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Conjugate Hydrostannation of Unsaturated Esters by Iodotin Hydride Ate Complex

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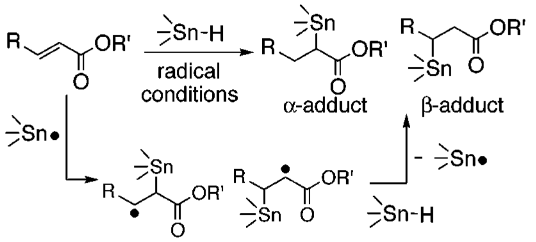
Stannylketene acetals bear high reactivity to afford effective carbon−carbon bond formation with electrophiles.[1] Although the conjugatge hydrostannation of α,*β*-unsaturated esters with tin hydrides could provide the reagents, no such examples have been reported so far. Until now, all the hydrostannation of α,*β*-unsaturated esters has been performed under radical conditions using elevated temperatures,[2] UV irradiation,[2] ultrasound,[3] and Et_3B[4] and gave only the α- and *β*-stannylated adducts where the α/*β*-selectivity is dependent on the stability of the radicals (Scheme 1).[5]

An ionic promotion could allow the conjugate hydrostannation to form stannylketene acetals. However, no ionic method such as metal-catalyzed hydrostannation of α,*β*-unsaturated esters has been known so far.[6] Furthermore, it is known that tri-*n*-butylstannylketene acetals are labile and easily isomerize to less reactive α-stannylesters at temperatures over −78 °C.[1] Hence, to achieve the conjugate hydrostannation and prevent the isomerization of the resulting stannylketene acetals, novel tin hydride reagents must be applied other than tri-*n*-butylstannyl hydride reagents.[7] We have already reported iododi-*n*-butyltin hydride and its ate complex such as $n\text{-}Bu_2SnIH$[8] and $Li^+[n\text{-}Bu_2SnI_2H]^-$,[9] which promote effective conjugate hydrostannation of α,*β*-unsaturated ketones and aldehydes, respectively. However, these tin hydrides have no reducing ability for α,*β*-unsaturated esters. Quite recently, we have reported the novel tin hydride ate complex $[MgBr]^+[n\text{-}Bu_2SnBrIH]^-$ to promote addition to aliphatic alkynes.[10] The complex was prepared only by mixing $n\text{-}Bu_2SnIH$ and $MgBr_2{\cdot}OEt_2$. Using EtOAc as a solvent is particularly effective for the formation of the complete 1:1 complex. This solvent efffect indicates that the magnesium cation of $[MgBr]^+[n\text{-}Bu_2SnBrIH]^-$ would interact with ester functionalities. We found here that the complex effectively reacted with α,*β*-unsaturated esters **1**, and the conjugate hydrostannation could be accomplished for the first time (Scheme 2).

Scheme 1



Scheme 2

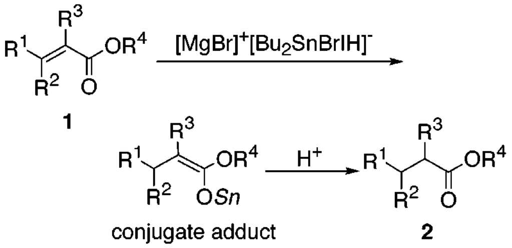
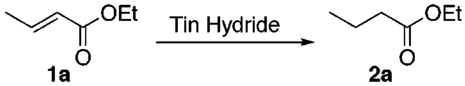


Table 1. Reduction of 1a by Various Tin Hydrides[a]



entry	tin hydride	time/h	yield/%
1	$n\text{-}Bu_3SnH$	22	0
2	$n\text{-}Bu_2SnIH$	0.5	trace
3	$Li^+[n\text{-}Bu_2SnI_2H]^-$	7	0
4	$n\text{-}Bu_2SnIH/MgBr_2{\cdot}OEt_2$	1	80
5	$n\text{-}Bu_2SnIH/BF_3{\cdot}OEt_2$	22	0
6	$n\text{-}Bu_2SnIH/ZnCl_2$	20	0
7	$n\text{-}Bu_3SnH/MgBr_2{\cdot}OEt_2$	22	17

[a] Tin hydride (1 mmol), **1a** (1 mmol), THF (1 mL), room temperature.

