40**) (96.1 mg), after evaporation of the solvent under reduced pressure, which was used for the next reaction without purification.

A solution of the crude acid (**40**) (96.1 mg) in benzene (2 ml) was refluxed using a Dean-Stark apparatus for 16.5 h. The mixture was diluted with Et₂O and washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (4 g) using Et₂O-hexane (1:4 v/v) as eluent to give the butenolide (**42**) (45.1 mg, 40% overall from **8**) as a colorless oil; $[\alpha]_D^{26} -99.8^\circ$ (*c* 1.01, CHCl₃). Ir (film) $\nu_{\max}$: 1790, 1760 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.42 (dd, *J*=5.7, 1.4 Hz, 1H), 7.33 (s, 5H), 6.12 (dd, *J*=5.7, 2.0 Hz, 1H), 5.79-5.58 (m, 2H), 4.50 (s, 2H), 3.98 (d, *J*=4.9 Hz, 2H), 2.78-2.30 (m, 1H), 1.14 (d, *J*=7.1 Hz, 3H); ms (*m/z*): 259 (*M*⁺+1), 91 (100%). Anal. Calcd for C₁₈H₁₈O₃: C 74.39, H 7.02. Found: C 74.31, H 7.22.

Methyl (4*R*,5*S*)-(E)-8-Benzyloxy-4-*tert*-butyldimethylsilyloxy-5-methyl-oct-6-en-2-ynoate (**41**) ——— A mixture of the eneyne (**8**) (2.10 g, 9.55 mmol) *tert*-butyldimethylsilyl chloride (2.67 g, 17.7 mmol), and imidazole (2.80 ml, 41.3 mmol) in DMF (30 ml) was stirred at room temperature for 12 h. The mixture was diluted with Et₂O and was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (60 g) using Et₂O-hexane (1:30 v/v) as eluent to give the silyl ether of **8** (2.96 g, 93%); bp 190-200 °C/0.4 Torr (Kugelrohr); $[\alpha]_D^{24} +17.61^\circ$ (*c* 0.99, CHCl₃). Ir (film) $\nu_{\max}$: 3320 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.32 (s, 5H), 5.80-5.60 (m, 2H), 4.50 (s, 2H), 4.21 (dd, *J*=5.6, 2.2 Hz, 1H), 4.01 (d, *J*=4.6 Hz, 2H), 2.40 (m, 1H), 2.38 (d, *J*=2.2 Hz, 1H),

1.10 (d, $J=6.8$ Hz, 3H), 0.90 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H); ms (m/z): 344 (M^+), 75 (100%).

To a stirred solution of the above silyl ether (5.40 g, 15.7 mmol) in THF (100 ml) was treated with *n*-butyllithium (1.6 M in hexane) (12.5 ml, 20.0 mmol) at -78 °C for 30 min, then methyl chloroformate (1.80 ml, 23.6 mmol) was added at -50 °C and the mixture was stirred for 30 min. The mixture was treated with saturated aqueous NH_4Cl (30 ml) and extracted with Et_2O . The extract was washed with saturated aqueous $NaHCO_3$, brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified on a silica gel column (210 g) using Et_2O -hexane (1:20 v/v) as eluent to give the ester (**39**) (5.77 g, 92%) as a pale yellow oil; bp 175 °C/0.5 Torr (Kugelrohr); $[\alpha]_D^{25} +21.75^\circ$ (c 1.00, $CHCl_3$). Ir (film) ν_{max} : 2325 , 1730 cm^{-1} ; 1H nmr ($CDCl_3$) δ : 7.33 (s, 5H), 5.70 (m, 2H), 4.50 (s, 2H), 4.32 (d, $J=5.6$ Hz, 1H), 4.04 (m, 2H), 3.74 (s, 3H), 2.50 (m, 1H), 1.11 (d, $J=6.8$ Hz, 3H), 0.90 (s, 9H), 0.15 (s, 3H), 0.10 (s, 3H); ms (m/z): 402 (M^+), 91 (100%). Anal. Calcd for $C_{23}H_{34}O_4Si$: C 68.62, H 8.51. Found: C 68.43, H 8.47.

