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A Sn atom-economical approach toward arylstannanes: Ni-catalysed stannylation of aryl halides using Bu_3SnOMe†

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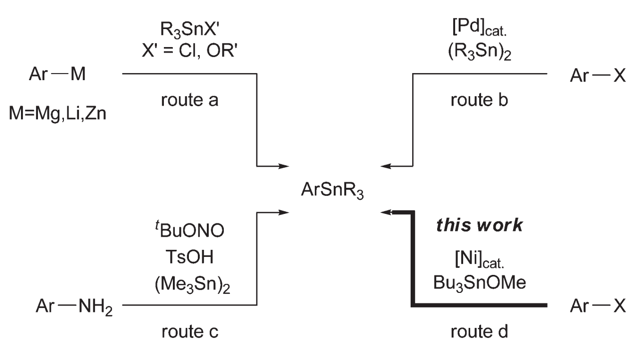
Stannylation of carbon–halogen bonds is one of the most promising and straightforward approaches for the preparation of organostannane compounds. Although a wide variety of methods are now available, all protocols require the use of highly nucleophilic organometals or wasteful stannyl sources like distannanes. Here, we report a new nickel-catalysed stannylation of aryl and alkenyl-halides using Bu_3SnOMe as a stannyl source to afford aryl and vinyl-stannanes, respectively. This method enables the stannylation of not only bromides, but also chlorides and triflates to furnish functionalized aryl- and alkenyl-stannanes without the release of wasteful and toxic stannyl byproducts.

Arylstannanes are useful synthetic intermediates because of their versatility in the construction of aryl-C,[1] -NR_2,[2] -F,[3] and -OCF_3 [4] bonds. The most promising route to afford arylstannanes relies on the trapping of arylmetal species (Mg, Li, and Zn)[3a,5] using trialkylstannyl electrophiles R_3SnX' (route a, Scheme 1). However, these protocols have some drawbacks: poor functional group tolerance and/or delicate conditions for the preparation of arylmetal species. In contrast, the Pd-catalysed stannylation of aryl halides (Scheme 1b)[6] and the recently proposed Sandmeyer-type reaction of anilines (Scheme 1c)[7] using hexaalkyl distannanes have been demonstrated as alternative procedures. Although both of the above methods are useful and powerful for functionalized arylstannane synthesis, the release of highly toxic stannyl byproducts is unavoidable. These disadvantages drastically reduce the efficiency of organostannane chemistry in both academia and industrial pursuits.



Scheme 1 Representative synthetic method for arylstannanes.

On the other hand, a few transition metal-catalysed reactions involve nucleophilic stannylation processes using trialkylstannyl alkoxides $ROSn(alkyl)_3$ as terminal electrophiles. For instance, the interception of alkynylzinc[8] and alkenylcopper intermediates[9] generated *in situ* using stannyl alkoxides quickly transforms into the corresponding alkynyl or alkenyl stannane compounds, respectively.[10] However, these catalytic processes have never been applied to the stannylation of ubiquitous carbon (sp^2)–halogen bonds because of their low reactivity for zinc and copper complexes. In this paper, we report a Ni-catalysed stannylation of aryl halides using Bu_3SnOMe in the presence of manganese powder (Scheme 1d). This stannylation process could be an ideal and straightforward approach to afford aryl or vinyl stannanes from both organohalides and organotriflates. The proposed process possesses the following advantages: (1) available substrates, (2) a broad scope of functional groups, and (3) Sn atom-economy without the release of wasteful toxic inorganic stannyl residues.

