Copper- and Manganese-Catalyzed Cross-Coupling of Organostannanes with Organic Iodides in the Presence of Sodium Chloride[†]

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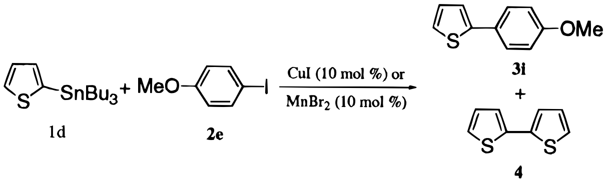
The palladium-catalyzed cross-coupling of organostannanes with aryl or vinyl halides and triflates, known as the Stille reaction, has emerged into an extremely powerful tool for carbon−carbon bond formation.[1] It is known[2] that the use of cocatalytic copper(I) dramatically enhances the reaction rate. In the copper effect, transmetalation of the R group from $RSnBu_3$ to CuI was suggested, and recent studies support the tin to copper transmetalation.[3] Recently, cross-coupling of organostannanes with organic halides mediated by stoichiometric amounts of copper alone was performed by Piers,[4] Takeda,[5] and Liebeskind.[6] Falck et al.[7] reported the copper (I)-catalyzed cross-coupling of α-heteroatom-substituted alkyltributylstannanes with organic halides. Here, we now report the cuprous iodide- and manganese bromide-catalyzed cross-coupling of organostannanes with iodides in the presence of sodium chloride without using palladium (eq 1).

$$R^1SnBu_3 \quad + \quad R^2I \xrightarrow[\text{NMP, 90–100 °C; NaCl (1 equiv), 6–16h}]{\text{CuI (10 mol \%) or } MnBr_2\text{(10 mol \%)}} R^1\text{-}R^2$$

1a	R^1 = vinyl	**2a**	R^2 = (*E*)-β-styryl	**3a–n**
1b	R^1 = (*E*)-β-styryl	**2b**	R^2 = (Z)-β-styryl	
1c	R^1 = phenyl	**2c**	R^2 = phenyl	
1d	R^1 = 2-thienyl	**2d**	R^2 = *p*-tolyl	
1e	R^1 = 2-furyl	**2e**	R^2 = *p*-anisyl	
1f	R^1 = phenylacetylenic	**2f**	R^2 = *p*-diiodophenyl	

Initially, we have examined the copper-catalyzed cross-coupling of 2-thienylorganostannane with *p*-iodoanisole to determine optimum reaction conditions. A series of experiments were performed, and the results are shown in Table 1. The yields of the coupled product **3i** are highly dependent on the salts employed. Among the salts tested, NaCl and KCl were the most suitable (Table 1, entries 1 and 2). With KF and CsF as salts, the homocoupled product **4** was formed. Accordingly, we have tested manganese bromide as the catalyst to discover a palladium-free Stille protocol, and the cross-coupling of the organostannane **1d** with iodide **2e** has been accomplished. Of the salts used, KCl and NaCl were the most preferable. The solvent DMF can be used instead of NMP.[8] In the experiment, it is necessary to add organostannanes slowly *via* a syringe pump to avoid the homocoupling of organostannanes.

Table 1. CuI- and $MnBr_2$-Catalyzed Cross-Coupling of 2-Thienyltributylstannane (1d) with *p*-Iodoanisole (2e)[a]



entry	catalyst[b]	salts[c]	yields[d] (%) 3i	yields[d] (%) 4
1	CuI	NaCl	85	traces
2	CuI	KCl	85	traces
3	CuI	LiCl	80	traces
4	CuI	KF	40	22(10)[e]
5	CuI	CsF	10	30(16)[e]
6	$MnBr_2$	NaCl	88	traces
7	$MnBr_2$	KCl	86	traces
8	$MnBr_2$	KF	20	50(10)[e]
9	$MnBr_2$	LiCl	10	35(12)[e]
10	$MnBr_2$	CsF	trace	20(8)[e]

[a] Reaction conditions for CuI as catalyst: CuI (10 mol %), NMP, 90 °C, 7 h, salt (1 equiv). For $MnBr_2$ as catalyst: $MnBr_2$ (10 mol %), NMP, 100 °C, 8 h, salt (1 equiv). [b] As the catalyst, two kinds of copper(I) iodide (99.999% from Aldrich Chem. Co.) and copper(I) iodide (98% from Janssen Chimica.) can be used. [c] In the case of NaCl and KCl, if 0.90 equiv of organostannane was used, the homocoupled product was not detected with CuI. [d] Of the manganese catalysts tested, $MnBr_2$ was the best choice, and with $MnCl_2{\cdot}4H_2O$ the yield was lower. The use of MnI_2 did not give the coupled product. [e] The yields of 4,4-dimethoxybiphenyl.

