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FULL PAPER

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Novel (N-heterocyclic carbene)Pd(pyridine)Br_2 complexes for carbonylative Sonogashira coupling reactions: Catalytic efficiency and scope for arylalkynes, alkylalkynes and dialkynes

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New *N*,*N*′-substituted imidazolium salts and their corresponding dibromidopyridine–palladium(II) complexes were successfully synthesized and characterized. Reactions of palladium bromide with the newly synthesized *N*,*N*′-substituted imidazolium bromides (**2a** and **2b**) in pyridine afforded the corresponding new N-heterocyclic carbene pyridine palladium(II) complexes (**3a** and **3b**) in high yields. Their single-crystal X-ray structures show a distorted square planar geometry with the carbene and pyridine ligands in *trans* position. Both complexes show a high catalytic activity in carbonylative Sonogashira coupling reactions of aryl iodides and aryl diiodides with arylalkynes, alkylalkynes and dialkynes.

KEYWORDS
alkynones, aryl diiodides, carbonylative Sonogashira coupling, dialkynes, Pd–NHC complex

1 | INTRODUCTION

Ynones (α,β-acetylenic carbonyl compounds) are important structural moieties found in natural products, biologically active compounds and agrochemicals.[1] They are also precursors for the synthesis of a variety of organic compounds, especially aromatic heterocycles such as pyrazoles,[2,3] quinolones,[4] furans[5] and pyrimidines.[1,6–8]

Traditional methods for the synthesis of ynones often involve multistep reactions and they are also associated with side reactions.[9] Another way for their synthesis is the catalytic carbonylative Sonogashira coupling reaction of aryl halides with terminal alkynes in the presence of palladium complexes.[10] This method offers access to a variety of ynones via a single step and under mild reaction conditions. Palladium-catalysed carbonylation reactions are now widely recognized as a very important tool in industrial and organic chemistry. Palladium-catalysed carbonylation chemistry allows the direct synthesis of carbonyl compounds using readily available feedstocks such as carbon monoxide (CO).[10–13] Several palladium complexes and supported palladium catalysts have been considered and tested in catalytic carbonylative Sonogashira coupling reactions.[14–36] However, the use of phosphine, the low catalyst activity, the relatively large loading of catalyst and the need for high CO pressure were drawbacks.[37–42]

Recently, much attention has been paid to the development of N-heterocyclic carbene (NHC) metal complexes, and notable advances have been made especially for their applications as organometallic catalysts.[43–58] This is attributed to the ability of NHC ligands to provide highly active and stable transition metal catalysts for various organic transformations. The highly sigma-donating NHC ligands prevent the formation of inactive palladium

black during catalysis.[43,46] In addition to the NHC moieties, the presence of ancillary N- or P-donating ligands attached to the metal centre enhances the catalytic activity of the metal carbene complexes.[46]

We have previously reported the synthesis and catalytic activities of palladium(II) bis(oxazoline) complexes,[50–53] and recently triazole-derived NHC–palladium(II) complexes.[49] In the present paper, we report the synthesis and crystal structures of two new mixed ligand palladium–carbene–pyridine (Pd–NHC–Py) complexes. They were found to be active catalysts in the carbonylative Sonogashira coupling reactions of aryl iodides and aryl diiodides with arylalkynes, alkylalkynes and dialkynes. We also report the synthesis of a new compound, 1,1′-benzene-1,4-diylbis(4,4-dimethylpent-2-yn-1-one), via the carbonylative Sonogashira coupling reaction of 1,4-diiodobenzene with 4,4-dimethylpent-2-yne using one of the new Pd–NHC–Py complexes as a catalyst.

2 | EXPERIMENTAL

2.1 | Materials and Instrumentation

Materials for the synthesis of the carbene ligand precursors and palladium carbene complexes were purchased from Sigma Aldrich and were used as received. All solvents (reagent grade) used in the synthesis were distilled and dried under molecular sieves. The products were purified either using flash column chromatography (packed with 60 F silica gel from Fluka Chemie AG, Buchs, Switzerland) or by washing with the appropriate solvent.

^{1}H NMR and ^{13}C NMR spectral data were obtained using a 500 MHz NMR machine (Joel 1500). Chemical shifts were recorded in ppm using tetramethylsilane as reference and $CDCl_3$ as solvent. Fourier transform infrared (FT-IR) spectra were recorded using a PerkinElmer 16F FT-IR spectrometer. Elemental analyses were performed with a PerkinElmer Series 11 (CHNS/O) Analyzer 2400. Merck 60 F_{254} silica gel plates (250 μm layer thickness) were used for TLC analyses. A Varian Saturn 2000 GC-MS machine (30 m capillary column) was used to analyse the products. An Agilent 6890 GC instrument was used to monitor reactions and analyse products.

