Synthesis and Catalytic Activity of a Pincer-Type Bis(imidazolin-2-ylidene) Nickel(II) Complex

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*Summary: An air- and moisture-stable nickel(II) complex of bis-carbene pincer complex **2** has been synthesized, and its catalytic activity for the Heck reaction and the Suzuki coupling reaction was investigated.*
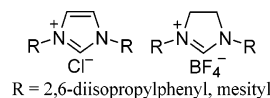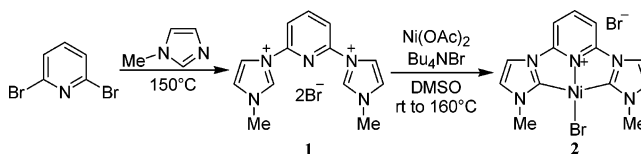
R = 2,6-diisopropylphenyl, mesityl

Figure 1. *N*-Heterocyclic carbene (NHC) precursors.

Scheme 1. Synthesis of NHC-Derived Pincer Complexes 1 and 2

Introduction

Since its discovery, the palladium-catalyzed arylation of alkenes (Heck reaction) has occupied a prominent position in organic synthesis.[1] The scope of this method has been extensively enhanced by the discovery of novel catalyst systems.[2−5] Various palladium-pincer complexes from these are among the best Heck catalysts known,[6] exhibiting extremely high turnover numbers and frequencies.

Although numerous studies on palladium catalysts have been reported to date, nickel-based catalysts had been thought generally ineffective.[7,8] However, we have very recently established the first general catalyst system consisting of Ni(acac)$_2$

and *N*-heterocyclic carbene (NHC)[9] precursors (Figure 1) for the Heck reaction.[10]

We now report herein that a novel NHC-derived nickel-pincer complex **2**, readily prepared and air- and moisture-stable, can catalyze the Heck reaction. The catalytic activity of **2** is much higher than that of the Ni(acac)$_2$/NHC catalyst system; thus aryl chlorides as well as aryl iodides and bromides successfully reacted in our system. Indeed, to the best of our knowledge, the procedure reported herein provides the first general catalytic use of a nickel-pincer complex for the carbon−carbon bond coupling reaction.[11] In addition, we also describe the catalytic use of complex **2** in the Suzuki coupling reaction.

Results and Discussion

The synthetic route for a novel NHC-derived nickel-pincer complex is shown in Scheme 1. The carbene precursor **1** was readily produced from 2,6-dibromopyridine and *N*-methylimidazole in one step,[12] and the subsequent cyclometalation of **1** with Ni(OAc)$_2$ in the presence of Bu$_4$NBr afforded the desired complex **2**. Complex **2** is highly air- and moisture-stable and can be recrystallized from MeOH into yellow-brown needles. The solid-state structure of **2** was determined by single-crystal X-ray diffraction, which showed the nickel in a distorted square planar conformation (Figure 2), similar to that of the NHC-derived palladium-pincer complex.[3c]

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(12) Carbene precursor **1** was prepared according to Crabtree's method; see ref 3c.
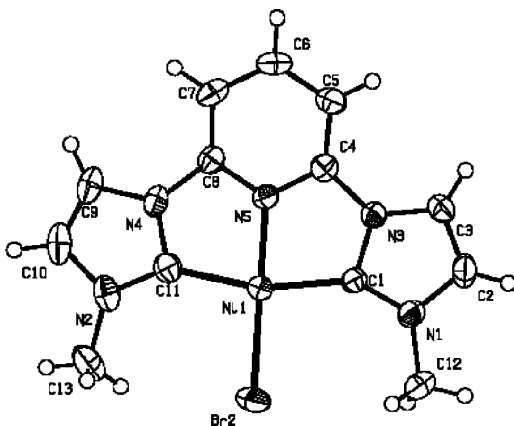
Figure 2. Molecular structure of **2**. The noncoordinating bromide anion is not shown. Selected bond lengths (Å) and angles (deg): Ni1−Br2 = 2.2783(7), Ni1−N5 = 1.862(3), Ni1−C1 = 1.932(4), Ni1−C11 = 1.920 (5), N1−C1 = 1.348(6), N3−C1 = 1.386(5), N2−C11 = 1.350(6), N4−C11 = 1.382(6); Br2−Ni1−N5 = 176.36 (11), Br2−Ni1−C1 = 98.05(13), N5−Ni1−C1 = 81.49(16), N5−Ni1−C11 = 81.53(18), C11−Ni1−Br2 = 98.89 (14), C11−Ni(1)−C1 = 163.02(19), N1−C1−N3 = 103.4(3), N2−C11−N4 = 102.6(4).

