Articles

Intramolecular Carbostannation Reaction of Active Methine Compounds with an Unactivated C−C π-Bond Mediated by $SnCl_4$−Et_3N

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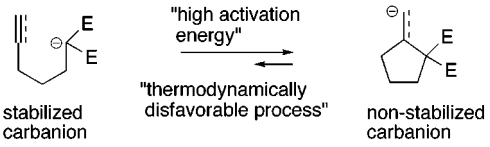
Received May 22, 2000

In the presence of $SnCl_4$ and Et_3N, intramolecular carbostannation reaction of various active methine compounds having an unactivated alkenyl, alkynyl, or allenyl group proceeds in good yields with complete regioselectivity. The subsequent reaction of the resulting Sn intermediates with some electrophiles provides functionalized cyclopentane and cyclohexane derivatives.

Introduction

It has been well documented that intramolecular carbometalation reaction of nonstabilized organometallic carbanions having an unactivated C−C π-bond proceeds smoothly,[1] while the reaction of strongly stabilized carbanions such as metal enolates derived from active methine compounds should be difficult to achieve[2] due to higher activation energy than that in the reaction of a nonstabilized carbanion and an endothermic process involving the conversion of a stabilized enolate anion to a nonstabilized sp^3 or sp^2 carbanion (Scheme 1).[3] Especially, a limited number of examples have been reported on the carbometalation of active methine enolates having a less reactive unactivated alkenyl group in place of an alkyny or an allenyl group.[4] One such reaction, the Pd-catalyzed carbocyclization of the enolate of alkenylated active methines, has been reported by Balme et al.[4a,b]

Scheme 1



In the course of our work in relation to iodocarbocyclization reaction of active methines having an unactivated C−C π-bond,[5] we unexpectedly found that intramolecular carbotitanation reaction of various active methines having an unactivated alkynyl group proceeds in good yields in the presence of $TiCl_4$ and Et_3N (Scheme 2).[6] In this reaction, addition of a trichlorotitanium enolate to the alkyne bond proceeded in a completely *cis*-selective manner, and the subsequent reaction with I_2 gave *Z*-iodomethylencyclopentane, which is in remarkable contrast to the *E*-stereochemistry of the iodocarbocyclization product.[7] The powerful activation of the alkyne bond by a strong Lewis acid such as $TiCl_4$ and the formation of a stabilized intermediate due to intramolecular coordination of an ester group to the Ti atom may be the driving force of the present carbocyclization reaction. However,

(1) (a) Knochel, P. In *Comprehensive Organic Synthesis*; Trost, B., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, pp 865−911. (b) Bailey, W. F.; Ovaska, T. V. *J. Am. Chem. Soc.* **1993**, *115*, 3080−3090, and references therein. (c) Marek, I.; Normant, J. F. In *Cross Coupling Reactions*; Diederich, D., Stang, P., Eds.; VCH: New York, 1998.

(2) Examples of intramolecular carbometalation reaction of enolates prepared from active methines with unactivated alkynyl or allenyl group. For alkyne, see: (a) Fournet, G.; Balme, G.; Gore, J. *Tetrahedron* **1991**, *47*, 6293−6304. (b) Monteiro, N.; Gore, J.; Balme, G. *Tetrahedron* **1992**, *48*, 10103−10114. (c) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F. *Synlett* **1993**, 65−68. (d) Cruciani, P.; Aubert, C.; Malacria, M. *Tetrahedron Lett.* **1994**, *35*, 6677−6680. (e) McDonald, F. E.; Olson, T. C. *Tetrahedron Lett.* **1997**, *38*, 7691−7692. (f) Tsukada, N.; Yamamoto, Y. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2477−2479. (g) Kadota, I.; Shibuya, A.; Gyoung, Y.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 10262−10263. (h) Bouyssi, D.; Monterio, N.; Balme, G. *Tetrahedron Lett.* **1999**, *40*, 1297−1300, and references therein. For allene, see: (i) Besson, L.; Bazin, J.; Gore, J.; Cazes, B. *Tetrahedron Lett.* **1994**, *35*, 2881−2884. (j) Yamamoto, Y. Al-Masum, M.; Asao, N. *J. Am. Chem. Soc.* **1994**, *116*, 6019−6020. (k) Trost, B. M.; Gerusz, V. J. *J. Am. Chem. Soc.* **1995**, *117*, 5156−5157. (l) Meguro, M.; Kamijo, S.; Yamamoto, Y. *Tetrahedron Lett.* **1996**, *37*, 7453−7456, and references therein.

(3) (a) Kubota, K.; Nakamura, E. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2491−2493. (b) Nakamura, E.; Kubota, K. *Tetrahedron Lett.* **1997**, *38*, 7099−7102.

(4) (a) Fournet, G.; Balme, G.; Gore, J. *Tetrahedron* **1990**, *46*, 7763−7774. (b) Balme, G.; Bouyssi, D.; Faure, R.; Gore, J. Hemelryck, B. V. *Tetrahedron* **1992**, *48*, 3891−3902. (c) Lorthiois, E.; Marek, I.; Normant, J. F. *J. Org. Chem.* **1998**, *63*, 2442−2450.

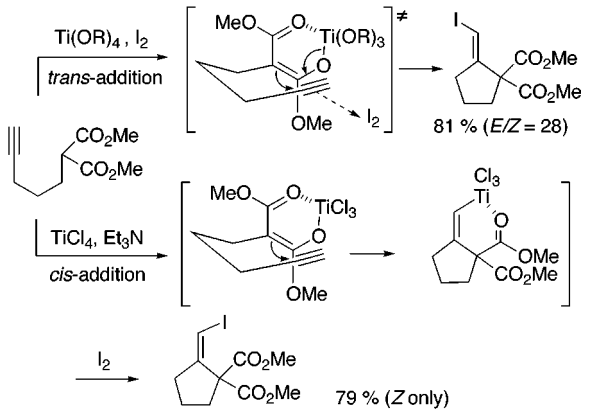
(5) Recent reviews in relation to iodocarbocyclization reaction. (a) Kitagawa, O.; Inoue, T.; Taguchi, T. *Rev. Heteroat. Chem.* **1996**, *15*, 243−262. (b) Kitagawa, O.; Taguchi, T. *Synlett* **1999**, 1191−1199. See also: (c) Inoue, T.; Kitagawa, O.; Saito, A.; Taguchi, T. *J. Org. Chem.* **1997**, *62*, 7384−7389, and references therein.

