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A macrocyclic Pd(II)–Ni(II) complex in Heck and Suzuki reactions

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ABSTRACT

A heterodinuclear Pd(II)–Ni(II) macrocyclic Schiff base complex was applied as a catalyst for Heck and Suzuki cross-coupling reactions. In reaction of 4-bromoanisole with styrene, 4-methoxy-trans-stilbene was formed as the main product with a yield of up to 87%. In the Suzuki coupling of 4-bromoanisole with $PhB(OH)_2$ in a 2-propanol/water solution, up to 96% of the product was obtained. Analyses of the post-reaction mixtures confirmed the high stability of the macrocyclic Pd(II)–Ni(II) complex under the reaction conditions. The partial decomposition of the complex started at the Ni(II) site.

1. Introduction

Palladium-catalyzed C–C bond forming reactions have become a very powerful tool of organic synthesis [1–11]. Organic products formed in these reactions, such as arylated olefins, unsymmetrical biaryls, arylalkynes, or conjugated enynes, are industrially important substrates for the pharmaceutical and agrochemical industries. They are also used as natural products, molecular organic materials and components for optical device production [1–11].

An increasing market for the products of C–C bond forming reactions motivates searching for new, more efficient catalysts for such processes, preferably operating under mild conditions. Different classes of palladium species have been tested in the Heck and the Suzuki cross-coupling reactions, such as palladacycles [12–17] and complexes with N-heterocyclic carbenes [18–23]. Good results have also been obtained for immobilized palladium catalysts [24–27] as well as for Pd(0) nanoparticles [28–30].

The main problem associated with the use of palladium catalysts is the low stability of Pd(0) forms, which easily undergo agglomeration in the absence of stabilizing agents [31,32]. At the beginning of the catalytic cycle, Pd(0) is needed for the activation of the substrate, aryl halide, according to the oxidative addition pathway. However, at the end of the catalytic process, non-stabilized Pd(0) can agglomerate and finally form inactive palladium black. To overcome this unfavourable process, strong ligands, polymers, or inorganic oxides are used.

Another concept was presented by Köhler and co-workers [33,34]. It was based on the slow and controlled release of palladium from the precursor to the solution. As a result, the concentration of palladium in the solution remained very low, and agglomeration was limited, which allowed a high catalytic activity even for deactivated substrates [33,34].

While palladium catalysts are first choice in C–C bond forming reactions, there is growing interest in catalysts based on the much cheaper and less toxic nickel complexes. In some cases the nickel based catalysts even surpass palladium catalysts in cross-coupling reactions [35,36]. In a recent communication a very interesting effect of cooperative catalysis by palladium–nickel binary nanocluster in Suzuki–Miyaura reaction has been reported [37]. In this case the mixture of Pd and Ni compounds turned out to be much more effective catalytic system than the catalytic systems based on the Pd alone or Ni alone.

Inspired by the results obtained in Heck and Suzuki reactions with the application of a Pd(II)–Pd(II) macrocyclic bimetallic complex $[Pd_2L](ClO_4)_2$, we decided to study the catalytic activity of a Ni(II)–Pd(II) analogue $[NiPdL](ClO_4)_2{\cdot}3MeCN$ (Scheme 1) [38,39]. In particular, it was interesting to learn whether the presence of Ni(II) would influence palladium activity via formation of mixed Pd–Ni nanoparticles/clusters originating from the same molecular precursor.

2. Experimental

Macrocyclic complexes $[NiPdL](ClO_4)_2{\cdot}3MeCN$, $[Ni(H_2L)](ClO_4)_2{\cdot}H_2O$, $[Ni_2L]Cl_2{\cdot}2H_2O$ were obtained according to the literature [38,39].

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2.1. Heck reaction

The Heck reaction was carried out under an N_2 atmosphere using a standard Schlenk technique. The reagents were introduced to the Schlenk tube (50 mL) in the following order: catalyst (0.0375–0.225 mol%), 4-bromoanisole (3 mmol), styrene (1.5 mmol), base ($Ca(OH)_2$ or $NaHCO_3$ 0.9 mmol), solvent NMP or DMF (5 mL). The reaction was carried out at 160 °C for 6–26 h. Afterwards, the reaction mixture was quenched with H_2O (10 mL), and the organic products were separated by extraction with diethyl ether (3 times, 15, 5, and 5 mL). The products were analyzed by GC-FID.

