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PALLADIUM-BASED COMPLEXES BEARING *N*-HETEROCYCLIC CARBENE (NHC) AND TRIPHENYLPHOSPHINE (PPh_3) LIGANDS: SYNTHESIS, CHARACTERIZATION, AND ITS APPLICATION ON SONOGASHIRA CROSS-COUPLING REACTIONS IN AQUEOUS MEDIA

ABSTRACT

Herein, we reported the synthesis of a new series of Pd-based complexes bearing *N*-heterocyclic carbene (NHC) and triphenylphosphine (PPh_3) ligands. These complexes have been prepared from the (NHC)Pd(II)(pyridine) complexes and PPh_3. All (NHC)Pd(II)PPh_3 complexes have been characterized by using ^{1}H NMR, ^{13}C {^{1}H}NMR, ^{31}P {^{1}H}NMR, and FTIR spectroscopy and elemental analysis technique. Here, as a result of low catalyst [(NHC)Pd(II)PPh_3] loading (0.01 mmol), acetylene derivatives with various functional groups were synthesized from the coupling of phenylacetylene with various aryl bromides in the aqueous medium.

Keywords: Aqueous Medium, *N*-heterocyclic carbenes, Palladium Complex, Sonogashira Reaction, Triphenylphosphine

1. INTRODUCTION

Carbenes are reactive intermediates with 6 electrons in their valence shell. Cyclic carbenes containing nitrogen atoms in their structure are called *N*-heterocyclic carbenes (NHCs). In 1968, the metal-NHC (M-NHC) complex was synthesized using NHC ligands [1 and 2]. After this development, NHC ligands gained importance in the fields of organic and organometallic chemistry. A new era in this topic has begun, particularly with the synthesis of the first stable and storable ligand by Arduengo et al [3]. NHCs can form stable complexes with almost all transition metals thanks to their structural and electronic properties [4]. Its properties allow the formation of strong metal carbene bonds, increasing the thermal stability of the M-NHC complexes formed [5].

Phosphine ligands have made rapid advances in organometallic chemistry. These ligand types are still widely used in industry because they are inexpensive and readily available [6]. By altering traditional Pd-phosphine catalysts, water-soluble Pd catalysts for cross-coupling processes have recently been developed [7]. However, there are some limitations. These ligands are sensitive to air and moisture, limiting catalyst reuse and causing unwanted waste under aqueous reaction conditions. However, a significant issue still exists with the generation of hazardous intermediates during the synthesis of phosphine ligands [8]. The choice of more stable and less hazardous ligands needs to be chosen because these circumstances present a

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challenge for green chemistry. NHCs are therefore a possible substitute for phosphines as support ligands for several Pd-catalyzed crosslinking processes [9].

The development of water-soluble Pd complexes as efficient catalysts for cross-coupling reactions in aqueous media has attracted a great deal of research since the second half of the 20th century [10]. Recently, water-soluble catalysts have been developed using Pd-based complexes containing NHC ligands [11]. In recent years, it is of great importance in the chemical industry to use cheap and environmentally friendly solvents (such as water), which are also important in terms of green chemistry, and to prefer safer and more beneficial reactions [12]. Palladium-catalyzed cross-coupling reactions in aqueous environments are among the most popular processes for the synthesis of delicate compounds, useful materials, and industrially important building blocks in this regard [13].

In the Sonogashira cross-coupling process, terminal acetylenes are combined with aryl, heteroaryl, or vinyl halides in the presence of a stoichiometric transition metal ion to produce alkynes. In terms of producing alkynes with different functional groups, it is one of the most significant and effective processes in organic synthesis. This method was developed and led to the development of many synthetic methodologies such as the widely used Pd-catalyzed aryl coupling reactions [14]. In recent years, new Pd-based complexes containing NHC/phosphine ligand mixture have been synthesized and their catalytic activities in cross-linking reactions have been investigated [15,16]. In addition, these new complexes have been reported to be active catalysts in Sonogashira reactions [17].

In this study, we presented the synthesis and characterization of a new series of 3-cyanobenzyl substituted Pd-based (NHC)Pd(II)PPh_3 complexes and their catalytic activity in Sonigashira reactions in the aqueous medium.

2. RESEARCH SIGNIFICANCE

Today, the synthesis of new chemicals is of great importance in the field of medicine, pharmacology, agriculture, and materials science. It is vital that these chemicals are obtained in a cleaner way (green chemistry), with lower energy, and in a shorter time. Therefore, the synthesis of new, selective, and effective catalysts is of great importance.

Highlights:

- A new series of (NHC)Pd(PPh_3) complexes have been synthesized as selective and effective catalysts.
- All (NHC)Pd(II)PPh_3 complexes have been characterized by using ^{1}H NMR, ^{13}C {^{1}H}NMR, ^{31}P {^{1}H}NMR, and FTIR spectroscopy and elemental analysis technique.
- The catalytic activities of all complexes were investigated in Sonogashira reactions in an aqueous medium.

