

Ring Enlargement of α -Ethylidenecycloalkanones to β -Alkylidenecycloalkanones Induced by Trimethylstannyl lithium/Aldehyde Equivalents/Lewis Acids

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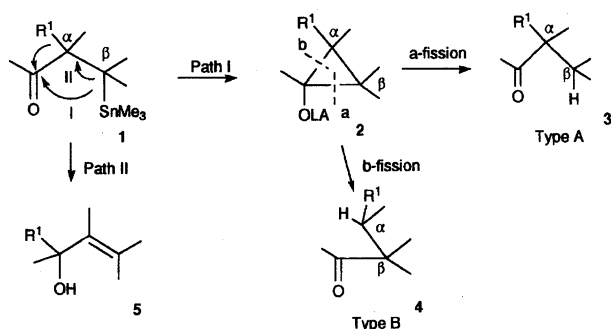
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α -Ethylidenecycloalkanones underwent a ring enlargement to β -alkylidenecycloalkanones upon a treatment with trimethylstannyl lithium/aldehyde equivalents/Lewis acids with high stereoselectivity.

We have reported that the Lewis acid-induced reaction of β -stannyl ketones **1** usually proceeds via cyclopropanol intermediates **2** (Path I), and affords saturated ketones **3** or **4**, according to the position of the bond cleavage of the cyclopropanol ring of **2**, a or b, in Scheme 1.^{1,2)} We call these reactions Type-A and Type-B, respectively. The general trend is that an increase in the number of substituents on the α -carbon favors the Type-A reaction, while an increase on the β -carbon favors the Type-B reaction. The Type-B reaction becomes the exclusive reaction pattern when the β -carbon is fully substituted. Only when an alkyl group of sufficient migratory aptitude occupies the antiperiplanar position against the stannyl group does the 1,2-alkyl migration compete with the cyclopropanation, affording products derived from **5** (Path II).^{3,4)} The Type-B reaction involves a carbon-skeleton rearrangement; we have utilized the reaction for the ring contraction of *endo*-type cyclic α,β -enones. It is expected that the Type-B reaction could be applied for a ring enlargement if it proceeds effectively with *exo*-type cyclic α,β -enones. Actually, the reaction proceeded as expected under specific conditions.

Results and Discussion

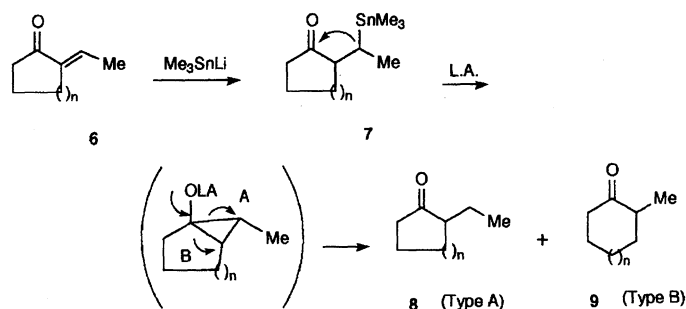
When β -stannyl ketones **7a–7d**, prepared by the



Scheme 1.

conjugate addition of Me_3SnLi upon corresponding ethylidene cycloalkanones **6**, were treated with Lewis acids, the Type-A and Type-B reactions proceeded to afford the corresponding **8** and **9**, as shown in Scheme 2 and Table 1.⁵⁾ Evidently, the selectivity between the Type-A and Type-B reactions was not necessarily satisfactory, probably because both of the α and β -carbons of the cyclopropanol intermediate are tertiary. We have already found that one of the effective ways to increase the selectivity of the Type-B reaction is to introduce leaving groups into the 1'-position of the α -substituent, as shown in Scheme 3, thus facilitating an effective ring contraction to form **11** when applied to cyclic compounds, such as **10**.⁶⁾ Therefore, we intended to prepare **15**, which might proceed through the Type-B reaction, as shown in Scheme 4. The desired **15a–15g** were prepared by a conjugate addition of Me_3SnLi to **12**, followed by quenching the lithium enolates **13** either with appropriate electrophiles directly (Method A), or first with trimethylsilyl chloride to afford silyl enol ether **14**, and then with aldehydes or acetals (Method B). The results are shown in Table 2. Products **15a–15d** were obtained as single stereoisomers to which the *anti* structure was assigned in view of the generally accepted reaction pattern of trapping the enolates with electrophiles.⁷⁾ Products **15e–15g** were obtained as mixtures of two diastereomers. It would be reasonable to assume that, here again, the relative stereochemistry of the carbon-tin bond and the newly created carbon-carbon bond is fixed to the *anti* relation, and that diastereomeric scrambling arises from the configuration of the aldol moiety. This was further confirmed by the following observations.

As shown in Runs 5 and 6, the diastereomer ratio of **15e** reversed according to the preparation methods, methods A and B. Each of the diastereomers was separable by column chromatography; their stereochemistries were unequivocally determined in the following way by utilizing our recent finding that the



a: n = 1; b: n = 2; c: n = 3; d: n = 4

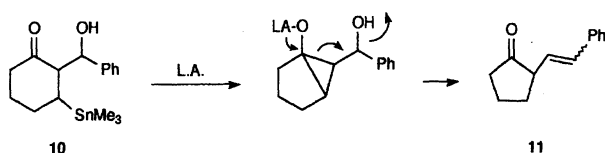
Scheme 2.

Table 1. Reaction of **7** with Lewis Acid

Run	Starting material	Lewis acid	Product ratio		Yield/%
			8	9	
1	7a	TiCl ₄	0	100	44
2	7b	TiCl ₄	89	11	69
3	7c	TiCl ₄	74	26	86
4	7c	TMSOTf	11	89	78
5	7d	TiCl ₄	51	49	82

Table 2. Reaction of **12** with Stannyl Anion and Electrophile

Run	Electrophile	Method	Product and yield/%		Diastereomer ratio
1	ClCH ₂ I	A	15a	47	—
2	ClCH ₂ I	A	15b	50	—
3	Me ₂ N ⁺ =CH ₂ I ⁻ /MeI	A	15c	78	—
4	CH ₂ O	B	15d	69 ^{a)}	—
5	MeCHO	A	15e	76	75 : 25
6	MeCHO	B	15e	71 ^{a)}	35 : 65
7	MeCH(OMe) ₂	B	15f	40 ^{a)}	17 : 83
8	PhCH(OMe) ₂	B	15g	48 ^{a)}	11 : 89

a) Yields from **14a**, which was prepared from **12a** in 97% yield.

