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Efficient N-heterocyclic carbene palladium(II) catalysts for carbonylative Suzuki-Miyaura coupling reactions leading to aryl ketones and diketones

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ABSTRACT

New N, N'-substituted imidazolium salts (L1 and L2) and their corresponding diiodopyridinepalladium(II) complexes (C1 and C2) were successfully synthesized and characterized. Reactions of palladium iodide with the newly synthesized N, N'-substituted imidazolium iodides in pyridine afforded the corresponding new palladium-N-heterocyclic carbene pyridine complexes in high yields. The new palladium(II) complex C1 was characterized by single crystal X-ray diffraction analysis. The Pd(II) ion is bonded to the nitrogen atom of the pyridine, the carbon atom of the NHC carbene ligand and two trans iodides resulting in distorted square planar geometry. The two Pd-NHC-Py complexes C1 and C2 displayed higher catalytic activity in the carbonylative Suzuki-Miyaura coupling reactions with much lower catalyst loading as compared to the catalytic systems reported in the literature.

Keywords: Pd-NHC-Py complex, carbonylative Suzuki, diiodides, diboronic acid, diarylketone.

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1. Introduction

Biaryl ketones are valuable structural moieties present in natural products, pharmaceuticals, cosmetics and agrochemicals [1-3]. The carbonylative cross coupling reactions of various organometallic reagents with aryl electrophiles [4-7] and the Friedel-Crafts acylation of acyl halides with aromatic compounds [1, 8] represent the common approaches for the synthesis of biaryl ketones. Another attractive method for the synthesis of biaryl ketones is the palladium catalyzed carbonylative Suzuki–Miyaura coupling reaction of aryl halides with aryl boronic acids, utilizing carbon monoxide as the carbon source. Several palladium catalysts have been tested in this regard. However, high catalyst loading, high CO pressure, long reaction time or the need to handle air and moisture sensitive phosphines were some of the drawbacks [9-16].

Recently, much attention has been paid to the development of N-heterocyclic carbene metal complexes and remarkable advances have been made especially on their applications as organometallic catalysts [17-23]. This was attributed to the ability of N-heterocyclic carbene ligands to provide highly active and stable metal complexes for various catalytic applications. The highly sigma donating property of NHC ligands prevents the formation of inactive palladium black during the catalytic reactions [17, 20].

We have previously reported the synthesis and catalytic activities of new palladium(II)bis(oxazoline) complexes [24-26] and recently new triazole-derived NHC-palladium(II) complexes [23]. In the present work, we report the synthesis and characterization of two new mixed ligand diiodo-palladium-carbene pyridine (I₂-Pd-NHC-Py₂) complexes (C1 and C2). These palladium(II) complexes were found to be active catalysts in the carbonylative Suzuki-Miyaura coupling reactions of aryl iodides and aryl diiodides with arylboronic acids and diboronic acids. We also report the synthesis of the new compound, 4,4'-(benzene-1,4 diyldicarbonyl)dibenzonitrile (**6ak**), via the carbonylative Suzuki-Miyaura coupling reaction of 1,4-diiodobenzene with 4-cyanophenylboronic acid using the new I₂-Pd-NHC-Py complex C1 as a catalyst.

2. Experimental

2.1. General

Materials for the synthesis of the N-heterocyclic carbene ligand pre-cursors and palladium-N-heterocyclic carbene complexes were purchased from Sigma Aldrich and used as received.

All solvents (reagent grade) used in the synthesis were distilled and dried under molecular sieves. The products were purified either using flash column chromatography (packed with 60 F Silica gel from Fluka Chemie AG, Buchs, Switzerland) or by washing with the appropriate solvent.

¹H and ¹³C NMR spectral data were obtained using 500 MHz NMR machine (Joel 1500 model). IR spectra were recorded in wave numbers (cm⁻¹) using FT-IR spectrometer (Perkin-Elmer 16F model). Elemental analysis was performed on Perkin Elmer Series 11 (CHNS/O) Analyzer 2400. Merck 60 F_{254} silica gel plates (250 µm layer thickness) were used for thinlayer chromatography (TLC) analysis. A Varian Saturn 2000 GC-MS machine (30 m capillary column) was used to analyze the products. Agilent 6890 gas chromatography (GC) was used to monitor the reactions and analyze the products.

2.2 Synthesis of 5-(4-methoxyphenyl)-1-methyl-1H-imidazole (1) and 4-(1-methyl-1Himidazol-5-yl)benzonitrile (2)

5-Bromo-1-methyl-1*H*-imidazole (0.50 mmol), $Pd(PPh_3)_2Cl_2$ (0.025 mmol, 5.0 mol%), K_2CO_3 (1.0 mmol, 2.0 mol equivalent), DMF (2.0 mL), distilled water (2.0 mL) and the corresponding phenylboronic acid (0.60 mmol), were added in a 10 mL round bottom flask. The mixture was stirred at 90 °C for 24 h. After completion of the reaction, the mixture was cooled down to room temperature and extracted 3 times with ethyl acetate. The combined ethyl acetate extract was dried using anhydrous MgSO₄. The solvent was removed under reduced pressure and the product was purified by silica gel column chromatography using hexane-ethyl acetate (1:1) followed by 7 % methanol in ethyl acetate as an eluent.

