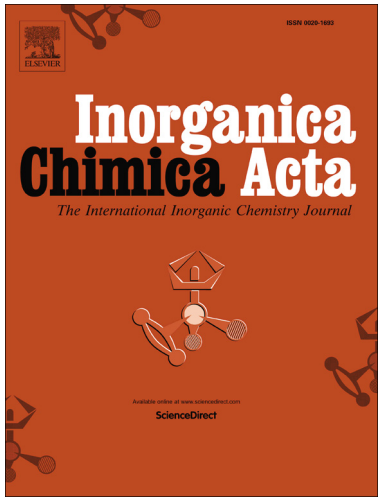

Research paper

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Palladium PEPPSI complexes: synthesis and catalytic activity on the Suzuki-Miyaura coupling reactions for aryl bromides at room temperature in aqueous media

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Running Head: Benzimidazole based Pd-PEPPSI complexes and Suzuki coupling reaction for aryl bromide substrate at room temperature

Abstract

A new series of palladium *N*-heterocyclic carbene complexes having methoxyethyl on the side chain (**3a-d**, **4a-e)** have been synthesized and fully characterized by NMR, HRMS and IR. Next, the palladium-NHC-PEPPSI complexes **3a-e** and **4a-e** were used as catalyst in Suzuki-Miyaura coupling reactions were investigated for aryl bromides at room temperature in aqueous media. **3a-d** and **4a-e** complexes showed good catalytic activity for electron-donating or electron-drawing aryl bromides with arylboronic acid. Complex **4b** exhibited higher activity compared to other analogues due to bearing more electronically donating NHC ligands.

Keywords: Palladium *N*-heterocyclic carbene complex; benzimidazole; Suzuki-Miyaura cross coupling; C-C bond formation; aqueous media

1. Introduction

The coordination chemistry of palladium has attracted a special interest in the field of catalysis for C-C bond formations for over 40 years. For this purpose, palladium based complexes or palladium salts are commonly used as catalyst. Cross-coupling reactions are the most important and accepted methods to produce fine chemicals in organic synthesis and for industry and academia. Suzuki-Miyaura reaction is one of the most beneficial and studied C-C bond forming reactions due to its reputation which comes from use of non-toxic chemicals, substrate tolerance, green solvents, mild reaction conditions and easy separation of product from reaction media.[1-3] Some excellent reviews were published on this area.[4] When the history of the Suzuki-Miyaura coupling reaction is examined, generally, phosphines have dominated as the ligand used.[5] However, some limitations of phosphine ligands include toxicity and sensitivity to air and moisture.[6] Therefore, to overcome these disadvantages, development of phosphine-free catalytic system is one of the most challenging and demanding issue in Suzuki-Miyaura cross-coupling reactions.

After 1991, *N*-heterocyclic carbenes (NHCs) are firmly occupied an important place in the ancillary ligands for organometallic chemistry and homogeneous catalysis. Since this date, NHCs have begun to replace phosphine ligands.[7-10] High thermal stability, nontoxic chemistry, resistance to oxidation, strong σ-donor ligands ability[13] with weak π-acceptor capability, tuneable of electronic and steric properties and easily handling are some of the superior advantageous of NHCs.[7,11-13] The commonly used NHC ligands for transition metals are generated from imidazolium, imidazolidinium and benzimidazolium based salts in presence of strong bases. Herrmann et al reported well-define Pd-NHC complexes used as effective catalysts in C-C bond formation reactions.[14] Other research groups reported well-

defined NHC-Pd complexes used successfully as effective catalyst in C-C bond formation reaction.[15-18] Herrmann study's encouraged Nolan[19-21] and others [22] to further investigate Pd-NHC complex as catalysts in Suzuki-Miyaura cross-coupling. Glorius et al. succeed in the production of sterically demanding biaryls via Suzuki-Miyaura coupling reaction at room temperature with low catalyst loadings in high yields.[23] Organ's studies take a very important place in cross-coupling reactions.[24] They synthesized a series of Pd-PEPPSI (PEPPSI= **P**yridine-**E**nhanced **P**recatalyst **P**reparation, **S**tabilisation and **I**nitiation) complexes with various NHC ligands. These catalyst displayed high reactivity with wide range of substrates and inorganic bases. Research showed that the activity of the Pd-PEPPSI complexes was attributed to NHC ligands.[25-28] Our group also synthesized and investigated the catalytic activity of Pd-PEPPSI type complexes in Suzuki-Miyaura cross-coupling reactions of aryl chlorides.[29]

Carbenes are most effectively stabilized after coordinated to transition metals, and many of them are stable in water. The properties of various transition-metal-carbene complexes in aqueous media have been studied.[30] The use of water as a solvent in Suzuki-Miyaura cross-coupling reactions helps with the solvation of these organic-insoluble materials and inorganic bases. Also, organoboron compounds are often quite stable to protolytic decomposition by water. In addition to being cheap and safe solvent,[31–33] water has the additional advantage that the Suzuki-Miyaura cross-coupling reactions products are often poorly soluble in water. Thus, they can be easily separated from the reaction mixture. This advantage, though, also turns out to be a drawback, as the aryl halides are poorly soluble in water.[34] To overcome this problem, addition of a minumum volume of a protic co-solvent such as alcohol should led to even faster Suzuki coupling reactions. There are certain key challenges for development of methodologies using water or aqueous medium as solvents.

Herein, we report the synthesis and characterization of nine new palladium-PEPPSI complexes bearing methoxyethyl on the side chain and the catalytic activity in Suzuki-Miyaura cross-coupling reactions at room temperature in aqueous media.

2. Experimental Section

2.1 Materials

All reactions for the preparation of benzimidazolium salts (**1-2**) and palladium-(NHC)-PEPPSI complexes (**3-4**) were carried out under air. $PdCl_2$, pyridine and solvents were purchased from Sigma-Aldrich and used as obtained. Elemental analyses were performed by ElementarVario EL III Carlo Erba 1108. The melting points of the complexes and NHC precursors were determined using Stuart automatic melting point apparatus (SMP-40). IR spectra were recorded with a PerkinElmer Spectrum 100 GladiATR FT/IR spectrophotometer. ^{1}H, ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d^6 solutions operating on a Bruker Avance III HD 400 MHz NMR spectrometer and chemical shifts were reported relative to tetramethylsilane for ^{1}H, ^{13}C NMR spectra as standard. Signals are quoted in parts per million as δ downfield from tetramethylsilane (δ 0.00) as an internal standard. Coupling constants (*J* values) are given in hertz. NMR multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, m = multiplet signal. The HRMS (ESI) electrospray ionization mass spectra were recorded on a Shimadzu LCMS-IT-Toff spectrometer in $CH_3CN/CHCl_3$. Column chromatography was performed using silica gel 60 (70-230 mesh). Solvent ratio is given as v/v.

2.2 General procedure for the synthesis of NHC precursors, 1a-d and 2a-e.

For the preparation of benzimidazolium salts 1a-d and 2a-e., 1-(2-Methoxyethyl)benzimidazole (1 mmol) was dissolved in anhydrous dimethylformamide (DMF), (3 mL) and alkyl halide (1.2 mmol) was added at room temperature. The reaction

mixture was stirred at 70 ^{o}C for 48 h. After completion of the reaction, the DMF was removed by vacuum and diethyl ether (15 mL) was added to obtain a white crystalline solid, which was filtered off. The solid was washed with diethyl ether (3x10 mL) and dried under vacuum. The crude product was recrystallized from dichloromethane–diethyl ether and completely dried under vacuum to give the title compounds as white crystals.