3. EXPERIMENTAL

The (NHC)Pd(II)PPh_3 complexes (1a-g) bearing cyanobenzyl group were synthesized in an inert atmosphere using the standard Schlenk technique. The chemical used in this study was purchased by Acros, Isolab, Merck, and Sigma-Aldrich Chemical Co., and used as received without any purification procedure. Melting points were identified in glass capillaries with an Electrothermal-9200 m.p. apparatus. FTIR spectra were saved in the range of 400–4000 cm^{-1} on Perkin Elmer Spectrum 100 FTIR spectrometer. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded using either a Bruker Avance III 400 MHz NMR spectrometer

operating at NMR (400 MHz for ^{1}H and 100 MHz for ^{13}C NMR) in the $CDCl_3$ with tetramethylsilane as an internal reference.

3.1. Dibromo[1-benzyl-3-(3-cyanobenzyl)benzimidazol-2-ylidene] triphenylphosphinepalladium(II), 1a

Dibromo[1-benzyl-3-(3-cyanobenzyl)benzimidazol-2-ylidene]pyridine palladium(II) (114 mg 0,17 mmol) and PPh_3 (45 mg 0,17 mmol) were mixed in chloroform (20 mL) at room temperature for 24 hours. Then, the excess solvent was evaporated under a vacuum. The crude product was crystallized from a dichloromethane/pentane mixture [18]. Yield: 77% (112 mg); m.p.: 201-202 °C; $\nu_{(CN\ 2\text{-}C)}$: 1425 cm^{-1}; $\nu_{(CN\ nitrile)}$: 2227 cm^{-1}. Elemental Analysis% Calculated: $C_{40}H_{32}Br_2N_3PPd$: C: 56.40; H: 3.79; N: 4.93. Found: C: 56.37; H: 3.82; N: 4.95.

^{1}H NMR (400 MHz, $CDCl_3$), δ; 6.16 (s, 2H, $-C\boldsymbol{H}_2C_6H_5$); 6,19 (s, 2H, $-C\boldsymbol{H}_2C_6H_4$-3-CN); 7.07-7.54 (m, 13H, Ar-***H***). ^{13}C NMR (100 MHz, $CDCl_3$), δ; 53.6 ($-\boldsymbol{C}H_2C_6H_5$); 57.8 ($-\boldsymbol{C}H_2C_6H_4$-3-CN); 118.4 (Ar-***C***N); 108.4, 108.7, 110.6, 111.8, 114.8, 115.9, 123.6, 128.1, 128.5, 128.6, 128.9, 130.5, 131.4 and 135.6 (Ar-***C***); 168.5 (*Pd*-$\boldsymbol{C}_{carbene}$).

3.2. Dibromo[1-(3-cyanobenzyl)-3-(2-methylbenzyl)benzimidazol-2-ylidene]triphenylphosphinepalladium(II), 1b

The compound **1b** was obtained from dibromo[1-(3-cyanobenzyl)-3-(2-methylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II) (116 mg. 0.17 mmol) and PPh_3 (45 mg. 0.17 mmol) by using a same method to compound **1a**. Yield: 72% (106 mg); m.p.: 204-205 °C; $\nu_{(CN\ 2\text{-}C)}$: 1430 cm^{-1}; $\nu_{(CN\ nitrile)}$: 2224 cm^{-1}. Elemental Analysis% Calculated: $C_{41}H_{34}Br_2N_3PPd$: C: 56.87; H: 3.96; N: 4.85. Found: C: 56.91; H: 3.95; N: 4.89.

^{1}H NMR (400 MHz, $CDCl_3$), δ; 2.35 (s, 3H, $-CH_2C_6H_4$-2-$C\boldsymbol{H}_3$); 4.72 and 4.89 (d, *J*: 12 Hz, 2H, $-C\boldsymbol{H}_2C_6H_4$-2-CH_3); 5.14 (s, 2H, $-C\boldsymbol{H}_2C_6H_4$-3-CN); 6.40-7.91 (m, 27H, Ar-***H***). ^{13}C NMR (100 MHz, $CDCl_3$), δ; 19.8 ($-CH_2C_6H_4$-2-$\boldsymbol{C}H_3$); 50.5 ($-\boldsymbol{C}H_2C_6H_4$-2-CH_3); 52.4 ($-\boldsymbol{C}H_2C_6H_4$-3-CN); 118.3 (Ar-***C***N); 111.2, 112.1, 112.7, 123.6, 123.7, 126.6, 127.9, 128.2, 128.5, 128.6, 129.2, 130.1, 130.4, 134.2, 134.7, 138.7, 149.9 110.8, 111.4, 112.8, 117.7, 123.1, 128.0, 128.3, 129.8, 130.9, 131.3, 132.0, 132.1, 132.2, 133.2, 134.2, 134.5, 134.9, 135.2 and 135.5 (Ar-***C***); 178.0 (*Pd*-$\boldsymbol{C}_{karben}$).

