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Highly active Pd^{II} cyclometallated imine catalyst for the Suzuki reaction

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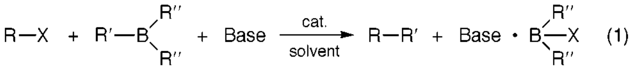
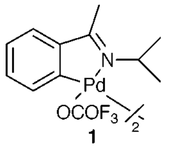
The cyclopalladated, phosphine-free imine complex 1 is an excellent catalyst for the Suzuki cross-coupling, leading to more than 10^5 turnovers with non-activated aryl bromides; the catalyst is air and thermally stable.

The Suzuki palladium-catalyzed cross-coupling reaction of organoboron compounds with organic halides or related electrophiles [eqn. (1)] represents a useful synthetic method for carbon–carbon bond formation and has attracted much current interest.[1] Usually palladium phosphine complexes are utilized as catalysts and the reactions are conducted under inert atmosphere. Palladium–carbene complexes and other phosphine-free catalysts have been recently utilized.[2] Very efficient catalysis of the Suzuki reaction using palladium complexes incorporating cyclometallated phosphine and phosphite complexes have recently been reported.[3]



$$\mathrm{R{-}X} + \mathrm{R'{-}BR''_2} + \mathrm{Base} \xrightarrow[\text{solvent}]{\text{cat.}} \mathrm{R{-}R'} + \mathrm{Base\cdot BR''_2{-}X} \quad (1)$$

We have reported on highly active PCP-type[4] and cyclometallated imine[5] catalysts for the Heck reaction. The phosphine-free imine complexes lead to more than a million turnovers in some cases. Furthermore, the catalysts are very thermally and air stable and can be recovered after catalysis. We now find that the palladium imine catalyst **1**[†] is among the best known for the Suzuki reaction. It catalyzes the coupling of aryl bromides with phenylboronic acid in extremely high efficiency [eqn. (2)].



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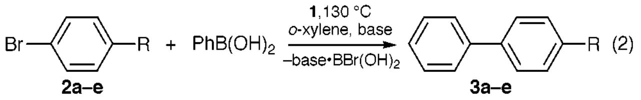

2a–e **3a–e**

R = Ac, CF$_3$, H, Me, OMe

The general procedure for the coupling reaction is as follows: to a solution containing 2.5 × 10^{-5} mmol of catalyst **1** were added 5 mmol of 4-BrC$_6$H$_4$R (1 : 200000 catalyst : substrate ratio), 7.5 mmol of PhB(OH)$_2$ and 10 mmol of K$_2$CO$_3$. The mixture was heated to 130 °C with stirring in 13 ml of *o*-xylene (distilled from Na/benzophenone) under air or N$_2$ atmosphere. The reaction was usually over after 2 h. The reaction mixture was sampled and analyzed by GC and GC-MS techniques. Typical results are presented in Table 1.

Our catalytic system is one of the most active, especially with respect to the non-activated aryl bromides **2a–c**. Increasing the amount of phenylboronic acid (from 1.5 to 2 equiv. relative to the bromide) had a beneficial effect on the yield. Similar results were obtained when a nitrogen atmosphere was used. The reaction is not very sensitive to the solvent used, as similar results were obtained in dioxane.[‡]

In order to gain insight into the mechanism of the reaction, a competitive reaction with the five aryl bromides **2a–e** was performed under pseudo-first order conditions with respect to PhB(OH)$_2$. A solution containing 2.5 × 10^{-5} mmol of catalyst **1**, 5 mmol of each of the bromides **2a–e**, 0.75 mmol of PhB(OH)$_2$ and 1 mmol of K$_2$CO$_3$ was heated at 130 °C with stirring in 13 ml of *o*-xylene under air. The concentrations of the various coupling products were determined by GC. The resulting Hammett plot is exhibited in Fig. 1.

The use of σ_P^- constants results in a better fit than σ_P constants, indicating some conjugation of π-electron density with the *para* substituent in the transition state. The correlation yields a value of $\rho \approx 1$. While this electronic effect is not surprising, since electron withdrawing substituents are expected to accelerate the Ar–Br oxidative addition step, the ρ value is too low to fit a rate-determining nucleophilic aromatic substitution. For example, a ρ value of 5.2 was obtained for oxidative addition of aryl chlorides to electron rich Pd^0 complexes.[6] This indicates a subsequent rate-determining step with different electronic requirements, such as the transmetallation step. It is noteworthy that a similar value of ρ = 1.34 was obtained for the Heck reaction of aryl iodides involving PCP–Pd^{II} catalysts, which is unlikely to proceed by the traditional Pd^0/Pd^{II} mechanism.