Scheme 3.

treatment of β' -hydroxy- β -stannyl ketones with PCl_3 or MeSO_2Cl (MsCl) induced a cyclopropanation,⁸⁾ with an inversion of the configuration at both reaction centers.⁹⁾

When the major isomer in Run 5 was treated with MsCl , a spirocyclopropane **18** was obtained, while the major isomer in Run 6 gave another spirocyclopropane **19** under the same conditions (Chart 1). In view of the ^1H NMR datum of **18**, which showed a single methyl signal and a single cyclopropane ring proton signal, we assigned the *cis*-dimethyl structure for this compound. On the other hand, the *trans*-dimethyl structure was assigned for **19**, because each of the signals of methyl and the cyclopropane ring proton appeared as a pair. These observations indicate that the major isomer in

Run 5 has a stereostructure shown as *threo*-**15e**, while another isomer as *erythro*-**15e**. The assignment is consistent with the general scheme that the reaction from lithium enolate proceeds through a Zimmerman-type cyclic transition state **20**, while the F^- -assisted aldol reaction with silyl enol ether proceeds through an open-chain transition state **21**. In view of the ^{13}C NMR spectra, **15f** and **15g** were found to be diastereomer mixtures, although the stereochemistries have not been assigned.

When **15a**–**15e** were treated with Lewis acids, they underwent the Type-B reaction, affording *exo*-type β,γ -enones **17** with a ring enlargement as shown in Table 3. Only in the case of Run 5, did further isomerization of the double bond occur to give α,β -enone **22**. The reaction proceeded with high stereospecificity, affording only (*E*)-**17e** from *threo*-**15e**, while only (*Z*)-**17e** from *erythro*-**15e**. The geometry of the double bond in **17e** was assigned based on the ^{13}C NMR signals of C2 carbon, which appeared at a higher field ($\delta=48.64$) for the (*Z*)-isomer than that for the (*E*)-isomer ($\delta=55.32$),

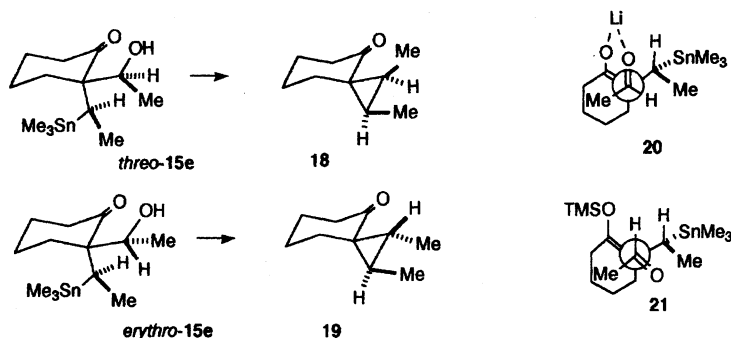
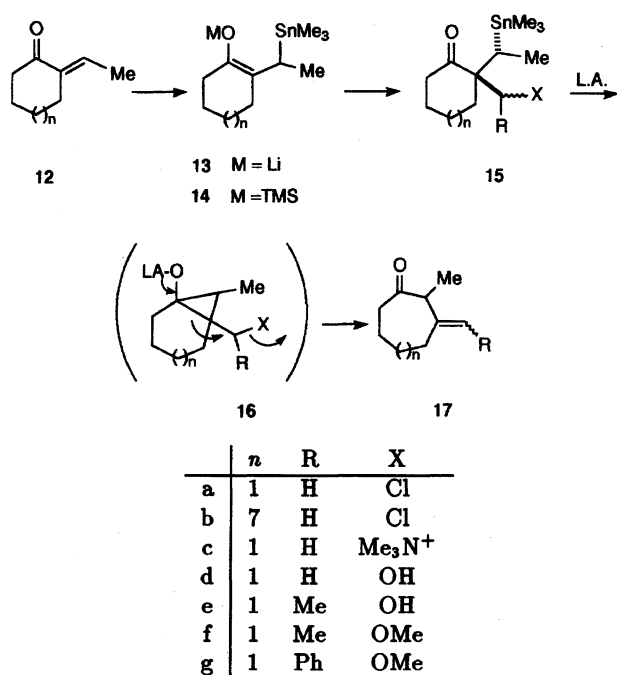


Chart 1.

Table 3. Reaction of **15** with Lewis Acid

Run	Starting material	Ratio	Lewis acid	Temp/°C	Time/min	Product	Yield/%	Ratio
1	15a	—	TiCl ₄	0	30	17a	92	—
2	15b	—	TiCl ₄	0	10	17b	82	—
3	15c	—	TiCl ₄	R.T.	48(h)	17a	75	—
4	15c	—	EtAlCl ₂	R.T.	48(h)	17a	65	—
5	15c	—	TMSOTf	R.T.	48(h)	22	75	—
6	15d	—	TiCl ₄	0	5	17a	63	—
7	<i>t</i> - 15e	100 : 0	TiCl ₄	-78	5	(<i>E</i>)- 17e	84	100 : 0
8	<i>e</i> - 15e	100 : 0	TiCl ₄	0	5	(<i>Z</i>)- 17e	83	100 : 0
9	15f	90 : 10	TiCl ₄	-78	30	(<i>E</i>)- 17e	92	99 : 1
10	15g	89 : 11	TiCl ₄	-78	10	(<i>E</i>)- 17g ^a	40	99 : 1
11	<i>t</i> - 15e	95 : 5	EtAlCl ₂	R.T.	5	25e	79	80 : 20
12	<i>e</i> - 15e	99 : 1	EtAlCl ₂	R.T.	15	25e	54	90 : 10
13	15f	90 : 10	EtAlCl ₂	R.T.	30	25f	59	93 : 7
14	15g	89 : 11	EtAlCl ₂	0	10	25g	47	60 : 40

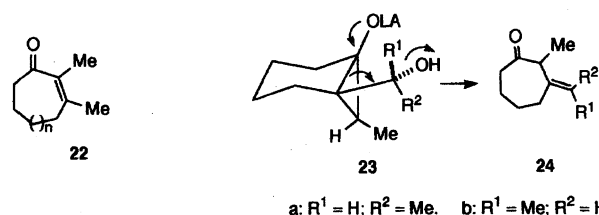
a) The starting enone **12a** (27%) was recovered.

Scheme 4.

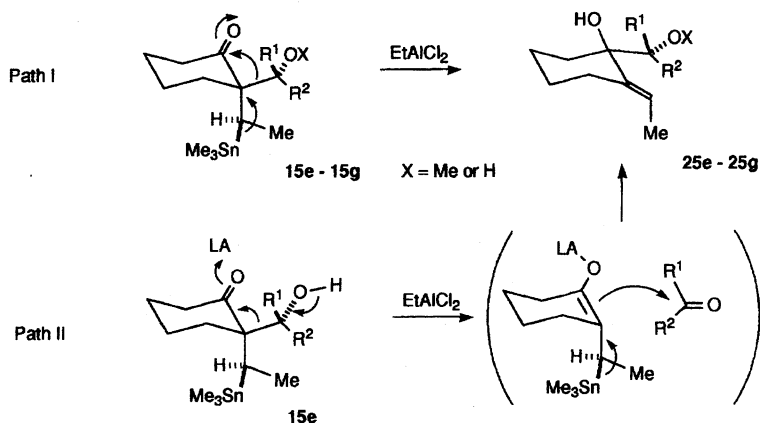
due to stereochemical compression. The observation of a 5% NOE enhancement between two methyl groups in the (*Z*)-isomer also supported the assignment.

