Synthesis of Dictyopterene A: Optically Active Tributylstannylcyclopropane as a Chiral Synthon

Toshiyuki Itoh,* Hitomi Inoue, and Sachie Emoto

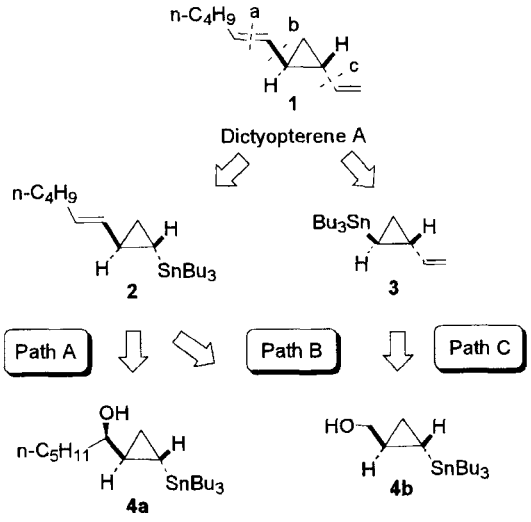
Department of Chemistry, Faculty of Education, Okayama University, Okayama 700-8530

(Received July 7, 1999)

Synthesis of (1*S*,2*R*)-1-[(*E*)-hex-1-en-1-yl]-2-vinylcyclopropane (dictyopterene A), which was isolated from the essential oil of algae of the genus *Dictyopteris* in Hawaii, has been demonstrated using optically active tributylstannylcyclopropane as a starting chiral synthon.

The cyclopropyl group is found as a basic structural element in a wide range of naturally occurring biologically active compounds in plants and in microorganisms, both fungal and bacterial.[1] Dictyopterene A (**1**) was isolated from the essential oil of the genus *Dictyopteris* in Hawaii and is known as a sex pheromone of the algae.[2] We were attracted by its unique structure in which a chiral cyclopropane moiety was involved at the center position between two double bonds.[3] Investigating the synthesis of dictyopterene A should provide important information on the chemistry related to the syntheses of various types of chiral cyclopropane compounds, and we therefore chose compound **1** as the synthetic target molecule of the present study using two kinds of optically active tributylstannylcyclopropane derivatives as chiral synthons.

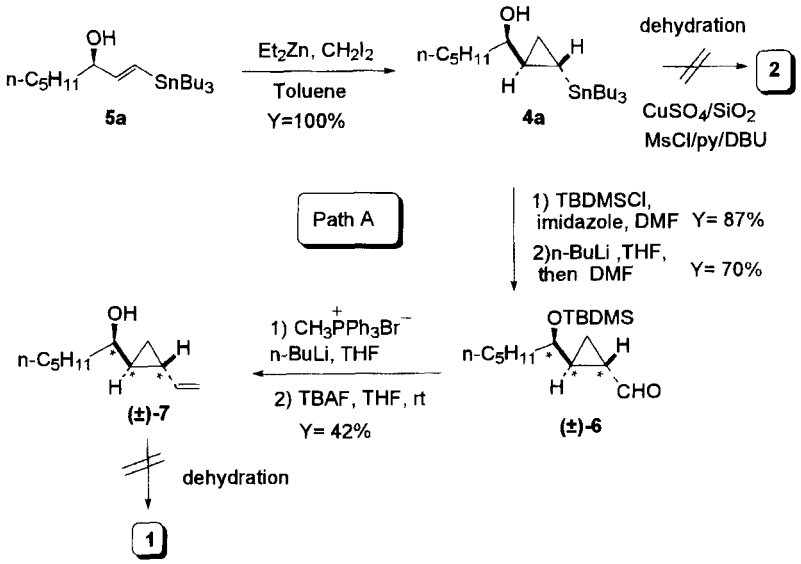
The retrosynthetic analysis suggests three pathways to access the target molecule **1** as shown in Scheme 1, since 1-[2-(tributylstannyl)cyclopropyl]alkan-1-ols, **4a**[4] and **4b**,[5] are the starting chiral materials. It is well known that the various functional groups are derived from the tributylstannyl group through metal exchange reaction with perfect retention of its absolute configuration.[6] Therefore we postulated that dictyopterene A may be accessible through intermediate **2**; the stannyl group of **2** is changed to the formyl group via lithiation and subsequent treatment with *N*,*N*-dimethylformamide (DMF), and the next Wittig type reaction may provide the target compound **1**. The key intermediate **2** seems to be derived from optically active **4a** (Path A) or **4b** (Path B). We recently reported that optically pure vinylstannane **5a**[4] was converted to stannylcyclopropane **4a** by the Simmons–Smith type reaction modified by Charette and colleagues[7] in quantitative yield. Another pathway to access **1** is the palladium-catalyzed coupling reaction of vinylcyclopropylstannane **3** with 1-iodohex-1-ene or 1-tributylstannylhex-1-ene, and in this Path, the key intermediate **3** would be derived from **4b** (Path C).



Scheme 1.

Path A is the shortest route to access the target molecule **1**, though this path was anticipated to be an ambitious strategy because McCormick and Barton reported that the ring opening reaction of the cyclopropane moiety occurred easily if the reaction was carried out under acidic reaction conditions.[8] We tested several dehydration methods that proceeded under mild reaction conditions using racemic (±)-**4a** (Scheme 2).[9] Initially, (±)-**4a** was treated with anhydrous $CuSO_4$ in the presence of silica gel,[10] however, none of the reaction took place at rt, and (±)-**4a** was recovered in almost quantitative yield, but (±)-**4a** was completely decomposed under reflux conditions in toluene. It was reported that dehydration took place easily as methanesulfonate in the presence of a base such as diazabicycloundecene (DBU)[11a] or ethyldiisopropylamine.[11b] Unfortunately, (±)-**4a** was decomposed even by treatment with methanesulfonyl chloride in the presence of triethylamine,[12] and unidentified compounds which possessed no cyclopropyl ring and tributylstannyl group were obtained instead of methanesulfonate.