2.2.1 5-(4-Methoxyphenyl)-1-methyl-1H-imidazole (1)

Yellow solid; isolated yield (83%); ¹H NMR (500 MHz, CDCl₃) δ (ppm): 7.48 (s, 1H, C-*H*-arom), 7.30 (d, 2H, *J*=8.8 *Hz*, C-*H* arom), 7.03 (s, 1H, C-*H*-arom), 6.96 (d, 2H, *J*=8.5 *Hz*, C-*H* arom), 3.84 (s, 3H, C*H*₃), 3.62 (s, 3H, C*H*₃). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 32.20, 55.20, 114.03, 122.06, 127.39, 129.54, 129.78, 133.07, 138.47, 159.28 (*C*- arom); IR (*v*, *cm*⁻¹): 3084, 2947, 1899, 1720, 1611, 1552,1491, 1234, 1116, 1023; GC-MS m/z: 188 (M⁺¹). Anal. Calc. for C₁₁H₁₂N₂O (188): C, 70.19; H, 6.43; N, 14.88. Found: C, 70.35; H, 6.83; N, 14.80.

2.2.2 4-(1-Methyl-1H-imidazol-5-yl)benzonitrile (2)

Light green solid; isolated yield (78%); ¹H NMR (500 MHz, CDCl₃) δ (ppm): 7.73 (d, 2H, *J*=7.9 *Hz*, C-*H* arom), 7.57 (s, 1H, C-*H*- arom), 7.52 (d, 2H, *J*=8.2 *Hz*, C-*H* arom), 7.22 (s, 1H, C-*H*-arom) 3.73 (s, 3H, C*H*₃). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 32.87, 111.28, 118.49, 128.30, 129.78, 131.66, 132.58, 134.33, 140.47 (*C*- arom); IR (*v*, *cm*⁻¹): 3084, 2283, 2219, 1926, 1671,1606, 1491, 1230, 1118, GC-MS m/z: 183 (M⁺¹). Anal. Calc. for C₁₁H₉N₃ (183): C, 72.11; H, 4.95; N, 22.94. Found: C, 72.01; H, 4.76; N, 22.60.

2.3 Synthesis of the precursors for N-Heterocyclic carbene ligands (L1 and L2)

5-(4-Methoxyphenyl)-1-methyl-1*H*-imidazole (1) or 4-(1-methyl-1*H*-imidazol-5-yl) benzonitrile (2) (0.50 mmol) and 1-iodo-2-methylpropane (2.0 mL) were added into a 10 mL round bottom flask. The mixture was stirred at 100 $^{\circ}$ C for 48 hours. The mixture was cooled down to room temperature. Diethyl ether (5 mL) was added and stirred for 15 minutes. The ether was decanted. The product was washed several times with ether. The pure product was dried under vacuum.

2.3.1 5-(4-Methoxyphenyl)-1-methyl-3-(2-methylpropyl)-1H-imidazol-3-ium iodide (L1)

Brown gummy solid; isolated yield (84%); ¹H NMR (500 MHz, CDCl₃) δ (ppm): 9.97 (s, 1H, C-*H* arom), 7.40 (d, 2H, *J*=8.5 *Hz*, C-*H* arom), 7.24 (s, 1H, C-*H* arom), 7.04 (d, 2H, *J*=8.5 *Hz*, C-*H* arom), 4.17 (d, 2H, *J*=7.3 *Hz*, CH₂), 3.90 (s, 3H, CH₃), 3.87 (s, 3H, CH₃), 2.30 (m, 1H, CH), 1.04 (d, 6H, *J*=6.7 *Hz*, 2xCH₃). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 19.69 (CH₃x2), 29.45 (CH), 35.28 (CH₃), 55.53 (CH₂), 57.03 (CH), 114.90, 119.06, 130.78, 130.97, 135.88, 137.07, 161.40 (*C*- arom); IR (*v*, *cm*⁻¹): 2951, 2354, 2041, 1610, 1510, 1448, 1365, 1262, 1168, 1026; GC-MS m/z: 372 (M⁺¹) Anal. Calc. for C₁₅H₂₁IN₂O (372): C, 48.40; H, 5.69; N, 7.53. Found: C, 48.45; H, 5.72; N, 7.66.

2.3.2 5-(4-Cyanophenyl)-1-methyl-3-(2-methylpropyl)-1H-imidazol-3-ium iodide (L2)

Brown gummy solid; isolated yield (78%); ¹H NMR (500 MHz, CDCl₃) δ (ppm): 9.86 (s, 1H, C-*H*- arom), 7.87 (d, 2H, *J*=8.5 *Hz*, C-*H*- arom), 7.74 (d, 2H, *J*=8.5 *Hz*, C-*H* arom), 7.43 (s, 1H, C-*H* arom), 4.22 (d, 2H, *J*=7.3 *Hz*, CH₂), 4.06 (s, 3H, CH₃), 2.33 (m, 1H, CH), 1.08 (d, 2H, *J*=8.5 *Hz*, CH₃x2). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 19.73 (CH₃x2), 29.45 (CH₂), 36.17 (CH₃), 57.72 (CH), 114.68 (CN), 117.59, 120.89, 128.95, 130.47, 132.71, 133.17, 138.16 (*C*-arom); IR (*v*, *cm*⁻¹) 2958, 2352, 2230, 1669, 1568, 1458,1384, 1154; GC-

MS m/z: 367 (M⁺¹); Anal. Calc. for C₁₅H₁₈IN₃ (367): C 49.06; H, 4.94; N, 11.44. Found: C, 49.21; H, 4.46; N, 11.80.

