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Lewis Acid-induced Reaction of Silicon-containing Stannyl Ketones and Its Application to the Synthesis of (+)-β-Cuparenone

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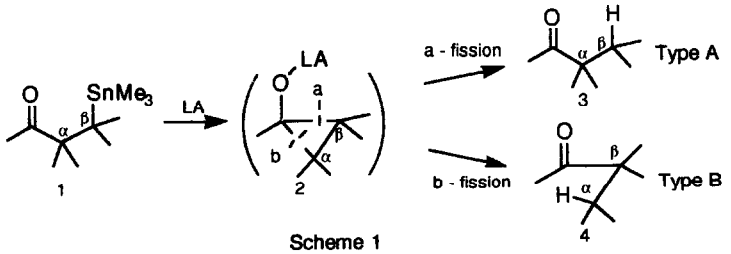
Key Words: β-Silyl-β'-stannyl ketone; (+)-β-Cuparenone; Cyclopropanation; 1,5-Hydride shift

Abstract: *Lewis acids activated only stannyl group in the silicon-containing stannyl ketones. The silyl group neither participated in the reaction directly, nor excerted any influences upon the reaction mode of the stannyl group. The reaction was applied for the synthesis of (+)-β-cuparenone.*

We have reported that the tin-bearing carbon behaves as a latent carbanion, and undergoes several types of reactions with cationic center within the same molecule.[1] Typical reaction types are cyclization and hydride or alkyl shift, and the reaction types depend upon the relative positions of the cationic center to the carbon-tin bond, the number of the substituents on the tin-bearing carbon, and the activation methods. As a continuation of the study, we extended the reaction system to stannyl ketones having silicon or another tin atom, with a view to compare the reactivities of the carbon-silicon and carbon-tin bonds located at appropriate positions from carbonyl group, and those of two carbon-tin bonds located at different positions from the activating group.

The Reaction of β*-Stannyl Ketones with Lewis Acids.* We have so far investigated the Lewis acid-induced reaction of β-stannyl ketones **1**, and found that the reaction usually proceeded *via* cyclopropanol intermediates **2**, which afforded saturated ketones **3** or **4**, according to the position of the bond cleavage of the cyclopropanol ring of 2, a or b, as shown in Scheme 1.[2] We termed Type A and Type B reactions,

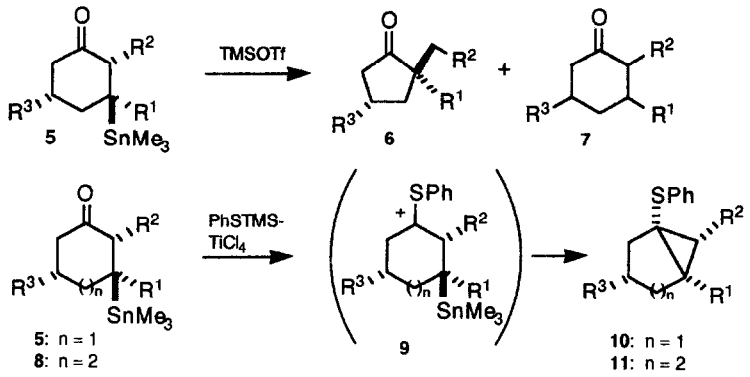


Scheme 1

respectively, for these reactions. The general trend is that, (1) the ring cleavage of the cyclopropanol intermediates **2** occurs at bond leading to the less substituted carbon, (2) in cases where both α and β-carbons have the same number of substituents, trimethylsilyl trifluoromethanesulfonate (TMSOTf) facilitates the Type B reaction, while titanium(IV) chloride induces the both reactions unselectively, (3) the introduction of a group having leaving ability (-OH or -Cl) into the α-substituent induces the Type B reaction, irrespective of the substitution pattern or the nature of Lewis acid, and (4) if both of α and β-positions of the β-stannyl ketones are fully substituted, a 1,2-alkyl migration-dehydration affording hydrocarbons competes with the cyclopropanation.[3]

Since these types of the reaction have not been known in the corresponding silicon compounds, we examined the behaviors of silicon-containing β-stannyl ketones towards the TMSOTf treatment. The requisite β-silyl-β'-stannyl ketones **5a** ~ **5e** were prepared by conjugate addition of trimethylstannyllithium to the corresponding 5-trimethylsilyl-2-cyclohexen-1-one derivatives, followed by quenching the intermediate enolates with benzyl bromide or proton. It has been established that the stannyl group occupies *trans* position to the C2 and C5 substituents (R^2 and R^3, respectively) in compounds prepared in this way.[4]

Upon treatment with TMSOTf, **5a** ~ **5e** afforded cyclopentanones **6a** ~ **6e**, resulted from the Type B reaction, as major products (Table 1, runs 1 ~ 7). Only in case of **5a**, the Type A reaction competed to afford **7a** in minor amounts, particularly when the reaction temperature was higher (runs 1 ~ 3). The products were isolated as a single stereoisomer in all cases except **6a**, which contained a minor amount (1 : 4) of *cis*-isomer. The stereochemistry of **6** was assigned as indicated (R^3 *vs* CH_2R^2 : *trans*), in view of our conclusion obtained



a: $R^1 = R^2 = H$, $R^3 = TMS$; b: $R^1 = Me$, $R^2 = H$, $R^3 = TMS$
c: $R^1 = Me$, $R^2 = Bn$, $R^3 = TMS$; d: $R^1 = p$-tol, $R^2 = H$, $R^3 = TMS$
e: $R^1 = PhCH_2CH_2$, $R^2 = H$, $R^3 = TMS$;
f: $R^1 = R^2 = R^3 = H$; g: $R^1 = Me$, $R^2 = H$, $R^3 = Me_2$

previously from the NOE experiment that the cyclopropanation proceeded with inversion of the tin-bearing carbon.[2] The conclusion was now further confirmed by utilizing optically active compounds, as will be discussed in later part of the paper. The results show that the carbon-silicon bond could not be activated under the present conditions. Actually **7a** was recovered unchanged upon treatment with TMSOTf (run 8).

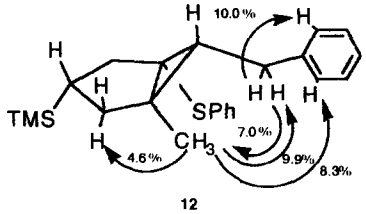
When the compounds **5a-5d** were treated with trimethylsilyl phenylthiolate/titanium(IV) chloride ($Me_3SiSPh/TiCl_4$) in dichloromethane,[5] cyclopropane derivatives **10a** ~ **10d** were obtained (Table 1, runs 9 ~ 12). Presumably the reaction proceeded through the intermediacy of the thionium cation **9**. The reaction of **5a** (run 9) was exceptional in that the product contained the Type A and Type B products in minor amounts, and **10a** was a diasteromer mixture (1 : 2). The cyclopropanation by this reagent was also accomplished with

stannyl compounds having no silyl group, **5f**, **5g**, and **8f** (runs 13-15), indicating that the silyl group did not excert any influences for the cyclopropanation. Referring to the ^{13}C- and/or 400 MHz ^{1}H-NMR analyses, all the products except **10a** were stereochemically pure, and we assigned the structures of the products as shown, in view of the NOE experiment with **10c**, which showed signal enhancements between benzyl and angular methyl groups as shown in **12**. The result is compatible with the generality that the cyclopropanation proceeded with inversion of the tin-bearing carbon. The NOE result is inconsistent with the structure **13**, which would result from the reaction involving retention of the tin-bearing carbon.

Table 1. Reactions of β-Stannyl Ketones with TMSOTf and TMSSPh/$TiCl_4$.

run	substrate	Lewis acid[a)]	temp (°C)	time (min)	product and yield (%)
1	**5a**[b)]	A	-78 ~ 0	60	**6a**[c)] (70) **7a** (5)
2	**5a**[b)]	A	0	180	**6a**[c)] (51) **7a** (5)
3	**5a**[b)]	A	rt	180	**6a**[c)] (67) **7a** (12)
4	**5b**	A	-78 ~ rt	120	**6b** (99)
5	**5c**	A	0	240	**6c** (82)
6	**5d**	A	0 ~ rt	180	**6d** (90)
7	**5e**	A	0 ~ rt	180	**6e** (61)
8	**7a**	A	rt	180	**7a** (recovery)
9	**5a**	B	rt	15	**10a** (60) **6a** (20) **7a** (14)
10	**5b**	B	0	15	**10b** (97)
11	**5c**	B	0	15	**10c** (93)
12	**5d**	B	0	15	**10d** (84)
13	**5f**	B	rt	15	**10f** (93)
14	**5g**	B	rt	15	**10g** (86)
15	**8f**	B	rt	15	**11f** (44)
16	**14a**	B	0	15	**15a** (99)
17	**14b**	B	0	15	**15b** (96)

a) A: TMSOTf; B: TMSSPh/$TiCl_4$; b) Diastereomer mixture (*c* : *t* = 1 : 10); c) Diastereomer mixture (*c* : *t* = 1 : 4)