As shown in Table 1, the reduction of ethyl crotonate (**1a**) was examined by using various tin hydride systems. No reaction proceeded with $n\text{-}Bu_3SnH$ (entry 1). As described above, $n\text{-}Bu_2SnIH$ and $Li^+[n\text{-}Bu_2SnI_2H]^-$ were not effective (entries 2 and 3). However, when $MgBr_2{\cdot}OEt_2$ was added to $n\text{-}Bu_2SnIH$, saturated ester **2a** was obtained in 80% yield (entry 4). Thus, the reaction could be performed effectively at room temperature. Here, $MgBr_2{\cdot}OEt_2$ does not simply work as a Lewis acid because other types of Lewis acids such as $BF_3{\cdot}OEt_2$ and $ZnCl_2$ did not promote the reactions (entries 5 and 6). Moreover, the combination of $MgBr_2{\cdot}OEt_2$ with $n\text{-}Bu_3SnH$ gave little effect (entry 7). The formation of ate complex $[MgBr]^+[Bu_2SnBrIH]^-$ is essential for conjugate hydrostannation. Thus, an anion in the complex has a trigonal bypiramidal structure in which two halogens occupy the apical positions and a hydrogen and two butyl groups are located at the equatorial positions

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(1) Shimada, E.; Inomata, K.; Mukaiyama, T. *Chem. Lett.* **1974**, 689−690.

(2) Pereyre, M.; Colin, G.; Valade, J. *Tetrahedron Lett.* **1967**, 4805−4808.

(3) Nakamura, E.; Imanishi, Y.; Machii, D. *J. Org. Chem.* **1994**, *59*, 8178−8186.

(4) Nozaki, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2585−2587.

(5) For example, the hydrostannation of *n*-hexyl crotonate with Ph_3SnH/Et_3B gives the *β*-adduct, whereas the reaction of methyl crotonate under the same conditions gives the α-adduct.[4]

(6) Smith, N. D.; Mancuso, J.; Lautens, M. *Chem. Rev.* **2000**, *100*, 3257−3282.

(7) Tin hydride chemistry; see, for example: Pereyre, M.; Quintard, J. P.; Rahm, A. *Tin in Organic Synthesis*; Butterworth: London, 1987; p 35.

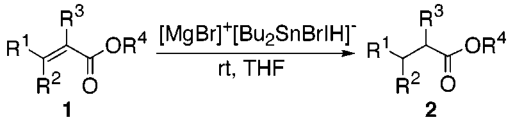
(8) (a) Kawakami, T.; Miyatake, M.; Shibata, I.; Baba, A. *J. Org. Chem.* **1996**, *61*, 376−379. (b) Suwa, T.; Nishino, K.; Miyatake, M.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **2000**, *41*, 3403−3406.

(9) Suwa, T.; Shibata, I.; Baba, A. *Organometallics* **1999**, *18*, 3965−3967.

(10) Shibata, I.; Suwa, T.; Ryu, K.; Baba, A. *J. Am. Chem. Soc.* **2001**, *123*, 4101−4102.

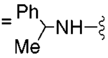
10.1021/jo016081e CCC: $20.00

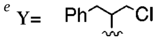
Table 2. Hydrostannation of α,β-Unsaturated Esters by Tin Hydride Ate Complex[a]



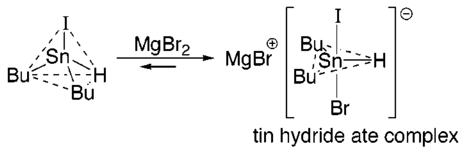
entry	R¹	R²	R³	R⁴		product	time/h	yield/%
1	Ph	H	H	Et	**1b**	**2b**	5	51
2	Ph	H	H	Bn	**1c**	**2c**	5	90
3	Ph	H	H	Bn	**1c**	**2c**	5	87[b]
4	p-MeC$_6$H$_4$	H	H	Me	**1d**	**2d**	6	76
5	p-NO$_2$C$_6$H$_4$	H	H	Me	**1e**	**2e**	1	62
6	p-ClC$_6$H$_4$	H	H	Me	**1f**	**2f**	1	67
7	X[d]	Me	H	Me	**1g**	**2g**	5	61
8	H	H	Me	^{t}Bu	**1h**	**2h**	0.5	75
9	H	H	H	Y[e]	**1i**	**2i**	0.5	78
10	H	H	H	Et	**1j**	**2j**	0.5	90
11	H	H	H	Et	**1j**	**2j**	18	0[c]
12	Me	Me	H	Et	**1k**	**2k**	24	10
13	Me	Me	H	Et	**1k**	**2k**	18	18[c]

[a] [MgBr]$^+$[Bu$_2$SnBrIH]$^-$ (1 mmol), **1** (1 mmol), THF (1 mL). [b] Galvinoxyl (0.1 mmol) was added. [c] Yields are described in ref 2 using Bu$_3$SnH under UV irradiation at 70 °C.

