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Synthesis and characterization of new 3,3`-bipyrazole-4,4`-dicarboxylic acid derivatives and some of their palladium(II) complexes as pre-catalyst for Suzuki coupling reaction in water

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ABSTRACT

The 1,3-dipolar cycloaddition reaction of *bis*-hydrazonyl chlorides with methyl propiolate afforded dimethyl 1,1′-aryl-3,3`-bipyrazole-4,4`-dicarboxylates (5a,b). Heating the later compound 5a with a mixture of HCl/AcOH gave 3,3`-bipyrazole-5,5`-dicarboxylic acid derivative 6. Treatment of the hydrazonoyl chloride (1a) and 3,3`-bipyrazole-5,5`-dicarboxylic acid (6) with palladium(II) chloride gave the corresponding Pd-complexes 7 and 8, respectively. The catalytic activity of the prepared Pd-complexes was examined in the Suzuki cross-coupling reaction of phenylboronic acid with activated and deactivated aryl(hetaryl) bromides. The catalyst system provides very good to excellent yields, 85-94%. The structures of the obtained products were established from their elemental analysis, spectral data, XPS, EDX, and single crystal X-ray crystallography. Crystal data for $C_{10}H_7N_2O_2$ (6): triclinic, space group P-1 (no. 2), a = 3.9956(10) Å, b = 9.8917(18) Å, c = 10.810(3) Å, α = 94.167(15)°, β = 94.979(19)°, γ = 98.953(15)°, V = 418.83(16) Å^3, Z = 2, T = 296.(2) K, μ(Cu Kα) = 0.887 mm^{-1}, D_{calc} = 1.484 g/cm^3, 5469 reflections measured (11.72° ≤ 2Θ ≤ 133.24°), 1420 unique (R_{int} = 0.0633, R_{sigma} = 7.24%) which were used in all calculations. The final R_1 was 0.1055 (>2sigma(I)) and wR_2 was 0.3620 (all data).

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1. Introduction

Pyrazoles, as a class of multi-donor nitrogen ligands with changing coordination patterns, has played important roles in organometallic, inorganic and materials chemistry and were also used to establish pyrazolyl-bridged multi-metal and metal-metal bonding coordination systems [1,2]. Chemistry of the coordination of pyrazole and its derivatives have received special attention because of its structural diversity, such as metal-based polymers, [3,4]. Furthermore, pyrazole-based palladium(II) complexes were reported as examples for interesting coordination chemistry [5-7]. Pyrazolyl palladium complexes proved to be efficient catalysts for cross-coupling reactions [8,9]. Besides, pyrazoline ligands coordinated to palladium(II) were also assigned as very efficient DNA intercalator and artificial metallonuclease [10].

Bipyrazoles were found to be potential bioactive compounds [11], where they were reported to have antitumor [12], anti-inflammatory [13], antimicrobial [14] and cytotoxic [15] activities and scavengers for free radicals [16]. Further, pyrazole scaffold is a component of some commercial drugs in the market such as celecoxib and rimonabant [17,18].

1,3-Dipolar cycloaddition was reported as one of the most valuable synthetic routes for the construction of pyrazole heterocycles [19,20]. In continuation of our research work about *bis*-hydrazonoyl chlorides [21-24], we report herein the *hitherto* unreported regioselective double 1,3-dipolar cycloaddition of the *bis*-hydrazonoyl chlorides (**1a**,**b**) with methyl propiolate followed by acid hydrolysis of one of the products and its reaction with palladium(II) chloride and with urea. The regioselectivity of the obtained structures was confirmed from the single crystal X-ray analysis. Applications of the palladium(II) complex in Suzuki cross-coupling was also examined.

2. Experimental

2.1. Instrumentations

Melting points were measured on a Gallenkamp melting point apparatus. IR spectra were recorded using KBr disks using a Perkin-Elmer System 2000 FT-IR spectrophotometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded at 25 °C using DMSO-d_6 as a solvent with TMS as internal standard on a Bruker DPX 400 or 600 superconducting NMR spectrometer. Chemical shifts are reported in ppm.

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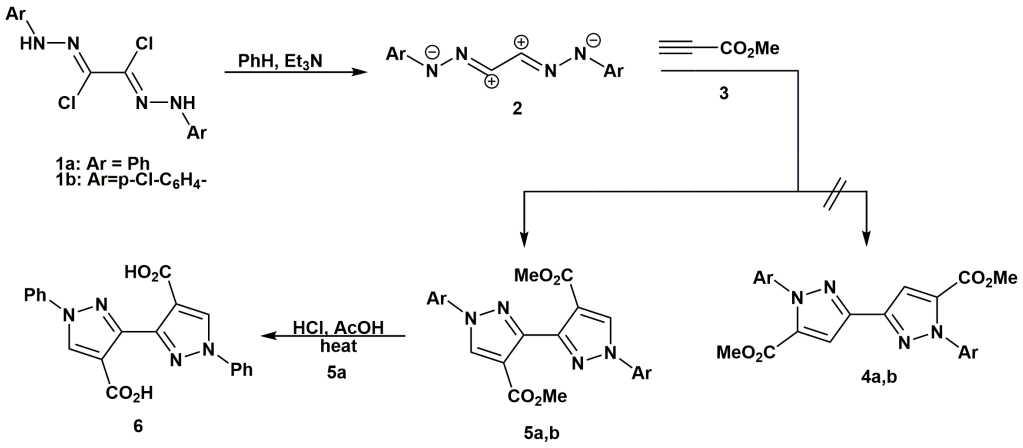


Scheme 1. Synthesis of 1,1`-diphenyl-3,3`-bipyrazole derivatives **5** and **6**.