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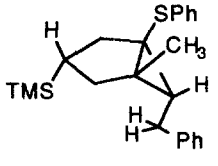

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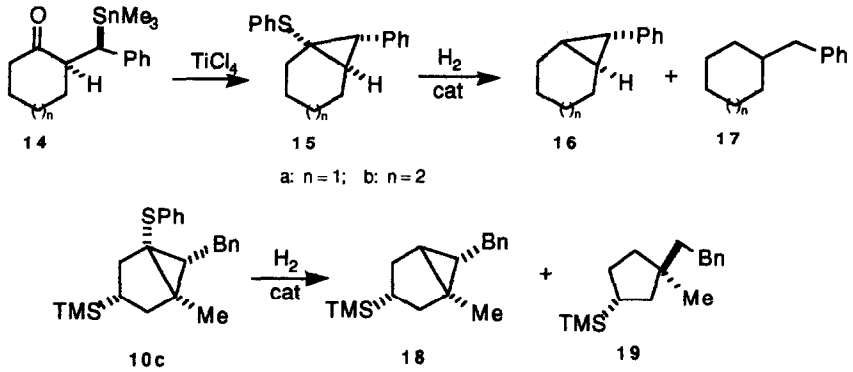
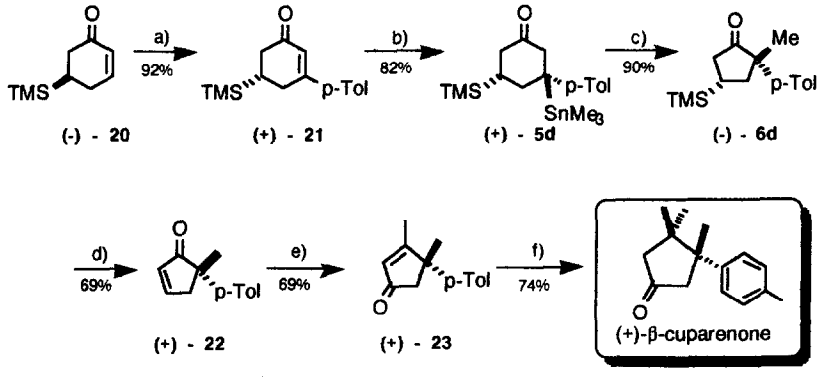
The cyclopropanation also proceeded with the *exo*-type stannyl compounds **14a** and **14b** (runs 16 and 17), which gave **15a** and **15b**, respectively, as single stereoisomers. Since cyclopropanethiol derivatives have potential synthetic capabilities, the present reaction could be utilized for this purpose, particularly for the preparation of stereochemically defined products. As an instance, **15b** and **10c** afforded **16** + **17** (2 : 8) and **18** + **19** (1 : 1), respectively, in quantitative yields as single stereoisomers, upon hydrogenation over Raney nickel (W-7). With less active Raney nickel, **18** was obtained selectively from **10c** in 89% yield.



Since it has been well-documented that the carbon-silicon bond can be easily activated by fluoride anion, we wondered if the nucleophilic reaction of the carbon-silicon bond towards the carbonyl group could be realized by fluoride anion, in a similar fashion as observed in the TMSOTf-induced reaction of the stannyl ketones. Actually, however, neither of the stannyl nor silyl ketones **5a**, **5f**, or **7a** underwent any reactions, when they were treated with four equivalents of tetrabutylammonium fluoride at room temperature for 7 h in dichloromethane.

(+)-β-Cuparenone Synthesis. As described in our previous paper,[2] as well as in the present study, NOE experiments showed that the cyclopropanation proceeded with inversion of the tin-bearing carbon. Since it has now been established that the carbon-silicon bond was intact under the TMSOTf treatment, we envisioned a (+)-β-cuparenone synthesis from an optically active silyl ketone, with a view to demonstrate a synthetic applicability of the Type B reaction, and also to prove the proposed stereochemical pathway. We chose (−)-**20** as an ideal starting material, because it is available in both enantiomorph,[6] and has a suitable feature for the present purpose. The reaction scheme is shown in Scheme 2.[7]

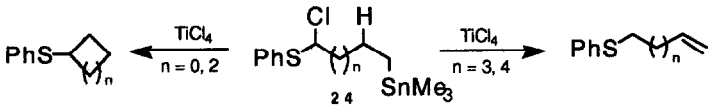


a) 1) p-TolLi, 2) PDC; b) 1) Me_3SnLi, THF; c) TMSOTf, CH_2Cl_2;
d) 1) MnO_2, TMSCl, 2) TBAF; e) 1) MeLi, 2) PDC; f) $MeCuBF_3$, ether

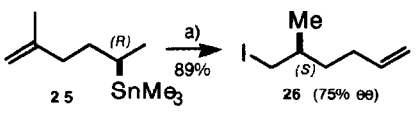
Scheme 2

The reaction of *p*-tolyllithium with (−)-**20**, followed by oxidation with PDC gave enone (+)-**21** in 92% overall yield in two steps.[7a] Treatment of (+)-**21** with trimethylstannyllithium in THF at −78 °C afforded crystalline β-silyl-β'-stannyl ketone (+)-**5d** in 82% yield. A trace amount of *cis*-epimer was detected, but it was easily separated from the major product by column chromatography. The major product was diastereomerically pure as evident from ^{13}C-NMR analysis. Treatment of (+)-**5d** with TMSOTf in dichloromethane gave (−)-**6d** in 90% yield with the carbon skeleton rearrangement. The silyl compound (−)-**6d** was converted into (+)-β-cuparenone according to the reported method,[7a] with slight modification (see Experimental part). The product, obtained in 23% overall yield from (−)-**20**, showed the same $[\alpha]_D$ value,[7a,8,9] as well as the spectroscopic data (NMR and IR) as those reported.[9] The intermediate (+)-**23** also indicated the same optical rotation as reported.[8] In view of these results, it is evident that the Type B reaction proceeds with complete inversion of the tin-bearing carbon, affording a single stereoisomer in high yield and selectivity.

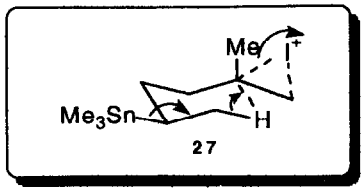
The Lewis Acids-induced Reaction of Stannyl Ketones having Tin Atom at Remote Positions from the Carbonyl Group. Macdonald observed that the cation-induced reaction of stannyl compounds having a cationic center separated from the carbon-tin bond by more than three carbons proceeds with cyclization or β-hydride shift, depending upon the type of the substrate and reaction conditions.[10] Some time ago, we carried out a systematic investigation of the thionium ion-induced reaction of primary alkylstannanes **24**, and found that the cyclization predominated when n = 0 or 2, while β-hydride shift predominated when n = 3 or 4.[11] We further



Scheme 3

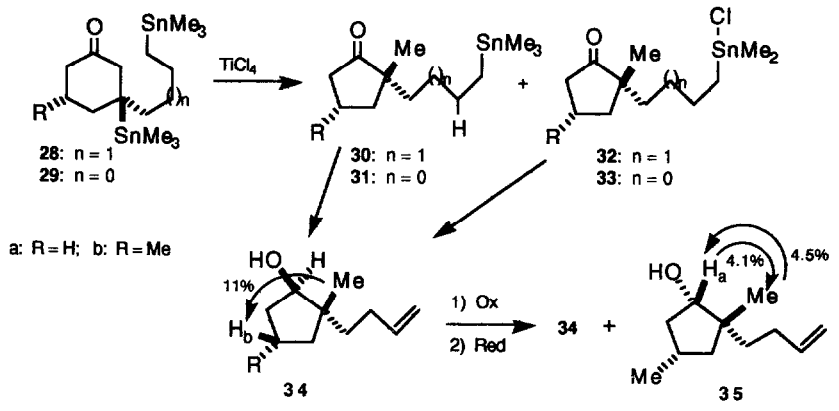


a) I_2/AgOTf, CH_2Cl_2, -78 °C



reported that a chiral stannyl olefin **25** gave an iodo olefin **26** with 75% ee upon treatment with silver triflate/iodine.[12] A cyclic transition state **27** was proposed for the 1,5-hydride shift to justify the chirality transfer. A similar hydride transfer has been observed with a carbonyl system by the Lewis acid treatment.[13]

With a view to compare the relative reactivity of the carbon-tin bond at β-position and that at positions separated farther from the carbonyl group, we treated **28a**, **28b**, and **29b** with Lewis acids. The starting materials were prepared in routes as shown in Scheme 4. The reaction afforded the corresponding Type B products **30a**, **30b**, and **31b**, respectively, as shown in Table 3, runs 18 ~ 22. In cases of runs 20 ~ 22, a chlorine replacement of one of the methyl groups on the tin atom occurred to afford **32b** and **33b**. Although we have not pursued the chlorine source, there is no candidate other than dichloromethane (solvent) in runs 20 and 21. Although the hydride-shift to **34b** was observed only when two equivalents of TMSOTf was used with prolonged reaction time (run 21), it proceeded smoothly when **30a** and **30b** were treated with titanium(IV) chloride (runs 23 and 24). The same reaction proceeded from **32b**, even though with lower yield (run 25), but no reaction occurred with **33b** (run 26). Reasonably no hydride shift could be expected from