2.2 | Synthesis of 1-Methyl-5-phenyl-1*H*-imidazole (1)

5-Bromo-1-methyl-1*H*-imidazole (0.50 mmol), $Pd(PPh_3)_2Cl_2$ (0.025 mmol, 5.0 mol%), K_2CO_3 (1.0 mmol, 2.0 mol equivalent), dimethylformamide (DMF; 2 ml), distilled water (2 ml) and phenylboronic acid (0.6 mmol) were added to a 10 ml round-bottom flask. The mixture was stirred at 90 °C for 24 h. After completion of the reaction, the mixture was cooled and extracted three times with ethyl acetate. The combined ethyl acetate extract was dried using anhydrous $MgSO_4$. The solvent was removed under vacuum and the product was purified by silica gel column chromatography using hexane–ethyl acetate (1:1) followed by 7% methanol in ethyl acetate as an eluent.

White solid; isolated yield 78%. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.50 (s, 1H, C-*H* arom), 7.41–7.38 (m, 2H, C-*H* arom), 7.35–7.33 (m, 3H, C-*H* arom), 7.07 (s, 1H, C-*H* arom), 3.62 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 32.45 (*C*H_3), 127.31, 127.69, 127.85, 128.40, 128.64, 129.62, 133.39, 133.57, 138.85 (*C*- arom). FT-IR (ν, cm^{-1}): 2353, 1718, 1489, 1444, 1115, 923, 824, 763, 701. GC-MS: m/z 158 (M^{+1}). Anal. Calcd for $C_{10}H_{10}N_2$ (158) (%): C, 75.92; H, 6.37; N, 17.71. Found (%): C, 76.11; H, 6.43; N, 17.80.

2.3 | Synthesis of Precursors for NHC Ligands (2a and 2b)

Compound **1** (0.50 mmol) and alkyl bromide (2.0 ml) were added to a 10 ml round-bottom flask. The mixture was stirred at 120 °C for 48 h. The mixture was cooled to room temperature. Diethyl ether (5 ml) was added and stirred for 15 min. The ether was decanted and the product was washed several times with ether. The pure product was dried in a vacuum.

2.3.1 | 1-Methyl-3-(2-methylpropyl)-5-phenyl-1*H*-imidazol-3-ium bromide (2a)

Yellow oil; isolated yield 71%. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 10.36 (s, 1H, C-*H* arom), 7.54–7.51 (m, 6H, C-*H* arom), 4.14 (d, 2H, J = 7.3 Hz, CH_2), 3.93 (s, 3H, CH_3), 2.21 (m, 1H, C*H*), 0.95 (d, 6H, J = 6.7 Hz, 2 × CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 19.51 (*C*H_3), 19.45 (*C*H_3), 29.28 (*C*H), 35.15 (*C*H_3), 56.86 (*C*H_2), 119.63, 124.33, 129.27, 130.55, 135.50, 137.29 (*C*- arom). FT-IR (ν, cm^{-1}): 2962, 2353, 1669, 1527, 1459, 1376, 1236, 1160, 771, 697. GC-MS: m/z 295 (M^{+1}). Anal. Calcd for $C_{14}H_{19}BrN_2$ (295) (%): C, 56.96; H, 6.49; N, 9.49. Found (%): C, 56.41; H, 6.72; N, 9.23.

2.3.2 | 3-Benzyl-1-methyl-5-phenyl-1*H*-imidazol-3-ium bromide (2b)

Brown oil; isolated yield 68%. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 10.44 (s, 1H, C-*H* arom), 7.60 (d, 2H, J = 7.0 Hz, C-*H* arom), 7.47 (d, 2H, J = 7.0 Hz, C-*H* arom), 7.39–7.36 (m, 6H, C-*H* arom), 5.67 (s, 2H, CH_2), 3.93 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 34.92 (*C*H_3), 53.19 (*C*H_2), 118.84, 124.47, 128.32, 128.90, 129.13, 129.17,

130.39, 133.00, 135.55, 137.54 (*C*- arom). FT-IR (ν, cm^{-1}): 2973, 2354, 1986, 1628, 1567, 1448, 1365, 1151. GC-MS: *m*/*z* 329 (M^{+1}). Anal. Calcd for $C_{17}H_{17}BrN_2$ (329) (%): C, 62.02; H, 5.20; N, 8.51. Found (%): C, 62.51; H, 5.33; N, 8.80.

2.4 | Synthesis of Palladium NHC Pyridine Complexes (3a and 3b)

NHC ligand precursor (**2a** or **2b**; 0.50 mmol), palladium(II) bromide (0.50 mmol), potassium carbonate (2.0 mmol) and pyridine (5 ml) were added to a 15 ml round-bottom flask. The reaction mixture was stirred at 90 °C for 24 h. The crude product was cooled to room temperature and diluted with 5 ml of dichloromethane. The mixture was then passed through a short silica column covered with a short pad of celite. The column was eluted with methanol. The solvents were removed using a rotary evaporator under reduced pressure. The complex was obtained as yellow crystals. The crystals were washed with ether and dried in vacuum. The complex was characterized with ^{1}H NMR, ^{13}C NMR and FT-IR spectroscopies, ESI-MS, elemental analysis and single-crystal X-ray diffraction analysis.

