## Regioselective Buta-1,3-dienylation of Aldehydes via Transmetallation of 2-Tributylstannylbuta-1,3-diene

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**Abstract:** Transmetallation of 2-tributylstannylbuta-1,3-diene with SnCl<sub>4</sub> followed by Lewis base promoted addition of the resulting 1-trichlorostannyl-2,3-butadiene to aldehydes in the presence of DMF allows their buta-1,3-dienylation to take place at the C2 position with complete regioselectivity in high yields.

**Key words:** buta-1,3-dienes, tin compounds, transmetallations, buta-1,3-dienylations, Lewis base promoted reaction

Dienols of general structure 1 are valuable precursors for the syntheses of a variety of natural products.<sup>1,2</sup> Buta-1,3dienylation of aldehydes utilizing 2-metallated buta-1,3dienes 2 derived from 2-chlorobuta-1,3-diene (chloroprene), an industrial material, is obviously the simplest approach for the synthesis of 1 although several other methods have already been developed.<sup>3</sup> However, existing methods<sup>4</sup> using 2 (M = MgCl or Li) following this approach have the serious disadvantage of poor regioselectivity or low chemical yield. We now report a facile and efficient buta-1,3-dienvlation of aldehydes giving 1 with complete regioselectivity by use of 2-tributylstannylbuta-1,3-diene 3, readily available from chloroprene.3e,5



Allylstannanes are known to react with Lewis acids  $(MX_n)$  to generate the corresponding allylmetal compounds through a transmetallation process normally with migration of the olefinic double bond.<sup>6</sup> We envisaged that such transmetallation of 2-tributylstannylbuta-1,3-diene **3** would produce buta-2,3-dienylmetal **4**, which is expected to react with aldehydes in 1,3-rearrangement fashion<sup>7</sup> to give dienols **1**.



Scheme 1

To assay the possibility of the above-mentioned approach we first surveyed various Lewis acids  $(SnCl_4, ^6 BCl_3,$  $TiCl_4$ ,<sup>6</sup> SiCl\_4, InCl\_3,<sup>8</sup> CoCl\_2<sup>9</sup>) in the reaction of **3** with hydrocinnamaldehyde. Thus, 2-tributylstannylbuta-1,3-diene **3** was treated with Lewis acid in  $CH_2Cl_2$  and after disappearance of 3 on TLC, hydrocinnamaldehyde was added to the reaction mixture. As shown in Table 1,<sup>10</sup> only SnCl<sub>4</sub> and BCl<sub>3</sub> turned out to promote the desired reaction to give dienol 1 ( $R = CH_2CH_2Ph$ ) although the yields were moderate (entries 2 and 4). 2-Tributylstannylbuta-1,3-diene 3 itself did not react with hydrocinnamaldehyde even under refluxing conditions when no Lewis acid was used (entry 1). It should be stressed that addition of DMF, HMPA, or isoquinoline N-oxide dramatically improved the yield of this reaction, in particular, when  $SnCl_4$  was used for the transmetallation (entries 5-7 and 9).





Entry	Lewis acid	Additive <sup>b</sup>	T (°C)	Time (h)	Yield $(\%)^{e}$
1	none	none	reflux	12	$0^{f}$
2	BCl <sub>3</sub>	none	-78 <sup>d</sup>	2	37
3	BCI,	DMF	rt	9	51
4	SnCl₄	none	$-30^{d}$	4	30
5	SnCl <sub>4</sub>	DMF	rt	12	88
6	SnCl <sub>4</sub>	$DMF^{c}$	rt	6	82
7	SnCl <sub>4</sub>	HMPA	rt	8	81
8	SnCl <sub>4</sub>	CH <sub>3</sub> CN <sup>c</sup>	0	2	52
9	SnCl <sub>4</sub>	isoquinoline N-oxide	rt	18	72

<sup>a</sup> See the representative procedure in ref. 10. <sup>b</sup> 3 equiv. of additive were used unless otherwise stated. <sup>c</sup> Half volume of  $CH_2Cl_2$  was used. <sup>d</sup> A complex mixture was obtained when the reaction was carried out at room temperature. <sup>e</sup> Isolated yield. <sup>f</sup> No reaction.

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Table 2 summarizes  $SnCl_4$  promoted addition of **3** to various aldehydes. It is evident that this reaction proceeds with complete regioselectivity and has broad applicability for the preparation of **1**. Entry 6 clearly indicates the chemoselectivity of this reaction and an acetal group is intact under the reaction conditions, showing its advantage in comparison with other buta-1,3-dienylations.<sup>3</sup> The diastereoselectivity of this reaction can be also evaluated by the examples listed in entries 7-9 and high *anti*-selectivity (80% de) was observed in the case of 2,3-*O*-isopropylidene-D-glyceraldehyde.