2.2.1 1-(2-Methoxyethyl)-3-(2,3,4,5,6-penthamethylbenzyl)benzimidazolium chloride, 1a

This NHC precursor was synthesized according to published procedure.[35]

2.2.2 1-(2-Methoxyethyl)-3-(2,4,6-trimethylbenzyl)benzimidazolium chloride, 1b

This NHC was synthesized according to published procedure.[36]

2.2.3 1-(2-Methoxyethyl)-3-(3,5-dimethylbenzyl)benzimidazolium bromide, 1c

Yield: 92% (3.1 g); m.p.= 311.1 °C. $\nu_{(CN)}$= 1560.26 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 2.28 [s, 6H, $CH_2C_6H_3(CH_3)_2$-3,5], 3.36 [s, 3H, $CH_2CH_2OCH_3$], 3.98 [t, J = 4 Hz, 2H, $CH_2CH_2OCH_3$], 4.89 [t, J = 4 Hz, 2H, $CH_2CH_2OCH_3$], 5.73 [s, 2H, $CH_2C_6H_3(CH_3)_2$-3,5], 6.96 and 7.06 [s, 3H, $CH_2C_6H_3(CH_3)_2$-3,5], 7.55 [m, 3H, NC_6H_4N], 7.82 [d, J = 8 Hz, 1H,NC_6H_4N], 11.40 [s, 1H, NCHN]. ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 21.3 [$CH_2C_6H_3(CH_3)_2$-3,5], 47.9 [$CH_2CH_2OCH_3$], 51.7 [$CH_2C_6H_3(CH_3)_2$-3,5], 59.2 [$CH_2CH_2OCH_3$], 70.5 [$CH_2CH_2OCH_3$], 113.5, 114.1 [NC_6H_4N-o], 126.1 [$CH_2C_6H_3(CH_3)_2$-3,5;$C_{2,4,6}$], 127.0 and 127.1 [NC_6H_4N-m], 131.0 and 131.0 [NC_6H_4N-i], 132.3 [$CH_2C_6H_3(CH_3)_2$-3,5;C_1], 139.2 [$CH_2C_6H_3(CH_3)_2$-3,5; $C_{3,5}$], 142.6 [NCHN]. Anal. Calc. for $C_{19}H_{23}N_2OBr$ (%): C, 60.81; H, 6.18; N, 7.46. Found (%): C, 60.88; H, 6.30; N, 7.59.

2.2.4 1-(2-Methoxyethyl)-3-(4-methylbenzyl)benzimidazolium chloride, 1d

Yield: 90% (2.9 g); m.p. = 302.5 °C. $\nu_{(CN)}$= 1557.32 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 2.29 [s, 3H, $CH_2C_6H_4(CH_3)$-4], 3.35 [s, 3H, $CH_2CH_2OCH_3$], 3.95 [t, J = 4 Hz, 2H, $CH_2CH_2OCH_3$], 4.87 [t, J = 4 Hz, 2H, $CH_2CH_2OCH_3$], 5.83 [s, 2H, $CH_2C_6H_4(CH_3)$-4], 7.10 and 7.29 [d, J = 8 Hz, 4H, $CH_2C_6H_4(CH_3)$-4], 7.52, 7.58, and 7.86 [d, J = 8 Hz, 4H, NC_6H_4N], 11.24 [s, 1H, NCHN]. ^{13}C NMR($CDCl_3$, 100 MHz, δ, ppm): 21.2 [$CH_2C_6H_4(CH_3)$-4], 47.9 [$CH_2CH_2OCH_3$], 51.3 [$CH_2C_6H_4(CH_3)$-4], 59.1 [$CH_2CH_2OCH_3$], 70.1 [$CH_2CH_2OCH_3$], 113.6, 114.1 [NC_6H_4N-*o*], 127.1 [NC_6H_4N-*m*], 128.4 [$CH_2C_6H_4(CH_3)$-4;$C_{2,3,5,6}$], 129.9 and 130.9 [NC_6H_4N-*i*], 132.2 [$CH_2C_6H_3(CH_3)_2$-3,5;C_1], 139.3 [$CH_2C_6H_4(CH_3)$-4;C_4], 142.9 [NCHN]. Anal. Calc. for $C_{18}H_{21}N_2OCl$ (%): C, 68.24; H, 6.68; N, 8.84. Found (%): C, 68.19; H, 6.75; N, 8.93%.

2.2.5 1-(2-Methoxyethyl)-3-(2,3,4,5,6-pentamethylbenzyl)-5,6-dimethylbenzimidazolium chloride, 2a

This NHC precursor was synthesized according to published procedure.[36]

2.2.6 1-(2-Methoxyethyl)-3-(2,4,6-trimethylbenzyl)-5,6-dimethylbenzimidazolium chloride, 2b

This NHC precursor was synthesized according to published procedure.[36]

2.2.7 1-(2-Methoxyethyl)-3-(3,5-dimethylbenzyl)-5,6-dimethylbenzimidazolium bromide, 2c

Yield: 89% (3.19 g); m.p. = 267.6 °C. $\nu_{(CN)}$= 1563.49 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 2.22 [s, 6H, $CH_2C_6H_3(CH_3)_2$-3,5], 2.31 and 2.35 [s, 6H, $NC_6H_2(CH_3)_2$N-5,6], 3.29 [s, 3H, $CH_2CH_2OCH_3$], 3.89 [t, J = 4 Hz, 2H, $CH_2CH_2OCH_3$], 4.73 [t, J = 4 Hz, 2H, $CH_2CH_2OCH_3$], 5.59 [s, 2H, $CH_2C_6H_3(CH_3)_2$-3,5], 6.90 and 6.95 [s, 3H, $CH_2C_6H_3(CH_3)_2$-3,5], 7.22 and 7.47 [s, 2H, $NC_6H_2(CH_3)_2$N-5,6], 11.05 [s, 1H, NCHN]. ^{13}C NMR($CDCl_3$, 100

MHz, *δ*, ppm): 20.6 and 20.7 [$NC_6H_2(CH_3)_2$N-5,6], 21.2 [$CH_2C_6H_3(CH_3)_2$-3,5], 47.5 [$CH_2CH_2OCH_3$], 51.2 [$CH_2C_6H_3(CH_3)_2$-3.5], 59.1 [$CH_2CH_2OCH_3$], 70.3 [$CH_2CH_2OCH_3$], 113.0, 113.5 [$NC_6H_2(CH_3)_2$N-*o*], 125.7 [$CH_2C_6H_3(CH_3)_2$-3,5;$C_{2,4,6}$], 130.8 and 132.6 [$NC_6H_2(CH_3)_2$N-*i*], 132.6[$CH_2C_6H_3(CH_3)_2$-3,5;C_1], 137.2 [$NC_6H_2(CH_3)_2$N-*m*], 139.1 [$CH_2C_6H_3(CH_3)_2$-3,5;$C_{3,5}$], 141.8 [NCHN]. Anal. Calc. for $C_{21}H_{27}N_2OBr$ (%): C, 62.53; H, 6.75; N, 6.95. Found (%): C, 62.59; H, 6.79; N, 7.13%.

2.2.8 1-(2-Methoxyethyl)-3-(4-methylbenzyl)-5,6-dimethylbenzimidazolium chloride, 2d

Yield: 87% (3.0 g); m.p. = 256.8 °C. $\nu_{(CN)}$= 1559.72 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz, *δ*, ppm): 2.32 [s, 3H, $CH_2C_6H_4(CH_3)$-4], 2.37and 2.41 [s, 6H, $NC_6H_2(CH_3)_2$N-5,6], 3.36 [s, 3H, $CH_2CH_2OCH_3$], 3.95 [t, *J* = 4 Hz, 2H, $CH_2CH_2OCH_3$], 4.78 [t, *J* = 4 Hz, 2H, $CH_2CH_2OCH_3$], 5.72 [s, 2H, $CH_2C_6H_4(CH_3)$-4], 7.18 and 7,36 [d, *J* = 8 Hz, 4H, $CH_2C_6H_4(CH_3)$-4], 7.31 and 7.53 [s, 2H, $NC_6H_2(CH_3)_2$N-5,6], 11.23 [s, 1H, NCHN]. ^{13}C NMR ($CDCl_3$, 100 MHz, *δ*, ppm): 20.6 and 20.7 [$NC_6H_2(CH_3)_2$N-5,6], 21.2 [$CH_2C_6H_4(CH_3)$-4], 40.2[$CH_2CH_2OCH_3$], 51.0 [$CH_2C_6H_4(CH_3)$-4], 59.2 [$CH_2CH_2OCH_3$], 70.3 [$CH_2CH_2OCH_3$], 113.0, 113.5 [$NC_6H_2(CH_3)_2$N-*o*], 128.2 [$NC_6H_2(CH_3)_2$N-*i]*, 130.0 [$CH_2C_6H_4(CH_3)$-4;$C_{2,3,5,6}$], 130.8 [$CH_2C_6H_4(CH_3)$-4;C_1], 137.2 [$CH_2C_6H_4(CH_3)$-4;C_4], 139.1 [$NC_6H_2(CH_3)_2$N-*m*], 141.8 [NCHN]. Anal. Calc. for $C_{20}H_{25}N_2OCl$ (%): C, 69,65; H, 7.31; N, 8.12. Found (%): C, 69.77; H, 7.43; N, 8.24.

