Transition-Metal-Free Conjugate Stannyl Transfer to α,β-Unsaturated Carbonyl and Carboxyl Compounds in Basic Aqueous Media

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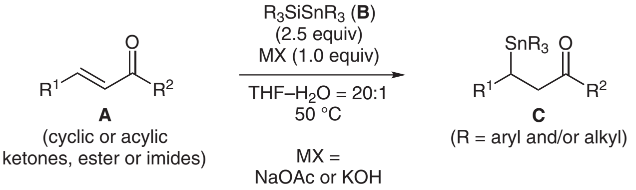
Abstract: An unpretentious procedure for the conjugate stannylation of several α,β-unsaturated acceptors using silyl stannanes is reported. Competing reaction pathways of conjugate addition and reduction are discussed.

Key words: aqueous media, conjugate addition, interelement linkages, silicon, tin



Scheme 1 Transition-metal-free conjugate stannyl transfer

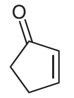
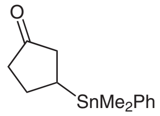
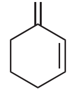
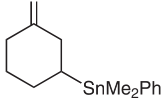
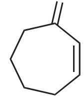
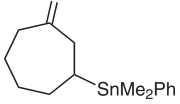
The carbon–tin bond belongs to the most widely used carbon–element linkages in organic chemistry.[1] A classic way of installing a triorganostannyl group at saturated carbon is the indirect 1,4-addition of stannyl lithiums to α,β-unsaturated acceptors,[2] a reaction that is believed to follow a 1,2-addition–1,3-allylic transposition pathway.[3] These anions also provide an entry into tin-based cuprates,[4] and there is a rich chemistry connected with that.[5] In order to bypass stannyl lithium generation by reductive metalation or deprotonation reactions,[2] alternative approaches were later elaborated, which rely on cleavage of tin–element bonds (element = hydrogen, silicon, and tin) by metalates.[6] Prior to this development, Chenard et al.[8] had realized that interelement linkages, namely silyl stannanes,[7] are chemoselectively activated by cyanide[8] or halides[9] thus enabling a (transition) metal-free stannyl transfer onto α,β-unsaturated acceptors.[10]

In the course of our investigations towards catalytic asymmetric conjugate carbon–element bond formation by activation of element–element bonds with chiral Rh^{I}OH complexes,[11,12] we also tested silyl stannanes as a source of nucleophilic tin. These catalyses are usually performed at elevated temperatures (45–60 °C) in basic aqueous media using 1,4-dioxane–H_2O solvent mixtures and Et_3N or KOH as bases. From control experiments, we quickly learned that, in fact, several acceptors **A** do undergo the desired 1,4-addition with silyl stannanes **B** in the absence of a rhodium catalyst (**A** → **C**, Scheme 1).[13] In this communication, we report an unpretentious conjugate stannyl transfer requiring neither a transition metal nor exclusion of water.

For simplification, we replaced 1,4-dioxane by THF in these reactions. In contrast to our previous work,[11,12] Et_3N was not effective, which is why we employed NaOAc as well as KOH as activators. We decided to use the novel silyl stannane $Me_3SiSnMe_2Ph$ (**1**)[14,15] in all transformations; in principle, related known silyl stannanes[6b,7–9] do also work in these reactions. Cyclic α,β-unsaturated ketones cleanly underwent the conjugate stannylation in high chemical yields (Table 1).[13] No conversion was seen when the acceptor and **1** were reacted in aqueous THF without NaOAc or KOH.

We next turned to acyclic α,β-unsaturated carbonyl and carboxyl compounds (Table 2).[13] Under reaction conditions identical to those for cyclic enones (Table 1, entries 1–6), chemical yields were markedly decreased for acyclic enones due to competing conjugate reduction (Table 2, entries 1–4). While only minor amounts (5–10%) of the reduced acceptor were formed from a β-alkyl-substituted acceptor (Table 2, entries 1 and 2), appreciable quantities were isolated in the case of a β-arylated substrate (Table 2, entries 3 and 4). A tentative mechanism of this undesired side reaction is outlined further below. Conversely, this 1,4-reduction was virtually not detected

Table 1 Transition-Metal-Free Conjugate Stannylation of Cyclic α,β-Unsaturated Carbonyl Acceptors[13]

Entry	Acceptor	Product[a]	Base	Yield (%)
1			NaOAc	85
2			KOH	60
3			NaOAc	92
4			KOH	72
5			NaOAc	90
6			KOH	93

[a] Satisfactory elemental analyses were obtained.