Initially, we explored the suitable reaction conditions for the stannylation of aryl bromides **1a** and **1b** using stannyl electrophile as model substrates based on the previous work by Tsuji and Fujihara (Table 1).[11] When **1a** was treated with Bu_3SnOMe (1.2 equiv.) in the presence of $NiBr_2$ (10 mol%), 2,2′-bipyridine (bpy, 10 mol%), and Mn powder (2.0 equiv. treated with 20 mol% of chlorotrimethylsilane), arylstannane **2a** was afforded in 72% yield along with biaryl **3a** in 14% yield

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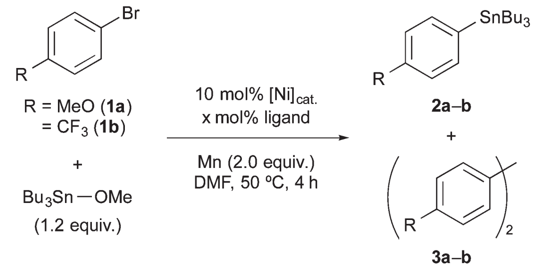
Table 1 Screening of the reaction conditions in the stannylation of 4-methoxy bromobenzene (**1a**) and 4-trifluoromethyl bromobenzene (**1b**)



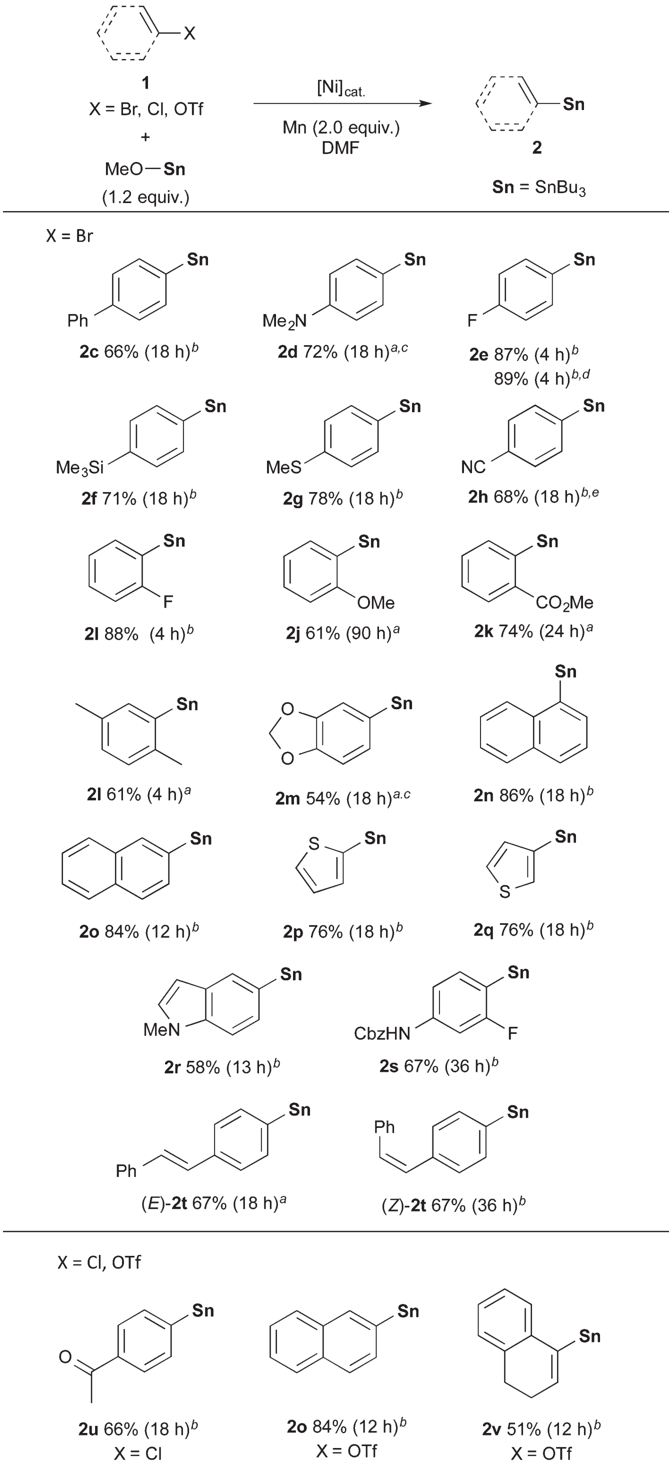
Entry	1	[Ni]$_{cat.}$	Ligand (*x* mol%)	Yield[a]/%	
				2	3
1	**1a**	NiBr$_2$	bpy (10)	72	14
2	**1a**	NiBr$_2$(bpy)	—	91 (85)	9
3	**1a**	NiBr$_2$	—	0	0
4	**1a**	NiBr$_2$	PPh$_3$ (20)	21	7
5	**1a**	NiBr$_2$	dppe (10)	0	0
6	**1a**	NiBr$_2$	*t*bpy[b] (10)	10	70
7	**1a**	—	bpy (20)	0	0
8[c]	**1a**	NiBr$_2$(bpy)	—	23	60
9[d,e]	**1a**	NiBr$_2$(bpy)	—	60	39
10[f]	**1b**	NiBr$_2$(bpy)	—	22	68
11[f]	**1b**	NiBr$_2$	PPh$_3$ (20)	75	12
12[f]	**1b**	NiBr$_2$	PPh$_3$ (30)	86	6
13[f,g]	**1b**	NiBr$_2$	PPh$_3$ (30)	96 (90)	4