2.2.9 1-(2-Methoxyethyl)-3-(4-*tert*-butylbenzyl)-5,6-dimethylbenzimidazolium bromide, 2e

Yield: 74% (2.85 g); m.p. = 255.4 °C. $\nu_{(CN)}$= 1559.06 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz, *δ*, ppm): 1.29 [s, 9H, $CH_2C_6H_4(C(CH_3)_3)$-4], 2.40 and 2.43 [s, 6H, $NC_6H_2(CH_3)_2$N-5,6], 3.38 [s, 3H, $CH_2CH_2OCH_3$], 3.98 [t, *J* = 4 Hz, 2H, $CH_2CH_2OCH_3$], 4.79 [t, *J* = 4 Hz, $CH_2CH_2OCH_3$], 5.73 [s, 2H, $CH_2C_6H_4(C(CH_3)_3)$-4], 7.34 and 7.53 [s, 2H, $NC_6H_2(CH_3)_2$N-5,6], 7.42 [s, 4H,

$CH_2C_6H_4$(C(CH_3)$_3$)-4], 11.27 [s, 1H, NC*H*N]. ^{13}C NMR ($CDCl_3$, 100MHz, δ, ppm): 20.6 and 20.7 [NC_6H_2(*C*H_3)$_2$N-5,6], 31.2 [$CH_2C_6H_4$(C(*C*H_3)$_3$)-4], 47.5[*C*$H_2CH_2OCH_3$], 50.9 [*C*$H_2C_6H_4$(C(CH_3)$_3$)-4], 59.2 [$CH_2CH_2OCH_3$], 70.3 [$CH_2CH_2OCH_3$], 112.9 and 113.5 [NC_6H_2(CH_3)$_2$N-*o*], 126.3 [$CH_2C_6H_4$(CH_3)-4;$C_{3,5}$], 128.0 [$CH_2C_6H_4$(*C*H_3)-4, $C_{2,6}$], 129.5 and 129.8 [NC_6H_2(CH_3)$_2$N-*i*], 130.8 [$CH_2C_6H_4$(CH_3)-4;C_1], 137.2 [NC_6H_2(CH_3)$_2$N-*m*], 141.8 [N*C*HN], 152.3 [$CH_2C_6H_4$(C(CH_3)$_3$)-4; C_4]. Anal. Calc. for $C_{23}H_{31}N_2OBr$ (%): C, 64.03; H, 7.24; N, 6.49. Found (%): C, 64.11; H, 7.30; N, 6.61.

2.3 General procedure for the preparation of the palladium-PEPPSI complexes, (3a-d, 4a-e)

In air, a pressure tube was charged with $PdCl_2$ (180 mg, 1 mmol), NHC precursors (1.1 mmol), K_2CO_3 (700 mg, 5 mmol) and 3 mL of pyridine. The reaction mixture was heated with vigorous stirring for 12 h at 80 ^{o}C then cooled to room temperature and diluted with dichloromethane (DCM). A short silica column was used for filtration. All volatiles were evaporated. Residue yellow solid was washed with hexane (2x10 mL) and diethyl ether (2x10 mL). The yellow solid was crystallized with DCM-Hexane (1:3) for further purification.

2.3.1 Dichloro[1-(2-methoxyethyl)-3-(2,3,4,5,6-pentamethylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II), 3a

Yield: 88% (0.4 g); m.p. = 243.9 °C. $\nu_{(CN)}$= 1447.16 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 2.25 [s, 6H, CH_2C_6(C*H*$_3$)$_5$-2,6], 2.32 [s, 6H, CH_2C_6(C*H*$_3$)$_5$-3,5], 2.34 [s, 3H, CH_2C_6(C*H*$_3$)$_5$-4], 3.38 [s, 3H, $CH_2CH_2OCH_3$], 4.23 [t, J = 4 Hz, 2H, $CH_2CH_2OCH_3$], 5.13 [t, J = 4 Hz, 2H, $CH_2CH_2OCH_3$], 6.26 [s, 2H, CH_2C_6(CH_3)$_5$-2,3,4,5,6], 6.44, 6.97 and 7.18 [t, 3H, NC_6H_4N], 7.54 [d, J = 8 Hz, 1H, NC_6H_4N], 7.39 [t, J = 8 Hz, 2H, NC_5H_5-H$_{3,5}$], 7.81 [t, J = 8 Hz, 1H, NC_5H_5-H$_4$], 8.98 [d, J = 8 Hz, 2H, NC_5H_5-H$_{2,6}$]. ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 16.9, 17.3 and 17.5 [CH_2C_6(*C*H_3)$_5$-2,3,4,5,6], 48.6 [*C*$H_2CH_2OCH_3$], 51.2

[*C*$H_2C_6(CH_3)_5$-2,3,4,5,6], 59.2 [$CH_2CH_2OCH_3$], 72.0 [$CH_2CH_2OCH_3$], 111.3 [N*C*$_6H_4$N-*o*], 122.7 [N*C*$_5H_5$, *C*$_{3,5}$], 123.0 [N*C*$_6H_4$N-*m*], 124.5 [$CH_2C_6(CH_3)_5$-2,3,4,5,6;*C*$_{3,5}$], 127.8 [$CH_2C_6(CH_3)_5$-2,3,4,5,6;*C*$_4$], 133.1 [N*C*$_6H_4$N-*i*], 134.7 [$CH_2C_6(CH_3)_5$-2,3,4,5,6;*C*$_{2,6}$], 135.9 [N*C*$_5H_5$;*C*$_4$], 138.1 [$CH_2C_6(CH_3)_5$-2,3,4,5,6;*C*$_1$], 151.2 [N*C*$_5H_5$;*C*$_{2,6}$], 163.3 [Pd-*C*carb]. HRMS(ESI), m/z=468,1243 $[M+Na+H]^+$ (calcd for $C_{22}H_{28}N_2OPdNa$:468,1217).

2.3.2 Dichloro[1-(2-methoxyethyl)-3-(2,4,6-trimethylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II), 3b

Yield: 82% (0.35 g); m.p. = 215.5 °C. $\nu_{(CN)}$= 1448.80 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, *δ*, ppm): 2.26 [s, 9H, $CH_2C_6H_2(CH_3)_3$-2,4,6], 3.28 [s, 3H, $CH_2CH_2OCH_3$], 4.14 [t, *J* = 4 Hz, 2H, $CH_2CH_2OCH_3$], 5.04 [t, *J* = 4 Hz, 2H, $CH_2CH_2OCH_3$], 6.11 [s, 2H, $CH_2C_6H_2(CH_3)_3$-2,4,6], 6.39 and 7.47 [d, *J* = 8 Hz, 2H, NC_6H_4N], 6.86 [s, 2H, $CH_2C_6H_2(CH_3)_3$-2,4,6], 6.89 and 7.10 [t, *J* = 8 Hz, 2H, NC_6H_4N], 7.31 [t, *J* = 8 Hz, 2H, NC_5H_5-$H_{3,5}$], 7.72 [t, *J* = 8 Hz, 1H, NC_5H_5-H_4], 8.91 [d, *J* = 8 Hz, 2H, NC_5H_5-$H_{2,6}$]. ^{13}C NMR ($CDCl_3$, 100 MHz, *δ*, ppm): = 20.8 and 21.1 [$CH_2C_6H_2(CH_3)_3$-2,4,6], 48.6 [$CH_2CH_2OCH_3$], 50.0 [$CH_2C_6H_2(CH_3)_3$-2,4,6], 59.2 [$CH_2CH_2OCH_3$], 72.0 [$CH_2CH_2OCH_3$], 111.1 and 111.4 [N*C*$_6H_4$N-*o*], 122.8 [N*C*$_5H_5$;*C*$_{3,5}$], 123.1 [N*C*$_6H_4$N-*m*], 124.5 [$CH_2C_6H_2(CH_3)_3$-2,4,6;*C*$_{3,5}$], 127.5 [$CH_2C_6H_2(CH_3)_3$-2,4,6;*C*$_4$], 134.7 [$CH_2C_6H_2(CH_3)_3$-2,4,6;*C*$_{2,6}$], 134.4 and 135.6 [N*C*$_6H_4$N-*i*], 138.2 [N*C*$_5H_5$;*C*$_4$], 138.8 [$CH_2C_6H_2(CH_3)_3$-2,4,6;*C*$_1$], 151.3 [N*C*$_5H_5$;*C*$_{2,6}$], 163.5 [Pd-*C*carb]. HRMS(ESI), m/z=440,0914 $[M+Na+H]^+$ (calcd for $C_{20}H_{24}N_2OPdNa$:440,0904); m/z=413,0680 $[M-H]^-$ (calcd for $C_{20}H_{24}N_2OPd$:413,0845).

