Pergamon

Tetrahedron Letters 40 (1999) 2549–2552

TETRAHEDRON
LETTERS

Intramolecular Carbostannation Reaction of Active Methine Compounds Having an Allenyl Group Mediated by $SnCl_4$-Et_3N

Osamu Kitagawa, Takashi Suzuki, Hiroki Fujiwara, and Takeo Taguchi*

Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan

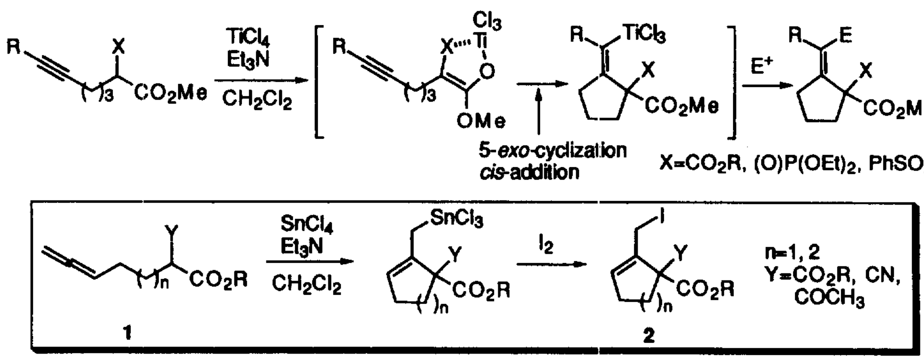
Received 18 December 1998; revised 18 January 1999; accepted 22 January 1999

Abstract: **In the presence of $SnCl_4$ and Et_3N, intramolecular carbostannation reaction of active methine compounds having an allenyl group proceeded in a completely regioselective manner to give cyclopentene and cyclohexene derivatives in good yields.** © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: allenes; cyclization; tin and compounds; cycloalkenes

Intramolecular carbometallation of unstabilized carbanions having an unactivated C-C π-bond such as unsaturated alkyl lithium or Grignard reagents is well known to smoothly proceed to give carbocyclic alkyl metal,[1] while that of stabilized carbanions such as metal enolates prepared from active methylene compounds should be difficult to achieve[2] because of endothermic process involving the conversion of a stabilized enolate anion to an unstabilized carbanion.[3] As very few examples of such reaction, Pd-catalyzed carbocylizations of active methine compounds with unactivated alkenyl, alkynyl or allenyl groups have been reported by several groups.[4] On the other hand, in the course of our work in relation to iodine-mediated carbocyclization reaction,[5] we recently found a carbocyclization reaction of various active methine compounds having an unactivated 4-alkynyl group mediated by a Lewis acid such as $TiCl_4$.[6] In contrast to Pd-catalyzed carbocyclization reaction which proceeds in a *trans*-addition manner to the C-C π-bond, this reaction proceeds through a *cis*-addition of trichlorotitanium enolate of active methines to alkynes, giving methylenecyclopentane derivatives with high stereoselectivity by further reaction of the resulting vinyltitanium intermediate with electrophiles (Scheme 1).

Scheme 1



In this paper, we report the result of intramolecular carbostannation reaction of active methine compounds having an allenyl group which proceeds in the presence of $SnCl_4$ and Et_3N.[7] The present reaction proceeds with complete regioselectivity through the attack of Sn-enolates of active methines at the

PII: S0040-4039(99)00199-9

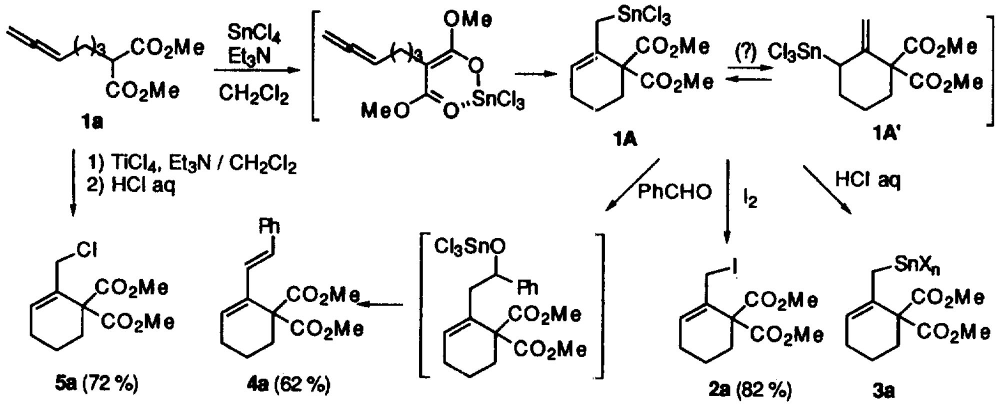
central carbon of an allene to give the corresponding cyclopentene and cyclohexene derivatives in good yields by the successive regioselective reaction of the allyl tin intermediate with electrophiles (Scheme 1).

