

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

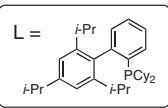
At first, aryl(fluoro)silanes and aryl(chloro)silanes were successfully coupled with aryl halides and triflates as disclosed from this laboratory to provide unsymmetrical biaryls in good yields.⁶ Recently, this method has been utilized in solid phase synthesis;⁷ various arylsilanols, trialkoxy(aryl)silanes, 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 PdCl₂, PCy₃, and TBAF in DMSO-H₂O 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 [(η³-C₃H₅)PdCl]₂ in the presence of a biaryl ligand introduced by Buchwald¹² played a key role to the cross-coupling reaction. Thus, our optimized conditions {(η³-C₃H₅)PdCl]₂ (2.5 mol %), 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (L,

10 mol %), TBAF (4.0 equiv. with respect to arylsilane) in THF-H₂O (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

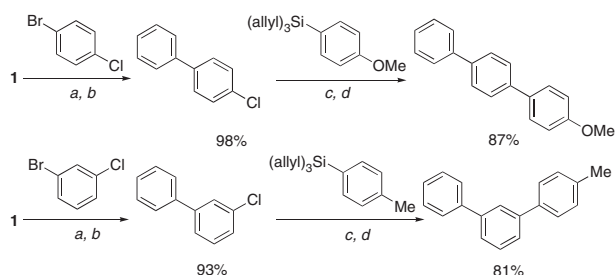
$\text{Ar}^1\text{-Si(allyl)}_3 \xrightarrow[\text{2) Ar}^2\text{-Cl (1.00 mmol), } [(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}]_2 \text{ (2.5 mol\%), L (10 mol\%), 80 }^\circ\text{C}]{\text{1) TBAF (5.0 mmol), THF-H}_2\text{O (20 : 1, 5 mL), rt, 1 h.}}$ $\text{Ar}^1\text{-Si(allyl)}_3$ (1.25 mmol) $\text{L} =$  $\text{Ar}^1\text{-Ar}^2$				
Entry	Ar ¹ –	Ar ² –	Time /h	Yield of Ar ¹ –Ar ² /% ^a
1	C ₆ H ₅ –	4-CF ₃ C ₆ H ₄ –	3	95
2	C ₆ H ₅ –	4-FC ₆ H ₄ –	3	91
3	C ₆ H ₅ –	4-NCC ₆ H ₄ –	3	77
4	C ₆ H ₅ –	2-CF ₃ C ₆ H ₄ –	3	86
5	C ₆ H ₅ –	2-FC ₆ H ₄ –	3	85
6	C ₆ H ₅ –	4-MeOC ₆ H ₄ –	12	97
7	C ₆ H ₅ –	3-MeOC ₆ H ₄ –	14	99
8	C ₆ H ₅ –	2-MeOC ₆ H ₄ –	14	94
9	C ₆ H ₅ –	2-MeC ₆ H ₄ –	16	88
10	C ₆ H ₅ –	1-Naphthyl–	14	94
11	C ₆ H ₅ –	2,6-Me ₂ C ₆ H ₃ –	12	87
12	C ₆ H ₅ –	3-Pyridyl–	14	98
13	C ₆ H ₅ –	2-Thienyl–	12	93
14	4-MeOC ₆ H ₄ –	4-MeC ₆ H ₄ –	4	95 ^b
15	4-MeOC ₆ H ₄ –	4-CF ₃ C ₆ H ₄ –	3	89 ^b
16	4-MeOC ₆ H ₄ –	3-Pyridyl–	6	92 ^b
17	4-MeC ₆ H ₄ –	4-MeOC ₆ H ₄ –	4	93 ^b
18	4-MeC ₆ H ₄ –	2-MeOC ₆ H ₄ –	4	85 ^b
19	2-MeC ₆ H ₄ –	4-CF ₃ C ₆ H ₄ –	4	78 ^c
20	2-MeC ₆ H ₄ –	4-MeOC ₆ H ₄ –	4	92 ^c
21	4-FC ₆ H ₄ –	4-MeC ₆ H ₄ –	11	99 ^d

^aIsolated yield based on aryl chloride. ^bArylsilane (1.20 mmol) was used. ^cArylsilane (1.30 mmol) was used. ^dArylsilane (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 hin-

dered 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 PdCl₂, PCy₃, and TBAF in DMSO-H₂O 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·3H₂O (4.4 equiv.), DMSO-H₂O (10:1), rt, 1 h. *b*. PdCl₂ (5 mol %), PCy₃ (10 mol %), 80 °C, 12 h. *c*. TBAF·3H₂O (4.4 equiv.), THF-H₂O (20:1), rt, 1 h. *d*. [(η³-C₃H₅)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 media¹⁴ 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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