

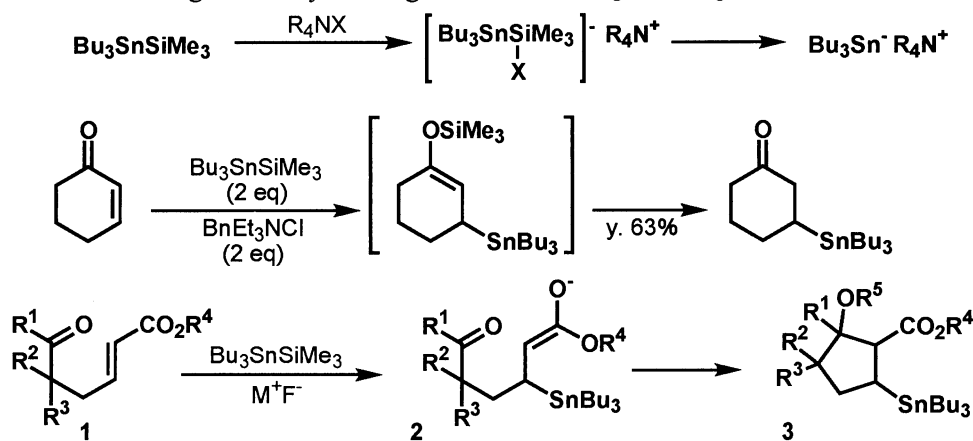
Novel Cyclization Reaction by Tandem Michael Addition -Dieckmann Condensation
Using Stannyl Anion Generated from $\text{Bu}_3\text{SnSiMe}_3$ and F^-

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A novel cyclization reaction was developed using stannyl anion generated from $\text{Bu}_3\text{SnSiMe}_3$ and TASF ($\text{Et}_3\text{S}^+\text{Me}_3\text{SiF}_2^-$). The reaction product was converted to the allylstannane, which was a useful intermediate for the synthesis of biologically active substances.

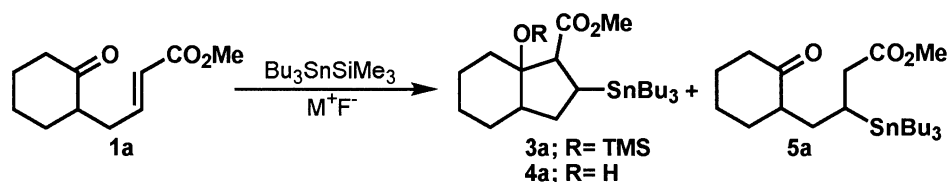
Stannyl anion, generated from $\text{Bu}_3\text{SnSiMe}_3$ and F^- , is a useful tool for organic synthesis.¹⁾ Recently, we reported a new reaction of an aryl or vinyl halide with the carbonyl group intramolecularly in the presence of $\text{Bu}_3\text{SnSiMe}_3$ and the halide ion. For this reaction, fluoride ion is the most effective because the harder silyl group is attacked by the harder fluoride ion. The stannyl anion generated from $\text{Bu}_3\text{SnSiMe}_3$ reacts with the α , β -unsaturated ketone to give the Michael addition product.^{1a,b, 2)} The formation of silyl enol ether prompted us to develop the new cyclization. We now want to report a new cyclization by Michael addition followed by Dieckmann condensation³⁾ using the stannyl anion generated from $\text{Bu}_3\text{SnSiMe}_3$ and F^- as shown in Scheme 1.



Scheme 1.

When keto-ester **1a** was treated with $\text{Bu}_3\text{SnSiMe}_3$ in the presence of TASF⁴⁾ at $-30\text{ }^\circ\text{C}$ in DMF, the cyclized product **3a** was obtained in 79% yield (Scheme 2). The reaction at lower temperature did not afford a good yield (Table 1, run 2). Using CsF or $\text{Bu}_4\text{NSnPh}_3\text{F}_2$ ⁵⁾ instead of TASF did not improve the yield of the cyclized product **3a** (Runs 3 and 4). The fact that the product is obtained as the silylether **3a** means that the reaction would proceed using a catalytic amount of F^- . Thus, using 17 mol% of TASF, the cyclized products, **3a** and **4a**, were obtained in 79% yield (Run 5).⁶⁾ The reaction proceeds even by use of 5 mol% of TASF. The cyclized product **3a** was converted into the destannylated product **9a** to confirm the structure of **3a**.