2.4 Synthesis of diiodo-palladium-N-heterocyclic carbene-pyridine complexes (C1 and C2)

N-Heterocyclic carbene ligand precursor (L1 or L2) (0.5 mmol), palladium(II) iodide (0.50 mmol), potassium carbonate (2.0 mmol) and pyridine (5.0 mL) were added into a 15 mL round bottom flask. The reaction mixture was stirred at 90°C for 24 h. The crude product was cooled down to room temperature and diluted with 5 mL dichloromethane. The mixture was then passed through a short silica column covered with a short pad of celite. The column was eluted with methanol. The solvents were removed using rotary evaporator under reduced pressure. The complexes were obtained as yellow crystals. The crystals were washed with ether and dried in a vacuum. The complexes were characterized with ¹H and ¹³C NMR, FT-IR, ESI-MS, elemental analysis and the molecular structure of **C1** was established using single crystal X-ray diffraction analysis.

2.4.1 Diiodido[5-(4-methoxyphenyl)-1-methyl-3-(2-methylpropyl)-1H-imidazol-2-ylidene] pyridinepalladium(II) (C1)

Yellow crystals; Yield (79%); ¹H NMR (500 MHz, CDCl₃) δ (ppm): 9.05 (d, 2H, *J*=4.88 *Hz*, C-*H*- arom), 7.73 (t, 1H, *J*=7.6 *Hz*, C-*H*- arom), 7.34–7.26 (m, 4H, C-*H* arom), 6.97 (d, 2H, *J*=8.54 *Hz*, C-*H* arom), 6.86 (s, 1H, C-*H* arom), 4.19 (d, 2H, *J*=7.6 *Hz*, CH₂), 3.94 (s, 3H, CH₃), 3.85 (s, 3H, CH₃), 2.79 (m, 1H, C-*H*), 1.08 (d, *J*=6.7 *Hz*, 6H, CH₃x2); ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 20.45, 28.21, 37.47, 55.37, 59.35, 114.20, 119.96, 120.06, 120.12, 124.40, 124.47, 130.59, 135.92, 137.50, 145.50, 153.36, 160.19 (*C*-arom). IR (*vcm*⁻¹): 2950, 1606, 1507, 1451, 1248, 1174, 1023; ESI-MS m/z: 684 (M⁺¹); Anal. Calc. for C₂₀H₂₅I₂N₃OPd (684): C, 35.09; H, 3.83%; N, 6.14. Found: C, 35.69; H, 3.99; N, 6.53.

2.4.2 Diiodo5-(4-cyanophenyl)-1-methyl-3-(2-methylpropyl)-1H-imidazol-2-ylidene] pyridinepalladium(II) (C2)

Yellow crystals; isolated yield (68%); ¹H NMR (500 MHz, CDCl₃) δ (ppm): 9.05 (s, 2H, CH₂-arom), 7.77 (d, 3H, J = 8.54 Hz, C-H- arom), 7.52 (d, 2H, J = 8.2 Hz, C-H arom), 7.36–7.32 (m, 2H, C-H arom), 7.02 (s, 1H, C-H arom), 4.23 (d, 2H, J = 7.9 Hz, CH₂), 4.03 (s, 3H,

 CH_3), 2.81 (m, 1H, C-*H*), 1.09 (d, J=6.4 Hz, 6H, $CH_3 \ge 2$), ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 20.34 (*C*H₃ ≥ 2), 28.14 (*C*H), 37.97 (*C*H₃), 59.60 (*C*H₂), 121.10, 124.49, 128.18, 129.31,132.66, 153.83 (*C*-arom); IR (*v*, *cm*⁻¹) 2931, 2353, 2224, 1717, 1598, 1453, 1386, 1073; ESI-MS m/z 679 (M⁺¹) Anal. Calc. for C₂₀H₂₃I₂N₄Pd, (679): C, 35.34; H, 3.41; N, 8.24. Found: C, 35.21; H, 3.35; N, 8.20.

2.5 X-Ray crystal structure

Single-crystal data collections were performed at 150 K on a Bruker APEX-II CCD diffractometer using a graphite mono-chromated MoK α radiation ($\lambda = 0.71073$ Å). The data were collected using APEX2 [27], integrated and reduced using SAINT [28]. An empirical absorption correction was carried out using SADABS [29]. The structure was solved with direct methods using SHELXS-97 and refined by full matrix least square methods based on F², using SHELXL [30]. Graphics were generated using ORTEP3 [31]. All non-hydrogen atoms were refined with anisotropic displacement parameters. All H atoms were included at calculated positions using a riding model. Crystal data and details of the data collection are summarized in Table 1.

