Synthesis of Biaryls Using the Coupling Reaction of Diaryldimethyltins with Copper(II) Nitrate

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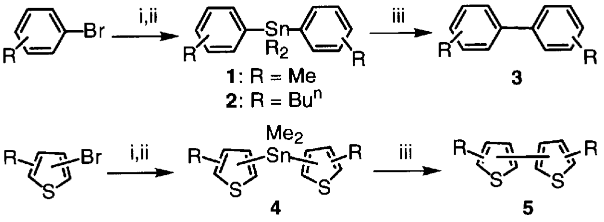
The coupling of diaryldimethyltins with $Cu(NO_3)_2\cdot 3H_2O$ in THF proceeds smoothly at room temperature under ambient atmosphere to produce the corresponding biaryls in good to high yields. Diaryldimethyltins can be prepared in high yields by the reaction of aryllithiums with dichlorodimethyltin.

Although a number of reactions have been reported for the homocoupling of aromatic and heteroaromatic halides to produce biaryls and their heteroaromatic analogues,[1,2] the Ullmann reaction is believed to be the best method because of its ease of operation.[3] Previously, we reported an improved Ullmann reaction using a copper(II)-mediated coupling of an organozinc species to produce biphenylene and its derivatives.[4] Recently, we have found another new improved method for the synthesis of biaryls and their heteroaromatic analogues using the coupling of diaryldimethyltins with $Cu(NO_3)_2\cdot 3H_2O$ (Scheme 1).

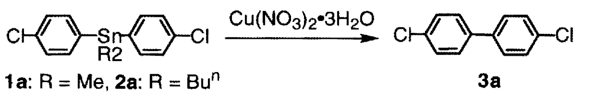


Scheme 1. Reagents and conditions: i) Bu^nLi (1.1 equiv.); ii) R_2SnCl_2 (0.5 equiv.); iii) $Cu(NO_3)_2\cdot 3H_2O$.

As shown in Scheme 1, the preparation of dialkyldiaryltins (**1** and **2**) was carried out starting from the corresponding aryl bromides. Thus, the reaction of aryl bromides with butyllithium (1.1 equiv.), followed by treatment with dialkyldichlorotin (0.5 equiv.) afforded dialkyldiaryltins (**1** and **2**) in moderate to high yields [**1a**: R = 4-Cl, 85%; **1b**: R = H, 93%; **1c**: R = 4-Me, 90%; **1d**: R = 3-Me, 76%; **1e**: R = 2-Me, 83%; **1f**: R = 4-OMe, 85%; **1g**: R = 3-OMe, 49%; **1h**: R = 2-OMe, 80%; **1i**: R = 3-Cl, 73%; **2a**: R = 4-Cl, 80%;]. In a similar manner, the reaction of bromothiophenes with butyllithium, followed by treatment with dichlorodimethyltin gave **4** in good yields [**4a**: R = H, 2-thienyl, 81%; **4b**: R = H, 3-thienyl, 72%].

The coupling reactions of dialkylbis(4-chloromethyl)tins (**1a** and **2a**) with $Cu(NO_3)_2\cdot 3H_2O$ are summarized in Table 1. Although the known couplings of organotin compounds using organometallic reagents can be carried out under an inert atmosphere,[5,6] the reaction of **1a** with $Cu(NO_3)_2\cdot 3H_2O$ in THF at 23 °C proceeded smoothly under ambient atmosphere or in an atmosphere of oxygen to produce 4,4'-dichlorobiphenyl (**3a**) in 91 and 88% yields, respectively (entries 1 and 2). A similar reaction of **1a** under nitrogen gave **3a** in lower yield (entry 3). The reaction rate of **1a** with $Cu(NO_3)_2\cdot 3H_2O$ (2.2 equiv.) at 0 °C in THF was much slower than that at 23 °C to afford the coupling product **3a** in 69-85% yields (entries 4-6). A similar reaction of dibutylbis(4-chlorophenyl)tin (**2a**) with $Cu(NO_3)_2\cdot 3H_2O$ (2.2 equiv.) in THF at 23 °C produced **3a** in 85% yield which was slightly lower than that of **1a** (entry 7). The coupling reaction needed 2 equiv. of $Cu(NO_3)_2\cdot 3H_2O$, and the reaction of **1a** with 1 equiv. of $Cu(NO_3)_2\cdot 3H_2O$ gave **3a** in 45% yield, together with the recovered starting material **1a**.

Table 1. Coupling of **1a** and **2a** with $Cu(NO_3)_2\cdot 3H_2O$[a]



Entry	Compound	Temp / °C	Atmosphere	Time / h	Yield of **3a**[b] / %
1	**1a**	23	Ambient	0.5	91
2	**1a**	23	Oxygen	0.5	88
3	**1a**	23	Nitrogen	0.5	73
4	**1a**	0	Ambient	1	85
5	**1a**	0	Oxygen	1	85
6	**1a**	0	Nitrogen	1	69
7	**2a**	23	Ambient	0.5	85

[a] To a solution of $Cu(NO_3)_2\cdot 3H_2O$ (2.2 mmol) in THF (1 ml) was added a solution of **1a** or **2a** (1 mmol) in THF (1 ml). [b] Isolated yield.