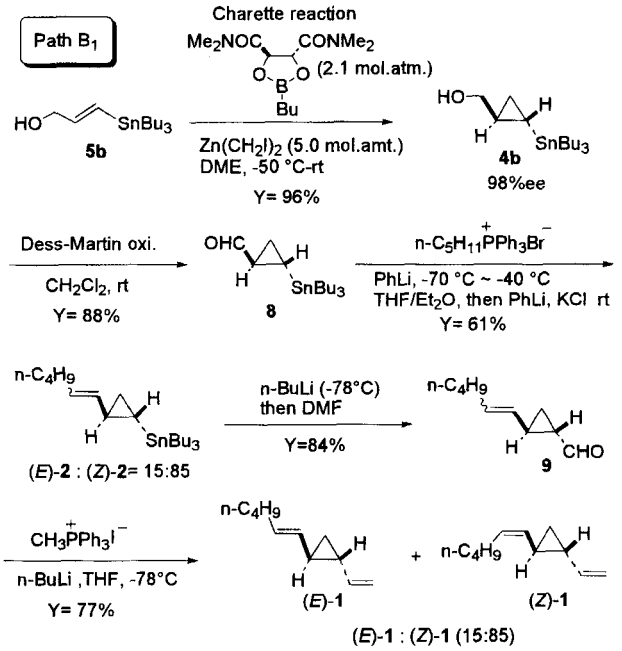
The stannane (±)-**4a** was therefore converted to vinylcyclopropane (±)-**7** through aldehyde (±)-**6**; the hydroxy group of (±)-**4a** was protected by *t*-butyldimethylsilyl ether (TBDMS), and lithium–tin exchange reaction by treatment



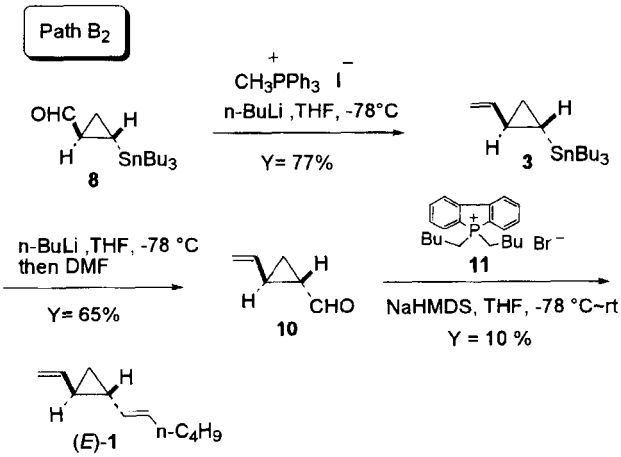
Scheme 2.

with butyllithium (*n*-BuLi), and subsequent treatment with DMF gave aldehyde (±)-**6** in 61% yield (two steps). Aldehyde (±)-**6** was subjected to the Wittig reaction, and deprotection of the TBDMS group by treatment with tetrabutylammonium fluoride (TBAF) afforded vinylcyclopropane (±)-**7** in 42% yield. However, we came up against a stone wall again when all attempts to convert (±)-**7** into the desired molecule (±)-**1** by the dehydration protocols previously mentioned were unsuccessful (Scheme 2). In addition, treatment with thionyl chloride ($SOCl_2$) in the presence of excess pyridine[12] also caused the decomposition of (±)-**7** and no identical compound was obtained; we therefore abandoned this route.

Synthesis of dictyopterene A was accomplished through path B (Schemes 3 and 4). The Charette asymmetric cyclopropanation was successfully employed to prepare the starting compound **4b** in optically active form.[13] It was found that the use of excess amounts of $Zn(CH_2I)_2$ (at least 5 molar amounts to the substrate) was essential to obtain **4b** in high optical purity (98%ee). Dess–Martin oxidation[14] of alcohol **4b** gave aldehyde **8** in good yield (83%). The key step of the synthesis of dictyopterene A through Path B is the introduction of (*E*)-hex-1-enyl group to the cyclopropane moiety via the Wittig reaction. The stereochemistry of the Wittig reaction has been intensively investigated, and the (*E*/*Z*)-selectivity of the product is known to be determined by the preference of oxaphosphetane intermediates and (*E*)-olefin to be derived from *trans*-oxaphosphetane.[15] We first used Schlosser's protocol for trans-selective olefin synthesis using pentyltriphenylphosphonium ylide in the presence of potassium chloride,[17] and obtained the coupling product **2** (61% yield) as a mixture of two stereo isomers with a ratio of 85 : 15. Although the stereoselectivity was insufficient, we decided to complete the synthesis of dictyopterene A using this product because we believed that (*E*)-**2** was obtained as a major product, though ^{1}H NMR spectra of the olefinic



Scheme 3. Synthesis of dictyopterene A.



Scheme 4. Synthesis of dictyopterene A.

protons of the major isomer of **2** disagreed with those of the speculated spectra of (*E*)-**2**. Conversion of the stannyl group of **2** to the formyl group to give aldehyde **9** in 84% yield, and subsequent Wittig reaction of aldehyde **9** using methyltriphenylphosphonium iodide in the presence of *n*-BuLi as base afforded the final product **1** in 77% yield. However, the specific rotation of the final compound **1** ($[\alpha]_D^{23}$ −30.7° ($CHCl_3$)) was completely different from those of the reported (*E*)-**1** ($[\alpha]_D$ +72°).[2b] We became aware of our mistake by ^{1}H NMR analysis, which showed that we had synthesized (*Z*)-**1** as a major product instead of the desired (*E*)-**1** (Scheme 3).

Separation of (*E*)-**1** and (*Z*)-**1**was impossible by a laboratory scale experiment such as silica gel column chromatography due to the low boiling point of the two, though it was confirmed that compound **1** was synthesized as optically pure form by capillary GC analysis using a chiral column (G-Ta). Since it was now obvious that the first Wittig reaction gave unexpected (*Z*)-isomer of **2** as a major product, we reinvestigated the reaction conditions in the Wittig reaction. The importance of the proper choice of the solvent system for the (*E*)-selective Wittig reaction is well known,[15b] and many protocols that provide (*E*)-olefin selectively have been developed.[15] According to one such means, aldehyde **8** was treated with pentyltriphenylphosphonium bromide using *n*-BuLi as base in a mixed solvent system (CH_2Cl_2–Et_2O) and subsequent treatment with *t*-BuOH and *t*-BuOK gave the corresponding cyclopropylstannane **2** in 99 % yield, but (*Z*)-product **2** was again obtained as a major product (*E*/*Z* = 24 : 76, Table 1, Entry 2).[18] Although several reaction conditions of the Wittig type reaction have been examined, all results obtained were far from satisfactory, as can be seen in Table 1 (Entries 2—11). The best ratio of (*E*)-**2** and (*Z*)-**2** was 1 : 1 when pentyltriphenylphosphonium bromide was employed using potassium *t*-butoxide as base in the presence of methanol (Entry 8).[20]