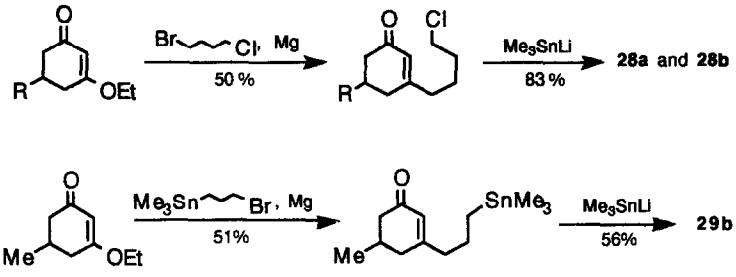


33b, in which no such a cyclic transition state is possible. In order to confirm the stereochemistry of **34b**, we prepared a diastereomer **35** from **34b** through a successive Swern oxidation and sodium borohydride reduction. A distinct NOE enhancement was observed between C2-methyl and H_b (11%) in **34b**, while it was observed between C2-methyl and H_a (4.1 ~ 4.5%) in **35**. Evidently these results show that β-carbon-tin bonds in **28** and **29** are more reactive than the terminal carbon-tin bonds, and that the 1,5-hydride shift proceeded through a cyclic transition state **40** to produce stereochemically-defined products. No cyclization products between carbonyl carbon and the terminal carbon were detected either.

Table 2. The Reaction of Stannyl Ketones having Tin Atom at Remote Positions from the Carbonyl Group with Lewis Acids.

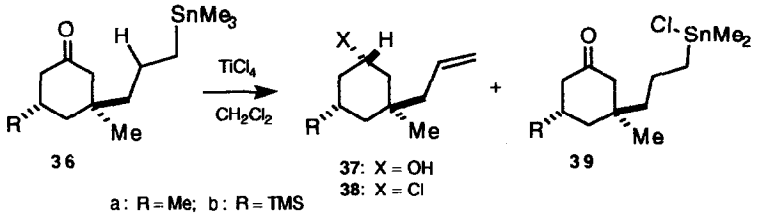
run	substrate	Lewis acids[a] (eq)	temp (°C)	time (h)	product and yield (%)
18	**28a**	A (1)	rt	2	**30a** (65)
19	**28b**	A (1)	rt	0.5	**30b** (50)
20	**28b**	A (1)	rt	2	**30b** (25) **32b** (~50)
21	**28b**	A (2)	0 ~ rt	17	**30b** (20) **32b** (33) **34b** (30)
22	**29b**	B (1)	-78 ~ 0	2	**31b** (7) **33b** (69)
23	**30a**	B (1)	rt	1	**34a** (49)
24	**30b**	B (1)	-78 ~ 0	2	**34b** (94)
25	**32b**	B (1)	-78 ~ rt	40	**34b** (37)
26	**33b**	B (1)	-78 ~ rt	24	**33b** (recovery)
27	**36a**	B (1.5)	-78	1	**37a** (63) **39a** (34)
28	**36a**	B (2.0)	-78 ~ rt	2	**37a** (70) **39a** (26)
29	**36b**	B (1.1)	-78	1	**37b** (66) **39b** (15)
30	**36b**	B (1.5)	-78 ~ 0	2	**38b** (62) **39b** (29)

a) A: TMSOTf; B: $TiCl_4$.

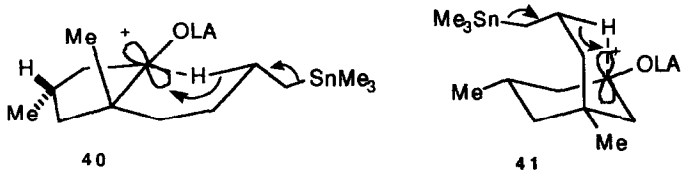


Scheme 4

We further prepared a silicon-containing compound **36b**, and compared its reaction mode with that of the non-silyl counterpart **36a**. These starting materials were prepared as single stereoisomers by conjugate addition of Grignard reagent prepared from 3-(trimethylstannyl)propyl bromide to the corresponding cyclohexenones according to the reported method.[14] The stereochemistry of the products was deduced from the well-documented observation that the incoming group occupies *trans* position to the C5 substituent.[15] When **36a** or **36b** were treated with titanium(IV) chloride at −78 °C, the hydride shift and chlorine substitution proceeded in both cases, affording **37a** and **39a**, or **37b** and **39b**, respectively, as single stereoisomers (Table 2, runs 27 and 29). The stereochemistry of **37a** and **37b** was assigned by assuming a cyclic transition state **41**,



corresponding to **40**. When the reaction was carried out at 0 °C ~ room temperature, the replacement of the hydroxyl group by chlorine was observed with the silyl compound **36b**, affording **38b** (run 30). However, no chlorine replacement was observed with **36a** under the same conditions (run 28). The chloride **38b** was stereochemically pure in view of the 400 MHz ^{1}H-NMR analysis, indicating that the chlorine substitution took place stereoselectively. It has been reported that the solvolysis of *cis*-3-(trimethylsilyl)cyclohexyl sulfonate is promoted by the participation of the γ-situated silyl group across the ring, and proceeds with retention of configuration.[16] In view of the apparent participation of the silyl group in the present case, we assumed the retention of configuration during the chlorine substitution, and assigned the *cis* structure (TMS *vs* Cl) for **38b**.



Conclusion. In this paper, we found the following points. (1) Lewis acids activated only stannyl group in the silicon-containing stannyl ketones. The silyl group neither participated in the reaction directly, nor excerted any influences upon the reaction mode of the stannyl group. (2) The stereochemical pathway of the TMSOTf-induced reaction of 3-stannylcyclohexanones was confirmed to proceed with inversion at the tin-bearing carbon, by correlating an optically active silyl stannyl ketone with natural product (+)-β-cuparenone, as well as by NOE experiments. (3) In reactions with stannyl ketones having two tin atoms, the cyclopropanation proceeded preferably to the 1,5-hydride shift. The 1,5-hydride shift proceeded through a cyclic transition state to afford stereochemically-defined products.

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Experimental Section

General Procedure and Instrumentation. GLC experiments were carried out on a 2.5 m x 3 mm stainless steel column packed with Silicone SE 30 on silanized Chromosorb W and 25 m x 0.25 mm capillary column (SE 30). Preparative TLC was carried out on DC-Alufolien Kieselgel 60 F254, Art. 5554, using solvents as indicated. Column chromatography was carried out on Kieselgel 60, Art. 7734 (70-230 mesh ASTM) using solvents as indicated. ^{1}H-NMR spectra (60 MHz) were recorded on a Hitachi R-24 or JEOL PMX 60 SI spectrometer. ^{1}H-NMR (90 MHz) and ^{13}C-NMR (22.5 MHz) spectra were measured on a Hitachi JNM-PMX 60 S R-90 H spectrometer, and 400 MHz ^{1}H-NMR spectra on a JEOL GSX-400 spectrometer. GC-MS spectra were taken on a Shimadzu QP-1000 mass spectrometer, and high resolusion mass spectra on a JEOL DX-300 mass spectrometer. IR spectra were recorded on a Perkin-Elmer 1640 type FT-IR. Unless otherwise stated, all the spectroscopic data were determined on pure samples obtained by either distillation, preparative TLC, or column chromatography; the mass spectra were obtained by EI method at 70 ev, the ^{1}H-NMR data on the 60 MHz machines with CCl_4 solutions, the ^{1}H-NMR data on the 400 MHz machine and ^{13}C-NMR data with $CDCl_3$ solutions, and IR spectra with neat samples.

All of the ^{1}H-NMR signal of the methyl group on tin atom at δ = ~0 ppm accompanied splitting signals by ^{117}Sn (7.54% abundance, J = 51 Hz) and ^{119}Sn (8.62% abundance, J = 53 Hz).

General Procedure for the Preparation of α-Unsubstituted-β-Stannyl Ketones. To a THF solution (5 ml) of Me_3SnLi (1.5 mmol)[17] was added a THF solution (2.5 ml) of appropriate enones (1.0 mmol) dropwise at −25 ~ −78 °C over 10 min, and the solution was stirred at this temperature for 30 min. The reaction mixture was diluted with hexane (30 ml), slowly warmed to room temperature, and stirred for another 1 h. The solution was quenched by sat NH_4Cl aq, diluted with ether, washed with brine, and dried over $MgSO_4$. The solvent was removed *in vacuo*, and the residue was purified on column chromatography (ether : hexane =1 : 5) to give the respective β-stannyl ketones.

