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N-Heterocyclic Carbene Adducts of Cyclopalladated Ferrocenylpyridine Complex: Synthesis, Structural Characterization and Application in Heck Reaction

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Palladium-catalyzed Heck reaction has become an extremely powerful method in organic synthesis for the formation of carbon-carbon bond.[1,2] A number of reports have shown that phosphine based Pd complexes are effective catalysts for this transformation.[3] However, these catalysts are often air sensitive, toxic and can be expensive. Thus, the drive to develop new phosphine-free, inexpensive and stable catalysts is still very much a current topic of interest. As an alternative, *N*-heterocyclic carbenes (NHCs) have become a paradigmatically new generation of strong σ-donor ligand[4-6] and widely used in palladium-catalyzed coupling reactions such as the Heck reaction.[7-10] Since the first report on the use of palladacycles for the Heck reaction by Herrmann and co-workers in 1995,[11] a wide variety of known and new palladacycles have been successfully used in organic synthesis.[12,13] Among them, *N*-heterocyclic carbene adducts combine the stability induced by the presence of a palladacycle framework with the highly donating and sterically demanding NHCs and were also demonstrated to be highly active.[14-17]

We have also found phosphine adducts of palladacycle are very efficient for the Heck reaction.[18] Furthermore, we have recently synthesized the carbene adducts of cyclopalladated ferrocenylpyridine and found these complexes exhibited high activity in Suzuki and amination.[19] These adducts were far more active than the corresponding dimeric palladacycles. As a continuation of our interest in palladium-catalyzed coupling reactions,[18-21] we prepared two new carbene adducts of palladacycle **1-2** *in situ* from the reaction of the chloride-bridged palladacyclic dimer **A** and 1,3-bis(4-bromophenyl) imidazolium chloride or 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride (IMesHCl) (Scheme 1) and examined their catalytic activity in Heck reaction. Here, we report that **2** is an extremely effective catalyst for the Heck reaction.

Complexes **1-2** are air- and moisture-stable, both in solid state and in solution. They are very soluble in chloroform, dichloromethane and acetone, but insoluble in petroleum ether and *n*-hexane. They were fully characterized by elemental analysis, IR, ESI-MS, ^{1}H and C^{13} NMR. These spectra

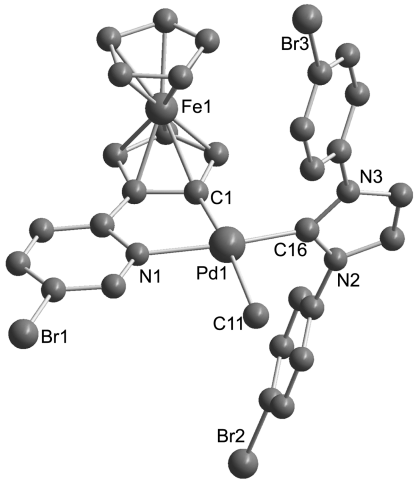
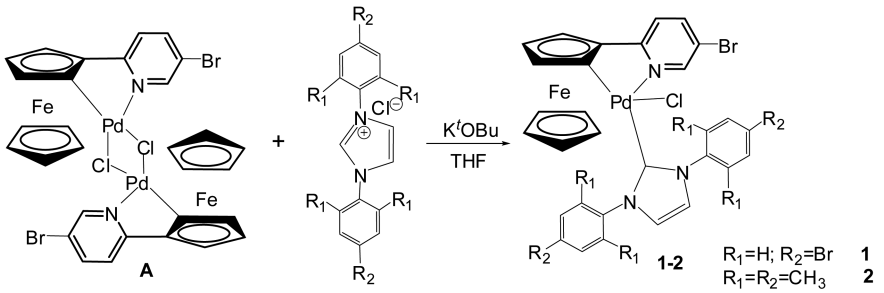


Figure 1. Molecular structure of complex **1**. Displacement parameters are drawn at the 50% level. H atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Pd(1)-C(1) 1.961(13), Pd(1)-C(16) 1.942(13), Pd(1)-N(1) 2.097(10), Pd(1)-Cl(1) 2.396(6), and C(1)-Pd(1)-Cl(1) 173.7(4), C(16)-Pd(1)-N(1) 172.3(5), C(16)-Pd(1)-C(1) 91.4(6), C(1)-Pd(1)-N(1) 81.0(5).