In view of the high stereospecificity in the ring-enlargement reaction, we schemed the reaction as involving a concerted mechanism. With the structures of the aldols and the β,γ -enones now confirmed, it was concluded that the ring enlargement proceeded through a synperiplanar orientation of the hydroxyl group and a cleaving bond of the cyclopropanol, as shown in Scheme 5.¹⁰⁾ This is in sharp contrast to the stepwise fragmentation of 2-(1-hydroxyalkyl)-1-cyclopropanols, in which two hydroxyl groups can not occupy the same side of the cyclopropane ring.¹¹⁾

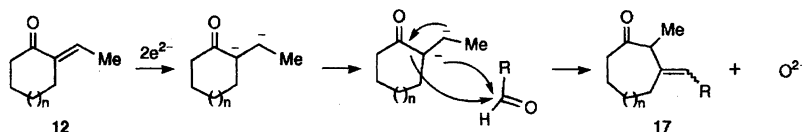
Diastereomer mixtures of **15f** and **15g** also underwent the ring enlargement with TiCl₄ to give **17f** and



Scheme 5.



Scheme 6.



Scheme 7.

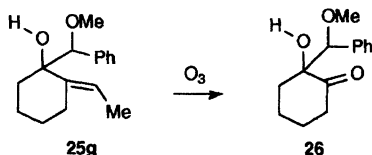


Chart 2.

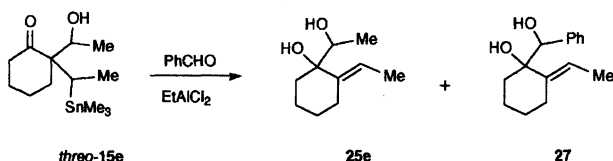


Chart 3.

17g, predominantly of *E*-geometry (Runs 9 and 10). Considering the *E/Z* stability of **17** under these conditions as revealed above, the high *E*-predominance could be rationalized by assuming a retro reaction of the minor diastereomer to the original enones. The retro reaction was actually observed in Run 10, where **12a** was recovered in 27% yield.

The nature of the Lewis acid is critical to induce the Type-B reaction. Although **15c** underwent the Type-B reaction with EtAlCl_2 as smoothly as with TiCl_4 (Run 4), **15e**–**15g** gave **25e**–**25g** by EtAlCl_2 , without producing any amounts of the Type-B reaction products (Runs 11, 12, 13, and 14). In each case, the product was a mixture of two inseparable isomers, as revealed by the ^{13}C NMR spectrum. In order to assign the origin of the isomerism, the double bond in **25g** was cleaved by ozone, using a sample of a 60:40 diastereomer mixture. Since the product ketone **26** was also a 60:40 mixture of two isomers, it was concluded that the isomerism originated in the stereochemical scrambling at the 1,2-diol moiety, while the double bond in **25g** is

fixed to a single geometry, probably the *E*-configuration (Chart 2). The reaction could be schemed either as involving 1,2-migration (Path I, Scheme 6) or, in the case of **15e**, a retroaldol reaction followed by coupling of the resulting γ -hydroxyallylstannane and aldehyde (Path II). As shown in Runs 11 and 12, both of the *threo* and *erythro*-**15e** gave a diastereomer mixture of **25e** with an identical stereochemical preference. While we have not assigned the stereochemistries of the diastereomers, the stereochemical scrambling favors a stepwise reaction mechanism through Path II. The stepwise intermolecular reaction scheme was further verified by the EtAlCl_2 -induced reaction of **15e** in the presence of benzaldehyde, which afforded **27** in 76% yield as well as **25e** in 12% (Chart 3). In contrast, no such aldehyde scrambling was observed with **15f** and **15g**, which favors the intramolecular reaction scheme (Path I).

Conclusion

In this study we found that although the stannyl compounds **7** underwent a ring enlargement to afford **9**, the reaction was not always selective, accompanied by the formation of **8**. In contrast, stannyl compounds **15** having leaving groups X underwent a ring enlargement stereoselectively to produce *E*, *Z*-defined **17**. In a previous paper¹²⁾ we proposed a synthon representation in order to characterize the reaction type typical of the tin-containing compounds, and represented Me_3SnLi as a reagent equivalent to a double electron. Thus, the present reaction can be represented essentially as shown in Scheme 7.

We have so far characterized the typical points of the reactions of the stannyl compounds as follows:¹²⁾ while the tin-bearing carbon exhibits a carbanionic nature, its low reactivity towards electrophilic centers allows us to prepare, as the first-stage reaction, stannyl compounds

having a variety of electrophilic centers within the same molecule, and we can activate the tin-carbon bond, as the second-stage reaction, in various ways by changing the nature of the electrophilic centers, reaction conditions, and activation methods. The present reaction is another example which demonstrates the diversity in the reaction mode on tin-containing compounds involving the activation of the tin-carbon bond by cooperation of the carbonyl group, aldehyde equivalents, and Lewis acids.

Experimental

General Procedure and Instrumentation. GC experiments were carried out on a 2.5 m×3 mm stainless-steel column packed with Silicone SE 30 on silanized Chromosorb W and 25 m×0.25 mm capillary column (SE 30). Column chromatography was carried out on Kieselgel 60, Art. 7734 (70–230 mesh ASTM). ^1H NMR spectra (60 MHz) were recorded on a Hitachi R-24 or JEOL PMX 60 SI spectrometer. ^1H NMR (90 MHz) and ^{13}C NMR (22.5 MHz) spectra were measured on a Hitachi JNM-PMX 60S R-90H spectrometer, and ^1H NMR (400 MHz) spectra on a JEOL GSX-400 spectrometer. GC-MS spectra were taken on a Shimadzu QP-1000 mass spectrometer, and high resolution 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 of the spectroscopic data were determined on pure samples obtained by either distillation or column chromatography, checking the purity by TLC or GC analyses; the mass spectra were obtained by the EI method at 70 eV, the ^1H NMR on the 60 MHz machines with CCl_4 solutions, the ^1H NMR data on the 90 and 400 MHz machines and the ^{13}C NMR data with CDCl_3 solutions, and IR spectra with neat samples.

All of the ^1H NMR signals of the methyl group on the tin atom at $\delta \approx 0$ ppm accompanied splitting signals by ^{117}Sn (7.54% abundance, $J=51$ Hz) and ^{119}Sn (8.62% abundance, $J=53$ Hz). Mass spectral peaks of the tin-containing fragments showed isotope pattern typical to the tin atom, but only values corresponding to ^{120}Sn were shown.