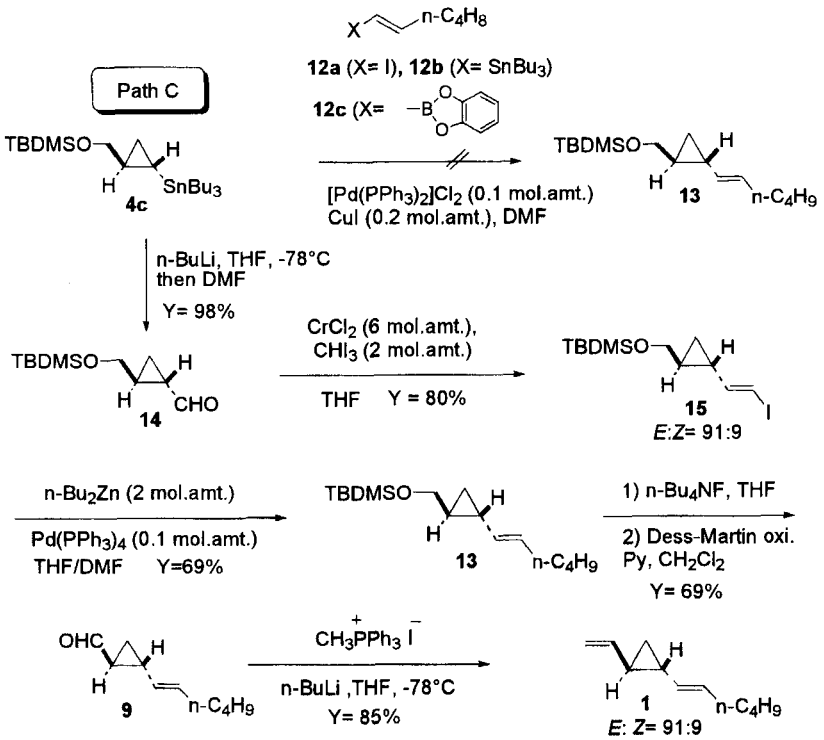
An interesting property in the stereoselectivity of the Wittig reaction of cyclopropanecarbaldehyde **8** was identified and it was suspected that such special reactivity may be caused by the bulky tributylstannyl group to which the cyclopropane ring was attached. The concept of the strategy in path B is using stannylcyclopropanemethanol **4b** as a synthetic equivalent of cyclopropanedicarbaldehyde, which possesses two formyl groups with different reactivity. It is possible to access **1** by changing the order of the Wittig type reactions (Scheme 4). Vinylcyclopropylstannane **3** was derived from carbaldehyde **8** via the Wittig reaction in 77% yield, and by subsequent conversion of the stannyl group to the formyl group giving aldehyde **10** in 65% yield. Among several methods we tested, most reactions again gave (*Z*)-olefin preferentially, but the use of 5,5-dipentyl-5*H*-dibenzophosphol-5-ium bromide (**11**) developed by Vedejs and Marth[22] gave the desired (*E*)-**1** (10%) in perfect (*E*)-stereoselectivity, while the chemical yield of the product was not sufficient. Significant decomposition of the product or substrate occurred during the reaction and, improvement of the chemical yield by this method was therefore unsuccessful in spite of using several different combinations of solvent systems and bases such as NaHMDS–THF at −78 °C, NaH–THF at −78 °C to r.t., and *t*-BuOK–THF–Et_2O at −78 to 0 °C.

Another pathway to access dictyopterene A from cyclopropane **4c** was path C using palladium chemistry (Scheme 5). Initially we attempted the coupling reaction of **4c** with vinyl compounds **12a** (X = I) and **12b** (X = $SnBu_3$) in the presence of palladium catalyst.[23] We recently reported dimerization of 1-(2-tributylstannylcyclopropyl)hexan-1-ol (**4a**) using palladium(0) catalyst in the presence of copper(I) iodide.[4,23] However no desired compound **13** was obtained under these reaction conditions and only the significant loss of the starting material **4c** was observed. Suzuki coupling reaction[24] using hexenyldihydroxyborane ester **12c**[25] was also unsuccessful and no identical compound was obtained. Because the starting material **4c** disappeared quickly in the course of the reaction and tributyltin iodide was formed when **4a** was

Table 1. Results of the Wittig Reaction of **8** under Various Reaction Conditions

Entry	Method	Reaction conditions		**2**	
		Base	Solvent	Yield (%)	*E*/*Z*
1	A[17]	PhLi (1.8 M)	THF/Et_2O	61	15 : 85
2	B[18]	*n*-BuLi (1.6 M)	CH_2Cl_2/Et_2O	99	24 : 76
3	B	*n*-BuLi (1.6 M)	THF	17	8 : 92
4	B	*n*-BuLi (1.6 M)	Et_2O	50	29 : 71
5	B	*n*-BuLi (1.6 M)	THF/Et_2O	76	34 : 66
6	C[19]	*n*-BuLi (0.24 M)	Et_2O	57	37 : 63
7	D	*n*-BuLi (0.24 M)	Et_2O	71	18 : 82
8	E[20]	*n*-BuLi (0.24 M)	Et_2O	35	50 : 50
9	E[21]	*n*-BuLi (0.24 M)	THF/Et_2O	59	40 : 60
10	F	*t*-BuOK	THF	61	2 : 98
11	G	*t*-BuOK	THF	31	5 : 95

Method: A: 1 mol. amt. PhLi (−70 to −40 °C) and 1 mol. amt. PhLi and KCl (prepared in situ from HCl–Et_2O and *t*-BuOK), r.t. 2 h. B: 1 mol. amt. *n*-BuLi (−70 to −40 °C) and *t*-BuOH (1.5 mol. amt.), *t*-BuOK (1.5 mol. amt.), r.t., 2 h. C: Addition of EtOH, −78 to −40 °C to r.t. D: Addition of MeOH, −78 °C to −40 °C to r.t. E: Addition of MeOH, −40 °C, 4 h, then added H_2O, r.t., 3 h. F: −78 °C to r.t., 18 h. G: 0 °C, 2 h.



Scheme 5. Synthesis of dictyopterene A using Pd chemistry.

reacted with hex-1-en-1-yl iodide (**12a**), this unsuccessful result seemed due to the instability of the cyclopropyl ring under the Pd-catalyzed reactions, though some possibilities still remained to find a good catalyst that realized the desired coupling reaction. So, the tributylstannyl group in **4c** was derived to the 2-iodovinyl group in **15** which possesses a reaction point apart from the cyclopropane ring (Scheme 5). Cyclopropane **4c** was converted to the aldehyde **14** and subjected to the Takai reaction[26] to afford vinyl iodide **15** with acceptable (*E*)-selectivity (*E* : *Z* = 91 : 9). Application of the Negishi protocol[27a] for $Pd(PPh_3)_4$-catalyzed coupling reaction of **15** with dibutylzinc[28] was successful,[27] and olefin **13** was obtained in 69% yield. Deprotection of TBDMS group and subsequent Dess–Martin oxidation gave the aldehyde **9** in 69% yield, and finally, the Wittig reaction of **9** with methyltriphenylphosphonium iodide using *n*-BuLi as base at −78 °C afforded the desired (1*S*,2*R*)-1-[(*E*)-hex-1-en-1-yl]-2-vinylcyclopropane (**1**) as a major product (*E* : *Z* = 91 : 9) in 85% yield. Although the stereoselectivity was not perfect, this route provided dictyopterene A in the highest yield with acceptable stereoselectivity.

Conclusion

Synthesis of dictyopterene A has been demonstrated using optically active tributylstannylcyclopropane derivatives as starting materials. 2-(Tributylstannyl)cyclopropanemethanol (**4**) is a synthetic equivalent of bisfunctional cyclopropane, in which **4a** possesses α-alkylmethanol group and tributylstannyl group, and **4b** has two formyl groups with different reactivity, though the tributylstannylcyclopropyl group of **4** showed a somewhat more special nature than those of simple alkylstannanes or vinylstannanes. Proper design of the synthetic strategy was essential using stannylcyclopropanemethanols as convenient chiral building blocks for asymmetric synthesis of cyclopropane derivatives. We believe that the present study should contribute to the chemistry of stannylcyclopropane compounds.

