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Selective Synthesis of Unsymmetrical Biaryls via Palladium-Catalyzed Cross-Coupling of Arylfluorosilanes with Aryl Iodides

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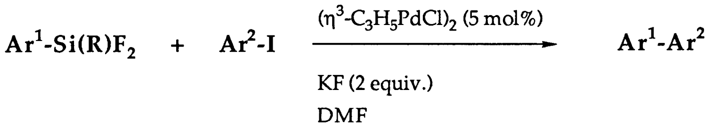
In the presence of potassium fluoride, arylfluorosilanes readily participate in Pd-catalyzed cross-coupling reaction of aryl iodides to give the corresponding unsymmetrical biaryls in good yields.

In view of recent progress of the display devices using liquid crystalline compounds as well as the recent interest in liquid crystalline polymers, selective synthesis of unsymmetrical biaryls renewedly has grown a major problem in organic synthesis.[1)] A straightforward approach should be that which involves transition metal catalyzed cross-coupling reactions of aryl metals with aryl halides.[2)] However, this is scarcely applicable to the preparation of highly functionalized biaryls. The methods presently available are the coupling of aryl halides with arylmagnesium halides,[3)] arylzinc chlorides,[3c,4)] aryltin compounds[5)] and arylboronic acids.[6)] Of these, heteroaryltin compounds[5b)] and arylboronic acids[6)] only are compatible with the carbonyl groups of esters and amides. In connection with our interest in synthetic applications of silicon-based cross-coupling reactions mediated by a palladium catalyst and fluoride ion,[7)] we have investigated the palladium catalyzed reaction of arylsilanes with aryl iodides promoted by potassium fluoride. We have found that the reaction can be extremely useful in aryl-aryl bond formation and describe herein its application to the synthesis of highly functionalized unsymmetrical biaryls.

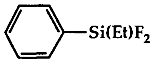
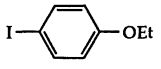
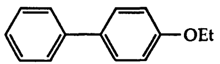
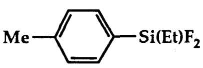
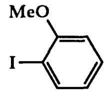
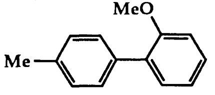
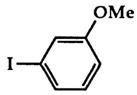
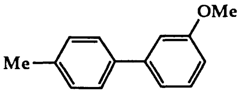
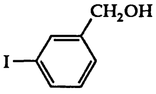
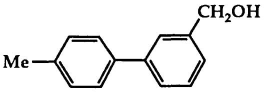
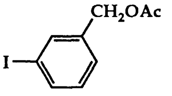
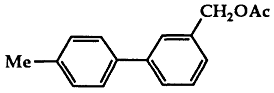
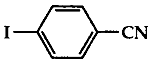
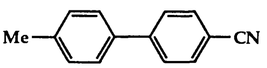
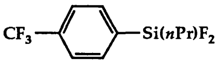
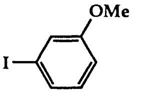
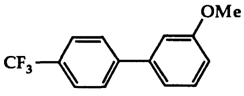
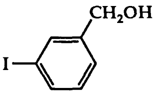
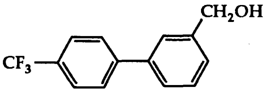
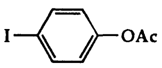
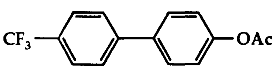
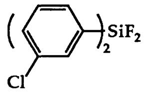
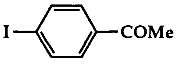
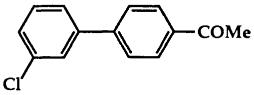
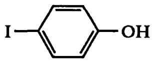
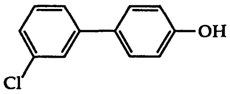
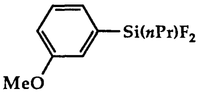
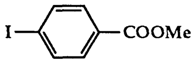
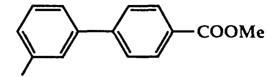
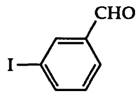
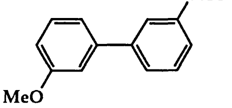
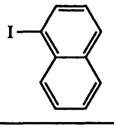
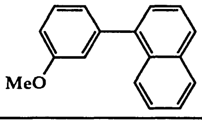


$$\mathrm{Ar^1\text{-}Si(R)F_2} \quad + \quad \mathrm{Ar^2\text{-}I} \quad \xrightarrow[\text{KF (2 equiv.)}\ \text{DMF}]{(\eta^3\text{-}C_3H_5PdCl)_2\ \text{(5 mol\%)}} \quad \mathrm{Ar^1\text{-}Ar^2}$$

The arylfluorosilanes used in this work can be conveniently prepared by the fluorination of the corresponding arylchlorosilanes with antimony trifluoride[8)] and stored in the air for a long period.

