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Catalytic activity of κ^3-X,N,Y-palladium pincer complexes (X, Y = O, S) with (thio)phosphoryl-substituted carbamoylmethylphosphine oxide and sulfide ligands in the Suzuki cross-coupling

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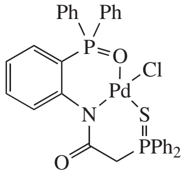
Palladium pincer complexes with *N*-{2-[diphenyl(thio)phosphoryl]phenyl}carbamoylmethylphosphine oxide and sulfide ligands provide moderate activity in the Suzuki cross-coupling.

Functionalized carboxamides have been the objects of intense research in coordination and organometallic chemistry for many years.[1] Introduction of ancillary donor centers both into acid and amine parts enables the realization of different coordination modes, either in N-monoanionic or neutral forms, thus allowing fine-tuning of physicochemical properties of the resulting complexes. As a rule, the ancillary coordination-active fragments are nitrogen-, phosphorus- and sulfur-containing groups such as pyridine, thioether, phosphoryl, and hydroxy groups.[2–4] Numerous palladium complexes are known in which functionalized amides act as mono-, bi- or tridentate ligands.[5] However, to the best of our knowledge, there is no literature data on catalytic activity of these complexes in the arylation of haloarenes with arylboronic acids (the Suzuki cross-coupling), serving as a powerful tool in organic synthesis.[6,7]

Recently we have shown that P(X)-modified carbamoylmethylphosphine oxides and sulfides (X = O, S), derived from the condensation of *o*-(thio)phosphorylaniline with (thio)phosphorylacetyl chlorides, can serve as monoanionic tridentate pincer-type ligands for Pd^{II} ions (complexes **1**–**3**).[8] Palladium pincer complexes were actively studied in recent years as (pre)catalysts for various chemical processes;[9,10] however, most of them belong to X,C,Y-type palladacycles (X, Y = P, S, N, *etc.*) containing the Pd–C central bond. Taking into account that S,C,S′- and N,C,S-pincer complexes with organothiophosphorus ligands are efficient (pre)catalysts for the Suzuki cross-coupling,[11] it seemed interesting to investigate the catalytic activity of their amido counterparts **1**–**3** in model reactions.



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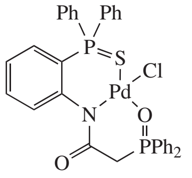

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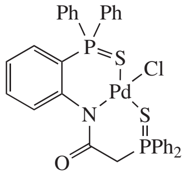

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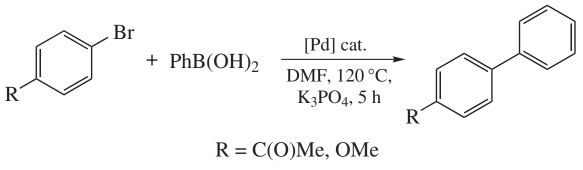
All the experiments were carried out under conditions previously suggested for sulfur-containing palladium pincer complexes[12] and successfully adopted for C-metallated organothiophosphorus systems:[11(c),(e)] heating in DMF at 120 °C for 5 h using K_3PO_4 as a base[†] (Scheme 1, Table 1).

Table 1 Catalytic activity of amido pincer complexes **1**–**3** in the Suzuki cross-coupling between 4-BrC_6H_4R and $PhB(OH)_2$.

Entry	R	Catalyst	Catalyst loading (mol%)	Product yield (%)
1	C(O)Me	**1**	1	100
2			0.1	100
3			0.01	99
4			0.001	8
5		**2**	1	87
6			0.1	98
7			0.01	18
8		**3**	1	5
9			0.1	6
10	OMe	**1**	1	90
11			0.1	76
12			0.01	15
13		**2**	1	76
14			0.1	61



Scheme 1

The preliminary studies under these conditions showed that isomeric S,N,O-palladocycles **1**, **2** (1 mol%) efficiently promote the coupling of 4-bromoacetophenone (Table 1, entries 1, 5), while their S,N,S′-analogue **3** was completely inactive already at this catalyst loading (entry 8). This is likely to be attributed to the hemilabile nature of ligands in **1**, **2** bearing the hard oxygen and soft sulfur donor centers, which is often indicated as a reason for the better catalytic performance of palladium pincer complexes.[11(e),13] The high level of activity of complexes **1**, **2** is

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[†] In a typical experiment, a solution of 0.25 mmol of bromoarene, 0.375 mmol of $PhB(OH)_2$, 0.5 mmol of K_3PO_4, and the specified amount of the corresponding palladium complex (used as titrated solutions in DMF) in 1 ml of DMF was heated at 120 °C for 5 h. The aliquots of the reaction mixture were treated with water, extracted with benzene, and analyzed by GC. In all cases, the chromatogram contained peaks only for the starting bromoarenes and cross-coupling products; no homocoupling or other side products were observed.