Experimental

Reagents and solvents were purchased from common commercial sources and were used as received or purified by distillation from appropriate drying agents. Reactions requiring anhydrous conditions were run under an atmosphere of dry argon. Silica gel (Wako gel 300E) was used for column chromatography and silica gel (Wako gel B-5F) for thin layer chromatography. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian VXR-200 spectrometer, and chemical shifts are expressed in ppm downfield from tetramethylsilane (TMS) in $CDCl_3$ as an internal reference (M = mol dm^{-3}).

(1*RS*,2*SR*)-2-[(*RS*)-1-(*t*-Butyldimethylsiloxy)hexyl]cyclopropanecarbaldehyde ((±)-6). To a solution of alcohol (±)-**4a**[4] (2.72 g, 6.34 mmol) and imidazole (1.34 g, 7.57 mmol) in DMF (30 ml) was added a DMF (8.0 ml) solution of *t*-butyldimethylsilyl chloride (TBDMSCl) (1.14 g, 7.57 mmol) dropwise at 0 °C and the mixture was stirred at r.t. for 1 h. The reaction was quenched by addition of a small amount of crushed ice and the mixture was extracted with ether. The organic layer was dried over $MgSO_4$ and was purified by silica gel flash column chromatography (hexane/ethyl acetate = 10 : 1) giving TBDMS ether of (±)-**4a** (3.00 g, 5.50 mmol) in 87% yield. To a solution of TBDMS ether of (±)-**4a** (3.00 g, 5.50 mmol) in tetrahydrofuran (THF) (27.5 ml) was added *n*-BuLi (6.4 mmol as 1.6 M hexane solution) (1 M = 1 mol dm^{-3}) at −78 °C and the mixture was stirred for 25 min at the same temperature. To this mixture was added dropwise 6.9 ml of dry DMF and the mixture was stirred for 1 h at −78 °C. The reaction was quenched by addition of water and extracted with ether. Silica gel flash column chromatography (hexane/ethyl acetate = 10 : 1)

afforded (±)-**6** (1.10 g, 3.87 mmol, 70%): R_f 0.33 (hexane/ethyl acetate = 10 : 1); bp 125 °C/2 Pa (Kugelrohr); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.034 (6H, d, J = 6.8 Hz), 0.87 (10H, m), 1.10—1.82 (14H, m), 3.52 (1H, dd, J = 10.8, 5.4 Hz), 9.02 (1H, d, J = 5.6 Hz) ; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 11.45, 13.98, 18.04, 22.57, 24.52, 25.77, 27.25, 27.38, 31.91, 37.93, 71.43, 200.89; IR (neat) 2955, 2930, 1713, 1464, 1254, 1091, 975, 836 cm^{-1}. Found: C, 67.54; H, 11.34%. Calcd for $C_{16}H_{32}OSi$: C, 67.55; H, 11.34%.

(*RS*)-1-[(1*SR*,2*RS*)-2-Vinylcyclopropyl]hexan-1-ol ((±)-7). To a solution of methyl triphenylphosphonium bromide (2.84 g, 7.03 mmol) in THF (15 ml) was added 3.5 ml of *n*-BuLi (5.3 mmol in hexane) dropwise at −20 °C. The mixture was stirred for 5 min, then a THF (5 ml) solution of aldehyde **6** (1.00 g, 3.51 mmol) was added at −78 °C and this mixture was again stirred for 15 min. The mixture was diluted with 10 ml of ether and was filtered through a florizil short column and the residue was eluted with ether several times. The combined organic layer was concentrated to the crude product. To a THF (1.3 ml) solution of the crude product was added tetrabutylammonium fluoride (TBAF) (0.56 ml in 1.0 M in THF) at r.t. and the mixture was stirred for 13 h. The reaction mixture was diluted with 10 ml of ether and washed with brine. The combined organic layers were dried ($MgSO_4$) and evaporated. Silica gel flash column chromatography (hexane/ethyl acetate = 5 : 1) gave **7** (248 mg, 1.47 mmol) in 42% yield: R_f 0.6 (hexane/ethyl acetate = 5 : 1); bp 130 °C/5 Pa (Kugelrohr); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.51—0.67 (2H, m), 0.77—0.85 (4H, m), 1.16—1.48 (9H, m) 2.92 (1H, dt, J = 8.2, 6.0 Hz), 4.77 (1H, dd, J = 10.0, 1.9 Hz), 4.95 (1H, dd, J = 17.1 Hz, 1.4), 5.55 (1H, ddd, J = 16.9, 10.0, 8.5 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 11.25, 14.01, 20.53, 22.61, 25.28, 27.26, 31.87, 37.30, 75.53, 112.25, 140.53; IR (neat) 3323, 2923, 1462, 1375, 1048 cm^{-1}. Found: C, 78.58; H, 12.01%. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98%.

[(1*R*,2*S*)-2-(Tributylstannyl)cyclopropyl]methanol (4b). To a solution of diethylzinc (50 ml, 50.0 mmol) in dichloromethane (35 ml) and freshly distilled DME (6.0 ml) was added diiodomethane (9.26 ml, 115 mmol) at a rate to keep the internal temperature below −10 °C (ca. 20 min) and to form $Zn(CH_2I_2)$/DMF complex, a clear colorless solution. This was used immediately for the next reaction. To a mixture of 3-tributylstannylprop-2-en-1-ol (**5b**) (4.40 g, 10.0 mmol), chiral 1,3,2-dioxabolane (4.9 g, 16.9 mmol), which was prepared from (*R*,*R*)-(+)-*N*,*N*,*N*′,*N*′-tetramethyltartaramide and butyldihydroxyborane according to the method of Charette,[7] was added $Zn(CH_2I_2)$/DMF complex solution dropwise at a rate to keep the internal temperature below −15 °C for 20 min in the presence of MS 4A (460 mg). The resulting mixture was stirred for 2 h at −10 °C, then further stirred for 20 h at r.t. The reaction was quenched by addition of saturated NH_4Cl aqueous solution and extracted with ether. To the combined organic layers were added 10 ml of 5 M KOH aqueous solution and the mixture was stirred for 9 h at r.t. The organic layer was washed with 10% HCl aqueous solution, saturated $NaHCO_3$ aqueous solution, water, brine, and dried over $MgSO_4$. Silica gel flash column (hexane/ethyl acetate = 10 : 1) afforded **4b** (3.45 g, 9.55 mmol) in 96% yield: $[\alpha]_D^{21}$ +17.2° (*c* 0.96, $CHCl_3$), lit,[5] −14.6° (1*S*,2*R*), 86%ee; ^{1}H NMR (200 MHz, $CDCl_3$) δ = −0.31 (1H, dt, J = 10.2, 6.7 Hz), 0.4—0.6 (2H, m), 0.7—0.95 (2H, m), 0.78 (3H, t, J = 7.9 Hz), 0.88 (9H, t, J = 7.1 Hz), 1.2—1.6 (25H, m) 1.7 (1H, brs, OH) 2.78 (1H, dt, J = 8.4, 6.1 Hz) ; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 2.61, 7.42, 8.62, 13.67, 18.03, 27.31, 28.86, 29.06, 69.53; IR (neat) 3323, 2923, 1462, 1375, 1048 cm^{-1}.

