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Reaction of Metal Free Bu_3Sn^- Generated from $Bu_3SnSiMe_3$-R_4NX with an Aryl or Vinyl Halide

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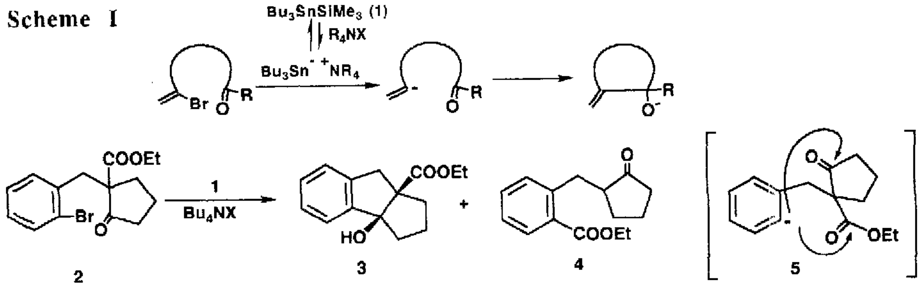
Key Words: $Bu_3SnSiMe_3$, Bu_3Sn^- R_4N^+, Metal free stannyl anion, Cyclization, Aryl or Vinyl anion

Abstract: *Metal free stannyl anion generated from $Bu_3SnSiMe_3$ and R_4NX in DMF reacted with an aryl or vinyl halide to produce the aryl or vinyl anion via so-called halogen-metal exchange process, which reacted with internal carbonyl group to afford cyclized product in good yield.*

Bimetallic reagents having Si-Sn bond have become interest in recent synthetic organic chemistry because the silyl and/or stannyl group can be introduced into unsaturated compounds[1] by use of them. During the course of our investigation of palladium catalyzed tandem transmetallation-cyclization reaction using $Bu_3SnSiMe_3$,[2] we found the new cyclization reaction by use of metal free Bu_3Sn^- generated from $Bu_3SnSiMe_3$ and R_4NX. Namely, keto ester **2** was treated with $Bu_3SnSiMe_3$ (**1**) and Bu_4NBr in DMF at 60 °C for 6 h to produce cyclized product **3**[3] and aryl ester **4** in 50% and 27% yields, respectively.

Scheme I

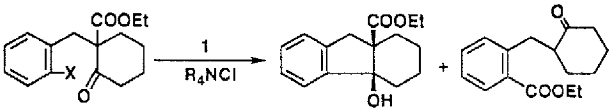


It seems likely that the metal free stannyl anion is generated from **1** *via* hypervalent silicate under the reaction conditions, which would provide an aryl anion **5** from **2**. In order to confirm the generation of stannyl anion, the effects of halide ion of ammonium salts were examined and the results are shown in Table I. In the absence of ammonium salt, the desired products were not obtained (Table I, run 1). When Bu_4NF was used in this reaction, cyclized product **3** was obtained in only 32% yield in spite of the rapid disappearance of the starting material on TLC[4] (run 2). Bu_4NCl as halide ion afforded the best result(run 3). These results suggest that the harder chloride ion gave a good result and it strongly coordinates at the hard silicon moiety of $Bu_3SnSiMe_3$ to form hypervalent silicate, thus generating metal free stannyl anion.[5] If the stannyl anion is generated under these reaction conditions, the effect of halide variation on the aromatic ring would be observed. As expected, aryl iodide **6a** gave a good result (Table II, run 2), suggesting that the aryl anion was produced by *so-called* halogen-metal exchange process[6] of stannyl anion and an aryl halide. Cationic part of ammonium salt did not affect this reaction significantly (run 1 and 2). Generation of the metal free stannyl anion was also supported by the following results: When **9a** or **9b** was treated with **1** and $BnEt_3NCl$ in DMF, stannylated compound **10a** or **10b** was obtained in 63% or 38% yield.[1b,7]