Low-resolution electron impact mass spectra [MS(EI)] and high-resolution electron impact mass spectra [HRMS (EI)] were performed on high resolution GC-MS (DFS) thermo spectrometers at 70.1 eV using magnetic sector mass analyzer. The crystal structures were determined by a Rigaku R-AXIS RAPID diffractometer and Bruker X8 Prospector and the single crystal X-ray diffraction data collections were made by using Mo-Kα radiation. The data were collected at room temperature. The structure was solved by direct methods and was expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. The structure was solved and refined using the Bruker SHELXTL Software Package (Structure solution program-SHELXS-97 and Refinement program-SHELXL-97) [25]. Data were corrected for the absorption effects using the multi-scan method (SADABS). Scanning Electron Microscopy (SEM) and Energy Dispersive X-ray analysis (EDX) were examined at room temperature (25 °C) in a model JSM 6300 JEOL scanning electron microscope (Akishima, Japan) at 20 kV. X-ray Photoelectron Spectroscopy (XPS) was conducted using a Thermo Scientific ESCALAB-250Xi spectrometer. The *bis*-hydrazonoyl chlorides (**1a**,**b**) was prepared following the literature procedure (Scheme 1) [26].

2.2. Synthesis of 1,1'-diaryl-3,3'-bipyrazole derivatives (5a,b)

To a solution of the appropriate *bis*-hydrazonoyl chloride **1a** or **1b** (10 mmol) in dry benzene (30 mL), methyl propiolate **3** (20 mmol) was added, followed by dropwise addition of triethylamine (0.2 mL). The reaction mixture was refluxed for 4 h then left to cool to room temperature. The solvent was evaporated under reduced pressure then the residue was treated with few drops of methanol. The precipitated product was filtered off, washed with methanol, dried and finally recrystallized from DMF to afford the corresponding 3,3'-bipyrazole derivatives **5a**,**b** (Scheme 1).

Dimethyl 1,1'-diphenyl-3,3'-bipyrazole-4,4'-dicarboxylate (**5a**): Color: Beige. Yield: 70%. M.p.: 260-262 °C. FT-IR (KBr, ν, cm^{-1}): 3084 (CH), 2989 (CH), 1733 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 7.53 (s, 2H, pyrazole-H), 7.52-7.34 (m, 10H, Ar-H), 3.45 (s, 6H, $2CH_3$). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 160.1 (2C, C=O), 144.9 (2C, pyrazole-C), 129.02 (2C, pyrazole-C), 116.6 (2C, pyrazole-C), 140.1 (2C, Ar-C), 128.9 (4C, Ar-C), 126.0 (2C, Ar-C), 121.1 (4C, Ar-C), 52.1 (2C, OCH_3). HRMS (EI, *m/z*) calcd. for $C_{22}H_{18}N_4O_4$: 402.10 (M^+); found: 402.13. Anal. calcd. for $C_{22}H_{18}N_4O_4$: C, 65.66; H, 4.51; N, 13.92. Found: C, 65.67; H, 4.32; N, 13.97%.

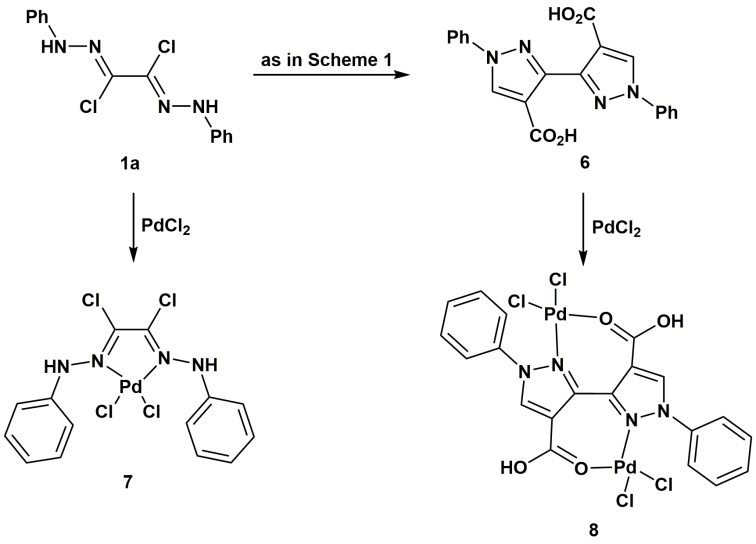
Dimethyl 1,1'-di(4-chlorophenyl)-3,3'-bipyrazole-4,4'-dicarboxylate (**5b**): Color: Yellow. Yield: 60%. M.p.: 232-233 °C. IR (KBr, ν, cm^{-1}): 3076 (CH), 2988 (CH), 1736 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 7.56 (s, 2H, pyrazole-H), 7.64, 7.62 (d, 2H, Ar-H, *J* = 8 Hz); 7.40, 7.38 (d, 2H, Ar-H, *J* = 8 Hz), 7.60, 7.58 (d, 2H, Ar-H, *J* = 8 Hz), 7.33 (d, 2H, Ar-H, *J* = 8 Hz), 3.76 (s, 6H, $2OCH_3$). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 160.2 (2C, C=O), 147.4 (2C, pyrazole-C), 129.2 (2C, pyrazole-C), 117.5 (2C, pyrazole-C), 139.6 (2C, Ar-C), 129.2 (2C, Ar-C), 126.0 (4C, Ar-C), 120.9 (4C, Ar-C), 54.3 (2C, OCH_3). HRMS (EI, *m/z*) calcd. for $C_{22}H_{16}Cl_2N_4O_4$: 470.05 (M^+); found: 470.10. Anal. calcd. for $C_{22}H_{16}Cl_2N_4O_4$: C, 56.07; H, 3.42; N, 11.89. Found: C, 56.16; H, 3.34; N, 11.91%.

