



**Copper(I) Iodide-Catalyzed Regioselective Allylation of  
 $\alpha$ -(2-Pyridylthio)allylstannanes.  
A New Route to  $\delta,\epsilon$ -Unsaturated Ketones**

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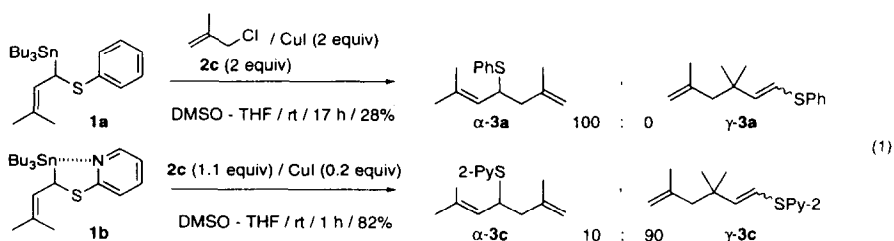
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**Abstract:** The reaction of  $\alpha$ -(2-pyridylthio)allylstannanes with allylic halides in the presence of a catalytic amount of copper(I) iodide in DMSO-THF produced the 1,5-dienes **3** in good yields. The  $\gamma$ -selective allylation using allyl chloride followed by the alkylation and hydrolysis of resulting vinyl sulfides gave  $\delta,\epsilon$ -unsaturated ketones. © 1997 Elsevier Science Ltd.

Recently efforts have been directed toward the investigation of the copper(I) salt promoted reaction of organotin compounds because of their synthetic utility and interest in their reaction mechanism.<sup>1</sup> In the course of studying reactions utilizing vinylstannanes, we recently found that copper(I) iodide-promoted allylation of various vinylstannanes with allylic halides occurred under mild reaction conditions in DMSO-THF.<sup>2</sup> This result suggests that the combined use of copper(I) iodide and allylic halides in dipolar aprotic solvents promotes the allylation of organotin compounds and prompted us to examine the broader application to allylstannanes.<sup>3</sup> Although the allylation of simple allylstannanes was found to be unsuccessful,<sup>4</sup> the reaction of 2-methyl-4-phenylthio-4-tributylstannylbut-2-ene (**1a**) with methallyl chloride (**2c**) in the presence of copper(I) iodide in DMSO-THF gave the  $\alpha$ -allylated product  $\alpha$ -**3a** in 28% yield, along with a small amount of unreacted starting material. The yield of allylated product was greatly improved when the allylstannane contained a 2-pyridylthio group (Eq. 1). What is striking is that this allylation proceeded with high  $\gamma$ -regioselectivity; opposite to that observed in the well-known allylation of lithium derivatives of allylic sulfides.<sup>5</sup>

It is assumed that the intramolecular coordination of nitrogen to tin as depicted in Eq. 1, or coordination to copper as an organocopper intermediate [f,j],<sup>6</sup> largely facilitates the reaction and probably is a major factor governing the high regioselectivity. This idea was substantiated when 2-methyl-4-(4-pyridylthio)-4-tributylstannylbut-2-ene, in which the intramolecular coordination is unlikely, was reacted with **2c** at room temperature for 24 h. No allylated product was observed and 72% of the starting material was recovered.

The  $\gamma$ -allylation of allylic sulfides<sup>7</sup> is of special interest because the products possess a vinyl sulfide



moiety which can be transformed into a variety of functional groups. We have further examined the regioselectivity of this copper(I)-catalyzed allylation of  $\alpha$ -(2-pyridylthio)allylstannanes **1b**, **c**, **d**, **e** and  $\gamma$ -(2-pyridylthio)allylstannane (**1f**) in detail (Eq. 2). As shown in Table 1, the allylated products **3** were produced in good yields using various allylic halides and a catalytic amount of copper(I) iodide. Variation of the leaving group on methallyl halide was found to favor  $\gamma$ -allylation in the order: Cl > Br > I (Entries 5, 6, and 7). The same trend was also observed for those reactions using allyl halides (Entries 1, 3, and 4). In general,  $\gamma$ -selectivity seems to decrease as the allyl halide becomes more substituted (Entries 1, 5, and 8). When less substituted allylstannanes were employed,  $\gamma$ -allylated product predominated in all cases (Entries 9-18). Allylation was also found to proceed when DMF (Entry 2) or protic solvent such as EtOH was employed. For instance, reaction of **1b** with **2c** carried out using DMSO-EtOH for 4.5 h gave the allylated product **3c** ( $\alpha : \gamma = 28 : 72$ ) in 73% yield along with a small amount of the protodestannylated compound, prenyl 2-pyridyl sulfide (8%).

