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Palladium-Catalyzed Carbonylative Coupling of Arylfluorosilanes with Aryl Iodides. A Convenient Synthesis of Diaryl Ketones

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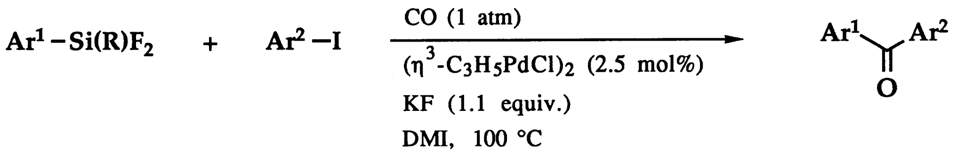
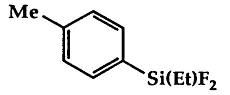
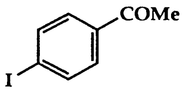
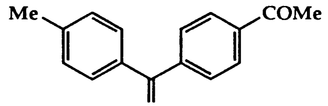
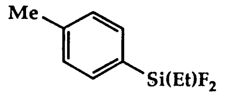
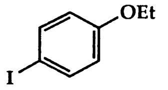
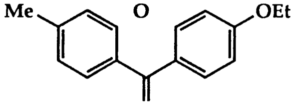
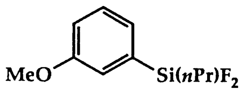
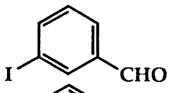
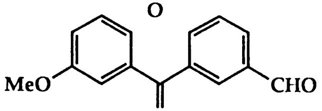
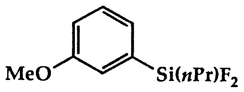
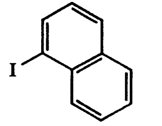
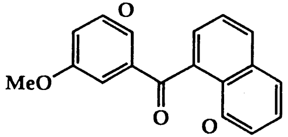
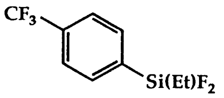
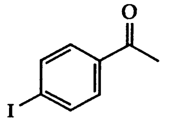
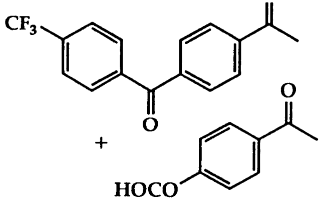
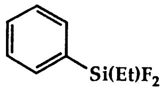
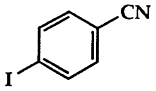
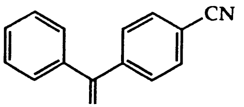
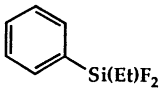
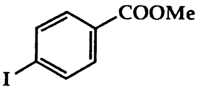
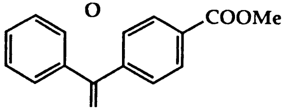
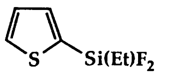
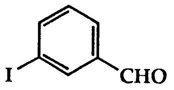
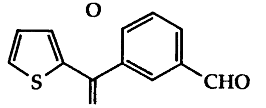
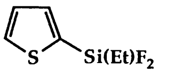
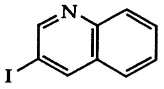
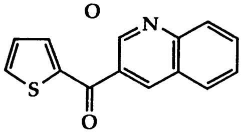
In the presence of 1 atm of carbon monoxide, arylfluorosilanes activated by potassium fluoride were found to participate in the Pd-catalyzed carbonylative coupling reaction of aryl iodides to give unsymmetrical diaryl ketones in good yields.

