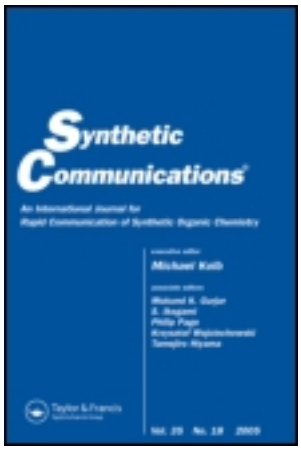


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Total Synthesis of (±)-Isocembrene: A Tactic for Both Diene Construction and Macrocycle Formation

Fengzhi Zhang [a] , Lizeng Peng [a] , Tao Zhang [a] , Tiansheng Mei [a] , Huawei Liu [a] & Yulin Li [a]

[a] National Laboratory of Applied Organic Chemistry , and Institute of Organic Chemistry , Lanzhou University , Lanzhou, Gansu, P.R. China

Published online: 16 Aug 2006.

To cite this article: Fengzhi Zhang , Lizeng Peng , Tao Zhang , Tiansheng Mei , Huawei Liu & Yulin Li (2003) Total Synthesis of (±)-Isocembrene: A Tactic for Both Diene Construction and Macrocycle Formation, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 33:21, 3761-3770, DOI: 10.1081/SCC-120025185

To link to this article: http://dx.doi.org/10.1081/SCC-120025185

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

SYNTHETIC COMMUNICATIONS®
Vol. 33, No. 21, pp. 3761–3770, 2003

Total Synthesis of (±)-Isocembrene: A Tactic for Both Diene Construction and Macrocycle Formation

Fengzhi Zhang, Lizeng Peng, Tao Zhang, Tiansheng Mei, Huawei Liu, and Yulin Li*

National Laboratory of Applied Organic Chemistry,
and Institute of Organic Chemistry,
Lanzhou University, Lanzhou, Gansu, P.R. China

ABSTRACT

The total synthesis of (±)-isocembrene **1**, a naturally occurring cembrene diterpenoid, has been achieved via a unified, convergent and highly efficient strategy by imploying an intramolecular Stille sp^2–sp^2 macrocyclization as the key step and it presents an ideal opportunity to extend the effectiveness of the tactic for both 1,3-diene construction and macrocycle formation.

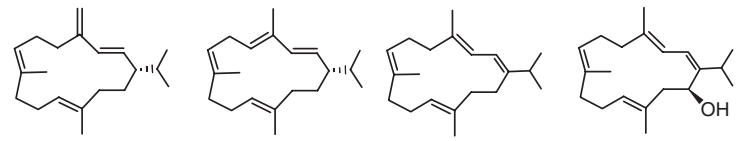
Key Words: Cembrane diterpenoid; Stille cyclization; Total synthesis.

*Correspondence: Yulin Li, National Laboratory of Applied Organic Chemistry, and Institute of Organic Chemistry, Lanzhou University, Lanzhou, Gansu 730000, P.R. China; E-mail: liyl@lzu.edu.cn.

DOI: 10.1081/SCC-120025185 0039-7911 (Print); 1532-2432 (Online)

