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Catalytic properties of several supported Pd(II) complexes for Suzuki coupling reactions

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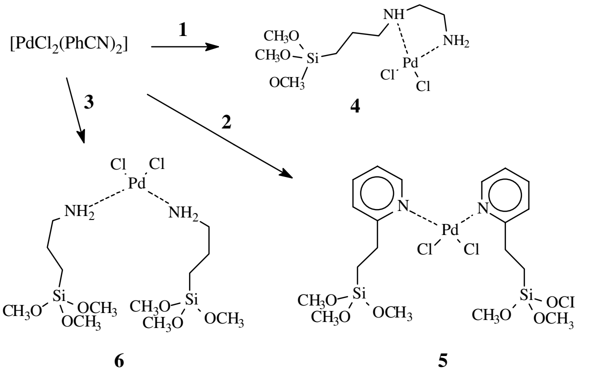
Abstract—Pd(II) complexes with N-ligands were synthesized and tested for Suzuki coupling reaction. These complexes were also heterogenized on silica. The resulting site-isolated catalysts showed a high catalytic activity. The most stable complex was supported *N*-(propyl)ethylenediamine, which did not display any notable leaching. The effects of reaction conditions and the nature of the boronic acid derivative on the conversion of the starting compounds were studied.

Palladium(II) complexes with nitrogen-containing ligands are well-known catalysts for Suzuki coupling reactions, which are of increasing importance for the formation of C–C bonds.[1] We recently used Suzuki couplings for the synthesis of bis-indenyl ligands for a chiral titanocene catalyst.[2] Homogeneous Pd complexes possess high activity for this reaction; however, their disadvantage is that they are hard to remove and recycle, leading to a contamination of products with the catalyst. Thus, heterogenization of the catalysts is a logical step to avoid these problems, as it allows for easy removal from the reaction mixture. However, inorganic heterogeneous Pd catalysts show low stability due to leaching of Pd from the surfaces.[3] In fact, in detailed studies it was shown that in most cases, the leached homogeneous Pd species is responsible for the catalytic activity.[4] A promising strategy to obtain stable heterogeneous catalysts is the synthesis of organic/inorganic hybrid materials, containing Pd complexes with an organic ligand anchored covalently on the support. This support may be an organic polymer or an inorganic oxide (e.g., silica).[5] When these catalysts are immobilized on a catalytically active material (e.g., zeolites), bifunctional catalysts may be obtained, where active sites of one kind are located in the zeolite pores and the Pd moieties on the external surface.[6]



Scheme 1. Synthesis of three different Pd(II)-complexes.

In this study, three ligands containing functional groups for their immobilization were chosen, that is, *N*-[3-(trimethoxysilyl)propyl]-ethylenediamine (**1**), 2-(2′-pyridyl)-ethyltrimethoxysilane (**2**), and 3-aminopropyltrimethoxysilane (**3**). Their Pd(II) complexes were prepared by the reaction of [PdCl$_2$(PhCN)$_2$] with the corresponding ligand (Scheme 1) under reflux with *i*-PrOH.[7] All three ligand–Pd complexes were not reported before for use as Suzuki coupling catalysts.

In order to obtain a heterogeneous catalyst, the ligands were first immobilized on the silica surface in toluene (Scheme 2) and then metalated with [PdCl$_2$(PhCN)$_2$].[8] This strategy was chosen due to the very low solubility of two of the resulting complexes (i.e., **4** and **6**) in most

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Keywords: Suzuki couplings; Catalysis; Pd leaching.

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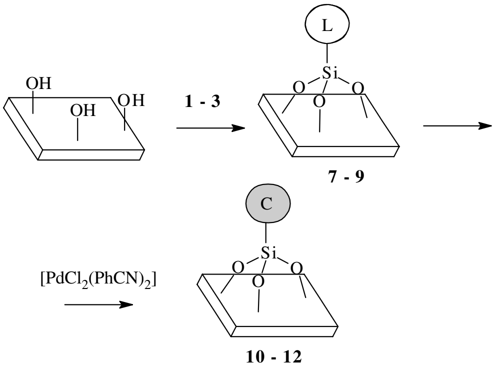


Ⓛ = $(CH_2)_3NH(CH_2)_2NH_2$ (**7**), $(CH_2)_2Py$ (**8**), $(CH_2)_3NH_2$ (**9**)

Ⓒ = $(CH_2)_3NH(CH_2)_2NH_2$-$PdCl_2$ (**10**), $(CH_2)_2Py$-$PdCl_2$ (**11**), $(CH_2)_3NH_2$-$PdCl_2$ (**12**)

Scheme 2. Preparation of supported Pd(II)-complexes.