Table 1. Catalytic Activity of Nickelacycle 2 in Heck Reaction[a]
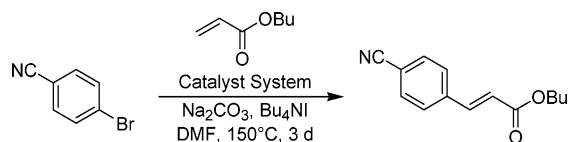
| entry	catalyst system	Bu$_4$NI	yield (%)[b]
1	5 mol % **2**	yes	65
2	1 mol % **2**	yes	64
3	5 mol % Ni(acac)$_2$ + **1**	yes	71
4	5 mol % Ni(acac)$_2$	yes	29
5	5 mol % **2**	no	trace
6[c]	5 mol % **2**	yes	61

[a] Reagents: 4-bromobenzonitrile (1.0 mmol), butyl acrylate (5.0 mmol), catalyst system (as listed above), Na$_2$CO$_3$ (3.0 mmol), Bu$_4$NI (3.0 mmol), and DMF (5 mL). [b] Isolated yield, average of two runs. [c] Under air atmosphere.

To evaluate the catalytic activity of nickelacycle **2** in the Heck reaction, we first carried out the reaction of 4-bromobenzonitrile with butyl acrylate. After exploring a wide array of reaction conditions, we determined that 5 mol % of **2** in the presence of Na$_2$CO$_3$ and Bu$_4$NI catalyzed this reaction in satisfactory yield (Table 1, entry 1). Reaction with reduced catalyst loading (1 mol %) proceeded without a drop in yield (Table 1, entry 2). The combination of Ni(acac)$_2$ and carbene precursor **1** displayed a similar catalytic activity (Table 1, entry 3).[13] In contrast, the use of only Ni(acac)$_2$ as a nickel source proved to be much less reactive (Table 1, entry 4). Essentially, none of the desired cinnamate was obtained in the absence of Bu$_4$NI (Table 1, entry 5). Finally, it is worthy of note that the reaction can also be carried out aerobically (Table 1, entry 6).

With optimized conditions in hand, we next carried out the nickel-catalyzed Heck reaction of a range of aryl halides. It is not surprising that nickelacycle **2** catalyzed the reaction of more reactive aryl iodide (Table 2, entry 1). Both electron-rich and electron-poor aryl bromides can be reacted in the presence of **2**, and corresponding cinnamates produced in good-to-high

Table 2. Nickelacycle 2-Catalyzed Heck Reaction of Aryl Halides[a]
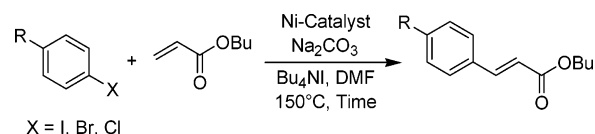
entry	X	Ni-catalyst	R	time (days)	yield (%)[b]
1	I	**2**	H	2	81
2	Br	**2**	H	2	66 (80)[c]
3[d]	Br	**2**	CHO	2	75
4[d]	Br	**2**	CO$_2$Bu	4	57
5	Br	**2**	Me	7	72
6	Cl	**2**	CN	5	65
7[d]	Cl	**2**	CHO	3	60
8	Cl	**2**	COMe	5	60
9	Cl	Ni(acac)$_2$ + **1**	CN	5	71
10[d]	Cl	Ni(acac)$_2$ + **1**	CHO	3	57
11	Cl	Ni(acac)$_2$ + **1**	COMe	5	68
12	Cl	**2**	H	5	15

