A Highly Effective and Practical Biaryl Synthesis with Triallyl(aryl)silanes and Aryl Chlorides

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A general and convenient approach for the palladium-catalyzed cross-coupling of triallyl(aryl)silanes, stable and easily accessible arylsilanes, with aryl chlorides has been demonstrated. The scope of the reaction is broad and a wide variety of functional groups are tolerant to the present catalyst system.

The biaryl subunit has seen a prominent presence not only in many biologically active molecules but also in many novel materials such as organic semiconductors and liquid crystals.[1] Transition metal-catalyzed cross-coupling reaction between arylmetal nucleophiles with aryl electrophiles has emerged as a unique and effective strategy to construct biaryls.[2] Although various organometallic reagents have been employed for the cross-coupling reactions,[2,3] the toxic by-products,[4] oxygen sensitivity, and less availability associated with many metallic reagents makes a great appeal to search for an alternative. To substantiate these cumulative problems, organosilanes have recently been introduced as a viable candidate due to their availability, stability, and non-toxic by-products.[5]

At first, aryl(fluoro)silanes and aryl(chloro)silanes were successfully coupled with aryl halides and triflates as disclosed from this laboratory to provide unsymmetrical biaryls in good yields.[6] Recently, this method has been utilized in solid phase synthesis;[7] various arylsilanols, trialkoxy(aryl)silanes, poly(phenylsiloxane)s, aryl(chloro or fluoro)silacyclobutanes, and arylsilatranes were employed for the cross-coupling reaction with aryl halides and triflates.[8–10]

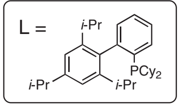
These arylsilanes, however, require at least one heteroatom on silicon to enhance the electrophilicity and thus are generally sensitive to water, base and/or acid. Cross-coupling of arylsilanes have been focused mainly on the reaction with aryl bromides, iodides and triflates; electron-deficient aryl chlorides couple with aryl(chloro)silanes and phenyltrimethoxysilane partly successfully, but electron-neutral and -rich aryl chlorides do only moderately.[6,8] To address the above drawbacks, we disclosed very recently an approach to the cross-coupling of stable all-carbon-substituted triallyl(aryl)silanes, as a notable alternative to the arylsilane nucleophile, easily accessible, quite stable toward moisture, bases, and acids, with various aryl bromides in the presence of $PdCl_2$, PCy_3, and TBAF in DMSO-H_2O to afford the corresponding biaryls in good to excellent yields.[11] Herein, we describe a general, quite effective, and an alternative method for the cross-coupling of an array of triallyl(aryl)silanes with electronically and sterically different aryl chlorides, readily available with low cost, in fairly good yields.

Among many trials under various catalyst/ligand/solvent systems, we were pleased to observe that the catalyst $[(\eta^3\text{-}C_3H_5)PdCl]_2$ in the presence of a biaryl ligand introduced by Buchwald[12] played a key role to the cross-coupling reaction. Thus, our optimized conditions $\{[(\eta^3\text{-}C_3H_5)PdCl]_2$ (2.5 mol %), 2-dicyclohexylphosphino-2′,4′,6′-triiospropylbiphenyl (L, 10 mol %), TBAF (4.0 equiv. with respect to arylsilane) in THF-H_2O (20:1), 80 °C$\}$ were applied to a wide array of electron-poor aryl chlorides to give the corresponding coupled products in good yields (Table 1, Entries 1–3).[13] The cross-coupling proceeded also with electron-rich aryl chlorides (Entries 6 and 7). One or two *o*-substituents did not affect the efficiency (Entries 4, 5, and 8–11). Pyridine- and thiophene-derived heteroaryl chlorides also cross-coupled smoothly (Entries 12 and 13).