On the basis of the results shown in Table 1, the coupling reactions of various kinds of diaryldimethyltins with $Cu(NO_3)_2\cdot 3H_2O$ were carried out (Table 2). As shown in Table 2, the reactions of diaryldimethyltins with $Cu(NO_3)_2\cdot 3H_2O$ in THF proceeded smoothly to produce biaryls in good to high yields. Thus, the reaction of dimethyldiphenyltin (**1b**) with $Cu(NO_3)_2\cdot 3H_2O$ in THF at 23 °C gave biphenyl (**3b**) in 97% yield (entry 2). Similar reactions of diaryldimethyltins (**1c-d**, **1f-g**, and **1i**) containing *para-* or *meta-*substituents produced the corresponding biaryls in 78-95% yields (entries 3-4, 6-7, and 9). In the case of *ortho-*substituted diaryldimethyltins, the reaction of dimethylbis(2-methylphenyl)tin (**1e**) with $Cu(NO_3)_2\cdot 3H_2O$ gave 2,2'-dimethylbiphenyl (**3e**) (entry 5) in 82% yield, whereas the reaction of dimethylbis(2-methoxyphenyl)tin (**1h**) with $Cu(NO_3)_2\cdot 3H_2O$ in THF was slow to produce 2,2'-dimethoxybiphenyl (**3h**) in 49% yield (entry 8). The reactions of dimethylbis(thienyl)tins (**4a** and **4b**) with $Cu(NO_3)_2\cdot 3H_2O$ afforded bithiophenes (**5a** and **5b**) in 62 and 68% yields, respectively (entries 10 and 11).

Although the reactions of tributylaryltin ($Ar\text{-}SnBu^n_3$) with $Cu(NO_3)_2\cdot 3H_2O$, $PdCl_2(CH_3CN)_2$, and $[PdCl(\pi\text{-}C_3H_5)]_2$ were reported to produce biaryls (**3**),[6,7] the reaction of diaryldimethyltins reported here gave higher yields of the products (Table 2). In addition, the intramolecular coupling of diaryldimethyltins with $Cu(NO_3)_2\cdot 3H_2O$ in THF can be carried out without an inert atmosphere, and hence this coupling can be widely employed for the construction of biphenyl frameworks under ambient atmosphere or under oxygen.

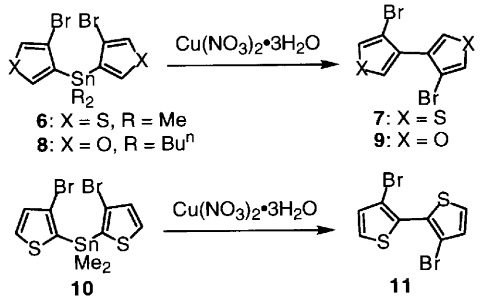
Table 2. Synthesis of biaryls using the coupling of diaryldimethyltins (**1a-i** and **4a,b**) with $Cu(NO_3)_2•3H_2O$[a]

$$\underset{\mathbf{1}}{\mathrm{Ar_2SnMe_2}} \xrightarrow{\mathrm{Cu(NO_3)_2•3H_2O}} \underset{\mathbf{3}}{\mathrm{Ar\text{-}Ar}}$$

Entry	Ar (Starting Material)		Time / h	Product	Yield of **3**[b] / %
1	4-ClC_6H_4	**1a**	0.5	**3a**	91
2	C_6H_5	**1b**	0.5	**3b**	97
3	4-MeC_6H_4	**1c**	0.5	**3c**	92
4	3-MeC_6H_4	**1d**	0.5	**3d**	78
5	2-MeC_6H_4	**1e**	0.5	**3e**	82
6	4-$MeOC_6H_4$	**1f**	0.5	**3f**	95
7	3-$MeOC_6H_4$	**1g**	0.5	**3g**	92
8	2-$MeOC_6H_4$	**1h**	4	**3h**	49
9	3-ClC_6H_4	**1i**	0.5	**3i**	81
10	2-Thienyl	**4a**	0.5	**5a**	68
11	3-Thienyl	**4b**	0.5	**5b**	62

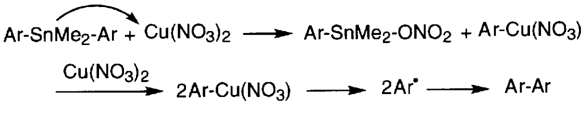
[a]To a solution of $Cu(NO_3)_2•3H_2O$ (2.2 mmol) in THF (1 ml) was added a solution of **1** or **4** (1 mmol) in THF (1 ml) at room temperature, and the mixture was stirred at room temperature. [b]Isolated yield.