[a] Reagents: aryl halide (1.0 mmol), butyl acrylate (5.0 mmol), **2** (0.05 mmol), Na$_2$CO$_3$ (3.0 mmol), Bu$_4$NI (3.0 mmol), and DMF (5 mL). [b] Isolated yield, average of two runs. [c] 0.075 mmol of **2** was used. [d] K$_2$CO$_3$ was used instead of Na$_2$CO$_3$.

yields (Table 2, entries 2−5). Activated aryl chlorides were also suitable substrates for the reaction catalyzed by **2**, although yields were moderate (Table 2, entries 6−8). Similar results were obtained in the reaction of aryl chlorides employing the combination of Ni(acac)$_2$ and **1** (Table 2, entries 9−11). In contrast, nonactivated aryl chlorides remain poorly reactive compounds (Table 2, entry 12).

Interestingly, the time-dependent profile of the Heck reaction of 4-bromobenzonitrile employing nickelacycle **2** or Ni(acac)$_2$/**1** was sigmoidal (Figure 3). The product yield increased slowly during the first 48 h and then accelerated sharply.[14] Furthermore, the reaction was completely suppressed by a drop of Hg[15] (Scheme 2), in contrast to Crabtree's results with NHC-derived palladium-pincer complexes.[3c,16] Although the precise reaction mechanism remains to be elucidated, these results suggest a heterogeneous catalytic species could be involved in our system, though the participation of other species cannot be ruled out.[17,18]

Moreover, the catalytic activity of complex **2** in the Suzuki coupling reaction was also probed. Reactions of various aryl bromides and chlorides with phenylboronic acid have been studied utilizing K$_3$PO$_4$ as a base and dioxane as a solvent. The results are summarized in Table 3. With 0.1−1mol % of catalyst loading, both activated (Table 3, entries 1−4) and deactivated (Table 3, entries 5 and 6) aryl bromides successfully reacted, and the desired coupling products were obtained in high yields. Similar yields were obtained with reaction of aryl chlorides using

(13) Ni(acac)$_2$ is more effective than other nickel sources in this reaction. For example, Ni(OAc)$_2$, 48%; NiBr$_2$, 27%; NiCl$_2$, 60%; Ni(cod)$_2$, 49%.

(14) Interestingly, the time-dependent reaction profile for the reaction employing the previously reported Ni(acac)$_2$/NHC catalyst system is also sigmoidal, although the reaction rate is different from **2** or Ni(acac)$_2$/**1**. Detailed studies to reveal the origin of the difference in catalytic activity between two catalyst systems are underway and will be reported in due course.

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(17) Eberhard suggested the possibility of formation of metallic Pd(0) from a PCP-type pincer ligand; see: Eberhard, M. R. *Org. Lett.* **2004**, *6*, 2125.

(18) For the synthesis of a heterogeneous Ni-nanoparticle and its use for Heck reaction of iodobenzenes, see: Houdayer, A.; Schneider, R.; Billaud, D.; Ghanbaja, J.; Lambert, J. *Synth. Met.* **2005**, *151*, 165.
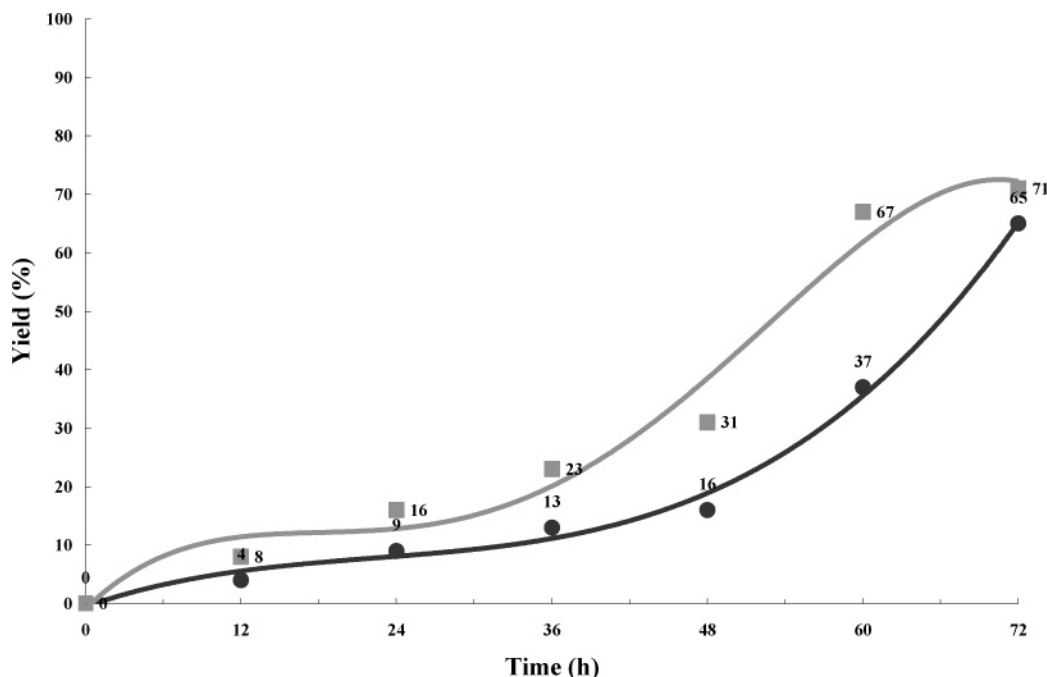
Figure 3. Plot of yield vs time in 5 mol % **2** (●)- or Ni(acac)$_2$/**1** (■)-catalyzed Heck reaction of 4-bromobenzonitrile.