2.3.3 Dichloro[1-(2-methoxyethyl)-3-(3,5-dimethylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II), 3c

Yield: 88% (0.32 g); m.p. = 205.5 °C. $\nu_{(CN)}$= 1445.58 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, *δ*, ppm): 2.21 [s, 6H, $CH_2C_6H_3(CH_3)_2$-3,5], 3.30 [s, 3H, $CH_2CH_2OCH_3$], 4.23 [m, 2H, $CH_2CH_2OCH_3$], 5.10 [d, *J* = 6 Hz, 2H, $CH_2CH_2OCH_3$], 6.07 [m, 2H, $CH_2C_6H_3(CH_3)_2$-3,5],

6.86 [s, 1H, NC_6H_4N], 7.05[m, 2H, NC_6H_4N], 7.48 [d, J = 8 Hz, 1H, NC_6H_4N], 7.15 and 7.19 [s, 3H, $CH_2C_6H_3(CH_3)_2$-3,5], 7.28 [m, 2H, NC_5H_5-$H_{3,5}$], 7.48 [d, J = 8 Hz, 1H, C_6H_4-H_4], 7.67-6.72 [m, 1H, NC_5H_5-H_4], 8.95 [m, 2H, NC_5H_5-$H_{2,6}$]. ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 21.3 [$CH_2C_6H_3(CH_3)_2$-3,5], 48.8 [$CH_2CH_2OCH_3$], 53.3 [$CH_2C_6H_3(CH_3)_2$-3,5], 59.2 [$CH_2CH_2OCH_3$], 71.7 [$CH_2CH_2OCH_3$], 111.2 and 111.5 [NC_6H_4N-o], 123.1 [NC_5H_5;$C_{3,5}$], 124.6 [NC_6H_4N-m], 125.9 [$CH_2C_6H_3(CH_3)_2$-3,5;$C_{2,6}$], 129.8 [$CH_2C_6H_3(CH_3)_2$-3,5;C_4], 134.8 and 134.3 [NC_6H_4N-i], 135.9 [$CH_2C_6H_3(CH_3)_2$-3,5;C_1], 138.1 [NC_5H_5;C_4], 138.4 [$CH_2C_6H_3(CH_3)_2$-3,5;$C_{3,5}$], 152.7 [NC_5H_5;$C_{2,6}$], 163.4 [Pd-Ccarb]. HRMS(ESI), m/z=571,6105 $[M+Na-H]^+$ (calcd for $C_{24}H_{27}N_3OCl_2PdNa$:571,0385); m/z=426,0798 $[M+Na+H]^+$ (calcd for $C_{19}H_{22}N_2OPdNa$:426,0786).

2.3.4 Dichloro[1-(2-methoxyethyl)-3-(4-methylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II), 3d

Yield: 86% (0.30 g); m.p. = 200.7 °C. $\nu_{(CN)}$= 1446.03 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 2.10 [s, 3H, $CH_2C_6H_4(CH_3)$-4], 3.30 [s, 3H, $CH_2CH_2OCH_3$], 4.16 [m, 2H, $CH_2CH_2OCH_3$], 5.02 [m, 2H, $CH_2CH_2OCH_3$], 6.06 [s, 2H, $CH_2C_6H_4(CH_3)$-4], 6.94-7.74 [m, 6H, $CH_2C_6H_4(CH_3)$-4,NC_6H_4N, NC_5H_5-H_4], 7.10 [t, J = 8 Hz, 2H, $CH_2C_6H_4(CH_3)$-4], 7.38 [d, J = 8 Hz, 2H, NC_5H_5-$H_{3,5}$], 7.48 [d, J = 8 Hz, 1H, NC_6H_4N], 8.96 [m, 2H, NC_5H_5-$H_{2,6}$]. ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm)= 21.2 [$CH_2C_6H_4(CH_3)$-4], 48.9 [$CH_2CH_2OCH_3$], 53.54 [$CH_2C_6H_4(CH_3)$-4], 59.2 [$CH_2CH_2OCH_3$], 71.4 [$CH_2CH_2OCH_3$], 111.3 and 111.5 [NC_6H_4N-o], 123.0 [NC_5H_5;$C_{3.5}$], 124.6 [NC_6H_4N-m], 128.0 [$CH_2C_6H_4(CH_3)$-4;$C_{2,6}$], 129.5 [$CH_2C_6H_4(CH_3)$-4;$C_{3,5}$], 131.8 [NC_6H_4N-i], 134.2 [$CH_2C_6H_4(CH_3)$-4;C_4], 136.0 [$CH_2C_6H_4(CH_3)$-4;C_1], 137.9 [NC_5H_5;C_4], 152.7 [NC_5H_5; $C_{2,6}$], 163.1 [Pd-Ccarb]. HRMS(ESI), m/z=467,1327 $[M+2H]^+$ (calcd for $C_{23}H_{25}N_3OPd$:467,1189); m/z=464,1175 $[M-H]^-$ (calcd for $C_{23}H_{25}N_3OPd$:464,0954).

2.3.5 Dichloro[1-(2-methoxyethyl)-3-(2,3,4,5,6-pentamethylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]pyridinepalladium(II), 4a

Yield: 81% (0.38 g); m.p. = 206.5 °C. $\nu_{(CN)}$= 1449.03 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 2.02 [s, 3H, $CH_2C_6(CH_3)_5$-4], 2.15 [s, 6H, $CH_2C_6(CH_3)_5$-3,5], 2.22 [s, 6H, $CH_2C_6(CH_3)_5$-4 and $NC_6H_2(CH_3)_2$N-5,6], 2.24 [s, 3H, $NC_6H_2(CH_3)_2$N-5,6], 3.30 [s, 3H, $CH_2CH_2OCH_3$], 4.12 [t, J = 5.6 Hz, 2H, $CH_2CH_2OCH_3$], 4.96 [t, J = 5.6 Hz, 2H, $CH_2CH_2OCH_3$], 6.04 [s, 2H, $CH_2C_6(CH_3)_5$-2,3,4,5,6], 6.18 and 7.18 [s, 2H, $NC_6H_2(CH_3)_2$N-5,6], 7.27 [d, J = 8 Hz, 2H, NC_5H_5-$H_{3,5}$], 7.70 [t, J = 7.2 Hz, NC_5H_5-H_4], 8.83 [d, J = 8 Hz, 2H, NC_5H_5-$H_{2,6}$]. ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 16.9, 17.2 and 17.5 [$CH_2C_6(CH_3)_5$-2,3,4,5,6], 20.2 and 20.4 [$C_6H_2(CH_3)_2$], 48.4 [$CH_2CH_2OCH_3$], 50.4 [$CH_2C_6(CH_3)_5$-2,3,4,5,6], 59.2 [$CH_2CH_2OCH_3$], 71.9 [$CH_2CH_2OCH_3$], 111.3 and 111.6 [$NC_6H_2(CH_3)_2$N-*o*], 124.4 [NC_5H_5, $C_{3,5}$], 128.2 and, 131.8 [$NC_6H_2(CH_3)_2$N-*i*], 133.0 [$CH_2C_6(CH_3)_5$-2,3,4,5,6;$C_{2,6}$], 133.3 [$CH_2C_6(CH_3)_5$-2,3,4,5,6;C_4], 134.1 [$NC_6H_2(CH_3)_2$N-*m*], 134.8 [$CH_2C_6(CH_3)_5$-2,3,4,5,6;$C_{2,6}$], 135.7 [NC_5H_5;C_4], 138.0 [$CH_2C_6(CH_3)_5$-2,3,4,5,6;C_1], 151.2 [NC_5H_5;$C_{2,6}$], 160.9 [Pd-*C*carb]. HRMS(ESI), m/z=494,1506 $[M+Na+H]^+$ (calcd for $C_{24}H_{32}N_2OPdNa$:494,1525).