(6) (a) Kitagawa, O.; Suzuki, T.; Inoue, T.; Taguchi, T. *Tetrahedron Lett.* **1998**, *39*, 7357−7360. (b) Kitagawa, O.; Suzki, T.; Inoue, T.; Watanabe, Y.; Taguchi, T. *J. Org. Chem.* **1998**, *63*, 9470−9475. In relation to this $TiCl_4$-mediated reaction, we also found *n*-BuLi-catalyzed hydrocarbocyclization of various 4-alkynylated active methines which proceeds through a proton-transfer mechanism. (c) Kitagawa, O.; Suzuki, T.; Fujiwara, H.; Fujita, M.; Taguchi, T. *Tetrahedron Lett.* **1999**, *40*, 4585−4588.

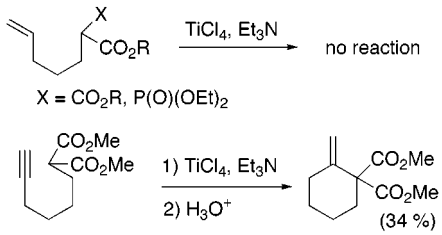
(7) Kitagawa, O.; Inoue, T.; Hirano, K.; Taguchi, T. *J. Org. Chem.* **1993**, *58*, 3106−3112.

10.1021/jo000784z CCC: $19.00
Published on Web 09/21/2000

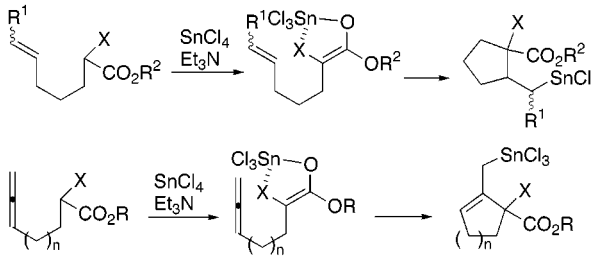
Scheme 2



Scheme 3



Scheme 4



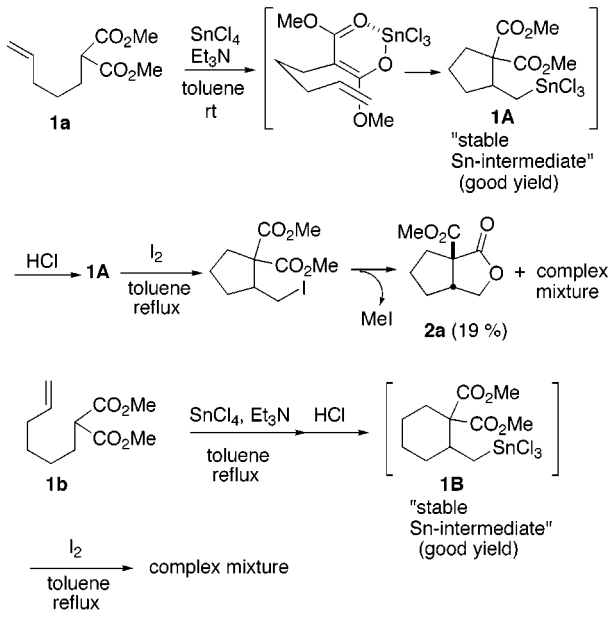
substrates applicable to the present reaction are limited to only 4-alkynylated active methines, and the reaction could not be applied to alkenylated derivatives and six-membered ring forming reaction using 5-hexynylmalonate (Scheme 3). In particular, in the reaction of 4-pentenylated active methines, no cyclized products were detected.

In this paper, we report the result of intramolecular carbometalation reaction mediated by $SnCl_4$ and Et_3N, which is applicable to alkenylated active methines and 5-hexynylmalonate (Scheme 4). Furthermore, the $SnCl_4$-mediated reaction was found to be applicable to various active methines having an allenyl group (Scheme 4). This reaction proceeded with complete regioselectivity through an intramolecular addition of trichlorotin enolates of active methine compounds to the unactivated C−C π-bond, and the subsequent reaction of the resulting Sn intermediate with some electrophiles gave functionalized cyclopentane or cyclohexane derivatives. The details of this reaction and the structure of the Sn intermediate are also described.[8]

Results and Discussion

Intramolecular Carbostannation Reaction of Alkenylated Active Methines and 5-Hexynylmalonate. In the presence of Lewis acids and Et_3N, intramolecular carbometalation reaction of 4-pentenylmalonate **1a** was

Scheme 5



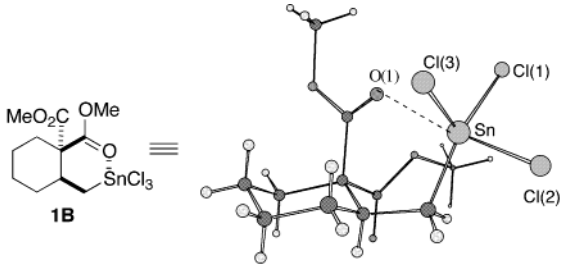
examined. Although various Lewis acids such as $TiCl_4$, $InCl_3$, $GaCl_3$, $AlCl_3$, $ZrCl_4$, SnF_4, $Sn(OTf)_2$, $La(OTf)_3$, $MgBr_2$, and $ZnCl_2$ were examined, formation of the cyclized product was not observed and the starting material **1a** was quantitatively recovered.

