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ORIGINAL PAPER

Ferrocene-tagged *N*-heterocyclic carbene-Pd complex for Suzuki–Miyaura coupling

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Abstract We demonstrate that the ferrocene-tagged *N*-heterocyclic carbene (NHC)-Pd(II) complex can act as an efficient heterogeneous catalyst for Suzuki–Miyaura cross-coupling in dimethylformamide (DMF)-water. This complex was found to be an active and efficient catalyst for coupling of aryl iodides, bromides, and even less reactive chlorides with boronic acids and pinacol ester of boronic acid.

Keywords Suzuki reaction · Boronic acid pinacol ester · *N*-heterocyclic carbene · Aerobic condition

Introduction

Transition-metal complexes of *N*-heterocyclic carbenes (NHCs) in cross-coupling reactions have made revolutionary changes in synthetic chemistry [1–14]. As compared with phosphine ligands, NHCs bind through stronger bonds with most of the metals, avoiding the necessity of excess ligand in catalytic reaction [15, 16]. Hence, they play a dual role of catalyst as well as ligand and overcome limitations raised due to use of phosphine ligands in catalytic reactions, viz. oxidation of phosphines to phosphine oxides, formation of stable phosphido-bridged catalytically inactive dimers, and also cleavage of P–C bond causing degradation of the ligand and thus termination of the catalytic cycle [17–19]. The difficulties involved in removal of these byproducts and the high price of phosphine ligands are other drawbacks that have spurned enormous interest in the discovery of new NHCs as superior alternatives to phosphine ligands.

Ferrocene-containing compounds have wide applications in the fields of catalysis, material science, and coordination chemistry [20–23]. Atkinson et al. have stated that "the ferrocene moiety has played a significant role as a backbone or a substituent in ancillary ligands in coordination chemistry, due to (1) the specific and unique geometries that the ferrocene provides and (2) its electronic (redox) properties, whereby the possibility of switching the redox state of the ferrocene backbone gives access to potential control of reactivity at a metal center" [23]. Hence, synthetic chemists have focused their attention on ferrocene-tagged NHC metal complexes of W(0), Pd(II), and Hg(II) containing a monodentate imidazolylidene ligand [24]. These ferrocene-tagged NHCs have been prepared in situ by deprotonation of the imidazolium precursor, viz. 1-(ferrocenylmethyl)-3-methylimidazolium iodide [24, 25]. There are also reports on synthesis of cyclopalladated ferrocenylimine palladium catalyst and its activity in cross-coupling reactions [26–30]. The first example of a ferrocene-based ligand containing two NHCs was reported by Coleman et al. [31], and later on NHCs possessing one or two 3,4-dimethylphosphaferrocenyl substituents were prepared by Ganter's group [32].

Impressed by these and in continuation of our interest in coupling reactions [33, 34], we wish to explore ferrocene-tagged NHC-Pd complex as an efficient heterogeneous catalyst for Suzuki–Miyaura coupling (Scheme 1), the most celebrated tool for constructing C–C bond [35, 36] which was recognized with the 2010 Nobel Prize in Chemistry.

Electronic supplementary material The online version of this article (doi:10.1007/s00706-013-0970-2) contains supplementary material, which is available to authorized users.

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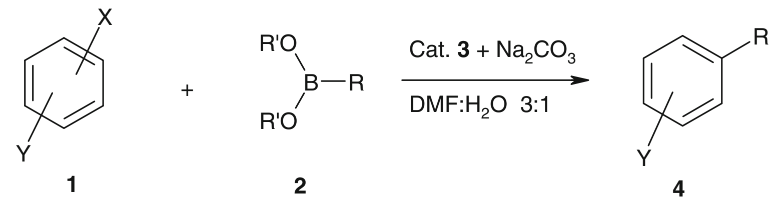
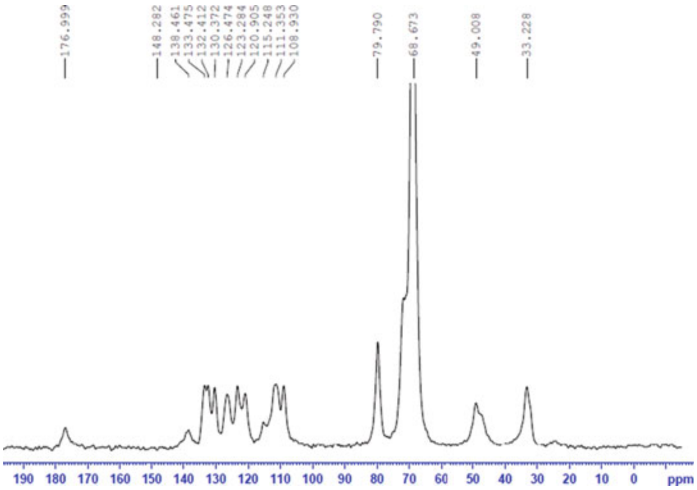
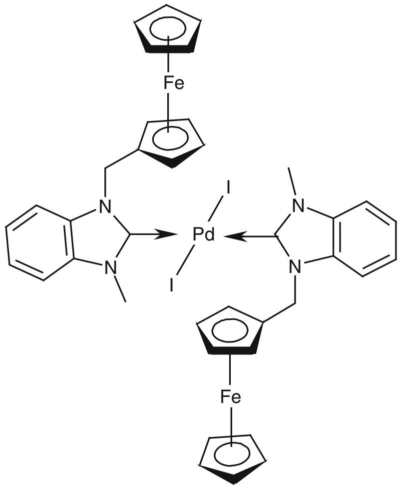
Scheme 1