2.3. 1,1'-Diphenyl-3,3'-bipyrazole-4,4'-dicarboxylic acid (6)

A solution of compound **5a** (1 mmol) in a mixture of glacial acetic acid (15 mL), hydrochloric acid (5 mL) and water (5 mL), was refluxed for 5 h during which compound **5a** was dissolved and a solid product was precipitated. The mixture was left to cool to room temperature and the precipitate was collected by filtration and recrystallized from acetonitrile : methanol (2:1, *v:v*) to give 3,3'-bipyrazole-4,4'-dicarboxylic acid (**6**) as pale gray crystals (2.32 g, 62%) (Scheme 1). M.p.: 208-210 °C. Color: Pale grey. Yield: 62%. IR (KBr, ν, cm^{-1}): 3427 (OH, acid), 3064 (CH), 2981 (CH), 1702 (C=O, acid). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 7.49-7.37 (m, 10H, Ar-H), 7.53 (s, 2H, pyrazole-H), 13.45 (br. s, 2H, CO_2H). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 158.2 (2C, C=O), 144.6 (2C, pyrazole-C), 128.6 (2C, pyrazole-C), 109.8 (2C, pyrazole-C), 140.0 (2C, Ar-C), 134.4 (4C, Ar-C), 128.5 (4C, Ar-C), 125.8 (2C, Ar-C). HRMS (EI, *m/z*) calcd. for $C_{20}H_{14}N_4O_4$: 374.1015 (M^+); found: 374.1014. Anal. calcd. for $C_{20}H_{14}N_4O_4$: C, 64.17; H, 3.77; N, 14.97. Found: C, 64.54; H, 3.73: N, 14.75%. Crystal Data: Crystal dimensions 0.060 × 0.080 × 0.200 mm, triclinic, *a* = 3.9956(10) Å, *b* = 9.8917(18) Å, *c* = 10.810(3) Å, V = 418.83 (16) $Å^3$, α = 94.167(15)°, β = 94.979(19)°, γ = 98.953(15)°, θ_{max} 66.62° (0.84 Å resolution), Space Group P-1, *Z* = 2, D_{calc} = 1.484 g/cm^3, F000 = 194, R1 = 10.55%, wR2 = 36.20%.

2.4. Synthesis of bis-hydrazonoyl chloride-$PdCl_2$ complex (7)

A solution of compound **1a** (0.307 g, 1 mmol) in DMF (25 mL) was added to a hot solution of palladium(II) chloride (0.177 g, 1 mmol) in methanol (30 mL). The reaction mixture was refluxed for 3 h, then left to cool to room temperature. The formed solid product was collected by filtration, washed with DMF then water and ethanol to give the Pd-complex **7** as pale gray solid (0.305 g, 63%) (Scheme 2). Color: Pale gray. Yield: 63%. M.p.: 280-281 °C. IR (KBr, ν, cm^{-1}): 3321 (NH), 3238 (NH), 3053 (CH), 1639 (C=N).



Scheme 2. Complexation of *bis*-hydrazonoyl chloride **1a** and bipyrazole-dicarboxylic acid **6** with $PdCl_2$.

^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 7.08-6.38 (m, 10H, Ar-H), 7.96 (br. s, 1H, NH), 10.66 (br. s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 156.2 (2C, C=N), 144.3 (2C, Ar-C), 130.2 (4C, Ar-C), 120.0 (2C, Ar-C), 118.23 (4C, Ar-C). MS (EI), *m/z* (%)): 484.50 (M^+, 73%), 271.0 (32%), 237.1 (44%), 214.0 (63%), 122.0 (23%). UV/Vis ($CHCl_3$, λ_{max}, nm, (ε)): 239.55, 292.0, 326.17. Anal. calcd. for $C_{14}H_{12}Cl_4N_4Pd$: C, 34.71; H, 2.50; N, 11.56. Found: C, 34.54; H, 2.73; N, 11.43%. EDX Anal. for Pd: calcd.: 21.96%, found 21.70%.

2.5. Synthesis of 1,1'-diphenyl-3,3'-bipyrazole-4,4'-dicar boxylic acid-palladium(II) chloride complex (8)

A solution of palladium(II) chloride (0.354 g, 2 mmol) in methanol (25 mL) was added to a solution of compound **6** (0.374 g, 1 mmol) in methanol (25 mL). The reaction mixture was refluxed for 5h, then left to cool to room temperature. The precipitated solid product was collected by filtration and recrystallized from DMF/acetonitrile (1:1) to yield the Pd-complex **8** as green solid (0.67 g) (Scheme 2). Color: Green. Yield: 92%. M.p.: 264-266 °C. IR (KBr, ν, cm^{-1}): 3435 (OH), 3062 (CH), 1725 (C=O), 1703 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 7.07 (s, 2H, pyrazole-H), 7.53-7.19 (m, 10H, Ar-H), 13.48 (br. s, 2H, CO_2H). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 159.7 (2C, C=O, CO_2H), 158.2 (2C, C=N, pyrazole-C), 144.6 (2C, Ar-C), 140.0 (4C, Ar-C), 134.4 (2C, pyrazole-C), 128.6 (2C, Ar-C), 125.8 (4C, Ar-C), 109.8 (2C, pyrazole-C). UV/Vis ($CHCl_3$, λ_{max}, nm, (ε)): 266. Anal. calcd. for $C_{20}H_{14}Cl_4N_4O_4Pd_2$: C, 32.95; H, 1.94; N, 7.69. Found: C, 32.75; H, 2.03; N, 6.87%. EDX Anal. for Pd: calcd. 29.20%, found. 29.6%.

2.6. Synthesis of poly-N-bis(3,3`-bi-pyrazolylcarbonyl)urea derivative (10)

To a solution of compound **6** (0.374 g, 1 mmol) in DMF (25 mL), urea (0.060 g, 2 mmol) were added. The reaction mixture was refluxed for 5 h then left to cool to room temperature. The precipitated product was collected by filtration and recrystallized from DMF/acetonitrile (1:1) to give the poly-*bis*(3,3`-bi-pyrazolylcarbonyl)urea derivative **10** as yellow powder (0.35 g) (Scheme 3). Colour: Yellow powder. M.p.: > 300 °C. IR (KBr, ν, cm^{-1}): 3208 (NH), 3122 (NH), 3069 (CH), 1726 (C=O), 1660 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 12.47 (br. s, 2H, NH), 7.99-7.39 (m, 10H, Ar-H), 7.59 (s, 2H, pyrazole-CH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 163.3 (1C, C=O), 159.6 (2C, C=O), 146.0 (2C, pyrazole-C), 138.8 (2C, Ar-C), 131.7 (4C, Ar-C), 129.8 (2C, pyrazole-C), 127.2 (2C, Ar-C), 118.9 (4C, Ar-C), 117.1 (2C, pyrazole-C). Anal. calcd. for repeating unit $C_{21}H_{14}N_6O_3$: C, 63.31; H, 3.54; N, 21.10. Found: C, 63.51; H, 3.72; N, 21.21%.