[a] Determined by GC yield with tridecane as the internal standard. Parenthetical value indicates isolated yield. [b] *t*bpy = 4,4′-di-*tert*-butyl-2,2′-bipyridine. [c] Zn was used instead of Mn. [d] 4-Iodoanisole was used instead of bromide **1a**. [e] 25 °C, 4 h. [f] 25 °C, 18 h. [g] Et$_4$NI (20 mol%) was added.

(entry 1).[12] The preformed [NiBr$_2$(bpy)] complex exhibited higher catalytic performance to afford **2a** in 91% yield (entry 2).[13] The 2,2′-bipyridine ligand and Ni catalyst were crucial (entries 3–7). The replacement of Mn or **1a** with Zn or 4-iodoanisole, respectively, induced the homocoupling reaction (entries 8 and 9). In contrast, the optimized conditions (entry 2) were not sufficient for the stannylation of electron-poor aryl bromides like **1b**; instead, the homocoupling mainly proceeded due to the high reactivity of low-valent Ni toward the aryl halides[14] and/or the poor nucleophilicity of the generated aryl nickel.[15] Fortunately, the low chemoselectivity was improved by replacing the bpy ligand with electron-donating PPh$_3$ (entry 10). Further improvement was achieved by increasing ligand loading (30 mol%) and by adding Et$_4$NI[11,16] (entries 11–13). In this stannylation, other stannyl electrophiles such as Bu$_3$SnCl, Bu$_3$SnO^{t}Bu, and Bu$_3$SnOAc also participated, leading to **2a** in 74%, 69%, and 54% yields, respectively (Table S1 in the ESI†). Additionally, hexane, toluene, tetrahydrofuran, 1,4-dioxane, and acetonitrile were not suitable solvents; most of the substrates remained unchanged.

With the optimized conditions in hand (entries 2 and 13, Table 1), we next investigated the substrate scope in the Ni-catalysed stannylation by employing various aryl or vinyl halides with Bu$_3$SnOMe (Table 2). Aryl bromides containing electron-donating (**1d**) and -withdrawing substituents (**1e–1g**) at the *para*-position were well tolerated, giving rise to the