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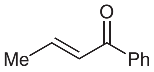
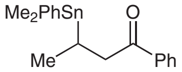
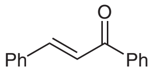
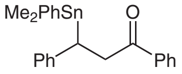
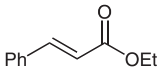
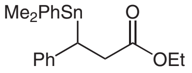
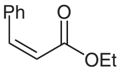
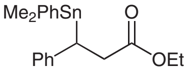
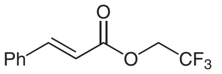
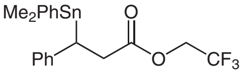
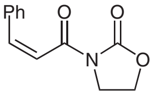
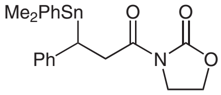
Table 2 Transition-Metal-Free Conjugate Stannylation of Acyclic α,β-Unsaturated Carbonyl and Carboxyl Acceptors[13]

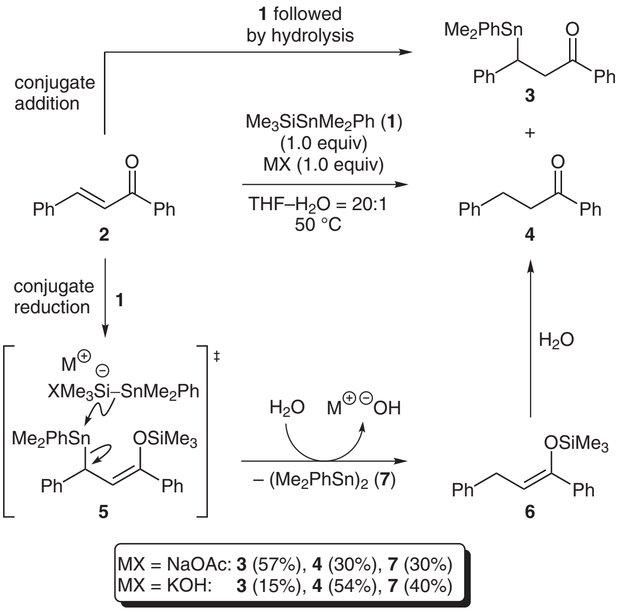
Entry	Acceptor	Product[a]	Base	Conjugate reduction Yield (%)	Conjugate stannylation Yield (%)
1			NaOAc	~5	55
2			KOH	~10	74
3			NaOAc	19	59
4			KOH	30	54
5			NaOAc	<5	57
6			KOH	<5	41
7			NaOAc	<5	22
8			KOH	<5	50
9			NaOAc	0	95
10			KOH	0	54
11			NaOAc	<5	77
12			KOH	<5	83

[a] Satisfactory elemental analyses were obtained except for entries 11 and 12.

for α,β-unsaturated carboxyl compounds, esters and imides (Table 2, entries 5–12). A standard ethyl ester afforded the stannylated product independent of the double bond geometry in modest yields (Table 2, entries 5–8); the more reactive trifluoroethyl ester performed very well (Table 2, entries 9 and 10). Imides are also possible precursors, which undergo the stannylation in high yields (Table 2, entries 11 and 12).

The origin of the aforementioned competition between conjugate addition and reduction might be understood on the basis of an interesting methodology developed by Takeda et al., by which β-aryl (not β-alkyl) α,β-unsaturated carbonyl as well as carboxyl compounds are reduced with the Me_3SiCl–NaI–H_2O reagent.[16] The proposed mechanism involves the 1,4-addition of Me_3SiI forming a β-iodo silyl enol ether with a substantially weakened allylic and benzylic carbon–iodine bond. Nucleophilic attack at iodine by iodide then breaks this bond accompanied by formation of diiodine followed by protolysis.

The same reaction sequence might apply to our $Me_3SiSnMe_2Ph$–MX–H_2O system (**2** → **3** and **4**, Scheme 2). An allylic and benzylic carbon–tin bond in the initially formed β-stannyl silyl enol ether (**2** → **5**) is also relatively labile and might be prone to nucleophilic attack at tin accordingly (**5** → **6**). The nucleophile might be Lewis base-activated **1** (= **1**·MX), a hypervalent silicon intermediate.[17] When exactly one equivalent of **1** was used, almost equimolar amounts of $(Me_2PhSn)_2$ (**7**) and the reduced acceptor **4** with acetate as an activator were isolated; that further supports this assumption (MX = NaOAc). As hydroxide is a good nucleophile itself (MX = KOH), it might also attack at tin in intermediate **5** thus producing more of **4** (54%) than expected on the basis of isolated **7** (40%).