3.3. Dibromo[1-(3-cyanobenzyl)-3-(3-methylbenzyl)benzimidazol-2-ylidene]triphenylphosphinepalladium(II), 1c

The compound **1c** was obtained from dibromo[1-(3-cyanobenzyl)-3-(3-methylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II) (116 mg. 0.17 mmol) and PPh_3 (45 mg. 0.17 mmol) by using a same method to compound **1a**. Yield: 79% (115 mg); m.p.:182-183°C; $\nu_{(CN\ 2\text{-}C)}$: 1427 cm^{-1}; $\nu_{(CN\ nitrile)}$: 2224 cm^{-1}. Elemental Analysis% Calculated: $C_{41}H_{34}Br_2N_3PPd$: C: 56.87; H: 3.96; N: 4.85. Found: C: 56.84; H: 3.98; N: 4.90.

^{1}H NMR (400 MHz, $CDCl_3$), δ; 2.32 (s, 3H, $CH_2C_6H_4$-3-$C\boldsymbol{H}_3$); 4.73 (dd, *J*: 16 Hz, 1H, $-C\boldsymbol{H}_2C_6H_4$-3-CH_3); 5.10 (d, *J*: 24 Hz, 1H, $-CH_2C_6H_4$-3-CH_3); 6.31 and 6.45 (d, 2H, J: 12 Hz, $-C\boldsymbol{H}_2C_6H_4$-3-CN); 6.69-8.18 (m, 27H, Ar-***H***). ^{13}C NMR (100 MHz, $CDCl_3$), δ; 21.4 ($-CH_2C_6H_4$-3-$\boldsymbol{C}H_3$); 52.3 ($-\boldsymbol{C}H_2C_6H_4$-3-CH_3); 53.6 ($-\boldsymbol{C}H_2C_6H_4$-3-CN); 118.3 (Ar-***C***N); 111.9, 112.2, 112.7, 114.2, 115.3, 123.5, 125.5, 128.4, 128.5, 128.6, 129.2, 129.4, 130.1, 130.4, 131.2, 131.3, 132.2, 133.3, 133.5, 134.2, 134.3, 134.7, 135.5, 136.1 and 138.8 (Ar-***C***); 171.7 (*Pd*-$\boldsymbol{C}_{karben}$).

3.4. Dibromo[1-(3-cyanobenzyl)-3-(4-methylbenzyl)benzimidazol-2-ylidene]triphenylphosphinepalladium(II), 1d

The compound **1d** was obtained from dibromo[1-(3-cyanobenzyl)-3-(4-methylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II) (116 mg.

0.17 mmol) and PPh_3 (45 mg. 0.17 mmol) by using a same method to compound **1a**. Yield: 82% (0.121 g); m.p.: 205-207°C; $\nu_{(CN\ 2\text{-}C)}$: 1428 cm^{-1}; $\nu_{(CN\ nitrile)}$: 2225 cm^{-1}. Elemental Analysis% Calculated: $C_{41}H_{34}Br_2N_3PPd$: C: 56.87; H: 3.96; N: 4.85. Found: C: 56.85; H: 3.94; N: 4.88.

^1H NMR (400 MHz, $CDCl_3$), δ; 2.28 (s, 3H, $-CH_2C_6H_4-4-C\boldsymbol{H}_3$); 4.67 and 4.81 (d, J: 12 Hz, 2H, $-C\boldsymbol{H}_2C_6H_4-4-CH_3$); 6.29 and 6.45 (d, *J*: 16 Hz, 2H, $-C\boldsymbol{H}_2C_6H_4-3-CN$); 6.62-7.94 (m, 27H, Ar-***H***). ^{13}C NMR (100 MHz, $CDCl_3$), δ; 21.2 ($-CH_2C_6H_4-4-\boldsymbol{C}H_3$); 50.3 ($-\boldsymbol{C}H_2C_6H_4-4-CH_3$); 53.5 ($-\boldsymbol{C}H_2C_6H_4-3-CN$); 118.3 (Ar-***C***N); 107.7, 111.1, 112.1, 112.7, 116.7, 123.4, 123.5, 128.4, 128.5, 128.7, 129.6, 129.9, 130.1, 130.4, 130.6, 131.2, 131.3, 132.2, 133.3, 134.1, 134.2, 134.3, 134.8 and 135.5 (Ar-***C***); 175.5 (*Pd-**C**karben*).

3.5. Dibromo[1-(3-cyanobenzyl)-3-(2,4,6-trimethylbenzyl) benzimidazol-2-ylidene]triphenylphosphinepalladium(II), 1e

The compound **1e** was obtained from dibromo[1-(3-cyanobenzyl)-3-(2,4,6-trimethylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II) (0.121 g. 0.17 mmol) and PPh_3 (45 mg. 0.17 mmol) by using a same method to compound **1a**. Yield: 80% (0.122 g); m.p.: 212-214°C; $\nu_{(CN\ 2\text{-}C)}$: 1422 cm^{-1}; $\nu_{(CN\ nitrile)}$: 2223 cm^{-1}. Elemental Analysis% Calculated: $C_{43}H_{38}Br_2N_3PPd$: C: 57.77; H: 4.28; N: 4.70. Found: C: 57.80; H: 4.25; N: 4.68.