2.3.6 Dichloro[1-(2-methoxyethyl)-3-(2,4,6-trimethylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]pyridinepalladium(II), 4b

Yield: 79% (0.35 g); m.p. = 208.9 °C. $\nu_{(CN)}$= 1410.35 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 2.03 [s, 3H, $CH_2C_6H_2(CH_3)_3$-4], 2.21and 2.26 [s, 6H, $NC_6H_2(CH_3)_2$N-5,6] 2.25[s, 6H, $CH_2C_6H_2(CH_3)_3$-2,6], 3.29 [s, 3H, $CH_2CH_2OCH_3$], 4.13 [t, J = 5.6 Hz, 2H, $CH_2CH_2OCH_3$], 4.96 [t, J = 5.6 Hz, 2H, $CH_2CH_2OCH_3$], 6.01 [s, 2H, $CH_2C_6H_2(CH_3)_3$-2,4,6], 6.19 [s, 1H, $NC_6H_2(CH_3)_2$N-5,6], 6.85 [s, 2H, $CH_2C_6H_2(CH_3)_3$-2,4,6], 7.19 [s, 2H, NC_5H_5-$H_{3,5}$], 7.29 [t,J = 8.8 Hz, 1H, $NC_6H_2(CH_3)_2$N-5,6], 7.71 [t,J = 8.8 Hz, 1H, NC_5H_5-H_4], 8.89 [d, J = 8.8Hz, 2H, NC_5H_5-$H_{2,6}$]. ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 20.2 and 20.42 [$NC_6H_2(CH_3)_2$N] 20.8 and 21.1 [$CH_2C_6H_2(CH_3)_3$-2,4,6], 48.3 [$CH_2CH_2OCH_3$], 49.5 [$CH_2C_6H_2(CH_3)_3$-2,4,6],

59.2 [$CH_2CH_2OCH_3$], 71.9 [$CH_2CH_2OCH_3$], 111.4 and 111.5 [$NC_6H_2(CH_3)_2N$-*o*], 124.4 [NC_5H_5;$C_{3,5}$], 127.9 [$CH_2C_6H_2(CH_3)_3$-2,4,6;$C_{2,6}$], 132.0 [$NC_6H_2(CH_3)_2N$-*i*], 133.0 [$NC_6H_2(CH_3)_2N$-*m*], 134.2 [$CH_2C_6H_2(CH_3)_3$-2,4,6;C_4], 138.1 [$CH_2C_6H_2(CH_3)_3$-2,4,6;$C_{3,5}$], 138.2 [NC_5H_5;C_4], 138.9 [$CH_2C_6H_2(CH_3)_3$-2,4,6;C_1], 151.3 [NC_5H_5;$C_{2,6}$], 161.2 [Pd-*C*carb]. HRMS(ESI), m/z=637,5322 $[M+2Na]^+$ (calcd for $C_{27}H_{33}Cl_2N_3OPdNa_2$:637,0831); m/z=489,1196 $[M+2Na+H]^+$ (calcd for $C_{22}H_{28}N_2OPdNa_2$:489,1110); m/z=468,1246 $[M+Na+H]^+$ (calcd for $C_{22}H_{28}N_2OPdNa$:468,1217).

2.3.7 Dichloro[1-(2-methoxyethyl)-3-(3,5-dimethylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]pyridinepalladium(II), 4c

Yield: 87% (0.33 g); m.p. =233.5 °C. $\nu_{(CN)}$= 1445.47 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz, δ, ppm): 2.23 and 2.33 [s, 6H, $NC_6H_2(CH_3)_2N$-5,6], 2.28 [s, 6H, $CH_2C_6H_3(CH_3)_2$-3,5], 3.39 [s, 3H, $CH_2CH_2OCH_3$], 4.22 [t, *J* = 5.6 Hz, 2H, $CH_2CH_2OCH_3$], 5.01 [t, *J* = 5.6 Hz, 2H, $CH_2CH_2OCH_3$], 5.95 [s, 2H, $CH_2C_6H_3(CH_3)_2$-3,5], 6.85 [m, 1H, $NC_6H_2(CH_3)_2N$-5,6], 6.93 [s, 1H, $NC_6H_2(CH_3)_2N$-5,6], 7.20 and 7.30 [s, 3H, $CH_2C_6H_3(CH_3)_2$-3,5], 7.33 [m, 2H, NC_5H_5-$H_{3,5}$], 7.76 [m, 1H, NC_5H_5-H_4], 9.02 [m, 2H, NC_5H_5-$H_{2,6}$]. ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 20.4 [$NC_6H_2(CH_3)_2N$], 21.3 [$CH_2C_6H_3(CH_3)_2$-3,5], 48.6 [$CH_2CH_2OCH_3$], 53.2 [$CH_2C_6H_3(CH_3)_2$-3,5], 59.2 [$CH_2CH_2OCH_3$], 71.4 [$CH_2CH_2OCH_3$], 111.4 and 111.6 [$NC_6H_2(CH_3)_2N$-*o*], 124.5 [NC_5H_5;$C_{3,5}$], 125.8 [$CH_2C_6H_3(CH_3)_2$-3,5;$C_{2,6}$], 129.7 [$CH_2C_6H_3(CH_3)_2$-3,5;C_4], 132.1, 133.0 [$NC_6H_2(CH_3)_2N$-*i*], 134.5 [$NC_6H_2(CH_3)_2N$-*m*], 135.0 [$CH_2C_6H_3(CH_3)_2$-3,5;C_1], 137.9 [NC_5H_5;C_4], 138.3 [$CH_2C_6H_3(CH_3)_2$-3,5;$C_{3,5}$], 151.7 [NC_5H_5;$C_{2,6}$], 160.8 [Pd-*C*carb]. HRMS(ESI), m/z=1102,3491 $[2M+4Na]^+$ (calcd for $C_{52}H_{58}N_6O_2Pd_2Na_4$:1102,2282); m/z=507,0180 $[M]^+$ (calcd for $C_{26}H_{31}N_3OPd$:507,1502); m/z=509,0369 $[M+2H]^+$ (calcd for $C_{26}H_{31}N_3OPd$:509,1506).

2.3.8 Dichloro[1-(2-methoxyethyl)-3-(4-methylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]pyridinepalladium(II), 4d

Yield: 75% (0.31 g); m.p. = 225.6 °C. $\nu_{(CN)}$= 1445.91 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm):2.21 [s, 3H, $CH_2C_6H_4(CH_3)$-4], 2.25 [s, 6H, $NC_6H_2(CH_3)_2$N-5,6], 3.32 [s, 3H, $CH_2CH_2OCH_3$], 4.14 [t, J = 6 Hz, 2H, $CH_2CH_2OCH_3$], 4.95 [t, J = 6 Hz, 2H, $CH_2CH_2OCH_3$], 6.04 [s, 2H, $CH_2C_6H_4(CH_3)$-4], 7.10 [m, 2H, $CH_2C_6H_4(CH_3)$-4], 7.19 and 7.22 [s, 1H, $NC_6H_2(CH_3)_2$N-5,6], 7.36 [m, 2H, $CH_2C_6H_4(CH_3)$-4], 7.40 [m, 2H, NC_5H_5-$H_{3,5}$], 7.68 [m, 1H, NC_5H_5-H_4], 8.96 [m, 2H, NC_5H_5-$H_{2,6}$]. ^{13}C NMR ($CDCl_3$, 100 MHz,δ, ppm): 20.3 [$NC_6H_2(CH_3)_2N$], 21.2 [$CH_2C_6H_4(CH_3)$-4], 48.5 [$CH_2CH_2OCH_3$], 53.0 [$CH_2C_6H_4(CH_3)$-4], 59.2 [$CH_2CH_2OCH_3$], 71.6 [$CH_2CH_2OCH_3$], 111.5 and 111.6 [$NC_6H_2(CH_3)_2$N-*o*], 124.5 [NC_5H_5;$C_{3.5}$], 127.9 [$CH_2C_6H_4(CH_3)$-4;$C_{2,6}$], 129.5 [$CH_2C_6H_4(CH_3)$-4;$C_{3,5}$], 132.2 and 132.7 [$NC_6H_2(CH_3)_2$N-*i*], 134.5 [$NC_6H_2(CH_3)_2$N-*m*], 138.0 [$CH_2C_6H_4(CH_3)_2$-4;C_4], 151.29 [$CH_2C_6H_4(CH_3)$-4; C_1], 152.1 [NC_5H_5; C_4], 152.7 [NC_5H_5;$C_{2,6}$], 161.0 [Pd-*C*carb]. HRMS(ESI), m/z=560,3253 $[M-3H]^-$ (calcd for $C_{25}H_{29}N_3OPdCl_2$:560,0488); m/z=415,0857 $[M+H]^+$ (calcd for $C_{20}H_{24}N_2OPd$:415,1002); m/z=440,0926 $[M+Na+2H]^+$ (calcd for $C_{20}H_{24}N_2OPdNa$:440,1056).