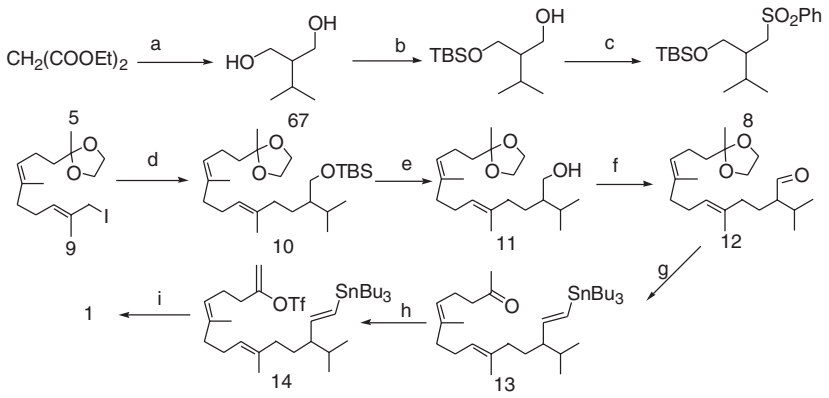
INTRODUCTION

Cembranoids, a large family of diterpenoid natural products characterized by the presence of a fourteen-membered ring, have been isolated from various marine sources as well as some terrestrial organisms since the 1960's.[1] These diterpenoids have become of great interest to synthetic chemists and biologists because of their unusual structural features and remarkably wide range of biological activities.[2] There is an important family of cembrane diterpenoids that are characteristic of bearing a 1,3-diene unit in the macrocyclic cembrane skeleton, such as isocembrene **1**,[3] cembrene **2**,[4] cembrane C **3**,[5] sarcophytol A **4**.[6] In continuation of our on-going project on the total synthesis and novel macrocyclization methods of cembrane-type diterpenoids, we intended to explore a novel macrocyclization method to construct the macrocyclic skeleton that bears a 1,3-diene unit. Intramolecular Pd-catalyzed cross coupling between alkenylstannane and alkenyl halide (or triflate) functionality is now firmly established as an important methodology for the construction of unsaturated heterocycles and carbocycles.[7,8] Furthermore, this reaction is relatively insensitive to moisture and air, tolerates a variety of functional groups on either coupling partner, and is both stereospecific and regioselective. Thus, this reaction appeared to be ideal for the synthesis of a variety of cembrane-type compounds. We reasoned that the unique architecture of the cembrane diterpenoids that was characteristic of bearing a 1,3-diene unit would present an ideal opportunity to extend the effectiveness of this tactic for both diene construction and macrocycle formation. To gain experience of this chemistry, it was decided initials to develop a total synthesis of isocembrene **1**, a cembrane diterpenoid isolated in 1968 by Kashtanova and co-workers from the Russia pine tree *Pinus sibirica*.[3,9]



(-)-Isocembrene 1 Cembrene 2 Cembrene C 3 Sarcophytol A 4

The diol **6,** readily available from **5**,[10] was selectively protected employing NaH/TBSCl in THF[11] to furnish the monosilylated product **7** (Sch. 1), which was then converted into the sulphone **8** in 2 steps. Allylic iodide **9**, readily available from (*E*)-geranyl acetone,[12] was used in the



Scheme 1. Reagents and conditions: (a) i. KOH, DMSO, isopropylbromide, 50°C; ii. LAH, Et_2O, 0°C (65% two steps); (b) NaH, THF, TBDMSCl, r.t. (95%); (c) i. Ph_3P, imidazole, I_2, Et_2O/CH_3CN (3:2); ii. $PhSO_2Na$, DMF, r.t. (60% two steps); (d) i. *n*-BuLi, **8,** THF, −40°C, then added **9**/HMPA, −40°C to r.t.; ii. Na (Hg), Na_2HPO_4, CH_3OH, r.t. (72% two steps); (e) *n*-Bu_4NF, THF, r.t. (95%); (f) oxalyl chloride, DMSO, Et_3N, CH_2Cl_2, −78°C (92%); (g) i. *p*-TsOH, acetone, 40°C; ii. $CrCl_2$, DMF, Bu_3SnCHI_2, 0°C to r.t. (70% two steps); (h) *N*-phenyl triflimide, hexamethyldisilazide (NaHMDS), THF, −78°C (84%); (i) tetrakis (triphenylphosphine)palladium, THF, LiCl, reflux (76%).