(1*R*,2*S*)-2-(Tributylstannyl)cyclopropanecarbaldehyde (8). To a dichloromethane (30.0 ml) solution of **4b** (1.06 g, 2.94 mmol) was added pyridine (1.20 ml, 14.8 mmol) and triacetato(benzoato-$\varkappa C^2$,$\varkappa O$)iodine(V) ($C_6H_4COOI(OAc)_3$) (2.50 g, 5.89 mmol) at r.t., and the mixture was stirred for 1 h. The reaction was quenched by addition of $NaHCO_3$ saturated aqueous solution and 10% $Na_2S_2O_3$ aqueous solution and extracted with ethyl acetate. Silica gel flash column chromatography (hexane/ethyl acetate = 50 : 1) gave aldehyde **8** as a colorless oil (927 mg, 2.58 mmol, 88%): $[\alpha]_D^{23}$ −25.3° (*c* 1.25, $CHCl_3$); R_f 0.40 (hexane/ethyl acetate = 10 : 1); bp 170 °C/2.5 Pa (Kugelrohr); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.54 (1H, ddd, J = 10.7, 8.4, 5.6 Hz), 0.80—0.90 (16H, m), 0.99 (1H, ddd, J = 8.4, 6.9, 4.3 Hz), 1,18—1.54 (12H, m), 1.65—1.73 (1H, m), 8.49 (1H, d, J = 6.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 1.67, 8.96, 11.07, 13.57, 26.81, 27.20, 28.85, 201.53; IR (neat) 2925, 1707, 1463, 1188, 1035, 915, 861 cm^{-1}. Found: C, 53.21; H, 8.75%. Calcd for $C_{16}H_{32}OSn$: C, 53.51; H, 8.98%.

(1*R*,2*S*)-1-(Hex-1-enyl)-2-tributylstannylcyclopropane (2). Pentyltriphenylphosphonium bromide (827 mg, 2.0 mmol) was suspended in 4.0 ml of THF and 4.0 ml of ether and stirred with 2.0 mmol of PhLi (1.8 M in cyclohexane/ether = 7 : 3) for 10 min. The solution was cooled to −70 °C and 2.0 mmol of aldehyde **8** (718 mg, dissolved in 4.0 ml of ether) was added. The mixture was stirred for 10 min, a further 2.0 mmol of PhLi solution (1.1 ml) was added and the whole kept at −40 °C for 10 min. This solution was treated with 2.2 mmol of ethereal hydrogen chloride and with 3.0 mmol of potassium *t*-butoxide (as 1 : 1 complex with *t*-butyl alcohol). The mixture was stirred for 2 h at r.t., and was extracted with ether. The combined organic layers were dried ($MgSO_4$), and evaporated. Silica gel flash column chromatography (hexane/ethyl acetate = 10 : 1) gave **2** (504 mg, 1.22 mmol, 61%). The ratio of the stereo isomers was determined as (*E* : *Z* = 15 : 85) by capillary GC analysis. R_f 0.90 (hexane/ethyl acetate = 10 : 1); bp 190 °C/4 Pa (Kugelrohr); $[\alpha]_D^{25}$ +1.9° (*c* 2.0, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = −0.25—−0.13 (1H, m), 0.62—0.74 (2H, m), 0.77—0.98 (18H, m), 1.22—1.59 (18H, m), 1.93—2.02 (1H, m), 4.91 (1H, ddt, J = 15.2, 8.6, 1.4 Hz), 5.48 (1H, dt, J = 15.2, 6.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 2.18(*Z*), 2.44(*E*), 8.70, 11.05(*Z*), 11.61(*E*), 13.73, 14.00, 18.18, 22.20(*Z*), 22.43(*E*), 27.34, 29.13, 31.99, 32.25, 127.23(*Z*), 127.35(*E*), 135.64 (*Z*), 135.73(*E*); IR (neat) 2921, 1655, 1457, 1375, 1041, 955 cm^{-1}. Found: C, 61.10; H, 10.41%. Calcd for $C_{21}H_{42}Sn$; C, 61.04; H, 10.24%.

(1*S*,2*R*)-2-(Hex-1-enyl)cyclopropanecarbaldehyde (9). To a solution of stannane **2** (290 mg, 0.70 mmol) in THF (4.0 ml) was added *n*-BuLi (0.56 ml, 0.90 mmol, hexane) at −78 °C dropwise. The mixture was stirred for 1 h at the same temperature and to this solution was added DMF (1.0 ml), followed by stirring for 1.5 h at the same temperature. The reaction was quenched by addition of a small volume of water and extracted with ether three times. After careful evaporation, subsequent silica gel flash column chromatography afforded aldehyde **9**. (90 mg, 0.59 mmol, 84%): $[\alpha]_D^{24}$ +96.4° (*c* 0.11, $CHCl_3$); R_f 0.47 (hexane/ethyl acetate = 10 : 1); bp 140 °C/135 Pa (Kugelrohr); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.83 (3H, t, J = 6.9 Hz), 1.00—1.12 (1H, m), 1.20—1.33 (4H, m), 1.43—1.52 (1H, m), 1.75—1.86 (1H, m), 2.01—2.14 (2H, m), 2.16—2.26 (1H, m), 4.96 (1H, ddt, J = 15.3, 8.1, 1.4 Hz), 5.54 (1H, dt, J = 15.3, 6.8 Hz), 9.06 (1H, d, J = 5.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 13.92, 15.07, 21.46, 22.14, 25.17, 31.40, 31.61, 32.03, 128.34, 132.35, 199.99; IR (neat) 2927, 2725, 1708, 1455, 1165, 1006 cm^{-1}. Found: C, 77.94; H, 11.06%. Calcd for $C_{10}H_{16}O$: C, 78.9; H, 10.59%.

(1*S*,2*R*)-1-[Hex-1-en-1-yl]-2-vinylcyclopropane (1). To a suspension of methyltriphenylphosphonium iodide (206 mg, 0.58 mmol) in THF (1.0 ml) was added potassium *t*-butoxide (61 mg,

0.54 mmol) at one portion and the mixture was stirred for 30 min at r.t., and cooled to −78 °C. To this mixture was added dropwise (*Z*)-aldehyde **9** (80.0 mg, 0.53 mmol) in THF (1.1 ml) and the reaction mixture was slowly warmed to r.t. for 3 h with stirring. The mixture was diluted with ether, concentrated under vacuum and silica gel flash column chromatography (pentane) afforded olefin **1** (65.0 mg, 0.41 mmol, 77%, *E*/*Z* = 15 : 85). The *E*/*Z* ratio was determined by capillary GC analysis ("Quadrex" bonded fused silica methyl silicone, ϕ 0.25 mm×25 m, N_2): R_t of (*E*)-**1**: 3.8 min. R_t of (*Z*)-**1**: 4.8 min, 100 °C to 250 °C/10 °C min^{-1}; $[\alpha]_D^{24}$ −30.7° (*c* 0.56, $CHCl_3$).