2.2. Suzuki–Miyaura reaction

The Suzuki–Miyaura reactions were carried out in a 50 mL Schlenk tube in an air atmosphere. The substrates were weighed and placed directly in the Schlenk tube: catalyst (0.55–2.1 mol%), phenylboronic acid (1.5 mmol, 0.183 g), base (KOH or K_3PO_4 2 mmol), aryl halide (4-bromoanizole or 4-iodoanisole, 1 mmol). Next, 5 mL of the solvent was added. The reaction mixture was stirred at 60 or 130 °C for 25.5 or 46.5 h. Afterwards, the reactor was cooled down, the reaction mixture was quenched with H_2O (3 mL), and the organic products were separated by extraction with diethyl ether (3 times, 4, 3 and 3 mL). The products were analyzed by GC-FID.

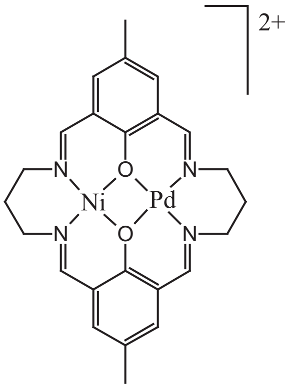
For recycling experiments the solution remaining after extraction of organic products was condensed in vacuo and used for the next experiment with new portion of substrates.

2.3. Instruments

GC analyses (GC-FID) were performed on Hewlett Packard 8454A instrument. Products were identified by GC–MS using Hewlett Packard 5890 II instrument with capillary column ELITE-5MS and stationary phase 5% diphenylpolysiloxane, 95% dimethylpolysiloxane.

MS spectra were performed on a Bruker Daltonics micrOTOF-Q. The ions were generated from electrospray ionization source. The electrospray flow rate was 10 μl/min^{-1}, which was maintained by a syringe pump; spray was directed into a heated glass capillary at a temperature 200 °C, and a high voltage of 4500 V between the endplate and the spray needle. Nebulizer vacuum 0.4 Bar; dry gas flow 4.0 l/min;

^{1}H NMR spectra were measured on Bruker 500 MHz spectrometer.



Scheme 1. Macrocyclic Pd(II)–Ni(II) cation ($[NiPdL]^{2+}$) of the $[PdNiL](ClO_4)_2 \cdot 3MeCN$ complex.

3. Results and discussion

3.1. Heck reaction

The model Heck reaction of styrene with 4-bromoanisole was performed according to Scheme 2.

The highest conversion of styrene, 95–99%, was obtained after 26 h at 160 °C using 0.0375–0.075 mol% of the catalyst. With a larger amount of the catalyst, 0.225 mol%, already after 6 h, 95% of styrene was converted to the products (Table 1).

A good result, 72% conversion, was also achieved in DMF. In this solvent, the best selectivity was noted with the 1:2 ratio amounting to 71. In all other cases, two products, 4-methoxy-trans-stilbene (1) and 1-(4-methoxyphenyl)-1-phenylethene (2), were formed with a ratio of ca. 10. Similarly, the formation of two products in the Heck reaction of styrene was reported for a macrocyclic palladium precursor [33,34] and phospha-palladacycle [40].

When $[NBu_4]Br$ was added to the reaction in DMF, conversion decreased to 44% and selectivity also dropped. The inhibiting effect of ammonium salt was also observed in the Heck reaction of styrene and chloroanisole catalyzed by a macrocyclic Pd(II) complex $[Pd_2L](ClO_4)_2$ [33,34]. It was explained by the formation of palladium black in reaction with tributylamine originated from the decomposition of the salt at 160 °C. The presence of tributylamine in the reaction mixture was confirmed in our system by GC–MS; however, we did not obtain confirmation of the formation of palladium black or Pd(0) nanoparticles by TEM.

In order to compare activity of $[NiPdL](ClO_4)_2$ and $[Pd_2L](ClO_4)_2$ complexes, one reaction was performed at 140 °C with 0.05 mol% of catalyst. Using mixed complex we obtained 76% of product 1, whereas 71% was formed with $[Pd_2L](ClO_4)_2$ [34]. Considering a lower content of palladium in the mixed precursor, the obtained results are quite satisfactory.

When more reactive butyl acrylate was used instead of styrene, only one product, substituted trans-stilbene, was obtained (Scheme 3). In this case formation of more stable product is favoured.

Attempts to perform the Heck coupling with 4-chloroanisole were unsuccessful and after 26 h the product was not formed.