2.4.1 | Dibromide(1-methyl-3-(2-methylpropyl)-5-phenyl-1*H*-imidazol-2-ylidene)pyridine palladium(II) (3a)

Yellow crystals; isolated yield 77%. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 9.04 (s, 2H, C-*H* arom), 7.75 (s, 1H, C-*H* arom), 7.43–7.34 (m, 7H, C-*H* arom), 6.89 (s, 1H, C-*H* arom), 4.31 (d, 2H, J = 7.6 Hz, CH_2), 4.09 (s, 3H, CH_3), 2.80–2.74 (m, 1H, C-*H*), 1.09 (d, J = 6.7 Hz, 6H, CH_3 × 2). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 20.15 (*C*H_3 × 2), 28.74 (*C*H), 36.61 (*C*H_3), 58.54 (*C*H_2), 120.08, 124.30, 127.54, 128.63, 128.84, 128.92, 135.74, 137.38, 148.06, 149.54, 152.29, 153.99 (*C*- arom). FT-IR (ν, cm^{-1}): 3039, 2933, 2296, 1599, 1437, 1386, 1008, 748, 690. ESI-MS: *m*/*z* 560 (M^{+1}). Anal. Calcd for $C_{19}H_{23}Br_2N_3Pd$ (559) (%): C, 40.78; H, 4.14; N, 7.51. Found (%): C, 40.89; H, 4.52; N, 7.63.

2.4.2 | Dibromide(3-benzyl-1-methyl-5-phenyl-1*H*-imidazol-2-ylidene)pyridine palladium(II) (3b)

Yellow crystals; isolated yield 82%. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 9.08 (d, 2H, J = 6.41 Hz, CH_2 arom), 7.77 (t, 1H, J = 7.6 Hz, C-*H* arom), 7.56 (d, 2H, J = 6.7 Hz, C-*H* arom), 7.41–7.26 (m, 11H, C-*H* arom), 5.82 (s, 2H, CH_2), 4.12 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 36.74 (*C*H_3), 55.13 (*C*H_2), 119.10, 124.50, 127.70, 128.52, 128.77, 128.93, 129.08, 129.17, 129.25, 137.84, 152.59 (*C* arom). FT-IR (ν, cm^{-1}): 3043, 2932, 2300, 1958, 1605, 1446, 1213, 1160, 1065, 745, 693. ESI-MS: *m*/*z* 594 (M^{+1}). Anal. Calcd for $C_{22}H_{21}Br_2N_3Pd$ (594) (%): C, 44.51; H, 3.57; N, 7.08. Found (%): C, 44.01; H, 3.25; N, 7.00.

2.5 | X-ray Crystal Structure

Single-crystal data collection for **3a** and **3b** was performed using a Bruker-Axs Smart Apex system equipped with graphite monochromatized Mo Ka radiation (k = 0.71073 Å). The data were collected using SMART and the integration was performed using SAINT.[54] An empirical absorption correction was carried out using SADABS.[55] The structures were solved by direct methods with SHELXS-97 and refined by full-matrix least-squares procedures on F2 using the program SHELXL-97.[56] Crystal data and details of the data collection are summarized in Table 1.

2.6 | Procedure for Carbonylative Sonogashira Coupling Reactions

A 45 ml stainless steel autoclave equipped with a glass liner, gas inlet valve and pressure gauge was used for carbonylative Sonogashira coupling reactions. Palladium complex (0.10 mol%), aryl iodide (1.0 mmol), alkyne (1.2 mmol), base (2.0 mmol) and solvent (3 ml) were added to the glass liner. Additional solvent (2 ml) was added in the autoclave. The glass liner was then placed in the autoclave. The autoclave was vented three times with carbon monoxide and then pressurized to 200 psi of CO. The mixture was heated to the required temperature and maintained under stirring for the required time. After completion of reaction, the mixture was cooled to room temperature and excess CO was vented under a fume hood. The mixture was diluted with 5 ml of water and extracted three times with 10 ml of ethyl acetate. The combined ethyl acetate extract was concentrated under reduced pressure in a rotary evaporator. The products were purified using column chromatography with hexane–ethyl acetate (9:1) as eluent. The products were analysed using GC-MS, ^{1}H NMR and ^{13}C NMR analyses. The spectral data of the alkynones prepared in this study were in full agreement with those reported in the literature and they are provided in the supporting information.[22,29,37,41,44,59–61]

Analytical and spectroscopic data of the new compound: 1,1′-benzene-1,4-diylbis(4,4-dimethylpent-2-yn-1-one) (**6fi**). White solid; yield 71%. ^{1}H NMR (500 MHz, CDCl3, δ, ppm): 8.20 (s, 4H, C-*H* arom), 1.40 (s, 18H, 6 × CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 177.42,