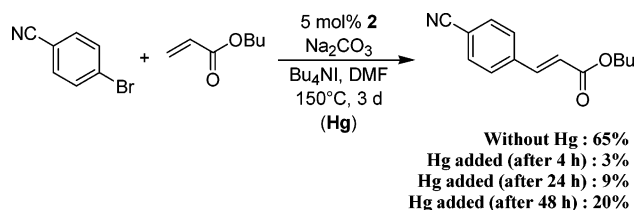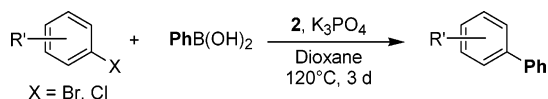**Scheme 2. Hg Drop Test in Nickelacycle 2-Catalyzed Heck Reaction**

5 mol% **2**
Na$_2$CO$_3$
Bu$_4$NI, DMF
150°C, 3 d
(**Hg**)

Without Hg : 65%
Hg added (after 4 h) : 3%
Hg added (after 24 h) : 9%
Hg added (after 48 h) : 20%

Table 3. Nickelacycle 2-Catalyzed Suzuki Coupling Reaction of Aryl Halides[a]

R'—⟨⟩—X + PhB(OH)$_2$ → R'—⟨⟩—Ph

2, K$_3$PO$_4$
Dioxane
120°C, 3 d

X = Br, Cl

entry	X	R'	**2** (mol %)	yield (%)[b]
1	Br	4-CN	1	77
2		4-CN	0.1	76
3		2-CN	1	93
4		4-CO$_2$Et	1	78
5		4-OMe	1	71
6		3-OMe	1	70
7[c]	Cl	4-CN	5	67
8[c]		4-COMe	5	66
9[c]		4-CO$_2$Me	5	68

[a] Reagents: aryl halide (1.0 mmol), PhB(OH)$_2$ (5.0 mmol), **2** (as listed above), K$_3$PO$_4$ (3.0 mmol), and dioxane (5 mL). [b] Isolated yield, average of two runs. [c] 4 days.

5 mol % of complex **2**, albeit with longer reaction time (Table 3, entries 7−9).

In conclusion, we have synthesized a novel nickel-pincer complex **2** and have shown its high catalytic activity in the Heck reaction. Indeed, this complex is an efficient catalyst for the Heck reaction of various aryl halides, including activated aryl chlorides. The method reported here has several appealing features, including easy accessibility to the nickel complex **2** from commercially available chemicals, its air- and moisture-stability, cost-effectiveness, and the unnecessariness of a strictly inert atmosphere during the reaction. Furthermore, in our

preliminary experiments, complex **2** has also shown catalytic activity for the Suzuki coupling reaction of aryl bromides and chlorides. These results further highlight the potential impact of nickel-pincer complexes in organic synthesis. Our current studies therefore focus on preparing various nickel-pincer complexes and applying them to a range of processes.