Methyl (4*R*,5*S*)-(2*Z*,6*E*)-8-Benzyloxy-4-*tert*-butyldimethylsilyloxy-5-methylocta-2,6-dienolate (41) — A suspension of the acetylene (**39**) (5.70 g, 14.18 mmol) and Lindlar catalyst (219 mg) in benzene (200 ml) containing quinoline (0.8 ml) was hydrogenated under atmospheric pressure at room temperature for 12 h. After filtration using Celite pad, the filtrate was evaporated under reduced pressure and the residue was purified on a silica gel column (180 g) using Et_2O -hexane (1:20 v/v) as eluent to give the (*Z*)-olefin (**41**) (5.58 g, 97%) as a colorless oil; bp 175 - 185 °C/0.5 Torr (Kugelrohr); $[\alpha]_D^{25} -5.39^\circ$ (c 1.04, $CHCl_3$). Ir (film) ν_{max} : 1725 cm^{-1} ; 1H nmr ($CDCl_3$) δ : 7.32 (s, 5H), 6.07 (dd, $J=11.7$, 8.3 Hz, 1H), 5.81-5.58 (m, 3H), 5.27 (dd, $J=8.3$, 5.6 Hz, 1H), 4.47 (s, 2H), 3.97 (d, $J=4.9$ Hz, 2H), 3.69 (s, 3H), 2.42 (m, 1H), 1.03 (d, $J=6.8$ Hz, 3H), 0.87 (s, 9H), 0.04 (s, 3H); ms (m/z): 404 (M^+), 229 (100%). Anal. Calcd for $C_{23}H_{36}O_4Si$: C 68.27, H 8.97. Found: C 68.07, H 9.08.

(4*R*,5*S*)-(2*Z*,6*E*)-8-Benzyloxy-4-hydroxy-5-methylocta-2,6-dienoic Acid Lactone (42) from the Silyl Ether (41) — To a stirred solution of the silyl ether (**41**) (5.50 g, 13.6

mmol) in MeOH (140 ml) was added 35% hydrochloric acid (14 ml) at room temperature and the stirring was continued for 30 min at the same temperature. The mixture was diluted with Et₂O and washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (150 g) using Et₂O-hexane (1:2 v/v) as eluent to give the butenolide (42) (3.20 g, 90%), as a colorless oil, which was identical with the material described above.

(3S,4S,5S)-(E)-8-Benzyloxy-4-hydroxy-3,5-dimethyloct-6-enoic Acid Lactone (43) —

— To a stirred suspension of CuI (100 mg, 0.52 mmol) in Et₂O (1 ml) was added methyllithium (1.09 M in Et₂O) (0.96 ml, 1.05 mmol) at 0 °C. After 1.5 h at the same temperature, to this mixture was added the butenolide (42) (45.1 mg, 0.18 mmol) in Et₂O (1 ml) at the same temperature. After 10 min, the mixture was diluted with Et₂O and was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (3 g) using Et₂O-hexane (1:4 v/v) as eluent to give the δ -lactone (43) (31.1 mg, 65%) as a colorless oil; $[\alpha]_D^{24}$ -3.03° (c 1.32, CHCl₃). Ir (film) $\nu_{\max}$: 1780 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.32 (s, 5H), 5.77-5.56 (m, 2H), 4.53 (s, 2H), 4.07-3.80 (m, 3H), 2.85-1.94 (m, 4H), 1.14 (d, $J=5.8$ Hz, 3H), 1.13 (d, $J=6.5$ Hz, 3H); ms (m/z): 274 (M⁺), 91 (100%). Exact Mass Calcd for C₁₅H₁₈O₂ (M⁺+1): 275.1648. Found: 275.1653. Anal. Calcd for C₁₅H₁₈O₂: C 74.42, H 8.08. Found: C 74.26, H 8.08.

(3S,4S,5S)-(E)-4-Hydroxy-8-iodo-3,5-dimethyloct-6-enoic Acid Lactone (44) —

To a stirred solution of the benzyloxylactone (43) (200 mg, 0.73 mmol) and NaI (543 mg, 3.6 mmol) in CH₂Cl₂-MeCN (2:1) (7 ml) was added trimethylsilyl chloride (0.46 ml, 3.6 mmol) at 0 °C and the stirring was continued for 4 h at room temperature. The mixture was treated with saturated aqueous NaHCO₃ (3 ml) and extracted with Et₂O. The extract was washed with 2% aqueous Na₂S₂O₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (10 g) using AcOEt:hexane (1:15 v/v) as eluent to give the iodide (44) (204 mg, 95%) as a pale yellow oil; $[\alpha]_D^{23}$ $+2.15^\circ$ (c 0.74, CHCl₃). Ir (film) $\nu_{\max}$: 1770 cm⁻¹,

