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Nickel(II)–aryl complexes as catalysts for the Suzuki cross-coupling reaction of chloroarenes and arylboronic acids

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Abstract—A series of air- and moisture-stable Ni(II)–(σ-aryl) complexes, $Ni(PPh_3)_2(aryl)X$ (X = Cl, Br), were employed as catalyst precursors in the Ni-catalyzed Suzuki cross-coupling reaction. These pre-catalysts easily form the catalytically active Ni(0) species in situ without the need of additional reducing agents. A general catalytic system involving $Ni(PPh_3)_2(1\text{-naph})Cl$ and PPh_3 proved to be highly effective for the Suzuki reaction of aryl chlorides under mild conditions (at 60 °C in THF in the presence of K_2CO_3 as the base).

The palladium-catalyzed Suzuki cross-coupling reaction represents a powerful and versatile methodology for the construction of C_{aryl}–C_{aryl} bonds.[1,2] During the past decades, various Pd catalytic systems have been developed that allow aryl iodides, bromides, triflates, and chlorides to be effectively coupled with arylboronic acids under mild reaction conditions.[2,3] Considering the high cost of palladium, the use of much cheaper Ni catalysts has attracted considerable interests. Since Percec's first report in 1995,[4a] remarkable advance has been made in the Ni-catalyzed version of Suzuki cross-couplings.[4–9] The key advantage of Ni-based catalysts over Pd systems lies in their high reactivity toward readily available but normally unreactive substrates (such as aryl chlorides or sulfonates) without the need of special ligands that are often electron rich (hence air sensitive) and expensive.

For the Ni-catalyzed Suzuki aryl–aryl cross-coupling, the Ni(0) species is generally regarded as being catalytically active and the mechanism follows a Ni(0)–Ni(II) catalytic cycle. The most commonly used Ni sources are the phosphine-coordinated nickel(II) halides, such as $NiCl_2(PPh_3)_2$, $NiCl_2(PCy_3)_2$, $NiCl_2(dppf)$, and $NiCl_2(dppe)$. These Ni(II) complexes are readily available and conveniently manipulated due to their air- and thermal-stability and non-hygroscopicity. Since the active Ni(0) species is essential for the Ni catalysis, the Ni(II) pre-catalysts need to be activated, that is, in situ reduction of Ni(II)–Ni(0). Unlike the Pd(II), the Ni(II) generally cannot be reduced to Ni(0) by the added base and/or solvent in the reaction system. A solution to this problem was that Ni(II) complexes were treated with additional reducing agents such as Zn[4] or *n*-BuLi[5] for in situ generating Ni(0). Afterwards, it was found that Ni(0) was more conveniently generated in situ from Ni(II) at elevated temperatures (80–130 °C) by the homocoupling of the reactant arylboronic acid.[6] Also, the Ni(0) on charcoal pre-treated from Ni(II) with *n*-BuLi was elaborated and then the reaction was conducted at 135 °C.[7] The simplest nickel salts, $NiCl_2$[8a] and $NiCl_2{\cdot}6H_2O$,[8b] were also used as the pre-catalyst for the Suzuki reaction, with nitrogen-containing ligands and with no ligand respectively, although they were effective only for aryl iodides and bromides and the elevated temperature (95–130 °C) was required. More recently, the room-temperature Ni-catalyzed Suzuki reaction has been demonstrated based on the direct use of $Ni(COD)_2$.[9] However, such Ni(0) source would be difficult to handle in practice due to its high air sensitivity. Besides, we noticed that K_3PO_4 (anhydrous or hydrated) seemed to be a sole effective base in almost all the reported Ni-catalyzed Suzuki reactions.[4–9]

Recently, we became interested in exploring Ni-based catalysts applicable in the cross-coupling reactions. The principle of choice is both convenient-to-handle

