Tetrahedron Letters, Vol. 34, No. 41, pp. 6567-6570, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

Novel Michael Addition Promoted by Tributylstannylcarbamate. Synthesis of Diacylcyclopropanes

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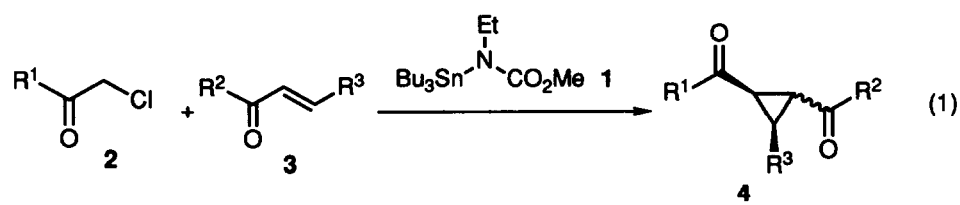
Abstract: Effective Michael addition of α-chloro ketones to α,β-unsaturated ketones was performed under mild conditions promoted by N-stannylcarbamate. Cyclopropane derivatives were obtained stereoselectively.

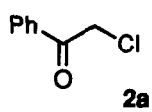
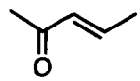
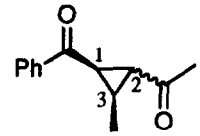
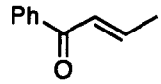
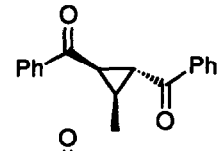
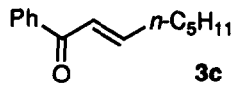
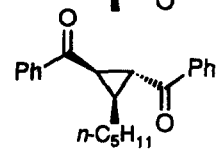
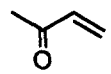
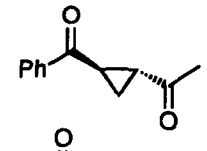
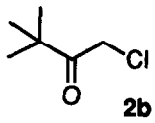
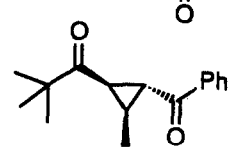
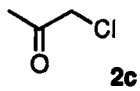
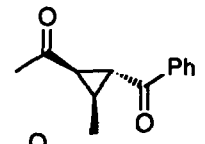
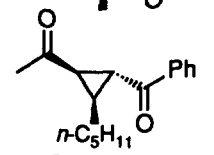
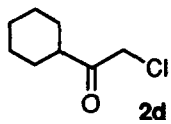
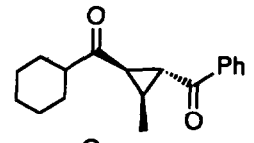
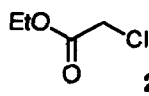
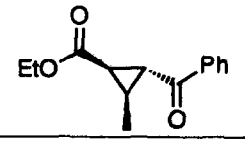
Trialkyltin enolates[1] have an advantage in terms of mild and neutral conditions to effect carbon-carbon bond formation with various electorophiles such as aldehydes, ketones[2] and organic halides.[3] Although effectively controlled chemo-[2e-f,3f-h] and stereoselective[2b-2e] reactions are accomplished, organotin enolates are scarcely reported to promote Michael addition to α,β-unsaturated ketones.[4] We have recently reported the novel Darzens reaction by using N-stannylcarbamate **1** which acted as an effective enolate generating reagent.[5,6] This reagent has an advantage that selective formation of halo enolate is established by the abstraction of α-hydrogen even in the reaction of halo acetones, where no side reactions derived from nucleophilic addition, nucleophilic substitution, and the abstraction of an α'-hydrogen occur. Here we have found that the stannylcarbamate promoted reaction enabled the effective preparation of cyclopropane derivatives (eq. 1). The products are derived from Michael addition of the halo enolate to α,β-unsaturated ketones.



(1)

Table 1 summarizes the reaction of α-chloro ketones **2** with enones **3** in the presence of an equimolar amount of **1**. The addition of LiBr as an additive induced higher yield of cyclopropane **4a** under mild and neutral conditions. Although **4a** was obtained in only 31% yield at 60°C without an additive (entry 1), the reaction in the presence of an equimolar LiBr proceeded even at room temperature to afford 78% yield of **4a** (entry 2). Similar to **3a**, various type enones were reactive. The reaction of aromatic enones, **3b** and **3c**, gave the corresponding products, **4b** and **4c**, respectively (entries 3 and 4). In the reaction of unsubstituted enones **3d**, product **4d** was obtained in 93% yield by using Bu_4NF as an additive (entry 6). Aliphatic chloro ketones **2b-2d** gave the corresponding cyclopropanes **4e-4h** (entries 7-10). α-Chloro ester **2e** also gave **4i** (entry 11). Noteworthy is that the regioselective carbon-carbon bond formation was performed at the α-position of the chloro ketone in the

Table 1. Michael Addition Promoted by Stannylcarbamate (**1**).[a]