Table 1. Composition of immobilized catalysts[10]

Ligand	Loading (mmol/g)		Surface density (molecules/nm^2)	
	Ligand	Pd(II)	Ligand	Pd(II)
1	1.40	1.38	2.52	2.48
2	1.20	0.99	2.16	1.78
3	1.19	0.93	2.14	1.68

solvents, which made it very difficult to immobilize them. As can be seen from Table 1, the loading of the ligands in all cases was similar (somewhat larger in the case of **4**). Assuming the surface area of silica to be 330 m^2/g and the estimated number of silanol groups on the surface to be 4.9 ± 0.8 molecules/nm[29] we conclude that most of the silanol groups were replaced by the ligand molecules.

The yields of the surface complexes of Pd(II) were between 78% and 98% (the highest loading of Pd was found for complex **10**). Considering the density of the ligand coverage (an average distance between their molecules is 0.8–0.9 nm), it is evident that the Pd atoms in the surface complexes **11**–**12** are bound to only *one* ligand molecule. This distance excludes influence of neighboring catalyst molecules on the active site.

Immobilization of Pd(II) was confirmed by IR studies of the samples. Spectra of the parent ligands contain strong bands related to the stretching vibrations of Si–O–C bonds at 1189 (asymmetric) and 771–807 (symmetric, doublets) cm^{-1}. In addition, the spectrum of ligand **2** contains a strong band at 789 cm^{-1} related to the vibrations of the pyridine ring, and medium doublets at 1434–1473 (overlapping of CH_2 bending and scissoring, and Py stretching vibrations) and 1568–1591 (Py stretching) cm^{-1}.

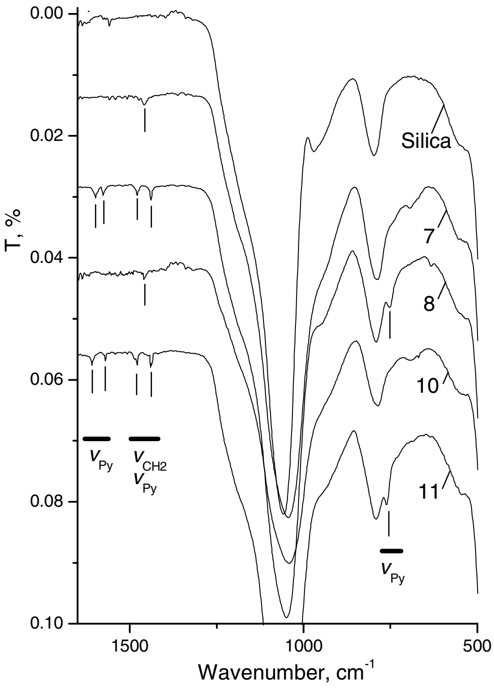
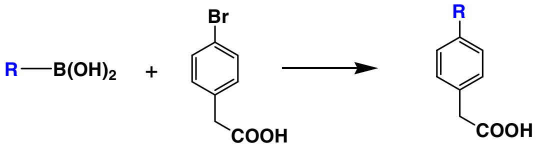


Figure 1. IR spectra of immobilized ligands **7**–**8** and Pd-complexes **10**–**11**.

Formation of the complexes resulted in some changes in the IR spectra. In **4**, the band of CH_2 bending and scissoring vibrations shifted insignificantly (from 1459 to 1457 cm^{-1}). In contrast to **4**, the corresponding doublet in the spectra of **5** shifted to 1448–1483 cm^{-1}. Band of the Py stretching vibrations shifted to 1568–1604 cm^{-1}. In addition, a new band at 770 cm^{-1} appeared.