The intramolecular carbometalltion reaction of 4,5-hexadienylmalonate **1a** was investigated by employing various Lewis acids and Et_3N. Among Lewis acids examined, the use of $SnCl_4$ was found to be the most effective; that is, the cyclization reaction of **1a** with $SnCl_4$ (1.8 eq) and Et_3N (1 eq) completed within 1h at rt (Scheme 2). The successive iodination of the resulting allyl tin intermediate **1A** gave iodomethylcyclohexene **2a** with complete regioselectivity in good yield (82 %),[8] while the quenching of **1A** by an acid gave allyl tin compound **3a** without the formation of a protonated product and a regioisomer of **3a** having *exo*-methylene. The iodonolysis of **1A** was carried out within 2 min, because prolonged reaction time resulted in a mixture of allyl iodide **2a** and chloride through halogen exchange of **2a** by tin chloride.

The exclusive formation of cyclohexenylmethyl tin **3a**[9] indicates that the cyclization of **1a** proceeds with complete 6-*exo*-selectivity through the attack of Sn-enolate at the central carbon of the allene. Although carbopalladation of allenes with a hard carbon nucleophile also generally favors C-C bond formation at the central carbon,[10] it has been reported that in the reaction of stabilized carbanion such as enolates from active methines, the attack of a carbon nucleophile exclusively occurs at an internal carbon and not at the central carbon of allene, because the reaction proceeds through the formation of a π-ally complex.[4e-4h] Thus, the $SnCl_4$-mediated carbocyclization should be complementarily used with the Pd-catalyzed reaction[4h] for the regioselective construction of carbocyclic compounds.

Furthermore, regioselective C-C bond formation of intermediate **1A** is also possible; the reaction of **1A** with benzaldehyde exclusively occurred at the *exo*-methyl carbon and not the carbon on the cyclohexene ring, giving diene **4a** in 62 % via the following dehydration. This regioselectivity may indicate that the C-C bond formation with aldehyde occurs through the reaction with reactive intermediate **1A'** which was possibly brought about by metallotropic rearrangement of stable intermediate **1A**.[11]

Scheme 2



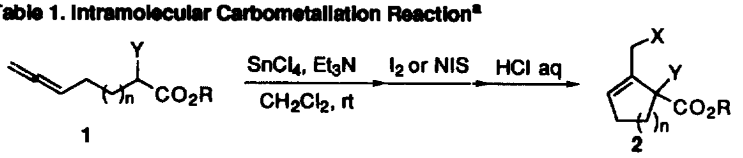
Although the reason is not clear, the reaction of **1a** with $TiCl_4$ which gave good results in the carbocyclization reaction of 4-alkynylmalonates,[6] led to the formation of allyl chloride **5a** after quenching by HCl (Scheme 2). On the other hand, as a Lewis acid, the use of $Ti(O\textit{i}\text{-}Pr)_4$ and $Sn(OTf)_2$ was ineffective, resulting in recovery of **1a**.

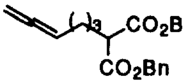
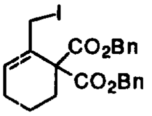
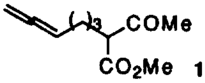
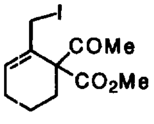
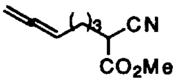
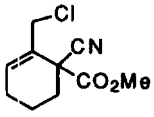
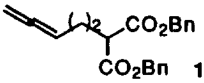
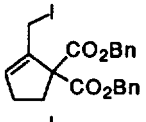
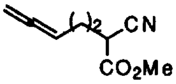
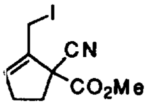
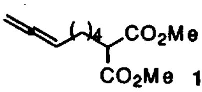
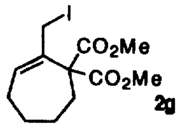
The results of intramolecular carbostannation reaction and the following iodonolysis of various allenylated active methine compounds **1** are shown in Table 1.[12]