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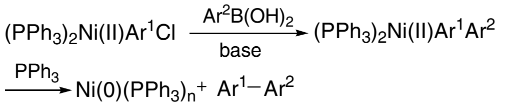
and easy-to-activate. We paid attention to a class of isolatable Ni(II)–(σ-aryl) complexes that were earlier established[10] but have rarely been successfully applied in the catalytic coupling reactions.[11] The Ni(II)–aryl complex is assumed to be an intermediate in the Ni(0)–Ni(II) catalytic cycle involving sequential oxidative addition, transmetalation, and reductive elimination.[4a,5b,6c] Thus, these complexes could undergo a process of sequential transmetalation and reductive elimination, prior to the normal cross-coupling reaction, to afford the active Ni(0) species (Scheme 1). A comparable protocol has been carried out in Pd-catalyzed cross-couplings, where the Pd(II)–(π-allyl) complex generates the active Pd(0) in situ by a sequential procedure of nucleophilic attacking at the η^3-coordinating allyl moiety and then reductive elimination.[12] Herein, we report our results on the use of simple and easily available Ni–(σ-aryl) complexes as pre-catalysts for the Suzuki cross-coupling reaction of aryl chlorides.

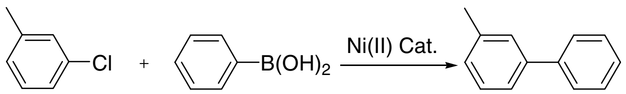
Four Ni(II)–aryl complexes, $Ni(PPh_3)_2$(1-naph)Cl, $Ni(PPh_3)_2$(*o*-tol)Cl, $Ni(PPh_3)_2$(1-naph)Br, and $Ni(PPh_3)_2$(phenyl)Br were synthesized according to the literature procedures.[10,11a] The effects of the catalyst, ligand, base and temperature on the cross-coupling reaction were first investigated using a model reaction of *m*-chlorotoluene and phenylboronic acid in THF. The results are shown in Table 1. Normal Ni(II) catalysts such as $NiCl_2(PPh_3)_2$ and $NiCl_2$(dppe) did not mediate the reaction at 60 °C in the presence of K_2CO_3 as the base at all (entries 1 and 2). After being replaced by $Ni(PPh_3)_2$(1-naph)Cl, the Suzuki reaction can be initiated, albeit in only 24% yield (entry 3). In this case, the color change of the reaction solution, turning dark-red and then black immediately after the addition of THF to the reaction mixture, clearly indicated that the Ni(II)–aryl complex is much easily activated. At the same time, the low conversion in the reaction also suggested that the in situ generated Ni(0) could not be stabilized very well in the absence of additional ligands. Indeed, the reaction yield increased drastically as extra two equiv of PPh_3 (per equiv of Ni) was added to stabilize the labile Ni(0) species (entry 4). It was found that moisture had no influence on this coupling reaction. Rather, the reaction was accelerated when little amounts of H_2O were added. This was likely because the added water increased the solubility of the base K_2CO_3 (entry 5 vs entry 4). Attempts either to reduce catalyst loading or to lower reaction temperature led to the decreased yields (entries 6 and 7). For the other nickel–aryl complexes, $Ni(PPh_3)_2$(phenyl)Br and $Ni(PPh_3)_2$(1-naph)Br were also effective but slightly inferior to $Ni(PPh_3)_2$(1-naph)Cl (entries 9 and 10), while $Ni(PPh_3)_2$(*o*-tol)Cl gave only a moderate yield of 62% (entry 8). The reason is yet unclear at the moment. For weak bases, Na_2CO_3 resulted in a yield of 75% (entry 11), and an excellent yield was obtained using $K_3PO_4·7H_2O$ as the base (entry 13). On the other hand, some stronger bases, $CsCO_3$ and KOH, did not promote the reaction (entries 12 and 14). At room temperature, the coupling reaction proceeded rather sluggishly even though K_3PO_4 was employed as the base (entries 15 and 16).



Scheme 1. Possible pathway for activation of the Ni(II)–aryl complex.