At first, series of experiments were effected with various types of phenylsilanes and 4-iodoacetophenone (**1**) to evaluate the reactivity of arylsilanes in the desired aryl-aryl cross-coupling. The coupling reaction worked well in *N,N*-dimethylformamide (DMF) solvent at 100 °C in the presence of 5 mol% of $(\eta^3\text{-}C_3H_5PdCl)_2$ catalyst and 2 equiv. of potassium fluoride to give 4-phenylacetophenone (**2**). Palladium complexes like $Pd(PPh_3)_4$, $PdCl_2(PPh_3)_2$ and $Pd(dba)_2$ did not work at all. Results obtained with various phenylsilanes are given in the order of phenylsilane,

Table 1. Pd-Catalyzed Coupling of Arylsilanes with Aryl Iodidies[a)]

Entry	Arylsilane	Aryl Iodide	Reaction temp Reaction time	Product (Yield/%)[b)]
1			70 °C 10 h	 (81)
2			80 °C 6 h	 (45)
3			80 °C 9 h	 (83)
4			100 °C 15 h	 (86)
5			100 °C 49 h	 (89)
6			100 °C 21 h	 (67)
7			80 °C 28 h	 (52)
8			100 °C 19 h	 (67)
9			100 °C 13 h	 (47)
10			70 °C 43 h	 (74)
11			70 °C 10 h	 (68)
12			70 °C 15 h	 (76)
13			100 °C 15 h	 (83)
14			100 °C 15 h	 (94)

a) All the reactions were carried out using 1 mol of halides and 1.2 to 1.5 mol of arylsilane in the presence of 2 mol of potassium fluoride and 2.5 to 5 mol% of the palladium catalyst in DMF.

b) Isolated yield. When the experiment of the entry 1 was carried out at 100 °C, a 1 : 1 mixture of 4,4'-diethoxybiphenyl and 4-ethoxybiphenyl was obtained in 88% yield.

reaction time, and product(s) (isolated yield). $PhSiMe_3$, 24 h, **2** (12%) and Ph-Ph (61%); Ph_4Si, 24 h, **2** (10%) and Ph-Ph (fair amount); Ph_3SiF, 12 h, **2** (84%); Ph_2SiF_2, 48 h, **2** (70%); $PhSiF_3$, 24 h, **2** (0%) and **1** (quantitative); $PhSi(Et)F_2$, 12 h, **2** (71%); $PhSi(nPr)F_2$, 12 h, **2** (87%); $PhSi(Me)F_2$, 12 h, **2** (68%) and $4\text{-}MeC_6H_4COMe$ (14%); $PhSi(Me)_2F$, 24 h, **2** (15%), $4\text{-}MeC_6H_9COMe$ (15%), and recovery of **1** (69%). Thus, tetraorganosilanes like $PhSiMe_3$ and Ph_4Si failed to give appreciable amounts of the coupled product **2** and produced instead biphenyl arising from the homo-coupling of phenylsilanes. Fluorinated silicon substrates such as Ph_3SiF and Ph_2SiF_2 afforded the desired product **2** in good yield. However, $PhSiF_3$ turned out totally inactive. These observations are consistent with our previous ones7b) and are ascribed to the ease with which the intermediate pentacoordinate anionic phenylsilicates are produced. We assume the pentacoordinate silicate species is the active one in the transmetallation step of the catalytic cycle.8) Noteworthy is that tetrabutylammonium fluoride (TBAF) effected the coupling reaction equally well, but this could be replaced by an inexpensive potassium fluoride. Tris(diethylamino)sulfonium difluorotrimethylsilicate was ineffective. When $PhSi(Et)F_2$ and $PhSi(nPr)F_2$ were employed, the phenyl group only underwent the coupling reaction in preference to the ethyl or propyl group, and the desired coupled product **2** was produced as the sole product. In contrast, the methyl group of $Ph(Me)SiF_2$ and $Ph(Me)_2SiF$ also reacted with **1** to give 4-methylacetophenone in comparable yields. These results clearly show the aryl(ethyl)difluorosilanes and aryl(propyl)difluorosilanes the reagent of choice. It is noteworthy that in the reaction of phenyl(alkyl)difluorosilanes with **1**, no symmetrical biaryl like biphenyl or 4,4'-diacetylbiphenyl was detected which should result from the homo-coupling reaction of phenylsilanes or **1**, respectively.

These successful observations were applied to various structural types of arylsilanes and aryl iodides, and the results are summarized in Table 1 which clearly shows the coupling reaction is applicable to aryl iodides having not only electron-donating but also electron-withdrawing substituents. However, the arylsilanes with a strongly electron-withdrawing group like CF_3 (σ_p = +0.54) gave somewhat lower yields of products.9) For example, 3-iodophenylmethanol coupled with $4\text{-}MeC_6H_4Si(Et)F_2$ in 86% yield but with $4\text{-}CF_3C_6H_4Si(nPr)F_2$ in 67% yield even after a prolonged reaction time (entries 4 and 8). Similarly, $3\text{-}IC_6H_4OMe$ coupled with $4\text{-}CH_3C_6H_4Si(Et)F_2$ in 83% yield, whereas the same iodide coupled with $4\text{-}CF_3C_6H_4Si(nPr)F_2$ in 52% yield (entries 3 and 7). The most striking feature of the process is its high chemoselectivity. The silicon-based cross-coupling reaction is tolerant of a wide variety of reactive functional groups, e.g. ester (entries 5, 9, and 12), ketone (entry 10) and aldehyde (entry 13) carbonyls, cyano (entry 6), and even hydroxyl (entries 4, 8, and 11). Accordingly, the procedure described herein should find wide application to construction of highly functionalized unsymmetrical biaryl structure of natural origin10) and of synthetic drugs.11)