Table 1 Suzuki coupling catalyzed by the imine complex **1** according to eqn. (2)

ArBr[a]	Catalyst/substrate ratio	Base (mmol)	PhB(OH)$_2$ (mmol)	Atmosphere	Yield (%)	TON (10^3)	t/h[b]
4-BrC$_6$H$_4$OMe	5 × 10^{-6}	K$_2$CO$_3$ (10)	7.5	N$_2$	51	102	16
	5 × 10^{-6}	K$_2$CO$_3$ (10)	7.5	air	57	114	16
	5 × 10^{-6}	K$_2$CO$_3$ (11.5)	10	air	60	120	3
	5 × 10^{-6}	K$_3$CO$_4$ (10)	7.5	air	68	136	22
4-BrC$_6$H$_4$Me[c]	5 × 10^{-6}	K$_2$CO$_3$ (10)	7.5	N$_2$	78	156	16
	5 × 10^{-6}	K$_2$CO$_3$ (10)	7.5	air	82	160	16
PhBr	5 × 10^{-6}	K$_2$CO$_3$ (10)	7.5	N$_2$	66	132	2
	5 × 10^{-6}	K$_2$CO$_3$ (11.5)	10	air	90	180	3
4-BrC$_6$H$_4$Ac	1 × 10^{-6}	K$_2$CO$_3$ (10)	7.5	air	59	590	16
	1 × 10^{-6}	K$_2$CO$_3$ (11.5)	10	air	84	840	16
4-BrC$_6$H$_4$CF$_3$	5 × 10^{-6}	K$_2$CO$_3$ (10)	7.5	N$_2$	93	186	16
	5 × 10^{-6}	K$_2$CO$_3$ (10)	7.5	air	90	180	14.5

[a] Amounts: ArBr (5 mmol) *o*-xylene (13 ml). Reaction temperature: 130 °C. [b] This is the time after which the reaction was analyzed. It might have been over at an earlier stage. [c] The same catalytic activity was observed in dioxane as a solvent.

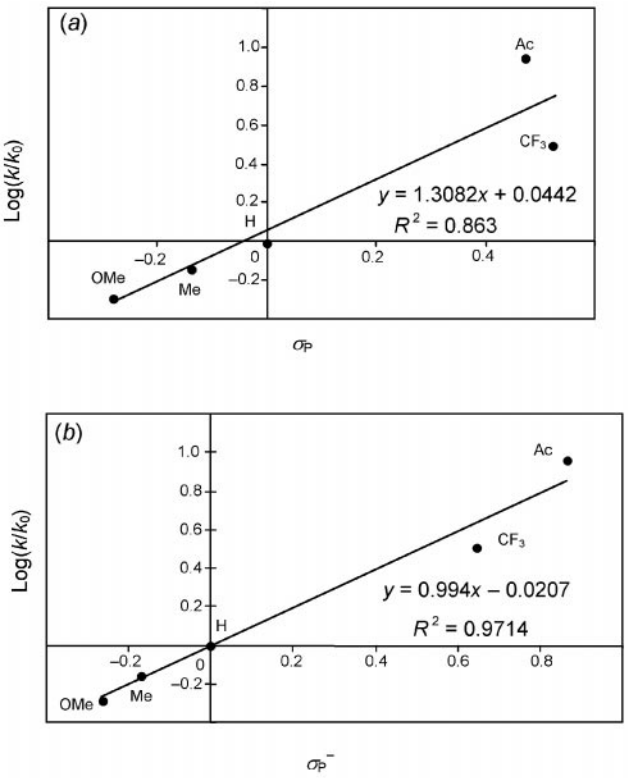

Fig. 1 Hammett correlation of the competitive reaction of aryl bromides with $PhB(OH)_2$ using (*a*) σ_P constants and (*b*) σ_P^- constants at 130 °C in *o*-oxylene.

In summary, the phosphine-free cyclopalladated imine complex **1** shows very high catalytic activity and yields in the Suzuki cross-coupling reaction of aryl bromides with phenylboronic acid. The system exhibits unprecedented turnovers with non-activated aryl bromides. The catalyst system is very thermally and air stable. Further investigations aimed at clarification of the scope and mechanism of this reaction are currently in progress.

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Notes and references

† X-Ray structure and NMR characterization have been reported in ref. 5.

‡ The reaction is sensitive to impurities in the solvent. Use of *o*-xylene not distilled from sodium may result in significantly lower efficiency.

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