Next, the cross-coupling reaction of several representative arylboronic acids with various aryl chlorides was carried out to determine the generality of our standard protocol (Table 2). As shown in Table 2, this transformation, generally, was very clean and highly efficient. *ortho*-Substituted aryl chlorides or arylboronic acids

Table 1. Reaction conditions for Ni(II)-catalyzed Suzuki reactions of *m*-chlorotoluene and phenylboronic acid[a]

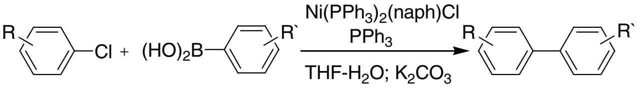


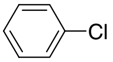
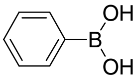
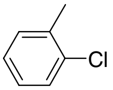
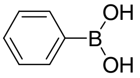
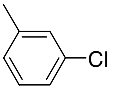
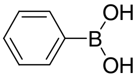
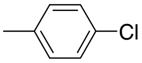
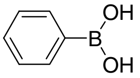
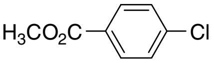
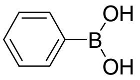
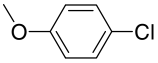
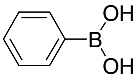
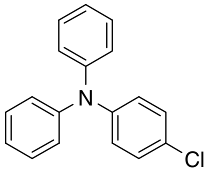
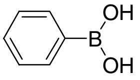
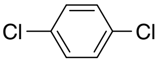
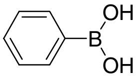
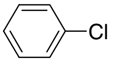
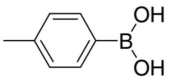
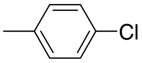
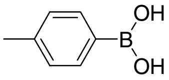
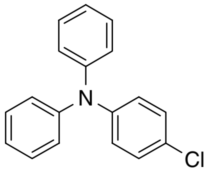
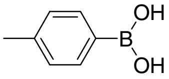
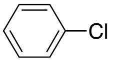
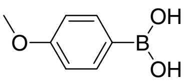
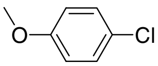
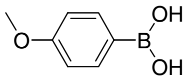
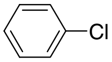
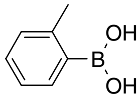
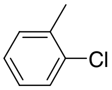
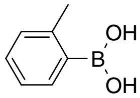
Entry	Catalyst (mol %)	Ligand (mol %)	Base	Solvent	Temperature (°C)	Time (h)	Yield[b] (%)
1	$NiCl_2(PPh_3)_2$ (5)	PPh_3 (10)	K_2CO_3	THF	60	5	No reaction
2	$NiCl_2$(dppe) (5)	dppe (5)	K_2CO_3	THF	60	5	No reaction
3	$Ni(PPh_3)_2$(1-naph)Cl (5)	No	K_2CO_3	THF	60	5	24
4	$Ni(PPh_3)_2$(1-naph)Cl (5)	PPh_3 (10)	K_2CO_3	THF	60	5	95
5	$Ni(PPh_3)_2$(1-naph)Cl (5)	PPh_3 (10)	K_2CO_3	THF–H_2O	60	3	96
6	$Ni(PPh_3)_2$(1-naph)Cl (2.5)	PPh_3 (10)	K_2CO_3	THF–H_2O	60	10	68
7	$Ni(PPh_3)_2$(1-naph)Cl (5)	PPh_3 (10)	K_2CO_3	THF–H_2O	40	10	72
8	$Ni(PPh_3)_2$(*o*-tol)Cl (5)	PPh_3 (10)	K_2CO_3	THF–H_2O	60	3	62
9	$Ni(PPh_3)_2$(1-naph)Br (5)	PPh_3 (10)	K_2CO_3	THF–H_2O	60	3	83
10	$Ni(PPh_3)_2$(phenyl)Br (5)	PPh_3 (10)	K_2CO_3	THF–H_2O	60	3	83
11	$Ni(PPh_3)_2$(1-naph)Cl (5)	PPh_3 (10)	$NaCO_3$	THF–H_2O	60	3	75
12	$Ni(PPh_3)_2$(1-naph)Cl (5)	PPh_3 (10)	$CsCO_3$	THF	60	3	15
13	$Ni(PPh_3)_2$(1-naph)Cl (5)	PPh_3 (10)	$K_3PO_4·7H_2O$	THF	60	3	94
14	$Ni(PPh_3)_2$(1-naph)Cl (5)	PPh_3 (10)	KOH	THF	60	3	12
15	$Ni(PPh_3)_2$(1-naph)Cl (5)	PPh_3 (10)	K_3PO_4	THF	rt	24	23
16	$Ni(PPh_3)_2$(phenyl)Br (5)	PPh_3 (10)	K_3PO_4	THF	rt	24	34

[a] Reaction conditions: *m*-Chlorotoluene (1.0 equiv), phenylboronic acid (1.2 equiv), base (3 equiv), THF (3 mL) or THF (3 mL)–H_2O (0.15 mL).