We found that the use of $SnCl_4$ as Lewis acid gives a good result.[9] That is, when **1a** was treated with $SnCl_4$ (1.8 equiv) and Et_3N (1 equiv) in toluene, carbostannation reaction smoothly proceeded at room temperature to give cyclopentylmethylstannan **1A** (Scheme 5).[10] The Sn intermediate **1A**, which was obtained after extractive workup (Et_2O−2% HCl) from the reaction mixture, was confirmed to be almost pure from the ^1H and ^{13}C NMR spectra, while the exact yield of Sn intermediate **1A** could not be determined because of the difficulty of further purification. For cleavage of the C−Sn bond in **1A**, treatment with acid (CF_3COOH, 10% HCl, 11 N H_2SO_4), peroxide (MCPBA, 30% H_2O_2, oxone), Pd catalyst [Pd(0)−PhI, Pd(0)−HCOOH], or halogenating reagents (Br_2, NBS, NIS) was attempted; however, all attempts were unsuccessful. Treatment of **1A** with these reagents resulted in the formation of a complex mixture (MCPBA), recovery of **1A** (CF_3COOH, 10% HCl, halogenating reagents, Pd catalyst), or the regeneration of pentenylmalonate **1a** (11 N H_2SO_4, 30% H_2O_2, oxone). When **1A** was treated with I_2 under toluene reflux conditions, bicyclic lactone **2a**[5c] was obtained in poor yield (19%) via iodination and subsequent lactonization (Scheme 5).

(8) Preliminary communication of this work. Kitagawa, O.; Suzuki, T.; Fujiwara, H.; Taguchi, T. *Tetrahedron Lett.* **1999**, *40*, 2549−2552.

(9) Intermolecular carbostannation reaction of silyl enol ether to alkynyl stannane which proceeds in the presence of $SnCl_4$ and Bu_3N has been reported by Yamaguchi et al. (a) Yamaguchi, M.; Hayashi, A.; Hirama, M. *J. Am. Chem. Soc.* **1993**, *115*, 3362−3363. (b) Hayashi, A.; Yamaguchi, M.; Hirama, M. *Synlett* **1995**, 51−53. (c) Yamaguchi, M.; Hayashi, A.; Hirama, M. *J. Synth. Chem. Org. Jpn.* **1996**, *54*, 267−279, and references therein.

(10) For a complete consumption of starting material **1a**, the use of 1.8 equiv of $SnCl_4$ was required, while the carbostannation reaction in the presence of 1 equiv of $SnCl_4$ and Et_3N gave the mixture of **1a** and Sn intermediate **1A** in a ratio of 3/2. In addition, we also examined the intermolecular reaction with dimethyl benzylmalonate and 1-alkene or 1-alkyne. However, in these cases, the formation of carbostannation product could not be observed.



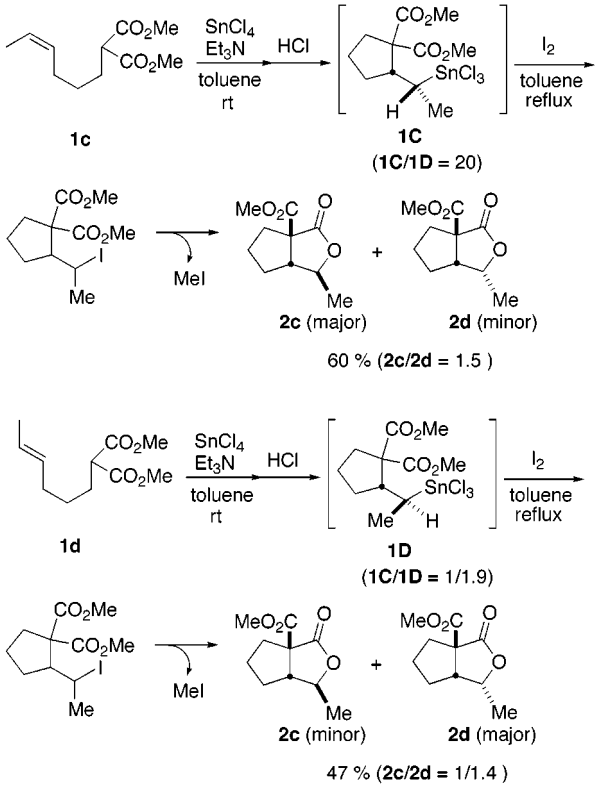
O(1)-Sn 2.400 Å, Cl(1)-Sn 2.269 Å, Cl(2)-Sn 2.365 Å, Cl(3)-Sn 2.299 Å
< O(1)-Sn-Cl(2) = 176.6 °

Figure 1. X-ray crystal structure of Sn intermediate 1B.

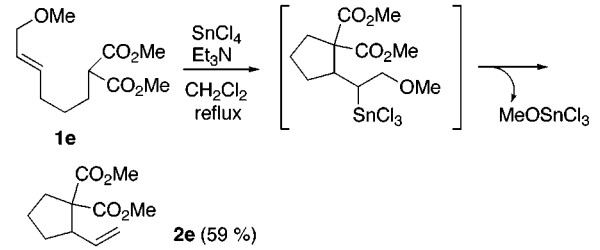
Although higher temperature (toluene reflux) was required in comparison with that in the reaction of **1a**, carbostannation of 5-hexenylmalonate **1b** also proceeded to give cyclohexylmethylstannan **1B** (Scheme 5). Similar to the case of **1A**, in the ^{1}H and ^{13}C NMR spectra of **1B** obtained after workup, signals corresponding to starting material **1b** and impurities could be hardly detected. The reaction of Sn intermediate **1B** with I_2 under toluene reflux conditions gave a complex mixture without the formation of any bicyclic lactone. At room temperature, both Sn intermediates **1A** and **1B** were unchanged by treating with I_2. The extremely low reactivity of the C−Sn bond in **1A** and **1B** may be due to the formation of a pentacoordinate Sn intermediate which was observed in the crystalline state by X-ray analysis of **1B** (Figure 1).[11] The X-ray crystal structure indicates an intramolecular coordination of a *cis*-ester group to the Sn atom, and the formation of this pentacoordinate Sn intermediate may enhance the stabilization of the C−Sn bond.[12] In solution state, the pentacoordinated structure should also be supported by the considerable downfield shift of an ester carbonyl carbon in the ^{13}C NMR of **1A** and **1B** in $CDCl_3$, (**1A** *175.8* and 170.7 ppm, **1B** *175.1* and 171.0 ppm).[13] These results possibly indicate that the formation of the stable Sn intermediate is the driving force of the present reaction.