^1H NMR (400 MHz, $CDCl_3$), δ; 2.35 and 2.36 (s, 9H, $-CH_2C_6H_2(C\boldsymbol{H}_3)_3-2,4,6$); 4.39 and 5.11 (d, *J*: 16 Hz, 2H, $-C\boldsymbol{H}_2C_6H_2(CH_3)_3-2,4,6$); 5.82 and 6.41 (d, *J*: 8 Hz, 2H, $-C\boldsymbol{H}_2C_6H_4-3-CN$); 6.50-7.90 (m, 25H, Ar-***H***). ^{13}C NMR (100 MHz, $CDCl_3$), δ; 20.7 and 21.1 ($-CH_2C_6H_2(\boldsymbol{C}H_3)_3-2,4,6$); 50.8 ($\boldsymbol{C}H_2C_6H_2(CH_3)_3-2,4,6$); 52.3 ($\boldsymbol{C}H_2C_6H_4-3-CN$); 118.3 (Ar-***C***N); 110.8, 111.8, 112.6, 123.9, 126.2, 128.6, 129.6, 130.1, 131.2, 131.3, 132.0, 132.1, 133.1, 133.9, 134.2, 134.9, 135.5 and 139.4 (Ar-***C***); 177.4 (*Pd-**C**karben*).

3.6. Dibromo[1-(3-cyanobenzyl)-3-(2,3,5,6-tetramethylbenzyl) benzimidazol-2-ylidene]triphenylphosphinepalladium(II), 1f

The compound **1f** was obtained from dibromo[1-(3-cyanobenzyl)-3-(2,3,5,6-tetramethylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II)(123 mg. 0.17 mmol) and PPh_3 (45 mg. 0.17 mmol) by using a same method to compound **1a**. Yield: 78% (0.120 g); m.p.: 233-235 °C; $\nu_{(CN\ 2\text{-}C)}$: 1425 cm^{-1}; $\nu_{(CN\ nitrile)}$: 2221 cm^{-1}. Elemental Analysis% Calculated: $C_{44}H_{40}Br_2N_3PPd$: C: 58.20; H: 4.44; N: 4.63. Found: C: 58.16; H: 4.47; N: 4.66.

^1H NMR (400 MHz, $CDCl_3$), δ; 2.23 (s, 12H, $-CH_2C_6H(C\boldsymbol{H}_3)_4-2,3,5,6$); 6.31 and 5.28 (d, *J*: 16 Hz, 2H, $-C\boldsymbol{H}_2C_6H(CH_3)_4-2,3,5,6$); 5.69 and 6.39 (d, *J*: 8 Hz, 2H, $-C\boldsymbol{H}_2C_6H_4-3-CN$); 6.56-7.92 (m, 24H, Ar-***H***). ^{13}C NMR (100 MHz, $CDCl_3$), δ; 16.3 and 20.5 ($-CH_2C_6H_2(\boldsymbol{C}H_3)_3-2,4,6$); 51.7 ($\boldsymbol{C}H_2C_6H_2(CH_3)_3-2,4,6$); 52.0 ($\boldsymbol{C}H_2C_6H_4-3-CN$); 118.3 (Ar-***C***N); 110.9, 111.7, 112.6, 122.8, 123.6, 128.4, 128.5, 128.6, 129.1, 130.1, 131.2, 131.4, 132.0, 132.1, 132.2, 133.1, 133.2, 133.7, 134.4, 134.5, 134.6, and 135.5 (Ar-***C***); 177.1 (*Pd-**C**karben*).

3.7. Dibromo[1-(3-cyanobenzyl)-3-(2,3,4,5,6-pentamethylbenzyl) benzimidazol-2-ylidene]triphenylphosphinepalladium(II), 1g

The compound **1g** was obtained from dibromo[1-(3-cyanobenzyl)-3-(2,3,4,5,6-pentamethylbenzyl) benzimidazole-2 ylidene]pyridinepalladium(II) (126 mg. 0.17 mmol) and PPh_3 (45 mg. 0.17 mmol) by using a same method to compound **1a**. Yield: 81% (125 mg); m.p.: 178-179°C; $\nu_{(CN\ 2\text{-}C)}$: 1425 cm^{-1}; $\nu_{(CN\ nitrile)}$: 2227 cm^{-1}. Elemental Analysis% Calculated: $C_{44}H_{39}Br_2N_3PPd$: C: 58.27; H: 4.33; N: 4.63. Found: C: 58.32; H: 4.35; N: 4.59.

^1H NMR (400 MHz, $CDCl_3$), δ; 1.97, 2.21 and 2.31 (s, 15H, $-CH_2C_6(C\boldsymbol{H}_3)_5-2,3,4,5,6$); 4.29 and 5.30 (d, J: 16 Hz, 2H, $-C\boldsymbol{H}_2C_6(CH_3)_5-$

