

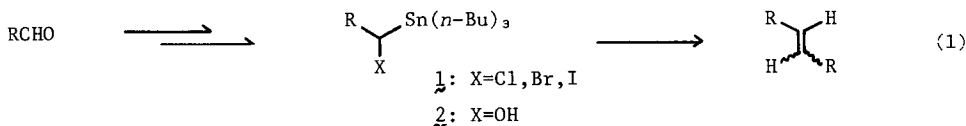
A NEW ALKYL TIN(IV)-MEDIATED COUPLING REACTION OF ALDEHYDES TO OLEFINS

Yasuhiro Torisawa, Masakatsu Shibasaki, and Shiro Ikegami\*

Faculty of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa 199-01, Japan

*Summary: Various olefins were synthesized by coupling reactions via the corresponding  $\alpha$ -stannylalkyl halides derived from aldehydes. A cross-coupling reaction using the different types of  $\alpha$ -stannylalkyl halides, based on the difference of their reactivities, was also achieved.*

In the course of our studies on natural product synthesis, we had a chance to investigate some synthetic utilities of  $\alpha$ -stannylalkyl halides (1), and have found a new interesting reactivity of 1, which allows a new coupling reaction of aldehydes to olefins as shown in eq. 1.



It has been found that 1 can be prepared efficiently from stannyl-carbinols (2) obtainable from the corresponding aldehydes according to Still's method.<sup>2</sup> In contrast to the rather unstable character of stannyl-carbinols (2),<sup>3</sup>  $\alpha$ -stannylalkyl halides (1) are unexpectedly stable and in handling, difficulties were not encountered.<sup>4</sup>

$\alpha$ -Stannylalkyl bromides<sup>5</sup> have been obtained in nearly quantitative yields by the reaction of stannyl-carbinols with triphenylphosphine and carbon tetrabromide in methylene chloride at room temperature for 1 hr.<sup>6</sup> On the other hand,  $\alpha$ -stannylalkyl chlorides could be prepared by treatment of stannyl-carbinols with 2 equiv of tosyl chloride in pyridine at room temperature for 5-7 hr in 60-70% yields,<sup>7</sup> and alternatively by reaction with triphenylphosphine and diethyl azodicarboxylate in methylene chloride at room temperature for 24 hr<sup>6,8</sup> in 60-70% yields. Similarly  $\alpha$ -stannylalkyl iodides could be prepared by treatment of stannyl-carbinols with triphenylphosphine, diethyl azodicarboxylate and methyl iodide in benzene at room temperature for 48 hr.<sup>6</sup> The results obtained with six stannyl-carbinols are summarized in Table I.<sup>9</sup>

Having established an efficient method for the preparation of various  $\alpha$ -stannylalkyl halides (1), we then turned our attention to some synthetic utilities of these  $\alpha$ -stannylalkyl halides.<sup>10</sup> As a first attempt, expecting the production of the  $\alpha$ -halocarbanion, the  $\alpha$ -stannylalkyl bromide derived from 4-phenylbutanal was treated with 1.2 equiv of *n*-butyllithium in THF at -78°. The starting  $\alpha$ -stannylalkyl bromide disappeared in a few minutes by rapid tin-lithium exchange, resulting in the clean formation of two major products (Entry 2, Table II). One of the major products was easily identified with tetra-*n*-butyltin and the other obtained in 60%

Table I. Conversion of Stannyl-Carbinols to  $\alpha$ -Stannylalkyl Halides
$$\begin{array}{c} \text{R} \\ | \\ \text{C} - \text{Sn}(n\text{-Bu})_3 \\ | \\ \text{OH} \end{array} \longrightarrow \begin{array}{c} \text{R} \\ | \\ \text{C} - \text{Sn}(n\text{-Bu})_3 \\ | \\ \text{X} \end{array}$$