In contrast with the low reactivity of the primary alkyl stannane derivative **1A** and **1B**, the secondary alkyl stannane derivative showed higher reactivity in the iodination reaction. The intramolecular carbostannation reaction of (*Z*)-4-hexenylmalonate **1c** proceeded under the above conditions to give Sn intermediate **1C**, and the following reaction of **1C** with I_2 gave a diastereomer mixture of known bicyclic lactones **2c** and **2d**[7] in 60% yield (Scheme 6). With (*E*)-4-hexenyl derivative **1d**, **2c** and **2d** were obtained in 47% yield (Scheme 6). Although the diastereoselectivities observed in the products were low, **1c** preferentially gave lactone **2c**, having a β-Me group (**2c**/**2d** = 1.5), and **1d** gave α-Me isomer **2d** as a major product (**2c**/**2d** = 1/1.4). Since the carbostannation reaction of **1c** gave the Sn intermediate **1C** with high diastereoselectivity (**1C**/**1D** = 20), the poor diastereoselectivity in the product should be due to the low diastereoselectivity at the iodination or lactonization step. On the other hand, in the carbostannation reaction of **1d**, low diasteroselectivity was observed (**1C**/**1D** = 1/1.9); thus, in this case, the low selectivity may reflect the poor diastereoselectivity of the lactone product. On the basis of the result of carbostannation of alkynylated malonate (see Scheme 9), the carbostannation reaction of **1c** and **1d** would be suggested to proceed in a stereospecific *cis*-addition manner, and this is in remarkable contrast to carbopalladation reaction of alkenylated malonate, which proceeds in a *trans*-addition manner.[4a,b]

Scheme 6



Scheme 7



It was expected that on using 6-methoxy-4-hexenylmalonate **1e** as a substrate, removal of the Sn moeity from the carbostannation product would easily occur through β-elimination of Sn alkoxide. Indeed, the reaction of **1e** gave vinylcyclopentane derivative **2e** in 59% yield (Scheme 7).

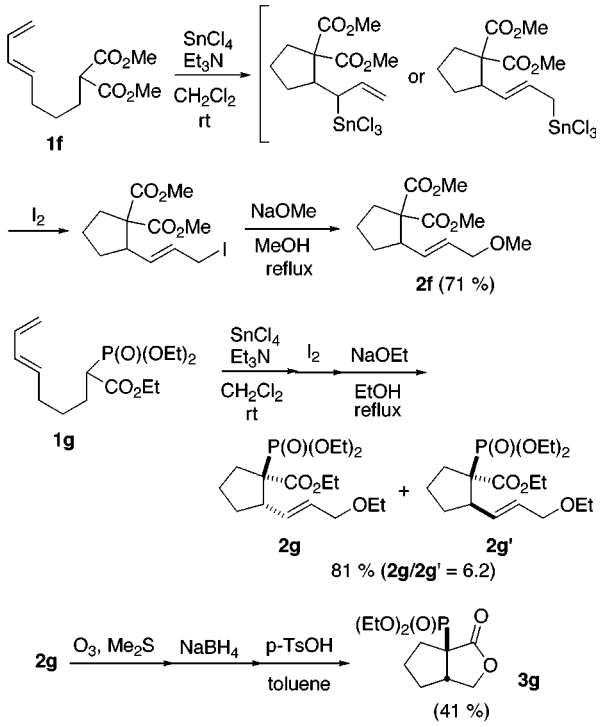
Good results were obtained with dienyl derivatives (Scheme 8). The carbostannation reaction of (4*E*)-4,6-heptadienylmalonate **1f** and -phosphonoacetate **1g** re-

(11) In addition to lower reactivity of the C−Sn bond, a ring-opening pathway which generates stabilized malonate anion is also another problem.

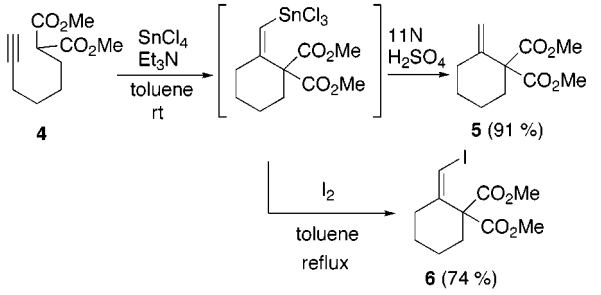
(12) The bond length (2.400 Å) of O(1)−Sn of **1B** (Figure 1) almost coincides with that (2.405 Å) of pentacoorinate stannane [$Cl_3Sn(CH_2)_3$-COOR], which has been previously reported by Howie et al. (a) Howie, R. A.; Paterson, E. S.; Wardell, J. L. *J. Organomet. Chem*. **1983**, *259*, 71−78. See also: (b) Howie, R. A.; Paterson, E. S.; Wardell, J. L.; Burley, J. W. *J. Organomet. Chem*. **1986**, *304*, 301−308. (c) Hayashi, A.; Yamaguchi, M.; Hirama, M.; Kabuto, C.; Ueno, M. *Chem Lett*. **1993**, 1881−1884.

(13) In the ^{13}C NMR of 1,1-bis(methoxycarbonyl)-2-iodomethylcyclopentane (ref 7), **2e** (Scheme 7), and **2f** (Scheme 8), slight differences in the chemical shifts of two carbonyl carbons were observed (iodomethylcyclopentane, 171.7 and 170.7 ppm; **2e**, 172.6 and 171.4 ppm; **2f**, 172.5 and 171.1 ppm).