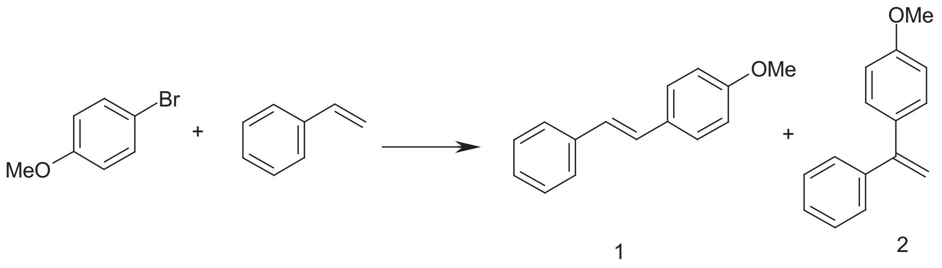
3.2. Suzuki reaction

The Suzuki reaction was performed according to Scheme 3, using the palladium–nickel complex $[NiPdL](ClO_4)_2$ and the nickel analogues: $[NiH_2L](ClO_4)_2$ and $[Ni_2L_4]Cl_2$, as catalysts. However, only Pd–Ni was active in the studied reaction.

The optimization of the reaction parameters resulted in the selection of the best solvents, namely 2-propanol/H_2O (1:1) and ethylene glycol, making it possible to obtain 96% or 80% of the cross-coupling product (Table 2). The concentration of the catalyst has an important influence on the reaction course and 1 mol% appeared the best. Using a smaller amount of the catalyst, 0.55 mol%, 78% of the product was obtained, whereas an increase of the catalyst amount to 2.1 mol% resulted in a decrease of the yield to 34%. The modification of the last reaction by the addition of 1 mmol TBAB made it possible to increase the yield to 71%. Interestingly, in the Suzuki reaction, the presence of $[Bu_4N]Br$ favourably influenced the reaction yield, while the same salt inhibited the Heck reaction (Scheme 4).

Attempts to reuse the Pd–Ni catalyst were not very promising, and in the best case 12% of product was found in the second run (Table 2).

Two experiments performed under conditions similar to these used earlier [34] for testing $[Pd_2L](ClO_4)_2$ complex gave 25–30% of product after 6 h.



Scheme 2. Heck reaction of styrene with 4-bromoanisole.

Table 1
Results of the Heck reaction of 4-bromoanisole with styrene catalyzed by [NiPdL]$(ClO_4)_2.CH_3CN$.

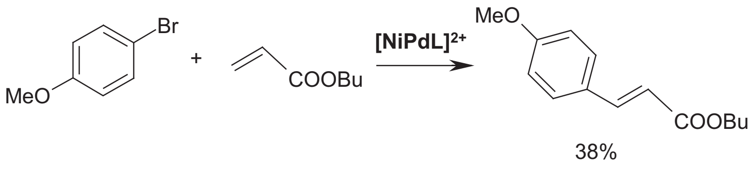
Time (h)	Solvent	Temp. (°C)	Catalyst amount (mol%)	Conversion (%)	Yield of 1 (%)	Yield of 2 (%)
26	NMP	160	0.075	99	87	8
26	NMP	160	0.0375	95	81	11
6	NMP	160	0.225	95	84	8
6[a]	DMF	160	0.075	72	71	1
6[a,b]	DMF	160	0.075	44	39	5
6[c]	DMF	160	0.05	43	38	5
6[c]	NMP	160	0.05	90	81	9
6[c]	NMP	140	0.05	85	76	9

Reaction conditions: styrene (1.5 mmol), 4-bromoanisole (3 mmol), $Ca(OH)_2$ (0.9 mmol), solvent (5 mL).

[a] Base: $NaHCO_3$ (0.9 mmol).

[b] 1 mmol $[Bu_4N]Br$ was added.

[c] Base: CH_3COONa.



Scheme 3. Heck coupling of 4-bromoanisole with butyl acrylate.

Table 2
Results of the Suzuki reaction catalyzed by [NiPdL]$(ClO_4)_2.CH_3CN$.

Substrate	Solvent	Time (h)	Temp. (°C)	Catalyst (mol%)	Conversion (%)	Yield (%)
4-Bromoanisole	Dioxane	25.5	130	1	16	16
4-Iodoanisole	Dioxane	46.5	130	2.1	96	96
4-Bromoanisole	Ethylene glycol	25.5	60	1	80	80
4-Bromoanisole	2-Propanol/water[a]	25.5	60	0.55	78	78
4-Bromoanisole	2-Propanol/water[b]	25.5	60		7	7
4-Bromoanisole	2-Propanol/water[a]	25.5	60	1	96	96
4-Bromoanisole	2-Propanol/water[b]	25.5	60		12	12
4-Bromoanisole	2-Propanol/water[a]	25.5	60	2.1	34	34
4-Bromoanisole	2-Propanol/water[a,c]	25.5	60	2.1	71	71
4-Bromoanisole	2-Propanol/water[d]	6	100	0.5	25	25
4-Bromoanisole	2-Propanol/water[d]	6	100	1	30	30