Experimental Section

General Procedures. All manipulations were carried out under an atmosphere of dry argon with standard Schlenk tube techniques or in a Vac glovebox, unless otherwise noted. Butyl acrylate (Wako), DMF (Wako), and DMSO (Wako) were distilled from 3 Å molecular sieves. Dioxane (Wako) was distilled from benzophenone ketyl. Inorganic bases such as Na$_2$CO$_3$ (Wako), K$_2$CO$_3$ (Wako), and K$_3$PO$_4$ (Wako) were dried with heating under reduced pressure. Ni(OAc)$_2$ (Wako), Ni(acac)$_2$ (Strem), and all other chemicals were used as received. ^{1}H NMR (600 or 400 MHz) and ^{13}C NMR (125 or 100 MHz) spectra were recorded on a JEOL JNM-ECA600 or JNM-AL400 using tetramethylsilane (TMS) as an internal standard. Mass spectra and high-resolution mass spectra were measured on JEOL JMS-DX303 and MS-AX500 instruments, respectively.

Synthesis of Nickel-Pincer Complex 2. A mixture of 2,6-dibromopyridine (6.4 g, 26.7 mmol) and 1-methylimidazole (8.8 g, 106.9 mmol) was heated in a sealed tube at 150 °C for 3 h. The resulting precipitate was collected by filtration, washed with CHCl$_3$ (10 mL × 3) and Et$_2$O (10 mL × 3), and dried in vacuo (7.8 g, 73%) and could be recrystallized from MeOH to give analytically pure **1**.[12] A mixture of thus obtained **1** (1.6 g, 4.0 mmol), Ni(OAc)$_2$ (0.80 g, 4.4 mmol), and Bu$_4$NBr (1.3 g, 4.0 mmol) in DMSO (20 mL) was stirred at 50 °C for 12 h and then 160 °C for 1 h. After cooling to room temperature, the resulting precipitate was collected by filtration, washed with CH$_3$CN (10 mL × 3) and CHCl$_3$ (10 mL × 3), and dried in vacuo (1.2 g, 63%) and could be recrystallized from MeOH. Mp: >300 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 4.00 (6H, s), 7.57 (2H, s), 7.85 (2H, d, $J =$ 8.4 Hz), 8.31 (2H, s), 8.45 (1H, t, $J =$ 8.4 Hz).[19] Anal. Calcd for

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(19) A satisfactory ^{13}C NMR spectrum of complex **2** could not be obtained due to its insolubility in various deuterated solvents.

$C_{13}H_{15}Br_2N_5Ni$: C, 34.11; H, 2.86; N, 15.30. Found: C, 34.01; H, 2.95; N, 15.12.

General Procedure for Heck Reaction. A mixture of an aryl halide (1.0 mmol), butyl acrylate (0.64 g, 5.0 mmol), Ni-pincer complex **2** (22.9 mg, 0.05 mmol), a base (3.0 mmol), and tetrabutylammonium iodide (1.1 g, 3.0 mmol) in DMF (5 mL) was allowed to react in a sealed tube at 150 °C. The reaction mixture was treated with H_2O (15 mL) followed by extraction with Et_2O (15 mL × 3). The combined extracts were washed with saturated aqueous NaCl (15 mL × 3) and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude material was purified by SiO_2 column chromatography using hexane−AcOEt as an eluent to give the desired cinnamate.

General Procedure for Suzuki Coupling Reaction. A mixture of an aryl halide (1.0 mmol), phenylboronic acid (0.61 g, 5.0 mmol), Ni-pincer complex **2** (22.9 mg, 0.05 mmol), and K_3PO_4 (0.64 g, 3.0 mmol) in dioxane (5 mL) was allowed to react in a sealed tube at 120 °C. The reaction mixture was treated with H_2O (15 mL) followed by extraction with Et_2O (15 mL × 3). The combined extracts were washed with saturated aqueous NaCl (15 mL × 3) and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude material was purified by SiO_2 column chromatography using hexane−AcOEt as an eluent to give the desired product.

Supporting Information Available: X-ray crystallographic data for complex **2** (CIF) and characterization data of coupling products (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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