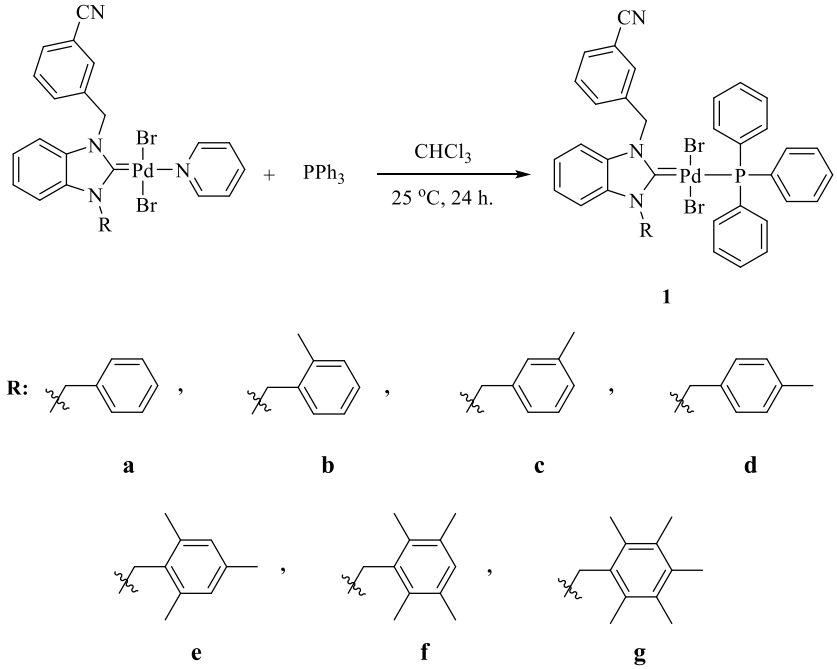
2,3,4,5,6); 5.77 and 6.38 (d, *J*= 8 and 16 Hz, 2H, -C***H***$_2$C$_6$H$_4$-3-CN); 6.40-7.95 (m, 23H, Ar-***H***). ^{13}C NMR (100 MHz, $CDCl_3$), δ; 16.9, 17.3 and 17.4 (-CH_2C_6(***C***H$_3$)$_5$-2,3,4,5,6); 52.1 (-***C***H$_2$C$_6$(CH$_3$)$_5$-2,3,4,5,6); 52.3 (-***C***H$_2$C$_6$H$_4$-3-CN); 118.4 (Ar-***C***N); 110.9, 111.9, 112.9, 122.9, 123.4, 126.5, 128.3, 128.7, 130.0, 131.0, 131.9, 133.1, 134.4, 135.8 and 136.9 (Ar-***C***); 177.0 (*Pd-**C**$_{karben}$*).

4. RESULTS AND DISCUSSION

4.1. Synthesis of (NHC)Pd(II)PPh$_3$ Complexes (1a-g)

In this work, the new (NHC)Pd(II)PPh$_3$ complexes bearing the 3-cyanobenzyl group are defined and their preparation is shown in Scheme 1. These complexes **1a-g** were prepared from the starting material Pd-PEPPSI complexes [19] and triphenylphosphine ligand. All complexes that are stable to air and moisture are soluble in halogenated solvents like dichloromethane and chloroform. However, it is also soluble in polar organic solvents such as ethyl alcohol, dimethylformamide, and dimethylsulfoxide. It was slightly soluble in polar solvents such as water and diethyl ether, but insoluble in nonpolar organic solvents such as pentane, hexane, and toluene. All complexes were obtained as a light-yellow solid in between 72% and 82% yields. The formation of the new (NHC)Pd(II)PPh$_3$ complexes bearing 3-cyanobenzyl group was confirmed using FT-IR, ^{1}H NMR ^{13}C NMR, and ^{31}P NMR spectroscopic methods and elemental analysis techniques. The spectra obtained as a result of the analysis are consistent with the suggested formulas. No peaks at about 9.00 ppm, which correspond to the pyridine protons of the starting material [19], were seen when the ^{1}H NMR spectra were examined. This demonstrates that the pyridine ligand has been removed from the structure. Moreover, an increase in the aromatic protons region due to the PPh$_3$ ligand was observed.

In this case, we could say that the PPh$_3$ ligand is added to the structure of the complexes. Furthermore, all aromatic proton peaks of the NHC ligands were between 6.50 and 8.00 ppm, while benzylic peaks were about 5.50 and 6.00 ppm and methyl peaks on benzene were seen at around 2.30 ppm. When ^{13}C NMR spectra were examined; the Pd-C$_{Carbene}$ peaks, which were seen at roughly 165 ppm in the starting materials, were found to have shifted to between 170 and 180 ppm. The carbon peak in the cyano group, which is attached to the benzene 3 position, was observed at around 120 ppm. Furthermore, aromatic carbon peaks between 110 and 140 ppm, benzylic carbon peaks between 50 and 55 ppm, and methyl carbon peaks on benzene between 20 and 22 ppm were observed. Finally, single peaks around 26 ppm observed in the ^{31}P NMR spectrum for all (NHC)Pd(II)PPh$_3$ complexes prove the presence of the Pd-P bond in the structure of the complexes. When the FT-IR spectra of all complexes are examined; ν(CN$_{benzimidazol}$) stretching bands showing between 1422 and 1430 cm^{-1} and ν(CN$_{nitrile}$) stretching bands showing at 2221 and 2227 cm^{-1} were clearly observed. When the elemental analysis results were evaluated, it was observed that the calculated values were very close to the found values. The findings of all data are consistent with previous research [17, 18 and 20].