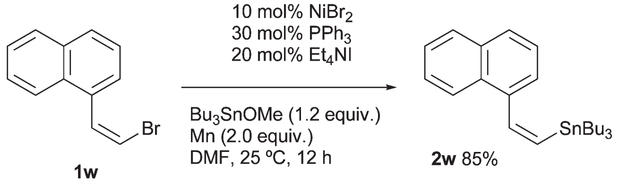
Table 2 Scope of aryl and vinyl halides



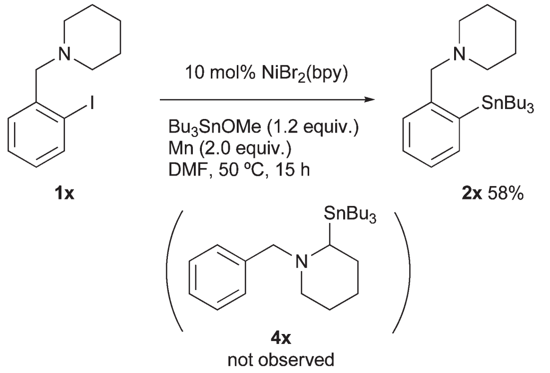
2c 66% (18 h)[b]
2d 72% (18 h)[a,c]
2e 87% (4 h)[b]
89% (4 h)[b,d]
2f 71% (18 h)[b]
2g 78% (18 h)[b]
2h 68% (18 h)[b,e]
2l 88% (4 h)[b]
2j 61% (90 h)[a]
2k 74% (24 h)[a]
2l 61% (4 h)[a]
2m 54% (18 h)[a.c]
2n 86% (18 h)[b]
2o 84% (12 h)[b]
2p 76% (18 h)[b]
2q 76% (18 h)[b]
2r 58% (13 h)[b]
2s 67% (36 h)[b]
(*E*)-**2t** 67% (18 h)[a]
(*Z*)-**2t** 67% (36 h)[b]
2u 66% (18 h)[b]
X = Cl
2o 84% (12 h)[b]
X = OTf
2v 51% (12 h)[b]
X = OTf

[a] 10 mol% NiBr$_2$(bpy), 50 °C. [b] 10 mol% NiBr$_2$, 30 mol% PPh$_3$, 20 mol% Et$_4$NI, 25 °C. [c] 1.5 equivalent of Bu$_3$SnOMe was used. [d] 2.05 g of **2e** was obtained. [e] Xantophos (20 mol%) was used instead of PPh$_3$ (30 mol%). Reaction temperature: 40 °C.

corresponding stannylated products (**2c–2g**) in good yields. In addition, the stannylation was successfully carried out on a gram-scale synthesis, giving rise to **2e** in 2.05 g (89% yield). For the efficient stannylation of 4-cyano bromobenzene (**1h**), bidentate phosphine ligands bearing large bite angles were effective (Table S2 in the ESI†). *ortho* and *meta*-substituents (**1i–1o**) also participated in the stannylation, leading to the corresponding stannylated products (**2i–2o**). Heteroaryl bromides (**1p–1r**) also underwent this transformation to afford the stannylation products in good-to-high yields. Slightly acidic N–H bonds did not prevent the reaction and afforded 4-amino-2-fluorophenyl stannane (**2s**), which is an intermediate in torezolid synthesis.[17] In addition, the stereochemistry of (*E*)- and (*Z*)-olefinic moieties (**1t**) was maintained during the stannylations. Furthermore, the present stannylation is active not only for bromides, but also for chloride **1u** and triflates **1o** and **1v**, yielding the corresponding stannylated products **2u**, **2o**, and **2v**, respectively.



1w **2w** 85% (1)



1x **2x** 58% (2)

4x
not observed

$$\mathrm{Ni(COD)_2}\ \xrightarrow[\text{2) }\mathbf{1a}\text{ (1.0 euiqv.) Bu}_3\text{SnOMe (1.2 equiv.) 50 °C, 4 h}]{\text{1) bpy (1.0 equiv.) DMF, 25 °C, 10 min}}\ \underset{20\%}{\mathbf{2a}} + \underset{60\%}{\mathbf{3a}} \tag{3}$$

