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NaOH-Promoted Cross-Coupling Reactions of Organosilicon Compounds with Organic Halides: Practical Routes to Biaryls, Alkenylarenes and Conjugated Dienes

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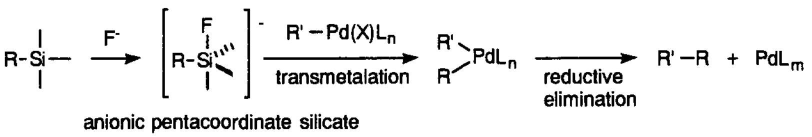
Abstract: The use of NaOH has been found to be extremely effective in promoting the palladium-catalyzed cross-coupling reactions of aryl and alkenylchlorosilanes with organic halides such as aryl bromides and chlorides under very mild conditions.

The palladium-catalyzed cross-coupling reaction of organosilicon compounds with a variety of electrophiles has provided one of the most practical and versatile methods for synthesizing functionalized organic compounds with high stereo- and regioselectivity.[1] This reaction is usually realized in the presence of KF or organic fluoride salts such as *n*Bu_4NF (TBAF) or $[(Et_2N)_3S]^+[Me_3SiF_2]^-$ (TASF) to activate the Si-C bonds of the silicon reagents by forming an anionic pentacoordinate silicate and facilitate the transmetalation with a palladium species. Subsequent reductive elimination of a resulting diorganopalladium species gives a coupled product.[1a, 2]



We report herein that NaOH is a better promotor than fluoride salts; the reactivity of the silicon reagents, when activated by NaOH, is significantly increased and the palladium-catalyzed cross-coupling reaction of aryl and alkenylchlorosilanes with organic halides proceeded under much milder reaction conditions compared to the fluoride salt-promoted reaction.

$$\text{R-}Si \quad + \quad \text{X-R'} \quad \xrightarrow{\text{NaOH / Pd cat}} \quad \text{R-R'}$$

R = aryl, alkenyl; *Si* = $SiEtCl_2$, $SiMeCl_2$; X = Cl, Br, I; R' = aryl, alkenyl.

The coupling reaction of Ar-$SiRCl_2$ (R = Me or Et) with aryl halides smoothly took place in the presence of NaOH (6 equiv. based on the silicon reagents) and a catalytic amount of $Pd(OAc)_2$ (0.5-1.0 mol %) and PPh_3 (1.0-2.0 mol %), giving high yields of the corresponding unsymmetrical biaryls (Table 1, entries 1- 6).[3]

In contrast to the KF-promoted coupling reaction of Ar-$SiRCl_2$ with aryl bromides which requires rather drastic conditions (e.g., heating at 120 - 150 °C for 20 h in *N,N*,-dimethylformamide),[4] the NaOH-promoted reaction smoothly completed at 60-80 °C in tetrahydrofuran (THF) or in benzene. In most cases, no significant side products such as symmetrical biaryls arising from homocoupling of the substrates were observed. Although the reaction conditions are strongly basic, the reaction tolerates a variety of reactive functionalities such as carbonyl group or cyano group on the aromatic ring without leading to serious side reactions.

The recent interest in organic functional materials, in particular in the area of aromatic polymers[5] and liquid crystals,[6] has created a need for a straightforward route to unsymmetrical biaryls. The synthetic utility of the present reaction is well demonstrated by the short synthesis of a liquid crystal, 3,4-difluoro-4'-(*trans*-4-propylcyclohexyl)-1,1'-biphenyl (**2**)[7] (entry 6). The liquid crystal **2** was successfully synthesized in 89% yield by the cross-coupling reaction of 1-bromo-3,4-difluorobenzene with (dichloro)(ethyl)[(4-*trans*-propylcyclohexyl)phenyl]silane (**1**), prepared from 1-bromo-4-(*trans*-4-propylcyclohexyl)benzene and trichloroethylsilane.