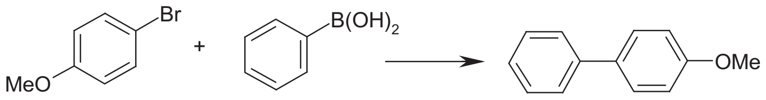
Reaction conditions: 4-bromoanisole (1 mmol), $PhB(OH)_2$ (1.5 mmol), K_3PO_4 (2 mmol), 130 °C.

[a] KOH (2 mmol).

[b] Recycling (second run with the same catalyst).

[c] $[Bu_4N]Br$ (1 mmol) was added.

[d] Na_2CO_3 (3.2 mmol), 4-bromoanisole (3 mmol), $PhB(OH)_2$ (3.2 mmol).



Scheme 4. Suzuki coupling of 4-bromoanisole with phenylboronic acid.

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3.3. Mechanistic studies

Similarly as was observed for the dipalladium complex $[Pd_2L]^{2+}$, a substantial amount of $[NiPdL]^{2+}$ survived the catalytic reactions. This fact is confirmed by the ^1H NMR spectrum of the residue obtained by the evaporation of the water phase from the reaction workup. Although the diamagnetic region is obscured by the signals of residual water and organic products, the characteristic signals of the paramagnetic complex $[NiPdL]^{2+}$ at 24.1, 11.9, and 10.0 ppm were observed. The presence of intact $[NiPdL]^{2+}$, left after the catalytic reaction, was also confirmed by the UV–Vis spectrum, which presented a band at 375 nm, and mass spectra that indicated a 284 signal at m/z, corresponding to $[NiPdL]^{2+}$, with a characteristic isotope pattern (Fig. 1).

In addition to the signal of intact $[NiPdL]^{2+}$, the mass spectra of the hexane post-reaction extract indicated a weak signal at m/z equal to 509, corresponding to the $[PdLH]^+$ complex, where the Ni(II) ion was removed and replaced by a proton. Additionally, there was a weak signal at m/z equal to 493, corresponding to the $[NaPdL']^+$ complex of an open ligand L′, resulting from the removal of the Ni(II) ion, the hydrolysis of the propylenediamine sidearm, and the binding of the Na(I) cation originating from sodium present in the base (Scheme 5). On the other hand we did not observed in ESI MS spectra signals of analogous $[NiLH]^+$ and $[NaNiL']^+$ decomposition products. Thus the two metal ions in the $[NiPdL]^{2+}$ complex are released at different rates; apparently the Ni(II) ion is bound less strongly and is removed first. These results indicate that the catalytic effect is similar to that proposed