Scheme 2 Tentative ionic mechanism for conjugate reduction

We are also aware of a report by Oshima and Utimoto et al., in which the Et_3B-induced 1,4-reduction of α,β-unsaturated carbonyls using Ph_3SnH is disclosed.[10b] The identical procedure yields β- and α-stannylated products for β-alkyl and β-aryl α,β-unsaturated carboxyls, respectively. We, however, currently rule out radical pathways in our system.

The reaction mechanism of this conjugate stannylation itself is not completely understood. As the presence of a Lewis base is essential, it might involve chemoselective nucleophilic activation of the silyl stannane at the silicon atom;[17] the water tolerance makes the intermediacy of a stannyl anion at least unlikely. Interaction of thus-activated silyl stannane with the carbonyl/carboxyl oxygen resulting in 1,2-addition followed by 1,3-allylic transposition[3] or direct 1,4-addition are conceivable scenarios.

In summary, we have elaborated a facile water-tolerant protocol for the 1,4-addition of a triorganostannyl group avoiding the generation of sophisticated tin-based organometallic reagents. We believe that these reaction conditions would be excellent for an asymmetric phase-transfer catalysis.[18]

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(12) For conjugate phosphination using silyl phosphines, see: Trepohl, V. T.; Oestreich, M. *Chem. Commun.* **2007**, 3300.

(13) **General Procedure for Conjugate Stannylation**: Under an inert atmosphere, a flame-dried Schlenk tube was charged with the indicated α,β-unsaturated acceptor **A** (0.10 mmol, 1.0 equiv) and the THF–H_2O solvent mixture (20:1, 2.1 mL). The base MX (0.1 mmol, 1.0 equiv) as well as **B** (**1**, 0.25 mmol, 2.5 equiv) were added, and the reaction mixture was heated to 50 °C. Conversion was monitored by TLC. After full consumption of **A** the reaction mixture was diluted with *tert*-butylmethylether (10 mL) at r.t. A small portion of silica gel was added and the solvents were removed in vacuo. The crude product **C** on silica gel was then subjected to flash chromatography on Et_3N-deactivated silica gel using cyclohexane–*tert*-butylmethylether solvent mixtures. Stannanes **C** (22–95%) were isolated as colorless oils.

(14) Reagent **1** is not particularly volatile, stable towards GLC measurements, and provides easy-to-interpret NMR spectra.

(15) **Preparation of Dimethylphenyl(trimethylsilyl)stannane (1)**: Neat dimethylphenylstannyl chloride[19] (3.00 g, 11.5 mmol, 1.00 equiv) was added dropwise to Me_3SiCl-activated lithium (large excess) in THF (40 mL) at 0 °C under ultrasonic irradiation, and the reaction mixture was then maintained at these conditions for 2 h. The supernatant blue-black-colored solution was subsequently transferred to another flask and slowly treated with trimethylsilyl chloride (3.10 mL, 24.3 mmol, 2.10 equiv) at 0 °C. After stirring at ambient temperature for additional 3 h, the solvent was removed under reduced pressure. Crude **1** was purified by flash chromatography on silica gel using cyclohexane as solvent. The title compound (3.22 g, 10.8 mmol, 94%) was obtained as a colorless oil. IR (ATR): 3062 (w), 2950 (w), 2893 (w), 1427 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.26$ [t, $^2J_{H,Sn} = 24$ Hz, 6 H, $SnMe_2$], 0.29 [t, $^3J_{H,Sn} = 3.0$ Hz, 9 H, $SiMe_3$], 7.27–7.55 (m, 5 H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -11.3$ [$SnMe_2$], 1.3 [$SiMe_3$], 128.2, 128.5, 137.1, 142.0 (Ph). ^{29}Si NMR (60 MHz, $CDCl_3$): $\delta = -9.3$. ^{119}Sn NMR (112 MHz, $CDCl_3$): $\delta = -138.9$. Anal. Calcd for $C_{11}H_{20}SiSn$: C, 44.18; H, 6.74. Found: C, 44.30; H, 7.01.

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