After immobilization of **1** and **3** on the surface, the band 771–807 disappeared due to replacement of the Si–O–C bonds onto Si–O–Si with a band at 797 cm^{-1} (Fig. 1). Only a weak shoulder can be seen that corresponds to a small number of remaining methoxy groups. For immobilized **2**, the band of the pyridine ring vibrations was observed, but shifted to 743 cm^{-1}. The bands at 1434–1473 cm^{-1} shifted insignificantly (1434–1477 cm^{-1} in the immobilized ligand **8** and 1437–1478 cm^{-1} in the immobilized complex **11**), but the bands at 1568–1591 cm^{-1} changed their position to 1576–1598 cm^{-1} (**8**) and 1569–1608 cm^{-1} (**11**), which is an evidence of complexation with Pd. For **9** and **12**, these bands appeared too weak to be detected.



Tests of catalysts **4**–**6** for the Suzuki coupling reaction in an isopropanol/water solution showed that the complexes with monodentate ligands **5**–**6** have a higher activity, while the complex with the bidentate ligand **4** appeared less active (Table 2). The activity of the immobilized version (catalyst **10**) was found significantly higher, which can be attributed to the effect of 'site isolation', that is, the absence of interactions between catalyst molecules,[12] which is followed by a decomposition of the

Table 2. Activity of Pd catalysts in Suzuki coupling[11]

Catalyst	R	Solvent	Base	*T* (°C)	Conversion, % (time, h)
4	Phenyl	IPA/H_2O (1:9)	Cs_2CO_3	80	1.9 (2), 16.6 (19)
4	Phenyl	DMA/H_2O (1:9)	Cs_2CO_3	90	1.5 (2), 18.6 (19)
5	Phenyl	IPA/H_2O (1:9)	Cs_2CO_3	80	100 (2)
6	Phenyl	IPA/H_2O (1:9)	Cs_2CO_3	80	90.4 (2)
10	Phenyl	IPA/H_2O (1:9)	Cs_2CO_3	80	80.1 (2), 99.9 (16)
11	Phenyl	IPA/H_2O (1:9)	Cs_2CO_3	80	100 (2)
12	Phenyl	IPA/H_2O (1:9)	Cs_2CO_3	80	93.6 (2)
13	Phenyl	IPA/H_2O (1:9)	Cs_2CO_3	80	20.7 (2), 99.8 (16)
13	Phenyl	Toluene	Et_3N	90	4.3 (2), 8.9 (22)
13	Phenyl	DMA/H_2O (1:9)	Cs_2CO_3	90	23.1 (2)
13	Phenyl	DMA/H_2O (1:9)	Na_2CO_3	90	55.5 (2), 99.7 (22)
10	Phenyl	Dioxane	Et_3N	80	2.0 (22)
10	Phenyl	Toluene	Et_3N	90	18.2 (2)
10	Phenyl	DMA/H_2O (1:9)	Cs_2CO_3	90	89.6 (2), 97.7 (22)
10	Phenyl	DMA/H_2O (1:9)	Na_2CO_3	90	98.3 (2), 100 (22)
10	Phenyl	DMA/H_2O (1:9)	K_2CO_3	90	85.5 (2), 99.8 (22)
10	Phenyl	DMA/H_2O (1:9)	Et_3N	90	28.3 (2), 94.6 (22)
10[a]	Phenyl	DMA/H_2O (1:9)	Na_2CO_3	90	100 (1)
10[b]	Phenyl	DMA/H_2O (5:6)	Na_2CO_3	90	81.8 (2), 100 (22)
10	3-Hydroxyphenyl	DMA/H_2O (1:9)	Na_2CO_3	90	89.7 (2), 99.8 (22)
10	3-(Hydroxymethyl)phenyl	DMA/H_2O (1:9)	Na_2CO_3	90	97.6 (2), 100 (22)
10	4-(Hydroxymethyl)phenyl	DMA/H_2O (1:9)	Na_2CO_3	90	97.3 (2)
10	3-Carboxyphenyl	DMA/H_2O (1:9)	Na_2CO_3	90	89.1 (2)
10	4-Carboxyphenyl	DMA/H_2O (1:9)	Na_2CO_3	90	100 (2)
10	4-Formylphenyl	DMA/H_2O (1:9)	Na_2CO_3	90	46.1 (2), 57.1 (22)
10	3-Thienyl	DMA/H_2O (1:9)	Na_2CO_3	90	2.0 (2)
10	Vinyl[c]	DMA/H_2O (2:9)	Na_2CO_3	90	22.3 (2), 49.8 (22)

[a] With 4-iodobenzoic acid.