Starting Materials and Reagents. The following compounds were prepared referring to the literature.¹³⁾ 2-Ethylidenecyclopentanone (**6a**),¹⁴⁾ 2-ethylidenecyclohexanone (**6b=12a**),¹⁵⁾ 2-ethylidenecycloheptanone (**6c**) [MS m/z 138 (M^+), 95, 81 (base), 68, 67. ^1H NMR, $\delta=1.70$ (br.s, 6H), 1.78 (d, $J=6.5$ Hz, 3H), 2.45 (br.s, 4H), 6.52 (q, $J=6.5$ Hz, 1H)], 2-ethylidenecyclooctanone (**12b**) [MS m/z 152 (M^+), 110, 109, 96, 95, 81, 68, 67 (base). ^1H NMR $\delta=1.55$ (br.s, 8H), 1.81 (d, $J=6.3$ Hz, 3H), 2.58 (br.s, 4H), 6.58 (q, $J=6.3$ Hz, 1H)], 2-ethylidenecyclododecanone [^1H NMR $\delta=1.26$ (br.s, 14H), 1.5–2.0 (m, 2H). 1.85 (d, $J=7.2$ Hz, 3H), 2.23–2.72 (m, 4H), 6.52 (q, $J=7.2$ Hz, 1H)]. Trimethylsilyl trifluoromethanesulfonate (TMSOTf) and TiCl_4 were obtained commercially, and purified by distillation. EtAlCl_2 was obtained commercially as hexane solution (0.93 M, 1 M=1 mol dm $^{-3}$), and used directly.

General Procedure for the Preparation of β -Stannyl Ketones 7. To a THF solution of Me_3SnLi (1.2–3.3 equiv) prepared as described in our previous report⁶⁾ was added a solution of the corresponding α,β -enones **6** (0.3–0.6, 1 equiv) in THF at 0 °C. After being stirred for the

periods described below, the solution was quenched with water at room temperature. The ether extracts, after being dried over MgSO_4 , were concentrated in vacuo. Column chromatography gave pure materials.

2-(1-Trimethylstannylethyl)-1-cyclopentanone (7a). The product was obtained in 29% yield (0.040 g) from **6a** (0.056 g, 0.509 mmol) by stirring for 15 min. ^1H NMR $\delta=-0.05$ (s, 9H), 1.10 (s, 3H), 1.4–2.4 (m, 8H).

2-(1-Trimethylstannylethyl)-1-cyclohexanone (7b). The product was obtained in 63% yield (0.636 g) from **6b** (0.433 g, 3.49 mmol) by stirring for 30 min. MS m/z 275 (M^+-15), 165, 135 (base). ^1H NMR $\delta=-0.13$ (s, 9H), 0.90–2.00 (m, 10H), 2.0–2.5 (m, 3H).

2-(1-Trimethylstannylethyl)-1-cycloheptanone (7c). The product was obtained in 86% yield (0.382 g) from **6c** (0.201 g, 1.46 mmol) by stirring for 15 min. ^1H NMR $\delta=-0.15$ (s, 9H), 0.85–2.00 (m, 12H), 2.1–2.4 (m, 3H).

2-(1-Trimethylstannylethyl)-1-cyclooctanone (7d). The product was obtained in 77% yield (0.855 g) from **6d** (0.534 g, 3.51 mmol) upon stirring for 30 min. Two diastereomers were separated by column chromatography (69:31). For major fraction: MS, m/z 303 (M^+-15), 165, 135 (base). ^1H NMR $\delta=-0.10$ (s, 9H), 1.00 (s, 3H), 1.15–2.00 (m, 11H), 2.10–2.30 (m, 2H), 2.60–2.90 (m, 1H). For minor fraction: MS m/z 303 (M^+-15), 165, 135 (base). ^1H NMR $\delta=-0.10$ (s, 9H), 0.90–2.50 (m, 17H).

General Procedure for the Preparation of β -Stannyl Ketones 15 (Method A). To a THF solution of Me_3SnLi (1.2–3.3 equiv) prepared as described in our previous report⁶⁾ was added a solution of the corresponding α,β -enones (0.3–0.6 M, 1 equiv) in THF at 0 °C. After being stirred for 1 h, the solution was reacted with appropriate electrophiles at room temperature for periods as described below. The ether extracts, after being dried over MgSO_4 , were concentrated in vacuo. Column chromatography gave pure materials.

2-Chloromethyl-2-(1-trimethylstannylethyl)-1-cyclohexane (15a). The product was obtained in 47% yield (0.643 g) from **12a** (0.500 g, 4.03 mmol) by a stepwise addition of a MeSnLi solution (10.0 mmol), and then chloriodomethane (1.77 g, 10.0 mmol), by stirring for 8 h. The product was purified by column chromatography (hexane:ether=4:1). MS m/z 323 (M^+-15), 303, 287, 185 (base), 165, 138, 110, 95, 81, 67, 55. ^1H NMR $\delta=0.09$ (s, 9H), 0.97 (d, $J=8.4$ Hz, 3H), 1.57–2.17 (m, 7H), 2.17–2.64 (m, 2H), 3.64 (s, 2H). HRMS. Found: m/z 323.0178. Calcd for $\text{C}_{11}\text{H}_{20}\text{OClSn}$: (M–Me), 323.0225.

2-Chloromethyl-2-(1-trimethylstannylethyl)-1-cyclododecanone (15b). The product was obtained in 50% yield (2.11 g) from **12b** (2.08 g, 10.0 mmol), Me_3SnLi solution (12.0 mmol), and chloriodomethane (2.66 g, 15.1 mmol) after stirring for 1 h. The product was purified by column chromatography (hexane:ether=19:1). MS m/z 407 (M^+-15), 371, 222, 193, 185, 165 (base), 151, 135, 123, 109, 95, 81, 67. IR 2931, 2864, 1694, 1468, 1443, 1127, 1054, 766, 727 cm^{-1} . ^1H NMR $\delta=0.08$ (s, 9H), 0.91 (d, $J=7.0$ Hz, 3H), 1.05–2.41 (m, 21H), 3.52 and 3.67 (ABq, $J=14.0$ Hz, 2H). HRMS (CI). Found: m/z 423.1463. Calcd for $\text{C}_{18}\text{H}_{36}\text{OClSn}$: (M+H), 423.1477.

2-(N,N,N-Trimethylammoniomethyl)-2-(1-trimethylstannylethyl)-1-cyclohexanone Iodide (15c).