TABLE 1 Crystallographic data for compounds **3a** and **3b**

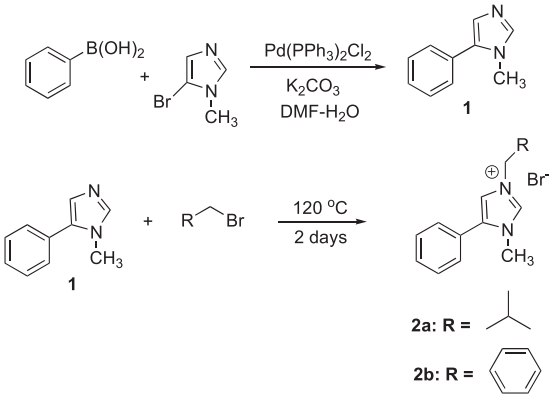
	3a	3b
Chemical formula	$C_{19}H_{23}Br_2N_3Pd$	$C_{22}H_{21}Br_2N_3Pd$
CCDC no.	1554542	1554544
Formula weight	559.62	593.64
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$
Temperature (K)	299	296
Radiation	Mo Kα (λ = 0.71073 Å)	
ρ_{calc} (g cm^{-3})	1.739	1.720
a (Å)	9.3722(5)	8.9016(7)
b (Å)	24.1786(14)	24.764(2)
c (Å)	9.4781(5)	10.4222(9)
β (°)	95.4890(10)	93.681(2)
V (Å^3)	2138.0(2)	2292.8(3)
Z	4	4
Refl. collect. / uniq.	29000 / 5308	31073 / 5685
Refl. obser. [$I > 2\sigma(I)$]	4653	4835
R(int)	0.0267	0.0329
Data / restr. / parameter	5308 / 0 / 229	5685 / 0 / 254
Goodness-of-fit on F^2	1.073	1.017
R indices [$I > 2\sigma(I)$]	R_1 = 0.0614; wR_2 = 0.2243	R_1 = 0.0305; wR_2 = 0.0740
R indices (all data)	R_1 = 0.0671; wR_2 = 0.2320	R_1 = 0.0384; wR_2 = 0.0782
Largest diff. peak, hole (e Å^{-3})	2.927, −2.097	1.320, −1.211

140.39, 137.79, 129.64, 105.33, 78.02, 30.07, 29.05. GC-MS: m/z 294 (M + 1). Anal. Calcd for $C_{20}H_{22}O_2$ (294) (%): C, 81.60; H, 7.53. Found (%): C, 81.91; H, 7.88.

3 | RESULTS AND DISCUSSION

3.1 | Synthesis of Ligands 2a and 2b

Compound **1** was prepared in good yield from the Suzuki–Miyaura cross-coupling reaction of 5-bromo-1-methyl-1*H*-imidazole with phenylboronic acid (Scheme 1). Ligands **2a** and **2b** were prepared in good yields by the direct alkylation of **1** with either isobutyl bromide or benzyl bromide (Scheme 1). Formation of the imidazolium bromides was confirmed by the presence of downfield singlet peaks at 10.21 ppm (**2a**) and 10.44 ppm (**2b**) in the ^{1}H NMR spectra, which are assigned to C-2 protons of the imidazole rings.



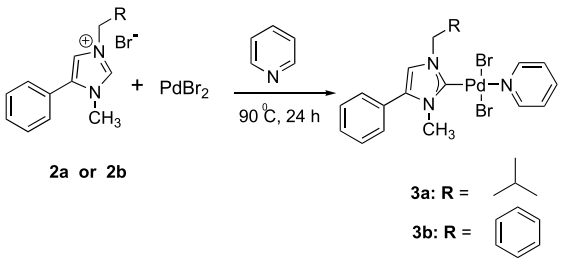
SCHEME 1 Synthesis of NHC ligand precursors

3.2 | Synthesis of Complexes 3a and 3b

The Pd–NHC–Py complexes **3a** and **3b** were prepared in good yields by reacting palladium bromide with 1.0 eq. of the appropriate ligand precursor (**2a** or **2b**) in pyridine (Scheme 2). Complexes **3a** and **3b** were purified by passing through a column of silica gel layered with a short pad of celite. Complexes **3a** and **3b** were isolated as yellow solids. The formation of the complexes was confirmed by the disappearance of the acidic C-2 protons of the imidazole rings, initially present in the *N*-substituted imidazolium salts, following palladation of the NHC ligand precursors. Furthermore, there is the appearance of a new signal at 152 ppm in the ^{13}C NMR spectra of both complexes assignable to the palladated carbon Pd—*C*. In the ESI-MS of the two complexes, base peaks were observed at 560 (**3a**) and 594 (**3b**) which confirmed the formation of the two Pd–carbene complexes.

3.3 | Molecular Structures of Palladium Complexes 3a and 3b

X-ray-quality single crystals were grown by slow evaporation of a solution of the compounds in a mixture of dichloromethane and diethyl ether. Both complexes crystallize in the monoclinic $P2_1/c$ space group with one molecule in the asymmetric unit. Selected bond distances and bond angles are listed in Tables 2 and 3. The molecular structures are depicted in Figures 1 and 2. In both



SCHEME 2 Synthesis of complexes **3a** and **3b**

TABLE 2 Selected bond distances and bond angles for **3a**

Bond distance (Å)		Bond angle (°)	
Pd1–C1	1.954(6)	C1–Pd1–N3	178.1(2)
Pd1–N3	2.124(6)	C1–Pd1–Br2	86.83(19)
Pd1–Br2	2.5123(8)	N3–Pd1–Br2	91.55(18)
Pd1–Br1	2.5565(8)	C1–Pd1–Br1	88.74(19)
N1–C1	1.370(8)	N3–Pd1–Br1	92.87(18)
N1–C3	1.377(8)	Br2–Pd1–Br1	175.53(3)
N1–C4	1.478(8)	C1–N1–C3	110.8(5)
N2–C1	1.342(8)	C1–N1–C4	122.2(6)
N2–C2	1.382(9)	C3–N1–C4	126.9(6)
N2–C5	1.473(8)	C1–N2–C2	110.6(6)
		C1–N2–C5	126.3(6)
		C2–N2–C5	123.0(6)