The following is a typical experimental procedure. To a flask charged with copper(I) iodide (38 mg, 0.2 mmol) was sequentially added DMSO (1 ml), a THF (3 ml) solution of 5-phenyl-1-(2-pyridylthio)-1-tributylstannylpent-2-ene (**1d**) (544 mg, 1 mmol), and allyl chloride (**2a**) (84 mg, 1.1 mmol) at room temperature under argon. After being stirred for 1 h, the reaction was quenched with 20 ml of 3.5% aqueous ammonia. The organic materials were extracted with ether, dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated. The residue was purified by column chromatography using silica gel (deactivated with 5 wt% of water) (hexane : AcOEt = 4 : 1) to give 3-(2-phenylethyl)-1-(2-pyridylthio)hexa-1,5-diene ( $\gamma$ -**3g**) (264 mg, 89%).

The synthetic utility of the product obtained by  $\gamma$ -selective allylation was demonstrated in the following synthesis of  $\delta,\epsilon$ -unsaturated ketones **4** (Eq. 3). 3-Phenyl-1-(2-pyridylthio)hexa-1,5-diene ( $\gamma$ -**3e**), obtained from Entry 9, was initially treated with butyllithium (1.1 equiv) in the presence of *N,N,N',N'*-tetramethylethylenediamine (TMEDA) (1.1 equiv) in THF at -78 °C for 30 min. Subsequent reaction with iodomethane (1.5 equiv) at -78 °C for 30 min and then at room temperature for 1 h afforded 4-phenyl-6-(2-pyridylthio)hepta-1,5-diene (**5a**) in 84% yield. Several reagents, such as mercury(II) chloride,<sup>8</sup> copper(II) chloride-copper(II) oxide,<sup>9</sup> and titanium(IV) chloride,<sup>10</sup> have been used for the hydrolysis of vinyl sulfides to carbonyl compounds. Unfortunately, we were unable to hydrolyze **5a** with any of these reagents due to the preferential formation of insoluble complexes of metal salts with the pyridine moiety. Alternatively, **5a** was treated with methyl *p*-toluenesulfonate (5 equiv) in DMF (90-100 °C / 25 h), followed by 1 M NaOH, to form the corresponding methyl sulfide **6a** in 80% yield. The hydrolysis of **6a** with mercury(II) chloride-MeCN-H<sub>2</sub>O (50 °C / 2 h) gave the  $\delta,\epsilon$ -unsaturated ketone **4a**. As shown in Table 2, several  $\gamma$ -allylated compounds  $\gamma$ -**3** were transformed to the unsaturated ketones **4** in good overall yields using above procedure.

Although the reaction mechanism and the role of the copper(I) salt are still unclear, the present study shows that the copper(I) iodide facilitates the reaction of certain organotin compounds with electrophiles when in the presence of dipolar solvent such as DMSO or DMF. We are continuing work in this area to further explore copper(I)-mediated reactions of organotin compounds.

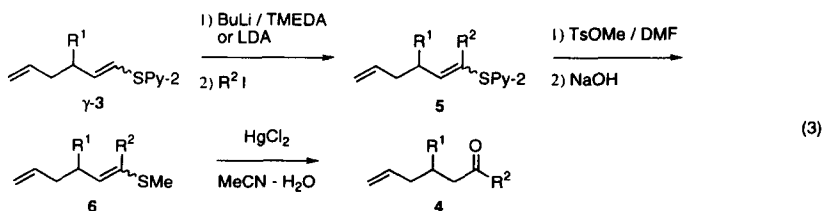
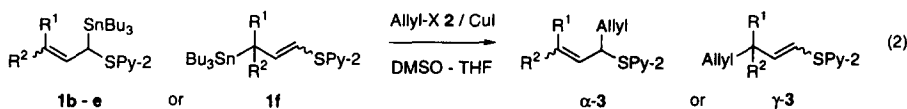
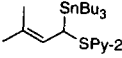


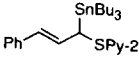




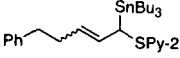
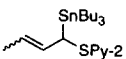

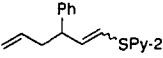
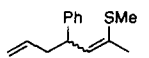
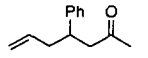
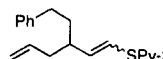
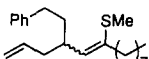
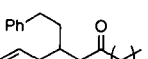
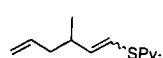
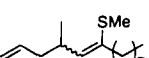
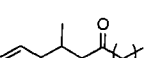
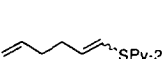
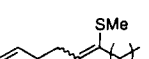
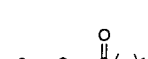