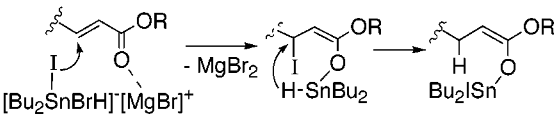
[d]


[e]


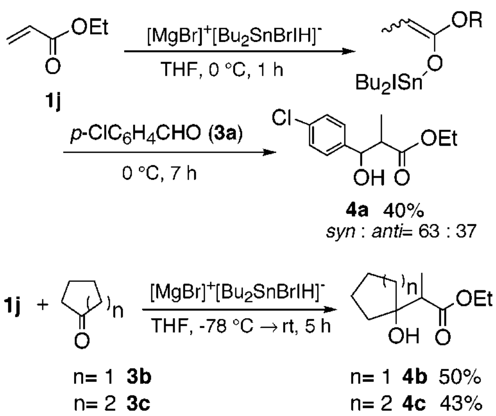
Scheme 3



Scheme 4



Scheme 5



(Scheme 3).[10] In this ate complex, it is assumed that the nucleophilicity of the iodine group is increased.[9] Namely, the preferential attack of iodine at the β-carbon is followed by rapid reduction of the carbon–iodine bond by tin hydride species to give the stannylketene acetal, which was hydrolyzed to saturated ester **2** (Scheme 4). Although the reason [MgBr]$^+$[n-Bu$_2$SnBrIH]$^-$ have a preference effect compared with Li$^+$[n-Bu$_2$SnI$_2$H]$^-$ is unclear as yet, unsaturated ester **1** would be activated by a countercation [MgBr]$^+$.[11]

Table 2 shows the conjugate reduction of various α,β-unsaturated esters with the ate tin hydride complex in THF. As in the case of **1a**, terminally monosubstituted alkenes **1b**–**1f** were reduced effectively to the corresponding saturated esters **2b**–**2f** (entries 1–6). The reducible functionalities such as nitro and halogen groups in **1e** and **1f** did not react (entries 5 and 6).[12] In the case of enamine type of substrate **1g**, good yield was obtained, and the amine group did not disturb the reactions at all (entry 7). A bulky O-substituent in **1h** was not problem and allowed the production of **2h** in good yield (entry 8). A reducible alkyl halide in **1i** was not affected (entry 9). It could be concluded that ionic processes determine the ate complex promoted hydrostannation. The yield of product scarcely changed in the presence of a radical inhibitor such as Galvinoxyl (entry 3). Of interest is that terminally nonsubstituted alkenes **1j** were more reactive than the substituted alkenes **1k** (entries 10 and 12) because the reactivity order is the reverse of that in the radical reactions (entries 11 and 13) where the nonsubstituted unsaturated esters do not react.[2] The reactions of terminally nonsubstituted unsaturated esters with [MgBr]$^+$[n-Bu$_2$SnBrIH]$^-$ went to completion within 30 min (entries 8–10).

This hydrostannation could develop the further reaction of the generated metal ketene acetal with an electrophile (Scheme 5). Thus, after completing the hydrostannation of unsaturated ester **1j**, the addition of the generated stannylketene acetal to p-chlorobenzaldehyde **3a** gave β-hydroxy ester **4a** in 40% yield. On the other hand, the hydrostannation of **1j** could be performed in the coexistence of cyclic ketone **3b** or **3c** to promote hydroxy ester **4b** or **4c** as the sole product, respectively, in which [MgBr]$^+$[n-Bu$_2$SnBrIH]$^-$ predominantly reduces **1j** beyond cyclic ketones. Although the yields of hydroxy

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(11) It has been already cleared that the 1:1 tin ate complex [MgBr]$^+$[n-Bu$_2$SnBrIH]$^-$ is formed more effectively in EtOAC than in THF.[8] However, no hydrostannation of α,β-unsaturated esters with [MgBr]$^+$[n-Bu$_2$SnBrIH]$^-$ proceeded in EtOAc. This would be because of the coordination of EtOAc to the tin complex. In THF solvent, we consider that effective coordination to α,β-unsaturated esters is possible.