coupling reaction with the lithium salt of **8** (formed by treatment with *n*-BuLi in THF at −40°C) in THF at −40°C proceeded smoothly to afford a coupling adduct, which gave the reduced product **10** by treatment with Na (Hg)[13] in MeOH. Desilylation of **10** with tetra-*n*-butylammonium fluoride in THF at room temperature gave the alcohol **11**, and this was converted into the desired product aldehyde **12** under Swern oxidation**.** Treatment of **12** with a catalytic amount of *p*-TsOH led to complete deprotection, and then the deprotected product was treated with gem-dichromium reagents ($CrCl_2/Bu_3SnCHI_2$, DMF) to furnish exclusively *E*-alkenylstannane **13**. For formation of the vinyl triflate **14** in high yields, Stork's procedure[14] was used. Adding sodium hexamethyldisilazide (NaHMDS) rapidly to a diluted solution of vinyl tin **13** and *N*-phenyl triflimide in excess (1.5–1.7 equiv.) at −78°C gave the triflate **14** containing only small amounts (<6% in 400 MHz ^{1}H NMR) of thermodynamic enolate in yield of 84%. Cyclization[15] of **14** containing the vinyl tin and vinyl triflate groups at the termini of the chain was accomplished with tetrakis(triphenylphosphine)palladium (5 mol%) in the presence of lithium chloride (3 equiv.) under high dilution

(10^{-3} M) in refluxing THF. Under these mild reaction conditions, no *E* to *Z* isomerization and no rearrangement of the exocyclic double bond occurred. Synthetic **1** showed identical spectral data with those of natural product **1** reported.[3,9]

In summary, the total synthesis of (±)-isocembrene **1** has been accomplished *via* an efficient palladium-catalyzed intramolecular Stille cross-coupling reaction as the key step. The approach proved highly convergent, straightforward and efficient. Thus, a novel strategy towards the 1,3-diene based cembrane-type macrocyclic diterpenoids, featuring sp^2–sp^2 coupling reaction, has been realized, which should be applicable to other cembrane-type diterpenoids, such as cembrene-C, sarcophytols, etc.

EXPERIMENTAL

^{1}H NMR and ^{13}C NMR spectra were recorded on Advance DXR-200 spectrometer or *Bruker* AM-400 *Bruker* in $CDCl_3$ solution using TMS as internal reference. IR spectra were obtained using a FT-170SX spectrophotometer. LRMS were measured on a *VG* ZAB-HS spectrometer by direct inlet at 70 eV, and signals given in *m*/*z* with relative intensity (%) in brackets. HRMS were determined on a *Bruker Daltonics* APEXII 47 e Fourier Transfer spectrometer with either of EI, CI, FAB or SIMS ionization methods. All solvents were freshly purified and dried by standard techniques prior to use. Organic extractive phases were dried over anhydrous $MgSO_4$. Purification of products was performed by Flash Column Chromatography (FCC) on silica gel (200–300 mesh) purchased from Qing Dao Marine Chemical Co. (Qingdao, China) and eluting with a solvent mixture (*v*/*v*) of petroleum spirit (60–90°C) (PS) and ethyl acetate (EA).

1,3-Dihydroxy-2-isopropylpropane 6

To a stirred solution of KOH (2.52 g, 45 mmol) in DMSO (60 mL) was added **5** (4.5 mL, 30 mmol), after 10 min isopropylbromide (4.5 mL, 45 mmol) was added slowly and the resulting mixture was stirred for 2 h at 50°C to complete the reaction. Diluted with Et_2O and washed with water (4×10 mL) and brine. Evaporation of the solvent afforded the alklated adduct, which was then added dropwise to the anhydrous Et_2O (30 mL) suspension of LAH (1.8 g, 48 mmol) at 0°C. The mixture was stirred at room temperature for 2 h, and the excess LAH was

quenched with MeOH (1 mL). Then the mixture was extracted with ether (3×50 mL), washed successively with 5% HCl, water and brine. Dried and concentrated in vacuum, followed by FCC (PS/EA, 2:1) gave the diol **6** (2.3 g, 65% two steps). ν_{max} (film)/cm^{-1} 3328, 2933, 2870, 1669, 1057, 1006, and 920. δ_H (400 MHz; $CDCl_3$) 0.91 (6H, d, *J* 6.8 Hz, $CH(CH_3)_2$), 1.51–1.55 (1H, m, $CH(CH_2)_2$), 1.68–1.74 (1H, m, $CH(CH_3)_2$), 3.40 (2H, brs, OH), 3.73 (2H, dd, *J* 10.6 and 7.8 Hz, CH_2), 3.83 (2H, dd, *J* 10.6 and 3.8 Hz, CH_2). *m*/*z* (EI) 100 (M^+-18, 29%).