Empirical formula	$C_{20} H_{25} I_2 N_3 O Pd$	
Formula weight	683.63	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 9.0779(5) Å	$\alpha = 90^{\circ}$
	b = 27.5230(17) Å	$\beta = 99.8203(10)^{\circ}$
	c = 9.2686(6) Å	$\gamma = 90^{\circ}$
Volume	2281.8(2) Å ³	
z	4	
Density (calculated)	1.990 g/cm ³	
Absorption coefficient	3.533 mm ⁻¹	
F(000)	1304	
Crystal size	0.257 x 0.125 x 0.066 mm	n ³
Theta range for data collection	1.480 to 26.999°.	
Index ranges	-11≤ h ≤11, -35≤ k ≤35, -	11≤1≤11
Reflections collected	33812	
Independent reflections	4972 [R(int) = 0.0323]	
Absorption correction	Semi-empirical from equi	valents

Table 1

Crystal data and	structure refinement for (C1.
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Max. and min. transmission
Refinement method
Data / restraints / parameters
Goodness-of-fit on F ²
Final R indices [I>2sigma(I)]
R indices (all data)
Largest diff. peak and hole

0.76 and 0.61

Full-matrix least-squares on F^2 4972 / 1 / 248 1.197 R1 = 0.0364, wR2 = 0.0801 R1 = 0.0441, wR2 = 0.0835 1.396 and -1.019 e.Å⁻³

2.6 Procedure for the carbonylative Suzuki-Miyaura coupling reaction

A 45 mL stainless steel autoclave equipped with a glass liner, gas inlet valve and pressure gauge was used for the carbonylative Suzuki coupling reaction. Palladium complex (0.010 mol%), aryl iodide (1.0 mmol), arylboronic acid (1.2 mmol), base (2.0 mmol) and solvent (3.0 mL) were added into the glass liner. The autoclave was vented three times with carbon monoxide and then pressurized to 200 psi of CO. The mixture was heated to the required temperature and maintained under stirring for the required time. After complete reaction, the mixture was cooled down to room temperature and extracted three times with 10 mL ethyl acetate. The combined ethyl acetate extract was concentrated under reduced pressure in a rotavapor. The product was analyzed with GC and GC-MS. The spectral data of the diarylketones prepared in this study were in full agreement with those reported in literature [1, 2, 32-37].

Analytical and Spectroscopic data of new compound: 4,4'-(benzene-1,4 diyldicarbonyl)dibenzonitrile (**6ak**),: White solid; yield 69%; ¹H NMR (500 MHz, DMSO): δ (ppm): 8.45 (s, 4H, C-*H* arom), 7.90 (d, *J*=7.32 Hz, 4H, C-*H* arom), 7.78 (d, *J*=7.32 Hz, 4H, C-*H* arom), ¹³C NMR (125 MHz, DMSO): δ (ppm): 194.50, 142.78, 134.87, 132.80, 130.17, 129.19, 119.11, 112.49; IR (*v* cm⁻¹): 2249, 2128, 1734, 1651, 1591, 1546; GC–MS: m/z 336 (M+1); Anal. Calcd for C₂₂H₁₂N₂O₂ (336): C, 78.56; H, 3.60; N, 8.33. Found: C, 78.71; H, 3.85; N, 8.46.

3. Results and Discussion

3.1 Synthesis of 5-(4-methoxyphenyl)-1-methyl-3-(2-methylpropyl)-1H-imidazol-3-ium iodide (L1) and 5-(4-cyanophenyl)-1-methyl-3-(2-methylpropyl)-1H-imidazol-3-ium iodide (L2)

The ligands L1 and L2 were prepared as shown on Scheme 1. The formation of the imidazolium iodides were confirmed by the presence of downfield singlet peaks at 9.97 ppm (L1) and 9.86 ppm (L2) in their proton NMR spectra, which are assigned to C-2 protons of the imidazole rings.

3.2 Synthesis of the Pd-NHC-Py complexes (C1 and C2)

The diiodo-palladium(II)-N-heterocyclic carbene-pyridine complexes (C1 and C2) were prepared by reacting palladium iodide with 1 equivalent of the appropriate ligand precursor in pyridine. The formation of the new complexes was confirmed by the disappearance of the acidic C-2 protons of the imidazole rings, initially present in the N-substituted imidazolium salts due to palladation of the NHC ligand precursors. Furthermore, there is appearance of new signal at 153 ppm in the ¹³C spectra of both complexes assignable to the Pd-*C*=N bond. The ESI mass spectra of the two complexes, base peaks were observed at 684 (C1) and 679 (C2) confirming the formation of the Pd-carbene complexes.