^1H nmr (CDCl_3) δ : 5.87 (dt, $J=15.1$, 7.1 Hz, 1H), 5.57 (dd, $J=15.1$, 7.1 Hz, 1H), 4.00-3.77 (m, 1H), 3.86 (d, $J=7.1$ Hz, 2H), 2.92-1.98 (m, 4H), 1.14 (d, $J=6.6$ Hz, 3H), 1.10 (d, $J=6.8$ Hz, 3H); ms (m/z): 295 (M^++1), 167 (100%). Exact Mass Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_2\text{I}$ (M^++H): 295.0195. Found: 295.0170.

(3*S*,4*S*,5*S*)-(E)-4,8-Dihydroxy-3,5-dimethyloct-6-enoic Acid Lactone (45) — A solution of the iodide (44) (204 mg, 0.69 mmol) and NaHCO_3 (1.0 g, 13.8 mmol) in 50% aqueous THF (20 ml) was stirred at room temperature for 4 days. The mixture was extracted with AcOEt and the extract was washed with 2% aqueous $\text{Na}_2\text{S}_2\text{O}_3$, brine, dried over MgSO_4 , and evaporated under reduced pressure. The residue was purified on a silica gel column (5 g) using Et_2O -hexane (1:1 v/v) as eluent to give the primary alcohol (45) (92 mg, 72%) as a pale yellow oil; $[\alpha]_{\text{D}}^{30} +5.66^\circ$ (c 0.99, CHCl_3). Ir (film) ν_{max} : 3400, 1760 cm^{-1} ; ^1H nmr (CDCl_3) δ : 5.96-5.41 (m, 2H), 4.12 (d, $J=4.2$ Hz, 2H), 3.92 (t, $J=5.9$ Hz, 1H), 2.86-1.98 (m, 4H), 1.60 (br s, 1H, exchangeable with D_2O), 1.13 (d, $J=5.9$ Hz, 3H), 1.11 (d, $J=6.6$ Hz, 3H); ms (m/z): 185 (M^++1), 99 (100%). Exact Mass Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_3$ (M^++H): 184.1090. Found: 184.1095.

(3*S*,4*S*,5*S*)-(E)-8-Benzyloxymethoxy-4-hydroxy-3,5-dimethyloct-6-enoic Acid Lactone (46) — A mixture of the primary alcohol (45) (44.8 mg, 0.24 mmol), benzyloxymethyl chloride (0.07 ml, 0.49 mmol), and (*i*-Pr) $_2\text{NEt}$ (0.17 ml, 0.98 mmol) in CH_2Cl_2 (1.5 ml) was stirred at room temperature for 12 h. The mixture was diluted with Et_2O and washed with 5% hydrochloric acid, saturated aqueous NaHCO_3 , brine, and dried over MgSO_4 . After evaporation the solvent under reduced pressure, the residue was purified on a silica gel column (6 g) using Et_2O -hexane (1:2 v/v) as eluent to give the ether (46) (60.0 mg, 81%) as a colorless oil; $[\alpha]_{\text{D}}^{23} -2.46^\circ$ (c 0.81, CHCl_3). Ir (film) ν_{max} : 1780 cm^{-1} ; ^1H nmr (CDCl_3) δ : 7.34 (s, 5H), 5.77-5.56 (m, 2H), 4.77 (s, 2H), 4.61 (s, 2H), 4.18-4.02 (m, 2H), 3.92 (t, $J=6.1$ Hz, 1H), 2.84-1.95 (m, 4H), 1.10 (d, $J=6.8$ Hz, 6H); ms (m/z): 305 (M^++1), 91 (100%). Anal. Calcd for $\text{C}_{18}\text{H}_{24}\text{O}_4$: C 71.02, H 7.95. Found: C 70.93, H 8.12.