2.7. Suzuki-Miyaura cross-coupling of aryl(hetaryl) bromides with phenylboronic acid in water

A mixture of the appropriate aryl(hetaryl) bromides **12**-**17** (1 mmol), phenylboronic acid **11** (146 mg, 1.2 mmol), tetrabutylammonium bromide (TBAB) (194 mg, 0.6 mmol), palladium complex **7** (7 mg, 1 mol%) and KOH (112 mg, 2 mmol) in distilled water (3 mL) was thermally heated with stirring at 100 °C under open air for the appropriate reaction time (monitored by TLC), as listed in Table 4. After the reaction was complete, the product was extracted with ethyl acetate (3×20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ then filtered and the solvent was evaporated under reduced pressure. The residue was then subjected to separation via flash column chromatography with hexane: ethyl acetate (10:1, *v:v*) as an eluent to give the corresponding pure cross-coupled products **18**-**23**. All experiments were done in triplicate.

4-Acetylbiphenyl (**18**): M.p.: 117-119 °C (Lit. M.p.: 118-120 °C [27]).

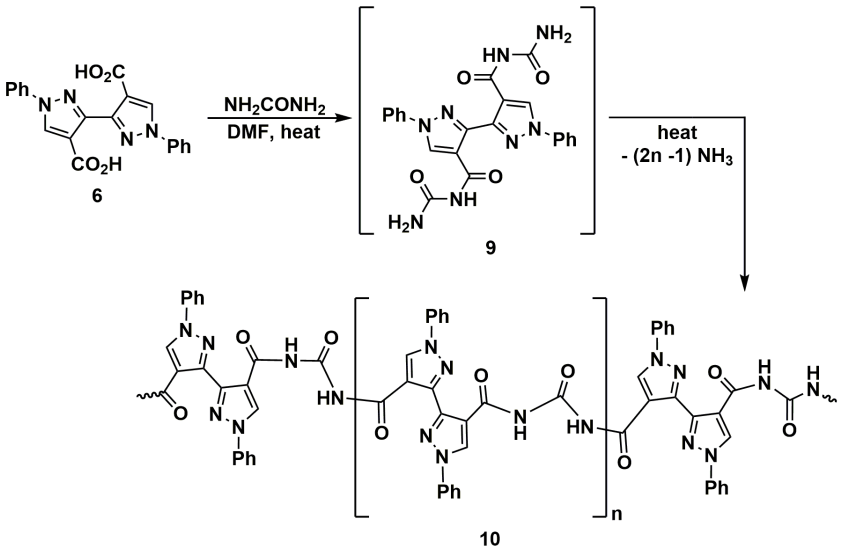
1,1'-Biphenyl-4-carbonitrile (**19**): M.p.: 85-86 °C (Lit. M.p.: 86-87 °C [28]).

3-Nitrobiphenyl (**20**): M.p.: 56-58 °C (Lit. M.p.: 57-59 °C [29]).

4-Phenylphenol (**21**): M.p.: 144-145 °C (Lit. M.p.: 146-147 °C [29]).

N-Acetyl-4-aminobiphenyl (**22**): M.p.: 152-154 °C (Lit. M.p.: 150-153 °C [29]).

4, 6-Dimethyl-2-oxo-5-phenyl-1, 2-dihydropyridine-3-carbo nitrile (**23**): Color: Brown crystals. Yield: 88%. M.p.: 230-231 °C. IR (KBr, ν, cm^{-1}): 3434 (NH), 2218 (C≡N), 1658 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 7.77-7.31 (m, 5H, Ar-H); 6.15 (br. s, 1H, NH, D_2O-exchangeable), 2.49 (s, 3H, CH_3), 2.21 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 160.93 (1C, C=O), 158.41 (1C, pyridine-C), 151.37 (1C, Ar-C), 134.01 (2C, Ar-C), 129.87 (2C, Ar-C), 127.26 (1C, Ar-C), 115.90 (1C, pyridine-C), 107.39 (1C, pyridine-C), 100.45 (1C, pyridine-C), 99.07 (1C, CN), 18.85 (1C, CH_3), 13.44 (1C, CH_3).



Scheme 3. Synthesis of poly-*bis*(3,3`-bi-pyrazolylcarbonyl)urea derivative **10**.

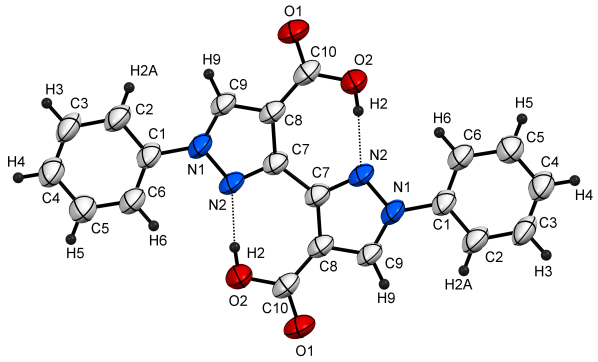


Figure 1. ORTEP plot of the X-ray crystallographic data of compound **6**.

HRMS (EI, *m/z*) calcd. for $C_{14}H_{12}N_2O$ (M^+): 224.09496; found: 224.09487. Anal. calcd. for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49. Found: C, 75.01; H, 5.33; N, 12.63%.