(1*S*,2*R*)-1-Tributylstannyl-2-vinylcyclopropane (3). To a suspension of methyltriphenylphosphonium iodide (1.49 g, 3.51 mmol) in THF (8.0 ml) was added potassium *t*-butoxide (394 mg, 3.69 mmol) and the mixture was stirred for 30 min at r.t., then cooled to −78 °C. To this solution was added dropwise a THF (5.0 ml) solution of aldehyde **8** (1.20 g, 3.34 mmol). The reaction mixture was allowed to warm to r.t. with stirring for 3 h, then diluted with ether and concentrated to dryness. Silica gel flash column chromatography (pentane) afforded **3** (990 mg, 2.77 mmol, 83%) as a colorless oil; $[\alpha]_D^{23}$ +3.48° (*c* 2.38, $CHCl_3$); R_f 0.93 (hexane/ethyl acetate = 10 : 1); bp 160 °C/2.5 Pa (Kugelrohr); ^{1}H NMR (200 MHz, $CDCl_3$) δ = −0.17—−0.05 (1H, m), 0.089 (9H, t, *J* = 7.2 Hz), 0.65—0.95 (7H, m), 1.22—1.62 (14H, m), 4.80 (1H, dd, *J* = 9.9, 2.0 Hz), 5.05 (1H, dd, *J* = 17.0, 2.1 Hz), 5.30 (1H, ddd, *J* = 17.0, 9.9, 8.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 2.59, 8.70, 11.46, 13.72, 19.44, 27.33, 29.10, 110.46, 144.53; IR (neat) 2957, 2925, 2853, 1633, 1463, 1375, 887 cm^{-1}. Found: C, 56.98; H, 9.56%. Calcd for $C_{17}H_{34}Sn$: C, 57.17; H, 9.60%.

(1*S*,2*R*)-2-Vinylcyclopropanecarbaldehyde (10). To a THF (11.0 ml) solution of stannane **3** (800 mg, 2.24 mmol) was added *n*-BuLi (2.48 mmol, 1.6 M hexane solution) at −78 °C dropwise and the mixture was stirred for 45 min at the same temperature. DMF (2.8 ml) was added and the solution was stirred for 1.5 h at −78 °C. The reaction was quenched by addition of water and extracted with ether. After careful evaporation and subsequent silica gel flash column chromatography (pentane) gave aldehyde **10** (140 mg, 1.46 mmol, 65%) as colorless liquid: $[\alpha]_D^{25}$ +149.9° (*c* 0.60, $CHCl_3$); R_f 0.47 (hexane/ethyl acetate = 10 : 1); bp 120 °C/11 Pa (Kugelrohr); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.13—1.24 (1H, m), 1.45—1.54 (1H, m), 1.85—1.97 (1H, m), 2.05—2.19 (1H, m), 5.02 (1H, dd, *J* = 9.8, 1.7 Hz), 5.18 (1H, dd, *J* = 17.0, 1.7 Hz), 5.42 (1H, ddd, *J* = 17.0, 9.8, 7.9 Hz), 9.15 (1H, d, *J* = 4.9 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 15.01, 25.68, 31.41, 115.48, 136.93, 199.67; IR (neat) 3083, 3006, 2928, 2834, 2728, 1707, 1639, 989, 908 cm^{-1}. Found: C, 73.97; H, 8.41%. Calcd for C_6H_8O: C, 74.97; H, 8.39%.

(+)-(1*S*,2*R*)-1-[(*E*)-Hex-1-enyl]-2-vinylcyclopropane (Dictyopterene A) (1). To a suspension of 5,5-dipentyldibenzophospholium bromide (**11**)[19] (231 mg, 0.570 mmol) in THF (5.0 ml) was added a THF (3.0 ml) solution of sodium hexamethyldisilazanide (NaHMDS) (255 mg, 0.556 mmol) at r.t. The mixture was stirred for 30 min at r.t., then a THF (4.0 ml) solution of aldehyde **10** (53.5 mg, 0.557 mmol) was added at −78 °C. The reaction mixture was allowed to warm to r.t. for 3 h with stirring and quenched by addition of water. The mixture was extracted with pentane and carefully evaporated. Silica gel flash column chromatography (pentane) and bulb-to-bulb distillation (150 °C, 760 Pa) afforded (*E*)-**1** (8.5 mg, 0.056 mmol, 10%). $[\alpha]_D^{25}$ +68.0° (*c* 0.34, $CHCl_3$), lit,[2b] +72 (*c* 6.74, $CHCl_3$); R_f 0.86 (hexane/ethyl acetate = 10 : 1); bp 100 °C/85 Pa (Kugelrohr); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.75—0.99 (5H, m), 1.24—1.42 (6H, m), 1.95—2.05 (2H, m), 4.96 (1H, dd, *J* = 10.1, 1.90 Hz), 5.04 (1H, dd, *J* = 17.0, 1.9 Hz), 5.38 (1H, ddd, *J* = 17.0, 10.3, 6.1 Hz), 5.49 (1H, dt, *J* = 15.2, 6.7 Hz) ; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 14.11, 14.75, 22.22, 23.57, 24.29, 31.77, 32.18, 111.83, 129.14, 131.55, 140.83; IR (neat) 2923, 2853, 1463, and 1376 cm^{-1}. These spectra data were completely identical with the reported one.[2b]

(1*S*,2*S*)-2-(*t*-Butyldimethylsiloxymethyl)cyclopropanecarbaldehyde (14). To a THF (5.2 ml) solution of **4c** (493 mg, 1.04 mmol) was added *n*-BuLi (1.12 mmol, 1.6 M hexane solution) at −78 °C and the mixture was stirred for 45 min at the same temperature. To this solution was added 1.3 ml of DMF and stirring continued for 2 h at −78 °C. Then the reaction was quenched by addition of water. The mixture was filtered through a silica gel short column eluted with ether, dried ($MgSO_4$), and evaporated. Silica gel flash column chromatography (hexane/ethyl acetate = 10 : 0 to 2 : 1) and bulb-to-bulb distillation gave **14** (218 mg, 1.02 mmol, 98%). $[\alpha]_D^{24}$ +60.0° (*c* 0.83, $CHCl_3$): R_f 0.45 (hexane/ethyl acetate = 10 : 1); bp 130 °C/11 Pa (Kugelrohr); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.028 (6H, s), 0.86 (9H, s), 1.06—1.17 (1H, m), 1.20—1.29 (1H, m), 1.64—1.88 (2H, m), 3.58—3.74 (2H, m), 9.07 (1H, d, *J* = 5.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 11.58, 18.23, 23.84, 25.80, 27.35, 62.63, 200.84; IR (neat) 2950, 2859, 1711, 1466, 1256, 1095, 839 cm^{-1}. Found: C, 61.60; H, 10.35%. Calcd for $C_{11}H_{22}O_2Si$: C, 61.63; H, 10.34%.