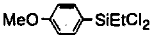
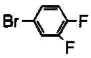
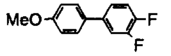
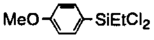
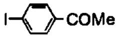
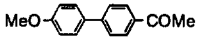
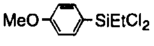
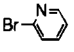
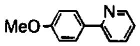
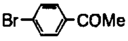
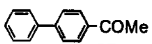
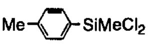
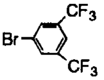
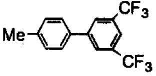
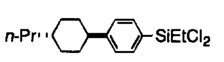
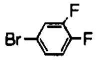
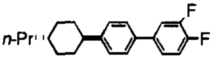
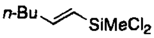
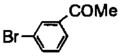
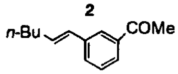
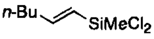
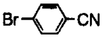
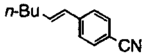
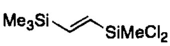
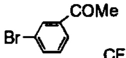
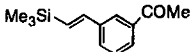
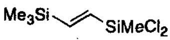
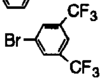
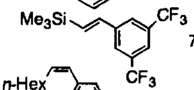
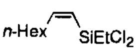
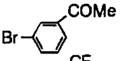
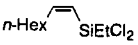
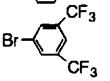
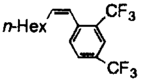
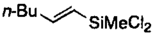
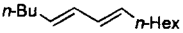
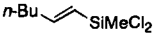
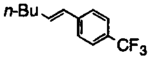
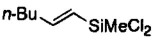
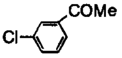
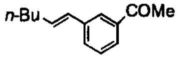
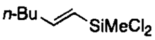
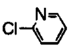
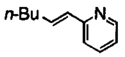
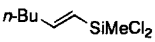
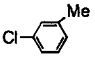
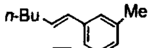
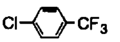
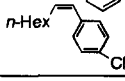
Surprisingly, the reaction is very sensitive to the variation of the base. A series of inorganic bases such as LiOH, KOH, K_2CO_3, and Na_2CO_3 were less effective under the similar conditions, affording only trace amount of the coupled products. The structure of the silyl groups also strongly influences the reactivity of the arylsilanes. The use of Ar-$SiEt_2Cl$ or Ar-$SiMe_2Cl$ gave the lower yields of the corresponding coupled products, and Ar-$SiCl_3$ failed to undergo the coupling reactions. It is noteworthy that the reaction can be effected even in a water-containing solvent; for example, the coupling reaction of (4-methoxyphenyl)(dichloro)(ethyl)silane with 4-bromoacetophenone smoothly took place in THF at 60 °C by adding aqueous NaOH (2 *M*), giving 4-acetyl-4'-methoxy-1,1'-biphenyl in 95% yield.

The coupling reaction of alkenylchlorosilanes with aryl bromides or alkenyl iodide successfully proceeded under the similar reaction conditions (e.g., heating at 60 °C in THF in the presence of $Pd(OAc)_2$ (2.5 mol %) and NaOH (6 equiv.)), giving alkenylarenes (entries 7-12) or conjugated dienes (entry 13) in good yields. Previously, we have reported the TBAF- or TASF-promoted cross-coupling reaction of alkenylsilanes with aryl halides, which is applicable to less available alkenylfluorosilanes and aryl iodides.[8] Thus, the use of readily accessible alkenylchlorosilanes[9] and aryl bromides as well as the use of NaOH in place of expensive TBAF or TASF makes the reaction much more practical.

When (*E*)-1-(methyldichlorosilyl)-2-(trimethylsilyl)ethene was allowed to react with aryl bromides, the coupling reactions selectively occurred at the carbon bonded to methyldichlorosilyl group, giving high yields of (*E*)-1-trimethylsilyl-2-arylethenes (entries 9 and 10). High stereospecificity of the reaction also deserves comment; (*Z*)-1-(dichloro)(ethyl)silyl-1-octene coupled with aryl bromides with the retention of the double bond geometry to furnish isomerically pure (*Z*)-1-aryl-1-octenes in good yields (entries 11 and 12).

Although aryl chlorides have been previously regarded as inert in the transition-metal-catalyzed coupling reaction with arylmetals or alkenylmetals,[10] we have recently found that trialkylphosphine-palladium complexes such as $(i\text{-}Pr_3P)_2PdCl_2$ or $(dcpe)PdCl_2$ (dcpe = $Cy_2PCH_2CH_2PCy_2$) effectively catalyze the coupling reaction of aryl chlorides with organochlorosilanes in the presence of TBAF or KF.[11, 12] The use of NaOH is also quite effective in accomplishing the coupling reaction of alkenylchlorosilanes with aryl chlorides at lower temperature in the presence of the same catalysts. The reaction stereospecifically proceeded at 80 °C in benzene, furnishing high yields of alkenylarenes (entries 14 - 18). This procedure would be of importance as a method for synthesizing alkenylarenes from less expensive aryl chlorides.