3. Results and discussion

3.1. Synthesis of the bipyrazole-dicarboxylic acid derivatives (5 and 6)

The *bis*-hydrazonoyl chlorides **1a**,**b** were prepared following our previously reported procedure [26]. Then, the reaction of *bis*-hydrazonoyl chloride **1a** with methyl propiolate **3**, in 1:2 molar ratio, was conducted in benzene at reflux temperature in the presence of triethylamine to afford only one product as checked by TLC. The obtained pure product was correctly analyzed for $C_{22}H_{18}N_4O_4$ based on its mass spectrum and elemental analyses. Structure of the obtained reaction product can be either dimethyl 1,1′-diphenyl-3,3`-bipyrazole-5,5`-dicarboxylate (**4a**) or its regioisomer dimethyl 1,1′-diphenyl-3,3`-bipyrazole-4,4`-dicarboxylate (**5a**) (Scheme 1). Spectroscopic analyses were fully compatible with structure **5a**. For example, the isolated product revealed a singlet signal at δ_H 7.54 ppm in its ^{1}H NMR spectrum due to the pyrazole-5-CH proton (structure **5a**) and not the pyrazole-4-CH proton (structure **4a**) (where pyrazole-4-CH proton appears at a lower chemical shift) [24]. Moreover, ^{13}C NMR spectrum exhibited a peak at δ_C 168.1 (C=O), 144.9, 128.8, 116.6 (pyrazole-carbons), 138.8, 130.3, 124.9, 121.2 (aromatic-carbons), 50.4 ppm (CH_3). In a similar manner, reaction of *bis*-hydrazonoyl chloride (**1b**) with methyl propiolate **3** under similar reaction condition yielded dimethyl 1,1′-di(4-chlorophenyl)-3,3`-bipyrazole-5,5`-dicarboxylate (**5b**) (Scheme 1). Structure of compound **5b** was confirmed from its elemental and spectral analyses.

Heating of dimethyl 1,1′-diphenyl-3,3`-bipyrazole-4,4`-dicarboxylate (**5a**) with a mixture of hydrochloric acid : acetic acid (1:3, *v*:*v*) led to the formation of a product that was determined as 3,3`-bipyrazole-5,5`-dicarboxylic acid (**6**). The structure of the product **6** was confirmed from all possible spectral analyses (IR, MS, ^{1}H- and ^{13}C-NMR) as well as its single crystal X-ray analysis as depicted in Figure 1 and Tables 1-3 (CCDC 1548525).

3.2. Synthesis of the palladium(II) complexes (7 and 8)

The complexation behaviour of the *bis*-hydrazonoyl chloride **1a** as a ligand (L) towards $PdCl_2$ was investigated. Thus, the addition of a hot solution of compound **1a** in DMF to the $PdCl_2$ solution in methanol at adjusted pH = 5.76 led to the formation of complex **7** of type $LPdCl_2$ (Scheme 2). Structure of the complex **7** was established based on its elemental analyses and spectral data. Besides, the experi-mental UV-visible absorption spectrum of the ligand **1a** exhibited two bands centred at 267.72 and 283.00 nm, while that of the Pd-complex **7** exhibited three peaks in the ultraviolet region at 239.55, 292.00 and 326.17 nm.

Table 1. Crystal data and details of the structure refinement for compound **6**.

Empirical formula	$C_{10}H_7N_2O_2$
Formula weight	187.18
Temperature (K)	296.(2)
Crystal system	Triclinic
Space group	P-1
a (Å)	3.9956(10)
b (Å)	9.8917(18)
c (Å)	10.810(3)
α (°)	94.167(15)
β (°)	94.979(19)
γ (°)	98.953(15)
Volume (Å^3)	418.83(16)
Z	2
ρ_{calc} (g/cm^3)	1.484
M (mm^{-1})	0.887
F(000)	194.0
Crystal size (mm^3)	0.200 × 0.080 × 0.060
Radiation	Cu Kα radiation (λ = 1.54178 Å)
2Θ range for data collection (°)	11.72 to 133.24
Index ranges	$-4 \le h \le 4, -11 \le k \le 11, -10 \le l \le 12$
Reflections collected	5469
Independent reflections	1420 [R_{int} = 0.0633]
Data/restraints/parameters	1420/0/130
Goodness-of-fit on F^2	1.422
Final R indexes [I≥2σ (I)]	R_1 = 0.1055, wR_2 = 0.3206
Final R indexes [all data]	R_1 = 0.1314, wR_2 = 0.3620
Largest diff. peak/hole (e Å^{-3})	0.43/-0.33
Absorption correction	Multi-scan
Max. and min. transmission	0.9487 and 0.8425
Structure solution technique	direct methods
Structure solution program	SHELXS-97 (Sheldrick, 2008)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-97 (Sheldrick, 2008)

Table 2. Bond lengths (Å) for compound **6.**

Atom-Atom	Bond length	Atom-Atom	Bond length
N2-C5	1.334(6)	C5-C5#1	1.465(9)
O2-C10	1.217(6)	C9-C10	1.466(8)
O3-H7	1.09(8)	N2-N1	1.356(5)
N1-C4	1.433(6)	O3-C10	1.326(6)
C1-C2	1.362(9)	N1-C8	1.344(7)
C2-C3	1.386(8)	C1-C6	1.359(8)
C3-C4	1.378(7)	C5-C9	1.427(6)
C4-C7	1.377(8)	C6-C7	1.386(7)

#1 Symmetry code: -*x*+1, -*y*+1, -*z*+1.

Table 3. Bond angles (°) for compound **6**.

Atom-Atom-Atom	Bond angle	Atom-Atom-Atom	Bond angle
C5-N2-N1	106.0(4)	C10-O3-H7	110.0(4)
C8-N1-N2	111.1(4)	C8-N1-C4	128.5(4)
N2-N1-C4	120.4(4)	C6-C1-C2	120.5(5)
C1-C2-C3	120.8(5)	C4-C3-C2	118.2(5)
C7-C4-C3	121.4(5)	C7-C4-N1	119.6(4)
C3-C4-N1	119.0(5)	N2-C5-C9	110.5(4)
N2-C5-C5#1	117.3(5)	C9-C5-C5#1	132.2(6)
C1-C6-C7	120.4(5)	C4-C7-C6	118.7(5)
N1-C8-C9	108.5(4)	C8-C9-C5	103.9(4)
C8-C9-C10	120.7(4)	C5-C9-C10	135.3(4)
O2-C10-O3	119.6(5)	O2-C10-C9	121.2(5)

#1 Symmetry code: -*x*+1, -*y*+1, -*z*+1.

