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#### COMMUNICATION

# Synthesis of Aryl Trimethylstannanes from Aryl Halides: An Efficient Photochemical Method

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An efficient transition-metal-free photochemical method featuring excellent functional group tolerance, mild reaction conditions and short reaction times has been discovered and developed for the synthesis of (hetero)aryl trimethylstannanes from (hetero)aryl halides. A photo-initiated radical chain mechanism was proposed based on preliminary mechanistic studies.

Through the palladium-catalysed C-C bond forming Stille reaction,<sup>[1]</sup> as synthetic building blocks, organotin reagents have found broad applications in synthesis of bioactive natural products,<sup>[2]</sup> drugs<sup>[3]</sup> and functional materials.<sup>[4]</sup> Carbonheteroatom bonds including C-N, C-F, C-OCF<sub>3</sub> bonds can also be reached by transformations of the C-Sn bond.<sup>[5]</sup> The conventional methods to generate arylstannane compounds involved reactions of arylmetallic intermediates with trialkyltin chloride (Scheme 1a).<sup>[6]</sup> In the past decades, catalytic stannylation reaction has been developed for conversion from Ar-X bond to Ar-Sn bond where X is a (pseudo)halide (Scheme **1b**).<sup>[7]</sup> A direct C-H stannylation of polyfluoroarenes based on transition-metal catalyst has also been reported.<sup>[8]</sup> Two transition-metal-free approaches toward Ar-Sn bond formation have been developed. Thus, the  $S_{\mbox{\tiny RN}}1$  reaction of aryl ammonium, or in some cases an aryl halide, with trialkylstannyl anion in liquid ammonia formed aryl stannane (Scheme 1c).<sup>[9]</sup> This reaction suffered from limited functional group tolerance and the inconvenience to handle liquid ammonia. A more direct and general stannylation method from aryl amines, under Sandmeyer-type conditions, was recently developed by Wang and co-workers (Scheme 1d).<sup>[10]</sup> In this case, an aryl radical, generated from the intermediate aryl diazonium salt, has been proposed in the possible mechanism.

Recently, we have been interested in developing new C-B and C-Si bond-forming reactions either via transition-metal mediated processes<sup>[11]</sup> or via radical pathways.<sup>[12]</sup> During these efforts, we have developed a borylation reaction of aryl

iodides and bromides under UV light irradiation.<sup>[13]</sup> This reaction features short reaction times, very mild conditions and broad functional group compatibility. Preliminary mechanistic investigations have suggested a reaction pathway involving aryl radical intermediates. Inspired by these results and Wang's Sandmeyer-type stannylation,<sup>[10]</sup> we hypothesized a photolytic stannylation reaction (Scheme 1e). Herein, we wish to report this transition-metal-free method for the synthesis of aryl trimethylstannanes from aryl halides using light as a clean reagent.

a) Ar-M + R₃SnCl ───►	Ar-SnR <sub>3</sub>						
(M = Mg, Li, Zn)							
b) Ar-X + R₃Sn-SnR₃ cat. [Pd or Ni]	Ar-SnR <sub>3</sub>						
(X = halogen, OTf)							
c) Ar-X + R₃Sn⁻ →	Ar-SnR <sub>3</sub>						
(X = NMe <sub>3</sub> , halogen)							
d) Ar-NH₂ + Me₃Sn-SnMe₃ <u>t-BuONO</u>	Ar-SnMe <sub>3</sub>						
e) this work							
Ar-X + Me₃Sn-SnMe₃ — hv →	Ar-SnMe <sub>3</sub>						
(X = I, Br, CI)							

 $\label{eq:scheme 1} \ensuremath{\mathsf{Scheme 1}}\xspace \ensuremath{\mathsf{Previous synthetic methods of aryl stannane compounds and the outline of this work}$ 

Initially, a solution of 4-iodoanisole (1a, 0.2 mmol, c = 0.1 M) and hexamethyldistannane (SnMe<sub>3</sub>)<sub>2</sub> (2, 1.0 equiv) in deoxygenated acetonitrile was placed in a quartz test tube and irradiated with a 300 W high pressure mercury lamp (maximum at 365 nm) for 2 hours (entry 1, Table 1). To our delight, the desired aryl-SnMe<sub>3</sub> product **3a** was formed in 26% yield based on <sup>1</sup>H NMR analysis of the crude product. Variations of the solvent system did not improve the reaction and more side product 4a due to hydrodehalogenation was observed (entry 2 and 3). Similar to our previous borylation reaction,<sup>[13]</sup> addition of tertiary amine bases could increase the conversion (entry 4-6). The highest yield of 3a (56%) was obtained when 1.0 equiv of N,N-Diisopropylethylamine (DIPEA) was added (entry 5). Variations of the amount of DIPEA could not improve the outcome (entry 7-9). The reaction time could be reduced to 1 hour without compromise of yield (entry 10-

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11). Using more  $(SnMe_3)_2$  (2) further increased the yields (entry 12-13) and 82% of **3a** was formed in the case of 1.5 equiv of **2**. Increasing the reaction concentration of **1a** to 0.2 M resulted in significantly lower conversion and yield (entry 14). Finally, when the reaction was conducted at 0.3 mmol scale, the yield was slightly improved to 85% and 83% of **3a** was isolated by flash chromatography (entry 15).