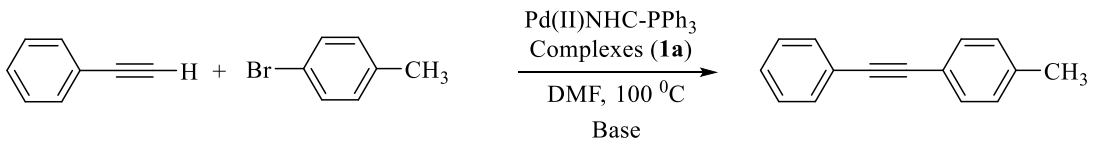
Scheme 1. Synthesis of the (NHC)Pd(II)PPh_3 Complexes Bearing 3-cyanobenzyl Group 1a-g

4.2. Determining Optimum Conditions

4.2.1. Base Determination

We started by choosing a variety of bases, including K_2CO_3, Cs_2CO_3, NaOH, and KOH. Phenylacetylene (1.5 mmol), 4-bromotoluen (1 mmol), and catalyst (0.01 mmol complex 1a) were mixed in 4 ml of DMF and heated to 100°C for four hours for each base under the same conditions. As a result of the experiments, DMF was evaporated under a vacuum. The reaction mixture was purified by passing through a silica gel column (1 cm thick) in ethylacetate: hexane (1:5) mixture. The conversion of phenylacetylene to diphenylacetylene was calculated from the conversion of 4-bromotoluene. The conversion of 4-bromotoluene was used to calculate yields (by GC). The results are illustrated in Table 1 as % conversion. When Cs_2CO_3 was utilized as the base, the maximum yield as the conversion was attained. So, subsequent experiments used Cs_2CO_3 as the base [21].

Table 1. Base determination for Sonogashira coupling reactions



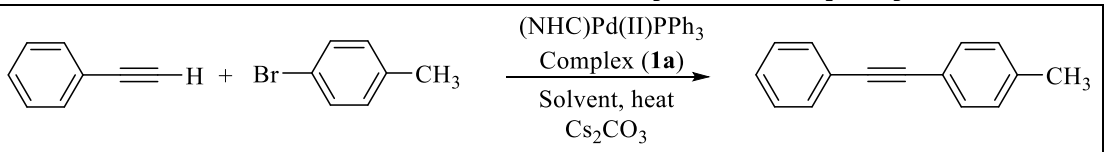
Entry	Solvent	Base	Temperature (°C)	Time (hour)	Conversion (%)
1	DMF	K_2CO_3	100	4	53
2	DMF	Cs_2CO_3	100	4	93
3	DMF	NaOH	100	4	27
4	DMF	KOH	100	4	45

Reaction conditions: Phenylacetylene (1.5 mmol), 4-bromotoluene (1 mmol), NHC-Pd(II)-PPh_3 complex 1a (0.01mmol), base (2 mmol) and DMF (4 ml) were added to the Schlenk tube, open to air. It was stirred at 100°C for 4 hours

4.2.2. Solvent Determination

For the solvent determination, phenylacetylene (1.5 mmol), 4-bromotoluene (1 mmol), Cs_2CO_3 (2 mmol) and NHC-Pd(II)-PPh_3 complex 1a (0.01 mmol) was dissolved various solvents (3 mL) . The temperature of the medium was adjusted by considering the boiling points of solvents. There are five different solvents used: DMF, $C_6H_5CH_3$, EtOH, H_2O, and THF. There are also two solvent mixtures: H_2O/EtOH (2:1) and H_2O/DMF (2:1). The conversion of 4-bromotoluene was used to calculate yields (by GC). The results are illustrated in Table 2 as % conversion. The highest yield and conversion were obtained when DMF and H_2O/DMF (2:1) were used as the solvent. However, later experiments employed an H_2O/DMF (2:1) mixture as the solvent because it was cheap and environmentally friendly [22].

Table 2. Solvent determination for Sonogashira coupling reactions



Entry	Solvent	Base	Temperature (°C)	Time (hour)	Conversion (%)
1	DMF	Cs_2CO_3	100	4	96
2	EtOH	Cs_2CO_3	78	4	72
3	CH_3CN	Cs_2CO_3	80	4	48
4	THF	Cs_2CO_3	67	4	61
5	$C_6H_5CH_3$	Cs_2CO_3	100	4	71
6	H_2O	Cs_2CO_3	100	4	77
7	H_2O/EtOH (2:1)	Cs_2CO_3	80	4	83
8	H_2O/DMF (2:1)	Cs_2CO_3	100	4	91

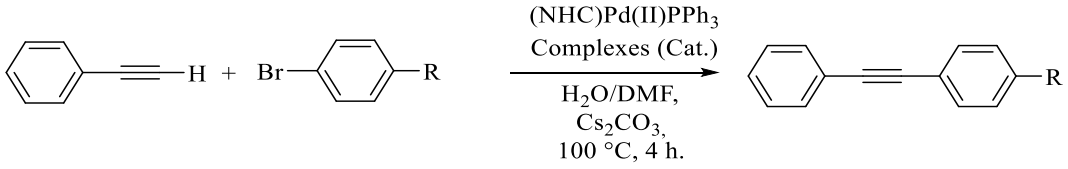
Reaction conditions: Phenylacetylene (1.5 mmol), 4-bromotoluene (1 mmol), NHC-Pd(II)-PPh_3 complex 1a (0.01 mmol), Cs_2CO_3 (2 mmol) and Solvent (3 ml) were added to the Schlenk tube, open to air. It was stirred for 4 hours at the appropriate temperature

