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High yield olefination of a wide scope of aryl chlorides catalyzed by the phosphinito palladium PCP pincer complex: [PdCl{$C_6H_3(OPPr^i{}_2)_2$-2,6}]

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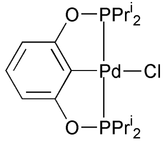
[PdCl{$C_6H_3(OPPr^i{}_2)_2$-2,6}] efficiently catalyzes the olefination of a broad scope of aryl chlorides; as a result of the high thermal stability of the catalyst, the coupled products are obtained in excellent and in many cases nearly quantitative yields.

The formation of vinylic C–C bonds from the palladium catalyzed coupling of aryl bromides, iodides and triflates with alkenes (the Heck reaction) is one of the "true power tools of contemporary organic synthesis".[1] However, the industrial application of the reaction has been very limited owing to the instability of the palladium catalysts and the high cost of the aryl starting materials. Recently a great deal of progress has been made toward overcoming these limitations.[2–9] In a pioneering study, Milstein and coworkers found that the olefination of relatively inexpensive aryl chlorides is catalyzed by [$Pd(OAc)_2$] in the presence of 1,3-bis(diisopropylphosphino)propane.[2] Higher turnovers and yields have recently been achieved with activated aryl chlorides using palladacycle,[3] carbene–palladium[4] and palladium–phosphite[5] catalysts. It has also been discovered that the activity of more traditional Heck coupling systems is enhanced by the addition of [PPh_4]Cl[6] or $PBu^t{}_3$[7] such that the chloro substrates can be utilized in the reaction. Notably, Littke and Fu found that in the presence of $PBu^t{}_3$, $Pd_2(dba)_3$ catalyzes the olefination of a broad scope of aryl chlorides.[7]

A key feature of several of these systems is the stabilization of the active catalysts by either ligand chelation or steric shielding of the metal center. Both of these stabilizing effects can be realized with mixed donor polydentate ligands. This combination has been used to good advantage in catalytic aliphatic dehydrogenation reactions by iridium PCP pincer complexes, [IrH_2{$C_6H_3(CH_2PR_2)_2$-2,6}]. The pincer ligand confers high stability on the complexes at the temperatures required for oxidative additions of aliphatic C–H bonds.[10] Similarly, the palladium PCP pincer complexes, [Pd{O-$C(O)CF_3$}{$C_6H_3(CH_2PPr^i{}_2)_2$-2,6}], [Pd{$OC(O)CF_3$}{C_6CH_2-1-$(CH_2PR_2)_2$-2,6-$(CH_2)_2$-3,5-H-4}] (R = Pr^i, Bu^t) have been found to be an extraordinarily active catalyst for the Heck couplings with iodo- and bromo-arenes.[11] However, the phosphino pincer complexes were found to be almost inactive with chloroarenes. Beller[5] and Zapf van Leeuwen and coworkers[9] have recently reported cases in which the catalytic activity of palladium complexes are remarkably enhanced upon substitution of phosphine ligands by alternative phosphorus ligands containing electron withdrawing groups.[5,9] We have found that unlike 1,3-bis(phos*phino*)benzenes, 1,3-bis(phos*phinito*)benzene, can be conveniently prepared in 95% yield from the reaction of inexpensive precursors.[12] It was therefore of interest to examine the activity of the phosphinito palladium complex, [PdCl{$C_6H_3(OPPr^i{}_2)_2$-2,6}] **1**, as a catalyst for Heck couplings of aryl chlorides. We report here that **1** is an efficient catalyst for this reaction, giving olefinated products in excellent, and in many cases nearly quantitative yields.

The results of our studies of the catalytic activity of **1** are presented in Table 1. In order to optimize the efficiency of the catalytic system, we initially examined the coupling of chlorobenzene and styrene by **1** under a variety of reaction conditions† and analyzed the product mixtures through gas chromatography. Unlike most previously reported systems for Heck couplings of aryl chlorides, additional cocatalyst such as excess LiBr,[3] $PBu^t{}_3$,[7] [NBu_4][Br][3–5] or [PPh_4]Cl,[6] are not required to achieve high catalytic activity. We found that > 99% isolated yield of *trans*-stilbene is obtained when the reaction is carried in dioxane solvent and caesium acetate is used as base. Employing this same combination of reagents in a preparative scale experiment, we were able to isolate the coupled product in nearly quantitative yield. At 120 °C, a reaction time of 5 days is required to achieve this high conversion. We found, however, that the catalyst can withstand prolonged heating to 180 °C and thus the request reaction time can be reduced to 24 h.



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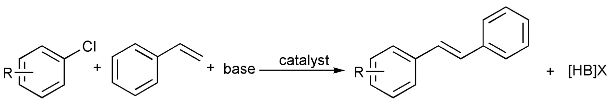
The reactivities of a variety of aryl chlorides were examined under the optimized conditions and uniformly showed > 99% selective for the *trans* configured product. The system is also one of the few reported systems to show high reactivity with electron-rich[2,7] and sterically hindered[7] aryl chlorides. The practical utility of this catalytic system was probed by carrying out preparative scale couplings of 4-chloroacetophenone and 4-chloroanisole with styrene. We obtained the corresponding *E*-

Table 1 Heck couplings of aryl chlorides with styrene using **2** as catalyst. Experiments conducted with 0.67 mol% catalyst and 1.1 equivalents of base in dioxane solution except where noted



Entry	Aryl chloride	Base	Yield[a] (%)	Yield[b] (%)
1	H	CsOAc	> 99	> 99
2	H	CsOAc		4.4[c]
3	H	CsOAc		2.0[d]
4	H	Cs_2CO_3		95
5	H	Na_2CO_3		87
6	H	KOAc		40
7	H	CsOH		31
8	H	$EtNPr^i{}_2$		3.0
9	4-MeC(O)	CsOAc	> 99	> 99
10	4-MeO	CsOAc	86	88
11	4-HC(O)	CsOAc	81	82
12	2-Me	CsOAc	83	85

[a] Yields obtained at 120 °C. [b] Yields obtained by GC analysis are based on chlorobenzene. In all experiments only the *trans* configured product was detected. [c] DMF solution. [d] Dimethylacetamide solution.