Table 1. The Reaction of  $\alpha$ -(2-Pyridylthio)allylstannanes **1** with Allylic Halides **2**<sup>a)</sup>

Entry	<b>1</b>	<b>2</b>	<b>Time</b> h	<b>3</b> <sup>b)</sup> (Yield / %)	Stereoisomeric ratios <sup>c)</sup>		
					$\alpha$ : $\gamma$	$E$ : $Z$ <sup>d)</sup>	
1			<b>2a</b>	2	<b>3b</b> (82)	$\gamma$ only	$E$ only
2c)		<b>2a</b>		6	<b>3b</b> (86)	$\gamma$ only	$E$ only
3	<b>1b</b>		<b>2b</b>	0.5	<b>3b</b> (82)	18 : 82	$E$ only
4		<b>2a</b> / NaI <sup>f)</sup>		18	<b>3b</b> (55)	75 : 25	$E$ only
5			<b>2c</b>	1	<b>3c</b> (82) <sup>g)</sup>	10 : 90	$E$ only
6			<b>2d</b>	1.5	<b>3c</b> (82)	26 : 74	$E$ only
7			<b>2e</b>	14	<b>3c</b> (71)	59 : 41	$E$ only
8			<b>2f</b>	1	<b>3d</b> (72) <sup>h)</sup>	87 : 13	$E$ only
9	<b>1c</b>	<b>2a</b>		1.5	<b>3e</b> (90) <sup>g)</sup>	$\gamma$ only	42 : 58
10		<b>2b</b>		1	<b>3e</b> (84)	9 : 91	55 : 45
11		<b>2c</b>		0.5	<b>3f</b> (82)	$\gamma$ only	76 : 24
12		<b>2a</b>		1	<b>3g</b> (89)	$\gamma$ only	51 : 49
13		<b>2a</b>		1	<b>3h</b> (84)	$\gamma$ only	56 : 44
14		<b>2c</b>		1	<b>3i</b> (77)	$\gamma$ only	75 : 25
15		<b>2d</b>		0.5	<b>3i</b> (63)	$\gamma$ only	81 : 19
16		<b>2a</b>		1.5	<b>3j</b> (83) <sup>g)</sup>	$\gamma$ only	57 : 43
17		<b>2c</b>		1.5	<b>3k</b> (70)	$\gamma$ only	76 : 24
18		<b>2d</b>		0.5	<b>3k</b> (82)	$\gamma$ only	80 : 20

a) All reactions were performed following the procedure described in the text, unless otherwise noted. b) The structures of these compounds were assigned by IR and NMR spectra. c) Determined by NMR spectroscopy. d) The ratio of stereoisomers of  $\gamma$ -allylated product  $\gamma$ -**3**. e) DMF (4 ml / 1 mmol of **1b**) was used as a solvent. f) 1.1 equiv of NaI was used. g) The product was contaminated by a small amount of the protodestannylated compound (2-3%) and the yield was corrected for the contaminant. h) The formal SN<sub>2</sub> and SN<sub>2</sub>' products of  $\alpha$ -**3** were formed in a ratio of 37 : 63, respectively. As for the  $\gamma$ -allylated product  $\gamma$ -**3**, the ratio of isomers was not determined. i)  $E$  :  $Z$  = 90 : 10. j)  $E$  :  $Z$  = 66 : 34. k)  $E$  :  $Z$  = 38 : 62.

Table 2. The Transformation of  $\gamma$ -Allylated Products  $\gamma$ -3 to  $\delta,\epsilon$ -Unsaturated Ketones 4.

Entry	$\gamma$ -3	R <sup>2</sup> I	6a) (Overall yield from $\gamma$ -3 / %)	4a) (Yield / %)
1		iodomethane	 6a (67)	 4a (76)
2		1-iodooctane <sup>b</sup> )	 6b (66)	 4b (58)
3		1-iodooctane <sup>b</sup> )	 6c (70)	 4c (72)
4		1-iodooctane <sup>b</sup> )	 6d (68)	 4d (80)

a) The structures of these compounds were assigned by IR and NMR spectra. b) The preparation of vinylolithium was performed using lithium diisopropylamide (LDA) (1.5 equiv / -40 °C / 30 min) and the reaction with 1-iodooctane (2 equiv) was carried out at -40 °C for 30 min and then at room temperature for 1 h in THF-HMPA.

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