Table 1. Cross-coupling Reactions of Organic halides with Organochlorosilanes Mediated by Palladium Catalyst and Sodium Hydroxide

Entry	Organosilane	Organic halides	Catalyst / Conditions	Product	Yield(%)[a]
1[b]			Pd(OAc)$_2$/2PPh$_3$ THF, 60 °C, 14 h.		75
2[b]			Pd(OAc)$_2$/2PPh$_3$ benzene, 80 °C, 17 h.		95
3[b]			Pd(OAc)$_2$/2PPh$_3$ THF, 60 °C, 39 h.		64
4[b]			Pd(OAc)$_2$/2PPh$_3$ benzene, 80 °C, 39 h.		89
5[b]			Pd(OAc)$_2$/2PPh$_3$ THF, 60 °C, 39 h.		85
6[b]	 1		Pd(OAc)$_2$/2PPh$_3$ benzene, 80 °C, 62 h.	 2	89
7[c]			Pd(OAc)$_2$ THF, 60 °C, 5 h.		79
8[c]			Pd(OAc)$_2$ THF, 60 °C, 12 h.		80
9[c]			Pd(OAc)$_2$ THF, 60 °C, 12 h.		62
10[c]			Pd(OAc)$_2$ THF, 60 °C, 36 h.		74
11[c]			Pd(OAc)$_2$ THF, 60 °C, 12 h.		70
12[c]			Pd(OAc)$_2$ THF, 60 °C, 12 h.		66
13[c]			Pd(OAc)$_2$ THF, 60 °C, 12 h.		58
14[d]			(*i*-Pr$_3$P)$_2$PdCl$_2$ benzene, 80 °C, 12 h.		95
15[d]			(*i*-Pr$_3$P)$_2$PdCl$_2$ benzene, 80 °C, 12 h.		65
16[d]			(*i*-Pr$_3$P)$_2$PdCl$_2$ benzene, 80 °C, 12 h.		79
17[d]			(*i*-Pr$_3$P)$_2$PdCl$_2$ benzene, 80 °C, 12 h.		91
18[d]			(dcpe)PdCl$_2$ benzene, 80 °C, 12 h.		55

[a] Isolated. [b] Arylsilanes (1.2 - 1.6 equiv), aryl halides (1.0 equiv), NaOH (6.0 equiv), Pd(OAc)$_2$ (0.5-1.0 mol % based on aryl halides), PPh$_3$ (1.0-2.0 mol % based on aryl halides). [c] Alkenylsilanes (1.2 equiv), organic halides (1.0equiv), NaOH (6.0 equiv), Pd(OAc)$_2$ (2.5 mol % based on organic halides). [d] Alkenylsilanes (1.2 equiv), aryl chlorides (1.0 equiv), NaOH (6.0 equiv), Pd cat (2.5 mol % based on aryl chlorides).

In summary, organosilicon compounds activated by NaOH undergo the palladium-catalyzed cross-coupling reactions with organic halides under the very mild conditions. The present method seems to be extremely useful as a general and practical route to a wide range of functionalized organic compounds in view of the use of NaOH as well as the great availability of organochlorosilanes.

REFERENCES AND NOTES

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1. For reviews on the cross-coupling reaction of organosilicon compounds, see: (a) Hatanaka, Y.; Hiyama, T. *Synlett* **1991**, 845-853. (b) Hiyama, T.; Hatanaka, Y. *Pure Appl. Chem.* **1994**, *66*, 1471-1478. (c) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371-1448. (d) Horn, K. A. *Chem. Rev.* **1995**, *95*, 1317-1350.
2. Recently, we have found that the palladium-catalyzed coupling reaction of allylic carbonates with alkenylfluorosilanes proceeds in the absence of fluoride salts. Matsuhashi, H.; Hatanaka, Y.; Hiyama, Kuroboshi, M. *Tetrahedron Lett.* **1995**, *36*, 1539-1540.
3. The following procedure for the preparation of 4-acetyl-1,1'-biphenyl is a representative (Table 1, entry 4). To a slurry of crushed NaOH (377 mg, 9.43 mmol; NaOH was crushed in a dry atmosphere) in benzene (5 ml), (dichloro)(ethyl)(phenyl)silane (360 mg, 1.90 mmol) was added at 0 °C. The resulting bright yellow suspension was stirred at room temperature for 3 h in an inert atmosphere. To this mixture 4-bromoacetophenone (313 mg, 1.6 mmol) and palladium catalyst, prepared by stirring the mixture of $Pd(OAc)_2$ (1.8 mg, 0.008 mmol) and PPh_3 (4.1 mg, 0.015 mmol) in benzene (1 ml) at room temperature for 40 min, were added. The reaction mixture was heated at 80 °C for 39 h with vigorous stirring. The usual work up of the reaction mixture, followed by column chromatography (silica-gel, ethyl acetate : hexane = 1: 7) gave a 275 mg of 4-acetyl-1,1'-biphenyl as a colorless solid (1.4 mmol, 89%). The physical properties of the obtained product were in good agreement with the reported data: Long, L. M.; Henze, H. R. *J. Am. Chem. Soc.* **1941**, *63*, 1939-1940.
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