The results of copper- and manganese-catalyzed cross-coupling of organostannanes with organic iodides are summarized in Table 2.[9] Vinylstannane **1a** was slowly added *via* a syringe pump to (*E*)-*β*-styryl iodide (**2a**) in NMP at 100 °C over 1 h and then heated at reflux for 10 h in the presence of CuI (10 mol %) and 1 equiv of NaCl to afford the diene **3a** in 71% yield (method A in entry 1 in Table 2). Under the same conditions but with $MnBr_2$ (10 mol %), the reaction gave the diene **3a** in comparable yield (method B). The addition of NaCl was crucial in these cross-couplings. In considering the mechanistic role of NaCl, it is presumed that the trasmetalation of $RSnBu_3$ with cuprate is reversible. By adding NaCl, *n*-Bu_3SnI formed from transmetalation of $RSnBu_3$ with CuI can be converted to *n*-Bu_3SnCl, which does not participate in a back-reaction with cuprate and thus drives the transmetalation favorable, although the mechanism remains unclear.

The reaction of (*E*)-*β*-styryltributylstannane (**1b**) with (*E*)-*β*-styryl iodide (**2a**) in NMP at 120 °C proceeded smoothly to give the (*E*,*E*)-diene **3b**[10] in 90% and 81% yields, respectively (Methods A and B in entry 2, Table 2). Similarly, when the stannane **1b** was treated with (*Z*)-*β*-styryl iodide (**2b**) (*E*,*Z*)-diene **3c**[10] was provided along with the (*E*,*E*)-diene **3b** (33%) in 59% yield (Method A in entry 3, Table 2). However, in the case of $MnBr_2$ (method B in entry 3, Table 2), the (*E*,*E*)-diene **3b** was

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[†] Dedicated to Professor Sang Chul Shim on the occasion of his 60th birthday.

[1] (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508−524. (b) Mitchell, T. N. *Synthesis* **1992**, 803−815.

[2] Farina, V. *Pure Appl. Chem.* **1996**, *68*, 73−78.

[3] Behling, J.; Babiak, K.; Ng, J.; Campbell, A.; Moretti, R.; Koerner, M.; Lipshutz, B. *J. Am. Chem. Soc.* **1988**, *110*, 2641−2643.

[4] Piers, E.; Romero, M. A. *J. Am. Chem. Soc.* **1996**, *118*, 1215−1216 and references therein.

[5] Takeda, T.; Matsunaga, K.; Kabasawa, Y.; Fujiwara, T. *Chem. Lett.* **1995**, 771−772.

[6] Allred, G. D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 2748−2749.

[7] Falck, J. R.; Bhatt, R. K.; Ye, J. *J. Am. Chem. Soc.* **1996**, *117*, 5973−5982.

[8] In the copper-catalyzed alkylation of organomanganese chlorides, the solvent THF/NMP (1:1) was used, and the influence of *N*-methylpyrrolidone (NMP) was remarkable. See: Cahiez, G.; Marquais, S. *Synlett* **1993**, 45−46.

[9] In our hands, aryl bromides and triflates did not couple.

[10] Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107*, 972−980.

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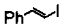
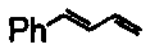
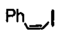
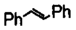
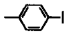
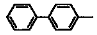
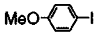
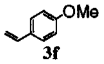
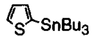
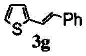
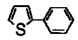
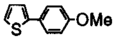
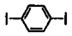
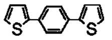
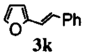
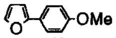
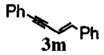
Table 2. Copper- and Manganese-Catalyzed Cross-Coupling of Organostannanes with Organic Iodides

Entry	Organo-stannanes	Iodides	Reaction Conditions[a]	Temp(°C)	Time(h)	Product	Yield(%)
1	 1a	 2a	A	100	10	 3a	71
			B	100	10		70
2	 1b	2a	A	120	12	 3b	90
			B	120	15		81
3	1b	 2b	A	100	16	 3c	59(33)[b]
			B	100	16		36(50)[b]
4	1b	PhI 2c	A	100	10	 3d	88
			B	120	10		80
5	PhSnBu$_3$ 1c	2a	A	120	12	3d	78
			B	120	14		72
6	1c	 2d	A	110	10	 3e	81
			B	120	10		76
7	1a	 2e	A	90	6	 3f	88
			B	90	6		85
8	 1d	2a	A	120	12	 3g	79
			B	120	13		75
9	1d	2c	A	100	12	 3h	92
			B	100	12		92
10	1d	2e	A	90	8	 3i	85
			B	100	8		86
11	1d	 2f	A	100	6	 3j	86
			B	110	10		80
12	 1e	2a	A	90	10	 3k	84
			B	100	10		80
13	1e	2e	A	90	8	 3l	90
			B	90	8		90
14	Ph—≡—SnBu$_3$ 1f	2a	A	120	12	 3m	74
			B	120	13		71
15	1f	2c	A	100	8	Ph—≡—Ph 3n	92
			B	100	9		88

[a] Method A: CuI (10 mol %), NMP, NaCl (1 equiv). Method B: MnBr$_2$ (10 mol %), NMP, NaCl (1 equiv). [b] The yield of (*E*,*E*)-diene.