5-Trimethylsilyl-3-(trimethylstannyl)cyclohexanone (5a). The product was obtained from 5-trimethylsilyl-2-cyclohexen-1-one[6] (0.600 g, 3.57 mmol) as an oil (1.102 g, 92%). Although the product showed two peaks (1 : 10) on GLC, the ^{1}H and ^{13}C-NMR signals corresponding to the minor component were hardly discernible. The GCMS data of the two peaks were identical. In view of our previous report,[2] we assigned *trans* structure for the major product. The IR, ^{1}H-NMR, and ^{13}C-NMR spectra were measured on the *cis-trans* mixture. MS, m/z 319 (M^+ − 15), 165, 73 (base peak, TMS). IR, 1709, 1249, 765 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.06 (s, 9H), 0.90 ~ 1.40 (m, 2H), 1.80 ~ 2.70 (m, 6H). ^{13}C-NMR, δ −10.34, −3.45, 26.37, 27.19, 29.65, 41.92, 45.26, 211.61.

3-Methyl-5-trimethylsilyl-3-(trimethylstannyl)cyclohexanone (5b). The product was obtained from 3-methyl-5-trimethylsilyl-2-cyclohexen-1-one[18] (0.500 g, 2.74 mmol) as a single *trans* isomer (oil, 0.855 g, 90%). MS, m/z 333 (base peak, M^+ - 15), 275, 233, 183, 165 (Me_3Sn), 93, 73. IR, 1711, 1248, 766 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.04 (s, 9H), 1.15 (s, 3H), 0.60 ~ 2.60 (m. 7H). HRMS, calcd for $C_{13}H_{28}OSiSn$ (M) 348.0931, found 348.0979.

(+)-3-*p*-Tolyl-5-trimethylsilyl-3-(trimethylstannyl)cyclohexanone ((+)-5d). The product was obtained from (+)-3-*p*-tolyl-5-trimethylsilyl-2-cyclohexen-1-one[7a] (0.600 g, 2.32 mmol, $[\alpha]_D^{23.5}$ +67.8°, (c 1.18, $CHCl_3$) as a single *trans* isomer (0.801 g, 82%), as confirmed by ^{13}C-NMR analysis. $[\alpha]_D^{23.2}$ +10.2°, (c 1.51, $CHCl_3$). MS, m/z 424 (M^+), 410, 409, 309, 259, 169, 165 (base peak, Me_3Sn), 129, 73. IR, 3027, 1712, 1512, 1249, 838, 767 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.15 (s, 9H), 1.0 ~ 3.3 (m, 7H), 2.37 (s, 3H), 6.8 ~ 7.2 (m, 4H). ^{13}C-NMR, δ -8.95, -3.66, 20.71, 25.17, 35.89, 41.35, 42.94, 50.35, 123.43, 128.88, 133.53, 145.79, 210.18. HRMS (EI, 20 ev), calcd for $C_{19}H_{32}OSiSn$ (M) 424.1244, found 424.1200.

3-(2-Phenylethyl)-5-trimethylsilyl-3-(trimethylstannyl)cyclohexanone (5e). The product was obtained from 3-(2-phenylethyl)-5-trimethylsilyl-2-cyclohexen-1-one[18] (0.460 g, 1.79 mmol) as a single *trans* -isomer (0.681 g, 92%). ^{1}H-NMR, δ 0.00 (s, 9H), 0.08 (s, 9H), 0.80 ~ 2.80 (m, 11H), 6.95 (s, 5H).

3-(Trimethylstannyl)cyclohexanone (5f). The product was obtained from 2-cyclohexen-1-one (0.500 mg, 5.2 mmol) as an oil (1.299 mg, 96%).[17] IR, 1709, 1224, 766 cm^{-1}. HRMS (DI), calcd for $C_8H_{15}OSn$ (M) 247.0145, found 247.0128.

3,5,5-Trimethyl-3-(trimethylstannyl)cyclohexanone (5g). The product was obtained from 3,5,5-trimethyl-2-cyclohexen-1-one (0.200 g, 1.45 mmol) as an oil (0.417 g, 95%).[17]

3-(Trimethylstannyl)cycloheptanone (8f). The product was obtained from 2-cyclohepten-1-one (0.100 g, 0.91 mmol) as an oil (0.207 g, 83%). IR, 1698, 1438, 765 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 1.00 ~ 2.53 (m, 11H).

2-(1-Trimethylstannylbenzyl)cyclohexanone (14a). The product was obtained from *trans*-2-benzylidenecyclohexanone[19] (0.230 g, 1.23 mmol) as a single stereoisomer (oil, 0.247 g, 57%), as evident from ^{13}C-NMR analysis. The starting material (12%) was recovered. MS (EI, 20 ev), m/z 352 (M^+), 337, 307, 253, 187, 165, 91. IR, 3059, 1703, 1492, 1449, 765 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 1.30 ~ 3,00 (m, 10H), 6.65 ~ 7.20 (m, 5H). ^{13}C-NMR, δ -9.04, 24.50, 27.51, 34.01, 36.09, 41.40, 53.80, 123.78, 127.13, 128.04, 144.32, 212.92.

2-(1-Trimethylstannylbenzyl)cycloheptanone (14b). The product was obtained from *trans*-2-benzylidenecycloheptanone[19] (0.140 g, 0.699 mmol) as a single stereoisomer (oil, 97.6 mg, 38%) as evident from ^{13}C-NMR analysis. MS, m/z 351 (base peak, M^+ - 15), 253, 165 (Me_3Sn), 117, 91. IR, 3021, 1691, 768 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 1.00 ~ 2.60 (m, 12H), 6.67 ~ 7.30 (m, 5H). ^{13}C-NMR, δ -8.82, 24.50, 28.56, 29.33, 32.69, 39.30, 42.63, 54.85, 123.96, 126.54, 128.19, 144.27, 215.21. HRMS, calcd for $C_{16}H_{23}OSn$ (M - Me) 351.0771, found 351.0749.

2-Benzyl-3-methyl-5-trimethylsilyl-3-(trimethylstannyl)cyclohexanone (5c). To a THF solution (35 ml) of Me_3SnLi (16.50 mmol) was added dropwise a THF solution (20 ml) of 3-methy-5-trimethylsilyl-2-cyclohexen-1-one[18] (1.50 g, 8.23 mmol) at -25 °C over 15 min, and stirred for 1 h. A THF solution (10 ml) of benzyl bromide (4.9 ml, 41.10 mmol) was added at -25 °C, and stirred at this temperature for 3 h, warmed slowly to room temperature, and stirred for another 20 h. The solution was quenched by sat NH_4Cl aq, and worked up in the same way as above. The residue was purified on column chromatography ($CHCl_3$) to give **5c** as a single stereoisomer (oil, 2.46 g, 68%). MS, m/z 423 (M^+ - 15), 347 (base peak, M^+ - 91), 317, 288, 273, 257, 181, 165 (Me_3Sn), 153, 123, 91, 73. IR, 3028, 1706, 1496, 1454, 1248, 759

cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.05 (s, 9H), 1.18 (s, 3H), 1.42 ~ 2.22 (m, 5H), 2.80 (br.s, 3H), 6.77 ~ 7.17 (m, 5H). ^{13}C-NMR, δ −9.77, −3.77, 24.37, 26.09, 31.63, 33.97, 37.10, 38.62, 60.33, 125.95, 128.20, 128.39, 139.11, 212.52. HRMS, calcd for $C_{19}H_{31}OSiSn$ (M − Me) 423.1166, found 423.1200.

General Procedure for the Reactions of β-Stannyl Ketones with TMSOTf (runs 1 ~ 8). To a solution of 3-stannylcyclohexanone derivatives (1.0 mmol) in CH_2Cl_2 (13 ml) was added slowly a solution of TMSOTf (1.5 mmol) in CH_2Cl_2 (8 ml) at temperatures as specified in Table 1. The mixture was stirred for 4 h, quenched by sat $NaHCO_3$ aq, and diluted with CH_2Cl_2. Organic phase was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the residue on a column chromatography gave the corresponding products.

Reaction of 5a. The product obtained from **5a** (0.150 g, 0.450 mmol) was purified on column chromatography (ether : hexane = 1 : 5) to give **6a** and **7a** in yields as specified in Table 1, run 1 ~ 3, depending upon the reaction temperature. In view of the ^{13}C-NMR spectrum, **6a** was a *cis-trans* mixture, although GLC analysis showed only one peak. The following spectroscopic data were measured on the *cis-trans* mixture. For **6a** : MS, m/z 170 (M^+), 169, 155, 75, 73 (base peak, TMS). IR, 1739, 1250, 835 cm^{-1}. ^{1}H-NMR , δ 0.00 (s, 9H), 1.03 (d, J = 6 Hz, 3H), 0.83 ~ 2.30 (m, 6H). ^{13}C-NMR ($CDCl_3$),[20] δ −3.38, [13.85, 15.83*], [20.00*, 21.53], [32.31*, 32.49], [39.10, 39.24*], [42.17*, 45.61], 222.36. (1 : 4). In view of our previous report,[2] we assigned *trans* structure for the major product. For **7a** : The authentic sample was prepared in 82% yield by the catalytic hydrogenation (Pd/C) of 5-trimethylsilyl-2-cyclohexen-1-one,[6] in ethyl acetate for 1 h at room temperature. MS, 170 (M^+), 169, 155, 127, 75, 73 (base peak, TMS). IR, 1712, 1249 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.90 ~ 2.50 (m, 9H).