Scheme 8



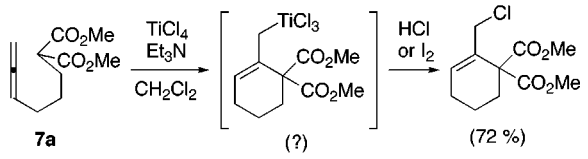
Scheme 9



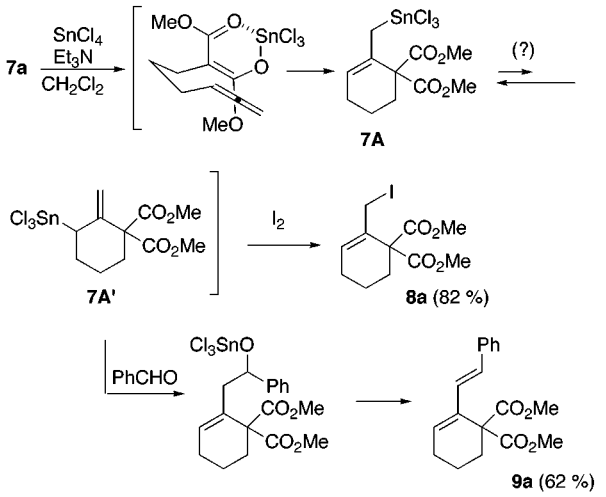
sulted in the formation of more reactive allyl stananne intermediates[14] than alkyl stannane, and the following iodination of the allyl stanannes at 0 °C proceeded in a regioselective manner to give allyl iodides in good yields.[15] Due to the instability of the allyl iodides thus formed, these were converted to methyl ether **2f** and ethyl ether **2g**, **2g′** without further purification (**2f** overall 71% from **1f**; **2g** and **2g′** overall 81% from **1g**). In these reactions, no *Z*-isomer and regioisomer were detected. In the reaction of phosphonoacetate **1g**, *trans*-isomer **2g** and *cis*-isomer **2g′** were obtained in a ratio of 6.2/1, and the stereochemistry of major isomer **2g** was determined by converting to known bicyclic lactone **3g**.[6b]

As shown in Scheme 3, intramolecular carbotitanation reaction of 5-hexynylmalonate **4** gave methylenecyclohexane **5** in a low yield (34%). On the other hand, intramolecular carbostannation reaction of **4** smoothly proceeded at room temperature to lead to the vinyl stannane intermediate, which affords methylenecyclohexane **5** in excellent yield (91%) by quenching with 11 N H_2SO_4 (Scheme 9). The carbostannation to the alkyne bond proceeded in a completely *cis*-addition manner, and the following iodination of the Sn intermediate gave *Z*-vinyl iodide **6** as a single isomer in 74% yield.[16]

Scheme 10



Scheme 11



Intramolecular Carbostannation Reaction of Allenylated Active Methines. It is well known that allenes have much higher reactivity than alkenes in the reaction with carbon nucleophiles. Indeed, Pd-catalyzed carbocyclization reaction of allenylated active methines, which proceeds without the use of a basic reagent, has been reported by several groups.[2j–l] In these reactions, the active methine enolate preferentially attacks the internal carbon of allene and not the central carbon, because the reaction proceeds via the formation of a π-allyl complex.[2i–l]

We found that carbocyclization of allenylated active methines can be achieved by the use of a Lewis acid such as $TiCl_4$ and $SnCl_4$ (Schemes 10 and 11). Contrary to the Pd-catalyzed reaction, in these Lewis acid-mediated reactions, the attack of enolate occurs on the central carbon with complete regioselectivity.[17] Although the reason is not clear, in $TiCl_4$-mediated reaction of 4,5-hexadienylmalonate **7a**, a chloromethylcyclohexene derivative was obtained in 72% yield even if the reaction was quenched by I_2 or 2% HCl (Scheme 10). Thus, the formation of an ally trichlortitanium intermediate and the subsequent reaction with some electrophiles could not be confirmed.

On the other hand, when **7a** was treated with $SnCl_4$ (1.8 equiv) and Et_3N (1.0 equiv) in CH_2Cl_2, the formation of carbostannation product **7A** was observed by ^1H and

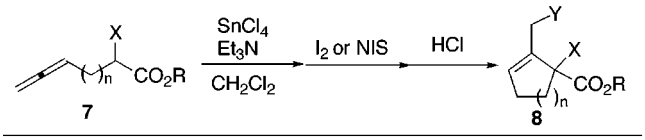
(14) For a review in relation to allylic metals. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207−2293, and references therein.

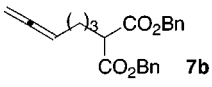
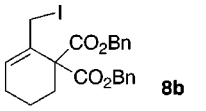
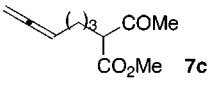
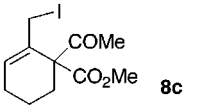
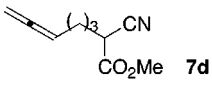
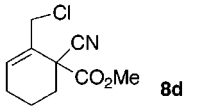
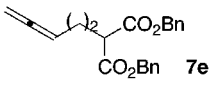
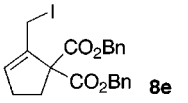
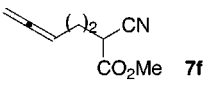
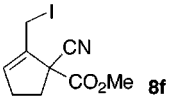
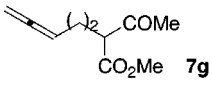
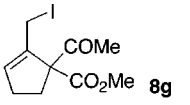
(15) The reaction of (4*E*)-4,6-heptadienylcyanoacetate and -acetoacetate was also examined. In the cases of these substrates, although the carbostannation reaction proceeded smoothly, the subsequent reaction of the resulting Sn intermediates with I_2 resulted in the formation of complex mixtures.

(16) The stereochemistry of *Z*-vinyl iodide **6** was determined on the basis of the NOE experiment.

(17) In carbopalladation reaction of allenes with a hard carbon nucleophile, preferential C−C bond formation at the central carbon has been observed. (a) Ma, S.; Negishi, E. *J. Am. Chem. Soc.* **1995**, *117*, 6345−6357. (b) Negishi, E.; Copéret, C.; Ma, S.; Liou, S.; Liu, F. *Chem. Rev.* **1996**, *96*, 365−393, and references therein.

Table 1. Intramolecular Carbostannation Reaction[a]



Entry	7	I_2 or NIS	8	Yield (%)[b]
1		I_2		84
2		I_2		61
3		NIS[c]		60[d]
4		I_2		96
5		I_2		62
6		I_2		79

[a] Carbostannation: 7 (1 mmol), $SnCl_4$ (1.8 mmol), Et_3N (1 mmol), CH_2Cl_2 (8 ml), rt, 1 h and then I_2 or NIS (2 mmol). [b] Isolated yields. [c] When I_2 was used as an electrophile, the corresponding iodide was obtained in 39% yield. [d] Allyl iodide was also obtained in 5% yield together with allyl chloride.