2.3.9 Dichloro[1-(2-methoxyethyl)-3-(4-tert-buthylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]pyridinepalladium(II), 4e

Yield: 79% (0.30 g); m.p. = 174.8 °C. $\nu_{(CN)}$= 1448.41 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.22 [s, 9H, $CH_2C_6H_4(C(CH_3)_3)$-4], 2.15 and 2.25 [s, 6H, $NC_6H_2(CH_3)_2$N-5,6], 3.31 [s, 3H, $CH_2CH_2OCH_3$], 4.15 [t, J = 6 Hz, 2H, $CH_2CH_2OCH_3$], 4.96 [t, J = 6 Hz 2H, $CH_2CH_2OCH_3$], 5.99 [m, 2H, $CH_2C_6H_4(C(CH_3)_3)$-4], 6.76 [m, 1H, $NC_6H_2(CH_3)_2$N-5,6], 7.23 [s, 1H, $NC_6H_2(CH_3)_2$N-5,6],7.19 [s, 1H, $CH_2C_6H_4(C(CH_3)_3)$-4], 7.26-7,45 [m, 4H, $CH_2C_6H_4(C(CH_3)_3)$-4, NC_5H_5-H_4], 7.43 [d, J = 8.4 Hz, 2H, NC_5H_5-$H_{3,5}$], 8.96 [m, 2H, NC_5H_5-$H_{2,6}$].^{13}C NMR ($CDCl_3$, 100 MHz,δ, ppm): 20.2 [$NC_6H_2(CH_3)_2N$], 31.3

[$CH_2C_6H_4(C(CH_3)_3)$-4], 34.6 [$CH_2C_6H_4(C(CH_3)_3)$-4], 48.5 [$CH_2CH_2OCH_3$], 52.9 [$CH_2C_6H_4(C(CH_3)_3)$-4], 59.2 [$CH_2CH_2OCH_3$], 71.6 [$CH_2CH_2OCH_3$], 111.5 and 111.6 [$NC_6H_2(CH_3)_2N$-*o*], 124.5 [NC_5H_5;$C_{3.5}$], 125.7 [$CH_2C_6H_4(C(CH_3)_3)$-4; $C_{3,5}$], 127.9 [$CH_2C_6H_4(C(CH_3)_3)$-4;$C_{2,6}$], 132.2 and 132.8 [$NC_6H_2(CH_3)_2N$-*i*], 134.5 [$NC_6H_2(CH_3)_2N$-*m*], 138.0 [$CH_2C_6H_4(C(CH_3)_3)$-4;C_1], 151.3 [NC_5H_5;C_4], 152.1 [$CH_2C_6H_4(C(CH_3)_3)$-4;C_4], 152.7 [NC_5H_5; $C_{2,6}$], 161.0 [Pd-*C*carb]. HRMS(ESI), m/z=455,1254 $[M-H]^-$ (calcd for $C_{23}H_{30}N_2OPd$:455,1315).

2.4 General Procedure for Suzuki-Miyaura Reactions

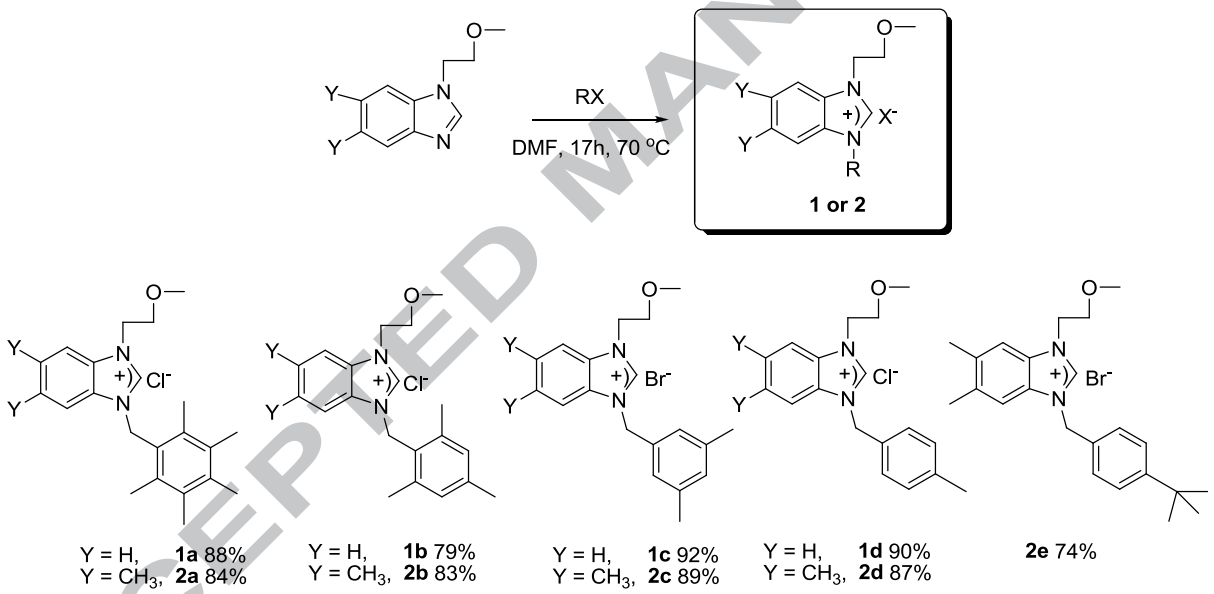
In air, Pd-PEPPSI complex (0.5 mol %), aryl bromide (1.0 mmol), phenylboronic acid (1.2 mmol), K_2CO_3 (1 mmol), and 4 mL of water/*i*-PrOH (3:1 v/v) were added to a small round bottom flask and the mixture stirred appropriate time. The reaction mixture was extracted with Et_2O. Products were purified by column chromatography using ethylacetate/hexane (0.5:9.5 v/v). All coupling products obtained via Suzuki-Miyaura coupling reactions are previously reported compounds, and were identified by comparison of our data with that available in the literature.

3. Results and Discussion

3.1 Materials and methods

Our strategy was based on the construction of the *N*-heterocyclic carbene precursors bearing a methoxyethyl which is grouped on the side chain to increase solubility in water as well as in electron density of palladium complexes (Scheme 1). To do so, new unsymmetrical 1-methoxyethyl-3-arylbenzimidazolium that based on precursors (**1a-d** and **2a-e**) were prepared according to literature.[29,35-36] Thus, the structure of **1a-d** and **2a-e** is shown in Scheme 1 and the **1c**, **2**c and **2e** compounds were also synthesised as the bromide salts due to corresponding aryl halides which commercially available on bromides form. Concerning the treatment of 1-

(2-methoxyethyl)benzimidazole with 1.2 equivalents, it yields of different aryl halides in DMF at 70 ^{o}C led to the formation of corresponding NHC precursors in 74-92% yields. The NHC precursors were fully characterized by ^{1}H and ^{13}C NMR, IR and elemental analysis. However, the assigned structures for the NHC precursors are supported by the ^{1}H NMR spectra where the resonances for C_2-***H*** (carben carbon= ***C_2***) were observed as sharp singlet signals at 10.96, 11.06, 11.40, 11.24, 10.01, 10.81, 11.05, 11.23 and 11.27 ppm, respectively, for **1a-d** and **2a-e**. The ^{13}C NMR data also supports the assigned structures of the NHC precursors by ***C_2*** chemical shifts that come to resonance at 143.0, 143.7, 142.6, 143.0, 141.4, 142.3, 141.8, 141.7 and 141.8 ppm, respectively, for **1a-d** and **2a-e**.