X = I, Br, Cl

Y = $COCH_3$, OCH_3, CN, CHO, NO_2, CH_3, NH_2





3

Fig. 1 Solid-state ^{13}C NMR of ferrocene-tagged NHC-Pd complex

Results and discussion

Initially, ferrocene-tagged NHC-Pd complex **3** (Fig. 1) was synthesized by using reported procedure from ferrocene and benzimidazole [25]. The Fourier-transform infrared (FT-IR) result for the synthesized complex **3** is in accordance with the literature [25]. Due to insufficient solubility of Pd complex in dimethyl sulfoxide (DMSO), we further characterized the complex by solid-state nuclear magnetic resonance (NMR) (Fig. 1), as a confirmation and supporting tool. The solid-state NMR of **3** exhibits signals at $\delta = 33.2$ and 49.0 ppm for *N*-methyl and methylene carbon, respectively. Cyclopentadiene (Cp) ring carbons were centered at 68.6 ppm, while the *ipso*-carbon of the substituted Cp ring appeared at 79.7 ppm. Aromatic carbons of benzimidazole moiety were observed in the region of 108.9–138.4 ppm, and –CH_2 of NHC appeared at 176.9 ppm.

The crystalline morphology with fibrous crystal growth was confirmed from scanning electron microscopy (SEM) micrograph, displayed in Fig. 2. Thermal gravimetric analysis (TGA) carried out in nitrogen atmosphere over the temperature range of 20–1,000 °C with heating rate of 10 °C/min showed that the catalyst is stable up to 200 °C, after which slow decomposition starts and continues until

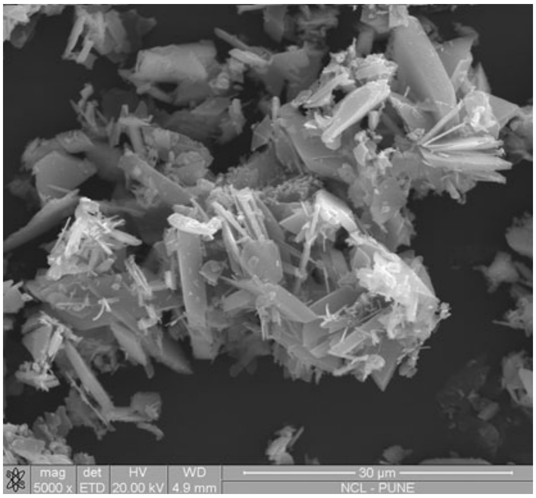


Fig. 2 SEM image of ferrocene-tagged NHC-Pd complex

Table 1 Effect of solvent, base, and amount of catalyst on Suzuki–Miyaura cross-coupling[a]

Entry	Catalyst/mol%	Solvent	Base	Time/h	Yield/%[b]
1	2	Toluene	Na_2CO_3	7	63
2	2	Toluene	K_3PO_4	7	60
3	2	Toluene	K_2CO_3	7	56
4	2	Acetonitrile	Na_2CO_3	8	54
5	2	Acetonitrile	K_3PO_4	9	52
6	2	Acetonitrile	K_2CO_3	9	50
7	2	Dioxane	Na_2CO_3	6	65
8	2	Dioxane	K_3PO_4	6	65
9	2	Dioxane	K_2CO_3	6	61
10	2	THF	Na_2CO_3	8	68
11	2	THF	K_3PO_4	7	60
12	2	THF	K_2CO_3	8	58
13	2	Water	Na_2CO_3	10	50
14	2	Water	K_3PO_4	10	45
15	2	Water	K_2CO_3	10	40
16	2	DMF	Na_2CO_3	3	75
17	2	DMF	K_3PO_4	3	71
18	2	DMF	K_2CO_3	3	65
19	2	DMF:water	Na_2CO_3	2	88
20	2	DMF:water	K_3PO_4	2.5	78
21	2	DMF:water	K_2CO_3	2.5	75
22	2.5	DMF:water	Na_2CO_3	2	89
23	1	DMF:water	Na_2CO_3	3	72
24	0.5	DMF:water	Na_2CO_3	4.5	58