Scheme 1. Synthesis of NHC Ligand (L1 and L2) Precursors



Scheme 2. Synthesis of Palladium(II)-NHC-Pyridine Complexes (C1and C2)

3.3 Molecular structure of the palladium complex C1

The palladium complex **C1** crystallizes in the P $2_1/c$ space group. The Pd(II) ion is bonded to two trans iodides, the nitrogen atom of the pyridine, in addition to the carbon atom of the NHC carbene ligand. The geometry around the metal ion is distorted square planar. The cisbond angles are in the range 85.32(13) - 93.78(12)°. The Pd-C, Pd-N and Pd-I_{average} bond lengths are 1.959(5) Å, 2.136(4) Å and 2.5806(5) Å respectively. These data are similar to those reported for other diiodidopyridine(imidazol-2-ylidene)palladium(II) complexes [38, 39]. In the Pd(II) coordination sphere, the trans imidazol-2-ylidene and pyridine ligands are not coplanar. The dihedral angle between the two corresponding mean planes is 48.8(2)°. In the case of the NHC ligand, the imidazol-2-ylidene and the phenyl group are also not coplanar likely due to the steric effect of the methyl substituent. The corresponding torsion angle N1-C3-C8-C13 is 41.7(7)°.



Figure 1. ORTEP diagram of the molecular structure of **C1** showing the atomic labeling scheme. Thermal ellipsoids have been drawn at 50% probability level.

Table 2	2
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I1-Pd1	2.5791(5)
I2-Pd1	2.5820(5)
N3-Pd1	2.136(4)
C1-Pd1	1.959(5)
C1-N2	1.339(6)
C1-N1	1.348(6)
C3-N1	1.398(6)
C2-N2	1.374(6)
C2-C3	1.345(7)
C1-Pd1-I1	87.66(13)
N3-Pd1-I1	93.28(12)
C1-Pd1-I2	85.32(13)
N3-Pd1-I2	93.78(12)
N2-C1-N1	106.0(4)
C1-N2-C2	110.1(4)
N2-C1-Pd1	127.7(3)
N1-C1-Pd	126.1(3)
C1-N1-C3	110.3(4)

Selected Bond lengths [Å] and angles [°] for C1.

3.4 Carbonylative Suzuki-Miyaura coupling reactions of aryl iodide with arylboronic acid by Pd-NHC-Py complexes. Optimization of the reaction conditions

The Pd(II)-NHC complexes have proven to be efficient and active catalysts for a wide range of cross coupling reactions, especially the C-C bond coupling [23, 30-31, 38-43]. On the other hand, the application of Pd(II)-NHC complexes in carbonylative cross coupling reactions is still limited. Therefore, we have examined in detail the applications of the newly synthesized I_2 -Pd-(II)-NHC-Pyridine complexes (C1 and C2) in the carbonylative Suzuki coupling reaction of aryl iodides with aryl boronic acids.

The carbonylative Suzuki coupling reaction of iodobenzene with phenylboronic acid in the presence of a catalytic amount of the Pd-NHC-Py (**C1**) was adopted as a model reaction (Eq. 1). The results of the optimization reactions are summarized in Table 3. A complete conversion of the iodobenzene was observed and 98% isolated yield of the aryl ketone were achieved at 120 $^{\circ}$ C (Table 3, entry 3). A more careful optimization of the reaction time reveals that the reaction essentially completed within 6 h (Table 3, entry 6-9). No product was observed when the reaction was carried out in the absence of a base (Table 3, entry 10). While KOH gave similar activity with K₂CO₃ (Table 3, entry 12), only traces of product were observed with Et₃N (Table 3, entry 11). Based on the above results, the subsequent reactions

were carried out using C1 (0.01 mol%), toluene, K_2CO_3 at 120 °C for 6 h. These optimized conditions (Toluene / K_2CO_3 / 120 °C / 6 h) were used with the palladium catalysts C2; similarly, excellent isolated yield (92%) was also obtained with the same aryl ketone (Table 3, entry 12). No Suzuki-Miyaura coupling product and no homocoupling products were detected in the reaction mixtures. A comparison of the catalytic carbonylative Suzuki-Miyaura coupling reactions under the optimized conditions using commercially available palladium catalysts (Table 3, entries 13-16) showed clearly the high efficiency of the palladium(II)-NHC-Pyridine catalysts C1 and C2.

Table 3

Carbonylative Suzuki-Miyaura coupling reaction of iodobenzene with phenylboronic acid.^a



Eq. 1

Entry	T °C	Base	Catalyst (mol %)	Time (h)	Yield (%) ^b
1	80	K ₂ CO ₃	C1 (0.01)	16	80
2	100	K ₂ CO ₃	C1 (0.01)	16	90
3	120	K ₂ CO ₃	C1 (0.01)	16	98
4	100	K ₂ CO ₃	C1 (0.02)	16	79
5	100	K ₂ CO ₃	C1 (0.01)	16	80
6	120	K ₂ CO ₃	C1 (0.01)	6	91
7	120	K ₂ CO ₃	C1 (0.01)	4	86
8	120	K ₂ CO ₃	C1 (0.01)	3	79
9	120	K ₂ CO ₃	C1 (0.01)	1	54
10	120	-	C1 (0.01)	6	Traces
11	120	Et ₃ N	C1 (0.01)	6	7
12	120	КОН	C1 (0.01)	6	88
13	120	K ₂ CO ₃	C2 (0.01)	6	92

14	120	K ₂ CO ₃	PdI ₂ (0.01)	6	70
15	120	K ₂ CO ₃	$Pd(PPh_3)_3Cl_2$ (0.01)	6	72
16	120	K ₂ CO ₃	$\begin{array}{c} Pd(OAc)_2\\ (0.01) \end{array}$	6	69

a. Iodobenzene (1.0 mmol), phenylboronic acid (1.2 mmol), base (2.0 mmol), toluene (5.0 mL), CO (200 psi).

b. Isolated yield.