Table 1. Optimization of reaction parameters<sup>a</sup>

MeO-	)—I + (8	6nMe <sub>3</sub> ) <sub>2</sub>	→ MeO-	├	+ MeO-
1a		2	38	l	4a
Entry	Equiv	Solvent	Additive	Time	Yield
	of 2		[mol %]		[%] <sup>[0]</sup>
	1.0			21	1a/3a/4a
1	1.0	MeCN	none	2 n	65/26/5
2	1.0	МеОН	none	2 h	0/25/40
3	1.0	$MeCN/H_2O$	none	2 h	32/5/28
4	1.0	MeCN	TMEDA	2 h	0/41/25
			(100)		
5	1.0	MeCN	DIPEA	2 h	0/56/29
			(100)		
6	1.0	MeCN	TMDAM	2 h	0/50/31
			(100)		
7	1.0	MeCN	DIPEA	2 h	0/48/28
			(200)		
8	1.0	MeCN	DIPEA	2 h	0/40/31
			(300)		
9	1.0	MeCN	DIPEA	2 h	0/49/24
			(50)		
10	1.0	MeCN	DIPEA	1 h	0/58/27
			(100)		
11	1.0	MeCN	DIPEA	0.5 h	21/48/26
			(100)		
12	1.2	MeCN	DIPEA	1 h	0/70/19
			(100)		
13	1.5	MeCN	DIPEA	1 h	0/82/17
			(100)		
14 <sup>[b]</sup>	1.5	MeCN	DIPEA	1 h	40/42/15
			(100)		
15 <sup>[c]</sup>	1.5	MeCN	DIPEA	1 h	0/85/13
			(100)		(83) <sup>[e]</sup>

<sup>a</sup>Reaction conditions: 4-iodoanisole (0.2 mmol), (SnMe<sub>3</sub>)<sub>2</sub> (0.2 mmol), MeCN/MeOH (2 ml, C = 0.1 M) under Ar atomosphere. <sup>b</sup>MeCN (1 ml, C = 0.2 M). <sup>c</sup>4-iodoanisole (0.3 mmol), (SnMe<sub>3</sub>)<sub>2</sub> (0.45 mmol), MeCN (3 ml, C = 0.1 M). <sup>d</sup>Yields based on <sup>1</sup>H NMR analysis of the crude products with 1,3,5-trimethoxybenzene added as an internal standard. <sup>e</sup> Isolated yield shown in parenthesis.

With the optimized conditions in hand, we then explored the substrate scope of this photochemical stannylation reaction. The results are summarized in Scheme 2. Iodoarenes with various electron-donating, -neutral and -withdrawing groups at *para-*, *meta-* or *ortho*-positions, including hydroxyl, amino, amide, ester, carboxylic acid, ketone, cyano, fluorine or trifluoromethyl group, were all effectively converted to the corresponding aryl stannane products in moderate to good yields (**3a-3r**). Interestingly, the aryl iodide containing a terminal allyl or propargyl ether groups was also good substrate (for **3n**, **3r**). This is remarkable considering the reaction might involve reactive radical intermediates and the multiple bond might be attacked. In the case of **3o** or **3p** where an *ortho*-substituent was present the diminished yield could be attributed to steric effect. It is known that in both the preparative and the following C-C cross-coupling reactions, heteroarylstannane compounds are often more productive than the corresponding heteroarylboron compounds because the latter suffer from protodeboronation reactions. Actually, our previous photochemical borylation reaction was not successful in some heteroarene substrates and sometimes the heteroaryl boronate could not be isolated.<sup>[13]</sup> In contrast, using the present photochemical stannylation reaction, pleasingly, several heterocyclic aryl iodides were smoothly converted to the corresponding heteroaryl stannanes in good yields (**3s-3x**).



Scheme 2 Substrate scope of the photo-induced stannylation reaction. <sup>a</sup>Reaction conditions: aryl iodide (0.3 mmol), (SnMe<sub>3</sub>)<sub>2</sub> (0.45 mmol), MeCN (3 ml, c = 0.1 M) under Ar atomosphere, 1 hour; <sup>b</sup>aryl bromide (0.3 mmol), 2 hours; <sup>c</sup>aryl chloride (0.3 mmol), 2 hours; <sup>6</sup>Yields based on <sup>1</sup>H NMR analysis of the crude products with 1,3,5-trimethoxybenzene added as an internal standard.

