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Cross-Coupling Reactions of Aryl Chlorides with Organochlorosilanes: Highly Effective Methods for Arylation or Alkenylation of Aryl Chlorides

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The transition-metal-catalyzed cross-coupling reactions of aryl halides with organometallic reagents[1] have been demonstrated to be a highly effective and practical method for preparing a number of valuable aromatic products such as aromatic polymers,[2] liquid crystals,[3] and natural products containing aryl parts.[4] Among various aryl halides, aryl chlorides should be the most attractive candidates for industrial applications of these reactions, because they are inexpensive and easily available in bulk quantities compared with aryl bromides and iodides. Thus, transition-metal-catalyzed activation and transformation of the inert Cl−C bonds in aryl chlorides has been one of the most challenging problems in synthetic chemistry.[5] However, unlike bromo and iodo analogs, aryl chlorides are usually unreactive in the cross-coupling reactions with organometallic reagents[6] except for the nickel-catalyzed alkylation using alkyl Grignard reagents.[7]

We report herein the first successful examples of alkenylation and arylation of aryl chlorides by means of the cross-coupling reactions using organochlorosilanes (Scheme 1).[8]

Scheme 1[a]

$$\mathrm{R}\mathit{Si} + \mathrm{ClAr} \xrightarrow{\text{Pd cat/F}^-} \mathrm{RAr}$$

[a] R = aryl, alkenyl; *Si* = $SiCl_3$, $Si(R)Cl_2$, $SiEtCl_2$, $SiMeCl_2$, $SiMe_2Cl$.

A series of alkenyl- and arylchlorosilanes have been found to undergo the palladium-catalyzed cross-coupling reactions with aryl chlorides in the presence of a fluoride salt, giving alkenylarenes or unsymmetrical biaryls in good yields.[9]

The cross-coupling reactions of aryl chlorides with arylchlorosilanes smoothly proceeded in the presence of a catalytic amount of [$(i\text{-}Pr_3P)_2PdCl_2$] (0.5 mol%)[10] and potassium fluoride in *N*,*N*-dimethylformamide at 120 °C, furnishing the corresponding unsymmetrical biaryls (Table 1). In most cases, no significant side products such as symmetrical biaryls arising from the homocoupling reactions were observed.[6d] However, reduction of the Si−Ar bonds occurred in some cases, producing volatile aromatic compounds (Table 1, entries 3−5). Since a wide range of functional groups on the aromatic rings of both the coupling partners could be tolerated under the reaction conditions, aryl chlorides containing cyano, acetyl, fluoro, and trifluoromethyl groups were easily involved in the reactions (Table 1, entries 1−6). Considering the commercial availabilities of a variety of arylchlorosilanes,[11] this method would be of great value as a convenient route to functionalized unsymmetrical biaryls from inexpensive aryl chlorides.[12]

A series of trialkylphosphine−palladium complexes were found to be highly effective in catalyzing the cross-coupling reactions of aryl chlorides. The highest yields of the coupled products were obtained by using [$(i\text{-}Pr_3P)_2PdCl_2$] as a catalyst. In some cases, catalytic activity of [$(dcpe)PdCl_2$] (dcpe = $Cy_2PCH_2CH_2PCy_2$)[13] was comparable (Table 1, entry 2). In contrast to the excellent catalytic activity of trialkylphosphine−palladium complexes, triphenylphosphine-palladium complexes such as $(PPh_3)_4Pd$ and $(PPh_3)_2PdCl_2$ exhibited negligible catalytic activity.

The structure of the silyl groups of arylchlorosilanes slightly influences the rate of the cross-coupling reactions. For instance, the reactivities of (dichloro)(methyl)-(4-methoxyphenyl)silane and (dichloro)[bis(4-methoxyphenyl)]silane in the coupling reactions with 4-chlorobenzonitrile were comparable to that of (dichloro)(ethyl)-(4-methoxyphenyl)silane (Table 1, entries 6−8). However, (trichloro)(4-methoxyphenyl)silane in the same reaction was slightly less reactive, giving the coupled product in lower yield even under the longer reaction time (Table 1, entry 9).

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Table 1. Cross-Coupling Reactions of Chloroarenes with Organochlorosilanes Mediated by Palladium Catalyst and Fluoride Salt

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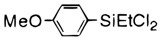
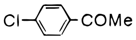
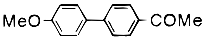
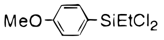
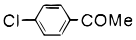
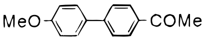
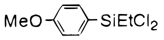
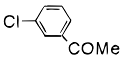
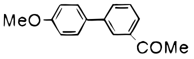
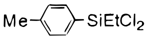
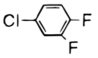
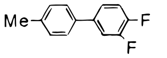
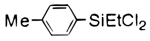
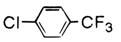
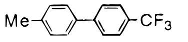
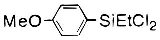
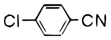
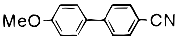
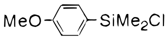
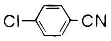
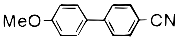
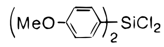
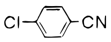
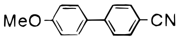
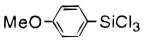
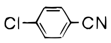
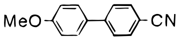
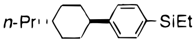
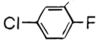
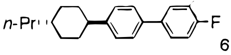
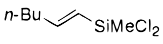
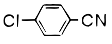
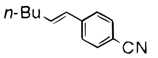
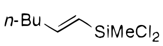
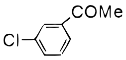
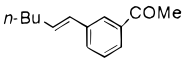
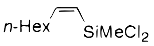
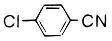
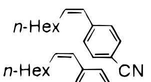
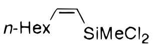
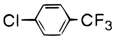
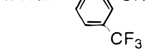
1[b]				62
2[c]				97
3[b]				62
4[b]				65
5[b]				68
6[b]				95
7[b]				93
8[b]				92
9[b]				73
10[d]	 **1**		 **2**	64
11[e]				83
12[e]				83
13[e]				91
14[e]				58