2-(*N,N*-Dimethylaminomethyl)-2-(1-trimethylstannylethyl)-1-cyclohexanone was obtained in 78% yield by treating the solution, prepared from **12a** (0.400 g, 3.23 mmol) and Me_3SnLi (4.00 mmol), with *N,N*-dimethyl(methylene)ammonium iodide (1.00 g, 5.40 mmol). MS (20 eV), m/z 332 ($\text{M}^+ - \text{Me}$), 289, 165, 58 (base). IR 2938, 2864, 2819, 2768, 1696, 1458, 1040, 764 cm^{-1} . ^1H NMR δ =0.21 (s, 9H), 1.06 (d, J =7.6 Hz, 3H), 1.50–2.50 (m, 9H), 2.27 (s, 6H), 2.60 (s, 1H), 2.67 (s, 1H). ^{13}C NMR δ =−7.56, 12.86, 20.87, 26.64, 26.93, 36.35, 39.20, 48.32, 56.44, 63.13, 214.55. HRMS (20 eV). Found: m/z 332.0978. Calcd for $\text{C}_{13}\text{H}_{26}\text{ONSn}$: ($\text{M} - \text{Me}$), 332.1036. The ammonium iodide **15c** was obtained as a white solid after stirring the resulting 2-(*N,N*-dimethylaminomethyl)-2-(1-trimethylstannyl)-1-cyclohexanone (0.85 g, 2.46 mmol) with CH_3I (40 ml) in methanol (40 ml) for two days, and evaporating the solvent. IR (KBr) 2994, 2940, 2869, 1699, 1482, 1466, 1120, 925, 888, 769 cm^{-1} . ^1H NMR δ =0.32 (s, 9H), 1.19 (d, J =7.6 Hz, 3H), 1.05–2.50 (m, 9H), 3.55 (s, 9H), 3.89, 4.06 (ABq, J =14.0 Hz, 2H). ^{13}C NMR δ =−7.56, 12.73, 20.23, 26.25, 26.62, 37.08, 39.42, 55.94, 56.29, 68.02, 212.78.

threo- and erythro-2-(1-Hydroxyethyl)-2-(1-trimethylstannylethyl)-1-cyclohexanone (15e). To a THF solution, prepared from **12a** (0.600 g, 4.84 mmol) and Me_3SnLi (5.57 mmol) was added a solution of acetaldehyde (0.639 g, 14.5 mmol) in THF (5 ml) at -78°C , and stirred for 40 min at this temperature. The solution was worked-up in the same way as above to afford a mixture of *threo*- and *erythro*-**15e** (75:25) in 76% yield. Each of the products was purified on a silica-gel column (hexane:AcOEt=5:1). For *threo*-**15e** (major component): IR 3462, 2938, 2867, 1690, 1458 cm^{-1} . ^1H NMR δ =0.19 (s, 9H), 1.05 (dist.d J =6.7 Hz, 6H), 1.27–2.53 (m, 10H), 3.79 (q, J =6.7 Hz, 1H). ^{13}C NMR δ =−7.92, 14.45, 18.35, 21.09, 25.80, 28.30, 32.55, 40.01, 58.98, 72.10, 217.06. For *erythro*-**15e** (minor component): IR 3498, 2938, 2867, 1682, 1455, 1108, 1054, 787, 764 cm^{-1} . ^1H NMR δ =0.14 (s, 9H), 1.05 (d, J =6.6 Hz, 3H), 1.20 (d, J =6.0 Hz, 3H), 1.26–2.76 (m, 10H), 4.17 (q, J =6.0 Hz, 1H). ^{13}C NMR δ =−6.81, 12.59, 19.36, 20.27, 25.92, 26.14, 30.31, 39.26, 58.45, 67.03, 213.95.

General Procedure for the Preparation of β -Stannyl Ketones 15 (Method B). 1-(Trimethylsilyloxy)-2-(1-trimethylstannylethyl)-1-cyclohexene (**14a**). To a THF solution of **13a**, prepared from **12a** (2.00 g, 16.2 mol) and Me_3SnLi (19.3 mmol), was added triethylamine (6.83 ml, 48.4 mmol) and then TMSCl (6.15 ml, 48.4 mmol) at room temperature. After being stirred for 10 min, the solution was quenched with sat. NaHCO_3 aq, and the product **14a** (5.70 g, 97%) was obtained. MS m/z 362 (M^+), 197 (base), 73. IR 2928, 2857, 2835, 1659, 1348, 1251, 1182, 920, 842 cm^{-1} . ^1H NMR δ =0.09 (s, 9H), 0.24 (s, 9H), 1.27 (d, J =7.6 Hz, 3H), 1.47–2.90 (m, 9H). ^{13}C NMR δ =−9.86, 1.08, 15.51, 22.08, 23.22, 23.89, 26.55, 30.42, 119.41, 139.42. HRMS (20 eV). Found: m/z 362.1128. Calcd for $\text{C}_{14}\text{H}_{30}\text{OSiSn}$: (M), 362.1088.

2-Hydroxymethyl-2-(1-trimethylstannylethyl)-1-cyclohexanone (15d). To a mixture of formalin (35%, 0.6 ml) and $\text{Yb}(\text{OTf})_3$ (0.020 g) was added a solution of **14a** (0.072 g, 0.20 mmol) in THF (1 ml) at room temperature. The solution was stirred for 55 h, and extracted with ether. The product was purified by column chromatography to afford **15d** (0.044 g, 69%). IR 3445, 2936, 2866, 1694, 1454,

1119, 1043, 766 cm^{-1} . ^1H NMR δ =0.17 (s, 9H), 1.05 (d, J =7.8 Hz, 3H), 1.22–2.75 (m, 9H), 3.20–3.91 (m, 3H). ^{13}C NMR δ =−8.19, 13.16, 20.50, 24.79, 27.11, 34.73, 39.29, 57.24, 66.37, 217.34.

threo- and erythro-2-(1-Hydroxyethyl)-2-(1-trimethylstannylethyl)-1-cyclohexanone (15e). A suspension of molecular sieve 4A (3 g) and TBAF (0.796 g, 3.04 mmol) in THF (7 ml) was stirred for 7 h at room temperature. To the mixture was added a solution of **14a** (0.330 g, 0.92 mmol) and acetaldehyde (0.405 g, 9.20 mmol) in THF (3 ml) at -78°C . After being stirred for 1 h, it was quenched with sat. NaHCO_3 aq. The product was a mixture of *threo*- and *erythro*-**15e** (35:65) in 70% yield. Each of the products was purified on a silica-gel column (hexane:AcOEt=5:1).

2-(1-Methoxyethyl)-2-(1-trimethylstannylethyl)-1-cyclohexanone (15f). To a mixture of **14a** (0.200 g, 0.55 mmol) and acetaldehyde dimethyl acetal (0.294 ml, 2.77 mmol) in CH_2Cl_2 (7 ml) was added TiCl_4 (0.06 ml, 0.55 mmol) at -78°C . After stirring for 30 min, the reaction mixture was treated with NaHCO_3 aq, and extracted with CH_2Cl_2 . The product was **15f** (0.076 g, 40%). A GC-MS analysis revealed that the product was a mixture of two diastereomers (83:17). MS m/z 333 ($\text{M}^+ - 15$), 289, 275, 165, 135, 125, 59 (base). ^1H NMR (as mixture) δ =0.15 (m, 9H), 1.15 (dist.d, J =7.2 Hz, 6H), 1.50–2.60 (m, 9H), 3.23 (s, 3H), 3.55 (q, J =6.4 Hz, 1H). HRMS. Found: m/z 333.0905. Calcd for $\text{C}_{13}\text{H}_{25}\text{O}_2\text{Sn}$: ($\text{M} - \text{Me}$), 333.0877.