3.5 Carbonylative Suzuki Coupling Reactions catalyzed by the complex C1. Scope of Substrates

We have adopted the optimized experimental conditions (0.010 mol% of **C1**, 2.0 equivalent of K_2CO_3 , 5 ml of toluene, 200 psi CO, 120 °C, 6 h) to study the substrate scope. Various aryl iodides with a range of functionalized aryl boronic acids were considered (Eq. 2, Table 4). The carbonylative Suzuki-Miyaura coupling reaction of phenylboronic acid with un-activated aryl iodide (Table 4, entry 1), deactivated aryl iodides (Table 4, entries 2 and 3) and activated aryl iodides (Table 4, entries 4 and 5) afforded the corresponding diaryl ketones in excellent yields (94-98%). The carbonylative Suzuki-Miyaura coupling reactions of aryl iodide with activated aryl boronic acids (Table 4, entries 5-6) were also very successful. Deactivated aryl boronic acids were relatively less reactive when toluene was used as solvent. However, moderate to excellent isolated yields (71-94%) of the functionalized biaryl ketones were achieved using acetonitrile as solvent (Table 4, entries 7-10). This can be attributed probably to the relatively higher solubility of the aryl boronic acid in acetonitrile.

Table 4

Carbonylative Suzuki-Miyaura coupling reaction of different aryl iodides with various aryl boronic acids.^a



Eq. 2

Entry	Aryl iodide 4a-e	Aryl boronic acid 5a-g	Carbonylation Product 6aa-ah	Yield (%) ^c
1	4a	5a B(OH) ₂	6aa	97

2	4b	B(OH) ₂ 5a	6ab	95
3	NC	B(OH) ₂		94
	4c	Sa	6ac	
4	CH ₃ O	B(OH) ₂	CH30	98
	4u	5a	6ad	
5	CH ₃	B(OH) ₂		96
	4e	50	oae	
6	I	CH ₃ O	Осн3	98
	4a	50	6ad	
7 ^b		HO O	ОН	78
	4a	50	6af	
8^{b}	I	NC 50	CN CN	71
	4a	36	0 00	
9 ^b		F B(OH) ₂	F F	94
	4a	5f	6ag	
10 ^b		O ₂ N 5a		80
	та	Jg	6ah	

- a. **C1** (0.010 mol %), aryl iodide (1.0 mmol), aryl boronic acid (1.2 mmol), K₂CO₃ (2.0 mmol), toluene (5.0 mL), CO (200psi), 120 °C, 6 h.
- b. CH_3CN was used as solvent, 20 h
- c. Isolated yield

3.6 Carbonylative Suzuki-Miyaura coupling reaction of aryl iodides or aryl diiodides with aryl boronic acids or aryl diboronic acids catalyzed by the complex C1

Considering the high catalytic performance of the I_2 -Pd-NHC-Py complexes **C1** and **C2**, we have investigated the carbonylative Suzuki-Miyaura coupling reactions of aryl diiodides with aryl boronic acids and aryl iodides with aryl diboronic acids. For instance, we have considered the carbonylative Suzuki-Miyaura coupling of 1,4-diiodobenzene with phenyl

boronic acid. The reaction successfully proceeded to give a symmetrical diaryl ketone in very good yield (78%) (Table 5, entry 1). Similarly, the carbonylative Suzuki coupling of 1,4diiodobenzene with 4-methoxy phenylboronic acid was also successful (82%) (Table 5, entry 2). Additionally, the new Pd-NHC-complex **C1** showed high catalytic performance in the carbonylative Suzuki coupling of 1,4-diidobenzene with 4-cyanophenyl boronic acid to yield 4,4'-(benzene-1,4-diyldicarbonyl) dibenzonitrile in good yield (69%) (Table 5, entry 3). The carbonylative coupling reaction of 1,4-benzene diboronic acid with iodobenzene and with 4-iodo anisole were also successful and yielded the corresponding symmetrical diarylketones in good yields (70-76%) (Table 5, entries 4 and 5).

Table 5

Carbonylative Suzuki-Miyaura coupling reaction of aryl iodides or aryl diiodides with aryl boronic acids or aryl diboronic acids by the palladium complex C1.^a



Entry	Aryl iodide 4a-f	Arylboronic acid 5a-h	Carbonylation product 6ai - ak	Isolated Yield (%) ^c
1 ^a	I Af	B(OH) ₂ 5a	6ai	78
2		CH ₃ O 5 C	CH ₃ O O O O O O CH ₃ O O O CH ₃ O O O O O O O O O O O O O O O O O O O	82
3 ^b	I I I I I I I I I I I I I I I I I I I	NC B(OH) ₂ 5e	NC O CN 6ak	79
4 ^b	4a	B(OH)2 5h	6ai	70



a. **C1** (0.010 mol%), aryl diiodide (0.50 mmol), aryl boronic acid (1.2 mmol), K₂CO₃ (2.0 mmol), toluene (5.0 mL), CO (200 psi), 120 °C, 20 h.

b. Acetonitrile was used as solvent.

c. Isolated yield.

