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Double Alkylation of Tin Enolate Derived from Diketene and Bis(tributyltin) Oxide

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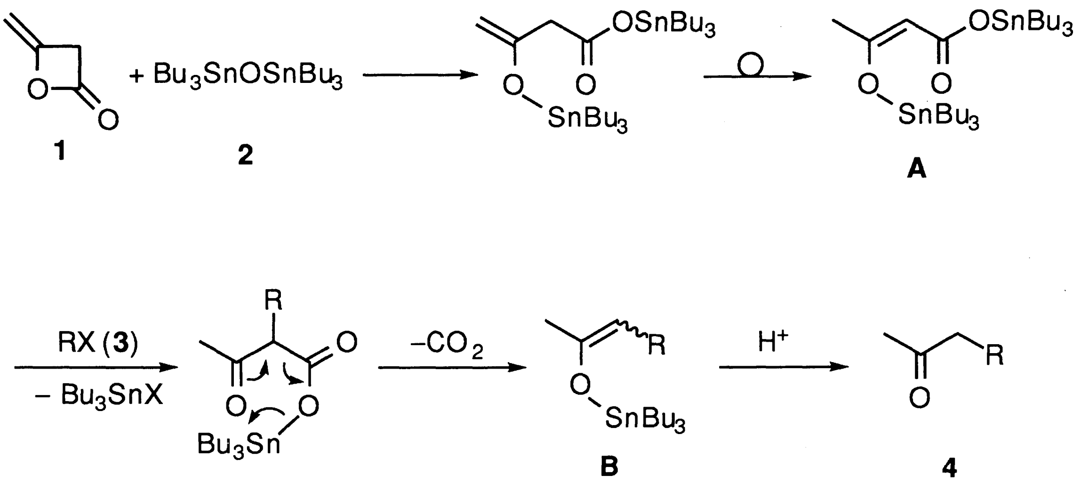
Tin enolate derived from diketene and $(n\text{-}Bu_3Sn)_2O$ was alkylated by alkyl halides, leading to mono-alkylated enolate *via* facile decarboxylation, which successively react with other electrophiles like an aldehyde and alkyl halides to furnish double-alkylated acetones.

Organotin enolates are used as mild and selective reagents for carbon-carbon bond formation.1) It is still an important subject to explore a novel type of tin enolate. We already found the tributyltin methoxide (Bu_3SnOMe) promoted regioselective ring opening2) of diketene (**1**) to afford a tin enolate.3) In addition, we recently reported that a novel tin enolate **A**, derived from bis(tributyltin) oxide [$(Bu_3Sn)_2O$] (**2**) and **1**, reacted with carbonyl compounds such as aldehydes and α,β–unsaturated ketones effectively.4)



Scheme 1.

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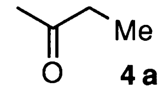
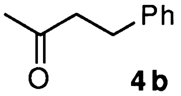
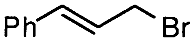
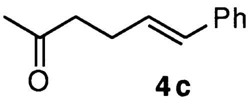
Table 1. Preparation of Methyl Ketone Derivatives by the alkylation of **A**[a]

Entry	RX (**3**)	Additive	Conditions[b]	Product(**4**)	Yield / %
1	MeI **3a**	–	40 °C, 12 h	 **4a**	5
2		LiBr	rt, 12 h		70
3		HMPA	rt, 12 h		51[c]
4		Bu_4NBr	rt, 12 h		61[d]
5	 **3b**	LiBr	rt, 24 h	 **4b**	59
6	 **3c**	LiBr	rt, 24 h	 **4c**	84

a) Enolate **A** was prepared *in situ* by the reaction of **1** (2 mmol) and **2** (2 mmol) at 0 °C for 10 min, then RX (**3**) 2 mmol, Additive 2 mmol, and THF 2 mL were successively added.
b) Alkylation step of **A**. c) Methyl isopropyl-ketone was accompanied in 21% yield.
d) Methyl isopropyl-ketone was accompanied in 17% yield.

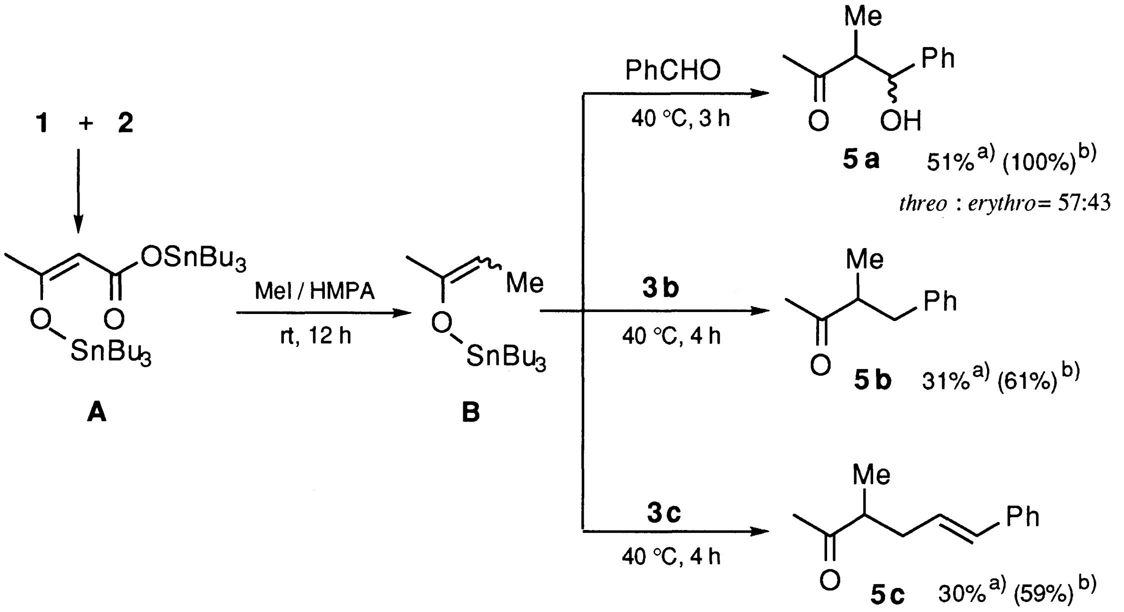
We have now found that the enolate **A** participated in the effective reaction with alkyl halides **3**. In contrast to the reaction with carbonyl compounds, the formation of alkylated tin enolate **B** was formed *via* facile decarboxylation *in situ*, which was proved by hydrolysis to monoalkylated acetone **4**. Moreover, successive alkytlation of **B** was achieved in the one-pot reaction.