Similar to dimethyl malonate derivative **1a**, the reaction of dibenzyl malonate **1b** gave the 6-*exo*-cyclized products **2b** in good yield in the presence of $SnCl_4$ and Et_3N (Entry 1), while in the carbocyclization of **1b** with $TiCl_4$ and Et_3N, the formation of a complex mixture due to cleavage of the benzyl ester by $TiCl_4$ was observed. Not only malonate, the reaction of acetacetate and cyanoacetate derivatives **1c** and **1d** also proceeded smoothly to give products **2c** and **5d**, respectively (Entries 2, 3). In the reaction of cyanoacetate **1d**, although the use of iodine as an electrophile resulted in a decrease in the chemical yield, on using NIS, chloromethylcyclohexene **5d** was obtained as the major product in 60 % yield through the following halogene exchange of the resulting allyl iodide by $SnCl_4$ (Entry 3). The effect of $SnCl_4$ in these reactions should be noteworthy, because the reaction of **1d** with $TiCl_4$ and Et_3N did not proceed, resulting in recovery of **1d**.

The present reaction can be also applied to cyclopentene forming reaction with 3,4-pentadienyl active methine compounds **1e** and **1f**; in these reactions, 5-*exo*-cyclized products **2e** and **2f** were obtained in good yields, respectively (Entries 4, 5). In the reactions of entries 1-5, since the formation of other regio-isomers was not observed, these reactions should proceed with complete 5- or 6-*exo* cyclization and the following selective iodonolysis of the allyl tin intermediates. Unfortunately, reaction of 5,6-heptadienylmalonate **1g** hardly proceeded to give cycloheptene derivative **2g** in poor yield (Entry 6).

Table 1. Intramolecular Carbometallation Reaction[a]



Entry	1	I_2 or NIS	2	Yield (%)[b]
1	 **1b**	I_2	 **2b**	84
2	 **1c**	I_2	 **2c**	61
3	 **1d**	NIS[c]	 **5d**	60[d]
4	 **1e**	I_2	 **2e**	96
5	 **1f**	I_2	 **2f**	62
6	 **1g**	I_2	 **2g**	10

[a] Carbometallation: 1 (1 mmol), $SnCl_4$ (1.8 mmol), Et_3N (1 mmol), CH_2Cl_2 (8 ml), rt, 1h 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] Iodide was also obtained in 5 % yield together with chloride 5d.

In conclusion, we have succeeded in the development of an intramolecular carbostannation reaction of various allenylated active methine compounds which proceeds in a completely regioselective manner in the presence of $SnCl_4$ and Et_3N. Furthemore, the following regioselective reaction of the resulting allyl tin intermediates with electrophiles gave functionalized cyclopentene and cyclohexene derivatives in good yields. The present reaction should be complementarily used with the Pd-catalyzed reaction[4h] which was previously reported by Yamamoto *et al.* for the regioselective construction of carbocyclic compounds.

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8. Typical procedure of carbostannation: To dimethyl 4,5-pentadienyllmalonate **1a** (212 mg, 1 mmol) in CH_2Cl_2 (8 ml) was added Et_3N (0.14 ml, 1 mmol) and 1 M CH_2Cl_2 solution of $SnCl_4$ (1.8 ml, 1.8 mmol) under argon atmosphere at rt. 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 rt. 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 **2a** (277 mg, 82 %). **2a**: ^{1}H-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.
9. **3a**: ^{1}H-NMR ($CDCl_3$) δ: 6.15 (1H, t, J = 4.0 Hz), 3.87 (6H, s), 3.09 [2H, s, ($J_{Sn\text{-}H}$ = 120 Hz)], 2.16-2.27 (4H, m), 1.62-1.72 (2H, m); ^{13}C-NMR ($CDCl_3$) δ: 172.6 ($J_{Sn\text{-}C}$ = 42 Hz), 134.5 ($J_{Sn\text{-}C}$ = 145, 157 Hz), 125.3 ($J_{Sn\text{-}C}$ = 130 Hz), 57.9, 54.3, 41.1 ($J_{Sn\text{-}C}$ = 784, 819 Hz), 29.9, 25.0 ($J_{Sn\text{-}C}$ = 41 Hz), 18.2.
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