The procedure for the preparation of 3-(3-methoxyphenyl)benzaldehyde is representative (entry 13). To a mixture of potassium fluoride (0.26 g, 4.4 mmol), $(\eta^3\text{-}C_3H_5PdCl)_2$ (18 mg, 2.5 mol%) and 3-iodobenzaldehyde (0.46 g, 2.0 mmol) in dry DMF (10 ml) was added 3-methoxyphenyl(propyl)difluorosilane (0.48 g, 2.2 mmol) with a syringe under an argon atmosphere. The reaction mixture was heated to 100 °C for 15 h, then cooled down to ambient temperature, and diluted with ether. The precipitated material was filtered, and the filtrate was washed with aq sodium hydrogencarbonate solution, dried over anhydrous magnesium sulfate, and concentrated. Purification by column chromatography (silica gel, ethyl acetate-hexane 1 : 10) afforded 3-(3-methoxyphenyl)benzaldehyde (0.35 g, 83% yield).[12]

In conclusion, the KF/Pd catalyst promoted cross-coupling reaction of arylsilanes with aryl iodides provides a straightforward route to highly functionalized unsymmetrical biaryls which have been hardly accessible by the conventional methods. That potassium fluoride can be employed makes this coupling reaction highly practical.

References

1) M. Sainsbury, Tetrahedron, 36, 3327 (1980).
2) R. F. Heck, "Palladium Reagents in Organic Syntheses," Academic Press, Orlando (1985), pp 179-295.
3) a) A. Sekiya, and N. Ishikawa, J. Organomet. Chem., 118, 349 (1976); b) A. Minato, K. Suzuki, K. Tamao, and M. Kumada, J. Chem. Soc., Chem. Commun., 1984, 511; c) A. Minato, K. Tamao, T. Hayashi, K. Suzuki, and M. Kumada, Tetrahedron Lett., 22, 5319 (1981); d) D. A. Widdowson and Y. Z. Zhang, Tetrahedron, 42, 2111 (1986).
4) E. Negishi, A. O. King, and N. Okukado, J. Org. Chem., 42, 1821 (1977).
5) a) I. P. Beletskaya, J. Organomet. Chem., 250, 551 (1983); b) T. R. Bailey, Tetrahedron Lett., 27, 4407 (1986).
6) M. J. Sharp, W. Cheng, and V. Snieckus, Tetrahedron Lett., 28, 5093, 5097 (1987); N. Miyaura, T. Yanagi, and A. Suzuki, Synth. Commun., 11, 513 (1981); M. Ishikura, M. Kamada, and M. Terashima, Synthesis, 1984, 396; M. Ishikura, M. Kamada, and M. Terashima, Heterocycles, 22, 265 (1984); 23, 2375 (1985); M. Ishikura, T. Ohta, and M. Terashima, Chem. Pharm. Bull., 33, 4755 (1985); R. B. Miller, and S. Dunger, Organometallics, 3, 1261 (1984); W. J. Thompson and J. Gaudino, J. Org. Chem., 49, 5237 (1984).
7) Y. Hatanaka and T. Hiyama, J. Org. Chem., 53, 918 (1988); 54, 268 (1989); Y. Hatanaka and T. Hiyama, Tetrahedron Lett., 29, 97 (1988); 30, 2403 (1989).
8) Some of phenylsilicates possessing two or more fluorines are isolable. See, R. Damrauer and S. E. Danahey, Organometallics, 5, 1490 (1986).
9) The electron-withdrawing substituent on the aromatic ring of arylsilanes might have retarded the transfer of the aryl group from the silicon to the palladium catalyst in the transmetallation step. See, M. G. Voronkov, N. F. Chernov, and E. M. Perlova, J. Organomet. Chem., 341, 225 (1988).
10) For representative examples, see footnote 1 of Ref. 3d.
11) D. Lednicer, "The Organic Chemistry of Drug Synthesis," Wiley-Interscience, New York (1977-1984), Vols. 1-3.
12) ^{1}H NMR (90 MHz, $CDCl_3$) δ 3.87 (s, 3 H), 6.95-8.18 (m, 8 H), 10.15 (s, 1 H); IR (neat) 2950, 2730, 1695, 1600, 1225, 1160, 780, 690 cm^{-1}. Found: C, 79.11; H, 5.58%. Calcd for $C_{14}H_{12}O_2$: C, 79.23; H, 5.70%.

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