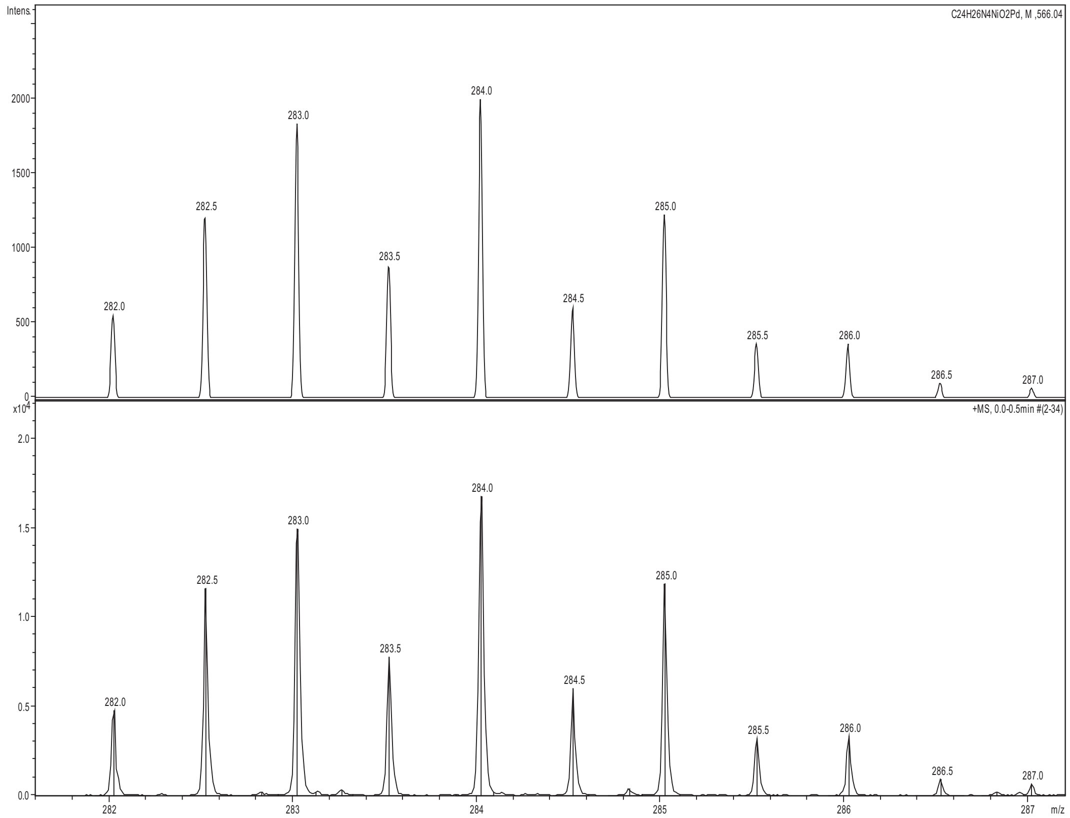
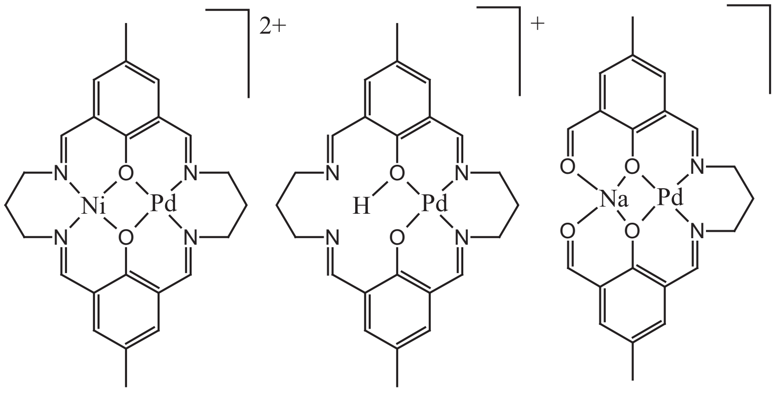


Fig. 1. Simulated (top) and experimental (bottom) isotope pattern of $[NiPdL]^{2+}$ ($m/z = 284$) found in the sample after Suzuki reaction.



Scheme 5. Cations $[NiPdL]^{2+}$, $[PdLH]^+$ and $[NaPdL']^+$ identified in ESI-MS spectra of the post-reaction mixture.

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previously for the dipalladium analogue. It is based on the high stability of the applied Pd(II) catalyst, which very slowly releases minute amounts of Pd to the reaction medium. This slow release prevents the formation of Pd clusters and palladium black. Indeed, in our case, Pd(0) nanoparticles and palladium black were not observed according to TEM results. On the other hand, the ESI MS data mentioned above suggest that the partial decomposition of the complex is actually started at the Ni(II) site.

4. Conclusions

A Pd(II)–Ni(II) macrocyclic complex exhibited good catalytic activity in the Heck coupling of 4-bromoanisole with styrene and the Suzuki coupling of 4-bromoanisole with phenylboronic acid. A high conversion of the substrates was obtained in the Heck reaction using MNP or DMF as a solvent. The addition of $[Bu_4N]Br$ caused an inhibiting effect leading to a yield decrease. The performance of the Suzuki reaction in a 2-propanol/water mixture made it possible to obtain 96% of the coupling product. Here, a positive effect of $[Bu_4N]Br$ was observed.

The catalytic activity of the Pd(II)–Ni(II) complex can be explained by the slow release of palladium to the reaction solution from the stable macrocyclic structure, similarly as was proposed for the Pd(II)–Pd(II) analogue. Some amount of the complex underwent decomposition, which started at the Ni(II) site. On the other hand, the mixed Ni–Pd clusters were probably not formed in the studied reactions and no increased activity was achieved due to cooperative effect. The reason for this was the different rate of release of nickel and palladium from the $[NiPdL](ClO_4)_2{\cdot}3MeCN$ complex. The presence of the unchanged complex in the post-reaction mixtures can be rationalized by its high stability or by reconstruction of the structure at the end of the catalytic cycle. Accordingly, the formation of Pd(0) nanoparticles or palladium black was efficiently prevented.

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