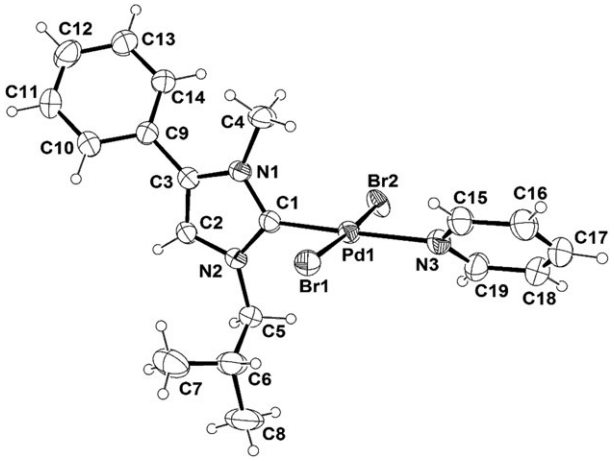


FIGURE 1 ORTEP diagram of **3a** showing the atomic labelling scheme. Thermal ellipsoids are drawn at 30% probability level

palladium(II) complexes **3a** and **3b**, the NHC carbene and pyridine ligands are in *trans* positions and the geometry is distorted square planar. The Pd—C, Pd—Br and Pd—N bond distances are in the same range as those reported for analogous palladium complexes.[57,58] The dihedral angles between the NHC and [$PdBr_2CN$] mean planes are 89.6(2)° and 86.68(9)° for **3a** and **3b**, respectively, while those between the pyridine and [$PdBr_2CN$] mean planes are 42.9(2)° and 53.4(1)°, respectively. This significant difference is likely due to van der Walls packing contacts with the ligands of neighbouring complex molecules.

3.4 | Carbonylative Sonogashira Coupling of Iodobenzene and Phenylacetylene Catalysed by Complexes 3a and 3b: Optimization of Reaction Conditions

Pd(II)–NHC complexes have proven to be efficient and active catalysts for a wide range of cross-coupling reactions, especially C—C bond coupling. A plethora of articles have been published on this topic.[43,45–49] However, the application of Pd(II)–NHC complexes in carbonylative cross-coupling reactions is limited. In previously reported works, higher catalyst loading[37] and long reaction time[44] limited the scope of these reactions.

However, we have examined in detail the applications of the newly synthesized complexes **3a** and **3b** in the carbonylative Sonogashira coupling reactions of aryl iodides with arylalkynes and alkylalkynes.

The carbonylative Sonogashira coupling reaction of iodobenzene with phenylacetylene in the presence of a catalytic amount of **3a** was adopted as a model reaction (equation (1)). The results of the optimization reactions are summarized in Table 4. When the reaction was run with triethylamine as base, at 60 °C for 6 h, only 20% of 1,3-diphenylprop-2-yn-1-one (Table 4, entry 1)

TABLE 3 Selected bond distances and bond angles for **3b**

Bond distance (Å)		Bond angle (°)	
Pd1–C1	1.967(2)	C1–Pd1–N3	176.85(10)
Pd1–N3	2.103(2)	C1–Pd1–Br2	87.00(7)
Pd1–Br2	2.4148(4)	N3–Pd1–Br2	90.60(7)
Pd1–Br1	2.4226(4)	C1–Pd1–Br1	91.50(7)
N1–C1	1.339(3)	N3–Pd1–Br1	90.87(7)
N1–C9	1.384(3)	Br2–Pd1–Br1	178.067(17)
N1–C2	1.467(3)	C1–N1–C9	110.4(2)
N2–C1	1.349(3)	C1–N1–C2	125.5(2)
N2–C1	1.396(3)	C9–N1–C2	124.0(2)
N2 C17	1.459(3)	C1–N2–C10	110.6(2)
		C1–N2–C17	122.9(2)
		C10–N2–C17	126.5(2)

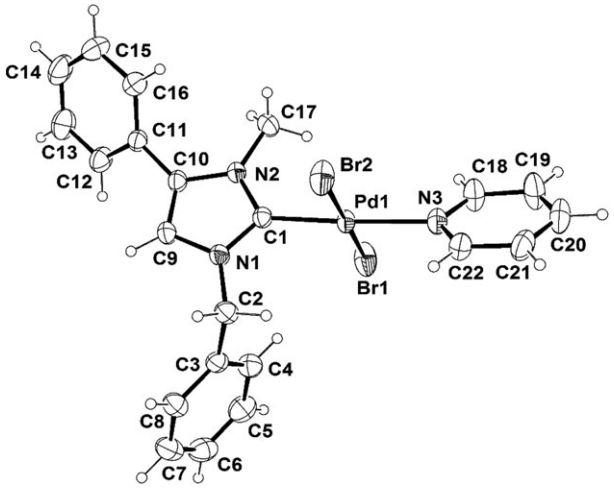
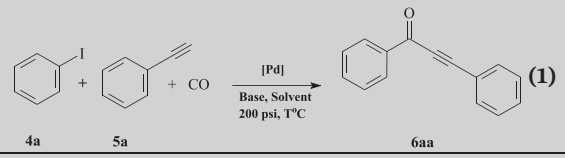