Aryl bromides were also tested in this photo-induced stannylation reaction (Scheme 2). Generally, the reaction times were somewhat longer than the aryl iodides (2 hours). Aryl bromides bearing electron-withdrawing groups were converted to the desired arylstannanes in moderate to good yields (**3d**, **3f**, **3j**, **3y** and **3z**). The stannylation of 3-bromopyridine was also possible (**3w**, 42%). However, in the cases of electron-rich aryl bromides, no reactions were observed based on <sup>1</sup>H NMR of the crude mixture (**3aa**, **3ab**).

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Lastly, it should be mentioned that the stannylation of 4chlorobenzonitrile also afforded **3d** in moderate yield (56%).

To gain insights into the reaction mechanism, we have carried out a series of control experiments (Table 2). When the reaction of ethyl 4-iodobenzoate 1f with the  $(SnMe_3)_2$  (2) was run under the standard conditions, 10% of hydrodeiodination product 4f was formed accompanying the stannylation product 3f (83% <sup>1</sup>H NMR yield) (entry 1). In the absence of light, no conversion was observed at room temperature (entry 2). However, small amount of 3a (12%) could be formed when the dark reaction was performed at 70  $^{\circ}\text{C}$  overnight (entry 3). When 1.5 equiv of TEMPO (2,2,6,6-tetramethylpiperidine-1oxyl) was added in the reaction, the yield of **3f** dropped to 17% (entry 4). The amount of the side product **4f** was significantly increased when 9,10-dihydroanthracene (1.5 equiv) was added (entry 5). When the photolytic reaction was stopped at 10 min immediately before workup, 82% of conversion and 70% of 3f were observed (entry 6). In contrast, if the 10 min irradiation was followed by another 50 min dark reaction, the outcome was essentially same to the result of the standard condition (entry 7 vs. entry 1). Finally, a dark reaction using 10% of AIBN as a radical initiator could also promote the formation of **3a**, albeit in lower yield (entry 8).

Table 2 Control experiments for preliminary mechanistic study

$EtO_2C - \swarrow + (SnMe_3)_2 \xrightarrow{h\nu} EtO_2C - \swarrow - SnMe_3 + EtO_2C - \swarrow$							
	1f	2	3f		4f		
Ent	Light	Additive	Conver-	Yield of	Yield of		
ry	Light	(equiv)	sion [%]	<b>3f</b> [%]	<b>4f</b> [%]		
1	on	-	100	85	10		
2	off	-	0	0	0		
3 <sup>b</sup>	off	-	15	12	3		
4	on	TEMPO (1.5)	79	17	9		
5	on	DHA (1.5)	100	47	50		
6 <sup><i>c</i></sup>	on	-	82	70	9		
7 <sup>d</sup>	on/off	-	100	85	8		
8	off	AIBN (0.1)	100	65	32		

<sup>a</sup>Reactions were run for 1 h unless otherwise stated, yields were determined by <sup>1</sup>H NMR spectroscopic analysis with 1,3,5-trimethoxybenzene as an internal standard; <sup>b</sup> The reaction was run at 70 <sup>o</sup>C for 12 h in dark; <sup>c</sup>The reaction mixture was irradiated under UV light for 10 min immediately before workup; <sup>d</sup>The reaction mixture was irradiated under UV light for 10 min and then stirred in dark for another 50 min before workup; DIPEA: N,N-Diisopropylethylamine; DHA: 9,10-dihydroanthracene; TEMPO: (2,2,6,6-tetramethylpiperidin-1-yl)oxyl; AIBN: azobisisobutyronitrile.

Based on the experimental results and related reports on photolytic reactions of aryl iodides,<sup>[14]</sup> we propose a radical reaction pathway involving a photolytically generated aryl radical as the possible mechanism (Scheme 3a). Thus, the excited state of the aryl iodide may be generated by UV irradiation and then undergo homolytic C-I bond cleavage to form the aryl radical and an iodine atom. The aryl radical may react with hexamethyldistannane (2) to produce the stannylation product **3** and a trimethylstannyl radical, which may be trapped by the iodine atom to form trimethyltin iodide. An alternative radical chain pathway can not be excluded, wherein a trimethylstannyl radical might react with aryl iodide to generate another aryl radical (Scheme 3b).

a) Ar-I 
$$\xrightarrow{hv}$$
  $[Ar-I]^* \longrightarrow Ar^* + I^*$   
Ar' + (SnMe\_3)<sub>2</sub>  $\longrightarrow$  Ar-SnMe\_3 + Me\_3Sn'  
Me\_3Sn' + I'  $\longrightarrow$  Me\_3SnI  
b) Me\_3Sn' + Ar-I  $\longrightarrow$  Ar' + Me\_3SnI

Scheme 3 Proposed reaction mechanism

In conclusion, we have designed and developed an efficient photo-induced transition-metal-free stannylation reaction to synthesize aryl trimethylstannanes from various aryl and heteroaryl halides. In comparison with the previous methods, this reaction features mild reaction conditions, broad functional group tolerance, generally good yields and simple experimental operation. Further investigations on the reaction mechanism and expansion of the substrate scope are currently ongoing.

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