2-(1-Methoxybenzyl)-2-(1-trimethylstannylethyl)-1-cyclohexanone (15g). To a mixture of benzaldehyde dimethyl acetal (0.304 g, 2.00 mmol) and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (0.245 ml, 2.00 mmol) in CH_2Cl_2 (10 ml) was added **14a** (0.600 g, 1.66 mmol) at -78°C . After strring for 4 h, the reaction mixture was treated with NaHCO_3 aq, and extracted with CH_2Cl_2 . The product was **15g** (0.325 g, 48%). A GC-MS analysis revealed that the product was a mixture of two diastereomers (89:11). MS m/z 395 ($\text{M}^+ - 15$), 289, 165, 121 (base). IR 3062, 3029, 2934, 2867, 2822, 1691, 1452, 1249, 1133, 1094, 1075, 840, 759 cm^{-1} . ^1H NMR (as mixture) δ =0.11 (s, 9H), 1.10 (br.s, 3H), 1.30–2.71 (m, 9H), 3.09 (s, 3H), 4.42 (s, 1H), 7.20 (br.s, 5H). HRMS. Found: m/z 395.0990. Calcd for $\text{C}_{18}\text{H}_{27}\text{O}_2\text{Sn}$: ($\text{M} - \text{Me}$), 395.1033.

General ProcEDURE for the Lewis Acid-Induced Reactions of 7 or 15. A solution of stannyl ketones **7** or **15** and Lewis acid in CH_2Cl_2 was kept under the conditions specified below. The mixture was quenched with sat. NaHCO_3 aq, and the residue was purified by column chromatography. The results for **7** are given in Table 1, and for **15** in Table 3, respectively.

Reaction of 7a with TiCl_4 . The reaction of **7a** (0.040 g, 0.145 mmol) and TiCl_4 (0.5 M, 0.291 ml) at 0°C for 15 min afforded **9a** (0.030 g, 44%) as a single product. **9a** was identical with the commercial sample.

Reaction of 7b with TiCl_4 . The reaction of **7b** (0.100 g, 0.345 mmol) in CH_2Cl_2 (3.46 ml) and TiCl_4 (0.5 M, 0.692 ml) at 0°C for 15 min afforded a mixture of **8b** and **9b** (0.030 g, 69%, 89:11 by GLC analysis). **9b** was identical with the sample prepared by the ring contraction of 2-cycloocten-1-one by $\text{Me}_3\text{SnLi/TMSOTf}$.⁶⁾

For **8b**: MS m/z 126 (M^+), 111, 98 (base), 97, 84, 83, 82, 70, 69, 67.

For **9b**: MS m/z 126 (M^+), 111, 98 (base), 97, 84, 83, 82,

70, 69, 68, 67. $^1\text{H NMR}$ $\delta=1.00$ (d, $J=6.6$ Hz, 3H), 1.20—2.10 (m, 8H), 2.10—2.80 (m, 3H).

Reaction of 7c with TiCl_4 . The reaction of 7c (0.050 g, 0.165 mmol) in CH_2Cl_2 (1.65 ml) and TiCl_4 (0.5 M, 0.330 ml) at 0 °C for 15 min afforded a mixture of 8c and 9c (0.020 g, 87%, 74:26 by GLC analysis).

For 8c: MS m/z 140 (M^+), 125, 112, 111, 98, 97, 83, 69, 55 (base).

For 9c: MS m/z 140 (M^+), 125, 112, 111, 98, 97 (base), 69.

Reaction of 7c with TMSOTf . The reaction of 7c (0.050 g, 0.165 mmol) in CH_2Cl_2 (1.65 ml) and TMSOTf (0.5 M, 0.330 ml) at 0 °C for 15 min afforded a mixture of 8c and 9c (0.018 g, 78%, 11:89 by GLC analysis).

Reaction of 7d with TiCl_4 . The reaction of 7d (0.100 g, 0.315 mmol) in CH_2Cl_2 (3.15 ml) and TiCl_4 (0.5 M, 0.631 ml) at 0 °C for 15 min afforded a mixture of 8d and 9d (0.040 g, 82%, 51:49 by GLC analysis).

For 8d: MS m/z 154 (M^+), 139, 126, 98, 83, 69, 55 (base).

For 9d: MS m/z 154 (M^+), 139, 97 (base), 69, 55.

Reaction of 15a with TiCl_4 . The reaction of 15a (0.098 g, 0.30 mmol) and TiCl_4 (0.057 g, 0.30 mmol) in CH_2Cl_2 (5 ml) at 0 °C for 30 min afforded 17a (0.384 g, 92%). MS m/z 138 (M^+), 123, 110, 95, 81, 67 (base), 55. IR 3395, 3092, 2933, 2860, 1709, 1641, 1448, 1256, 1154, 897 cm^{-1} . $^1\text{H NMR}$ $\delta=1.14$ (d, $J=6.6$ Hz, 3H), 1.51—1.98 (m, 4H), 1.98—2.59 (m, 4H), 3.08 (q, $J=6.6$ Hz, 1H), 4.94 (br.s, 1H), 4.90 (br.s, 1H). HRMS. Found: m/z 138.1052. Calcd for $\text{C}_9\text{H}_{14}\text{O}$: (M), 138.1045.

Reaction of 15b with TiCl_4 . The reaction of 15b (0.160 g, 0.37 mmol) and TiCl_4 (0.37 mmol) in CH_2Cl_2 (5 ml) at 0 °C for 10 min afforded 17b (0.069 g, 82%). MS m/z 222 (M^+), 207, 193, 175, 123, 109, 95 (base), 82, 81. IR 3082, 2931, 2860, 1712, 1639, 1458, 1369, 1120, 898 cm^{-1} . $^1\text{H NMR}$ $\delta=1.12$ (d, $J=7.0$ Hz, 3H), 1.06—1.85 (m, 16 H), 1.85—2.75 (m, 4H), 3.12 (q, $J=7.0$ Hz, 1H), 4.91 (br.s, 1H), 4.95 (br.s, 1H). $^{13}\text{C NMR}$ $\delta=15.61$, 22.15, 24.79, 24.90, 25.08, 25.23, 25.34, 32.69, 39.57, 53.77, 112.45, 147.58, 210.95. HRMS. Found: m/z 222.1965. Calcd for $\text{C}_{15}\text{H}_{26}\text{O}$: (M), 222.1984.

Reaction of 15c with TiCl_4 or EtAlCl_2 . A mixture of 15c (0.140 g, 0.29 mmol) and TiCl_4 (0.06 ml, 0.57 ml) in CH_2Cl_2 (5 ml) was kept at room temperature for 48 h. The work-up gave 17a (0.030 g, 75%). The reaction with EtAlCl_2 gave identical results.

Reaction of 15c with TMSOTf . The reaction of 15c (0.170 g, 0.349 mmol) with TMSOTf (0.155 g, 0.697 mmol) in CH_2Cl_2 (4 ml) at 0 °C for 2 h and then at room temperature for 46 h gave the product 22¹⁶ in 75% yield.

Reaction of 15d with TiCl_4 . The reaction of 15d (0.100 g, 0.13 mmol) with TiCl_4 (0.07 ml, 0.63 mmol) at 0 °C for 5 min gave 17a (0.029 g, 63%).