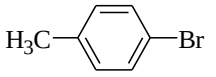
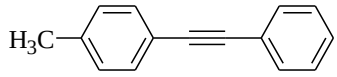
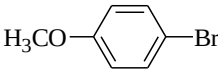
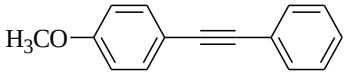
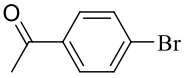
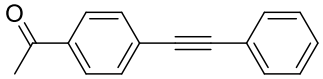
After the optimum conditions were determined, the catalytic activities of the prepared NHC-Pd(II)-PPh_3 complexes **1a-g** in Sonogashira coupling reactions were investigated under optimum conditions. Reaction conditions; phenylacetylene (1.5 mmol), aryl halides (1 mmol), Cs_2CO_3 (2 mmol), and NHC-Pd(II)-PPh_3 complexes **1a-g** (0.01 mmol) H_2O/DMF (2ml /1ml) open to the air in solvent system was added to the Schlenk tube and stirred for 4 hours at 100 °C. At the end of the experiment, the organic phase was extracted by adding ethyl acetate to the reaction mixture. After the organic phase was separated, it was dried with $MgSO_4$. It was passed through a 1 cm thick silica gel column using a solvent mixture of ethyl acetate: hexane (1:5). After the excess solvent was evaporated, the control of the products was examined by GC. The conversion of the aryl halide was taken into consideration while calculating the reaction yield. Conversions are given in Tables 3 and 4 as percent (%).

Catalytic experiments using iodinated substrates in Sonogashira coupling reactions were carried out with high yield in a short time under mild conditions. No differences in the activity of the catalysts were found when the catalytic experiments using 4-iodotoluene as the substrate in Sonogashira reactions were studied. When the catalytic activities of the synthesized NHC-Pd(II)-PPh_3 complexes **1a-g** in Sonogashira coupling reactions are compared with similar studies, it can be said that these complexes are active catalysts (Table 3) [23].

In experiments with aryl chlorides, it was observed that the complexes were less active. Quite low conversions were observed at 100°C for 8 hours. However, slightly better conversions were achieved at 100°C for 16 hours. Chlorobenzene and 4-chloroacetophenone containing electron withdrawing group were used as substrates. The sterical bulky **1a** complex and the sterical bulky **1g** complex were utilized as catalysts. Although complex **1a** with small steric bulky appeared more active, no significant activity difference was observed (Table 3.)

Table 3. Use of (NHC)Pd(II)PPh_3 complexes as catalysts in Sonogashira coupling reactions



Entry	Substrate	Product	Catalyst	Conversion (%)
1			1a	99
2			1b	96
3			1c	72
4			1d	99
5			1e	95
6			1f	88
7			1g	81
8			1a	80
9			1b	99
10			1c	66
11			1d	96
12			1e	93
13			1f	68
14			1g	65
15			1a	99
16			1b	100
17			1c	99
18			1d	98
19			1e	100
20			1f	100
21			1g	100

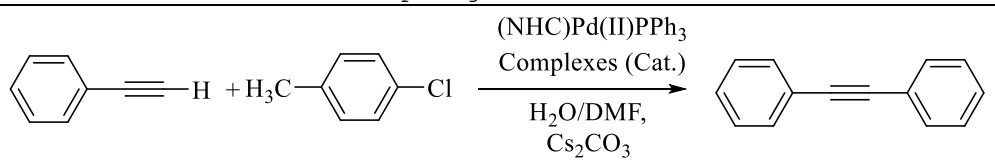
Reaction conditions: Phenylacetylene (1.5 mmol), 4-arylbromide (1 mmol), (NHC)Pd(II)PPh_3 complex 1a-g (0.01mmol), Cs_2CO_3 (2 mmol) and H_2O/DMF (2:1) (3 ml) was added to the Schlenk tube open to air. It was stirred at 100°C for 4 hours

All complexes displayed extremely high catalytic activity. Regardless of whether the substituents were steric bulky, all complexes could say to be very active (Table 3).

It was observed that the electronic properties of the substrates had a significant impact on the catalytic activity. When findings with brominated substrate are studied, it becomes clear that substrates with electron-withdrawing groups, like $-COCH_3$, convert at a higher efficiency than those with electron-donating groups, such as $-OCH_3$ and $-CH_3$. In our work, 4-bromotoluene, 4-bromoacetophenone and 4-bromoanisole were used as aryl bromides. When aryl halides are compared, it is seen that the conversion of 4-bromoacetophenone bearing electron withdrawing group ($-COCH_3$) is more than 4-bromoanisole bearing electron donating group ($-OCH_3$) (Table 3.). The product conversion of substrates containing methyl ($-CH_3$) substituents is higher than that of substrates containing methoxy ($-OCH_3$) group because the methoxy ($-OCH_3$) group has a stronger electron-donating property than the methyl ($-CH_3$) group. The bond between the carbon atom and the

bromine atom (C-Br) in the benzene, as well as the higher polarization of the electron-withdrawing group in the para position on the benzene, may be responsible for this condition [24]. Similar works also obtained outcomes that were similar [23, 24, 25, 27, and 28].