[b] With 4-iodoanisole.

[c] Dibutyl ester.

complex and formation of less active Pd nanoclusters.[13] The significantly higher activity of the immobilized catalyst proved that heterogeneous and not homogeneous Pd contributed to its activity. The catalysts **11**–**12** displayed a higher activity as well, however a filtration test[14] indicated some leaching for them to occur (in contrast to catalyst **10**, where the filtration test indicated no detectable leaching). The concentration of homogeneous Pd after reaction with catalyst **10** as determined by IPC was found to be below reliable detection limits, while for catalyst **11** it reached 3 ppm.

After reduction of Pd(II) in the catalyst **10** to Pd(0),[15] the activity of **13** was lower, and leaching of Pd was detected. Thus, the stability of the Pd(II) complex appeared higher than that of the Pd(0) complex. For this reason, we continued to work with catalyst **10** only.

Effect of the solvent on the activity of **10** was studied with different solvent systems. The highest conversion of phenylboronic acid was found using a DMA/water mixture. In contrast to the data reported by LeBlond et al., high water content in this mixture did not lead to the homocoupling of phenylboronic acid.[16] The conversion in *i*-PrOH/water mixture was somewhat lower, but higher than in toluene. Surprisingly, a very low catalytic activity was seen in dioxane, while no reaction occurred in DMA and THF. In contrast to a mixture of *i*-PrOH/water, some insignificant leaching of Pd was detected in DMA/water.

Comparison of different bases indicated that Na_2CO_3 is the most favorable one. It seems that the nature of the optimal base is unique for each catalyst and that no general dependence exists (Artok and Bulut[17] and Weskamp et al.[18] reported better performance of Cs_2CO_3 in comparison to Na_2CO_3, while Phan et al.[5a] found a reverse dependence. However, they found a much higher activity in the presence of TEA). This difference in the activating effect of the base is caused by the formation of a transition complex with Pd, which depends on its coordination sphere.

The activity of **10** was also studied for the conversion of different substituted boronic acids. In order to elucidate the effect of the substituent in the aromatic ring, we tested the catalyst for the coupling of phenylboronic acids with hydroxy, hydroxymethyl, and carboxy groups in 3- and 4-positions. The position of a CH_2OH group in the ring did not affect the conversion. For an electron-withdrawing COOH substituent, the reactivity of (4-carboxyphenyl)boronic acid was higher (Table 2). In the case of an electron-releasing OH group, a high conversion was observed for the 3-substituted ring, while no cross-coupling product was detected for (4-aminophenyl)boronic acid pinacoline ester and (4-hydroxyphenyl)boronic acid (not shown in Table 2). Non-identified peaks in the HPLC chromatograms of the reaction mixtures for these cases probably belong to products of homocoupling of boronic acid and its deboronation, while (4-bromophenyl)acetic acid remained unconsumed. Earlier, Lei and Zhang reported much higher ability of (4-methoxyphenyl)boronic acid to homocoupling in comparison with non-substituted substrate even in non-aqueous solution.[19] The possibility of deboronation of arylboronic acids with an electron-donor group in the benzene ring under mild conditions was mentioned by Lapert[20] and Lange,[21] and the promoting effect of silica for this pathway was reported by Schilling and Kaufmann.[22] We assume that the OH group in the 4-position favored these side-reactions.

The conversion of other boronic acids was low as well. As reported earlier, the low conversion of (4-formylphenyl)boronic acid did not depend on the experimental conditions.[23] Only an insignificant conversion of 3-thienylboronic acid was detected. Surprisingly, no reaction occurred with (4-vinylphenyl)boronic acid. Recently, we found that for most catalysts (except $Pd(PPh_3)_4$), (4-vinylphenyl)boronic acid does not react with arylbromides in the presence of water, while its conversion in non-aqueous solvent systems remains low.[24] As to the non-aromatic boronic acids, vinylboronic acid dibutyl ester yielded moderate conversions, while *cis*-1-propenylboronic acid did not react. (Reactions with 0% yield are not shown in Table 2.)