^{13}C NMR. The carbostannation reaction of **7a** proceeds in a regioselective manner (6-*exo* cyclization) to give cyclohexylmethyl stannane **7A** exclusively (Scheme 11). Similar to the Sn intermediate shown in Scheme 8, since **7A** is a reactive allylstannane intermediate,[14] iodination of **7A** easily proceeded at room temperature to give iodomethylcyclohexene derivative **8a** in good yield (82%). This iodination step should be finished within a few minutes at room temperature to prevent halogene exchange of the resulting allyl iodide **8a** by $SnCl_4$. Furthermore, C−C bond forming reaction with Sn intermediate **7A** is also possible; the reaction of **7A** with benzaldehyde gave diene **9a** in 62% yield via the addition to aldehyde and subsequent dehydration. In these reactions, the attack of I_2 and aldehyde to **7A** exclusively occurred at the *exo* carbon and not at the carbon on the cyclohexene ring. In the carbostannation reaction of **7a**, the formation of methylene cyclohexylstannan **7A′** could not be detected by NMR. However, the exclusive reaction with aldehyde at the *exo* carbon may indicate the existence of **7A′** based on the equilibrium with **7A**, because in general the reaction of allyl stannane with aldehyde proceeds via allylic rearrangement.[14]

The results of intramolecular carbostannation reaction and the following iodonolysis of various allenylated active methine compounds **7** are shown in Table 1.

Similar to dimethyl malonate derivative **7a**, the reaction of dibenzyl malonate **7b** also gave the 6-*exo*-cyclized products **8b** in good yield (84%) in the presence of $SnCl_4$ and Et_3N (entry 1). The reaction of not only malonate but also acetoacetate and cyanoacetate derivatives **7c** and **7d** proceeded smoothly to give products **8c** and **8d**, respectively (entries 2, 3). In the case of cyanoacetate **7d**, on using NIS as an electrophile, chloromethylcyclohexene **8d** was obtained as the major product in 60% yield through the subsequent halogene exchange of the resulting allyl iodide by $SnCl_4$, while the use of iodine resulted in a decrease in the product yield (entry 3). The reactions of **7b** and **7d** with $TiCl_4$ and Et_3N were also investigated; however, no cyclized products could be obtained. In the case of **7b**, a complex mixture due to the cleavage of the benzyl ester by $TiCl_4$ resulted, while in the case of **7d** cyclization reaction did not proceed, resulting in quantitative recovery of **7d**. Thus, the effect of $SnCl_4$ in these reactions should be noteworthy.

The $SnCl_4$-mediated reaction can also be applied to cyclopentene-forming reaction with 3,4-pentadienyl active methine compounds **7e, 7f**, and **7g**; in these reactions, 5-*exo*-cyclized products **8e**, **8f,** and **8g** were obtained in good yields, respectively (entries 4−6). In all reactions in Scheme 11 and Table 1, since the formation of other regioisomers was not observed, these reactions should proceed in a completely 5- or 6-*exo* cyclization mode with subsequent regioselective iodonolysis of the allyl stannane intermediates.

In conclusion, we have succeeded in the development of an intramolecular carbostannation reaction of various active methines having an unactivated C−C π-bond which proceeds with complete regioselectivity in the presence of $SnCl_4$ and Et_3N. The subsequent reaction of the resulting Sn intermediates with some electrophiles gave functionalized cyclopentane and cyclohexane derivatives. The present reaction should provide a new methodology for the synthesis of cyclopentane and cyclohexane derivatives.

Experimental Section

Melting points were uncorrected. ^1H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer. In ^1H and ^{13}C NMR spectra, chemical shifts were expressed in δ (ppm) downfield from $CHCl_3$ (7.26 ppm) and $CDCl_3$ (77.0 ppm), respectively. Mass spectra were recorded by electron impact or chemical ionization. Column chromatography was performed on silica gel (75−150 μm). Medium-pressure liquid chromatography (MPLC) was performed on a 30 × 4 cm i.d. prepacked column (silica gel, 50 μm) with a RI detector.

Starting Materials. Alkenylated malonates **1a**−**e**,[4a,7] 5-hexynylmalonate **4**,[2a,b] and allenylated active methines **7a**−**f**[18] were prepared according to reported procedures. Dienylated active methines **1f** and **1g** were prepared from (4*E*)-4,6-heptadienol[19] according to the following procedure (see also Supporting Information).

(4*E*)-Dimethyl 4,6-Heptadienylmalonate (1f). To a solution of (4*E*)-4,6-heptadienol[19] (1.12 g, 10.0 mmol) and Et_3N (2.1 mL, 15.0 mmol) in CH_2Cl_2 (30 mL) was added MsCl (0.93 mL, 12.0 mmol) at 0 °C. After being stirred for 30 min at 0 °C, the mixture was poured into water and extracted with Et_2O. The Et_2O extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 3) gave the mesylate. To a suspension of the NaH (60% assay, 600 mg, 15.0 mmol) in THF (40 mL) was added dimethyl malonate (2.3 mL, 20.0 mmol) under an argon atmosphere at 0 °C. After being stirred for 30

(18) Bates, R. W.; Rama-Devi, T.; Ko, H. *Tetrahedron* **1995**, *51*, 12939−12954.
(19) Clasby, M. C.; Craig, D.; Slawin, A. M. Z.; White, A. J. P.; Williams, D. J. *Tetrahedron* **1995**, *51*, 1509−1532.

min at room temperature, the above mesylate was added to the reaction mixture, and the mixture was refluxed for 11 h. The mixture was poured into 2% HCl and extracted with AcOEt. The AcOEt extracts were successively washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 50) gave **1f** (1.12 g, 50%). **1f**: colorless oil; IR (neat) 1739 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.30 (1H, td, J = 10.4, 16.8 Hz), 6.06 (1H, dd, J = 10.4, 15.1 Hz), 5.66 (1H, td, J = 7.1, 15.1 Hz), 5.10 (1H, d, J = 16.8 Hz), 4.97 (1H, d, J = 10.4 Hz), 3.75 (6H, s), 3.37 (1H, t, J = 7.6 Hz), 2.12 (2H, q, J = 7.1 Hz), 1.87−1.98 (2H, m), 1.37−1.49 (2H, m); ^{13}C NMR ($CDCl_3$) δ 169.8, 137.0, 134.0, 131.6, 115.1, 52.5, 51.5, 32.0, 28.3, 26.9; MS (*m*/*z*) 226 (M^+). Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.86; H, 7.84.