Scheme 1. Synthesis of **1-2**.

were well consistent with the title complexes. The ^{1}H NMR spectra of these complexes showed only one set of signals in a symmetrical surrounding indicating the exclusive formation of one isomer. Moreover, the molecular structure of **1** has been ascertained by means of X-ray studies. The molecule of **1** together with selected bond distances and angles is shown in Figure 1. The Pd atom is in a slightly distorted square-planar environment bonded to the C atom of NHC, the chlorine atom, the nitrogen atom and the C atom of the ferrocenyl moiety. The Pd-C_{carb} [1.961(13) Å] bond length of complex **1** is similar to those of related carbene adducts,[19,22] the imidazole ring plane of NHC is almost perpendicular to the square plane formed by the Pd(II) center (dihedral angle of 91.9°). In this type of arrangement the *N*-substituents of NHC reduce the steric interaction with palladacyclic ligand.

Initially, the Heck reaction of 4-bromotoluene with acrylic acid ethyl ester was carried out with various bases and solvents in the presence of 0.1 mol % of **2**. The results from this study are summarized in Table 1. After screening a variety of bases (entries 1-8), KOAc was found to be the most effective base (95% yield, entry 8) and K_3PO_4, Et_3N as well as NaOAc showed comparable results (entries 5-7). Other solvents such as toluene (at 100 °C), dioxane (at 100 °C), DMF (at 140 °C) and DMSO (at 140 °C) afforded the coupled product in 58%, 36%, 81% and 76% yields, respectively (entries 9-12). The relative catalytic activity of **1** and **A** was examined in the presence of KOAc as base in dimethylacetamide (DMA). **1** also displayed moderate efficiency, producing the coupled product in 73% yield (entry, 13). In comparison, the dimeric complex **A** generated the product in low yield under the same reaction conditions (52%, entry 14) and the yield was improved to 84% by the addition of IMesHCl suggesting that carbene ligand IMes participated in the catalytic cycles (entry 15).

The Heck reactions of a variety of aryl halides with acrylic acid ethyl ester catalyzed by **2** were carried out under the optimized reaction conditions (KOAc, DMA, 150 °C). The results are shown in Table 2. The catalyst system was very effective for the coupling of bromobenzene and 1-bromonaphthalene giving the coupled products in 97-98% yields (entries 1-2). The coupled products were isolated in good yields for deactivated aryl bromide substrates with this system (entries 3-5). For example, *ortho*-substituents were tolerated provided the products in 88-91% isolated yields. For activated aryl bromides, it was not surprising that excellent yields were obtained with a catalytic loading as low as 0.05 mol % (entries 6-8). In addition, heterocyclic bromides were found to be efficient coupling partners in this system (entries 9-10). In the case of 4-chlorotoluene, **2** was almost inactive under the same conditions (entry 11). Increasing catalyst loading to 1 mol % only gave 14% yield (entry 12). Furthermore, the addition of NBu_4Br cocatalyst, which was reported to be able to increase the activity of most catalytic systems,[17,23,24] did not give better results for the present catalytic system (entries 12-13). For activated chlorides such as 4-chloronitrobenzene and 4-chlorobenzonitrile, the yields of the coupled products could be reached 85% by using 1 mol % of **2** (entries 14-15). Finally, it was noteworthy that all of these reactions studied showed high regioselectivity for *trans*-coupling and *cis*-product was not found.

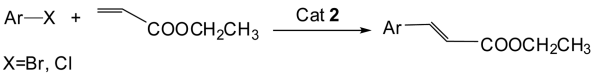
In conclusion, two carbene adducts of cyclopalladated ferrocenylpyridine **1-2** have been synthesized and characterized. Their catalytic activity was evaluated in Heck reaction of aryl halide. **2** was found to be very efficient for this reaction.