3-Methyl-2-(*tert*-butyldimethyl-silyloxymethyl)-1-butanol 7

To a stirred solution of NaH (0.5 g, 18 mmol, 80% wt.) in THF (70 mL) was added dropwise the diol **6** (2.1 g, 18 mmol) in THF (20 mL). The resulting mixture was stirred at room temperature for 1 h. TBSCl (2.7 g, 18 mmol) in THF (15 mL) was added dropwise into the mixture. The reaction mixture was stirred at room temperature for 2 h to complete the reaction, diluted with ether (200 mL), washed successively with 10% aq. K_2CO_3 (30 mL) and brine (30 mL). Dried and concentrated in vacuum followed by FCC (PS/EA, 6:1) to give the monosilylated product **7** (4.0 g, 95%). ν_{max} (film)/cm^{-1} 3405, 1450, 1310, 1154, 1080, and 745. δ_H (400 MHz; $CDCl_3$) 0.09 (6H, s, $2 \times CH_3$), 0.89 (9H, s, $C(CH_3)_3$), 0.91 (6H, d, *J* 7.3 Hz, $CH(CH_3)_2$), 1.48–1.53 (1H, m, $CH(CH_2)_2$), 1.70–1.78 (1H, m, $CH(CH_3)_2$), 3.73–3.88 (4H, m, $2 \times CH_2O$). *m*/*z* (EI) 189 (M^+-43, 9%).

3-Methyl-2-(*tert*-butyldimethyl-silyloxymethyl)-1-(penthylsulfonyl)butane 8

To a stirred solution of alcohol **7** (1.58 g, 6.8 mmol) in dry Et_2O (18 mL) and CH_3CN (12 mL) were added sequentially Ph_3P (2.67 g, 10.2 mmol), imidazole (0.81 g, 12 mmol) and I_2 (3.45 g, 13.6 mmol) at 0°C. The resulting mixture was stirred at r.t. for 0.5 h, diluted with ether (100 mL), and washed successively with aqueous $Na_2S_2O_3$, brine, and dried. Evaporation of the solvent in vacuum, the resulting residue was dissolved in anhydrous DMF (5 mL), anhydrous $PhSO_2Na$ (1.4 g, 7 mmol) was added, and the mixture was stirred for 24 h under Ar. Diluted with ether (100 mL), and washed with water, brine and dried. Concentrated in vacuum, followed by FCC (PS/EA, 8:1) to give the benzene sulphone **8** (1.45 g, 60% two steps). ν_{max} (film)/cm^{-1} 1477, 1448, 1425, 1307, 1110, 827, and 755. δ_H (200 MHz; $CDCl_3$) 0.02 (6H,

s, $2 \times CH_3$), 0.89 (9H, s, $C(CH_3)_3$), 0.81 (6H, d, *J* 7.3 Hz, $CH(CH_3)_2$), 0.89 (9H, s, $C(CH_3)_3$), 1.91–1.97 (2H, m, $2 \times CH$), 2.94–3.30 (2H, m, CH_2SO_2Ph), 3.64 (2H, d, *J* 4.6 Hz, CH_2O), 7.48–7.93 (5H, m, ArH). *m*/*z* (EI) 341 ($M^+ - CH_3$, 6%).

(5*E*,9*E*)-2-Ethylenedioxy-6,10,14-trimethyl-13-(*tert*-butyldimethyl-silyloxymethyl)pentadeca-5,9-diene 10