We first examined the reaction of **A** with methyl iodide. As can seen from the data in Table 1, addition of LiBr afforded the most effective alkylation at rt, after hydrolysis furnishing **4a** in 70% yield (entry 2),[5] whereas without additives the reaction proceeded hardly even at 40 °C (entry 1). Vigorous decarboxylation was observed during alkylation. Other alkyl halides, benzyl bromide (**3b**), cinnamyl bromide (**3c**) afforded the corresponding ketones **4b** and **4c** in good yields (entries 5 and 6). When either hexamethylphosphoric triamide (HMPA) or tetrabutylammonium bromide (Bu_4NBr) was used instead of LiBr, methyl isopropylketone was isolated as a by-product being derived *via* double methylation of the enolate **A** (entries 3 and 4). The double methylation suggests the favorable stability and reactivity of the tin enolate **B** which is thought to be formed *via* the route depicted in Scheme 1; the ring opening of **1** by tin alkoxide **2**, migration of double bond into a stable enolate **A**, the addition of alkyl halide, and decarboxylation to the enolate **B**.[6]

The formation of **B** encouraged us to investigate the further alkylation of **B** by other electrophiles than methyl iodide, affording unsymmetrical double alkylated acetones **5** (Scheme 2).

A typical procedure is as follows. Under nitrogen, tin alkoxide **2** (2 mmol) was added to the THF (2 mL) solution of **1** (2 mmol). After stirring at 0 °C for 10 min., enolate **A** was formed. Next, the reaction with MeI (2 mmol) in the presence of HMPA (2 mmol) at rt for 12 h afforded the enolate **B**. Without isolation of **B**, benzaldehyde (2 mmol) was further added, and heated at 40 °C for 3 h. After quenching with MeOH (5 mL), aldol product **5a** was isolated by column chromatography with silica gel eluted by hexane/EtOAc.

Similarly, the reaction with alkyl halides, **3b** and **3c**, gave double alkylated acetones **5b** and **5c**, respectively.7) Although the yields of **5** based on the starting diketene **1** was not so high, the effective trapping of **B** was performed because the formation of **B** by using HMPA is 51% yield (Table 1, entry 3).8)



Scheme 2.

a) Based on **1**. b) Based on **B**.

In summary, tin enolate **A** derived from diketene was employed as an effective acetonylating agent of alkyl halides. Presented method would enlarge not only the organotin chemistry but also the utility of diketene.

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References

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5) HMPA and LiBr are reported to accelerate the reaction of tin enolates with alkyl halides. M. Pereyre, G. Colin, and J. Valade, *C. R. Acad. Sci. Paris Ser. C*, **264**, 1204 (1967); M. E. Jung and R. B. Blum, *Tetrahedron Lett.*, **43**, 3791 (1977); Y. Odic and M. Pereyre, *J. Organomet. Chem.*, **55**, 273 (1973).

6) Similar formation of tin enolate *via* decarboxylation is reported by using β-keto esters. F. Guibe, Y. T. Xian, A. N. Zinga, and G. Balavoine, *Tetrahedron Lett.*, **26**, 3559 (1985).

7) For example, the spectral data of **5c** is as follows. IR (neat) 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.15 (d, 3H, J=6.84 Hz, CH_3), 2.17 (s, 3H, $CH_3C{=}O$), 2.22-2.69 (m, 3H, CHMe and CH_2), 6.12 (dt, 1H, 15.62 and 7.32 Hz, vinyl), 6.41 (d, 1H, J=15.62 Hz, PhCH), 7.18-7.34 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ16.07, 28.44, 36.17, 47.74, 126.07, 127.19, 127.33, 128.51, 132.10, 137.32, 211.83; Found: m/z 188.1217. Calcd for $C_{13}H_{16}O$: M, 188.1201.

8) Tin enolates **B** generated by using LiBr as an additive did not afford good yields of **5**. And the enolates **B** bearing bulky substituents such as benzyl, cinnamyl group (generated as shown in Table 1, entries 5 and 6) were not reactive at all.

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