Reaction of *threo*-15e with TiCl_4 . The reaction of *threo*-15e (0.090 g, 0.27 mmol) and TiCl_4 (0.059 g, 0.54 mmol) in CH_2Cl_2 (6 ml) at -78 °C for 5 min afforded (*E*)-17e (0.035 g, 84%). MS m/z 152 (M^+), 109, 95 (base), 81, 67. IR 2939, 2860, 1708, 1446, 1151, 788 cm^{-1} . $^1\text{H NMR}$ $\delta=1.15$ (d, $J=7.2$ Hz, 3H), 1.68 (d, $J=6.8$ Hz, 3H), 1.40—2.62 (m, 8H), 3.05 (q, $J=6.9$ Hz, 1H), 5.48 (q, $J=6.9$ Hz, 1H). $^{13}\text{C NMR}$ $\delta=13.11$, 15.26, 26.86, 28.78, 29.30, 42.12, 55.32, 122.83, 139.50, 214.86. HRMS. Found: m/z 152.1162. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}$: (M), 152.1201.

Reaction of *erythro*-15e with TiCl_4 . The reaction of *erythro*-15e (0.042 g, 0.126 mmol) and TiCl_4 (0.046 g, 0.252 mmol) in CH_2Cl_2 (5 ml) at 0 °C for 5 min afforded (*Z*)-17e (0.016 g, 83 %). MS m/z 152 (M^+), 109, 95 (base), 81, 67. IR 2930, 2860, 1711, 1660, 1446, 1158 cm^{-1} . $^1\text{H NMR}$ (400 MHz) $\delta=1.09$ (d, $J=7.0$ Hz, 3H), 1.67 (d, $J=7.0$ Hz, 3H), 1.35—1.65 (m, 2H), 1.59—1.73 (m, 2H), 1.75—1.98 (m, 2H), 2.21—2.37 (m, 2H), 3.42 (q, $J=6.8$ Hz, 1H), 5.51 (q, $J=6.8$ Hz, 1H). $^{13}\text{C NMR}$ $\delta=13.36$, 13.93, 26.69, 32.26, 34.55, 42.66, 48.64, 123.49, 139.61, 214.43. HRMS. Found: m/z 152.1184. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}$: (M), 152.1201.

Reaction of 15f with TiCl_4 . The reaction of 15f (90:10 diastereomer mixture, 0.104 g, 0.30 mmol) and TiCl_4 (0.080 ml, 0.69 mmol) in CH_2Cl_2 (5 ml) at -78 °C for 30 min afforded (*E*)-17e (0.042 g, 92%).

Reaction of 15g with TiCl_4 . The reaction of 15g (89:11 diastereomer mixture, 0.300 g, 0.73 mmol) and TiCl_4 (0.16 ml, 1.47 mmol) in CH_2Cl_2 (6 ml) at -78 °C for 10 min afforded (*E*)-17g (0.063 g, 40 %). MS m/z 214 (M^+ , base), 199, 171, 157, 143, 129, 118, 115, 95, 91. IR 2932, 2861, 1704, 1644, 1446, 699 cm^{-1} . $^1\text{H NMR}$ $\delta=0.61$ —2.72 (m, 8H), 1.24 (d, $J=6.6$ Hz, 3H), 3.19 (q, $J=6.6$ Hz, 1H), 6.42 (br.s, 1H), 7.27 (br.s, 1H). $^{13}\text{C NMR}$ $\delta=15.53$, 26.14, 29.97, 30.20, 42.59, 55.69, 126.49, 128.13, 128.22, 128.26, 128.37, 128.59, 137.33, 141.82, 212.98. HRMS. Found: m/z 214.1335. Calcd for $\text{C}_{15}\text{H}_{18}\text{O}$: (M), 214.1357.

Reaction of *erythro*- and *threo*-15e with EtAlCl_2 . The reaction of *threo*-15e (containing 5% of *erythro*-isomer, 0.200 g, 0.60 mmol) and EtAlCl_2 (0.93 M-hexane, 1.94 ml, 1.80 mmol) at room temperature for 5 min gave 25e (0.080 g, 79%). MS m/z 170 (M^+), 152, 137, 125 (base), 79, 67, 55. IR 3416, 2931, 2859, 1449, 1375, 1094, 1055, 1005, 982, 904, 787 cm^{-1} . $^1\text{H NMR}$ $\delta=0.93$ (d, $J=6.2$ Hz, 3H), 1.10—2.90 (m, 10H), 1.57 (d, $J=6.4$ Hz, 3H), 3.91 (q, $J=6.2$ Hz, 1H), 5.52 (q, $J=6.4$ Hz, 1H). $^{13}\text{C NMR}$ $\delta=[12.40^*$, 12.75], [15.22, 17.03*], [22.67, 23.36*], [25.65, 26.00*], [26.84, 27.02*], [36.33, 37.63*], [67.14*], [67.71], [76.58, 77.00*], [114.90*], [117.06], [141.32, 140.86*], (90:10). HRMS. Found: m/z 152.1190. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}$: (M-H₂O), 152.1201. The reaction of *erythro*-15e gave almost identical results.

Reaction of 15f with EtAlCl_2 . The reaction of 15f (90:10 diastereomer mixture, 0.255 g, 0.74 mmol) and EtAlCl_2 (0.93 M-hexane, 2.66 ml, 2.48 mmol) at room temperature for 30 min gave 25f (0.067 g, 54 %). MS m/z 184 (M^+), 152, 137, 125 (base), 79, 67. IR 3479, 2932, 2860, 1447, 1373, 1316, 1134, 1097, 1087, 985, 788 cm^{-1} . $^1\text{H NMR}$ $\delta=1.10$ —2.82 (m, 8H), 1.18 (d, $J=6.2$ Hz, 3H), 1.69 (d, $J=7.0$ Hz, 3H), 2.45 (br.s, 1H), 3.29 (s, 3H), 3.59 (q, $J=6.2$ Hz, 1H), 5.43 (q, $J=7.0$ Hz, 1H). $^{13}\text{C NMR}$ $\delta=12.84$, 13.03, 22.54, 25.81, 27.09, 36.26, 57.77, 76.18, 78.10, 115.23, 141.74. HRMS. Found: m/z 184.1507. Calcd for $\text{C}_{11}\text{H}_{20}\text{O}_2$: (M), 184.1463.

Reaction of 15g with EtAlCl_2 . The reaction of 15g (89:11 diastereomer mixture, 0.170 g, 0.42 mmol) and EtAlCl_2 (0.93 M-hexane, 0.89 ml, 0.83 mmol) at 0 °C for 10 min gave 25g (0.049 g, 47%) as a mixture of 60:40 diastereomer mixture. The minor component was isolated in pure state. The data for major component was deduced from those of the mixture. For minor component: MS (20 eV) m/z 246 (M^+), 228, 214, 213, 125 (base), 121. IR 3023, 2952, 2928, 2858, 1448, 1334, 1089, 1068, 990, 695 cm^{-1} .