FIGURE 2 ORTEP diagram of **3b** showing the atomic labelling scheme. Thermal ellipsoids are drawn at 30% probability level

TABLE 4 Optimization of carbonylative Sonogashira coupling reactions of iodobenzene (**4a**) and phenylacetylene (**5a**)[a]



Entry	Solvent	Temp. (°C)	Base	Catalyst	Time (h)	Yield of 6aa (%)[b]
1	Toluene	60	Et_3N	**3a**	6	20
2	Toluene	80	Et_3N	**3a**	6	51
3	Toluene	100	Et_3N	**3a**	6	70
4	Toluene	110	Et_3N	**3a**	6	83
5	Toluene	120	Et_3N	**3a**	6	95
6	DMF	120	Et_3N	**3a**	6	67
7	CH_3CN	120	Et_3N	**3a**	6	81
8	Dioxane	120	Et_3N	**3a**	6	43
9	Toluene	120	—	**3a**	6	0
10	Toluene	120	K_2CO_3	**3a**	6	Trace
11	Toluene	120	KOH	**3a**	6	Trace
12	Toluene	120	Et_3N	**3a**	1	38
13	Toluene	120	Et_3N	**3a**	2	65
14	Toluene	120	Et_3N	**3a**	3	82
15	Toluene	120	Et_3N	**3a**	4	97
16	Toluene	120	Et_3N	**3b**	6	95
17	Toluene	120	Et_3N	$Pd(PPh_3)_2Cl_2$	6	78
18	Toluene	120	Et_3N	$Pd(PhCN)_2Cl_2$	6	48
19	Toluene	120	Et_3N	$PdBr_2$	6	40

[a]Reaction conditions: [Pd] (0.10 mol%), iodobenzene (1.0 mmol), phenylacetylene (1.5 mmol), base (2.0 mmol), solvent (5 ml), CO (200 psi).

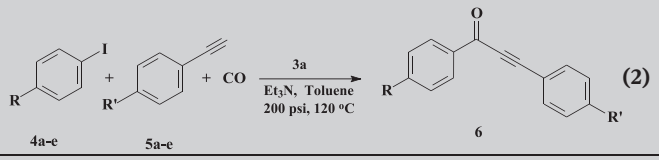
[b]Isolated yield.

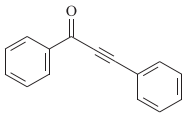
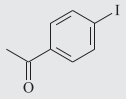
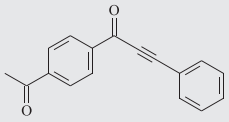
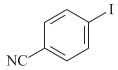
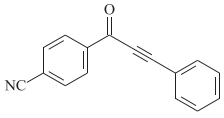
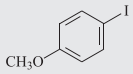
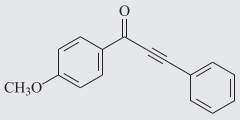
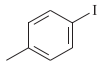
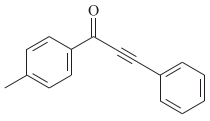
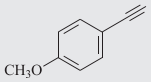
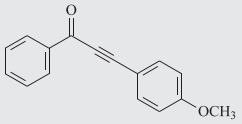
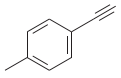
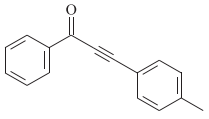
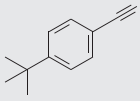
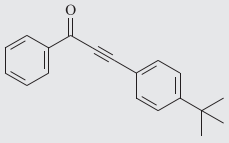
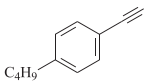
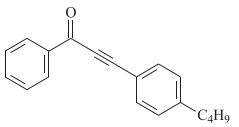
as a product was obtained. The yield of the product gradually increased with an increase in temperature (Table 4, entries 1–4). Complete conversion of iodobenzene and 95% isolated yield of alkynone were achieved at 120 °C (Table 4, entry 5). A substantial decrease in the isolated yield was noted when DMF (Table 4, entry 6), acetonitrile (Table 4, entry 7) or dioxane (Table 4, entry 8) was used in place of toluene as a solvent. No product was observed when the reaction was carried out in the absence of a base (Table 4, entry 9). Moreover, only traces of product were observed with K_2CO_3 (Table 4, entry 10) and KOH (Table 4, entry 11) as bases. Based on the above results, the subsequent reactions were carried out using toluene as a solvent, Et_3N as a base and at 120 °C for 6 h. These optimized conditions were adopted, under which the other catalyst (**3b**) gave similar results (Table 4, entry 16). For comparison, commercially available palladium catalysts were also investigated (Table 4, entries 17–19).