[b] Isolated yields (average of two runs).

Table 2. Ni(II)–Aryl complex-catalyzed Suzuki cross-couplings of chloroarenes and arylboronic acids[a]



Entry	ArX	ArB(OH)$_2$	Yield[b] (%)
1			99
2			91
3			96
4			94[c]
5			98
6			90[c]
7			87[c]
8			88[d]
9			96
10			92[c]
11			92[c]
12			94
13			92[c]
14			91
15			88

[a] Reaction conditions: aryl chlorides (1.0 equiv), arylboronic acids (1.2 equiv), $Ni(PPh_3)_2$(1-naph)Cl (5 mol %), PPh_3 (10 mol %), K_2CO_3 (3 equiv), THF (3 mL)–H_2O (0.15 mL), 60–70 °C, 2.5–3 h.

[b] Isolated yields (average of two runs).

[c] Arylboronic acids 1.4 equiv.

[d] Phenylboronic acid 2.4 equiv.

were coupled smoothly (entries 2, 14, and 15), indicating that the steric hindrance of coupling partners had less influence on this coupling reaction. On the other hand, the electronic effects of either coupling partner also produced no significant impact on the reaction yields (Table 2). The chloride bearing ester group reacted with phenylboronic acid to give an almost quantitative yield (entry 5), demonstrating the tolerance of the reaction toward functional groups. For aryl chlorides bearing electron-donating groups at the para position, excellent yields could be obtained by addition of a little more excess of arylboronic acids (1.4 equiv vs 1.2 equiv) (entries 4, 6, 7, 10, 11, and 13). For arylboronic acids bearing electron-donating groups at the para position, the reaction proceeded smoothly under the standard conditions (entries 9–13). Although the cross-coupling reaction of *p*-chloroaniline (with free amino group) was not achieved at this time, (4-chlorophenyl)diphenylamine was coupled smoothly (entries 7 and 11). Finally, *p*-terphenyl was easily synthesized in high yield via the double coupling of *p*-dichlorobenzene with phenylboronic acid (entry 8).

In summary, Ni(II)–(σ-aryl) complexes have first been successfully applied in the Ni-catalyzed Suzuki cross-coupling reaction. Ni(II)–(σ-aryl) complexes seem to be activated conveniently and easily, hence this coupling reaction of aryl chlorides and arylboronic acids proceeds under very mild conditions with excellent yields. $Ni(PPh_3)_2$(1-naph)Cl was the most efficient pre-catalyst and K_2CO_3 was an effective base. These Ni(II)–aryl complexes are readily prepared and manipulated due to their stability toward air and moisture. This new protocol provides a very convenient, highly efficient and less expensive alternative for the synthesis of biaryls. Further work to extend this type of Ni catalysts to other catalytic cross-coupling reactions, for instance the C–N coupling reaction, is underway in our laboratory.

General procedure: An oven-dried 50-mL three-necked flask was charged with $Ni(PPh_3)_2$(1-naph)Cl (5 mol %, relative to aryl chloride), PPh_3 (10 mol %, relative to aryl chloride), K_2CO_3 (3.0 mmol), the arylboronic acid (1.2 mmol). The aryl halide (1.0 mmol) was added at this time if it is solid. The flask was evacuated and backfilled with nitrogen, with the operation being conducted twice. The aryl halide (1.0 mmol) was added at this time via syringe if it is liquid. THF (3 mL) and degassed water (0.15 mL) were added via syringe. The reaction mixture was heated in an oil bath of 60–70 °C for 2.5–3 h. After being quenched with water, the reaction mixture was extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure, and then the residue was purified by column chromatography on silica gel with hexane/ethyl acetate as the eluent to give the desired product. Yields are listed in Table 2.

Acknowledgments

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Supplementary data

Detailed experimental procedure and characterization of the products. This material is available free of charge. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.01.175.

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