On the other hand, all trials to chelate the bipyrazole-dicarboxylate ester derivative **5a** with $PdCl_2$ were failed. This may be interpreted in terms of the non-planarity of the bipyrazole ester derivative **5** due to the high steric hindrance of the ester groups and consequently, the nitrogen-dentates are not in the appropriate positions to interact with palladium ions. However, treatment of the bipyrazole-dicarboxylic acid derivative **6** with $PdCl_2$ in DMF resulted in the formation of the bipyrazole-palladium(II) complex structure **8** (Scheme 2).

3.3. XPS and EDX measurements of palladium(II) complexes

All attempts to get a single crystal of the obtained complex **7** and **8** were not successful. Therefore, X-ray Photoelectron Spectroscopy (XPS) technique was used to elucidate the chemical composition of the palladium complex **8**. The XPS analysis (Figure 2) confirmed the presence of palladium, carbon, nitrogen and oxygen elements in the complex **8**. In the XPS valence band spectra for the Pd, two pairs Pd 3d peaks were observed (Figure 2A). The binding energy values of 338.1, 343.3 and 345.1 eV were assigned to incarcerate Pd (II) [30,31]. The peak at 339.86 was assigned to Pd-O bond. N1s high-resolution spectra (Figure 2B) showed two peaks, the first peak falling at binding energy 399.9 eV was assigned to Pd-N bond [32,33] and the second one, falling at binding energy 406.7 eV attributed to oxidized N. O1s peak (Figure 2C) at binding energy 531.46 eV assigned to C–O and O-H bond. C1s high-resolution spectra for Pd-complex are reported in Figure 2D. They were assigned to C–C, and C=C (284.5 eV), C–O (285.82 eV) and C=O and may be for C-O-M (M metal ion) at binding energy 287.4 eV) groups. Moreover, the binding energies 198.23 and 199.82 eV were assigned for Cl 2p, 3/2 and Cl 2p, 1/2.

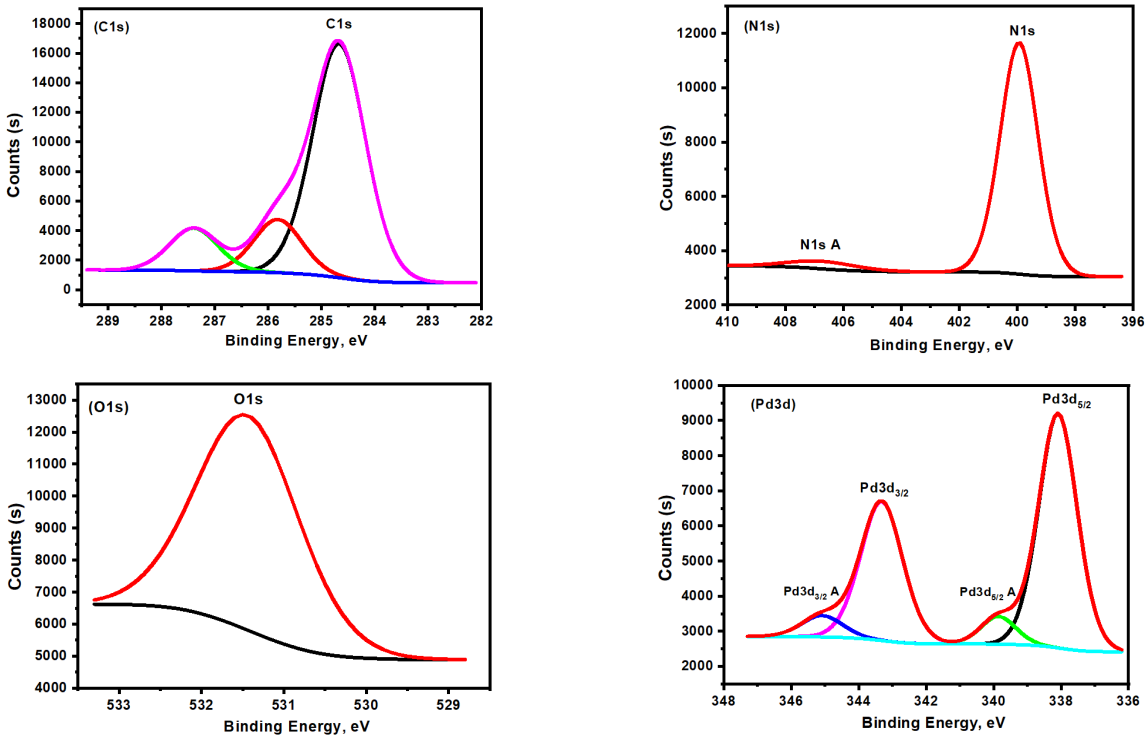


Figure 2. XPS of Pd-complex **8**, binding energy of C, N, O and Pd.

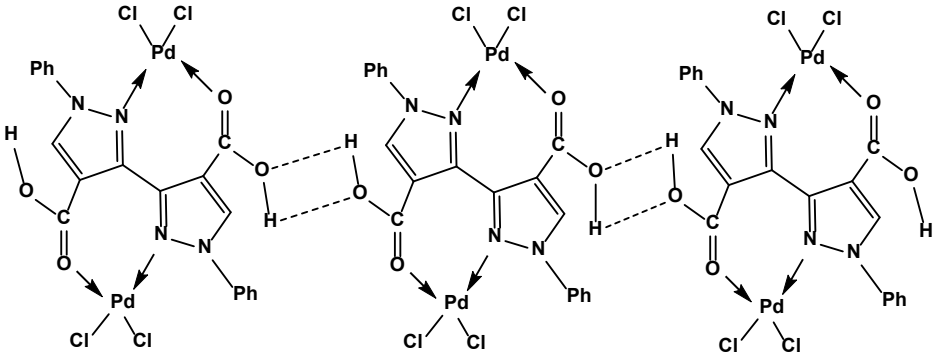


Figure 3. H-bonding between compound **8** forms consecutive layers.