Reaction of 5b. The product obtained from **5b** (0.200 g, 0.576 mmol) was an oil **6b** (0.106 g, 99%). MS, m/z 184 (M^+), 169, 128, 73. IR, 1738, 1250 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.97 (s, 3H), 1.00 (s, 3H), 1.15 ~ 2.37 (m, 5H). HRMS, calcd for $C_{10}H_{20}OSi$ (M) 184.1283, found 184.1268.

Reaction of 5c. . The product obtained from **5c** (0.130 g, 0.297 mmol) was an oil **6c** (66.6 mg, 82%) of a single stereoisomer, as evident from 400 MHz ^{1}H-NMR spectrum. MS (EI, 20 ev), m/z 275 ($M^+ + 1$), 274 (M^+), 183, 171, 170 (base peak), 96, 80, 73. IR, 3027, 1733, 1496, 1454, 1249 cm^{-1}. ^{1}H-NMR (400 MHz), δ 0.00 (s, 9H), 1.11 (s, 3H), 1.29 ~ 1.39 (m, 1H), 1.49 (t, J = 13.2 Hz, 1H), 1.64 ~ 1.70 (m, 2H), 1.97 (dd, J = 18.5 and 13.2 Hz, 1H), 2.02 (ddd, J = 13.2, 6.6, and 2.5 Hz, 1H), 2.37 (ddd, J = 18.5, 8.3, and 2.5 Hz, 1H), 2.54 ~ 2.60 (m, 2H), 7.12 ~ 7.29 (m, 5H). HRMS, calcd for $C_{17}H_{26}OSi$ (M) 274.1753, found 274.1732.

Reaction of (+)-5d. The product obtained from (+)-**5d** (0.139 g, 0.328 mmol) was an oil **6d** (75.4 mg, 90%) of a single stereoisomer as evident from 400 MHz ^{1}H-NMR spectrum. $[\alpha]_D^{24.2}$ −72.6°, (c 0.95, $CHCl_3$). MS (DI), m/z 260 (M^+), 245, 170, 143, 73. IR, 3026, 1737, 1514, 1250, 836 cm^{-1}. ^{1}H-NMR (400 MHz), δ 0.00 (s, 9H), 1.37 (s, 3H), 1.35 ~ 1.45 (m, 1H), 2.01 ~ 2.14 (m, 3H), 2.27 (s, 3H), 2.44 (ddd, J = 18.1, 7.2, and 2 Hz, 1H), 7.09 and 7.19 (A_2B_2, J = ~8 Hz, 4H). HRMS (DI), calcd for $C_{16}H_{24}OSi$ (M) 260.1597, found 260.1603.

Reaction of 5e. The product obtained from **5e** (0.390 g, 0.892 mmol) was an oil **6e** (0.150 g, 61%). ^{1}H-NMR, δ 0.00 (s, 9H), 1.00 (s, 3H), 1.40 ~ 2.65 (m, 9H), 6.85 (s, 5H).

(+)-5-Methyl-5-*p*-tolyl-2-cyclopenten-1-one ((+)-22). The chlorination of (−)-**6d** was carried out referring to the reported method as follows.[21] To an acetic acid solution (0.5 ml) of MnO_2 (20.2 mg, 0.232 mmol) and (−)-**6d** (55.0 mg, 0.211 mmol) was added slowly TMSCl (0.112 ml, 0.887 mmol) at room temperature. The resulting mixture was stirred at that temperature for 2 ~ 3 h, until the solution color changed from deep purple to colorless, and poured into water (5 ml). The mixture was extracted with ether, washed with 0.025 M NaOH several times, dried over $MgSO_4$, and the solvent was removed *in vacuo*. The residue

was dissolved in THF (0.3 ml), and was added to a THF solution of TBAF (1.103 g, 0.422 mmol). The solution was stirred at room temperature for 5 min, and hexane (3 ml) was added. The mixture was filtered through Hyflo Super Cell, the solvent was removed *in vacuo*, and the residue was purified by column chromatography (ether : hexane = 1 : 5 v/v) to afford (+)-**22** as an oil (26.1 mg, 66%). $[\alpha]_D^{23.2}$ +9.0°, (c 0.82, $CHCl_3$). MS, m/z 186 (M^+), 171, 157, 143, 128, 115, 91, 77, 65. ^{1}H-NMR, δ 1.60 (s, 3H), 2.45 (s, 3H), 2.90 and 3.25 (dd, J = 3 and 2 Hz, of ABq, J = 20 Hz, 2H), 6.25 (dt, J = 6 and 2 Hz, 1H), 7.18 (s, 4H), 7.73 (dt, J = 6 and 3 Hz, 1H).

(+)-3,4-dimethy-4-*p*-tolyl-2-cyclopenten-1-one ((+)-23). The compound was prepared from (+)-**22** in the same way as reported.[7a] $[\alpha]_D^{21.9}$ +235.2°, (c 0.91, $CHCl_3$), lit.[8] $[\alpha]_D^{20}$ +253°, (c 1.7, $CHCl_3$). ^{1}H-NMR, δ 1.60 (s, 3H), 1.80 (s, 3H), 2.30 (s, 3H), 2.60 (br.s, 2H), 6.00 (br.s, 1H), 7.10 (s, 4H).

(+)-β-Cuparenone. The product was obtained from (+)-**23** (20 mg, 0.100 mmol) by conjugate addition of methylcuprate as an oil (15.9 mg, 74%) in accordance with the literature.[12a] $[\alpha]_D^{24.6}$ +48.5°, (c 1.36, $CHCl_3$); lit: $[\alpha]_D^{23}$ +44.4°, (c 2.47, $CHCl_3$)[7a]; $[\alpha]_D^{29}$ +45°, (c 1.4, $CHCl_3$)[8]; $[\alpha]_D^{30}$ +48° ($CHCl_3$).[9] MS, m/z 216 (M^+), 132, 117, 91. IR and ^{1}H-NMR data were identical with those reported.[9] HRMS, calcd for $C_{15}H_{20}O$ (M) 216.1514, found 216.1547.

General Procedure for the Reactions of β-Stannyl Ketones with $Me_3SiSPh/TiCl_4$ (Runs 9 ~ 17). To a solution of β-stannyl ketones (1.0 mmol) in CH_2Cl_2 (6 ml) was added TMSSPh (2.0 mmol),[22] and then a solution of $TiCl_4$ (1.0 mmol) in CH_2Cl_2 (12 ml) over 20 min at 0 °C ~ rt. The solution was stirred at 0 °C ~ rt for 15 min and the resulting solution was quenched by sat $NaHCO_3$ aq, filtered through a short pad of Celite 545, diluted with CH_2Cl_2, and washed with sat NaCl aq. Organic phase was dried over $MgSO_4$, and the solvent was removed *in vacuo*. Purification of the residue by column chromatography (hexane) afforded cyclopropane derivatives. When the CH_2Cl_2 solution of $TiCl_4$ was poured into the reaction mixture, the Type A and Type B reaction products were also detected.

Reaction of 5a. The products obtained from **5a** (70.3 mg, 0.21 mmol) were **10a** (oil, 30.1 mg, 60%), as well as **6a** (10.4 mg, 20%) and **7a** (7.0 mg, 14%). The compound **10a** showed a single peak on a GLC equipped with packed column, it showed two peaks (1 : 2) on a GLC equipped with a capillary column. For **10a** (diastereomer mixture): MS, m/z 262 (M^+), 247, 182, 167, 153, 110, 91, 79, 73 (base peak, TMS), 58. IR, 3060, 1479, 1438, 1249, 833 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.65 ~ 2.2 (m, 8H), 7.10 (br.s, 5H)

Reaction of 5b. The product obtained from **5b** (0.100 g, 0.288 mmol) was an oil **10b** (77.3 mg, 97%) of a single stereoisomer, in view of 400 MHz ^{1}H- and ^{13}C-NMR analyses. MS, m/z 276 (M^+), 261, 167, 97, 73. IR, 3059, 1585, 1478, 1439, 1249 cm^{-1}. ^{1}H-NMR (400 MHz), δ 0.00 (s, 9H), 0.65 (d, J = 5.1, 1H), 0.79 (tt, J = 12.5 and 8.1 Hz, 1H), 1.20 (d, J = 5.1 Hz, 1H), 1.39 (s, 3H), 1.66 (t, J = 12.5 Hz, 1H), 1.90 ~ 1.97 (m, 2H), 2.10 (dd, J =12.5 and 8.1 Hz, 1H), 7.28 ~ 7.33 (m, 5H). ^{13}C-NMR, (100 MHz),.δ -3.06, 18.97, 19.00, 20.36, 21.22, 21.25, 32.44, 36.23, 36.43, 124.73, 127.24, 128.63, 137.39. HRMS (EI, 20 ev), calcd for $C_{16}H_{24}SSi$ (M) 276.1368, found 276.1353.

