1,4-Addition of Arylsiloxanes to Enones Catalyzed by Dicationic Palladium(II) Complexes in Aqueous Media

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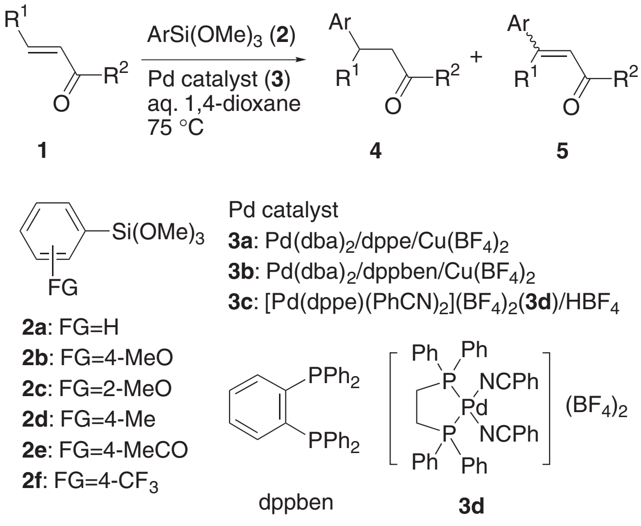
Catalytic 1,4-addition of arylsiloxanes to enones was carried out at 75 °C in the presence of a dicationic palladium(II) catalyst in aqueous 1,4-dioxane. A nitrile-free complex generated in situ from $Pd(dba)_2$ and $Cu(BF_4)_2$ in the presence of dppe or dppben was recognized to be the best catalyst to achieve high yields for the representative enones and enals.

Metal-catalyzed 1,4-addition of organometallic reagents to α,β-unsaturated carbonyl compounds is a widely used process in organic chemistry. Since the reaction yields a stereogenic center at the β-carbon, considerable efforts have been devoted to the development to asymmetric syntheses. Among these studies, rhodium complexes have recently been found to be excellent catalysts for 1,4-addition of aryl- or alkenylboron,[1] -silicon,[2] -bismuth,[3] -tin,[4] -titanium,[5] and zirconium[6] compounds. Although divalent palladium complexes have rarely been used for such a catalytic cycle starting from transmetalation, Pd(II) complexes in acidic media have been successfully used for 1,4-addition of aryltin[7] and -boron[8] compounds to enones. Very recently, we also reported 1,4-addition of arylboronic acids catalyzed by $[Pd(dppe)(PhCN)_2](BF_4)_2$ (**3d**).[9] Since arylsiloxanes are convenient reagents that are easily available via transmetalation[10] or cross-coupling reaction of $HSi(OR)_3$,[11] the protocol was extended to an analogous reaction of silicone compounds (Scheme 1).

Reaction between trimethoxyphenylsilane and 2-cyclohexenone was carried out at 75 °C in dioxane/water (2/1) (Table 1). $[Pd(dppe)(PhCN)_2](BF_4)_2$ (**3d**) unexpectedly resulted in no reaction (Entry 1), but a nitrile-free complex generated in situ from $Pd(dppe)Cl_2$ and $AgBF_4$ gave an addition product in 38% yield (Entry 2). Addition of HBF_4 (20 mol%) was also effective, presumably for accelerating the dissociation of benzonitrile (Entry 3). Although cationic Pd(II) complexes have been synthesized from Pd(II) halide complexes and silver salts (Entry 2) or by electrochemical oxidation of $Pd(PPh_3)_4$,[12] $Cu(BF_4)_2$ was found to be a mild oxidizing reagent of palladium(0) species for in situ preparation of nitrile-free catalysts. The catalyst synthesized from $Cu(BF_4)_2{\cdot}6H_2O$ (20 mol%) and $Pd(dba)_2$ (5 mol%) in the presence of dppe (5 mol%) provided the product in 80% yield (Entry 5), whereas other copper(II) salts such as $Cu(ClO_4)_2$ and $Cu(OTf)_2$ were not effective (Entries 6 and 7). The presence of an oxidant may also serve to recycle Pd(0) species that are generated by double transmetalation giving a homocoupling product or by other side reactions, since **3a** and **3b** resulted in much higher yields than did the catalyst generated from $Pd(dppe)Cl_2$ and $AgBF_4$ (Entries 2, 5, and 8). Although the reaction provided a mixture of **4** and **5**, the formation of alkene product (**5**) derived from β-hydride elimination decreased when the reaction was carried out at 50 °C (48%, **4**/**5**=96/4). Dppben was a better ligand than dppe to suppress the formation of **5** at 75 °C (Entry 8). On the other hand, other bidentate ligands such as dppm, dppp, dppb and dppf were not effective, and the reaction was strongly retarded by addition of a silicone activator such as CsF and $Bu_4NF{\it n}H_2O$.