Table 1. Cross-coupling of triallyl(aryl)silanes with aryl chlorides

$$\underset{(1.25\ \mathrm{mmol})}{\mathrm{Ar^1\text{-}Si(allyl)_3}} \xrightarrow[\substack{\text{2) }\mathrm{Ar^2\text{-}Cl}\ (1.00\ \mathrm{mmol})\\ [(\eta^3\text{-}\mathrm{C_3H_5})\mathrm{PdCl}]_2\ (2.5\ \mathrm{mol\%})\\ \mathrm{L}\ (10\ \mathrm{mol\%}),\ 80\ {}^\circ\mathrm{C}}]{\substack{\text{1) TBAF (5.0 mmol),}\\ \mathrm{THF{-}H_2O}\ (20:1,\ 5\ \mathrm{mL}),\ \mathrm{rt},\ 1\ \mathrm{h.}}} \mathrm{Ar^1\text{-}Ar^2}$$

L =

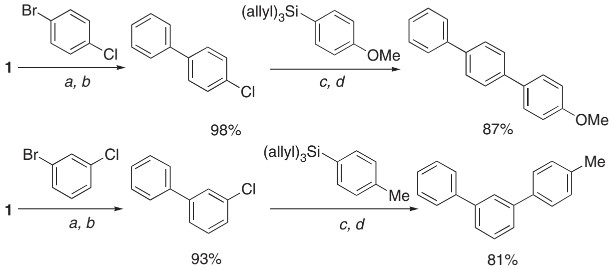


Entry	Ar^1–	Ar^2–	Time /h	Yield of Ar^1–Ar^2/%[a]
1	C_6H_5–	4-$CF_3C_6H_4$–	3	95
2	C_6H_5–	4-FC_6H_4–	3	91
3	C_6H_5–	4-NCC_6H_4–	3	77
4	C_6H_5–	2-$CF_3C_6H_4$–	3	86
5	C_6H_5–	2-FC_6H_4–	3	85
6	C_6H_5–	4-$MeOC_6H_4$–	12	97
7	C_6H_5–	3-$MeOC_6H_4$–	14	99
8	C_6H_5–	2-$MeOC_6H_4$–	14	94
9	C_6H_5–	2-MeC_6H_4–	16	88
10	C_6H_5–	1-Naphthyl–	14	94
11	C_6H_5–	2,6-$Me_2C_6H_3$–	12	87
12	C_6H_5–	3-Pyridyl–	14	98
13	C_6H_5–	2-Thienyl–	12	93
14	4-$MeOC_6H_4$–	4-MeC_6H_4–	4	95[b]
15	4-$MeOC_6H_4$–	4-$CF_3C_6H_4$–	3	89[b]
16	4-$MeOC_6H_4$–	3-Pyridyl–	6	92[b]
17	4-MeC_6H_4–	4-$MeOC_6H_4$–	4	93[b]
18	4-MeC_6H_4–	2-$MeOC_6H_4$–	4	85[b]
19	2-MeC_6H_4–	4-$CF_3C_6H_4$–	4	78[c]
20	2-MeC_6H_4–	4-$MeOC_6H_4$–	4	92[c]
21	4-FC_6H_4–	4-MeC_6H_4–	11	99[d]

[a]Isolated yield based on aryl chloride. [b]Arylsilane (1.20 mmol) was used. [c]Arylsilane (1.30 mmol) was used. [d]Arylsilane (1.8 equiv. with respect to aryl chloride) was used.

Regardless of the substituent in the arylsilane component, the cross-coupling proceeds effectively. Thus, chlorine in electron-rich, -poor chlorobenzenes was successfully substituted by 4-methoxyphenyl in good yields by the catalyst system (Entries 14 and 15). 3-Chloropyridine is not exception (Entry 16). Triallyl(4-methylphenyl)silane also successfully coupled with various aryl chlorides (Entries 17 and 18). Further, sterically hindered 2-methylphenyl and less nucleophilic 4-fluorophenyl groups were allowed to couple with a range of aryls in ArCl to afford the corresponding biaryls in acceptable yields (Entries 19–21).