Table 4. Use of (NHC)Pd(II)PPh_3 complexes as catalysts in Sonogashira coupling reactions



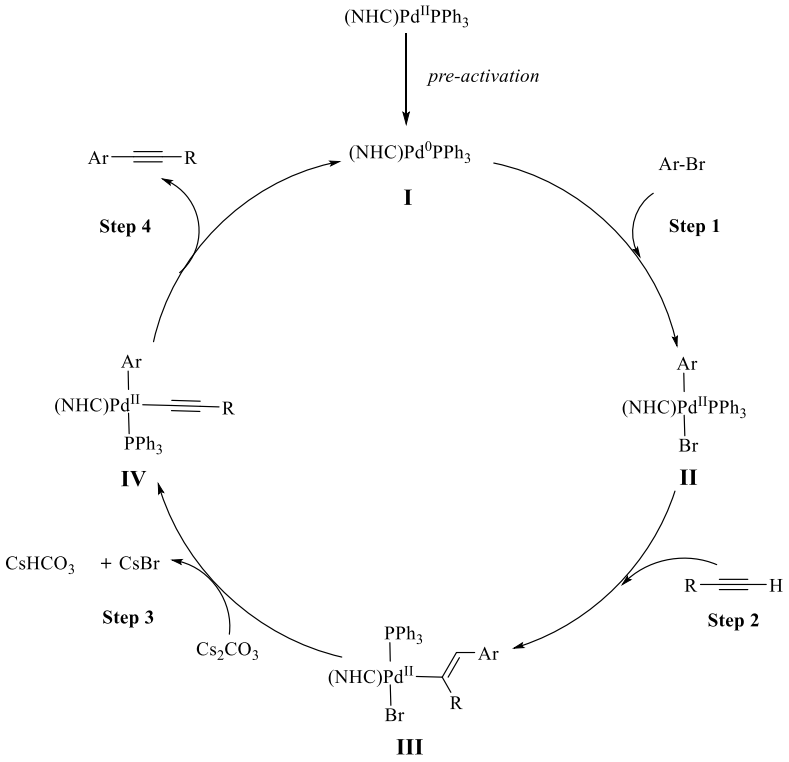
Test	Time (hour)	Catalyst	Conversion (%)
1	8	1e	12
2	8	1f	17
3	16	1e	78
4	16	1f	80

Reaction conditions: Phenylacetylene (1.5 mmol), arylchloride (1 mmol), (NHC)Pd(II)PPh_3 complex 1a-g (0.01mmol), Cs_2CO_3 (2 mmol) and H_2O/DMF (2:1) (3 ml) added to the Schlenk tube open to air and stirred at 100°C

When the proposed catalytic cycling mechanism for cross-coupling reactions was investigated, it was reported that the electronic properties of the catalyst affected oxidative addition. Also, the steric bulky of the catalysts facilitate reductive elimination [25]. Because of this, the 3-cyanobenzyl group in the structure of the (NHC)Pd(II)PPh_3 complexes (catalysts) may facilitate oxidative addition during the catalytic cycle (electronic properties). Additionally, it could ease reductive elimination in the catalytic cycle due to the steric bulky (structural properties) of the 3-cyanobenzyl group on catalysts.

4.3. Proposed Catalytic Cycling Mechanism

The Sonogashira cross-coupling process, which is catalyzed by Cu-NHC, has a known mechanism [26]. The copper-free Sonogashira cross-coupling reaction's mechanism, however, is unknown [23 and 24]. Pre-activation occurs in this pathway, much like in other cross-coupling reactions, and a palladium(0)complex is created (Scheme 2). In the first step, the aryl halide palladium(0) complex is added oxidatively. Step 2 is important due to a carbopalladation formation takes place in the absence of an amine [26 and 27]. The cyclopalladation at this point is a syn addition in which a cis adduct is formed and the aryl group transfers to a position that is less inhibited. The latter two steps (steps 3 and 4) follow the same established Sonogashira cross-linking reaction process.



Scheme 2. Proposed catalytic mechanism for Sonogashira cross-coupling reaction

5. CONCLUSION

As a result, we present the synthesis of the new (NHC)Pd(II)PPh$_3$ complexes bearing the 3-cyanobenzyl group. All complexes have been prepared from the triphenylphosphine and starting material (NHC)Pd(II)(pyridine) complexes. These compounds' catalytic abilities were tested in aqua media during the Sonogashira cross-coupling process and displayed good activity.

NOTICE

This study was presented as oral presentation and reconstructed at the 5th International Science Symposium between 01-03 September 2022.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

FINANCIAL DISCLOSURE

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DECLARATION OF ETHICAL STANDARDS

The authors of this article declare that the materials and methods used in this study do not require ethical committee permission and/or legal-special permission.

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