**Table 2.** SnCl<sub>4</sub> promoted addition of **3** to aldehydes giving  $1^{a}$ 



Entry	R	T (°C)	Time (h)	Yield (%) <sup>b</sup>
1	Ph	rt	12	89
2	PhCH <sub>2</sub>	rt	12	73
3	(E)-PhCH=CH	rt	12	70 (98) <sup>°</sup>
4	$CH_3(CH_2)_6$	rt	12	82
5	$c - C_6 H_{11}$	rt	12	79
6	$(CH_3O)_2CH(CH_2)_2$	0	4.5	69
7	Ph(CH <sub>3</sub> )CH	rt	12	$65(58:42)^{a}$
8	CH <sub>3</sub> (OBn)CH	rt	12	92 (60 : 40) <sup>e</sup>
9	$\frac{1}{2}$	rt	12	98 (90 : 10) <sup>e</sup>

<sup>a</sup> See the representative procedure in ref. 10. <sup>b</sup> Isolated yield. <sup>c</sup> Yield in parenthesis based on the consumed aldehyde. <sup>d</sup> Not determined which is *anti*- or *syn*-isomer. <sup>e</sup> *anti* : *syn*.

In order to further understand this reaction, the following NMR experiments were undertaken. Thus, 3 was treated with 1 equivalent of  $SnCl_4$  at -60 °C in CDCl<sub>3</sub> and after completion of the transmetallation, 3 equivalent of DMF were added and then the mixture was allowed to warm to room temperature. After 30 min at room temperature, 1-trichlorostannylbuta-2,3-diene 5<sup>11</sup> and 2-trichlorostannylbuta-1,3-diene  $6^{12}$  were observed in a ratio of ca. 1:1 each as complex with DMF and this ratio changed only slightly even after 6 h.13 Interestingly, when hydrocinnamaldehyde was added to this mixture, dienol 1  $(R = CH_2CH_2Ph)$  was produced in ca. 40% yield by <sup>1</sup>H NMR-measurement. On the other hand, in a control experiment without DMF, 5 isomerized to 6 completely within 6 h and addition of hydrocinnamaldehyde and DMF to this mixture did not cause production of dienol 1  $(R = CH_2CH_2Ph)$  at all. These results suggest that addition of DMF retards the isomerization rate from 5 to 6 by coordination and only coordinated **5** participates in the reaction with an aldehyde possibly via six-centered cyclic transition structure **7** even if both **5** and **6** exist as coordinated complexes. This reaction, therefore, can be regarded as Lewis base promoted reaction of 1-trichlorostannylbuta-2,3-dinene with an aldehyde, similar to the recently discovered reactions of allylhalosilanes<sup>14</sup> and allylhalostannanes.<sup>6c,15</sup>



Scheme 2

In conclusion, we have developed a simple buta-1,3-dienylation of aldehydes giving **1** using readily available 2tributylstannylbuta-1,3-diene **3** as the diene source. The present work exhibits the first example of Lewis base promoted reaction of 1-trichlorostannylbuta-2,3-dinene **5** prepared in situ by transmetallation of 2-tributylstannylbuta-1,3-diene **3** with SnCl<sub>4</sub>. The development of an asymmetric version of this reaction using a chiral Lewis base ligand is the focus of current investigations.

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- (10) Representative procedure (entry 5 in Table 1): To a stirred solution of **3** (342 mg, 1.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (4 ml) at -78 °C under argon was added SnCl<sub>4</sub> (117 µl, 1.0 mmol). After stirring at -78 °C for 45 min, DMF (232 µl, 3.0 mmol) was added and the mixture was stirred at -78 °C for 10 min. Hydrocinnamaldehyde (67 mg, 0.5 mmol) was added and the mixture was basified with 5% NaOH (5 ml) and extracted with Et<sub>2</sub>O. The extract was washed with water, dried over MgSO<sub>4</sub>, and concentrated in vacuo. Purification by column chromatography [SiO<sub>2</sub> (10 g) pretreated with Et<sub>3</sub>N (1 g), *n*-hexane : AcOEt = 8:1] afforded **1** (R = Ph(CH<sub>2</sub>)<sub>2</sub>) (82.5 mg, 88%).
- (11) <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  5.37 (m), 5.01 (dt, *J* = 6.6, 2.5 Hz, 2H), 3.03 (dt, *J* = 8.2, 2.5 Hz, 2H); <sup>2</sup>*J*(<sup>117 and 119</sup>Sn-<sup>1</sup>H) are

not given. When DMF was added, two methylene peaks shifted to 4.84 and 2.65, respectively but the corresponding methine peak could not be clearly identified.

- (12) <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  6.75 (dd, *J* = 16.8, 10.2 Hz, 1H), 6.23 (s, 1H), 5.90 (s, 1H), 5.56 (d, *J* = 16.8 Hz, 1H), 5.56 (d, *J* = 10.2 Hz, 1H)); <sup>2</sup>*J*(<sup>117 and 119</sup>Sn-<sup>1</sup>H) are not given. When DMF was added, these peaks shifted to 6.72, 6.15, 5.89, 5.43, and 5.32, respectively.
- (13) DMF-complex of **5** isomerized to DMF-complex of **6** almost completely 30 h later.
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