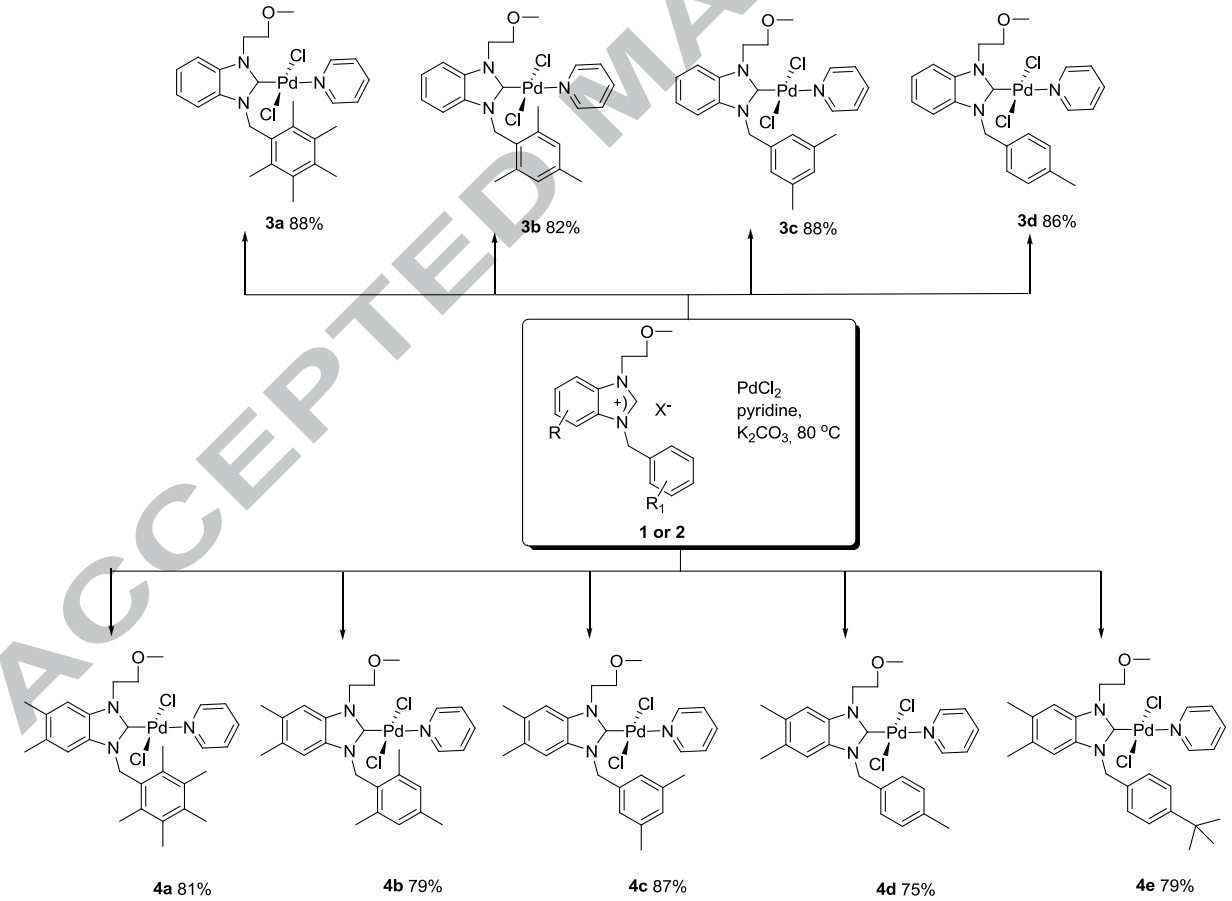


Scheme 1. Synthesis of NHC precursors.

The Pd-PEPPSI complexes **3a-d and 4a-e** were synthesized according to literature reported by Organ (Scheme 2);[24] and the reaction of NHC precursors with $PdCl_2$ in pyridine at 80 ^{o}C in the presence of excess of K_2CO_3 afforded the palladium PEPPSI complexes **3a-d** and **4a-e** in 75-88% yields.

Finally, all complexes were purified by crystallization using dichloromethane DCM/hexane (1:2) and characterized by ^{1}H and ^{13}C NMR, HRMS and IR. For the ^{1}H NMR spectra of the palladium-NHC-PEPPSI complexes **3a-d**, and **4a-e**, sharp peaks in the lower field region

belonging to the acidic imino proton of benzimidazolium salts (NCHN) were not observed between δ=10.0-12.0 ppm. Similarly, in the ^{13}C NMR spectra, imino carbon of benzimidazolium salts (NCHN) were not observed between δ=150-155 ppm. In the 1 H NMR and ^{13}C NMR spectra of the complexes **3a-d**, and **4a-e**, loss of the characteristic peak of the acidic imino proton (NC***H***N) and imino carbon (N***C***HN), signal suggests the formation of the palladium-NHC-PEPPSI complexes. The ^{13}C{^{1}H} N-C-N signals of **1a-c** and **2a-c**, which are respectively equal to 143.0, 143.7, 142.6, 143.0, 141.4, 142.3, 141.8, 141.7 and 141.8 ppm were shifted to 163.3, 163.5, 163.4, 163.1, 160.9, 161.2, 160.8, 161.0 and 161.0 ppm, respectively, in **3a-d** and **4a-e**.

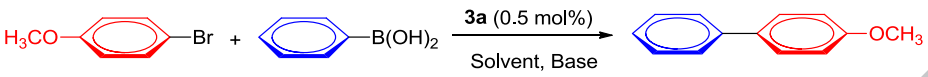


Scheme 2. Synthesis of Pd-PEPPSI complexes.

3.2 Suzuki-Miyaura cross-coupling reaction

As know from the literature, water and alcohol took very important place as solvent in the Suzuki-Miyaura reactions. [29,34,37-41a-h]

Table 1. The optimization for the Suzuki-Miyaura reaction of 4-bromoanisole[a]



[a]Entry	Solvent	Base	Yield(%)[b]
1	*i*-PrOH/H_2O(1:3)	K_2CO_3	80
2	*i*-PrOH/H_2O(1:3)	Na_2CO_3	58
3	*i*-PrOH/H_2O(1:3)	Cs_2CO_3	48
4	*i*-PrOH/H_2O(1:3)	K_3PO_4	59
5	*i*-PrOH/H_2O(1:3)	KOH	49
6	*i*-PrOH	K_2CO_3	75
7	H_2O	K_2CO_3	45
8	DMF	K_2CO_3	53
9	EtOH	K_2CO_3	69
10	MeOH	K_2CO_3	68
11	Acetone	K_2CO_3	45
12	*i*-PrOH/H_2O(1:1)	K_2CO_3	78
13	DMF/H_2O(1:3)	K_2CO_3	49
14	EtOH/H_2O(1:3)	K_2CO_3	57
15	MeOH/H_2O(1:3)	K_2CO_3	50
16[c]	*i*-PrOH/H_2O(1:3)	K_2CO_3	78
17[d]	*i*-PrOH/H_2O(1:3)	K_2CO_3	65

[a]Reaction Condition:1 mmol of 4-bromoanisole, 1.2 mmol of phenylboronic acid, 1 mmol of base, 0,5 mol% 3**a**, 4 mL solvent, room temperature, 1 hour. Yields are the average of the two

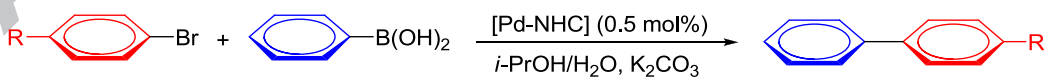
runs. [b] Isolated yield. [c] Reaction performed under nitrogen atmosphere. [d] **3a** used as catalyst, room temperature, 1.5 h