Interestingly, the reaction of bis(4-bromo-3-thienyl)dimethyltin (**6**)[8] with $Cu(NO_3)_2·3H_2O$ produced 4,4'-dibromo-3,3'-bithiophene (**7**)[9,10] in 76% yield (Scheme 2). Similarly, the reaction of bis(4-bromo-3-furyl)dimethyltin and bis(3-bromo-2-thienyl)dimethyltin (**8** and **10**)[8] with $Cu(NO_3)_2·3H_2O$ afforded 4,4'-dibromo-3,3'-bifuran and 3,3'-dibromo-2,2'-bithiophene (**9** and **11**)[9,10] in 72 and 52% yields, respectively. These reactions gave selectively the coupling products without loss of the bromo substituents.



Scheme 2.

We anticipated that the first step of the reaction of diaryldimethyltins with $Cu(NO_3)_2·3H_2O$ involves an electron-transfer process and transmetallation to afford an organocopper(II) species and dimethyltin dinitrate as depicted in Scheme 3. Since the reaction of a mixture of **1a** (0.5 mmol) and **6** (0.5 mmol) with $Cu(NO_3)_2·3H_2O$ (2.2 mmol) in THF (2 ml) at room temperature for 1 h produced **3a** (26%) and **7** (25%) with the corresponding cross-coupling product (30%), the intermediates for biaryls may be radical-like species which dimerizes to produce the coupling products.



Scheme 3.

The reaction reported here can be widely applied for the synthesis of biaryls and heterobiaryls. Further studies on the coupling reactions of diaryldialkyltins with transition metal catalysts are now under way.

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References and Notes

1 For reviews, see, a) E. Negishi, *Acc. Chem. Res.*, **15**, 340 (1982). b) F. Naso and G. Marchese, in "Carbon-carbon bond formation involving organic halides and transition metal compounds," in "The Chemistry of Functional Groups, Supplement D," ed by S. Patai and Z. Rappoport, John Wiley & Sons Ltd., New York (1983), p 1353. c) D. W. Knight, in "Coupling Reactions Between *sp*^{2} Carbon Center," in "Comprehensive Organic Synthesis," ed by B. M. Trost and I. Fleming, Pergamon Press, London (1991), Vol. 3, p. 499.

2 For examples, see, a) D. J. Cram, M. deGrandpre, C. B. Knobler, and K. N. Trueblood, *J. Am. Chem. Soc.*, **106**, 3286 (1984). b) B. Krische, J. Hellberg, and C. Lilja, *J. Chem. Sco., Chem. Commun.*, **1987**, 1476. c) M. Iyoda, H. Otsuka, K. Sato, N. Nisato, and M. Oda, *Bull. Chem. Soc. Jpn.*, **63**, 80 (1990). d) V. Penalva, J. Hassan, L. Lavenot, C. Gozzi, and M. Lemaire, *Tetrahedron Lett.*, **39**, 2559 (1998). e) N. Leadbeater and S. M. Resouly, *Tetrahedron Lett.*, **40**, 4243 (1999).

3 For reviews, see, a) P. E. Fanta, *Synthesis*, **1974**, 9. b) W. E. Bachmann and R. A. Hoffman, *Org. React.*, **2**, 224 (1962).

4 M. Iyoda, S. M. H. Kabir, A. Vorasingha, Y. Kuwatani, and M. Yoshida, *Tetrhedron Lett.*, **39**, 5393 (1998).

5 a) J. K. Stille, *Angew. Chem., Int. Ed. Engl.*, **25**, 508 (1986). b) T. N. Mitchell, *Synthesis*, **1992**, 803.

6 a) G. Ghosal, G. P. Luke, and K. S. Kyler, *J. Org. Chem.*, **52**, 4296 (1987). b) R. L. Beddoes, T. Cheeseright, J. Wang, and P. Quayle, *Tetrahedron Lett.*, **36**, 283 (1995). c) E. Piers, E. J. McEachern, and M. A. Romero, *Tetrahedron Lett.*, **37**, 1173 (1996). d) E. Piers and M. A. Romero, *J. Am. Chem. Soc.*, **118**, 1215 (1996). e) R. Durr, S. Cossu, V. Lucchini, and O. De Lucchi, *Angew. Chem., Int. Ed. Engl.*, **36**, 2805 (1997).

7 a) L. Alcaraz and R. J. K. Taylor, *Synlett*, **1997**, 791. b) E. Shirakawa, Y. Murota, Y. Nakao, and T. Hiyama, *Synlett*, **1997**, 1143.

8 The compounds (**6**, **10**, and **8**) were prepared starting from 3,4- and 2,3-dibromothiophenes and 3,4-dibromofuran in 63, 59, and 65% yields, respectively.

9 S. Gronowitz, *Acta Chem. Scand.*, **15**, 1393 (1961).

10 S. M. H. Kabir, M. Miura, S. Sasaki, G. Harada, Y. Kuwatani, M. Yoshida, and M. Iyoda, *Heterocycles*, in press.