3.5 | Carbonylative Sonogashira Coupling Reactions of Aryl Iodides with Arylalkynes Catalysed by 3a

Since the optimized conditions showed excellent results for the newly synthesized Pd complexes in carbonylative Sonogashira coupling reactions, the scope of substrates was considered using catalyst **3a**. Using optimized conditions (0.10 mol% of **3a**, 2.0 eq. of Et_3N, 5 ml of toluene, 200 psi CO, 120 °C), various aryl iodides were reacted with a range of functionalized arylalkynes (equation (2), Table 5). A variety of electron-withdrawing and electron-donating substituted aryl iodides were reacted efficiently with arylalkynes and CO to produce the corresponding alkynones in excellent yields. The carbonylative Sonogashira coupling reaction of phenylacetylene with unactivated aryl iodide (Table 5, entry 1), deactivated aryl iodides (Table 5, entries 2 and 3) and activated aryl iodides (Table 5, entries 4 and 5) afforded the corresponding

TABLE 5 Carbonylative Sonogashira coupling reactions of aryl iodides (**4a–e**) with arylalkynes (**5a–e**) catalysed by **3a**[a]



Entry	Aryl iodide (4)	Arylalkyne (5)	Product (6)	Yield (%)[b]
1	 4a	 5a	 6aa	96
2	 4b	5a	 6ba	92
3	 4c	5a	 6ca	94
4	 4d	5a	 6da	93
5	 4e	5a	 6ea	94
6	4a	 5b	 6ab	96
7	4a	 5c	 6ac	95
8	4a	 5d	 6ad	93
9	4a	 5e	 6ae	92

[a]Reaction conditions: **3a** (0.10 mol%), aryl iodide (1.0 mmol), alkyne (1.5 mmol), Et_3N (2.0 mmol), toluene (5 ml), CO (200 psi), 120 °C, 6 h.

[b]Isolated yield.

alkynones in excellent yields (92–96%). The carbonylative Sonogashira coupling reactions of iodobenzene with various arylalkynes (Table 5, entries 6–9) were also very successful.

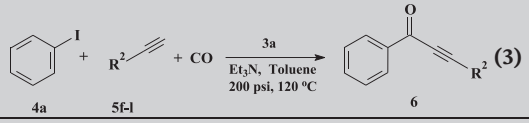
3.6 | Carbonylative Sonogashira Coupling Reactions of Aryl Iodides with Alkylalkynes

The phosphine-free carbonylative Sonogashira cross-coupling reactions of aryl iodides with alkylalkynes have been rarely investigated. Interestingly, complexes **3a** and **3b** were found to be highly active in the carbonylative coupling reactions of aryl iodides with alkylalkynes with a catalyst loading as low as 0.10 mol% (equation (3), Table 6). For instance, the carbonylative coupling reactions of iodobenzene with 1-pentyne (Table 6, entry 1), 1-hexyne (Table 6, entry 2) and 1-decyne (Table 6, entry 3) were successful to afford the expected alkynones in very good to excellent yields (80–91%). The yields of the reactions were found to vary slightly with the alkyl chain lengths. Alkylalkynes having fewer carbon atoms, such as 1-pentyne (Table 6, entry 1), were found to be more reactive as compared to alkylalkynes with higher numbers of carbon atoms such as 1-decyne (Table 6, entry 3) under the same experimental conditions. Similarly, the carbonylative Sonogashira coupling reaction of iodobenzene with 3,3-dimethyl-1-butyne yielded 94% of the expected alkynone (Table 6, entry 4). The reactivity of phenyl-substituted alkylalkynes with iodobenzene is also comparable with that of other alkylalkynes (Table 6, entries 5 and 6).

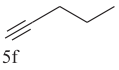
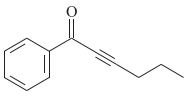
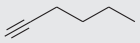
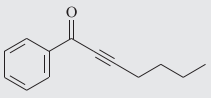
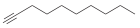
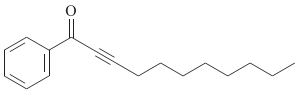
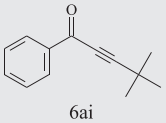
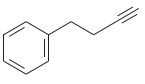
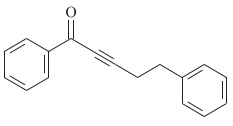
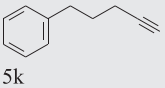
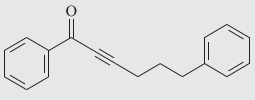
3.7 | Carbonylative Sonogashira Coupling Reactions of Aryl Iodides with Dialkynes and Aryl Diiodides with Alkynes Catalysed by 3a

Considering the high catalytic performance of the newly synthesized Pd–NHC–Py complexes **3a** and **3b**, we investigated the carbonylative Sonogashira coupling reactions of aryl iodides with dialkynes and of aryl diiodides with alkynes. Notably, the reactions successfully proceeded to give symmetrical dialkynones in good to very good isolated yields. For instance, the coupling reaction of 1,4-diethynylbenzene and 1,3-diethynylbenzene with 2 eq. of iodobenzene proceeded smoothly to afford the

TABLE 6 Carbonylative Sonogashira coupling reactions of iodobenzene (**4a**) with alkylalkynes (**5f–l**) catalysed by **3a**[a]



4a 5f-l 6

Entry	Aryl iodide	Alkylalkyne	Product	Yield (%)[b]
1	 4a	 5f	 6af	91
2	4a	 5g	 6ag	87
3	4a	 5h	 6ah	80
4	4a	 5i	 6ai	94
5	4a	 5j	 6aj	81
6	4a	 5k	 6ak	77

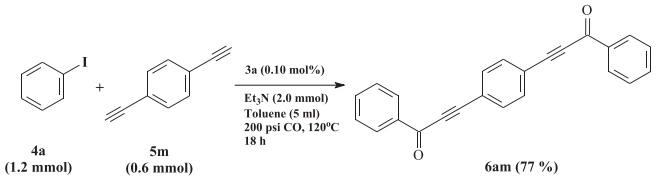
[a]Reaction conditions: **3a** (0.10 mol%), aryl iodide (1.0 mmol), alkyne (1.5 mmol), Et_3N (2.0 mmol), toluene (5 ml), CO (200 psi), 120 °C, 18 h.