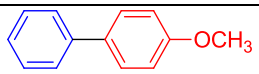
To study the efficiency of the palladium-NHC complexes **3a-d** and **4a-e** in Suzuki-Miyaura coupling reactions, we first studied the impact of the solvent and volume ratio. Then, the cross-coupling of 4-bromoanisole (1 mmol) with phenylboronic acid (1.2 mmol) in 4 mL *i*-PrOH/H_2O (1:3 v/v) under air was selected as a model reaction with **3a** (0.5 mol%) and K_2CO_3 (1 mmol) at room temperature in air (Table 1). In the literature, water soluble inorganic bases have been conveniently used in Suzuki-Miyaura cross-coupling reactions in aqueous media. [29,34] Thus, the first survey of this study was screening the performance of different inorganic bases in *i*-PrOH/H_2O (1:3 and 1:1 v/v). Different bases led to different activity in the present protocol for Suzuki reactions (Table 1, entries 1-5) but the most efficient base in this condition is K_2CO_3, which provides a 80% isolated yield in 1h. Comparatively, lower yields were obtained with other bases (Table 1). Therefore, we think that this catalytic differentiation is caused by better solubility of potassium carbonate in water.When single type of solvent such as H_2O, EtOH, MeOH, DMF or *i*-PrOH used, lower coupling product took place compared to product obtained *via* *i*-PrOH/H_2O (1:3) solvent system (Table 1, entries 6-11). Different solvent mixtures such as EtOH/H_2O, DMF/H_2O, and MeOH/H_2O (1:3 v/v), were led to lower cross-coupling product (Table 1, entries 13-15). Morever, single type solvent and solvent/H_2O mixtures (except isopropanol) led to lower yield are also observed. This may be attributed to low solubility of base in single type solvent as shown in (Table 1, entries 7-11) or low solubility of complex in too polar solvent or solvent/H_2O mixtures (Table 1, entries 7-15). As a result of the optimisation experiments, a very good yield (80%) was obtained with *i*-PrOH/H_2O (1:3 and 1:1 v/v) solvent system in open air (Table 1, entries 1 and 12). Hence, we selected 1:3 ratio for obtaining good yields. We are quite satisfied to report that 1-2% undesired homo-coupling product was observed in

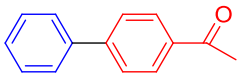
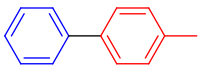
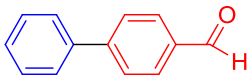
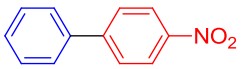
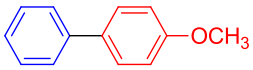
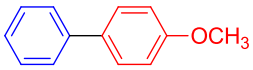
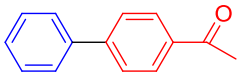
optimization of Suzuki the coupling reaction proceeding at room temperature in open air. Additionally, this protocol also compared to the reaction performed under nitrogen atmosphere and the results showed that there is not any significance difference among the yields obtained from reaction under nitrogen atmosphere (Table 1, entry 16). To show how importance of the methoxy chain, we compared the activity of the **4c** with a very similar complex which is not bear a methoxy chain. The palladium complex which *N*,*N*-substituted with 3,5 dimethyl benzyl group is already synthesised and published[41h] by our group (See the paper for **3a** compound). From our previous study, this complex tested in different conditions but totally needs temperature to catalyse Suzuki coupling reaction of aryl bromides. The reaction of complex **3a** in the same catalytic condition gives lower yields in longer time at room temperature (Table 1, entry 17). From these results, it is clear that a methoxy chain is very important for the increase solubility of the complexes **3a-d** and **4a-e**.

To evaluate the scope our catalytic system, different aryl bromides were examined (Table 2). As shown in Table 2, both electron-donating and electron-withdrawing groups bearing aryl bromides effectively afford the corresponding products (61-97 %) in short time at room temperature (Table 2, entries 1-6). For example, 4-bromoacetophenone afforded a good yield in 10 min, resulting in a TOF of 1000 h^{-1} (Table 2, entry 2). However, -CH_3 and -OCH_3

Table 2. Catalytic activities of **3a-d** and **4a-e** complexes in the Suzuki-Miyaura coupling reactions under optimized conditions.[a]



Entry	Product	[Pd-NHC]/yield (%)[b]								
		3a	**3b**	**3c**	**3d**	**4a**	**4b**	**4c**	**4d**	**4e**
1		80	82	75	54	72	93	68	88	78

2[c]		96	88	91	87	89	95	93	77	85
3		80	67	52	51	57	89	57	77	57
4		66	71	74	54	65	86	72	63	86
5[c]		94	96	85	88	91	96	88	91	96
6[c]		90	81	83	74	90	92	86	84	87
7[d]		98	95	92	94	96	98	95	98	98
8[e]		-	-	-	-	-	-	-	-	-
9		trace	trace	trace	trace	trace	trace	trace	trace	trace

[a]reaction condition: 0.5 mol% [Pd-NHC], 1 mmol *p*-R-C_6H_4Br, 1.1 mmol phenylboronic acid, 1.0 mmol K_2CO_3, rt, 1h. Yields are average of two runs.
[b] Isolated yield
[c]10 min.
[d] 1 mol%[Pd-NHC]
[e] 1 mmol 4-(OCH_3)-C_6H_4Cl

substituted aryl bromides showed slightly lower activity than $–NO_2$, and -$COCH_3$ substituted aryl bromides due to the high nuclophilicity of the electron donating substituents (Table 2, entries 1,3). However, increasing the catalyst loading up to 1 mol% resulted in an increased yield (98%) (Table 2, entry 7). Catalyst **4b** and others did not show any activity when 4-chloro anisole used as substrate (Table 2, entry 8). Trace amount products were observed with 4-chloroacetophenon used as substrate (Table 2, entry 9). This low catalytic activity of complexes with 4-chloroaryl substrates may be attribute to low oxidative addition rate of aryl chlorides to palladium(0) in this catalytic conditions. When the catalytic activities of the complexes **3a-d** and **4a-e** are compared among themselves, the complex **4b** has showed slightly higher catalytic activity, independent from the nature of the substrate. It may be due

to well-balanced electronic and steric properties of **4b** than other complexes. All tested complexes have similar steric bulky. Thus, we think that electronic properties of the complexes are more prevalent than steric parameters of the complexes. Also, this catalytic system is almost equally effective for electronically rich and poor aryl bromides. Thus, our study is pretty significant for the production of coupled product at room temperature in very short time using green solvents with low catalyst loading (0.5 mol%) without need to any additives such as NaX, $NaSO_4$ etc.

These new catalysts have a different and superior advantage. The presence of a NHC ligand bearing a second different donating group such as $–OCH_3$ on the metal may radically increase the catalytic performance of catalyst. The chelating nature of these ligands promote production of highly stable complexes. [41i-k] The hemilable part in such ligands is capable of reversible dissociation to produce vacant coordination sites allowing complexation of substrates during the catalytic cycle. At the same time the strong donor carbene moiety remains connected to the metal center.

To compare the catalytic activity of our system with existing catalysts, there are a few reports in the literature on Suzuki-Miyaura cross-couplings of aryl bromides running in our catalyst system. [42-49] When considering the amount of catalyst, time, temperature and solvent, the yield is better than the literature by our catalyst system. [41] It is believed that this performance is due to the presence of a second donor group on the catalyst that mentioned above. However, there are more effective catalyst reported on literature for Suzuki cross-coupling reaction of aryl chlorides or bromides.

4. Conclusion

In summary, new palladium-NHC complexes bearing a methoxyethyl on the side chain have been synthesised and characterised by different spectroscopic techniques. The catalytic reactivity of these complexes in Suzuki-Miyaura cross-coupling reactions with aryl bromides

at room temperature in aqueous media. Among these complexes, complex **4b** exhibited good catalytic performance with different types of aryl bromides when other complexes showed lower catalytic activity. The catalyst system described here has several advantages including low catalyst loading, substrate tolerance, very good yields, room temperature, green solvents, short reaction times and very simple procedure. These results represent a significant improvement in the field of the C-C bond formation reactions.

Acknowledgements

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Highlights

- New N-heterocyclic carben ligands bearing methoxyethyl on the side chain have been synthesized.
- New palladium- NHC-pyridine complexes have been synthesized.
- palladium- NHC-pyridine complexes performed lovely catalytic activity at room temperature in open air.
- With this catalyse system aryl bromides arylated under mild reaction condition.