Diaryl ketones are used in photo-induced reduction,1) cycloaddition,2) enolization,3) and remote oxidation,4) and as useful precursors of synthetic drugs.5) Current methods of the preparation include an addition of organometallics to a carbon dioxide equivalent,6) the cross-coupling of aryl metals with aroyl halides,7) and the transition metal-catalyzed carbonylative coupling of arylmetals with aryldiazonium salts or aryl halides.8) Although the last two methods seem to be convenient, limitation still remains yet to be studied.9) Recent development by us10) and other authors11) of the Pd-catalyzed cross-coupling reaction of organosilicon compounds with organic halides has provided us with a new method for the highly selective carbon-carbon bond formation. Reported herein are our preliminary results on the chemoselective synthesis of unsymmetrical diaryl ketones via Pd-catalyzed carbonylative coupling of arylfluorosilanes with aryl iodides employing potassium fluoride and atmospheric pressure of carbon monoxide.12)



We first studied the reaction of various types of 4-tolylsilanes with 4-iodoacetophenone (**1**) in the presence of 1 atm of carbon monoxide, 1.1 equiv. of potassium fluoride, and 2.5 mol% of $(\eta^3-C_3H_5PdCl)_2$ as a catalyst. The reaction of 4-tolyl(ethyl)difluorosilane13) with **1** at 100 °C in *N,N*-dimethyl-2-imidazolidinone (DMI) solvent proceeded smoothly to afford 4-acetylphenyl 4-methylphenyl ketone (**2**) in 91% yield (entry 1 in Table 1), whereas **2** was not produced in THF nor dioxane. In *N,N*-dimethylformamide or *N,N*-dimethylacetamide, the reaction proceeded under the similar reaction conditions albeit in 53-42% isolated yield. As the catalysts, $PdCl_2(PPh_3)_2$ and $Pd(PPh_3)_4$ were less potent and gave low yields of **2** with a significant amount of the carboxylated product of the starting aryl iodide. The product distribution depended greatly on the silyl substituent of the arylsilane also; the reaction of 4-tolyltri(methyl)silane and 4-tolyltrifluorosilane with **1** gave a large amount of 4-acetylbenzoic acid (76% and 50% yield respectively) in addition to the expected product **2** (8% and 15% respectively). The acid seems to be derived from of an intermediate 4-acetylbenzoyl fluoride.[14] The formation of the aroyl fluoride should be ascribed to the substitution of ArCO-Pd-I by fluoride ion to give ArCO-Pd-F which undergoes reductive elimination. This process competes with the transmetallation of pentacoordinate arylsilicate formed by the reaction of fluoride ion with arylfluorosilane. When the reaction was carried out under 10 atm

Table 2. Pd-Catalyzed Carbonylative Coupling of Arylsilanes with Aryl Iodidies[a)]

Entry	Arylsilane	Aryl iodide	Reaction time	Products (Yield/%)[b)]
1			3 h	 (91)
2			19 h	 (69)
3			5 h	 (80)
4			15 h	 (67)
5			18 h	 (38) (50)
6			5 h	 (60)
7			5 h	 (61)
8			6 h	 (72)
9			19 h	 (78)

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a) All the reactions were carried out at 100 °C using 1 mol of the iodide and 1.5 mol of the arylsilane under 1 atm of carbon monoxide in the presence of 1.1 mol of potassium fluoride and 2.5 mol% of $(\eta^3\text{-}C_3H_5PdCl)_2$ in DMI.

b) Isolated yield.

of carbon monoxide pressure, the formation of 4-acetylbenzoic acid predominated at the expense of the desired carbonylative coupling product. At the reaction temperature above 130 °C, a considerable quantity of a non-carbonylative coupling product, 4-acetyl-4'-methylbiphenyl was obtained as well as the diaryl ketone. For example, the reaction of 4-tolyl(ethyl)difluorosilane with **1** at 150 °C (CO 1 atm) afforded the biaryl in 73% yield. The pathway leading either to the biaryl formation[10e] or to the carbonylative coupling is evidently determined by the relative rate of carbon monoxide insertion and the transmetallation of pentacoordinate arylsilicate to arylpalladium complex. The latter pathway is preferred at higher temperature and under lower carbon monoxide pressure.