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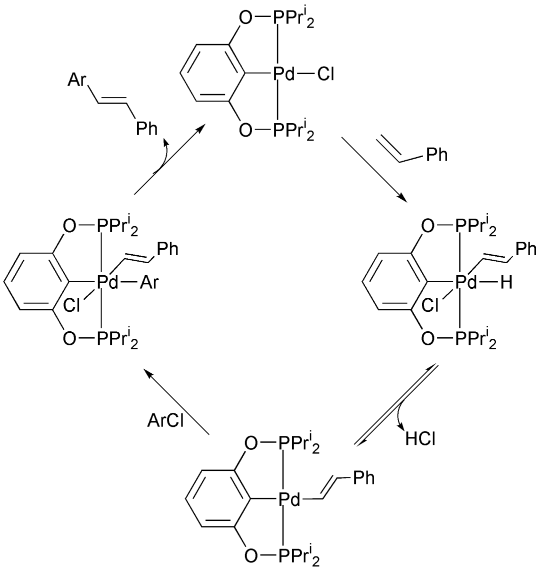

Scheme 1 Proposed mechanism for the catalytic olefination of aryl chlorides by $[PdCl\{C_6H_3(OPPr^i_2)_2\text{-}2,6\}]$.

stilbenes in > 95% and 85% isolated yields respectively. To our knowledge, these yields are the highest that have been achieved to date for the Heck coupling of these aryl chlorides with styrene.

In order to verify that the high catalytic activity of **1** requires the presence of phosphinito rather than a phosphino PCP ligand, we examined the catalytic activity of, $[PdCl\{C_6H_3(CH_2PPr^i_2)_2\text{-}2,6\}]$ **2**† under the conditions that were optimized for **1**. The chloro complex **2**, like $[Pd\{OC(O)CF_3\}\{C_6H_3(CH_2PPr^i_2)_2\text{-}2,6\}]$,[11] showed only a very low level of activity with aryl chlorides.

It has been suggested that Heck couplings catalyzed by PCP complexes proceed through Pd(II) and Pd(IV) rather than Pd(0) and Pd(II) intermediates.[11,13] Additionally, it seems unlikely that catalytic sequence in our system could be initiated by the oxidative addition of aryl chlorides to **1** as the resulting 18-electron complex would not be expected to undergo further reaction. We therefore conclude that the mechanism of the catalytic olefination of aryl chlorides by **1** is fundamentally different from those commonly considered for palladium catalyzed Heck couplings[1c] and operates through a mechanism like that seen in Scheme 1. Our suggestion is that the catalytic process is initiated by the oxidative addition of a vinyl C–H bond of the alkene reactant. This hypothesis is supported by the recent observation that the reaction of the palladium PCP pincer complex, with tributylstannyl furan results in the substitution of the triflate by an η^1-vinyl ligand.[14] Also the deuterium labeling studies of the reaction of *tert*-butylethylene with the related PCP pincer complex, $[IrH_2\{C_6H_3\text{-}(CH_2PBu^t_2)_2\}\text{-}2,6]$ have shown that activation of vinyl C–H bonds at the metal center occurs rapidly at room temperature.[15] The Pd(IV) intermediate resulting from the vinyl C–H oxidative addition would be expected to undergo a reductive elimination of HCl. It is well established that reductive elimination is promoted by decreasing ligand donor strengths.[16] Thus the finding that the phosphinito PCP complex has markedly higher activity than its phosphino analog suggests that this step is rate determining. The catalytic cycle is completed by oxidative addition of the aryl chloride followed by reductive elimination of the coupled product. Similar mechanistic considerations may explain the extraordinary high catalytic activities that Beller and Zapf[5] and van Leeuwen and coworkers[9] have observed respectively for palladium phosphite and phosphorus amidite complexes.

In summary, the relatively inexpensive, phosphinito PCP pincer complex **1** catalyzes the high yield olefination of broad scope of aryl chlorides. It should be noted, that while most of the reactions reported here were expedited by heating to 180 °C, high yields of coupled products can be obtained at longer times at temperatures as low as 120 °C. Thus it should be possible to apply this catalytic system to the synthesis of commercially important, structurally complex fine chemicals containing thermally sensitive groups.

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Notes and references

† *General procedure* for the olefination of aryl chlorides. Under an atmosphere of nitrogen, a solution of 0.924 mmol of aryl chloride, 1.83 mmol of olefin, 3.0 mg of **2** (0.0062 mmol) and 202 mg (0.924 mmol) of diethylene glycol di-*n*-butyl ether (internal standard) in 1.0 mL of dioxane, was introduced into a Schlenk tube containing a magnetic stir bar and charged with 1.01 mmol of base. The tube was sealed and fully immersed in a 180 (120) °C silicon oil bath. After 24 (120) h, the reaction mixture was cooled to room temperature and, the organic phase analyzed by gas chromatography (GC/FID, GC–MS). For quantitative analysis a gas chromatograph GC HP 5980A with flame ionization detector (FID), and a HP-1 capillary column (25.0 m) from Hewlett Packard was used.

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