(1*S*,2*S*)-1-[(*t*-Butyldimethylsiloxy)methyl]-2-(2-iodovinyl)cyclopropane (15). Chromium(II) chloride (279 mg, 2.27 mmol) was placed in a three necked flask under argon, aldehyde **14** (81.0 mg, 0.378 mmol) in THF (1.5 ml) and iodoform (298 mg, 0.757 mmol) in THF (1.5 ml) at 0 °C and the mixture was stirred for 2.5 h at the same temperature. The reaction was quenched by addition of water (9.45 ml) and extracted with ether. The combined organic layers were dried and evaporated. Silica gel flash column chromatography (hexane/ethyl acetate = 100 : 0 to 10 : 1) gave vinyl iodide **15** (102 mg, 0.302 mmol, 80%). Capillary GC analysis revealed that the product was a mixture of (*E*)- and (*Z*)-**15** with a ratio of 91 : 9. Because this compound **15** was unstable, distillation was unsuccessful. The compound was immediately used for the next reaction after ^{1}H NMR analysis and specific rotation measurement. $[\alpha]_D^{23}$ +32.9° (*c* 0.65, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.037 (6H, m), 0.64—0.78 (1H, m), 0.88 (9H, s), 1.08—1.25 (2H, m), 1.33—1.46 (1H, m), 3.55 (2H, d, *J* = 3.7 Hz), 5.95 (1H, d, *J* = 14.4 Hz), 6.06 (1H, dd, *J* = 14.4, 8.1 Hz); IR (neat) 2949, 2858, 1465, 1255, 1089, 838 cm^{-1}.

(1*S*,2*R*)-1-[(*t*-Butyldimethylsiloxy)methyl]-2-(hex-1-enyl)cyclopropane (13). To a THF (3.73 ml) solution of $ZnCl_2$ (0.746 mmol) was added *n*-BuLi (0.746 mmol, 1.6 M hexane solution) at −78 °C and the mixture was allowed to warm to r.t. for 1.5 h to form dibutylzinc reagent. To this solution was added the iodide **15** (126 mg, 0.373 mmol) in THF (2.0 ml), $Pd(PPh_3)_4$ (46 mg, 0.040 mmol), and 0.75 ml of DMF at 0 °C in one portion. The reaction mixture was stirred for 12 h at r.t. and was quenched by addition of water and filtered through a celite short column eluted with ether. The resulting elute was evaporated. Silica gel flash column chromatography afforded **13** (69 mg, 0.257 mmol, 69%). $[\alpha]_D^{23}$ +18.8° (*c* 1.70, $CHCl_3$); R_f 0.70 (hexane/ethyl acetate = 10 : 1); bp 130 °C/11 Pa (Kugelrohr); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.047 (6H, s), 0.50—0.70 (2H, m), 0.88 (3H, t, *J* = 6.9), 0.89 (9H, s), 0.90—1.05 (2H, m), 1.20—1.40 (4H, m), 1.96 (2H, dt, *J* = 12.8, 6.0 Hz), 3.47 (1H, dd, *J* = 10.9, 7.3 Hz), 3.61 (1H, dd, *J* = 10.9, 5.9 Hz), 5.01 (1H, ddt, *J* = 15.2, 8.3, 4.1 Hz), 5.21 (dt, *J* = 15.2, 6.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 11.25, 13.95, 15.21, 18.40, 19.08, 22.19, 22.50, 25.97, 31.81, 32.16, 65.99, 128.59, 132.32; IR (neat) 2930, 1463, 1253, 1090, 838, 776 cm^{-1}. Found: C, 71.77;

H, 12.03%. Calcd for $C_{16}H_{32}OSi$: C, 71.57; H, 12.01%.

Dictyopterene A (1). To a stirred solution of **13** (52 mg, 0.194 mmol) in THF (1.7 ml) was added a THF (0.25 ml) solution of *n*-Bu_4NF (1.0 M in THF) at r.t., and the solution was stirred at r.t. for 4.0 h. The reaction mixture was diluted with ether saturated with water and the solvent was removed under vacuum to give the alcohol (30 mg). This was treated with freshly prepared $C_6H_4COOI(OAc)_3$ (91.4 mg, 0.215 mmol),[14] and pyridine (56 mg, 0.72 mmol) in CH_2Cl_2 (1.4 ml) at r.t. for 2 h. Silica gel flash column chromatography gave aldehyde **9** (20 mg, 69%) as a colorless liquid: $[\alpha]_D^{22}$ +24.4° (*c* 0.50, $CHCl_3$). Methyltriphenylphosphonium iodide (488 mg, 1.21 mmol) was placed in a flask and suspended in THF (20 ml). *n*-BuLi (1.11 mmol, 0.70 ml of hexane solution) was added at −20 °C, and the mixture was stirred for 5 min at the same temperature. To this solution was added a THF (5.0 ml) solution of aldehyde **9** (153 mg, 1.00 mmol) at −78 °C and the mixture was stirred for 15 min at the same temperature. The reaction was quenched by addition of ether saturated with water and the solvent was carefully removed by evaporation. The residue was filtered through a florisil short column eluted with pentane, and evaporated by bulb-to-bulb distillation (40—50 °C at 45 Pa) to afford **1** (128 mg, 85%) as a colorless liquid. Capillary GC analysis revealed that the product was a mixture of desired (*E*)-**1** and undesired (*Z*)-**1** (91 : 9). $[\alpha]_D^{22}$ +60.6° (*c* 1.05, $CHCl_3$).

This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas No. 283, "Innovative Synthetic Reactions" from The Ministry of Education, Science, Sports and Culture. The authors are grateful to the SC-NMR Laboratory of Okayama University for the NMR measurements and to the MALDI-TOF MS laboratory of the Graduate School of Okayama University for elemental analyses.

References

1 A review for utilization cyclopropane in organic synthesis, see: H. N. C. Wong, M. -Y. Hon, C. -W. Tse, Y. -C. Yip, J. Tanko, and T. Hudlicky, *Chem. Rev.*, **89**, 165 (1989). For recent examples, see: A. G. M. Barrett and W. Tam, *J. Org. Chem.*, **62**, 4653 and 7673 (1997), and references cited therein.