Table I. Effect of Halide Ion of Ammonium Salt in Reaction of 2 with 1[a]

run	Bu_4NX	temp	3	4	2
1	none	60 °C	——	——	85%
2	F	60 °C	32%	——	——
3	Cl	60 °C	52%	12%	——
4	Br	60 °C	20%	6%	37%
5	Cl	rt	53%	19%	2%

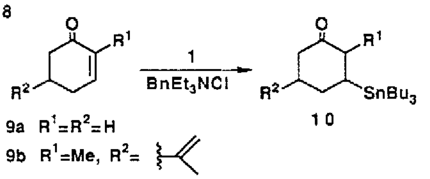
[a] All reactions were carried out in DMF (*ca.* 0.15 M) in the presence of 2 equiv. of **1** and 3 equiv. of Bu_4NX for 1 h.



6a X=I
6b X=Br
6c X=Cl
6d X=H

7

8



9a $R^1=R^2=H$
9b $R^1=Me$, $R^2=$

10

Table II. Reactivity of Various Aryl Halides[a]

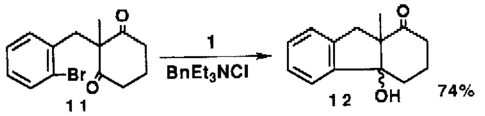
run	6	R_4NCl	7	8	6 d	SM[b]
1	6a (X=I)	Bu_4NCl	21%	30%	15%	—
2	6a (X=I)	$BnEt_3NCl$	30%	33%	19%	2%
3	6b(X=Br)	$BnEt_3NCl$	32%	18%	17%	24%
4	6c(X=Cl)	$BnEt_3NCl$	—	—	—	98%

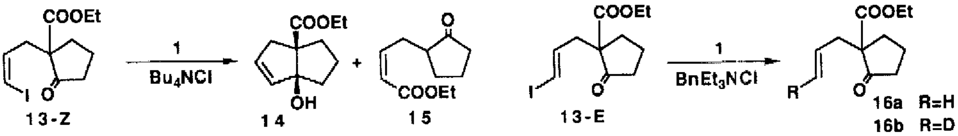
[a] All reactions were carried out in DMF (*ca.* 0.15 M) in the presence of 2 equiv of 1 and 2 equiv of R_4NCl at room temperature for 6 h.

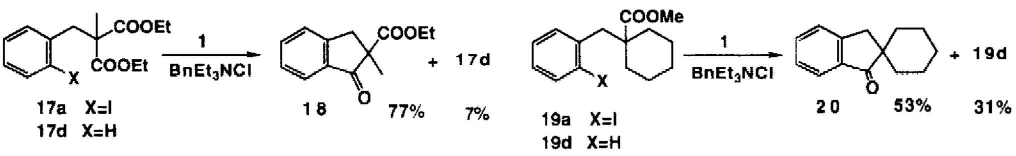
[b] Recovered starting material.

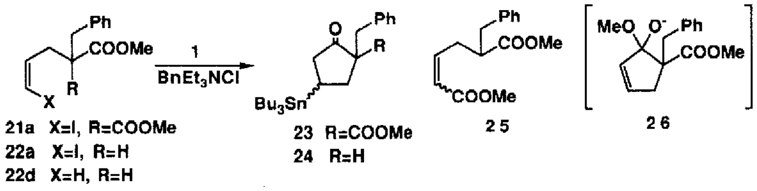
Diketone **11** was treated with **1** and $BnEt_3NCl$ in DMF to afford compound **12** in 74% yield. Furthermore, generation of vinyl anion was examined. Thus, compound **13-Z** was treated with **1** and Bu_4NCl in DMF at 60 °C and to our delight that the desired cyclized product **14** was obtained in 41% yield along with unsaturated ester **15** (21% yield). In contrast these products were not obtained from **13-E** and the main product was dehalogenation compound **16a** (83% yield). Hydrogen source of **16a** appears to be a trace of water in the reaction mixture because the same reaction was carried out in the presence of D_2O (5 equiv) or *i*-PrOD (20 equiv) to provide **16b** (R=D) in 74% or 50% yield, respectively.