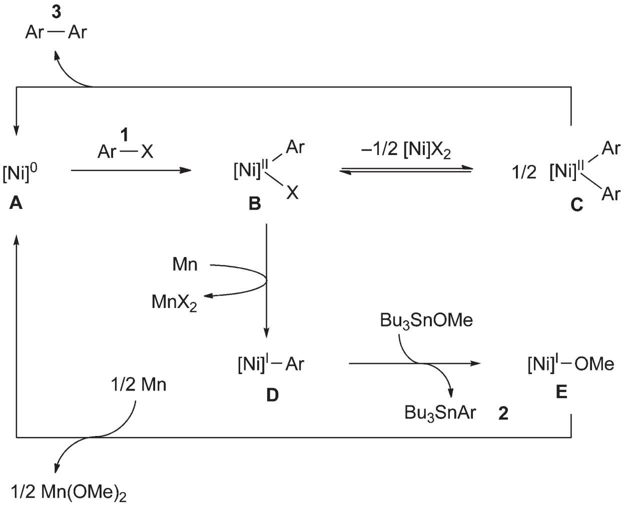
$$\mathrm{NiBr_2(bpy)}\ \xrightarrow[\text{2) }\mathbf{1a}\text{ (1.0 euiqv.) Bu}_3\text{SnOMe (1.2 equiv.) 50 °C, 4 h}]{\text{1) Mn (0.9–2.3 equiv.) DMF, 25 °C, 30 min}}$$

Mn /equiv.	**2a** /%	**3a** /%
0.9	9	70
1.0	14	68
1.1	20	60
1.5	47	42
2.3	90	5

Scheme 2 Stoichiometric reaction of NiBr$_2$(bpy) with **1a** (1.0 equiv.) and Bu$_3$SnOMe (1.2 equiv.) in the presence of Mn powder (*x* equiv.).

A stereocontrol study was conducted using (*Z*)-1-(bromovinyl)naphthalene (**1w**), as shown in eqn (1). The reaction of **1w** with Bu$_3$SnOMe exclusively yielded (*Z*)-vinyl stannane **2w** with complete retention of the stereo-integrity.[18] In addition, it is known that the aryl radical possessing a (dialkylamino) methyl group at the *ortho*-position, derived from the halogen atom abstraction of 1-(2-iodobenzyl)piperidine (**1x**), rapidly undergoes 1,5-hydrogen atom transfer to afford an α-amino alkyl radical.[19] This radical might be converted to alkyl stannane **4x** through the formation of alkyl nickel species *via* recombination between Ni and the alkyl radical.[20] However, the reaction of **1w** provided simple arylstannane **2x** (eqn (2)). Furthermore, the addition of a hydrogen atom donor like 9,10-dihydroanthracene[21] into the reaction media did not fully block the stannylation; 45–62% yields of **2a** were obtained even if excess scavenger (2.0–3.0 equiv.) was present in the reaction media.[22] These findings imply that the primary pathways for oxidative addition of Ni into organohalides **1** do not generate free organic radicals.

The stoichiometric reaction of NiBr$_2$(bpy) with **1a** and Bu$_3$SnOMe in the presence of various amounts of Mn powder (Scheme 2) provided some important information about the mechanism. As the loading of Mn was increased, the yield of stannylated product **2a** increased, while that of the homocoupling product **3a** decreased. Particularly note that the lower loading (0.9–1.1 equiv.) of Mn powder mainly produced the homocoupling product **3a**. A similar product distribution was observed in the reaction of Ni(COD)$_2$/bpy with **1a** and Bu$_3$SnOMe in the absence of an Mn reductant (eqn (3)). These results could indicate that monovalent Ni is an active intermediate in the Ni-catalysed stannylation. Thus, the present stannylation could be initiated by the generation of [Ni]^0 complex **A** from the reduction of the initial Ni(II) with Mn powder (Scheme 3). The oxidative addition of aryl halides (Ar–X: **1**) to **A** afforded Ar–[Ni]^{II}–X **B**. Although the divalent Ni intermediate **B** might be slightly active in the interception of Bu$_3$SnOMe (Scheme 2 and eqn (3)), disproportionation of **B**