Entry	R	Conditions	X	Yield, %
1	Ph(CH <sub>2</sub> ) <sub>2</sub>	a	Cl	65
2	Ph(CH <sub>2</sub> ) <sub>2</sub>	b	Cl	65
3	Ph(CH <sub>2</sub> ) <sub>2</sub>	c	Br	~100
4	Ph(CH <sub>2</sub> ) <sub>2</sub>	d	I	60
5	Ph(CH <sub>2</sub> ) <sub>3</sub>	c	Br	~100
6	PhCH <sub>2</sub> O(CH <sub>2</sub> ) <sub>4</sub>	c	Br	~100
7	PhCH(CH <sub>3</sub> )CH <sub>2</sub>	c	Br	~100
8	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub>	c	Br	90
9	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub>	d	I	50
10	Ph(CH <sub>2</sub> ) <sub>2</sub> CH(CH <sub>3</sub> )	c	Br	~100

a: TsCl-pyridine, r.t., 7 hr. b: (Ph)<sub>3</sub>P-DAD-CH<sub>2</sub>Cl<sub>2</sub>, r.t., 24 hr. c: (Ph)<sub>3</sub>P-CBr<sub>4</sub>-CH<sub>2</sub>Cl<sub>2</sub>, r.t., 1 hr. d: (Ph)<sub>3</sub>P-DAD-CH<sub>3</sub>I-PhH, r.t., 48 hr.

Table II. Conversion of  $\alpha$ -Stannylalkyl Halides to Olefins
$$\begin{array}{c} \text{R} \\ | \\ \text{C} - \text{Sn}(n\text{-Bu})_3 \\ | \\ \text{X} \end{array} \longrightarrow \begin{array}{c} \text{R} \quad \text{H} \\ \diagdown \quad / \\ \text{C} = \text{C} \\ / \quad \diagdown \\ \text{H} \quad \text{R} \end{array}$$

Entry	R	X	Yield, % <sup>a</sup>	<i>trans:cis</i> <sup>b</sup>	
1	Ph(CH <sub>2</sub> ) <sub>2</sub>	Cl	65	77	23
2	Ph(CH <sub>2</sub> ) <sub>2</sub>	Br	65	79	21
3	Ph(CH <sub>2</sub> ) <sub>2</sub>	I	60	50	50
4	Ph(CH <sub>2</sub> ) <sub>2</sub>	OMs <sup>c</sup>	25	35	65
5	Ph(CH <sub>2</sub> ) <sub>3</sub>	Br	60	79	21
6	PhCH <sub>2</sub> O(CH <sub>2</sub> ) <sub>4</sub>	Br	32	91	9
7	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub>	Br	60 <sup>d</sup>	87	13
8	PhCH(CH <sub>3</sub> )CH <sub>2</sub>	Br	73 <sup>e</sup>	-	-
9	Ph(CH <sub>2</sub> ) <sub>2</sub> CH(CH <sub>3</sub> )	Br	0	-	-

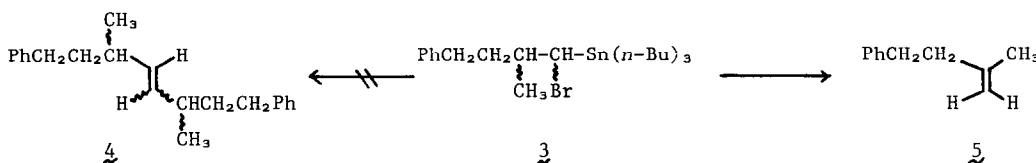
a: Isolated yield is shown. b: *trans:cis* Ratio was determined by glpc analysis. c: The stannyl-mesylates could be prepared from stannyl-carbinols in nearly quantitative yields by treatment with mesyl chloride and triethylamine in methylene chloride at -25°C. d: The olefinic product was converted to the epoxide to separate from tetra-*n*-butyltin and at this stage the yield was determined. e: The product consisted of a mixture of the *threo* and *erythro* isomers, and therefore, a ratio of *trans:cis* was not determined.