Desilylation of compound **3a** followed by treatment with SOCl_2 in the presence of pyridine afforded the unsaturated ester **6a** and **7**. The latter compound **7** could be easily converted into the former ester **6a** by treatment with DBU. DIBAH reduction of compound **6a** followed by treatment with Ac_2O -pyridine and then $\text{CrO}_3 \cdot 2\text{Py}$ gave the ketone **9a** (Scheme 3), whose structure was confirmed by spectral data.

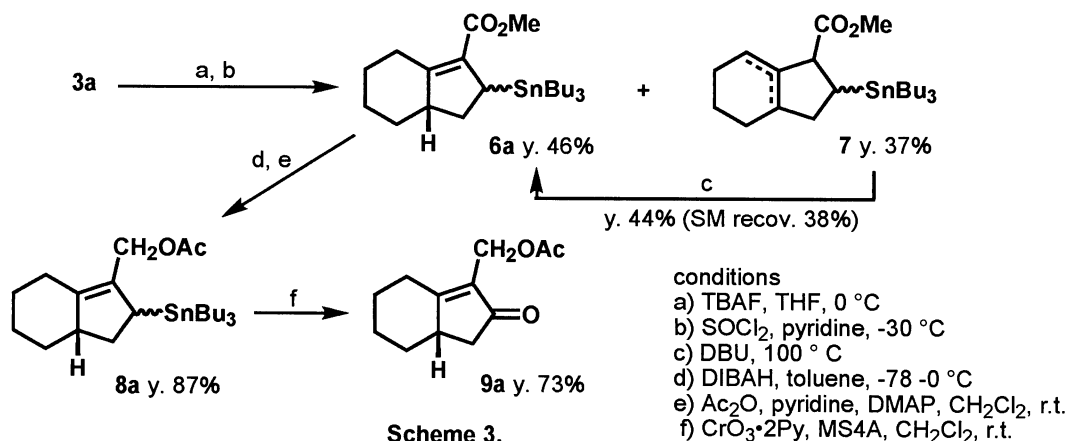


Scheme 2.

Table 1. Reaction of **1a** with $\text{Bu}_3\text{SnSiMe}_3$ in the presence of F^-

run	M^+F^-	$\text{Bu}_3\text{SnSiMe}_3$	temp. / °C	time / h	yield (%) of		
					3a	4a	5a
1	TASF (2 eq)	2 eq	-30	2	79	-	7
2	TASF (2 eq)	2 eq	-50	14	16	-	22
3	CsF (2 eq)	2 eq	0	2	53	-	11
4	$\text{Bu}_4\text{NSnPh}_3\text{F}_2$ (2 eq)	2 eq	-30~0	2	26	-	9
5	TASF (17 mol%)	1.1 eq	-30	1	45	34	2
6	TASF (17 mol%) ^{a)}	1.1 eq	-30	1	24	14	22
7	TASF (5 mol%)	1.1 eq	-30	12	32	31	18

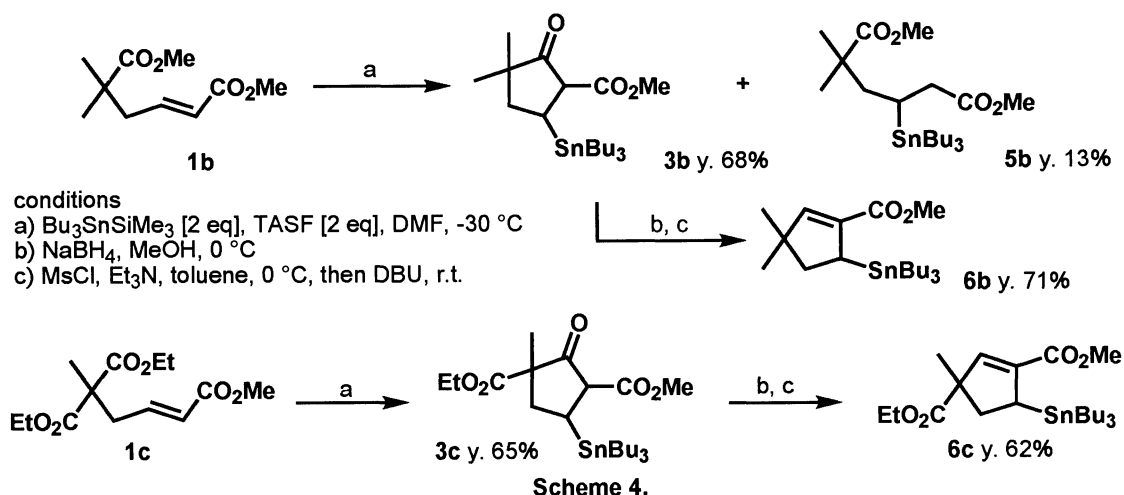
a) THF was used as the solvent.