To a stirred solution of **8** (0.97 g, 2.7 mmol) in anhyd. THF (6 mL) was added *n*-BuLi (1.7 mL, 2.7 mmol, 1.6 M in *n*-hexane) at −40°C over 5 min under Ar. After stirring for 30 min at −40°C, a solution of iodide **9** (1.27 g, 3.5 mmol) in anhyd. THF (7 mL) was added over 5 min the resulting mixture was stirred at −78°C for 30 min, allowed to warm to r.t. over 4 h, and quenched with sat. NH_4Cl. The mixture was extracted with Et_2O (3×50 mL); the organic phase was washed with water and brine, and dried. Evaporation of the solvent in vacuum, followed by FCC (PS/EA, 8:1) to give the coupling adduct, which was then dissolved in absolute MeOH (15 mL) without purification. To the stirred mixture was added Na_2HPO_4 (0.75 g, 5.3 mmol) and Na (Hg) (2.9 g, 7.2 mmol, 6% wt) at 0°C, and the mixture was stirred at r.t. for 6 h, diluted with ether, washed successively with 5% HCl, sat. $NaHCO_3$, water and brine, and dried. Concentration in vacuum was followed by FCC (PS/EA, 16:1) to give **10** (0.88 g, 72% two steps) as oil (Found: C, 71.55; H, 11.68. $C_{27}H_{52}O_3Si$ requires C, 71.62; H, 11.58%). ν_{max} (film)/cm^{-1} 1254, 1111, 1065, 836 and 776. δ_H (400 MHz; $CDCl_3$) 0.02 (6H, s, $2 \times CH_3$), 0.87 (3H, d, *J* 6.8 Hz, CH_3), 0.90 (3H, d, *J* 6.8 Hz, CH_3), 0.92 (9H, s, $3 \times CH_3$), 1.33 (6H, s, $2 \times CH_3$), 1.59–2.12 (13H, m, $6 \times CH_2$, CH), 3.55 (2H, d, *J* 5.6 Hz, CH_2OTBS), 3.92–3.95 (4H, m, OCH_2CH_2O), 5.10–5.14 (2H, m, $2 \times CH{=}$). *m*/*z* (EI) 395 ($M^+ - 57$, 12).

(5*E*,9*E*)-2-Ethylenedioxy-13-hydroxy-6,10,14-trimethylpentadeca-5,9-diene 11

To a stirred solution of **10** (0.68 g, 1.5 mmol) in THF (4 mL) was added dropwise *n*-Bu_4NF (3 mL, 3 mmol, 1 M in THF). The resulting mixture was stirred at r.t. for 2 h. Diluted with Et_2O (50 mL), the combined organic layer was washed successively with water and brine, dried. Evaporation of the solvent in vacuum was followed by FCC (PS/EA, 8:1) to give the desilylated product **11** (0.48 g, 95%) (Found: C, 74.39; H, 11.40. $C_{21}H_{38}O_3$ requires C, 74.51; H, 11.31%). ν_{max}

(film)/cm^{-1} 3386, 1254, 1111, 1065, 836 and 776. δ_H (400 MHz; $CDCl_3$) 0.86 (3H, d, *J* 6.8 Hz, CH_3), 0.89 (3H, d, *J* 6.8 Hz, CH_3), 1.33 (3H, s, CH_3), 1.58 (3H, s, CH_3), 1.61 (3H, s, CH_3), 1.65–1.79 (5H, m, $2 \times CH_2$, CH), 1.83 (1H, m, CH), 1.98–2.25 (8H, m, $4 \times CH_2$), 3.58–3.59 (2H, m, CH_2OH), 3.94–3.96 (4H, m, OCH_2CH_2O), 5.10–5.14 (2H, m, $2 \times CH=$). *m*/*z* (EI) 320 (M^+-18, 9).