N-[(3*S*,4*S*,5*S*)-(E)-8-Benzyloxymethoxy-4-hydroxy-3,5-dimethyloct-6-enoyl]-pyrrolidine (47) — To a stirred solution of pyrrolidine (0.46 ml) in benzene (7.64

ml) was added Et_3Al (19% solution in hexane, 5 mmol) (1.9 ml) dropwise at room temperature. This complex (1 ml, 0.5 mmol) was then added to a solution of the lactone (**46**) (34.5 mg, 0.11 mmol) in benzene (1 ml) at 5 °C with stirring. After stirring for 1 h at the same temperature, the mixture was treated with saturated aqueous NH_4Cl (2 ml) and extracted with AcOEt . The extract was washed with saturated aqueous NaHCO_3 , brine, dried over MgSO_4 , and evaporated reduced pressure. The residue was purified on a silica gel column (5 g) using AcOEt -hexane (3:1 v/v) as eluent to give the amide alcohol (**47**) (41.1 mg, 97%) as a colorless oil; $[\alpha]_{\text{D}}^{29} +11.76^\circ$ (*c* 0.88, CHCl_3). Ir (film) ν_{max} : 3380, 1610 cm^{-1} ; ^1H nmr (CDCl_3) δ : 7.30 (s, 5H), 5.98-5.39 (m, 2H), 4.75 (s, 2H), 4.60 (s, 2H), 4.09 (d, $J=5.1$ Hz, 2H), 3.58-3.10 (m, 5H), 2.70-1.60 (m, 9H, exchangeable with D_2O), 1.07 (d, $J=6.6$ Hz, 3H), 0.98 (d, $J=5.7$ Hz, 3H); ms (*m/z*): 375 (M^+), 70 (100%). Exact Mass Calcd for $\text{C}_{22}\text{H}_{33}\text{NO}_4$: 375.2409. Found: 375.2408. Anal. Calcd for $\text{C}_{22}\text{H}_{23}\text{NO}_4$: C 70.35, H 8.86, N 3.73. Found: C 69.94, H 8.74, N 3.95.

N-[*(3S,4S,5S)*-(*E*)Benzyloxymethoxy-4-*tert*-butyldimethylsilyloxy-3,5-dimethyloct-6-enoyl]pyrrolidine (**48**) — A mixture of the alcohol (**47**) (38.4 mg, 0.10 mmol), *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.05 ml, 0.03 mmol) and 2,6-lutidine (0.05 ml, 0.41 mmol) was stirred at room temperature for 10 min and the mixture was treated with saturated aqueous NaHCO_3 (2 ml) and extracted with Et_2O . The extract was washed with 5% hydrochloric acid, saturated aqueous NaHCO_3 , brine, dried over MgSO_4 , and evaporated under reduced pressure. The residue was purified on a silica gel column (5 g) using Et_2O -hexane (1:3 v/v) as eluent to give the silyl ether (**48**) (34.0 mg, 68%) as a colorless oil accompanied by the lactone (**46**) (6.3 mg, 26%); $[\alpha]_{\text{D}}^{24} -21.25^\circ$ (*c* 0.89, CHCl_3). Ir (film) ν_{max} : 1640 cm^{-1} ; ^1H nmr (CDCl_3) δ : 7.34 (s, 5H), 5.93-5.34 (m, 2H), 4.76 (s, 2H), 4.61 (s, 2H), 4.07 (d, $J=5.2$ Hz, 2H), 3.58-3.23 (m, 5H), 2.60-1.65 (m, 8H), 1.10-0.85 (m, 6H), 0.92 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ms (*m/z*): 489 (M^+), 284 (100%). Exact Mass Calcd for $\text{C}_{28}\text{H}_{47}\text{NO}_4\text{Si}$: 489.3280. Found: 489.3274. Anal. Calcd for $\text{C}_{24}\text{H}_{47}\text{NO}_4\text{Si}$: C 68.67, H 9.68, N 2.86. Found: C 68.93, H 9.79, N 2.99.