The conversion of iodo-substituted aromatic compounds was much higher than the bromo-substituted ones. In the case of 4-iodobenzoic acid, the reaction was completed within 1 h. For the reaction with 4-iodoanisole, we used a solvent system with lower water content in order to provide a sufficient solubility of all reactants.

In summary, immobilized dichloro(*N*-(3′-trimethoxysilyl)propyl-1,2-ethanediamine-*N*,*N*′)-Pd showed a high activity for Suzuki coupling reactions, which makes it a useful system for biaryl compound synthesis. Most importantly, leaching appeared negligible. Future work will be devoted to the understanding of leaching in different solvent systems and to the use for other reactions.

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7. Synthetic procedure for complexes **4**–**6**. 0.011 mol of ligands **1**–**3** was dissolved in 10 mL of CH_2Cl_2, and a solution of 0.01 mol of $[PdCl_2(C_6H_5CN)_2]$ in 10 mL of CH_2Cl_2 was added at room temperature. The solvent was removed in vacuum, the residue was washed by pentane and diethyl ether. Dichloro(*N*-(3′-trimethoxysilyl)propyl-1,2-ethanediamine-*N*,*N*′)-palladium (**4**): white crystals (dioxane/ethanol, decomp. >180 °C); IR (cm^{-1}): 774 (Si–O–C), 909, 1074, 1189 (Si–O–C), 1456 (CH_2), 2838, 2941 (CH_2). Dichloro-bis[2-(2′-trimethoxysilyl)ethylpyridine]-palladium (**5**): yellow crystals (dioxane, decomp. >200 °C); ^1H NMR (δ): 1.61 (t, 2H, $SiCH_2$), 3.73 (s, 9H, OCH_3), 4.03 (t, 2H, Py-CH_2), 7.20–7.34 (m, 2H, Py-CH), 7.69 (t, 1H, Py-CH), 9.01 (d, 1H, Py-CH); IR (cm^{-1}): 747 (Si–O–C), 770, 791 (Py), 912, 1073, 1190 (Si–O–C), 1448, 1483 (CH_2), 1568, 1604 (Py), 2839, 2940 (CH_2). Dichloro-bis[1-(3′-trimethylsilyl)propaneamine]-palladium (**6**): white crystals (dioxane/ethanol, decomp. >210 °C); IR (cm^{-1}): 774 (Si–O–C), 911, 1024, 1189 (Si–O–C), 1487 (CH_2), 2935 (CH_2).
8. Preparation of immobilized complexes **10**–**12**. 0.01 mol of ligands **1**–**3** was dissolved in 25 mL of toluene. Two grams of previously dehydrated silica was suspended, and the reaction mixture was kept at 100 °C for 18 h. The silica was filtered, washed with hot toluene and dried in a vacuum. Obtained hybrid materials **7**–**9** were suspended in a solution of 0.01 mol of $[PdCl_2(C_6H_5CN)_2]$ in 25 mL of *i*-PrOH and refluxed for 4 h. The brown product was filtered, washed with 2-C_3H_7OH, CH_2Cl_2, and dried in a vacuum.
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10. Loadings of the ligands and Pd were calculated on the basis of elemental analysis.
11. For all tests, a halide aryl compound (1 mmol), a boronic acid (1 mmol) and a base (3 mmol) were dissolved in 10 mL of a solvent. A catalyst (amount containing 0.01 mmol of Pd) was then added to the reaction mixture. The reaction was monitored by HPLC (Shimadzu SCL-10A with Discovery C18 column, 15 cm × 4.6 mm, 5 μm; eluent: methanol/water, 60:40).
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14. The reaction was carried out until a conversion of 30–50% was reached. Then, the catalyst was filtered and the

reaction mixture was stirred at the same temperature for 22 h. The absence of further conversion proves the absence of homogeneous Pd in the solution.

15. Reduction was carried out by dropping a methanol suspension of $NaBH_4$ to the catalyst in CH_3OH at 40 °C for 1 h. The black product was then filtered, washed with CH_3OH and CH_2Cl_2, and dried in a vacuum.
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