(5*E*,9*E*)-2-Ethylenedioxy-6,10,14-trimethyl-13-formylpentadeca-5,9-diene 12

To a stirred mixture of oxalyl chloride (0.5 mL, 5.6 mmol) in dry CH_2Cl_2 (20 mL) was added dropwise DMSO (0.8 mL, 11.2 mmol) under a nitrogen atmosphere at −78°C. After stirring for a period of 15 min at that temperature, a solution of desilylated alcohol **11** (1.4 g, 4.0 mmol) in CH_2Cl_2 (4 mL) was added and the reaction mixture was stirred for 30 min at −78°C. Et_3N (2.5 mL, 17.6 mmol) was added dropwise and the solution was allowed to warm to room temperature gradually. The mixture was diluted with Et_2O and washed with water and brine, dried over $MgSO_4$. Evaporation of the solvent in vacuuo was followed by FCC (PS/EA, 20/1) to give the title compound **12** (1.2 g, 92%) as a colorless oil (Found: C, 74.98; H, 10.71. $C_{21}H_{36}O_3$ requires C, 74.95; H, 10.78%). ν_{max} (film)/cm^{-1} 3413, 2962, 2379, 1720, 1442, 1260, and 1061. δ_H (400 MHz; $CDCl_3$) 0.96 (6H, d, *J* 7.3 Hz, $CH(CH_3)_2$), 1.33 (3H, s, CH_3), 1.56–2.25 (17H, m, $6 \times CH_2$, $2 \times CH$, CH_3), 3.91–3.94 (4H, m, OCH_2CH_2O), 5.10–5.12 (2H, m, $2 \times CH=$), 9.65 (1H, d, *J* 3.0 Hz, CHO). *m*/*z* (EI) 336 (M^+, 5).

(1*E*,6*E*,10*E*)-6,10-Dimethyl–3-isopropyl-1-tributylstannyl-14-oxopentadeca-1,6,10-triene 13

A mixture of **12** (0.15 g, 0.46 mmol) and *p*-TSOH (3 mg, 16 μmmol) in acetone (15 mL) was stirred at 40°C for 4 h under Ar. The mixture was diluted with ether (50 mL), washed with sat. $NaHCO_3$, H_2O and brine, and dried, evaporation of the solvent in vacuum was followed by FCC (PS/EA, 8:1) to give the deprotected keto aldehyde (0.13 g), which was used for the following step. Dry, deoxygenated DMF (7 mL) was added dropwise to well-stirred $CrCl_2$ (0.527 g, Aldrich 95% w/w pure, 4.3 mmol) in a flask under argon in an ice-bath. After allowing the flask to warm to room temperature over 15 min, it was surrounded by aluminium foil to exclude light and a mixture of keto aldehyde (0.13 g, 0.43 mmol) and

Bu_3SnCHI_2 (478 mg, 0.86 mmol) in dry, deoxygenated DMF (2 mL) was added dropwise to the reaction mixture. After 2.5 h at 25°C, water (14 mL) was added and the mixture was extracted with ether (3 × 10 mL). The combined organic layers were washed with water (10 mL), brine (10 mL), and dried. And evaporated under reduced pressure. Purification by FCC (PS/EA, 20:1) gave exclusively *E*-alkenylatannane **13** (0.18 g, 70% two steps) as colourless oil (Found: C, 66.11; H, 10.51. $C_{32}H_{60}OSn$ requires C, 66.32; H, 10.44%). ν_{max} (film)/cm^{-1} 2956, 2926, 2871, 1716, 1617, 1596, 1464, 1376, and 997. δ_H (400 MHz; $CDCl_3$) 0.78–0.91 (21H, m, $Sn(CH_2CH_2CH_2CH_3)_3$ and $CH(CH_3)_2$), 1.22–1.29 (6H, m, $Sn(CH_2CH_2CH_2CH_3)_3$), 1.39–1.66 (7H, m, $Sn(CH_2CH_2CH_2CH_3)_3$ and $CH(CH_3)_2$), 1.90–2.45 (13H, m, CH, 6 × CH_2), 2.15 (3H, s, CH_3CO), 5.07–5.10 (2H, m, 2 × CH=), 5.65 (1H, dd, *J* 18.9 and 8.7 Hz, CH=CHSn), 5.75 (1H, d, *J* 18.9 Hz, =CHSn).