The most striking feature of this reaction is that an aryl or vinyl halide reacted with ester. The cyclization of compounds **17a** and **19a** smoothly proceeded in the presence of **1** and $BnEt_3NCl$ in DMF at 60 °C to give desired cyclized products **18** and **20** in good yields. When vinyl iodide **21a** was treated in a similar manner at room temperature, only a small amount of cyclized product **23** was obtained and the main product was compound **25** (*E*/*Z*=2/1, 61% yield). It seems likely that the reaction of vinyl iodide **21a** with internal ester proceeds to give **26** and then the bond cleavage occurs to provide **25**. Thus, when ester **22a** was treated with **1** (3 equiv) in DMF in the presence of molecular sieves 4A at room temperature, the desired cyclized product **24** was obtained in 50% yield.



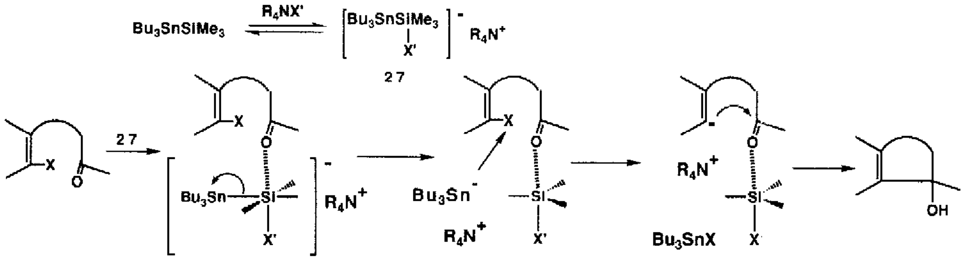






The probable reaction mechanism is shown as follows and the key step in the proposed mechanism is the generation of metal free stannyl anion. Namely, (i) The coordination of Cl^- at silicon of $Bu_3SnSiMe_3$ in DMF is followed by the concerted attack of carbonyl group at silicon[8] with the formation of hypervalent silicate, which would give rise to the metal free stannyl anion. Then, (ii) *so-called* halogen-metal exchange[9] of an aryl or vinyl halide with metal free stannyl anion provides the aryl or vinyl anion.[10] (iii) The last step is that the resulting aryl or vinyl anion attacks to the carbonyl group activated by silyl group. In this reaction, solvent must play an important role such as the stabilization of the hypervalent silicate or of the metal free stannyl anion.[11]

Figure 1 Possible Reaction Pathway



The remarkable characteristic of this reaction is as follows: For the formation of hypervalent silicate from $Bu_3SnSiMe_3$ in DMF, bromide ion shows the enough reactivity and the metal free stannyl anion is generated.

The aryl or vinyl anion generated by *so-called* halogen-metal exchange process of an aryl or vinyl halide with metal free stannyl anion can react with carbonyl compounds such as aldehyde,[11] ketone and even ester.

References and Notes

1. a) Michell, T. N.; Killing, H.; Dicke, R.; Wickenkamp, R. *J. Chem. Soc.,Chem. Commun.* **1985**, 354. Michel, T. N.; Wickenkamp, R.; Amamria, A.; Schnider, U. *J. Org. Chem.* **1987**, *52*, 4868. b) Chenald, B. L.; Laganis, E. D.; Davidson, F.; RajanBabu, T. V. *J. Org. Chem.* **1985**, *50*, 3666. Chenald, B. L.; Van Zyl C. M.; Sanderson, D. R.*Tetrahedron Lett.* **1986**, *27*, 2801. Chenald, B. L.; Van zyl, C. M. *J. Org. Chem.* **1986**, *51*, 3561. c) Ito, Y.; Bando, T.; Matsuura, T.; Ishikawa, M. *J. Chem. Soc., Chem. Commun.* **1986**, 980. d) Lipshutz, B. H.; Reuter, D. C.; Ellsworth, E. L. *J. Org. Chem.* **1989**, *54*, 4975. e) Liebeskind, L. S.; Fengl, R. W. *J. Org. Chem.* **1990**, *55*, 5359.
2. Mori, M.; Kaneta, N.; Shibasaki, M. *J. Org. Chem.* **56**, 3486 (1991). When compound **28** was treated with $Bu_3SnSiMe_3$ and $PdCl_2(PPh_3)_2$(cat.) in the presence of n-Bu_4NBr and Li_2CO_3 in toluene,[2] cyclized product **30** was not obtained. This reaction was carried out in DMF instead of toluene to give another cyclized product **29** in 31 % yield, whose structure was confirmed by spectral data. We are very surprized to find that this reaction proceeded without palladium catalyst and none of the cyclized product was obtained without n-$Bu_3SnSiMe_3$ (Table 3).