The efficiency of our strategy is demonstrated by sequential cross-coupling of polyhalobenzenes. For example, applying different reaction parameters to bromochlorobenzenes, unsymmetrical terphenyls are readily prepared. Thus, cross-coupling reaction of triallyl(phenyl)silane (**1**) with 4-bromochlorobenzene by the catalyst system including $PdCl_2$, PCy_3, and TBAF in DMSO-H_2O afforded the corresponding biaryls without affecting the chloro group in 98% yield.[11] Subsequent cross-coupling with triallyl(4-methoxyphenyl)silane gave the unsymmetrical *p*-terphenyl in 87% yield as shown in Scheme 1. Similarly, the synthesis of 4-methyl-*m*-terphenyl was also achieved by performing the identical reaction sequences with 3-bromochlorobenzene in good yields as depicted in Scheme 1.



Scheme 1. Reagents and Conditions: *a*. TBAF·$3H_2O$ (4.4 equiv.), DMSO-H_2O (10:1), rt, 1 h. *b*. $PdCl_2$ (5 mol %), PCy_3 (10 mol %), 80 °C, 12 h. *c*. TBAF·$3H_2O$ (4.4 equiv.), THF-H_2O (20:1), rt, 1 h. *d*. $[(\eta^3\text{-}C_3H_5)PdCl]_2$ (2.5 mol %), L (10 mol %), 80 °C, 8 h.

Although the reactive intermediates that were generated on treatment of TBAF with triallyl(phenyl)silane were not identified yet, we presume that the three-allyl groups on Si would be cleaved upon treatment with TBAF and an appropriate amount of water in the reaction media[14] to form possibly activated silicate species such as fluorosilanes, silanepolyols, siloxanes, and/or their mixed forms.[15,16]

In summary, we have demonstrated a general and novel approach for the cross-coupling of aryl chlorides with triallyl(aryl)silanes. It is noteworthy to emphasize that triallyl(aryl)silanes serve as a highly practical and convenient agent and are fairly stable toward moisture, acid and/or bases. The catalyst system described herein effectively runs the cross-coupling of a wide range of substrates to provide the desired biaryls in excellent yields. Because of easy accessibility of aryl chlorides and stability of organosilane reagents as well as the non-toxic by-products associated with the triallyl(aryl)silanes, the present methodology would likely to find a widespread use in synthetic organic chemistry. Current efforts are directed towards the practical cross-coupling of aryl electrophiles by use of activators other than TBAF.

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References and Notes

1 a) G. Bringmann, W. Rainer, and R. Weirich, *Angew. Chem., Int. Ed.*, **29**, 977 (1990). b) S. P. Stanforth, *Tetrahedron*, **54**, 263 (1998). c) J. Hassan, M. Sevignon, C. Gozzi, E. Schulz, and M. Lemaire, *Chem. Rev.*, **102**, 1359 (2002).

2 For reviews of metal-catalyzed cross-coupling reactions, see: a) *Top. Curr. Chem.*, **219** (2002). b) "Handbook of Organopalladium Chemistry for Organic Synthesis," ed. by E.-I. Negishi, Wiley-Interscience, New York (2002).

3 a) K. Tamao, K. Sumitani, and M. Kumada, *J. Am. Chem. Soc.*, **94**, 4374 (1972). b) R. J. P. Corriu and J. P. Masse, *Chem. Commun.*, **1972**, 144. c) J. K. Stille, *Angew. Chem., Int. Ed. Engl.*, **25**, 508 (1986). d) N. Miyaura and A. Suzuki, *Chem. Rev.*, **95**, 2457 (1995).

4 For discussions of the toxicity of triorganotin compounds, see: M. Pereyre, J.-P. Quintard, and A. Rahm, "Tin in Organic Synthesis," Butterworth & Co. Ltd. (1987).