$^1\text{H NMR}$ δ =1.20–2.87 (m, 9H), 1.31 (d, J =6.6 Hz, 3H), 3.15 (s, 3H), 4.23 (s, 1H), 5.05 (q, J =6.6 Hz, 1H), 7.00 (br.s, 5H). $^{13}\text{C NMR}$ δ =12.29, 23.53, 26.27, 26.87, 37.10, 57.44, 77.00, 83.64, 117.32, 127.18, 127.29, 128.02, 137.24, 138.49. For major component: $^1\text{H NMR}$ δ =1.20–2.87 (m, 9H), 1.68 (d, J =6.6 Hz, 3H), 3.05 (s, 3H), 4.18 (s, 1H), 5.35 (q, J =6.6 Hz, 1H), 7.00 (br.s, 5H).

cis-1,2-Dimethylspiro[4.2]octan-4-one (18). To a solution of *threo*-**15e** (0.070 g, 0.21 mmol) in hexane (6 ml) were added triethylamine (0.12 ml, 0.54 mmol) and mesyl chloride (0.08 ml, 0.54 mmol) at 0 °C. After being stirred for 10 min, the solution was stirred at room temperature for another 20 min. It was quenched with sat. NaHCO_3 aq. and the product was purified on a silica-gel column (hexane:AcOEt=15:1) to afford product (0.012 g, 36%). MS m/z 152 (M^+), 137 (base), 123, 109, 95, 81, 79, 67. IR 2932, 2866, 1686, 1456, 1292, 1182, 1141, 1081, 787 cm^{-1} . $^1\text{H NMR}$ (400 MHz) δ =0.93 (m, 6H), 1.47–1.89 (m, 8H), 2.34 (t, J =6.9 Hz, 2H). $^{13}\text{C NMR}$ δ =7.21, 22.45, 23.57, 25.64, 34.56, 39.73, 212.37. HRMS. Found: m/z 152.1208. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}$: (M), 152.1201.

trans-1,2-Dimethylspiro[4.2]octan-4-one (19). To a solution of *erythro*-**15e** (0.260 g, 0.78 mmol) in hexane (16 ml) were added triethylamine (0.44 ml, 3.13 mmol) and mesyl chloride (0.31 ml, 3.13 mmol) at 0 °C. After being stirred for 10 min, the solution was stirred at room temperature for another 20 min, and quenched with sat. NaHCO_3 aq. The product was purified on a silica-gel column (hexane:AcOEt=15:1) to afford product (0.043 g, 37%). MS m/z 152 (M^+), 137 (base), 123, 109, 95, 81, 79, 67. IR 2931, 2868, 1690, 1448, 1287, 1130, 1076, 962 cm^{-1} . $^1\text{H NMR}$ (400 MHz) δ =0.71 (quint, J =5.9 Hz, 1H), 0.89 (d, J =5.9 Hz, 3H), 0.98 (d, J =6.2 Hz, 3H), 1.36–2.07 (m, 8H), 2.46 (m, 1H). $^{13}\text{C NMR}$ δ =12.34, 12.39, 23.14, 24.11, 24.84, 30.46, 34.08, 38.24, 42.15, 209.54. HRMS. Found: m/z 152.1161. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}$: (M), 152.1201.

Reaction of *threo*-15e with EtAlCl_2 in the Presence of Benzaldehyde. The EtAlCl_2 -induced reaction of *threo*-**15e** (0.21 mmol) was carried out in the presence of benzaldehyde (0.63 mmol) under otherwise the same conditions as described above. The crossed product **27** was isolated in 76% yield, as well as 12% of **25e**. For **27**: MS (20 eV) m/z 214 ($\text{M}^+ - 18$), 199, 196, 185, 181, 125 (base), 105. IR 3427, 3352, 3019, 2923, 2858, 1451, 1216, 1042, 756 cm^{-1} . $^1\text{H NMR}$ δ =1.39 (d, J =6.6 Hz, 3H), 1.06–2.73 (m, 10H), 4.60–5.13 (m, 2H), 7.07 (br.s, 5H). $^{13}\text{C NMR}$ δ =12.37, 23.36, 26.47, 26.89, 37.36, 74.20, 77.53, 116.99, 127.11, 127.42, 127.86, 127.91, 128.04, 139.47, 140.24. HRMS. Found: m/z 214.1342. Calcd for $\text{C}_{15}\text{H}_{18}\text{O}$: (M– H_2O), 214.1358.

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References

- 1) T. Sato, *Synthesis*, **1990**, 259.
- 2) T. Sato, M. Hayashi, and T. Hayata, *Tetrahedron*, **48**, 4099 (1992).
- 3) J. Fujiwara, T. Yamamoto, and T. Sato, *Chem. Lett.*, **1992**, 1775.
- 4) J. Fujiwara and T. Sato, *Bull. Chem. Soc. Jpn.*, **66**, 1258 (1993).
- 5) Except **9a** and **9b**, the structures of products were tentatively assigned only by GC-MS analyses (see Experimental), because the reactions, albeit clean, gave two products which were inseparable by column chromatography. Each sets of the products showed very similar mass spectra, typically M-15 and M-28, and we assigned the structure **9** for compounds having M-15 peak stronger than M-28 peak.
- 6) T. Sato, M. Watanabe, T. Watanabe, Y. Onoda, and E. Murayama, *J. Org. Chem.*, **53**, 1894 (1988).
- 7) W. C. Still, *J. Am. Chem. Soc.*, **99**, 4836, (1977); M. Ochiai, T. Ukita, Y. Nagano, and E. Fujita, *J. Chem. Soc., Chem. Commun.*, **1985**, 637.
- 8) J. Fujiwara, S. Nagatsuka, and T. Sato, "40th Symposium on Organometallic Chemistry," Sapporo, Japan, October 1993, Abstr., B 118.
- 9) I. Fleming and C. J. Urch, *J. Organomet. Chem.*, **285**, 173 (1985).
- 10) A six-membered cyclic transition state with synperiplanar conformation has been proposed for the bond cleavage of γ -silyl alcohols: T. Fujiwara, A. Suda, and T. Takeda, *Chem. Lett.*, **1992**, 1631.
- 11) T. Sato, T. Kikuchi, H. Tsujita, A. Kaetsu, N. Sootome, K. Nishida, K. Tachibana, and E. Murayama, *Tetrahedron*, **47**, 3281 (1991).
- 12) J. Fujiwara and T. Sato, *J. Organomet. Chem.*, **473**, 63 (1994).
- 13) J. T. A. Reuvers and A. De Groot, *Synthesis*, **1982**, 1105.
- 14) J. T. Sharp and R. H. Findlay, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 102.
- 15) F. A. Van-Catledge, D. W. Boerth, and J. Kao, *J. Org. Chem.*, **47**, 4096 (1982).
- 16) L. Blanco, P. Amice, and J.-M. Conia, *Synthesis*, **1981**, 289.
- 17) The figures in brackets are chemical shifts of the same carbon in a set of diastereomers, with the major signal marked with an asterisk. The figures in the parentheses refer to the average intensity ratios of the pair signals.