obtained as a major product. The stannane **1b** with iodobenzene (**2c**) afforded the stilbene (**3d**) in 88% yield with CuI (10 mol %) (method A) and 80% yield with MnBr$_2$ (Method B in entry 4, Table 2). The stilbene (**3d**) was readily obtained by reacting phenyltributylstannane (**1c**) with the iodide **2a** under similar conditions (methods A and B) in 78 and 72% yields (entry 5, Table 2). This method was also extended to aryl−aryl cross-coupling. The arylstannane **1c** was coupled with *p*-iodotoluene (**2d**) to give unsymmetrical biphenyl **3e** (method A, entry 6, Table 2). Under similar conditions with MnBr$_2$, biphenyl **3e** was obtained (method B, entry 6, Table 2). With *p*-iodoanisole (**2e**), the coupling reaction with **1a** in the presence of CuI gave *p*-methoxystyrene (**3f**) as the sole product in 88% yield (method A in entry 7, Table 2). Under the same conditions wtih MnBr$_2$ the coupling gave **3f** in 85% yield (method B).[11] For 2-thienylstannane (**1d**), treatment with **2a** gave the coupled product **3g** (entry 8, Table 2). Alternatively, for aryl−aryl coupling, 2-thienylstannane (**1d**) was reacted with iodobenzene (**2c**) and *p*-iodoanisole (**2e**) to give biaryls **3h** and **3i** (entries 9 and 10, Table 2).[12−14] The *p*-diiodobenzene (**2f**) was reacted with 2-thienylstannane **1d** to afford bisthiophene **3j** in 86% yield in method A and 86% in method B (entry 11, Table 2). Similarly, 2-furylstannane **1e** was successfully coupled with **2a** and **2e** to furnish **3k** and **3l** (entries 12 and 13, Table 2). This method was also applied to the coupling reaction of alkynyl-substituted organostannanes. The alkynylstannane **1f** was coupled with vinyl iodide **2a** and aromatic iodide **2c** to afford the substituted alkynes **3m** and **3n**, respectively (entries 14 and 15, Table 2).

In summary, the cuprous iodide- and manganese bromide-catalyzed cross-couplings of organostannanes with iodides in NMP in the presence of NaCl were accomplished without using palladium. We believe that the methods described here may be valuable alternatives to Stille coupling.

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Supporting Information Available: Experimental procedures and analytical data for the compounds (3 pages).

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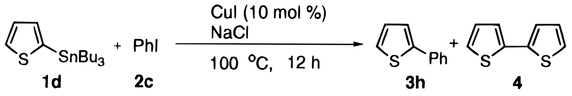
(11) The typical procedure is as follows. Method B: To a stirred solution of 4-iodoanisole (**2e**) (200 mg, 0.85 mmol) and NaCl (50 mg, 0.85 mmol) in NMP (2 mL) was added MnBr$_2$ (18.3 mg, 10 mol %), the mixture was heated to 90 °C, and then tributylvinyltin (**1a**) (0.27 g, 0.85 mmol) in NMP (2 mL) was added slowly for 1 h *via* a syringe pump. The reaction mixture was stirred at 90 °C for 6 h and cooled to rt, and saturated KF solution was added. The reaction mixture was extracted with ether, and the organic layer was dried over anhydrous MgSO$_4$ and evaporated *in vacuo*. The crude product was separated by SiO$_2$ column chromatography (hexanes, $R_f = 0.25$) to afford the coupled product **3f** (98 mg, 85%).

(12) The typical procedures is as follows. Method A: To a stirred solution of 4-iodoanisole (**2e**) (200 mg, 0.85 mmol) and NaCl (50 mg, 0.85 mmol) in NMP (2 mL) was added CuI (16.2 mg, 10 mol %), the mixture was heated to 90 °C, and then 2-(tributylstannyl)thiophene (**1d**) (320 mg, 0.85 mmol) in NMP (2 mL) was added slowly for 1 h *via* a syringe pump. The reaction mixture was stirred at 90 °C for 8 and cooled to rt, and saturated KF solution was added. The reaction mixture was extracted with ether, and the organic layer was dried over anhydrous MgSO$_4$ and evaporated *in vacuo*. The crude product was separated by SiO$_2$ column chromatography (hexanes, $R_f = 0.28$) to afford the coupled product **3i** (138 mg, 85%).

(13) In the MgBr$_2$(10 mol %)-catalyzed coupling of organostannane **1d** with iodobenzene (**2c**) (Table 2, entry 9, method B), we could get the product **3h** in 90% yield when DMF was used as solvent instead of NMP.

(14) In a control experiment for the reaction of organostannane **1d** with iodobenzene (**2c**) (Table 2, entry 9, Method A), when organostannane **1d** in NMP was added slowly for 1 h *via* a syringe pump, the coupled product **3h** was obtained in 92% yield. However, when organostannane **1d** was added in one portion, the coupled product **3h** was obtained in 60% yield along with the homocoupled product **4** (34%). The cross-coupling by adding organostannane **1d** slowly with DMF as solvent was also carried out to give the coupled product **3h** in 88% yield.



	3h	4	
slow addition	92%	trace	(NMP)
	88%	trace	(DMF)
one-pot addition	60%	34%	