5 a) T. Hiyama, in "Metal-Catalyzed Cross-Coupling Reactions," ed. by F. Diederich and P. J. Stang, Wiley-VCH, Weinheim (1998), p 421. b) T. Hiyama and E. Shirakawa, *Top. Curr. Chem.*, **219**, 61 (2002).

6 a) Y. Hatanaka, S. Fukushima, and T. Hiyama, *Chem. Lett.*, **1989**, 1711. b) Y. Hatanaka, K.-i. Gouda, Y. Okahara, and T. Hiyama, *Tetrahedron*, **50**, 8301 (1994). c) K.-i. Gouda, E. Hagiwara, Y. Hatanaka, and T. Hiyama, *J. Org. Chem.*, **61**, 7232 (1996). d) Y. Hatanaka and T. Hiyama, *J. Org. Chem.*, **53**, 918 (1988). e) T. Huang and C.-J. Li, *Tetrahedron Lett.*, **43**, 403 (2002).

7 F. Homsi, K. Hosoi, K. Nozaki, and T. Hiyama, *J. Organomet. Chem.*, **624**, 208 (2001).

8 a) K. Hirabayashi, J. Kawashima, Y. Nishihara, A. Mori, and T. Hiyama, *Org. Lett.*, **1**, 299 (1999). b) K. Hirabayashi, A. Mori, J. Kawashima, M. Suguro, Y. Nishihara, and T. Hiyama, *J. Org. Chem.*, **65**, 5342 (2000). c) M. E. Mowery and P. DeShong, *J. Org. Chem.*, **64**, 1684 (1999). d) M. E. Mowery and P. DeShong, *Org. Lett.*, **1**, 2137 (1999). e) K. Shibata, K. Miyazawa, and Y. Goto, *Chem. Commun.*, **1997**, 1309. f) H. N. Lee and S. P. Nolan, *Org. Lett.*, **2**, 2053 (2000). g) A. Mori and M. Suguro, *Synlett*, **2001**, 845. h) T. Koike and A. Mori, *Synlett*, **2003**, 1850. i) S. Riggleman and P. DeShong, *J. Org. Chem.*, **68**, 8106 (2003).

9 S. E. Denmark and Z. Wu, *Org. Lett.*, **1**, 1495 (1999).

10 S. E. Denmark and M. H. Ober, *Org. Lett.*, **5**, 1357 (2003).

11 Y. Nakao, T. Oda, A. K. Sahoo, and T. Hiyama, *J. Organomet. Chem.*, **687**, 570 (2003).

12 a) J. P. Wolfe, R. A. Singer, B. H. Yang, and S. L. Buchwald, *J. Am. Chem. Soc.*, **121**, 9550 (1999). b) H. N. Nguyen, X. Huang, and S. L. Buchwald, *J. Am. Chem. Soc.*, **125**, 11818 (2003).

13 Reaction of 4-$MeOC_6H_4$–I and 4-$MeOC_6H_4$–Br with triallyl(phenyl)silane (**1**) under these conditions gave the corresponding coupling products in 77 and 76% yield (GC) respectively. Stoichiometric reaction of **1** with 4-$MeOC_6H_4$–Cl gave 90% yield (GC) of the product.

14 ^1H NMR analysis of the reaction mixture showed no detectable peaks corresponding to allyl groups on silicon upon treatment of **1** with TBAF in THF-H_2O at rt for 20 min.

15 a) S. E. Denmark, D. Wehrli, and J. Y. Choi, *Org. Lett.*, **2**, 2491 (2000). b) S. E. Denmark and R. F. Sweis, *Acc. Chem. Res.*, **35**, 835 (2002).

16 A silicon activating group like 2-Py and benzyl are employed for the cross-coupling: a) K. Itami, T. Nokami, Y. Ishimura, K. Mitsudo, T. Kamei, and J.-i. Yoshida, *J. Am. Chem. Soc.*, **123**, 11577 (2001). b) B. M. Trost, M. R. Machacek, and Z. T. Ball, *Org. Lett.*, **5**, 1895 (2003).