Table 1. Influence of base, solvent and catalyst on the Heck reaction of 4-bromotoluene with acrylic acid ethyl ester[a]

Entry	Catalyst (mol %)	Base	Solvent	Yield (%)[b]
1	**2**(0.1)	Na_2CO_3	DMA	68
2	**2**(0.1)	K_2CO_3	DMA	75
3	**2**(0.1)	NaOH	DMA	71
4	**2**(0.1)	Na^{t}OBu	DMA	63
5	**2**(0.1)	K_3PO_4	DMA	92
6	**2**(0.1)	Et_3N	DMA	89
7	**2**(0.1)	NaOAc	DMA	93
8	**2**(0.1)	KOAc	DMA	95
9	**2**(0.1)	KOAc	toluene	58
10	**2**(0.1)	KOAc	dioxane	36
11	**2**(0.1)	KOAc	DMF	81
12	**2**(0.1)	KOAc	DMSO	76
13	**1**(0.1)	KOAc	DMA	73
14	**A**(0.05)	KOAc	DMA	52
15	**A**/IMesHCl (0.05/0.15)	KOAc	DMA	84

[a]Reaction conditions: 4-bromotoluene (1.0 mmol), acrylic acid ethyl ester (1.5 mmol), base (1.5 mmol), DMA (3 mL), 150 °C, 12 h. [b]Isolated yields (average of two experiments).

Table 2. Heck reaction of aryl halide with acrylic acid ethyl ester catalyzed by **2**[a]



Entry	Ar	X	Catalyst (mol %)	Yield (%)[b]
1	Ph	Br	0.1	97
2	1-$C_{10}H_7$	Br	0.1	98
3	*p*-$OMeC_6H_4$	Br	0.1	93
4	*o*-MeC_6H_4	Br	0.1	91
5	*o*-$OMeC_6H_4$	Br	0.1	90
6	*p*-$NO_2C_6H_4$	Br	0.1	99
7	*p*-$NO_2C_6H_4$	Br	0.05	97
8	*p*-CNC_6H_4	Br	0.05	96
9	pyridin-2-yl	Br	0.1	89
10	thiophen-2-yl	Br	0.1	83
11	*p*-MeC_6H_4	Cl	0.1	trace
12[c]	*p*-MeC_6H_4	Cl	1	14
13[c]	Ph	Cl	1	19
14[c]	*p*-$NO_2C_6H_4$	Cl	1	85
15[c]	*p*-CNC_6H_4	Cl	1	81

[a]Reaction conditions: aryl halide (1.0 mmol), acrylic acid ethyl ester (1.5 mmol), KOAc (1.5 mmol), DMA (3 mL), 150 °C, 12 h. [b]Isolated yields (average of two experiments). [c]NBu_4Br (1.0 mmol).

Experimental Section

Materials and Measurement. The chloride-bridged pall-

adacyclic dimer **A** was prepared according to published procedure.[25] All other chemicals were used as purchased. Elemental analyses were determined with a Thermo Flash EA 1112 elemental analyzer. IR spectra were collected on a Bruker VECTOR22 spectrophotometer using KBr pellets. NMR spectra were recorded on a Bruker DPX-400 spectrometer in $CDCl_3$ with TMS as an internal standard. Mass spectra were measured on a LC-MSD-Trap-XCT instrument. Crystallographic data were collected on a Bruker SMART APEX-II CCD diffractometer. CCDC reference number 847982 for **1**. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

General Procedure for the Synthesis of Carbene Adducts of Cyclopalladated Ferrocenylpyridine 1-2. A Schlenk tube was charged with the chloride-bridged palladacyclic dimer (0.1 mmol), the corresponding imidazolium salt (0.25 mmol) and K^{t}OBu (0.3 mmol) under nitrogen. Dry THF was added by a cannula and stirred at room temperature for 2 hours. The product was separated by passing through a short silica gel column with CH_2Cl_2 as eluent, the second band was collected and afforded the corresponding carbene adduct of cyclopalladated ferrocenylpyridine complex **1-2**.