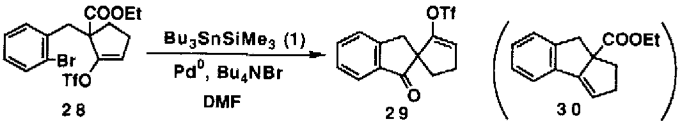


Table 3

$PdCl_2(PPh_3)_2$	$Bu_3SnSiMe_3$	29	28
3 mol%	1.1 eq	31%	——
3 mol%	——	——	95%
——	1.1 eq	38%	34%

3. All the new compounds reported in this manuscript exhibited spectral (^{1}HNMR, MASS HR-MASS and IR spectra) data consist with the assigned structure.
4. Reaction of **2** with $Bu_3SnSiMe_3$ was carried out in the presence of $(Et_2N)_3S{\cdot}TMSF_2$ in DMF at -50 °C for 1 h to provide **3** and **4** in 41 % and 18 % yields, respectively.
5. Generation of silyl anion from $Me_3SiSiMe_3$ by fluoride ion has been reported: Hiyama, T.; Obayashi, M.; Mori, I.; Nozaki, H. *J. Org. Chem.* **1983**, *48*, 912.
6. Kuivila has reported that the reaction of ArX with Bu_3SnNa proceeds through halogen-metal exchange process to produce $[Ar^-{\cdot}Na^+{\cdot}X\text{-}SnBu_3]$ and then $ArSnBu_3$ is formed. In our case, counter cation is NR_4^+. Thus, the term "halogen-metal exchange process" is not the proper designation, but the process would be same as that : Wursthorn, K. R.; Kuivila H. G.; Smith, G. F. *J. Am. Chem. Soc.* **1978**, *100*, 2779.
7. Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836.
8. Corriu R. J. P.; Yong, J. C. *The Chemistry of Organic Silicon Compounds*, S. Patai S.; Rappoport, Z. Eds., John Wiley & Sons, Chichester, **1989**, p. 1279.
9. The reaction mixtures of halogen-metal exchange of **2** with Bu_3SnLi (THF, 0 °C), *t*-BuLi (DME, -78 °C) and BuLi (THF, -78 °C) showed many spots on TLC.
10. A fair amount of $Bu_3SnSnBu_3$ was obtained in these reactions. Thus a more complex mechanism involving initial electron transfer from the metal free stannyl anion to the aryl halide[6] would be considered.
11. Ashby E. C.; Pham, T. N. *Tetrahedron Lett.* **1987**, *28*, 3183.
12. Representative Procedure: To a solution of **2** (50 mg, 0.16 mmol) and $BnEt_3NCl$ (130 mg, 0.47 mmol) in DMF (1 mL) was added $Bu_3SnSiMe_3$ (114 mg, 0.32 mmol) at room temperature under argon and the solution was stirred for 1 h. To the solution was added 10% NH_4OH solution and the whole solution was stirred for 30 min. The aqueous layer was extracted with ether, and the organic layer was washed with 10% HCl, sat. $NaHCO_3$ solution and brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel eluting with ethyl acetate-hexane (1:20) to give colorless oil of **3** (20 mg, 53%), **4** (7 mg, 19%) and **2** (1 mg, 2%).
13. Intermolecular reaction of benzaldehyde with iodobenzene in the presence of **1** and $BnEt_3NCl$ in DMF afforded diphenyl carbinol (16% yield).

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