yield was surprisingly found to be the olefinic compounds in a ratio of 79(*trans*): 21(*cis*) (Entry 2, Table II), which were probably formed via an intermolecular nucleophilic substitution and subsequent elimination. Since this reaction provides an alternative method for the coupling of aldehydes to olefins, which can be carried out under rather mild conditions in comparison

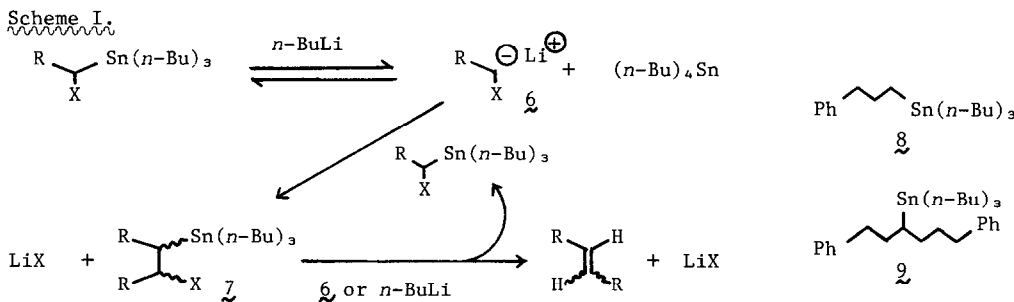
with the reported methods,<sup>11</sup> we were interested in the applicability of this new coupling reaction to synthetic chemistry. The results of olefin formation are summarized in Table II.

$\alpha$ -Stannylalkyl chlorides could be rapidly converted to the corresponding olefins even at  $-78^\circ\text{C}$  like the bromides (Entry 1, Table II), while the iodides were found to be less reactive under the same conditions and it was necessary to warm up the reaction mixture to  $0^\circ\text{C}$  to allow tin-lithium exchange and subsequent olefin formation<sup>12</sup> (Entry 3, Table II).

Different from  $\alpha$ -stannylalkyl halides prepared from aldehydes carrying no substituent on the  $\alpha$ -carbon, the  $\alpha$ -stannylalkyl bromide (**3**) obtainable from 2-methyl-4-phenylbutanal furnished no coupling product (**4**). However, 2-methyl-4-phenyl-1-butene (**5**) was exclusively formed in 83% yield, presumably via the carbene intermediate,<sup>13</sup> indicating that this reaction will be useful for the conversion of aldehydes containing one  $\alpha$ -substituent to terminal olefins such as **5**.



In regard to a possible mechanism for a new carbon-carbon bond forming reaction, it seems likely that the reaction of the lithiocarbanion (**6**), generated by tin-lithium exchange, with a  $\alpha$ -stannylalkyl halide is much faster than the nucleophilic attack by *n*-butyllithium, resulting in the coupled  $\beta$ -stannylalkyl halide (**7**), which is immediately followed by destannylation with the lithiocarbanion (**6**) or *n*-butyllithium to provide an olefinic coupling product as shown in Scheme I. This mechanism was also supported by the following fact. The reaction of the  $\alpha$ -stannylalkyl bromide (Entry 2, Table II) with *n*-butyllithium yielded two minor products (**8** in 5% yield and **9** in 8% yield), which were resulted from anions formed by the competitive bromine-lithium exchange of the starting bromide (**1**) and the coupled  $\beta$ -stannylalkyl bromide (**7**), in addition to the major olefinic coupling product.



Although the present reaction offers an alternative method for the coupling of aldehydes to olefins, it has been restricted to the preparation of homo-coupled products. On the bases of the observation that  $\alpha$ -stannylalkyl iodides are fairly stable under mild tin-lithium exchange conditions ( $-78^\circ\text{C}$ ) and the expectation that  $\alpha$ -stannylalkyl iodides should be more easily attacked by nucleophiles than  $\alpha$ -stannylalkyl chlorides, possibilities for development of a cross-coupling reaction were pursued.

A solution of the iodide (**10**) (1mM) and the chloride (**11**) (1mM) in THF was treated with *n*-