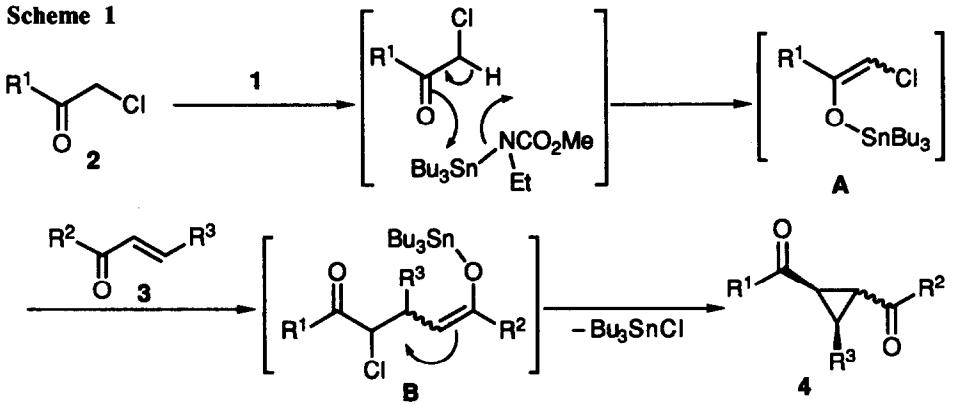
entry	chloro ketone (**2**)	enone (**3**)	time (h)	product (**4**)	yield (%)
1	 **2a**	 **3a**	2	 **4a**	31[b]
2			2		78[c]
3		 **3b**	1	 **4b**	97
4		 **3c**	5	 **4c**	92
5		 **3d**	4	 **4d**	69
6			4		93[d]
7	 **2b**	**3b**	4	 **4e**	67
8	 **2c**	**3b**	4	 **4f**	81
9	**2c**	**3c**	7	 **4g**	54
10	 **2d**	**3b**	7	 **4h**	26
11	 **2e**	**3b**	7	 **4i**	65

[a]Stannylcarbamate(**1**) 1mmol, LiBr 1 mmol, chloro ketone (**2**) 1 mmol, enone (**3**) 1 mmol, $ClCH_2CH_2Cl$ 1 mL, r.t.. [b]60°C, without LiBr, 1,2-*trans* : *cis*= 84 : 16. [c]1,2-*trans* : *cis*= 93 : 7. [d]Bu_4NF was used instead of LiBr.

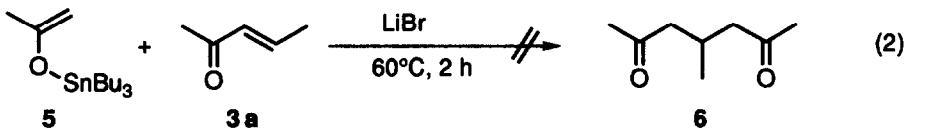
case of producing **4f-4h**. No side reaction at the α'-proton occurred at all even in the reaction of chloro acetone **2c**. Moreover, almost these reactions proceeded with high stereoselectivity. In the reaction of **3a**, the stereochemistry of major stereoisomer of **4a** is 1,2-*trans*, 1,3-*cis* conformation and that of minor one is 1,2-*cis* 1,3-*cis* conformation. In particularly, using LiBr as an additive afforded 93% 1,2-*trans* stereoselectivity (entry 2). Furthermore, products **4b-4i** were obtained as single stereo isomers (entries 3-11). In this way, the reaction proceeded with high stereoselectivity, hence, opposite diastereoisomers, **4a** and **4f**, could be prepared individually only by exchanging the Ph and Me group on the substrates **2** and **3** (entries 2 and 8).

The reaction course can be illustrated in Scheme 1 in which the tin halo enolate **A** is a key intermediate. Namely, stannylcarbamate **1** acts as a base, and abstracts an α-hydrogen of **2** regioselectively to form **A**. Next, **A** reacts with aldehyde **3** to afford the crossed aldol intermediate **B**. Finally, cyclization induces the product **4**. The stereoselectivity is explained in Scheme 2. First, **A** reacts with **3** through the acyclic transition state **C**,[2c] in which 1,3-stereochemistry is determined. Next, the subsequent cyclization proceeds through the non-chelation manner **D** rather than **E**.[8] 1,2-Stereochemistry is determined in this cyclization. The preference of **D** is increased by the coordination of Br^- ion to the tin atom.

Scheme 1



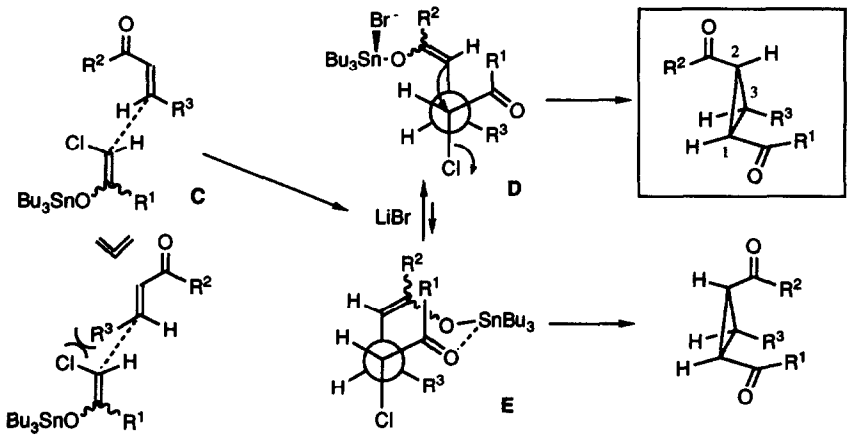
In this way, enolate **A** exhibits unusual reactivity compared with conventional organotin enolates,[9] because tributytin enolates are not reactive with α,β-unsaturated ketones. In fact, no Michael adduct **6** was obtained at all in the reaction of tin enolate **5** with **3a** (eq. 2).



In conclusion, halo enolates derived by stannylcarbamate **1** acted as an effective agent for Michael reaction. Various types cyclopropane derivatives were obtained in this one-pot procedure.

Acknowledgment: This work was supported by the Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture. Thanks are due to Mrs. Y. Miyaji, and Mr. H. Moriguchi, Faculty of Engineering, Osaka University for assistance in obtaining NMR (JEOL, JNM-GSX-400) and MS (JEOL, JMS-DX-303) spectra.

Scheme 2



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(Received in Japan 24 May 1993)