Furthermore, the IR spectrum of compound **8** showed a shift in the carbonyl absorption, $\Delta\nu_{C=O}$ = 23 cm^{-1}, and hydroxyl absorption, $\Delta\nu_{OH}$ = 10 cm^{-1} when compared with the IR of compound **6**, this result is attributed to the hydrogen bonding between the carboxylic groups (Figure 3).

Moreover, the microanalyses of palladium in compounds **7** and **8** were determined from the Energy Dispersive X-ray analysis (EDX), which is a technique of elemental analysis associated to electron microscopy based on the generation of characteristic X-rays that reveals the presence of elements present in the samples. The EDX analyses of compounds **7** and **8** exhibited the presence of Pd in 21.7 and 29.6% that were very closer to the calculated values 21.96 and 29.2%, respectively, as depicted in Figure 4.

3.4. Structure morphology

In general, the change in the surface morphology is attributed to the introduction of metal ions into the matrix. The mode of chelation of the palladium ions within the consecutive layers of the *bis*-pyrazole-carboxylic acid **6** was examined by measuring the SEM of the Pd-complex **8** as outlined in Figure 5. The results of the SEM provided consecutive layers which is consistent with $PdCl_2$-bipyrazole-$PdCl_2$ layers. The morphology of the metal complex **8** is shown in Figure 5, with 10000 and 40000 magnifications.

Heating of 3,3`-bipyrazole-5,5`-dicarboxylic acid **6** with double equivalents of urea led to the formation of the poly-*bis*(3,3`-bi-pyrazolylcarbonyl)urea derivative **10** (Scheme 3). The structure of the product **10** was formed through the intermediate **9** via loss of ammonia molecules in a step-type polymerization reaction. Comparing with its carboxylic acid precursor **6**, the IR spectrum of the polyamide **10** showed new broad bands for the NH groups at 3208 and 3122 cm^{-1} in addition to, two carbonyl absorptions at 1726 and 1660 cm^{-1}. Moreover, the structure of the polyamide **10** was investigated using SEM analysis. The results of SEM provided consecutive layers which is consistent with the postulated structure **10**. The morphological structure of the polymeric product **10** is shown in Figure 6, with 10000 and 40000 magnifications. It was observed that the bipyrazole-based polyamide **10** has a high degree of crystallinity.

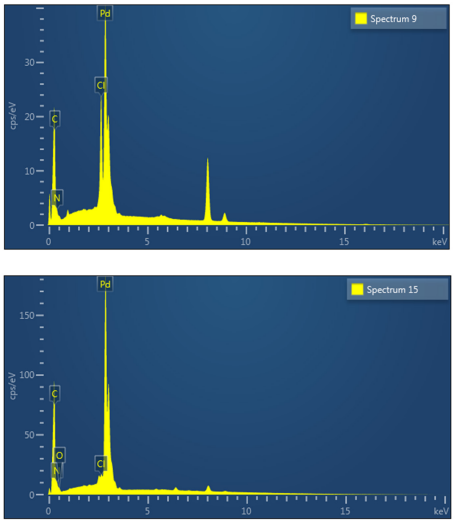


Figure 4. EDX of compounds **7** and **8** (Spectrum 9 represent compound 7 and spectrum 15 represent compound 8).

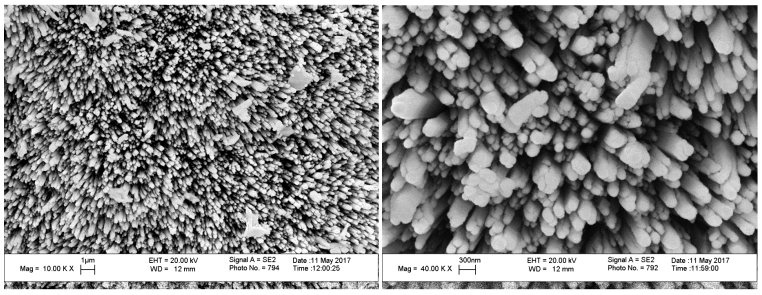


Figure 5. SEM micrograph of palladium complex **8**.

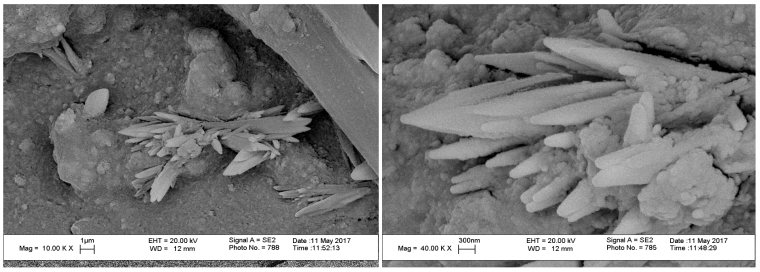


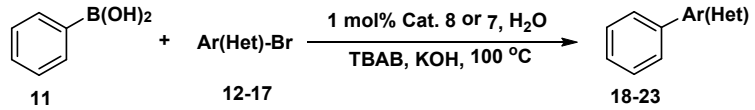
Figure 6. SEM micrograph of the polyamide product **10**.