Scheme 3 Plausible reaction pathway for the Ni-catalysed stannylation of aryl halides.

would spontaneously occur to afford $[Ni]^{II}X_2$ and $[Ni]^{II}Ar_2$ **C**,[14a,23] which would lead to the homocoupling product **3** and **A** *via* reductive elimination. In contrast, in the presence of excess Mn, **B** could be preferentially reduced to $[Ni]^{I}$–Ar **D**, which would be more active than **B** for interception because of the higher nucleophilicity of monovalent Ni.[15,16] This would afford the stannylated product **2** as well as $[Ni]^{I}$–OMe **E**, followed by the regeneration of **A** with Mn.

Conclusions

In conclusion, we have demonstrated a simple and atom-economical stannylation using stannyl electrophiles catalysed by Ni complexes in the presence of an Mn reductant. This stannylation can be tolerated by a diverse set of functional groups on aryl halides and does not release wasteful stannyl residues. Preliminary mechanistic studies suggest that aryl Ni(I) species are intermediates in this transformation. Further mechanistic studies and synthetic applications of this transmetalation process of the C–Ni bond are underway.

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Notes and references

1 (*a*) J. K. Stille, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 508; (*b*) M. Kosugi and K. Fugami, *Handbook of Organopalladium Chemistry for Organic Synthesis*, ed. E. Negishi, Wiley, New York, 2002, p. 263.

2 P. Y. S. Lam, G. Vincent, D. Bonne and C. G. Clark, *Tetrahedron Lett.*, 2002, **43**, 3091.

3 (*a*) T. Furuya, A. E. Strom and T. Ritter, *J. Am. Chem. Soc.*, 2009, **131**, 1662; (*b*) Y. Ye and M. S. Sanford, *J. Am. Chem. Soc.*, 2013, **135**, 4648.

4 C. Huang, T. Liang, S. Harada, E. Lee and T. Ritter, *J. Am. Chem. Soc.*, 2011, **133**, 13308.

5 (*a*) L. Adam Shih-Yuan and D. Wen-Chin, *Tetrahedron Lett.*, 1996, **37**, 495; (*b*) T. Hayashi and M. Ishigedani, *Tetrahedron*, 2001, **57**, 2589; (*c*) P. Knochel and R. D. Singer, *Chem. Rev.*, 1993, **93**, 2117; (*d*) C. Gosmini and J. Périchon, *Org. Biomol. Chem.*, 2005, **3**, 216.

6 (*a*) D. Azarian, S. S. Dua, C. Eaborn and D. R. Walton, *J. Organomet. Chem.*, 1976, **117**, C55; (*b*) H. Azizian, C. Eaborn and A. Pidcock, *J. Organomet. Chem.*, 1981, **215**, 49.

7 D. Qiu, L. Jin, S. Wang, S. Tang, X. Wang, F. Mo, Y. Zhang and J. Wang, *Angew. Chem., Int. Ed.*, 2013, **52**, 11581.

8 K. Kiyokawa, N. Tachikake, M. Yasuda and A. Baba, *Angew. Chem., Int. Ed.*, 2011, **50**, 10393.

9 (*a*) Y. Takemoto, H. Yoshida and K. Takaki, *Chem. – Eur. J.*, 2012, **18**, 14841; (*b*) T. Wakamatsu, K. Nagao, H. Ohmiya and M. Sawamura, *Angew. Chem., Int. Ed.*, 2013, **52**, 11620.

10 Interception of the carbon–silver bond using other stannyl electrophiles was reported. See: J. Liu, X. Xie and Y. Liu, *Chem. Commun.*, 2013, **49**, 11794.