(5*E*,9*E*,14*E*)-6,10-Dimethyl-13-isopropyl-2-((trifluoromethyl)sulfonyl)oxy)-15-tributyl-stannylpentadeca-1,5,9,14-tetraene 14

In a flame-dried 10-mL round-bottom flask fitted with an argon inlet on a rubber septum was placed a solution of Keto **13** (46 mg, 0.084 mmol) and *N*-phenyltrifluonimide (54 mg, 0.15 mmol) in tetrahydrofuran (4 mL), The mixture was cooled to −78°C. To this solution was added sodium *bis*(trimethylsilyl)amide (90 μL, 0.09 mmol, 1.0 M in THF) by syringe. The resulting solution was stirred at −78°C for a period of 20 min. Into the solution was introduced phosphate buffer (pH 7.0, 5%, 5 mL) to quench the reaction. The cold mixture was poured into hexane (200 mL) in a separation funnel and washed with saturated sodium chloride solution (2 × 10 mL), the organic layer drived over magnesium sulfate and concentrated under reduced pressure. The excess of *N*-phenyltrifluomethanesulfonimide was separated by crystallization in hexane at −20°C. The residue was purified by flash chromatography (PS/EA, 16:1); the product **14** was obtained as pale yellow oil (50 mg, 84%), which contained <6% of thermodynamic enolate (Found: C, 55.35; H, 8.14. $C_{33}H_{59}F_3O_3SSn$ requires C, 55.70; H, 8.36%). ν_{max} (film)/cm^{-1} 2957, 2927, 1601, 1472, 1072, and 1016. δ_H (400 MHz; $CDCl_3$) 0.78–0.91 (21H, m, $Sn(CH_2CH_2CH_2CH_3)_3$ and $CH(CH_3)_2$), 1.22–1.29 (6H, m, $Sn(CH_2CH_2CH_2CH_3)_3$), 1.39–1.66 (7H, m, $Sn(CH_2CH_2CH_2CH_3)_3$ and $CH(CH_3)_2$), 1.90–2.00 (8H, m, 4 × CH_2), 2.20–2.28 (2H, m, $CH_2C(OTf)=C$), 4.85 (1H, d, *J* 3.4 Hz, *cis*-TfOC=CH*H*), 5.02 (1H, d, *J* 3.4 Hz, *trans*-TfOC=C*H*H), 5.11 (2H, m, 2 × CH=), 5.65 (1H, dd,

J 18.9 and 8.7 Hz, C*H*=CHSn), 5.75 (1H, d, *J* 18.9 Hz, =CHSn). *m*/*z* (EI) 655 (M^+−Bu, 5), 547 (12), 505 (42).

(1*E*,5*E*,10*E*)-9-Isopropyl-2,6-dimethyl-12-methylene-1,5,10-cyclotetradecatriene 1

In a flame-dried 50-mL round-bottom flask fitted with a reflux condenser was placed the precusor **14** (70 mg, 0.1 mmol) in the presence of tetrakis(triphenylphosphine) palladium (2.3 mg, 2 mol %), lithium chloride (13 mg, 0.3 mmol) under high dilution (10^{-3} M) in THF, the resulting solution was stirred to accomplish the coupling under refluxing conditions. Diluted with ether (50 mL), the combined organic layer was washed with water and brine. Dried and concentrated in vacuum followed by FCC (pure PE) to give the target product **1** (21 mg, 76%) as colorless oil. ν_{max} (film)/cm^{-1} 2930, 2855, 1470, and 978; δ_H (400 MHz; $CDCl_3$) 0.84 (3H, d, *J* 7.0 Hz, Me), 0.89 (3H, d, *J* 7.0 Hz, Me), 1.25–1.40 (2H, m, C*H*$(Me)_2$ and C*H*CH$Me)_2$), 1.68 (3H, s, CH=C*Me*), 1.70 (3H, s, CH=C*Me*), 1.90–2.00 (8H, m, $4 \times CH_2$), 2.45 (1H, m, C*H*HC=CHH), 4.85 (1H, br s, C=CH*H*), 4.90 (1H, br s, C=CH*H*), 5.09 (1H, t, *J* 7.0 Hz, CH=CMe), 5.19 (1H, t, *J* 7.0 Hz, CH=CMe), 5.50 (1H, dd, *J* 15.6 and 9.6 Hz, CH=C*H*CH), 5.94 (1H, d, *J* 15.6 Hz, CH_2=CC*H*=CH). δ_C (100 MHz, $CDCl_3$) 146.0, 137.8, 135.8, 134.0, 132.3, 124.9, 123.8, 113.6, 50.0, 34.2, 33.0, 32.6, 32.2, 29.6, 28.4, 28.0, 24.0, 23.5, 20.7, and 19.8. *m*/*z* (EI) 272 (M^+, 5), 257 (M^+−Me, 12) [Found (HRMS) (ESI): $M^+ + H$, 273.2571. Calc. for $C_{20}H_{32} + H$: $M^+ + H$, 273.2577].