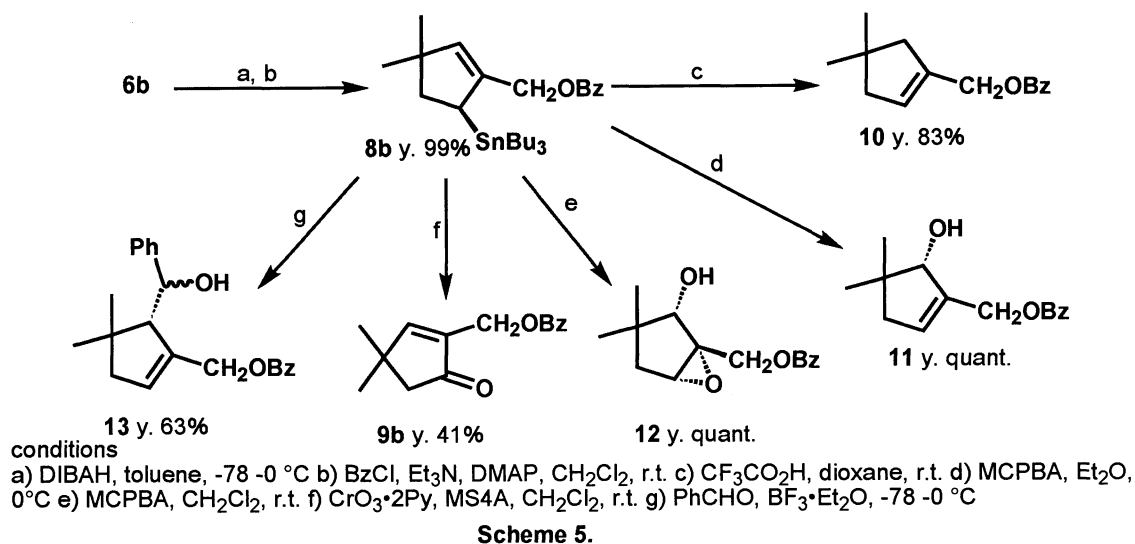
Scheme 3.

The reaction was further developed for the reaction of the ester-carbonyl with α, β -unsaturated ester. Compound **1b** was treated with $\text{Bu}_3\text{SnSiMe}_3$ in the presence of TASF at -30°C in DMF to give the cyclized product **3b** in 68% yield along with the Michael addition product **5b** (13% yield). As solvents, DMF is suitable and the use of THF (25% yield) and Et_2O (18% yield) did not afford good results. The reduction of **3b** with NaBH_4 followed by treatment with MsCl and then DBU gave **6b** (71% yield from **3b**), whose structure was confirmed by spectral data. In a similar manner, compound **1c** was treated with $\text{Bu}_3\text{SnSiMe}_3$ in the presence of TASF to give the cyclized product **3c** in 65% yield, which was converted into compound **6c** in a same manner with 62% yield (Scheme 4).

Compound **6** was a useful product because the β -position of the α, β -unsaturated ester group of **6** is an allylic position of the stannyl group. Thus, both of the electrophiles and the nucleophiles can be introduced at this position in **6**. Subsequently, we demonstrate the reactivity of the allylstannane **6**.