Reaction of 5c. The product obtained from **5c** (0.130 g, 0.297mmol) was an oil **10c** (0.101 g, 93%) of a single stereoisomer, in view of 400MHz ^{1}H-NMR analysis. MS (DI), m/z 366 (M^+), 290, 275 (base peak), 201, 91, 73. IR, 3060, 1584, 1478, 1249 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$), δ 0.00 (s, 9H), 0.94 (tt, J = 12.5 and 8.1 Hz, 1H), 1.34 (s, 3H), 1.58 (dd, J = 8.1 and 6.2 Hz, 1H), 1.75 (t, J = 12.5 Hz, 1H), 2.02 (t, J = 12.5 Hz, 1H), 2.04 (dd, J = 12.5, J = 8.1 Hz, 1H), 2.24 (dd, J = 12.5 and 8.1 Hz, 1H), 2.92 and 3.05 (ABq, J = 14.3 Hz, upper half splitted into doublets with J = 8.1 Hz, and lower half to doublets with J = 6.2 Hz, 2H), 7.21 ~ 7.35 (m, 10H). HRMS (DI), calcd for $C_{23}H_{30}SSi$ (M) 366.1838, found 366.1796.

Reaction of 5d. The product obtained from **5d** (80.1 mg, 0.189 mmol) was **10d** of a single stereoisomer (55.7 mg, 84%). MS (DI), m/z 352 (M^+), 243, 169, 73. IR, 3058, 3021, 1584, 1518, 1478, 1438, 1249,

834 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.27 ~ 2.40 (m, 7H), 2.30 (s, 3H), 6.80 ~ 7.33 (m, 9H). HRMS (DI), calcd for $C_{22}H_{28}SSi$ (M) 352.1681, found 352.1647.

Reaction of 5f. The product obtained from **5f** (0.100 g, 0.38 mmol) was an oil **10f** (67.5 mg, 93%). MS, m/z 190 (M^+), 110, 81 (base peak), 82. IR, 3059, 1582, 1478, 1438, 737 cm^{-1}. ^{1}H-NMR, δ 0.87 ~ 0.97 (m, 2H), 1.00 ~ 2.20 (m, 7H), 7.00 ~ 7.38 (m, 5H). HRMS, calcd for $C_{12}H_{14}S$ (M) 190.0817, found 190.0845.

Reaction of 5g. The product obtained from **5g** (0.100 g, 0.33 mmol) was an oil **10g** (77.7 mg, 86%). MS, m/z 232 (M^+), 228, 217, 123, 107, 91, 81, 77, 65. IR, 3060, 1585, 1478, 1438 cm^{-1}. ^{1}H-NMR, δ 1.00 (s, 3H), 1.08 (s, 3H), 1.35 (s, 3H), 0.77 ~ 1.23 (m, 2H), 1.77 (br.s, 2H), 2.0 ~ 2.1 (m, 2H), 7.00 ~ 7.50 (m, 5H). HRMS, calcd for $C_{15}H_{20}S$ (M) 232.1286, found 232.1301.

Reaction of 8f. The product obtained from **8f** (0.100 g, 0.364 mmol) was an oil **11f** (32.7 mg, 44%). MS, m/z 204 (M^+), 171, 110, 95 (base peak), 79, 67. IR, 3060, 1585, 1478, 1438 cm^{-1}. ^{1}H-NMR, δ 0.55 ~ 2.33 (m, 11H), 7.00 ~ 7.44 (m, 5H). HRMS, calcd for $C_{13}H_{16}S$ (M) 204.0973, found 204.0952.

Reaction of 14a. The product obtained from **14a** (0.100 g, 0.285 mmol) was a single stereoisomer of **15a** (oil, 79.6 mg, 99%), as evident from GLC analysis. MS (EI, 20 eV), m/z 280 (M^+), 247, 171, 129, 91. IR, 3058, 1583, 1478, 1438, 737, 693 cm^{-1}. ^{1}H-NMR, δ 1.23 ~ 2.27 (m, 9H), 2.10 (d, J = 6.2 Hz, 1H), 6.87 (s, 5H), 6.97 (s, 5H). HRMS (EI, 20 eV), calcd for $C_{19}H_{20}S$ (M) 280.1286, found 280.1287.

Reaction of 14b. The product obtained from **14b** (0.100 g, 0.274 mmol) was a single stereoisomer of **15b** (oil, 77.4 mg, 96%), as evident from 400 MHz ^{1}H-NMR analysis. MS, m/z 294 (M^+), 261, 185 (base peak), 167, 143, 129, 107, 91, 81. IR, 3058, 1582, 1499, 1478, 1438, 1452, 737, 693 cm^{-1}. ^{1}H-NMR (400 MHz), δ 1.16 ~ 1.33 (m, 2H), 1.38 ~ 1.52 (m, 2H), 1.62 ~ 1.72 (m, 2H), 1.79 ~ 1.87 (m, 1H), 1.80 ~ 1.96 (m, 1H), 1.96 ~ 2.08 (m, 1H), 2.27 (d, J = 5.9 Hz, 1H), 2.36 ~ 2.43 (m, 2H), 6.91 ~ 7.07 (m, 5H), 7.20 ~ 7.30 (m, 5H). HRMS, calcd for $C_{20}H_{22}S$ (M) 294.1443, found 294.1449.

General Procedure for the Reduction of Phenylthiocyclopropane with Raney Ni (W-7). A suspension of Raney Ni (W-7)[23] (catalytic amount) in an ethanol solution (2 ml) of phenylthiocyclopropane derivatives (0.1 mmol) was vigorously stirred at room temperature for 10 min. The resulting solution was filtered and the solvent was evaporated *in vacuo*. The residue was purified on a short column of Florisil (hexane).

Reaction of 15b. The product obtained from **15b** (25.0 mg, 0.085 mmol) was purified by column chromatography to give an oil (16.0 mg, ~100%). Although the product showed only one spot on TLC plate, two peaks were detected by GC analysis in a ratio of 1 : 4. Referring to the HRMS, we assigned the structures **16b** and **17b**, respectively, for the components corresponding to these peaks. ^{1}H-NMR and IR spectra are those of the mixture. IR, 3020, 1445, 691 cm^{-1}. ^{1}H-NMR, δ 0.75 ~ 2.35 (m, 13H), 2.50 (d, J = 6.8 Hz, 2H), 6.80 ~ 7.35 (m, 5H). For **16b**: MS, m/z 186 (M^+), 143, 129, 117, 104, 95, 91, 79, 67. HRMS, calcd for $C_{14}H_{18}$ (M) 186.1409, found 186.1391. For **17b**: MS, m/z 188 (M^+), 115, 97, 96, 92, 91, 81, 69, 67, 65, 52. HRMS, m/z calcd for $C_{14}H_{20}$ (M) 188.1565, found 188.1587.

Reaction of 10c. The product obtained from **10c** (60.0 mg, 0.164 mmol) was purified by column chromatography to give an oil (42.0 mg, ~99%). Although the product showed only one spot on TLC plate, two peaks were detected by GLC analysis in a ratio of 1 : ~1. Referring to HRMS, we assigned the structures **18** and **19** for the components corresponding to these peaks. ^{1}H-NMR and IR spectra are those of the mixture. IR, 3020, 1249, 834 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H x 1/2), 0.03 (s, 9H x 1/2), 1.08 (s, 3H x 1/2), 1.28 (s, 3H x 1/2), 0.80 ~ 1.87 (m, (7H + 9H) x 1/2), 2.43 ~ 2.73 (m, 4H x 1/2), 7.03 ~ 7.10 (two peaks, 10H x 1/2). For **18**: MS, m/z 258 (M^+), 243, 184, 167, 144, 93, 73 (TMS). HRMS, calcd for $C_{17}H_{26}Si$ (M^+) 258.1804, found 258.1773. For **19**: MS, 260 (M^+), 245, 219, 186, 114, 91, 73 (TMS). HRMS, calcd for $C_{17}H_{28}Si$ (M) 260.1960, found 260.1916.

When the deactivated catalyst (several days after preparation) was used, **18** was isolated in 89% yield in pure state. IR, 3026, 1604, 1495, 1453, 1248, 834, 697 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.80 ~ 1.90 (m, 7H), 1,30 (s, 3H), 2.65 (d, J = 6.5 Hz, 2H), 7.10 (s, 5H).

3-(Trimethylstannyl)-3-(4-trimethylstannylbutyl)cyclohexanone (28a). A solution of 1-bromo-4-chlorobutane (0.858 g, 5 mmol) in THF (4 ml) was slowly added to a suspension of Mg (0.146 g, 6 mmol) in THF (4 ml), and the mixture was stirred for 30 min. To this mixture was added a solution of 3-ethoxy-2-cyclohexen-1-one (0.630 g, 5 mmol) in a mixture of benzene/THF (1 : 2, 2.5 ml), and the solution was stirred for 20 h at room temperature. The reaction mixture was poured into ice-water, and acidified with 5% HCl aq. The product was extracted with ether, dried over Na_2SO_4, and purified by column chromatography (AcOEt : hexane = 1 : 1) to afford 3-(4-chlorobutyl)-2-cyclohexen-1-one (0.731 g, 78%). ^{1}H-NMR, δ 1.60 ~ 2.40 (m, 12H), 3.50 (br.t, J = 6 Hz, 2H), 5.70 (br.s, 1H). A solution of the cyclohexenone derivative obtained above (0.471 g, 2.53 mmol) in THF (6.5 ml) was reacted with a THF solution (6.4 ml) of Me_3SnLi, prepared from Me_3SnCl (1.01 g, 5.06 mmol) for 20 h at room temperature. The work up in the same way as described above gave **28a** (0.728 g, 67%) as a single stereoisomer. MS, m/z 317 (M^+ − 165), 285, 165, 150, 135. ^{1}H-NMR, δ 0.00 (s, 18H), 0.90 ~ 2.40 (m, 16H). HRMS, calcd for $C_{13}H_{25}OSn$ (M − Me_3Sn) 317.0928, found 317.0917.

