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Palladium-catalyzed coupling of aryl halides with arylhalosilanes in air and water

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Abstract—In the presence of a palladium catalyst, various aryl halides reacted with arylhalosilanes in aqueous media and under an air atmosphere to give the corresponding unsymmetrical aryl–aryl coupling products conveniently. © 2002 Elsevier Science Ltd. All rights reserved.

Palladium-catalyzed reductive couplings are among the most important carbon–carbon bond forming reactions in modern synthetic organic chemistry.[1] The Stille[2] and the Suzuki reactions[3] have been widely used to generate aryl–aryl coupling products. Although both reactions are highly successful, a drawback of the Stille coupling is the involvement and generation of relatively toxic tin reagents and by-products and the limitations with regard to synthesis and stability of boron reagents were also noted.[4] The use of hypervalent silicon reagents for palladium-catalyzed cross couplings has been established recently by Hiyama,[5] DeShong[6] and others. On the other hand, Denmark and co-workers have developed highly activated silicon reagents for palladium-catalyzed couplings with aryl halides.[7] More recently, Hiyama and co-workers reported the coupling of silanols, silanediols and silanetriols with aryl iodides in THF.[8] In an effort to develop air[9] and water-stable[10] catalytic reactions, previously we reported a palladium-catalyzed Ullmann-type reductive coupling of aryl halides in aqueous conditions and under an air atmosphere.[11] Although the reaction offers synthetic convenience, it is limited to the generation of symmetrical biaryls. Recently, we found that arylhalosilanes underwent conjugated additions catalyzed by rhodium in air and water effectively.[12] In this paper, we report that in the presence of a palladium catalyst, arylhalosilanes reacted with various aryl halides in air and water in the presence of base or NaF to give the corresponding unsymmetrical biaryl products conveniently (Eq. (1)).

$$\mathrm{ArX} + \mathrm{PhRSiCl_2} \xrightarrow[\mathrm{KOH\ (or\ NaF)/H_2O}]{\mathrm{Pd\ cat.}} \mathrm{Ar{-}Ph} \qquad (1)$$

Table 1. Coupling of 4-iodoanisole with arylhalosilanes under various conditions

Entry	Silicon reagent	Catalyst	Additive (equiv.)[a]	Yield (%)[b]
1	$PhSiCl_3$	$Pd(OAc)_2$	None	20
2	$PhSiCl_2$	$Pd(OAc)_2$	NaF	40
3	$PhMeSiCl_2$	$Pd(OAc)_2$	NaF	47
4	Ph_2SiCl_2	$Pd(OAc)_2$	KOH	70
5	$PhMeSiCl_2$	$Pd(OAc)_2$	KOH	71
6	$PhSiCl_3$	Pd/C	KOH	36
7	Ph_2SiCl_2	Pd/C	KOH	74
8	$PhMeSiCl_2$	Pd/C	KOH	80
9	$PhMeSiCl_2$	Pd/C	None	0

[a] 6–8 equiv. of additives were added.

[b] Isolated yields.

To begin the study, 4-iodoanisole was reacted with various arylhalosilanes under a variety of conditions (Table 1). Initially, $Pd(OAc)_2$ was used as the catalyst. The reaction of phenyltrichlorosilane with 4-iodoanisole under refluxing conditions overnight generated the desired product in 20% isolated yield together with a large amount of unreacted 4-iodoanisole. The use of diphenyldichlorosilane in combination with sodium fluoride slightly improved the yield. The yield was further improved by using phenylmethyldichlorosilane as the silicon reagent. The use of KOH instead of NaF provided higher yields for both diphenyldichlorosilane and phenylmethyldichlorosilane reactions. Very similar but slightly better results were observed with Pd/C as the catalyst. In this case, no reaction was observed in the absence of KOH.

Subsequently, a variety of aryl halides were examined under the Pd/C-catalyzed conditions (Table 2).[13] Nearly

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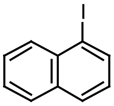
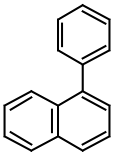
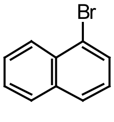
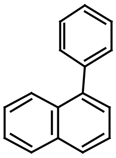
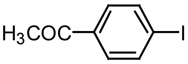
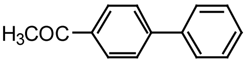
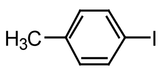
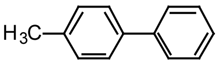
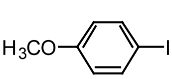
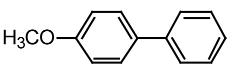
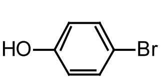
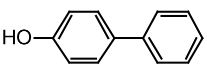
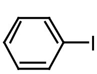
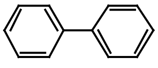
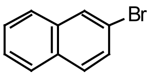
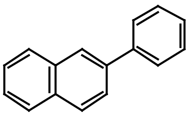
Table 2. Coupling of various aryl halides with methylphenylhalosilane

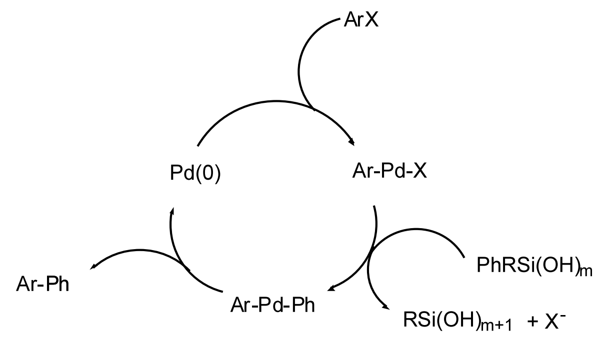
entry	aryl halide	product	yield (%)[a]
1			72
2			65
3			81
4			61
5			80
6			59
7			100
8			51

All reactions were carried out with Pd/C, KOH/H_2O, under refluxing conditions for 12-36h. a: Isolated yields.

the same results were obtained with either iodo or bromo derivatives. Iodo- and bromo-naphthalenes (entries 1, 2, and 8) reacted similarly. A slightly better yield was obtained with an electron-deficient aryl iodide than electron-rich aryl halides. It is noteworthy to mention that 4-bromophenol reacted smoothly to generate the desired product (entry 6). The use of simple iodobenzene provided the corresponding product quantitatively (entry 7) (part of the product may be due to homocoupling of the silicon reagent).

A tentative mechanism for the reaction involves the oxidative addition of the palladium catalyst to the aryl halides to generate a palladium intermediate (Scheme 1). The intermediate then reacts with the silicate generated from the arylhalosilane derivative and KOH or NaF to afford the cross-coupling product and regenerate the active palladium catalyst.

The following procedure is representative: A mixture of 4-iodoanisole (234 mg, 1 mmol), dichloromethylphenylsilane (382 mg, 2 mmol), KOH (448 mg, 8 mmol), and Pd/C (5 mol%) in 10 mL of water was stirred at 100°C for 12 h under an air atmosphere. The reaction mixture was cooled and extracted with ethyl acetate. After the combined organic phase was dried and concentrated in vacuo, the residue was separated by silica gel chromatography eluting with hexane to give the desired biaryl product (140 mg, 80%).



Scheme 1. Tentative mechanism for the palladium-catalyzed coupling of arylhalosilanes with aryl halides in air and water.

Acknowledgements

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