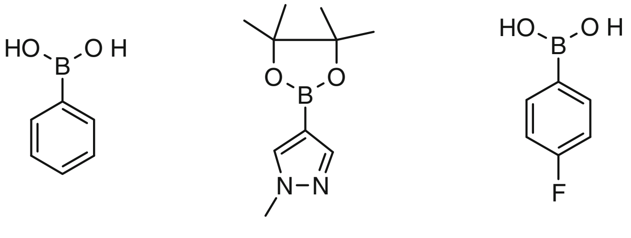
[a] Reaction conditions: bromobenzene (1 mmol), phenylboronic acid (1.2 mmol), base (3 mmol), 80 °C; for entries 19–24, DMF:water: 3:1 (v/v) is used

[b] Isolated yield

THF, tetrahydrofuran

850 °C. Finally, the residue of 22.71 % remaining at 1,000 °C is due to the elemental forms of Fe and Pd, since the possibility of alloy formation is ruled out due to the very high melting points of both Fe and Pd. This helped us to quantify the amount of Fe and Pd in **3**, which was calculated to be 11.63 and 11.08 %, respectively. CHNS elemental analysis of the catalyst showed 43.01 % C, 3.5 % H, and 4.8 % N. Thus, from these calculations, the content of iodine emerges as 25.98 %. All these elemental compositions agree with the molecular formula of the catalyst, i.e., $C_{38}H_{36}Fe_2I_2N_4Pd$.

We next shifted our attention towards screening for the best condition for Suzuki reaction of bromobenzene and phenylboronic acid by varying (1) solvent composition, (2) nature of the base, and (3) catalyst loading. The results of optimization are summarized in Table 1. The examination of solvent/base combination revealed that use of DMF/water with 3 mmol Na_2CO_3 is the best option, resulting in 88 % yield of the product.



5 **6** **7**

Fig. 3 Diversity of boronic acids

Various solvents, viz. toluene, acetonitrile, dioxane, tetrahydrofuran (THF), DMF, and water, were screened for Suzuki reaction, with observed yield of the desired product of 40–68 % (Table 1, entries 1–16). However, when DMF was employed, the yield was increased to 75 % (Table 1, entry 16). Water plays an important role in improving the reactivity of Suzuki reaction [37]. Hence, we tried the DMF:water system and observed that the yield of the desired product was boosted to 88 % (Table 1, entry 19). After further examination of the catalyst loading, a good result was obtained by using 2 mol % of the catalyst (Table 1, entries 19, 22–24), and we found the best condition for Suzuki reaction as mentioned in entry 19 (Table 1).

After optimization of the reaction conditions, to delineate this approach, particularly in regard to library construction, this methodology was evaluated by using aryl halides and different boronic acids (Fig. 3). A wide range of aryl halides, possessing electron-rich or electron-deficient substituents, worked well with arylboronic acids. In Suzuki coupling, activation of aryl chloride substrates has been limited as compared with activation of aryl bromides and iodides [38]. Recently, special emphasis on Suzuki coupling of aryl chlorides with boronic acid has been reported by Sau et al. [38] and Terashima et al. [39]. It is noteworthy that iodo-, bromo-, as well as less reactive chloro-substituted aromatic halides undergo smooth coupling with boronic acid under optimized reaction conditions. Coupling of heteroarylboronic acid pinacol ester (Table 2, entries g, o) with aryl halides was also performed smoothly under the optimized reaction conditions. We next examined the performance of the catalyst in the coupling of dihalide, viz. 1-bromo-4-iodobenzene with phenylboronic acid (Table 2, entry s) and found that the Suzuki–Miyaura coupling worked equally well to produce terphenyl.