Dimethyl 2-Trichlorostannylmethylcyclopentane-1,1-dicarboxylate (1A). To a solution of 4-pentenylmalonate **1a** (100 mg, 0.5 mmol) in toluene (4 mL) was added Et_3N (0.07 mL, 0.5 mmol) and a 1 M CH_2Cl_2 solution of $SnCl_4$ (0.9 mL, 0.9 mmol) under argon atmosphere at room temperature. After being stirred for 8 h at room temperature, the mixture was poured into 2% HCl and extracted with Et_2O. The Et_2O extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness to give **1A**. **1A**: ^1H NMR ($CDCl_3$) δ 3.88 (3H, d, J = 1.0 Hz), 3.84 (3H, d, J = 1.0 Hz), 2.72 (1H, m), 2.47 (1H, dd, J = 3.4, 13.2 Hz), 2.44 (1H, m), 2.17 (1H, dd, J = 11.6, 13.2 Hz), 2.02−2.22 (2H, m), 1.96 (1H, m), 1.58−1.84 (2H, m); ^{13}C NMR ($CDCl_3$) δ 175.8, 170.7, 60.6, 54.7, 53.5, 44.8 (J_{C-Sn} = 73.0 Hz), 35.3 (J_{C-Sn} = 826, 866 Hz), 33.0, 32.4, 20.9 (J_{C-Sn} = 16.6 Hz).

Dimethyl 2-Trichlorostannylmethylcyclohexane-1,1-dicarboxylate (1B). Similar to the preparation of **1A**, a mixture of 5-hexenylmalonate **1b** (107 mg, 0.5 mmol), Et_3N (0.07 mL, 0.5 mmol), and a 1 M CH_2Cl_2 solution of $SnCl_4$ (0.9 mL, 0.9 mmol) in toluene (4 mL) was refluxed for 9 h. The mixture was poured into 2% HCl and extracted with Et_2O. The Et_2O extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness to give **1B**. **1B**: ^1H NMR ($CDCl_3$) δ 3.91 (3H, s), 3.82 (3H, s), 2.56 (1H, m), 2.42 (1H, m), 2.36 (1H, dd, J = 3.6, 13.9 Hz), 2.13 (1H, dd, J = 5.2, 13.9 Hz), 1.60−1.92 (5H, m), 1.41 (1H, m), 1.22 (1H, m); ^{13}C NMR ($CDCl_3$) δ 175.8, 171.0, 57.4 (J_{C-Sn} = 24.0 Hz), 54.7, 53.4, 41.5 (J_{C-Sn} = 68.2 Hz), 37.8 (J_{C-Sn} = 838.0, 875.0 Hz), 32.6, 30.9, 25.0, 22.1

(2*R,1′*R**)-Dimethyl 2-(1′-Trichlorostannylethyl)cyclopentane-1,1-dicarboxylate (1C).** To a solution of (*Z*)-4-hexenylmalonate **1c** (107 mg, 0.5 mmol) in toluene (4 mL) was added Et_3N (0.07 mL, 0.5 mmol) and a 1 M CH_2Cl_2 solution of $SnCl_4$ (0.9 mL, 0.9 mmol) under argon atmosphere at room temperature. After being stirred for 8 h at room temperature, the mixture was poured into 2% HCl and extracted with Et_2O. The Et_2O extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Sn intermediate was obtained as a diastereomer mixture (**1C**/**1D** = 20). **1C**: ^1H NMR ($CDCl_3$) δ 3.89 (3H, d, J = 1.2 Hz), 3.82 (3H, d, J = 1.2 Hz), 3.11 (1H, m), 2.70 (1H, m), 2.48 (1H, m), 2.20−2.40 (2H, m), 1.60−1.82 (3H, m), 1.60 (3H, d, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 176.3, 170.8, 61.5, 54.9, 53.5, 53.3, 47.6 (J_{C-Sn} = 842.2, 880 Hz), 35.4, 31.2 (J_{C-Sn} = 67.2 Hz), 22.6, 18.6 (J_{C-Sn} = 30.2 Hz).

(3α,3aα,6aα)-Dihydro-3-methyl-6a-carbomethoxycyclopent[*c*]furan-1(3*H*)-one (2c). To the above Sn intermediate **1C** in toluene (4 mL) was added I_2 (635 mg, 2.5 mmol) under argon atmosphere at room temperature, and the reaction mixture was refluxed for 10 h. The mixture was poured into 2% HCl and extracted with Et_2O. The Et_2O extracts were washed with aqueous $Na_2S_2O_3$ solution, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 50) gave a mixture (**1c**/**1d** = 1.5) of **2c** and **2d** (60 mg, 60% from **1c**). ^1H NMR data of **2c** and **2d** were identical with those reported in our previous report.[7]

(*E*)-Dimethyl 2-(3-methoxy-1-propenyl)cyclopentane-1,1-dicarboxylate (2f). To (4*E*)-dimethyl 4,6-heptadienylmalonate **1f** (226 mg, 1 mmol) in CH_2Cl_2 (8 mL) was added Et_3N (0.14 mL, 1 mmol) and a 1 M CH_2Cl_2 solution of $SnCl_4$ (1.8 mL, 1.8 mmol) under argon atmosphere at room temperature. After the mixture was stirred for 1.5 h at room temperature, I_2 (508 mg, 2 mmol) was added at 0 °C, and then the reaction mixture was stirred for 4 min at 0 °C. The mixture was poured into 2% HCl and extracted with Et_2O. The Et_2O extracts were washed with aqueous $Na_2S_2O_3$ solution, dried over $MgSO_4$, and evaporated to dryness. To a MeOH solution (8 mL) of residue thus obtained (ally iodide) was added NaOMe (65 mg, 1.2 mmol) under argon atmosphere at room temperature, and then the reaction mixture was refluxed for 3.5 h. The mixture was poured into 2% HCl and extracted with Et_2O. The Et_2O extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 20) gave **2f** (182 mg, 71%). **2f**: colorless oil; IR (neat) 1732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.68 (1H, dd, J = 6.5, 15.4 Hz), 5.61 (1H, td, J = 5.2, 15.4 Hz), 3.85 (2H, d, J = 5.2 Hz), 3.73 (3H, s), 3.65 (3H, s), 3.28 (3H, s), 3.25 (1H, m), 2.46 (1H, td, J = 8.0, 13.7 Hz), 2.09 (1H, ddd, J = 4.9, 8.6, 13.7 Hz), 1.79−2.02 (2H, m), 1.56−1.74 (2H, m); ^{13}C NMR ($CDCl_3$) δ 172.5, 171.1, 132.8, 127.9, 72.8, 64.2, 57.6, 52.5, 52.0, 48.7, 33.8, 30.9, 23.0; MS (*m*/*z*) 256 (M^+). Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.94; H, 7.87.