The high yield and selectivity obtained in the catalytic carbonylative coupling of aryl iodides and aryl diiodides with aryl boronic acids and aryl diboronic acids showed the high catalytic efficiency of the new palladium complexes **C1** and **C2**. These complexes exhibited higher catalytic activity with much lower catalyst loading as compared to different catalytic systems reported in the literature (Table 6).

Table 6

Comparison of the activity of the new catalytic system including Pd-NHC-Py (C1) in the carbonylative Suzuki-Miyaura coupling reactions of aryl iodides and aryl boronic acids with previously published data.

Catalyst	Catalyst loading % mol	Base	Time (h)	Yield (%)	Ref.
Pd-NHC	1.0 mol %	K ₂ CO ₃	5	76 - 90	10
Pd(tmdh) ₂ *	2.0 mol %	K ₂ CO ₃	6	70 - 96	2
10% Pd/C	2.0 mol %	K ₂ CO ₃	8	60 - 93	12
Pd(dba) ₂	1.0 mol %	K ₂ CO ₃	20	67 - 98	13
Fe ₃ O ₄ @SiO ₂ -SH-Pd	1.0 mol %	K ₂ CO ₃	4-12	72 - 99	15
PdCl ₂ (PPh ₃) ₂	3.0 mol %	K ₂ CO ₃	5	63 - 89	32
$[PdCl_2(o-PPh_2) \\ C_6H_4CH=NCH(CH) \\ C_6H_4(p-NO_2)]$	0.02 mol %	K ₂ CO ₃	2	< 40	44
Pd-NHC-Py	0.01 mol %	K ₂ CO ₃	6	70 - 98	Present work

*tmdh: 2,2,4,6-tetramethyl-3,5-heptanedionate

3.7 Proposed mechanism for the carbonylative Suzuki-Miyaura coupling reaction

The proposed mechanism is illustrated in scheme 3. The activation of the palladium(II) precatalyst (I) proceeds first by transmetallation with aryl boronic acid in the presence of potassium carbonate, followed by a trans-cis isomerization step and a reductive elimination of the diaryl compound to generate the Pd(0) active catalyst (IV). The aryl iodide is then added to the Pd(0) in the oxidative addition step to form the palladium(II) intermediate (V). This addition is strongly favored by the carbene and the pyridine ligands [45]. This step is followed by CO insertion into the Ar-Pd bond to form the acyl Pd intermediate (VI). Transmetallation with aryl boronic acid in the presence of potassium carbonate, produces the intermediate VII followed by trans-cis isomerization and reductive elimination to yield the diaryl ketone as the product of the carbonylative Suzuki-Miyaura reactions accompanied with the regeneration of the Pd(0) active catalyst IV [46].



Scheme 3. A plausible mechanism for the carbonylative Suzuki-Miyaura coupling reaction catalyzed by I₂-Pd-NHC-pyridine complexes.

4. Conclusion

Two new diiodo palladium N-heterocyclic carbene pyridine complexes **C1** and **C2** have been successfully synthesized and characterized using various analytical and spectroscopic techniques. The molecular structure of **C1** was established based on a single crystal X-ray diffraction. The catalytic activities of the new complexes **C1** and **C2** were investigated in the carbonylative Suzuki-Miyaura coupling reactions of various aryl iodides and aryl diiodides with aryl boronic acids and aryl diboronic acids. Excellent yields of the expected aryl ketones were obtained. Similarly, very good yields were observed for the aryl diiodides and the aryl diboronic acids substrates.

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References

- [1] Y. Cui, X. Guo, Y. Wang, X. Guo, Chinese Journal of Catalysis 36 (2015) 322–327
- [2] P.J. Tambade, Y. P. Patil, A. G. Panda, B. M. Bhanage, Eur. J. Org. Chem. (2009) 3022–3025
- [3] N. De Kimpe, M. Keppens, G. Froncg, Chem. Commun. (1996) 635–636.
- [4] S. G. Davies, D. Pyatt, C, Thomson, J. Organomet. Chem. 387 (1990) 381.
- [5] Y, Hatanaka, T. Hiyama, Synlett (1991) 845.
- [6] S.-K. Kang, T. Yamaguchi, T-H. Kim, P-S. Ho, J. Org. Chem. 61 (1996) 9082.
- [7] Y. Hatanaka, S. Fukushima, T. Hiyama, Tetrahedron 1992.
- [8] S, Gmouh, H L. Yang, M. Vaultier, Org Lett 5 (2003) 2219.
- [9] P. Gautam, B. M. Bhanage, J. Org. Chem. 80 (2015) 7810–7815
- [10] S. Zheng, L. Xu, C. Xia, Appl. Organomet. Chem. 21 (2007) 772–776.
- [11] P. Wójcik, L. Sygellou, A. Gniewek, A. Skarżyńska, A. Trzeciak ChemCatChem. 9 (2017).
- [12) M. V. Khedkar, P. J. Tambade, Z. S. Qureshi, B. M. Bhanage, Eur. J. Org. Chem. (2010) 6981–6986.
- [13] H. Li, M. Yang, Y. Qi, J. Xue, Eur. J. Org. Chem. (2011) 2662–2667.
- [14] Z. S. Qureshi, K. M. Deshmukh, P. J. Tambade, B. M. Bhanage, Synthesis 2 (2011) 243–250.