To evaluate the role of the catalyst, viz. homogeneous/heterogeneous, hot filtration test was carried out by using optimized reaction conditions for coupling of bromobenzene

Table 2 Ferrocene-tagged NHC-Pd complex-catalyzed Suzuki–Miyaura cross-coupling[a]

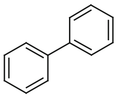
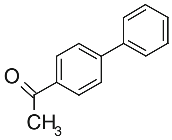
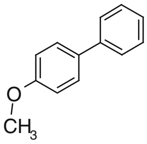
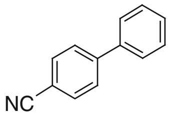
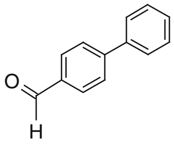
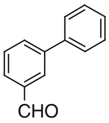
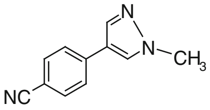
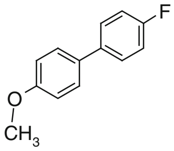
Entry	Product **4**	Boronic acid	Time/h	Yield/%[b]
a		**5**	2	88
b		**5**	2.5	93
c		**5**	2.5	84
d		**5**	2	93
e		**5**	2.5	82
f		**5**	3.5	78
g		**6**	3	78
h		**7**	2.5	79

Table 2 continued

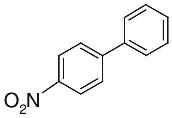
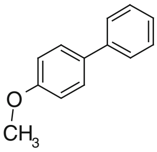
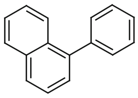
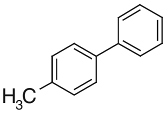
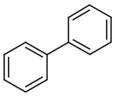
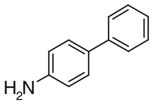
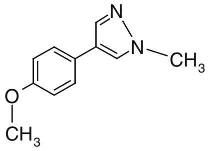
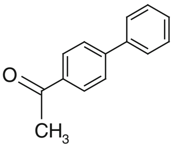
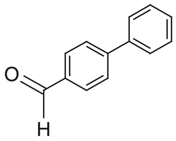
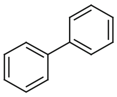
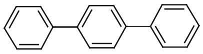
Entry	Product **4**	Boronic acid	Time/h	Yield/%[b]
i		**5**	3	85
j		**5**	2	81
k		**5**	2.5	76
l		**5**	2	78
m		**5**	2	83
n		**5**	2.5	75
o		**6**	2.5	79
p		**5**	4	69

Table 2 continued

Entry	Product **4**	Boronic acid	Time/h	Yield/%[b]
q		**5**	4	66
r		**5**	4	71
s		**5**	3.5	78

[a] Reaction conditions: aryl halide (1 mmol), boronic acid (1.2 mmol), Na_2CO_3 (3 mmol), Pd-NHC complex (2 mol%), DMF:water 3:1 (v/v), 80 °C; for entries a–h, i–o, p–r corresponding aryl bromides, iodide, and chloride used, respectively

[b] Isolated yield

with phenylboronic acid. After 50 % of the cross-coupling reaction was completed [30 min, gas chromatography (GC)], the catalyst was filtered off and the reaction was continued further. However, no further progress in the reaction was observed even after a prolonged reaction time (3 h, GC). These results revealed that Pd is not being leached out from **3** during the course of reaction, thus **3** acts as a heterogeneous catalyst in the present transformation.

Conclusions

We explored a ferrocene-tagged NHC-Pd complex as an efficient heterogeneous catalyst for Suzuki–Miyaura cross-coupling in DMF/water medium at 80 °C. All reactions were carried out in air atmosphere, illustrating the property of catalyst **3** as air and moisture stable. In the presence of NHC-Pd catalyst aryl bromides, iodides, and even less reactive aryl chlorides could be coupled with a variety of arylboronic acids to form biaryls in moderate to excellent yields. The protocol is also applicable to pinacol ester of boronic acid.

Experimental

IR spectra were recorded on a PerkinElmer FT-IR 783 spectrophotometer. NMR spectra were recorded on a Bruker AC-300 spectrometer in $CDCl_3$ using tetramethylsilane as internal standard. SEM analysis was recorded on Philips XL 30. Thermal gravimetric analysis (TGA) curves were obtained by using an STA 1500 instrument in the presence of static air at linear heating rate of 10 °C/min from 20 to 1,000 °C. C, H, N analysis of the complexes was obtained using a Carlo ERBA (Italy) model EA 1108 analyzer.

Typical Procedure

To a 25-cm^3 round-bottom flask, a mixture of aryl halide (1 mmol), arylboronic acid (1.2 mmol), Pd-NHC (2 mol %), and Na_2CO_3 (3 mmol) was added in DMF:water (3:1 cm^3). The reaction was stirred at 80 °C and monitored by thin-layer chromatography (TLC). After completion of reaction, the mixture was cooled and content of the flask was diluted with water and extracted with ethyl acetate (3 × 10 cm^3). The organic layer obtained was dried over anhydrous Na_2SO_4, filtered, and concentrated to furnish the desired biaryl compound, which was then purified by column chromatography (5 % ethyl acetate). All synthesized products were confirmed from physical constant [40–43], IR, and ^1H and ^{13}C NMR.

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