3.5. Catalytic activity of Pd-Complex in Suzuki cross-coupling reactions

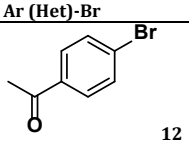
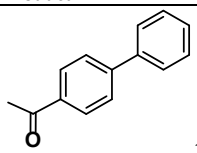
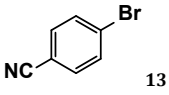
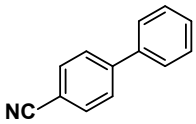
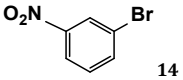
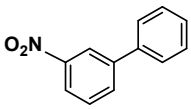
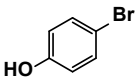
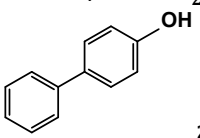
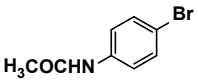
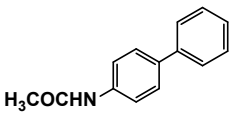
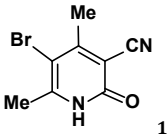
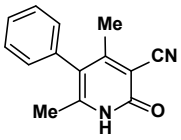
The palladium catalyzed Suzuki-Miyaura cross-coupling reaction represents one of the most widely and eco-friendly method for the construction of carbon-carbon bonds in organic molecules [34-36]. One of our goals in this work is to study the catalytic activity of the prepared Pd-complexes in Suzuki cross-coupling reaction. Thus, the catalytic activity of the Pd(II) complex **8** in the cross-coupling reaction between phenylboronic acid (**11**) and 4-bromoacetophenone (**12**) was examined and the results are shown in Table 4. The reaction was conducted in water (3 mL) at 100 °C using 1 mol% of the Pd(II) complex **8** with 1 mmol 4-bromoacetophenone (**12**), 1.2 mmol phenylboronic acid (**11**), 0.6 mmol TBAB and 2 mmoles of potassium hydroxide. TLC of the reaction mixture showed that 4-bromoacetophenone (**12**) was completely consumed after 45 min of heating and the product 4-acetylbiphenyl (**18**) was isolated in 90 % yield. Next, the utility of Pd-complex **8** in Suzuki-Miyaura cross-coupling reactions of further aryl and heteroaryl bromides under the above condition was also conducted. Thus, Suzuki coupling of the activated aryl bromides **13**, **14**, **15** and **16** with phenylboronic acid **11** resulted in the formation of the corresponding cross-coupled products **19**, **20**, **21** and **22**, respectively in excellent isolated yields as shown in Table 4. Cross-coupling of the 5-bromo pyridine-3-carbonitrile derivative **17** [37] with phenylboronic acid **11** in water using Pd-complex **8** (1 mol%) afforded the 5-phenylpyridine-3-carbonitrile derivative **23**, to the best of our knowledge, this is the first preparing by Suzuki-Miyaura cross-coupling reaction, (run 6, Table 4). The identities of the cross-coupled products were confirmed by HRMS, ^{1}H and ^{13}C NMR spectra.

In similar manner, the catalytic activity of Pd-complex **7** was investigated (Table 5). Thus, Suzuki coupling of the activated aryl bromides **12**-**16** with phenylboronic acid **11** resulted in the formation of the corresponding cross-coupled products **18**- **22** in excellent isolated yields as shown in Table 5.

Table 4. Suzuki coupling of aryl bromides with phenylboronic acid in water.



11 12-17 18-23

Run	Ar (Het)-Br	Product	Time (min)	Yield %[a]
1	 12	 18	45	90
2	 13	 19	45	91
3	 14	 20	45	92
4	 15	 21	60	91
5	 16	 22	60	85
6	 17	 23	45	88

[a] Reaction conditions: Bromide/boronic acid/KOH/TBAB/water: 1.0/1.2/2.0/0.6/3.0 mL at 100 °C temperature. All values refer to the isolated yields.

Table 5. Suzuki coupling of aryl bromides with phenylboronic acid in water using Pd-complex **7** as a catalyst.

Run	Ar (Het)-Br	Product	Time (min)	Yield (%)
1	**12**	**18**	45	91
2	**13**	**19**	45	90
3	**14**	**20**	45	94
4	**15**	**21**	60	90
5	**16**	**22**	60	85
6	**17**	**23**	45	91

Table 6. The comparison of the data obtained by Pd-complex 7 and 8 with that reported in literature.

Compound	Time (min)	Yield (%)	Comment or reference
18	1140	96	*Reference 28*
	45	90	Catalyst used: compound 8
	40	91	Catalyst used: compound 7
19	120	88	*Reference 28*
	45	91	Catalyst used: compound 8
	30	90	Catalyst used: compound 7
20	120	92	*Reference 29*
	45	92	Catalyst used: compound 8
	45	94	Catalyst used: compound 7
21	720	90	*Reference 29*
		91	Catalyst used: compound 8
		90	Catalyst used: compound 7
22	660	88	*Reference 29*
	60	85	Catalyst used: compound 8
	60	85	Catalyst used: compound 7
23			To the best of our knowledge, this is the first reporting for compound 23 for Suzuki coupling reaction
	45	88	Catalyst used: compound 8
	45	91	Catalyst used: compound 7

Cross-coupling of the 5-bromopyridine-3-carbonitrile derivative **17** [37] with phenylboronic acid **11** in water using Pd-complex **7** (1 mol%) afforded the 5-phenylpyridine-3-carbonitrile derivative **23** (run 6, Table 5). The identities of the cross-coupled products were confirmed by HRMS, ^{1}H and ^{13}C NMR spectra. The yield in case of compound **18**, **20** and **23** showed an improvement from 1 to 3% as compared by Pd-complex **8**.

Comparison between literature data and data obtained upon using catalytic compounds **7** and **8** showed an observed

improvement in the time of the reactions in addition to the yield % (cf. Table 6).

4. Conclusions

The current work described an efficient one-pot region-selective double 1,3-dipolar cycloaddition of bis-hydrazonoyl chlorides with two equivalents of the electron deficient alkyne; methyl propiolate to give the corresponding bipyrazole esters which underwent acid hydrolysis to give the bipyrazole dicarboxylic acid. Palladium(II)-complexes of the *bis*-hydrazonoyl chloride and bipyrazole dicarboxylic acid were synthesized and both of them was found to be an efficient catalyst for Suzuki cross-coupling reaction.

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Supporting information

CCDC-1548525 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033.

Disclosure statement

Conflict of interests: The authors declare that they have no conflict of interest.
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