[a] Isolated. [b] Arylchlorosilane (1.2 mmol), chloroarene (1.0 mmol), KF (6.0 mmol), (i-$Pr_3P)_2PdCl_2$ (0.005 mmol, 0.5 mol %), DMF (3 mL); 120 °C, 24−48 h. [c] Arylchlorosilane (0.9 mmol), chloroarene (0.45 mmol), KF (4.5 mmol), [(dcpe)$PdCl_2$] (0.01 mmol, 2.0 mol %), DMF (3 mL); 120 °C, 48 h. [d] The reaction was carried out at 150 °C for 20 h. [e] Alkenylchlorosilane (1.2 mmol), chloroarene (1.0 mmol), TBAF (3.6 mmol), [$(Et_3P)_2PdCl_2$] (0.005 mmol, 0.5 mol %), THF (3 mL); 90 °C, 20 h in a sealed tube.

In contrast, electronic property of the substituents has a strong influence on the reactivity of aryl chlorides. The cross-coupling reactions of aryl chloride substituted by an electron-withdrawing group smoothly proceeded and went to completion within 24 h, whereas aryl chlorides containing electron-donating groups such as 4-chlorotoluene and 4-chloroanisole reacted more slowly and failed to give satisfactory yields of the coupled products. The low reactivity of methyl- or methoxy-substituted aryl chlorides is probably due to the sluggish oxidative addition of the C−Cl bonds in the electron-rich aryl chlorides to a low valent palladium complex.[14]

The synthetic applicability of the present method has been well demonstrated by the simple preparation of a liquid crystal, 3,4-difluoro-4′-(*trans*-4-propylcyclohexyl)-1,1′-biphenyl (**2**).[15] The liquid crystal **2** was synthesized in 64% yield (Table 1, entry 10).

Alkenylchlorosilanes readily undergo the palladium-catalyzed cross-coupling reactions with aryl chlorides in the presence of n-$Bu_4N^+F^-$ (TBAF) in tetrahydrofuran (THF), giving alkenylarenes in good yields (Table 1, entries 11−14). The best conversions of chloroarenes to alkenylarenes were achieved with $(Et_3P)_2PdCl_2$[16] as a catalyst, whereas (dcpe)$PdCl_2$ and (i-$Pr_3P)_2PdCl_2$ were less effective. The reactivity of alkenylchlorosilanes was found to be strongly influenced by the structure of the silyl groups; the rate of the cross-coupling reaction of (*E*)-1-octenylchlorosilanes with 4-chlorobenzonitrile significantly decreases in the order $SiCl_3$, $SiMeCl_2 > SiMe_2Cl \gg SiMe_3$. It should be noted that the coupling reaction of alkenylchlorosilanes with aryl chlorides proceeded highly stereospecifically with the retention of the double bond geometry of the alkenylchlorosilanes.[17] Thus, the present reactions offer a convenient and highly stereospecific method for synthesizing stereodefined alkenylarenes from chloroarenes and alkenylchlorosilanes that are easily available from the hydrosilylation of alkynes with chlorosilanes.[18]

The mechanism of the present cross-coupling reactions of aryl chlorides has not been investigated in detail; however, it is reasonable to assume that an oxidative addition of the inert Cl−Ar bond to a low valent palladium complex is the rate-limiting step in the catalytic cycle. Recent studies on the oxidative addition of aryl chlorides to phosphine−palladium complexes have shown that cleavage of the Cl−Ar bond by a low-valent palladium complex proceeds via a typical S_NAr mechanism rather than one-electron transfer from the palladium complex to the aryl chlorides.[19] Thus, the excellent catalytic activity of the trialkylphosphine−palladium complexes is attributable to the enhanced nucleophilicity of the palladium, since the electron-donating trialkylphosphine ligands such as dcpe or i-Pr_3P would increase the electron-density of the palladium complexes, promoting the nucleophilic cleavage of the Cl−Ar bonds by the palladium.

In summary, the cross-coupling reactions of aryl chlorides with organochlorosilanes catalyzed by electron-donating trialkylphosphine-based palladium complexes provide a general and convenient route to functionalized unsymmetrical biaryls and alkenylarenes. The successful reactions can be ascribed to the exceptional thermal stability of the organochlorosilanes; unlike usual organometallic reagents, organochlorosilanes can effectively undergo the cross-coupling reactions without decomposition even under the drastic conditions (90−150 °C for 24−48 h) that are essential for the smooth catalytic activation of the inert Cl−Ar bonds.

Supporting Information Available: Text describing experimental details and spectral data of the coupled products and organochlorosilanes (7 pages).

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