Scheme 1.

Results of 1,4-addition of representative arylsiloxanes to enones or enals at 75 °C with a catalyst system (**3a**, **3b**, or **3c**) are summarized in Table 2. Among the substrates screened, 2-cyclopentenone (Entries 1 and 2) and 2-cyclohexenone (Table 1) have a strong tendency to yield an alkene product (**5**), though such a side reaction was negligible for 2-cycloheptenone (Entries 3 and 4), acyclic enones (Entries 5-20) and enals (Entries 21-23). The reactions of substituted arylsiloxanes often resulted in moderate yields due to formation of the correspond-

Table 1. Addition of $PhSi(OMe)_3$ to 2-cyclohexenone[a]

Entry	Catalyst	Yield/% (**4**/**5**)
1	**3d**	0
2	$Pd(dppe)Cl_2/AgBF_4$	38
3	**3c**	64 (72/18)
4	$Pd(dba)_2$/dppe	0
5	**3a**	80 (88/12)
6	$Pd(dba)_2/dppe/Cu(ClO_4)_2$	0
7	$Pd(dba)_2/dppe/Cu(OTf)_2$	0
8	**3b**	77 (92/8)

[a] All reactions were carried out at 75 °C for 23 h in the presence of 2-cyclohexenone (1 mmol), $PhSi(OMe)_3$ (2.5 mmol), a palladium complex (5 mol%), a ligand (if used, 5 mol%) and an additive (if used, 20 mol%) in 1,4-dioxane/water (2/1, 9 mL).

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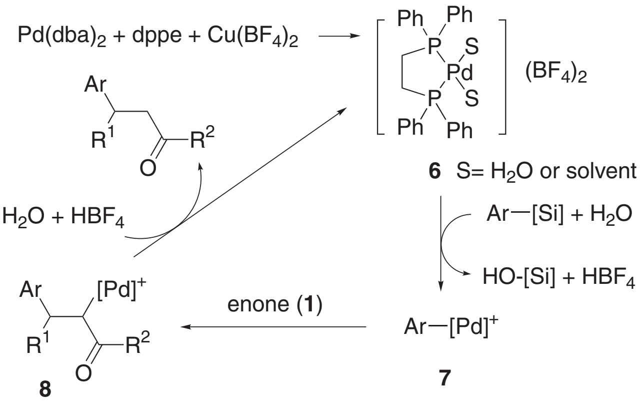
ing arenes (Entries 7, 10, 12), but they were improved significantly when the water content in 1,4-dioxane was decreased to 6:1 or 12:1 (Entries 8, 13, 14). Enals required a higher temperature than that of enones because the reactions were retarded by formation of hemiacetals in aqueous media (Entries 22 and 23).

A probable catalytic cycle is shown in Scheme 2. In contrast to a very smooth transmetalation of arylboronic acids to dicationic Pd(II)-nitrile complexes at room temperature, transmetalation of arylsiloxanes require a nitrile-free complex at 75 °C. Thus, a method for preparing nitrile-free catalysts (**6**) via oxidation of Pd(dba)$_2$ with Cu(BF$_4$)$_2$ was newly developed. The formation of a dicationic species (**6**) was confirmed by ^{31}P NMR, which exhibited a single signal at 74.9 ppm. Arylsilanols produced by hydrolysis may participate in transmetalation, giving **7**, as was demonstrated in the related rhodium-catalyzed 1,4-addition of arylsiloxanes to enones.[2] Insertion of an enone into the C-Pd bond yields a C-bound palladium enolate (**8**), which is highly susceptible to hydrolytic C-Pd bond cleavage.[13]

Table 2. Addition of ArSi(OMe)$_3$ to enones (Scheme 1)[a]