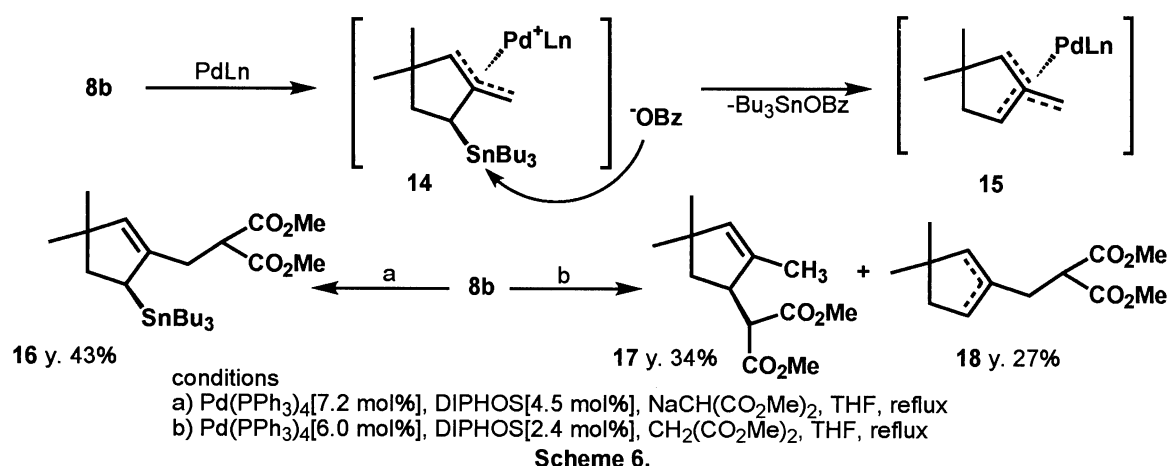


Compound **6b** was converted to the allyl benzoate **8b** in 99% yield. Treatment of **8b** with TFA afforded the allyl alcohol **10** in 83% yield. Oxidation of **8b** with 1.6 equiv. of MCPBA in Et_2O afforded the allyl alcohol **11** in quantitative yield and further oxidation of MCPBA (3.7 equiv.) in CH_2Cl_2 gave the epoxide **12** in quantitative yield. On the other hand, oxidation of **8b** with Collins reagent in the presence of 4A molecular sieves provided the α, β -unsaturated ketone **9b** (41% yield). The new carbon-carbon bond formation was established by the reaction of benzaldehyde in the presence of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (Scheme 5).



Scheme 5.

Moreover, compound **8b** can react with palladium catalyst to give π -allyl palladium complex **14**. When a THF solution of compound **8b**, dimethyl malonate and NaH in the presence of a catalytic amount of $\text{Pd}(\text{PPh}_3)_4$ and DIPHOS was refluxed for 8 h, the alkylated product **16** was obtained in 43% yield. On the other hand, the π -allyl palladium complex **14** would form the dialkylidenemethylenemethane palladium complex **15** without base.⁷⁾ In order to confirm the formation of **15**, a THF solution of compound **8b** and dimethyl malonate was refluxed with palladium catalyst without NaH to give the different alkylated product **17** in 34% yield along with **18** (27% yield). The fact that the product **17** was obtained from **8b** using a palladium catalyst without base is indicated that the dialkylidenemethylenemethane palladium complex **15** is generated from **8b** by palladium catalyst and acts as base.^{7b)}

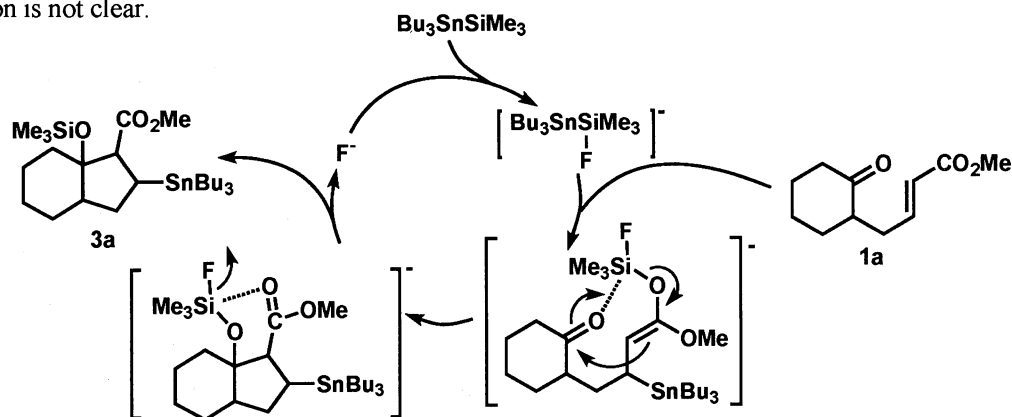


These results indicate that this tandem Michael addition-Dieckmann condensation reaction is very useful reaction for the synthesis of cyclic compounds and the products obtained as allylstannanes are the versatile intermediates for the synthesis of biologically active substances.

Further studies for the cyclization and for the reaction of the stannylated products are in progress.

References

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