The optimum conditions (1 atm of CO, 100 °C) were applied to various arylfluorosilanes and aryl iodides. Results are summarized in Table 1. It is easily observed that the reaction is quite general to the substrates possessing not only an electron-withdrawing substituent but an electron-donating one on the aromatic ring. However, the arylsilane substituted by a strong electron-withdrawing group like CF_3 gave a mixture of a carboxylated product and the expected ketone (entry 5), whereas an electron-withdrawing substituent on the aryl iodide partner accelerated the reaction rate of carbonylative coupling and afforded the unsymmetrical diaryl ketone in high yields.

Several features of the present reaction deserve comments. First, the reaction can be carried out under 1 atm of carbon monoxide, wherein the competitive direct cross-coupling reaction[10e] of arylfluorosilane and the aryl iodide is negligible. Second, the reaction is tolerant of a wide range of such reactive functional groups as ester- (entry 7), ketone- (entries 1 and 5), aldehyde-carbonyl groups (entries 3 and 8) and cyano group (entry 6). Thus, the silicon-based carbonylative coupling reaction provides a straightforward route to highly functionalized, unsymmetrical diaryl ketones. Third, since the reaction is not retarded by the heteroaromatic substrates, the method is applicable to the preparation of unsymmetrical heteroaryl ketones (entry 9) which has hitherto been hardly accessible by a conventional method like the Friedel-Crafts reaction.[15]

The following procedure for the preparation of 4-acetylphenyl 4-methylphenyl ketone (**2**) is representative (entry 1, Table 1). To a mixture of DMI (10 ml), potassium fluoride (0.19 g, 3.3 mmol), $(\eta^3\text{-}C_3H_5PdCl)_2$ (18 mg, 2.5 mol%) and 4-iodoacetophenone (0.5 g, 2 mmol) was added 4-tolyl(ethyl)difluorosilane (0.56 g, 2 mmol) under 1 atm of carbon monoxide (balloon). After stirring at an ambient temperature for 10 min, the reaction mixture was heated at 100 °C for 3 h. The bulk of the solvent and the catalyst were removed by passing the reaction mixture through a silica gel column with ethyl acetate/hexane (1:10) as the eluent. Evaporation of the solvent under reduced pressure afforded pure **2** (0.43 g, 1.82 mmol, 91%).[16]

In summary, the present carbonylative process allows us to prepare unsymmetrical diaryl ketones using readily available, stable arylfluorosilanes and aryl iodides possessing various functional groups.

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9) Pd-catalyzed carbonylative coupling reaction of aryltin and arylaluminium compounds (Ref. 8) with aryl halides are compatible with the functional groups such as ester and cyano, but use of toxic aryltrimethyltin reagents and HMPA as the solvent reduces their synthetic value.

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12) Although the transition-metal catalyzed carbonylative coupling reactions using main group organometallics are reported, these could not be applied to the synthesis of the diaryl ketones. See Ref. 7a; Y. Wakita, T. Yasunaga, and M. Kojima, J. Organomet. Chem., 288, 261 (1985); 301, C17 (1986); M. Tanaka, Synthesis, 1981, 47; Y. Tamaru, H. Ochiai, Y. Yamada, and Z. Yoshida, Tetrahedron Lett., 24, 3869 (1983).

13) The methyl group of phenyl(methyl)difluorosilane was found to react competitively with iodobenzene giving a fair amount of acetophenone.

14) The formation of 4-acetylbenzoyl fluoride was confirmed by ^{19}F NMR (60 MHz, DMI, CCl_3F as an internal standard) δ -26.0.

15) "Friedel-Crafts and Related Reactions," ed by G. A. Olah, Interscience, New York (1964), Vol. 3, p. 1.

16) Mp 110-112 °C; ^1H NMR (90 MHz, $CDCl_3$) δ 2.45 (s, 3H), 2.63 (s, 3H), 7.28 (d, J = 7.5 Hz, 2H), 7.70 (d, J = 7.5 Hz, 2H), 7.80 (d, J = 8.0 Hz, 2H), 8.04 (d, J = 8.0 Hz, 2H); IR (KBr) 1690, 1645, 1605, 1290, 1265, 930, 830, 760, 680 cm^{-1}.

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