(4*S*,5*S*,6*S*)-(E)-9-Benzoyloxymethoxy-5-*tert*-butyldimethylsilyloxy-4,6-dimethylnon-7-enyl-2-one (The Suzuki-Tsuchihashi C₁₋₈ Segment) (6) — To a stirred solution of the amide (48) (32.1 mg, 0.07 mmol) in THF (1 ml) was added methyllithium (1.4 M in THF) (0.1 ml, 0.13 mmol) at -78 °C and the stirring was continued for 45 min. The mixture was treated with saturated aqueous NH₄Cl (1 ml) and extracted with Et₂O. The extract was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (5 g) using Et₂O-hexane (1:5 v/v) as eluent to give the ketone (6) as a colorless oil; $[\alpha]_D^{20}$ -8.79° (*c* 0.91, CHCl₃) [lit.^{2b} $[\alpha]_D^{32}$ -9.2° (*c* 1.1, CHCl₃)]. Ir (film) $\nu_{\max}$: 1770 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.35-7.27 (m, 5H), 5.71 (dd, *J*=15.3, 7.6 Hz, 1H), 5.54 (dtd, *J*=15.3, 6.1, 1.2 Hz, 1H), 4.77 (s, 2H), 4.61 (s, 2H), 4.08 (d, *J*=6.1 Hz, 2H), 3.37 (dd, *J*=5.5, 3.7 Hz, 1H), 2.66 (dd, *J*=15.9, 2.4 Hz, 1H), 2.35 (sext, *J*=6.7 Hz, 1H), 2.20 (m, 1H), 2.15 (dd, *J*=15.9, 9.8 Hz, 1H), 2.09 (s, 3H), 1.01 (d, *J*=6.7 Hz, 3H), 0.91 (s, 9H), 0.89 (d, *J*=6.7 Hz, 3H), 0.06 (s, 3H), 0.05 (s, 3H); ms (*m/z*): 349 (M⁺-C₅H₉O), 229 (100%). Spectral data were virtually identical with those reported by Suzuki and Tsuchihashi.⁶

(3*R*,4*S*)-(E)-7-Benzoyloxymethoxy-3-*tert*-butyldimethylsilyloxy-4-methyl-hept-5-ene (49) — A mixture of the alcohol (30) (152.3 mg, 0.59 mmol), benzyloxymethyl chloride (0.25 ml, 1.77 mmol), and ethyldiisopropylamine (0.51 ml, 2.95 mmol) in CH₂Cl₂ (3 ml) was stirred at room temperature for 11.5 h. The mixture diluted with ether was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (15 g) using Et₂O-hexane (1:100 v/v) as eluent to give the silyl ether (49) (223.1 mg, 100%) as a colorless oil; $[\alpha]_D^{29}$ -3.59° (*c* 1.00, CHCl₃). Ir (film) $\nu_{\max}$: 1250, 1100, 855, 770, 695 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.34 (s, 5H), 5.88-5.33 (m, 2H), 4.77 (s, 2H), 4.62 (s, 2H), 4.08 (d, *J*=5.1 Hz, 2H), 3.45 (td, *J*=5.9, 4.2 Hz, 1H), 2.32 (m, 1H), 1.51-1.21 (m, 2H), 0.99 (d, *J*=6.8 Hz, 3H), 0.89 (s, 9H), 0.84 (t, *J*=7.6 Hz, 3H), 0.03 (s, 6H); ms (*m/z*): 349 (M⁺-C₂H₅), 173 (100%). Exact Mass Calcd for C₂₀H₂₃O₂Si (M⁺-C₂H₅): 349.2199. Found: 349.2220.

(3R,4S)-(E)-7-Benzoyloxymethoxy-4-methylhept-5-en-1-ol (The Suzuki-Tsuchihashi C₁₁₋₁₇ Segment) (7) — A mixture of the bis-ether (49) (174.0 mg, 0.46 mmol) and tetra-*n*-butylammonium fluoride (1 M in THF) (1.84 ml, 1.84 mmol) in THF (3 ml) was stirred at room temperature for 19.5 h. The mixture diluted with Et₂O was washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, and evaporated under reduced pressure. The residue was purified on a silica gel column (8 g) using Et₂O-hexane (1:4 v/v) as eluent to give the secondary alcohol (7) (92.2 mg, 80%) as a colorless oil; $[\alpha]_{\text{D}}^{30} -9.75^\circ$ (*c* 1.30, CHCl₃) [lit.^{2b} $[\alpha]_{\text{D}}^{21} -9.6^\circ$ (*c* 1.3, CHCl₃)]. Ir (film) ν_{max} : 3470 cm⁻¹; ¹H nmr (CDCl₃) δ : 7.35 (s, 5H), 5.71-5.61 (m, 2H), 4.78 (s, 2H), 4.62 (s, 2H), 4.10 (d, *J*=4.3 Hz, 2H), 3.33 (m, 1H), 2.25 (sext, *J*=6.5 Hz, 1H), 1.72-1.49 (m, 2H, 1H exchangeable with D₂O), 1.45-1.34 (m, 1H), 1.04 (d, *J*=7.3 Hz, 3H), 0.96 (t, *J*=7.3 Hz, 3H); ms (*m/z*): 265 (M⁺), 68 (100%). Spectral data were identical with those reported.^{6,18}

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