ACKNOWLEDGMENT

This work was financially supported by the National Natural Science Foundation of China (Grant No. 20072012) and the Special Research Grant for Doctoral Sites in Chinese Universities (Grant No. 20010730001).

REFERENCES

1. Tursch, B.; Bracekman, J.C.; Dolaze, D.; Kaisin, M. In *Marine Natural Products: Chemical and Biological Perspectives*; Scherer, P.J., Ed.; Academic Press: New York, 1978; Vol. 2, pp. 247.

2. (a) Tius, M.A. Chem. Rev. **1988**, *88*, 719; (b) Cox, N.J.G.; Mills, S.D.; Pattenden, G. J. Chem. Soc., Perkin Trans. 1 **1992**, 1313 and references cited therein.
3. Kashtanova, N.K.; Lisina, A.I.; Pentegova, V.A. Khim. Prir. Soedin. **1968**, *4*, 52.
4. Tadahiro, K.; Toyohiko, K.; Takashi, K.; Yoshio, K. Syn. Commun, **1976**, *6*, 365.
5. Yoel, K.; Shmuel, C.; Amiram, G. J. Org. Chem. **1981**, *46*, 3592.
6. Kobayashi, M.; Nakagawa, T.; Mitsuhashi, H. Chem. Pharm. Bull. **1979**, *27*, 2382.
7. For reviews see: (a) Stille, J.K. Angew. Chem. Int. Ed. Engl. **1986**, *25*, 508; (b) Farina, V.; Krishnamurthy, V.; Scott, W. Org. React. **1997**, *50*, 1.
8. Duncton, M.A.J.; Pattenden, G. J. Chem. Soc., Perkin Trans. 1 **1999**, 1235 and references cited therein.
9. Pattenden, G.; Smithies, A.J. J. Chem. Soc., Perkin Trans. 1 **1996**, 57.
10. Johnstone, R.A.W.; Tuli, D.; Rose, M.E. J. Chem. Research(s) **1980**, 283.
11. For the selective protection of one of two chemically equivalent primary hydroxyl groups in 1, *n*-diols using TBSCl, see: (a) McDougal, P.G.; Rico, J.G.; Oh, Y.-I.; Condon, B.D. J. Org. Chem. **1986**, *51*, 3388; (b) Yu, C.Z.; Liu, B.; Hu, L.Q. Tetrahedron Lett. **2000**, *41*, 4281 and references cited therein.
12. (a) Unbriet, M.; Sharpless, K.B. J. Am. Chem. Soc. **1977**, *99*, 5526; (b) Corey, E.J.; Pyne, S.G.; Su, W.G. Tetrahedron Lett. **1983**, *24*, 4883.
13. For a review see: Najera, C.; Yus, M. Tetrahedron **1999**, *55*, 10547.
14. (a) Stork, G.; Kraus, G.A.; Rathke, M.W. J. Am. Chem. Soc. **1980**, *102*, 3959; (b) Comins, D.L.; Dehghani, A.; Tetrahedron lett. **1992**, *42*, 6299; (c) Hodgson, D.M.; Foley, A.M.; Lovell, P.J. Tetrahedron Lett. **1998**, *39*, 6419.
15. (a) Hodgson, D.M.; Foley, A.M.; Boulton, L.T.; Lovell, P.J.; Maw, G.N. J. Chem. Soc., Perkin Trans. 1 **1999**, 2911; (b) Hodgson, D.M.; Foley, A.M.; Boulton, L.T.; Ovell, P.J. Synlett. **1999**, 744; (c) Stille, J.K.; Tanaka, M. J. Am. Chem. Soc. **1987**, *109*, 3785.

Received in Japan April 9, 2003