3-(Trimethylstannyl)-3-(4-trimethylstannylbutyl)-5-methylcyclohexanone (28b). The intermediate 3-(4-chlorobutyl)-5-methyl-2-cyclohexen-1-one was prepared in the same way as above. MS, m/z 202 (M^+ + 2),, 200, 187, 185, 160, 158, 123, 95, 82, 67, 53. The intensity ratios at (202; 200), (187; 185), and (160; 158) were 1 : 3. ^{1}H-NMR, δ 1.10 (br.d, J = 4.0 Hz, 3H), 1.60 ~ 2.50 (m, 11H), 3.5 (br.t, J = 6.0 Hz, 2H), 5.70 (br.s, 1H). HRMS, calcd for $C_{11}H_{17}O^{35}Cl$ (M) 200.0968, found 200.0952; calcd for $C_{11}H_{17}O^{37}Cl$ (M) 202.0238, found 202.0960. The overall yield of **28b** from 3-ethoxy-5-methyl-2-cyclohexen-1-one was 81%. MS, m/z 331 (M^+ − 165), 301, 165, 135. ^{1}H-NMR, δ 0.00 (s, 18H), 0.80 ~ 2.50 (m, 18H). HRMS, calcd for $C_{14}H_{27}OSn$ (M − Me_3Sn) 331.1084, found 331.1068.

5-Methyl-3-trimethylstannyl-3-(3-trimethylstannylpropyl)cyclohexanone (29b). To a suspension of Mg (0.255 g, 10.4 mmol) in THF (5 ml) was added a solution of 1-bromo-3-trimethylstannylpropane[24] in THF (5 ml) in the presence of a small amount of I_2. After stirred for 1 h at room temperature, a solution of 3-ethoxy-2-cyclohexen-1-one (1.00 g, 6.49 mmol) in THF (5 ml) was added slowly, and stirred for 1 h at room temperature. The reaction mixture was quenched with water, extracted with ether, washed with NaCl aq. After dried over $MgSO_4$, the product was purified by column chromatography to afford 5-methyl-3-(3-trimethylstannylpropyl)-2-cyclohexen-1-one (1.05 g, 51%). ^{1}H-NMR, δ 0.00 (s, 9H), 0.70 (t, J = 8.0 Hz, 2H), 1.00 (d, J = 4 Hz, 3H), 1.50 ~ 2.50 (m, 9H). The cyclohexenone derivative obtained above (0.73 g, 2.32 mmol) was reacted with Me_3SnLi solution prepared from Me_3SnCl (0.928 g, 4.66 mmol) in the same way as described above to afford **29b** (0.617 g, 56%). MS, m/z 317 (M^+ − 165), 287, 275, 165, 135. ^{1}H-NMR, δ 0.00 (s, 9H), 0.04 (s, 9H), 0.85 (t, J = 6.0 Hz, 2H), 1.05 (d, J = 4.0 Hz, 3H), 1.30 ~ 2.60 (m, 11H).

General Procedure for Reactions of Stannyl Ketones with Lewis Acids (runs 18 ~ 26). To a solution of the stannyl ketones (1.0 mmol) in CH_2Cl_2 (8 ml) was added a solution of $TiCl_4$ (1.1 ~ 2.0 mmol) or TMSOTf (1.0 ~ 2.0 mmol) in CH_2Cl_2 (10 ml) dropwise over 20 min, and the solution was stirred under conditions specified in Table 2. The mixture was extracted with CH_2Cl_2 and dried over $MgSO_4$. Organic phase was concentrated *in vacuo*, and the residue was purified on a column chromatography (ether : hexane = 1 : 5).

Reaction of 28a (Run 18). The product obtained from **28a** (0.253 g, 0.525 mmol) was **30a** (0.139 g, 65%). ^{1}H-NMR, δ 0.00 (s, 9H), 0.80 ~ 2.30 (m, 17H). ^{13}C-NMR, δ −10.06, 11.16, 19.02, 22.15, 27.63, 28.96, 35.95, 36.59, 38.02, 48.59, 224.22.

Reaction of 28b (Runs 19 ~ 21). The product obtained from **28b** (0.312 g, 0.629 mmol) under conditions in run 19 was **30b** (0.142 g, 68%). IR, 1730, 1028, 762 cm^{-1}. ^{1}H-NMR (400 MHz), δ 0.02 (s, 9H), 0.79 (t, J = 8.0 Hz, 2H), 0.97 (s, 3H), 1.11 (d, J = 6.6 Hz, 3H), 1.20 ~ 1.50 (m, 7H), 1.75 (dd, J = 19 and 12 Hz, 1H), 1.83 (ddd, J = 12.5, 6.0, and 2.0 Hz, 1H), 2.16 ~ 2,27 (m, 1H), 2.46 (ddd, J = 19, 7.0, and 2.0 Hz,1H). ^{13}C-NMR (except carbonyl carbon), δ −10.37, 10.87, 20.53, 22.60, 27.19, 27.60, 28.85, 37.17, 44.36, 46.92, 50.31. In runs 20 and 21, **32b** and **34b** were identified as well as **30b**. For **32b**: MS, m/z 337 (M^+ − 15), 317 (M^+ − 35), 296, 281, 185 (base peak), 149, 135, 109, 81.69. ^{1}H-NMR, δ 0.55 (s, 6H), 0.95 (s, 3H), 1.10 (d, J = 6.0 Hz, 3H), 0.80 ~ 2.70 (m, 13H). HRMS, calcd for $C_{12}H_{22}O^{37}Cl^{120}Sn$ (M − Me) 339.0351, found 339.0356; calcd for $C_{12}H_{22}O^{35}Cl^{120}Sn$ (M − Me) 337.0382, found 337.0412; calcd for $C_{12}H_{22}O^{35}Cl^{118}Sn$ (M − Me) 335.0375, found 335.0363. For **34b**: MS, m/z 167 (M^+ − 1), 153 (M^+ − 15), 135, 123, 112, 95, 83, 81, 71, 69, 67. ^{1}H-NMR (400 MHz, $CDCl_3$), δ 0.91 (s, 3H), 0.97 (d, J = 7.0 Hz, 3H), 0.99 (m, 1H), 1.32 (ddd, J = 13.2, 11.7, and 5.1 Hz, 1H), 1.43 (br.s, 1H), 1.51 (ddd, J = 13.6, 11.4, and 5.5 Hz, 1H), 1.62 (ddd, J = 13.6, 7.7, and 6.2 Hz, 1H), 1.69 (dd, J = 12.8 and 8.1 Hz, 1H), 1.73 (ddd, J = 13.6, 9.5, and 7.0 Hz, 1H), 1.98 ~ 2.15 (m, 2H), 2.13 ~ 2.25 (m, 1H), 3.83 (t, J = 7.3 Hz, 1H), 4.93 (dd, J = 10.3 and 1.5 Hz, 1H), 5.02 (dd, J = 18.7 and 1.5 Hz, 1H), 5.83 (ddt, J = 18.7, 10.3, and 7.0 Hz, 1H). ^{13}C-NMR δ 18.20, 22.32, 28.16, 29.41, 40.78, 41.13, 45.52, 46.13, 79.64, 113.77, 139.41. HRMS, calcd for $C_{10}H_{17}O$ (M − Me) 153.1279, found 153.1277.

The epimer **35** was prepared by the succeeding Swern oxidation and $NaBH_4$ reduction as a mixture of **34b** and **35** in a ratio of 2.3 : 1, which were separated by column chromatography. For **35**: ^{1}H-NMR (400 MHz), δ 0.88 (s, 3H), 1.05 (d, J = 6.75 Hz, 3H), 1.19 (ddd, J = 14.0, 6.7, and 3.4 Hz, 1H), 1.26 (dd, J = 12.4 and 9.9 Hz, 1H), 1.30 (br.s, 1H), 1.42 ~ 1.60 (m, 3H), 2.00 ~ 2.15 (m, 3H), 2.32 (tdd, J = 14.4, 9.3, and 5.8 Hz, 1H), 3.72 (dd, J = 5.3 and 3.5 Hz, 1H), 4.94 (dd, J = 10.2 and 1.9 Hz, 1H), 5.04 (dd, J = 17.1 and 1.8 Hz, 1H), 5.87 (ddt, J = 17.1, 10.2, and 6.6 Hz, 1H).