(12) (a) Kabalka, G. W.; Varma, R. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 8, Chapter 2, pp 363–380. (b) Imamoto, T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 8, Chapter 4, pp 793–810.

esters are not yet satisfactory, it should be noted that the result is the first generation of stannylketene acetal by the conjugate hydrostannation of unsaturated esters.

In conclusion, conjugate hydrostannation of various α,β-unsaturated esters could be performed with high chemoselectivity by using ate tin hydride complex, $[MgBr]^+[n\text{-}Bu_2SnBrIH]^-$. The resulting stannylketene acetals could be used for the aldol reactions to give β-hydroxy esters.

Experimental Section

Representative Procedure for Hydrostannation of an α,β-Unsaturated Ester 1c. To 1 mL of dry THF in a round-bottomed flask under dry N_2 were added $n\text{-}Bu_2SnH_2$ (0.118 g, 0.5 mmol) and $n\text{-}Bu_2SnI_2$ (0.244 g, 0.5 mmol). After 10 min at room temperature, the formation of $n\text{-}Bu_2SnIH$ (1 mmol) was confirmed by the shift of an IR band (ν(Sn−H)) from 1837 to 1846 cm^{-1}. Then, $MgBr_2\cdot OEt_2$ (0.258 g, 1 mmol) was added and stirring was continued for 10 min. IR absorption was observed at the same value, 1846 cm^{-1}. To the solution was added unsaturated ester **1c** (0.238 g, 1 mmol), and the resulting mixture was stirred at room temperature for 5 h. $CHCl_3$ (5 mL) was added to decompose the remaining tin hydride, and volatiles were removed under reduced pressure. The residue was subjected to column chromatography eluting with 1:1 hexanes−EtOAc to give product **2c** in 90% yield (0.216 g), which was consistent with the authentic sample.

Other reactions of unsaturated esters were performed in similar ways for the corresponding reaction time (Table 2).

Reaction of Stannylketene Acetal Generated by the 1,4-Hydrostannation of an α,β-Unsaturated Ester with an Aldehyde. A THF solution (1 mL) of $[MgBr]^+[n\text{-}Bu_2SnBrIH]^-$ (1 mmol) was prepared by the above-described method. The solution was cooled to 0 °C, and ethyl acrylate (**1j**) (0.100 g, 1 mmol) was added. After the mixture was stirred at 0 °C for 1.5 h, *p*-chlorobenzaldehyde (0.141 g) was added, and stirring was continued at 0 °C for 7 h. $CHCl_3$ (5 mL) was added to decompose the remaining tin hydride, and volatiles were removed under reduced pressure. The residue was subjected to column chromatography eluting with 1:1 hexanes−EtOAc to give product **4a** in 40% yield (0.097 g). The diastereomeric ratio was determined by ^1H NMR (syn:anti = 63:37).

Reaction of Stannylketene Acetal Generated by the 1,4-Hydrostannation of an α,β-Unsaturated Ester with a Cyclic Ketone. A THF solution of $[MgBr]^+[n\text{-}Bu_2SnBrIH]^-$ (1 mmol) was prepared by the above-described method. The solution was cooled to −78 °C, and ethyl acrylate (**1j**) (0.100 g, 1 mmol) and cyclohexanone (0.252 g, 3 mmol) were added. After the mixture was stirred at from −78 °C to room temperature for 5 h, $CHCl_3$ (5 mL) was added to decompose the remaining tin hydride and volatiles were removed under reduced pressure. The residue was subjected to column chromatography eluting with 1:1 hexanes−EtOAc to give product **4b** in 50% yield (0.093 g).

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Supporting Information Available: Experimental procedures, IR, ^1H NMR, ^{13}C NMR, and HRMS spectra fo r **2c**−**2g**, **2i**, and **4a**−**c**, and ^{13}C and ^{119}Sn NMR data for the tin hydride ate complex $[MgBr]^+[n\text{-}Bu_2SnBrIH]^-$. This material is available free of charge via the Internet at http://pubs.acs.org.

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