(*Z*)-Dimethyl 2-iodomethylenecyclohexane-1,1-dicarboxylate (6). Similar to the preparation of **2f**, after a mixture of dimethyl 5-hexynylmalonate **4** (106 mg, 0.5 mmol), Et_3N (0.07 mL, 0.5 mmol), and a 1 M CH_2Cl_2 solution of $SnCl_4$ (0.9 mL, 0.9 mmol) in toluene (4 mL) was stirred for 8 h at room temperature, I_2 (381 mg, 1.5 mmol) was added, and then the reaction mixture was refluxed for 11.5 h. The mixture was poured into 2% HCl and extracted with Et_2O. The Et_2O extracts were washed with aqueous $Na_2S_2O_3$ solution, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 20) gave **6** (126 mg, 74%). **6**: colorless oil; IR (neat) 1732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.40 (1H, s), 3.81 (6H, s), 2.35 (2H, t, J = 5.2 Hz), 2.24 (2H, t, J = 5.6 Hz), 1.48−1.64 (4H, m); ^{13}C NMR ($CDCl_3$) δ 169.7, 144.0, 73.3, 62.3, 52.9, 38.2, 34.3, 25.8, 22.3; MS (*m*/*z*) 338 (M^+). Anal. Calcd for $C_{11}H_{15}IO_4$: C, 39.07; H, 4.47. Found: C, 39.50; H, 4.63.

Typical Procedure of Carbostannation and Subsequent Iodination of Allenylated Active Methine. To a solution of dimethyl 4,5-pentadienylmalonate **7a** (212 mg, 1 mmol) in CH_2Cl_2 (8 mL) was added Et_3N (0.14 mL, 1 mmol) and a 1 M CH_2Cl_2 solution of $SnCl_4$ (1.8 mL, 1.8 mmol) under argon atmosphere at room temperature. After the mixture was stirred for 1 h, I_2 (508 mg, 2 mmol) was added, and then the reaction mixture was stirred for 1 min at room temperature. The mixture was poured into 2% HCl and extracted with Et_2O. The Et_2O extracts were washed with aqueous $Na_2S_2O_3$ solution, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 20) gave **8a** (277 mg, 82%).

Dimethyl 2-Iodomethyl-1-cyclohexene-3,3-dicarboxylate (8a). 8a: colorless oil; IR (neat) 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.38 (1H, t, J = 4.0 Hz), 4.17 (2H, s), 3.79 (6H, s), 2.24−2.28 (2H, m), 2.02−2.08 (2H, m), 1.52−1.60 (2H, m); ^{13}C NMR ($CDCl_3$) δ 170.9, 135.8, 131.5, 57.4, 53.0, 30.6, 25.5, 18.3, 7.3; MS (*m*/*z*) 339 (M^+ + 1). Anal. Calcd for $C_{11}H_{15}IO_4$: C, 39.07; H, 4.47. Found: C, 39.39; H, 4.70.

Dimethyl 2-(2′-Phenylethenyl)-1-cyclohexene-3,3-dicarboxylate (9a). After carbostannation reaction of **7a** (212 mg, 1 mmol) was carried out according to the above procedure, PhCHO (508 mg, 2 mmol) was added, and then the reaction mixture was stirred for 23 h at room temperature. Extractive workup (2% HCl and Et_2O) and purification of the residue by column chromatography (hexane/AcOEt = 30) gave **9a** (183 mg, 62%). **9a**: colorless solid; mp 110.5−112.0 °C; IR (KBr) 1731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35−7.39 (2H, m), 7.27−7.32 (2H, m), 7.20 (1H, m), 6.70 (1H, dd, J = 1.0, 16.2 Hz), 6.61 (1H, d, J = 16.2 Hz), 6.29 (1H, dt, J = 0.8, 4.1 Hz), 3.75 (6H, s), 2.23−2.31 (4H, m), 1.63−1.71 (2H, m); ^{13}C NMR ($CDCl_3$) δ 171.6, 137.5, 132.7, 129.9, 129.1, 128.4, 127.8, 127.1, 126.1, 58.0, 52.6, 31.2, 25.3, 18.7; MS (*m*/*z*) 330 (M^+). Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.83; H, 6.75.

Dimethyl Trichlorostannylmethyl-1-cyclohexene-3,3-dicarboxylate (7A). To a solution of dimethyl 4,5-pentadi-

enylmalonate **7a** (212 mg, 1 mmol) in CH_2Cl_2 (8 mL) was added Et_3N (0.14 mL, 1 mmol) and a 1 M CH_2Cl_2 solution of $SnCl_4$ (1.8 mL, 1.8 mmol) under argon atmosphere at room temperature. The reaction mixture was stirred for 1 h at room temperature. The mixture was poured into 2% HCl and extracted with Et_2O. The Et_2O extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness to give **7A**. **7A**: ^{1}H NMR ($CDCl_3$) δ 6.15 (1H, t, J = 4.0 Hz), 3.87 (6H, s), 3.09 [2H, s, (J_{Sn-H} = 120 Hz)], 2.16−2.27 (4H, m), 1.62−1.72 (2H, m); ^{13}C NMR ($CDCl_3$) δ 172.6 (J_{Sn-C} = 42 Hz), 134.5 (J_{Sn-C} = 145, 157 Hz), 125.3 (J_{Sn-C} = 130 Hz), 57.9, 54.3, 41.1 (J_{Sn-C} = 784, 819 Hz), 29.9, 25.0 (J_{Sn-C} = 41 Hz), 18.2.

Supporting Information Available: Characterization data and experimental procedures of starting material **1g**, products **2d, 2e, 2g**, **3g**, **5**, **8b**−**g**, and Sn intermediate **1D**, and X-ray crystal data of **1B**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO000784Z