Reaction of 29b (Run 22). The products obtained from **29b** (0.250 g, 0.521 mmol) were **31b** (12.2 mg, 7%) and **33b** (0.121 g, 69%), after the purification by column chromatography. For **31b**: MS, m/z 303 (M^+ − 15), 165, 135, 107. ^{1}H-NMR, δ 0.04 (s, 9H), 0.98 (s, 3H), 1.10 (d, J = 6 Hz, 3H), 1.20 ~ 2.50 (m, 11H). For 33b: IR, 1727, 1456, 1150, 778 cm^{-1}. ^{1}H-NMR, δ 0.62 (s, 6H), 0.98 (s, 3H), 1.13 (d, J = 6.0 Hz, 3H), 1.10 ~ 2.45 (m, 11H).

Reaction of 30a (Run 23). The product obtained from 30a (0.314 g, 0.987 mmol) was 34a (74.5 mg, 49%). MS, m/z 136 (M^+ − 18), 121, 112, 95, 81, 67, 55. ^{1}H-NMR, δ 0.90 (s, 3H), 1.10 ~ 2.30 (m, 10H), 3.50 ~ 3.80 (m, 1H), 4.75 ~ 5.10 (m, 2H), 5.50 ~ 6.00 (m, 1H). HRMS, calcd for $C_{10}H_{16}$ (M − H_2O) 136.1252, found 136.1290.

Reaction of 30b (Run 24). The product obtained from **30b** (0.353 g, 1.07 mmol) was **34b** (0.168 g, 94%).

3,5-Dimethyl-3-(3-trimethylstannylpropyl)cyclohexanone (36a). To a suspension of Mg (90.0 mg, 3.7 mmol) in THF (1 ml) was added 1-bromo-3-trimethylstannylpropane (2.5 ml, 3.43 mmol)[24] in the presence of a small amount of I_2. After the solution was stirred at room temperature for 1 h, the solution was added to a mixture of 3,5-dimethyl-2-cyclohexen-1-one (0.217 g, 1.75 mmol), CuBr·SMe_2 (18.0 mg, 0.088 mmol), HMPA (0.61 ml), and TMSCl (0.67 ml) in THF (20 ml).[14] The mixture was stirred at −78 °C for 1 h, diluted with hexane, and allowed to warm up to room temperature. The solution was quenched with brine, and the organic layer was concentrated *in vacuo*. The residue was treated with a small amount of KF in methanol for a few minutes, and water was added. The product was extracted with CH_2Cl_2 to afford **36a**

(468 mg, 81%). The product was a single stereoisomer, as confirmed by GLC and ^{13}C-NMR analyses. MS, m/z 317 (M^+ - 15), 289, 165 (base peak, Me_3Sn), 135, 73, 55. IR, 1714, 1455, 1273, 765 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.78 (t, J = 7.0 Hz, 2H), 0.93 (s, 3H), 1.00 (d, J = 4.0 Hz, 3H), 1.33 ~ 2.33 (m, 11H). HRMS (CI), calcd for $C_{13}H_{25}OSn$ (M - Me) 317.0927, found 317.0936.

In the same way, **36b** was prepared from 3-methyl-5-trimethylsilyl-2-cyclohexen-1-one as a single stereoisomer in 69% yield. MS, m/z 375 (M^+ - 15), 347, 275, 225, 165, 135, 73. IR, 1711, 1248, 841, 765 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.04 (s, 9H), 0.87 (t, J = 6.0 Hz, 2H), 0.97 (s, 3H), 1.0 ~ 2.17 (m, 11H). ^{13}C-NMR, δ -10.19, -3.91, 11.45, 20.29, 21.64, 28.32, 36.72, 40.08, 41.22, 41.42, 54.17, 211.72. HRMS (CI), calcd for $C_{16}H_{34}OSiSn$ (M) 390.1401, found 390.1397.

General Procedure for Reactions of Stannyl Ketones with Lewis Acids (runs 27 ~ 30). A solution of the stannyl ketones (1.0 mmol) in CH_2Cl_2 (8 ml) was cooled to -78 °C, and a solution of $TiCl_4$ (1.1 ~ 2.0 mmol) in CH_2Cl_2 (10 ml) was added dropwise over 20 min, and the solution was stirred under conditions specified in Table 2. The reaction mixture was poured into brine directly (method A), or after the reaction mixture was allowed to warm up to room temperature slowly, and then stirred for 1 ~ 2 h (method B). The mixture was extracted with CH_2Cl_2 and dried over $MgSO_4$. Organic phase was concentrated *in vacuo*, and the residue was purified on a column chromatography (ether : hexane = 1 : 5).

Reaction of 36a. The product obtained from **36a** (0.130 g, 0.393 mmol) by the method B gave **37a** (46.5 mg, 70%) and **39a** (35.9 mg, 26%) upon separation on a column chromatography. The method A also gave the same result. For **37a** : MS, m/z 153 (M^+ - 15), 109, 83, 67, 55. IR, 3346, 3074, 1639, 1026 cm^{-1}. ^{1}H-NMR, δ 0.70 ~ 2.07 (m, 8H), 0.92 (s, 3H), 0.93 (d, J = 6.0 Hz, 3H), 2.02 (br.d, J = 6.6 Hz, 2H), 3.4 ~ 4.00 (m, 1H), 4.77 ~ 5.20 (m, 2H), 5.43 ~ 6.05 (m, 1H). HRMS (CI), calcd for $C_{11}H_{20}O$ (M) 168.1514, found 168.1480. For **39a**: MS (EI, 20 ev), m/z 337 (M^+ - 15), 309, 185, 125, 109. IR, 1704, 1456, 1364, 1276, 1228, 777 cm^{-1}. ^{1}H-NMR, δ 0.58 (s, 6H), 0.83 ~ 2.37 (m, 13H), 0.97 (s, 3H), 0.98 (d, J = 5.0 Hz, 3H). HRMS (EI, 20 ev), calcd for $C_{12}H_{22}ClOSn$ (M - Me) 337.0382, found 337.0352.

Reaction of 36b. The products obtained from **36b** (0.135 g, 0.347 mmol) were **37b** (51.7 mg, 66%) and **39b** (21.0 mg, 15%) by the method A, while the products were **38b** (77.5 mg, 62%) and **39b** (61.1 mg, 29%) from **36b** (0.200 g, 0.514 mmol) by the method B. No trace of the alcohol **37b** was identified. For **37b**: MS (CI), m/z 227 (M^+ + 1), 226 (M^+), 209, 183, 137, 121, 107, 95, 75, 73, 67. IR, 3345, 3072, 1638, 1248 790 cm^{-1}. ^{1}H-NMR (400 MHz), δ -0.05 (s, 9H), 0.88 (s, 3H), 0.80 ~ 1.38 (m, 5H), 1.79 (br.d, J = 12.5 Hz, 1H), 1.92 (br.d, J = 12.5 Hz, 1H), 1.98 ~ 2.10 (m, 2H), 3.74 (tt, J = 7.2 and 3.9 Hz, 1H), 4.99 (br.d, J = 17.6 Hz, 1H), 5.02 (br.d, J = 10.3 Hz, 1H), 5.75 (ddt, J = 17.6, 10.3, and 7.1 Hz, 1H). HRMS (CI), calcd for $C_{13}H_{26}OSi$ (M) 226.1753, found 226.1725. For **39b**: mp, 107 ~ 109 °C. MS, m/z 395 (M^+ - 15), 367, 295, 225, 185, 181, 135, 93, 73, 55. IR ($CHCl_3$), 1694, 1250, 832, 757 cm^{-1}. ^{1}H-NMR, δ 0.00 (s, 9H), 0.57 (s, 6H), 0.77 ~ 2.23 (m, 13H), 1.00 (s, 3H). HRMS, calcd for $C_{15}H_{31}OSiSn$ (M^+ - 35) 375.1166, found 375.1170. For **38b**: MS (CI), m/z 231 (M^+ + 2 - 15), 229 (M^+ - 15), (M^+ + 2 - 15 : M^+ - 15 = 1 : 3), 209 (M^+ - 35), 135, 121, 107, 95, 93, 81, 73 (TMS), 67. IR, 3070, 1639, 1248, 865, 840 cm^{-1}. ^{1}H-NMR (400 MHz), δ -0.05 (s, 9H), 0.89 (s, 3H), 0.85 ~ 0.90 (m, 1H), 1.23 ~ 1.40 (m, 4H), 2.01 (br.d, J = 12.5 Hz, 1H), 2.05 (br.d, J = 6.8 Hz, 2H), 2.13 (br.d, J = 12.5 Hz, 1H), 4.04 (tt, J = 12 and 4 Hz, 1H), 5.00 (br.d, J = 17.7 Hz, 1H), 5.05 (br.d, J = 10 Hz, 1H), 5.72 (ddt, J = 17.7, 10, and 6.8 Hz, 1H). HRMS (CI), calcd for $C_{18}H_{25}Si$ (M - Cl) 209.1725, found 209.1733.

References and Footnotes

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