[PdCl{[(η^5-C_5H_5)]Fe[(η^5-C_5H_3)-NC_5H_3-Br]}($C_3N_2H_2$)-(C_6H_4-Br)$_2$] (1): Red solid, yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.12 (s, 1H, py), 8.38 (d, J = 8.4 Hz, 2H, Ar), 7.83 (d, J = 8.4 Hz, 2H, Ar), 7.77 (d, J = 8.4 Hz, 2H, Ar), 7.67 (d, J = 8.4 Hz, 1H, py), 7.41-7.49 (m, 4H, NCHCHN+py), 6.97 (d, J = 8.4 Hz, 1H, py), 4.40 (s, 1H, C_5H_3), 4.08 (s, 1H, C_5H_3), 3.45 (s, 5H, C_5H_5), 3.25 (s, 1H, C_5H_3). ^{13}C NMR (100 MHz, $CDCl_3$): 172.2, 164.7, 150.9, 140.6, 139.4, 135.0, 134.8, 132.9, 132.4, 130.7, 128.4, 128.2, 127.5, 126.9, 123.3, 122.9, 122.8, 122.6, 118.3, 114.6, 94.5, 87.4, 72.9, 69.9, 68.7, 63.2. MS-ESI$^+$: *m/z* 821.8 [M$^+$-Cl]. IR (KBr, cm^{-1}): 2920, 1594, 1490, 1422, 1393, 1376, 1339, 1307, 1278, 1103, 1072, 1030, 1012, 999, 943, 828, 820, 742, 695. Anal. Calcd for $C_{30}H_{21}Br_3ClFeN_3Pd$: C, 41.85; H, 2.46; N, 4.88. Found: C, 41.97; H, 2.23; N 4.55.

[PdCl{[(η^5-C_5H_5)]Fe[(η^5-C_5H_3)-NC_5H_3-Br]}($C_3N_2H_2$)-(C_6H_2-3CH_3)$_2$] (2): Red solid, yield 88%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.16 (s, 1H, py), 7.49 (d, J = 8.4 Hz, 1H, py), 7.03-7.14 (m, 5H, NCHCHN+Ar), 6.93 (s, 1H, Ar), 6.87 (d, J = 6.8 Hz, 1H, py), 4.50 (s, 1H, C_5H_3), 4.24 (s, 1H, C_5H_3), 3.94 (s, 1H, C_5H_3), 3.53 (s, 5H, C_5H_5), 2.71 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 1.96 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 171.9, 164.8, 150.9, 140.2, 140.1, 139.1, 138.6, 137.7, 136.9, 136.2, 134.9, 134.8, 134.6, 130.2, 129.6, 128.7, 124.2, 123.7, 117.4, 113.6, 95.1, 87.0, 72.5, 70.6, 68.6, 63.3, 27.9, 22.3, 21.1, 20.8, 19.8, 19.5. MS-ESI$^+$: *m/z* 750.0 [M$^+$-Cl]. IR (KBr, cm^{-1}): 2919, 1593, 1493, 1401, 1377, 1327, 1307, 1269, 1224, 1105, 1026, 999, 925, 908, 850, 828, 815, 737, 701. Anal. Calcd for $C_{36}H_{35}BrClFeN_3Pd$: C, 54.92; H, 4.48; N, 5.34. Found: C, 55.16; H, 4.34; N 5.58.

General Procedure for the Heck Reaction. In a Schlenk tube, a mixture of the prescribed amount of catalyst (**A** or **1** or **2**), aryl halide (1.0 mmol), acrylic acid ethyl ester (1.5 mmol) and the selected base (1.5 mmol) in solution (3 mL) was evacuated and charged with nitrogen. The reaction mixture was then placed in an oil bath and heated at 150 °C for 12 h, cooled and quenched with water. The organic layer was separated and the aqueous layer was extracted with ethylacetate. The solvent was evaporated and the pure products were isolated by flash chromatography on silica gel and identified by comparing melting points or ^{1}H NMR spectra.

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