- [15] J-R. Niu, X. Huo, F.-W. Zhang, H.-B. Wang, P. Zhao, W.-Q. Hu, ChemCatChem 5 (2013) 349–354.
- [16] J. Niu, M. Liu, P. Wang, Y. Long, M. Xie, R. Li, Ma, J. New J. Chem. 38 (2014) 1471–1476.
- [17] F. Rajabi, W. R. Thiel Adv, Synth. Catal. 356 (2014) 1873 1877.
- [18] C. Zhang, J. Liu, C. Xia, Org. Biomol. Chem. 12 (2014) 9702.
- [19] A. Chartoire, A. Boreux, A. R. Martin, S. P. Nolan, RSC Advances 3 (2013) 3840.
- [20] T. Wang, H. Xie, L. Liu, W.X. Zhao, Journal of Organometallic Chemistry 804 (2016) 73-79
- [21] K. Natte, J. Chen, H. Neumann, M. Beller, X. Wu, Org. Biomol. Chem., 12 (2014) 5590.
- [22] A. Chartoire, X. Frogneux, S. P. Nolan, Adv. Synth. Catal. 354 (2012) 1897 1901.
- [23] V. H. Nguyen, M. B. Ibrahim, W. W. Mansour, B. M. El Ali, H. V. Huynh, Organometallics 36 (2017) 2345–2353.
- [24] M. B. Ibrahim, B. El Ali, M. Fettouhi, L. Ouahab, Appl. Organometal. Chem 29 (2015) 400.
- [25] M. B. Ibrahim, S. M. S. Hussain, A. Fazal, M. Fettouhi, B. El Ali J. Coord. Chem. 68 (2015) 432.
- [26] S. M. S. Hussein, M. B. Ibrahim, A. Fazal, R. Suleiman, M. Fettouhi, B. El Ali, Polyhedron 70 (2014) 39.
- [27] Bruker, APEX2. Bruker AXS Inc., Madison, Wisconsin, USA (2014).
- [28] Bruker SAINT, Bruker AXS Inc., Madison, USA (2014).
- [29] G. M. Sheldrick, SADABS, Bruker AXS Inc., Madison, Wisconsin, USA (2014).
- [30] G. M. Sheldrick, Acta Cryst, C71 (2015) 3-8.
- [31] L. J. Farrugia, J. Appl, Cryst. 30 (1997) 565.
- [32] T. Ishiyama, H. Kizaki, T. Hayashi, A. Suzuki, N. Miyaura, J. Org. Chem. 63 (1998) 4726-473.
- [33] X. Zeng, D. Xu, C. Miao, C. Xia, W. Sun, RSC Adv 4 (2014) 46494.
- [34] D. Ogawa, K. Hyodo, M. Suetsugu, J. Li, Y. Inoue, M. Fujisawa, M. Iwasaki, K. Takagi, Y. Nishihara Tetrahedron 69 (2013) 2565.
- [35] T. Ohishi, M. Nishiura, Z. Hou, Angew. Chem. Int. Ed. 47 (2008) 5792.
- [36] Q. Zhou, S. Wei, W. Han, J. Org. Chem. 79 (2014) 1454.
- [37] W. Zhao, W. M. Carreira, Org. Lett. 8(1) (2006) 99.
- [38] D.M.Khramov, E.L.Rosen, J.A.V.Er, P.D.Vu, V.M.Lynch, C.W.Bielawski, Tetrahedron 64 (2008) 6853.
- [39] R.Maity, M.van der Meer, B.Sarkar, Dalton Trans. 44 (2015) 46.
- [40] A. Chartoire, A. Boreux, A. R. Martin and S. P. Nolan, RSC Advances 3 (2013) 3840.
- [41] T. Wang, H. Xie, L. Liu, W.X. Zhao, Journal of Organometallic Chemistry 804 (2016) 73 -79.

- [42] K. Natte, J. Chen, H. Neumann, M. Beller, X. Wu, Biomol. Chem. 12 (2014) 5590.
- [43] A. Chartoire, X. Frogneux, S. P. Nolan, Adv. Synth. Catal. 354 (2012) 1897 1901.
- [44] M. K. Yılmaz, H. Keleş, S. Ince, M. Keleş, Appl. Organometal. Chem. (2017) DOI: 10.1002/aoc.4002.
- [45] J. Jover, N. Fey, M. Purdie, G. C. Lloyd-Jones, J. N. Harvey, J Mol. Catal. a-Chem. 39 (2010) 324.
- [46] S. Roslin, L. R. Odell, Chem. Commun. 53 (2017) 6895.

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Highlights:

- New N, N'-substituted imidazolium salts was synthesized and characterized.
- New diiodopyridinepalladium(II) complexes were successfully synthesized and characterized.
- Single crystal x-ray structure reveals a distorted square planar geometry.
- The two palladium complexes were found to be highly active catalyst for carbonylative Suzuki-Miyaura coupling reactions.
- The catalyst functions effectively at lower loading.

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