2 a) R. E. Moore, J. A. Pettus, Jr., and M. S. Doty, *Tetrahedron Lett.*, **1968**, 4787. b) J. Mistysyn, R. E. Moore, J. A. Pettus, Jr., and J. Mistysyn, *J. Org. Chem.*, **39**, 2201 (1974). c) R. E. Moore, *Acc. Chem. Res.*, **10**, 40 (1977). d) L. Jaenicke and W. Boland, *Angew. Chem., Int. Ed. Engl.*, **21**, 643 (1982). Absolute configuration of dictyopterene A was wrong registered as (1*R*,2*R*) in these references. This should be corrected to (1*S*,2*R*); M. Hombeck, G. Pohnert, and W. Boland, *Chem. Commun.*, **1999**, 243.

3 Because of its unique biological activity, several syntheses of this compound have been reported. a) D. Grandjean, P. Pale, and J. Chuche, *Tetrahedron*, **47**, 1215 (1991). b) D. Wirth, I. F-Lui, W. Boland, D. Icheln, T. Runge, W. A. Kønig, J. Phillips, and M. Clayton, *Helv. Chim. Acta*, **75**, 734 (1992). c) W. Boland, G. Pohnert, and I. Maier, *Angew. Chem., Int. Ed. Engl.*, **34**, 1602 (1995). d) G. Pohnert and W. Boland, *Tetrahedron*, **53**, 13681 (1997).

4 T. Itoh, S. Emoto, and M. Kondo, *Tetrahedron*, **54**, 5225 (1998).

5 Several synthesis of optically active (**4a**) has been reported. a) Y. Ukaji, K. Sada, and K. Inomata, *Chem. Lett.*, **1993**, 1227. b) N. Imai, K. Sakamoto, H. Takahashi, and S. Kobayashi, *Tetrahedron Lett.*, **35**, 7075 (1994). c) N. Imai, K. Sakamoto, M. Maeda, K. Kouge, K. Yoshizane, and J. Nokami, *Tetrahedron Lett.*, **38**, 1423 (1997).

6 Recent examples, see: a) S. E. Denmark and S. P. O'Connor, *J. Org. Chem.*, **62**, 584 (1997). b) R. E. Taylor, M. K. Ameriks, and M. J. LaMarche, *Tetrahedron Lett.*, **38**, 2057 (1997). c) W. S. McDonald, C. A. Verbicky, and C. K. Zercher, *J. Org. Chem.*, **62**, 1215 (1997). d) J. Barluenga, P. L. Bernad, Jr., and J. M. Concellón, *J. Org. Chem.*, **62**, 6870 (1997). e) H. Wakamatsu, N. Isano, and M. Mori, *J. Org. Chem.*, **62**, 8917 (1997). f) J. Pietruska and M. Windenmeyer, *Synlett*, **1997**, 977. g) J. P. Hildebrand and S. P. Marsden, *Synlett*, **1996**, 893. h) N. Isano and M. Mori, *J. Org. Chem.*, **61**, 7867 (1996). g) M. Lautens, P. H. M. Delanghe, J. B. Goh, and C. H. Zhang, *J. Org. Chem.*, **60**, 4213 (1995), references cited therein.

7 A. B. Charette and H. Juteau, *J. Am. Chem. Soc.*, **116**, 2651 (1994). For review see: A. B. Charette and J. -F. Marcoux, *Synlett*, **1996**, 1197.

8 J. P. McCormick and D. J. Barton, *J. Org. Chem.*, **45**, 2566 (1980).

9 For various dehydration methods, see:, R. C. Larock, "Comprehensive Organic Transformation. A Guide to Functional Group Preparations," VCH Publishers, Inc., pp.151—153 (1989).

10 a) N. Porahmady, E. H. Vickery, and E. J. Eisenbraum, *J. Org. Chem.*, **47**, 2590 (1982). b) T. Nishiguchi, N. Machida, and E. Yamamoto, *Tetrahedron Lett.*, **28**, 4565 (1987).

11 a) J. Mulzer, B. List, and J. N. Bats, *J. Am. Chem. Soc.*, **119**, 5512 (1997). b) R. M. Williams and L. K. Maruyama, *J. Org. Chem.*, **52**, 4044 (1987). c) H. Kashihara, H. Suemune, T. Kawahara, and K. Sakai, *Tetrahedron Lett.*, **28**, 6489 (1987).

12 A. Schwartz and P. Madan, *J. Org. Chem.*, **51**, 5463 (1986).

13 a) A. B. Charette, H. Juteau, H. Lebel, and D. Deschenes, *Tetrahedron Lett.*, **34**, 7925 (1996). b) C. R. Theberge, C. A. Verbicky, and C. K. Zercher, *J. Org. Chem.*, **61**, 8792 (1996). c) W. S. McDonald, C. A. Verbicky, and C. K. Zercher, *J. Org. Chem.*, **62**, 1215 (1997).

14 a) D. B. Dess and J. C. Martin, *J. Org. Chem.*, **48**, 4156 (1983). b) R. E. Ireland and L. Liu, *J. Org. Chem.*, **58**, 2899 (1993).

15 Reviews see: a) M. Schlosser, *Top. Stereochem.*, **5**, 1 (1970). b) B. E. Maryanoff and A. B. Reitz, *Chem. Rev.*, **89**, 863 (1989).

16 J. M. Muchowski and M. C. Venuti, *J. Org. Chem.*, **46**, 459 (1981).

17 M. Schlosser and K. F. Christmann, *Angew. Chem., Int. Ed. Engl.*, **5**, 126 (1966).

18 R. J. Anderson and C. A. Henrick, *J. Am. Chem. Soc.*, **97**, 4327 (1975).

19 E. Vedejs, C. F. Marth, and R. Ruggeri, *J. Am. Chem. Soc.*, **110**, 3940 (1988).

20 M. Schlosser and K. F. Christmann, *Liebigs Ann. Chem.*, **708**, 1 (1967).

21 M. Schlosser, K. F. Christmann, and A. Piskala, *Chem. Ber.*, **103**, 2814 (1970).

22 E. Vedejs and C. Marth, *Tetrahedron Lett.*, **28**, 3445 (1987).

23 T. S. McDermott, A. A. Mortlock, and C. H. Heathcock, *J. Org. Chem.*, **61**, 700 (1996).

24 A review see: A. Suzuki, *Pure Appl. Chem.*, **63**, 419 (1991). For our employed reaction conditions see: I. D. Gridnev, N. Miyaura, and A. Suzuki, *J. Org. Chem.*, **58**, 5351 (1993).

25 H. C. Brown and S. K. Gupta, *J. Am. Chem. Soc.*, **94**, 4370 (1972).

26 K. Takai, K. Nitta, and K. Utimoto, *J. Am. Chem. Soc.*, **108**, 7408 (1986).

27 a) E-i. Negishi, M. Ay, Y. V. Gulcvich, and Y. Noda, *Tetrahedron Lett.*, **34**, 1437 (1993). b) D. R. Williams and W. S. Kissel, *J. Am. Chem. Soc.*, **120**, 11198 (1998).

28 Y. Kondo, N. Takazawa, C. Yamazaki, and T. Sakamoto, *J. Org. Chem.*, **59**, 4717 (1994).