Entry	**2**	Enone	Catalyst	Yield/% (**4**/**5**)
1	**2a**	2-cyclopentenone	**3b**	60 (43/57)
2	**2a**	2-cyclopentenone	**3a**	58 (50/50)
3	**2a**	2-cycloheptenone	**3b**	86 (**4**>99)
4	**2a**	2-cycloheptenone	**3c**	87 (**4**>99)
5	**2a**	n-$C_5H_{11}CH{=}CHCOCH_3$	**3b**	84 (**4**>99)
6	**2a**	n-$C_5H_{11}CH{=}CHCOCH_3$	**3c**	82 (**4**>99)
7	**2b**	n-$C_5H_{11}CH{=}CHCOCH_3$	**3b**	64 (**4**>99)
8[b]	**2b**	n-$C_5H_{11}CH{=}CHCOCH_3$	**3b**	77 (**4**>99)
9	**2c**	n-$C_5H_{11}CH{=}CHCOCH_3$	**3b**	74 (**4**>99)
10	**2d**	n-$C_5H_{11}CH{=}CHCOCH_3$	**3b**	61 (**4**>99)
11[c]	**2d**	n-$C_5H_{11}CH{=}CHCOCH_3$	**3b**	81 (**4**>99)
12	**2e**	n-$C_5H_{11}CH{=}CHCOCH_3$	**3b**	62 (**4**>99)
13[b]	**2e**	n-$C_5H_{11}CH{=}CHCOCH_3$	**3b**	85 (**4**>99)
14[d]	**2f**	n-$C_5H_{11}CH{=}CHCOCH_3$	**3b**	90 (**4**>99)
15	**2a**	$PhCH{=}CHCOCH_3$	**3b**	90 (**4**>99)
16	**2a**	$PhCH{=}CHCOCH_3$	**3b**	96 (**4**>99)
17	**2a**	i-$C_3H_7CH{=}CHCOCH_3$	**3b**	60 (**4**>99)
18	**2a**	i-$C_3H_7CH{=}CHCOCH_3$	**3c**	75 (**4**>99)
19	**2a**	$PhCH{=}CHCOPh$	**3c**	80 (**4**>99)
20	**2a**	$PhCH{=}CHCOPh$	**3b**	95 (**4**>99)
21	**2a**	$CH_3CH{=}CHCHO$	**3c**	56 (**4**>99)
22[c]	**2a**	n-$C_3H_7CH{=}CHCHO$	**3b**	72 (**4**>99)
23[c,e]	**2a**	$PhCH{=}CHCHO$	**3b**	74 (**4**>99)

[a] All reactions were carried out for 23 h in the presence of enone (1 mmol), ArSi(OMe)$_3$ (2.5 mmol) and a catalyst (5 mol%) in dioxane/water (2/1, 9 mL). E-isomers were used for all acyclic enones and enals. [b] dioxane/water=6/1. [c] At 95 °C. [d] dioxane/water=12/1. [e] For 9 h.



Scheme 2.

References

1 a) M. Sakai, H. Hayashi, and N. Miyaura, *Organometallics*, **16**, 4229 (1997). b) Y. Takaya, M. Ogasawara, T. Hayashi, M. Sakai, and N. Miyaura, *J. Am. Chem. Soc.*, **120**, 5579 (1998). c) T. Hayashi, M. Takahashi, Y. Takaya, and M. Ogasawara, *J. Am. Chem. Soc.*, **124**, 5052 (2002). For a review, d) K. Fagnou and M. Lautens, *Chem. Rev.*, **103**, 169 (2003).

2 a) T. Koike, X. Du, A. Mori, and K. Osakada, *Synlett*, **2002**, 301. b) S. Oi, Y. Honma, and Y. Inoue, *Org. Lett.*, **4**, 667 (2002).

3 a) T.-S. Huang and C.-J. Li, *Org. Lett.*, **3**, 2037 (2001). b) S. Venkatraman and C.-J. Li, *Tetrahedron Lett.*, **42**, 781 (2001).

4 S. Oi, M. Moro, H. Ito, Y. Honma, S. Miyano, and Y. Inoue, *Tetrahedron*, **58**, 91 (2002).

5 T. Hayashi, N. Tokunaga, K. Yoshida, and J. W. Han, *J. Am. Chem. Soc.*, **124**, 12102 (2002).

6 A. Kakuuchi, T. Taguchi, and Y. Hanzawa, *Tetrahedron Lett.*, **44**, 923 (2003).

7 a) S. Cacchi, D. Misiti, and G. Palmieri, *Tetrahedron*, **37**, 2941 (1981). b) T. Ohe and S. Uemura, *Tetrahedron Lett.*, **43**, 1269 (2002).

8 C. S. Cho, S. Motofusa, K. Ohe, and S. Uemura, *J. Org. Chem.*, **60**, 883 (1995).

9 T. Nishikata, Y. Yamamoto, and N. Miyaura, *Angew. Chem., Int. Ed. Engl.*, **42**, 2768 (2003).

10 W. P. Weber, in "Silicon Reagents for Organic Synthesis," Springer-Verlag, Berlin (1983).

11 M. Murata, M. Ishikura, M. Nagata, S. Watanabe, and Y. Masuda, *Org. Lett.*, **4**, 1843 (2002).

12 C. Amatore, A. Jutand, M. Mederious, and L. Mottier, *J. Electroanal. Chem.*, **422**, 125 (1997).

13 A. C. Albéniz, N. M. Catalina, P. Espinet, and R. Redón, *Organometallics*, **18**, 5571 (1999).

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