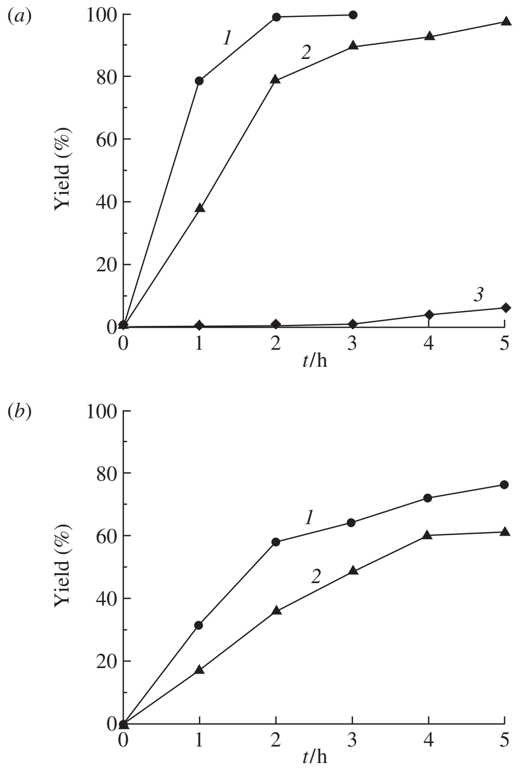

Figure 1 Plots of yields of the biaryls *vs.* time for the couplings of (*a*) 4-bromoacetophenone and (*b*) 4-bromoanisole catalyzed by complexes (*1*) **1**, (*2*) **2** and (*3*) **3** (catalyst loading 0.1 mol%).

retained also when the catalyst loading is decreased to 0.1 mol% (entries 2, 6). At the same time, the kinetic investigations revealed that complex **1** was more active than **2**, providing the complete conversion of 4-bromoacetophenone within 3 h *vs.* 5 h in the case of complex **2** [Figure 1(*a*)]. A difference in the activity of **1** and **2** became more apparent when the catalyst loading was diminished to 0.01 mol%: the yields of the biaryl were 99% and 18%, respectively (entries 3, 7). A further tenfold reduction of the loading of complex **1** dropped the conversion to only 8% (entry 4). Complexes **1**, **2** also catalyzed efficiently the coupling of electronically deactivated 4-bromoanisole, showing a satisfactory level of activity even at 0.1 mol% catalyst loading (61–76%, entries 11, 14). According to the kinetic studies, again complex **1** was more active than complex **2** [Figure 1(*b*)]. Note that for an easy-to-couple substrate, 4-bromoacetophenone, S,N,O-amido pincer complexes **1**, **2** show the same level of activity as the most active C-palladated pincer complexes with organothiophosphorus ligands,[11(*e*)] but towards 4-bromoanisole, they are considerably inferior, providing only 15% yield of the biaryl product at 0.01 mol% concentration *vs.* 98%.

Although complexes **1**–**3** are stable upon heating in DMF solution at 120 °C, according to the ^{31}P NMR monitoring of the complex destiny after the catalytic cycle,[‡] palladocycles **1**, **2** undergo decomposition, but no general tendency can be outlined in the decomposition pathways. Thus, the ^{31}P NMR spectrum of the reaction mixture bearing complex **1** demonstrates two singlet signals at *ca.* 34 and 26 ppm, being close to the signals of the free bis(phosphine oxide) ligand (37.0 and 27.8 ppm),[8] whereas in the case of complex **2** a set of signals in the range from 17.8 to 45.6 ppm was observed. Furthermore, despite the lack of activity, complex **3** also did not remain unchanged. This implies that the complexes obtained serve only as precatalysts, and the mechanisms of generation of catalytically active species may differ.

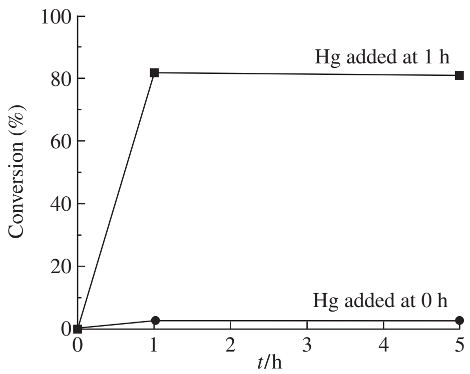

Figure 2 Time dependence of the conversion of 4-bromoacetophenone catalyzed by complex **1** (catalyst loading 0.1 mol%) in the presence of Hg^0.

A mercury poisoning test, which is used to distinguish between heterogeneous Pd^0 and homogeneous Pd^{II} catalysts,[14] revealed that the addition of excess Hg^0 to the reaction mixture bearing complex **1** either at the reaction beginning or in 1 h completely suppresses the conversion of 4-bromoacetophenone (Figure 2); Hg^0 should have exerted no effect on homogeneous organometallic complexes containing metals in high oxidation states. This indicates that some Pd^0 species are formed in the course of the catalytic reaction, which are likely to be true catalysts in the system involving complex **1** and which are trapped by the mercury metal. Furthermore, the conversion of 4-bromoacetophenone catalyzed by complex **3** in the presence of 2 mol% of Ph$_3$P reaches 29% (*cf.* 5% in the absence of phosphine). In small amount, phosphines as well as N-heterocyclic carbenes can coordinate to Pd^0 particles, preventing their agglomeration and precipitation in the form of palladium black.[15] This also supports the assumption that complexes **1**–**3** serve as depots for Pd^0 catalytically active particles.

In conclusion, although the amido pincer complexes of P(X)-functionalized carbamoylmethyl(thio)phosphoryl ligands show the lower activity than other N-metallated pincer systems,[16] serving only as precatalysts for Pd^0 catalytically active species, the results presented demonstrate that hemilabile pincer ligands based on functionalized carboxylic acid amides can be considered as a novel, promising class of ligands for transition metal catalysis. The interesting thing is that they are different in activity, which may give more insight into the pincer complex properties in general.

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[‡] A representative reaction was the coupling of 4-bromoacetophenone and phenylboronic acid at 0.1 mol% catatalyst loading.

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