11 T. Fujihara, K. Nogi, T. Xu, J. Terao and Y. Tsuji, *J. Am. Chem. Soc.*, 2012, **134**, 9106.

12 A possibility that the biaryl **3a** was formed through the Stille coupling of **1a** with the generated **2a** was completely ruled out in the reaction of **1a** with $PhSnBu_3$ under the identical conditions. D. A. Powell, T. Maki and G. C. Fu, *J. Am. Chem. Soc.*, 2005, **127**, 510.

13 The reaction of 4-anisyl chloride under the identical conditions (Table 1, entry 2) afforded **2a** in 33% yield, along with **3a** in 32%.

14 (*a*) T. T. Tsou and J. K. Kochi, *J. Am. Chem. Soc.*, 1979, **101**, 6319; (*b*) V. P. Ananikov, *ACS Catal.*, 2015, **5**, 1964.

15 J.-X. Hu, H. Wu, C.-Y. Li, W.-J. Sheng, Y.-X. Jia and J.-R. Gao, *Chem. – Eur. J.*, 2011, **17**, 5234.

16 (*a*) M. Zembayashi, K. Tamao, J.-I. Yoshida and M. Kumada, *Tetrahedron Lett.*, 1977, **18**, 4089; (*b*) M. Iyoda, H. Otsuka, K. Sato, N. Nisato and M. Oda, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 80; (*c*) V. Percec, J.-Y. Bae, M. Zhao and D. H. Hill, *J. Org. Chem.*, 1995, **60**, 176.

17 W. B. Im, S. H. Choi, J.-Y. Park, S. H. Choi, J. Finn and S.-H. Yoon, *Eur. J. Med. Chem.*, 2011, **46**, 1027.

18 J. J. Hirner and S. A. Blum, *Organometallics*, 2011, **30**, 1299.

19 (*a*) V. Snieckus, J. C. Cuevas, C. P. Sloan, H. Liu and D. P. Curran, *J. Am. Chem. Soc.*, 1990, **112**, 896; (*b*) M. Murakami, M. Hayashi and Y. Ito, *J. Org. Chem.*, 1992, **57**, 793; (*c*) N. Yoshikai, A. Mieczkowski, A. Matsumoto, L. Ilies and E. Nakamura, *J. Am. Chem. Soc.*, 2010, **132**, 5568.

20 (*a*) H. Yin, C. Zhao, H. You, K. Lin and H. Gong, *Chem. Commun.*, 2012, **48**, 7034; (*b*) D. A. Everson, B. A. Jones and D. J. Weix, *J. Am. Chem. Soc.*, 2012, **134**, 6146; (*c*) H. Xu, C. Zhao, Q. Qian, W. Deng and H. Gong, *Chem. Sci.*, 2013, **4**, 4022; (*d*) Y. Peng, X.-B. Xu, J. Xiao and Y.-W. Wang, *Chem. Commun.*, 2013, **50**, 472; (*e*) Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle and D. W. C. MacMillan, *Science*, 2014, **345**, 437; (*f*) L. K. G. Ackerman, L. L. Anka-Lufford, M. Naodovic and D. J. Weix, *Chem. Sci.*, 2014, **6**, 1115.

21 (*a*) B. L. Tran, B. Li, M. Driess and J. F. Hartwig, *J. Am. Chem. Soc.*, 2014, **136**, 2555; (*b*) S. K. Bose, K. Fucke, L. Liu, P. G. Steel and T. B. Marder, *Angew. Chem., Int. Ed.*, 2014, **53**, 1799.

22 Decreasing the solubility of Bu_3SnOMe by the addition of 9,10-dihydroanthracene would cause low yields. Indeed, as the amount of the scavenger increases (1.0–3.0 equiv.), the homocoupling reaction exclusively occurred to form **3a** in 16–31% yields. See Table S3 in the ESI.†

23 A. Nakamura and S. Otsuka, *Tetrahedron Lett.*, 1974, **15**, 463.