[b]Isolated yield.

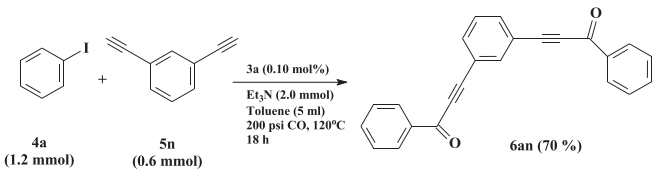
TABLE 7 Comparison of activity of new catalytic system **3a** in carbonylative Sonogashira coupling reactions of aryl iodides and alkynes with previously published data

Ref.	Catalyst	Co-catalyst/ligand/additive	Base	Time (h)	Yield (%)
[30]	$PdCl_2$ (5 mol%)	PPh_3 (10 mol%)	Et_3N	24	46–95
[16]	$Pd(OAc)_2$ (3 mol%)	PPh_3 (6 mol%), diisopropylcarbodiimide (2 eq.)	Et_3N	20	63–99
[21]	$Pd(OAc)_2$ (3 mol%)	PPh_3 (6 mol%)	Et_3N	17–24	43–88
[64]	$Pd(OAc)_2$ (5 mol%)	TBAAc (1.5 eq.)	Et_3N	12	45–84
Present work	Pd–NHC–Py (0.1 mol%)	—	Et_3N	6	88–94

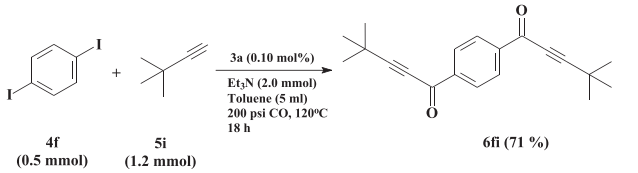
corresponding *para*-dialkynone (**6 am**; equation (4)) and *meta*-dialkynone (**6an**; equation (5)) in yields of 77 and 70%, respectively. Additionally, the new Pd–NHC–Py complexes show high catalytic performance in the carbonylative Sonogashira coupling of 1,4-diiodobenzene with alkylalkynes to yield the corresponding dialkynones **6fi** (equation (6)) and **6fo** (equation (7)), respectively.



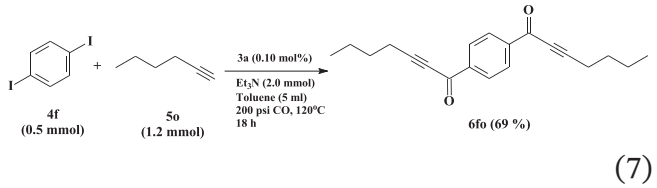
(4)



(5)



(6)

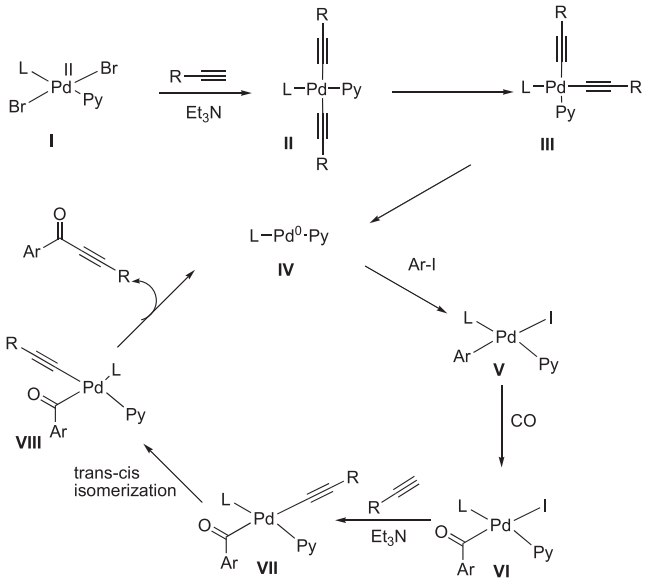


(7)

The high yields and selectivities obtained with the catalytic coupling of aryl iodides and diiodides with alkynes and dialkynes showed the high efficacy of the new complexes **3a** and **3b** in catalysis. Complex **3a** exhibited superior catalytic activity with much lower loading as compared to other catalytic systems reported in the literature (Table 7).

+B: 2.8 Plausible Mechanism for Carbonylative Sonogashira Coupling Reaction

The palladium(II) pre-catalyst undergoes first a substitution of bromides by acetylides, formed by deprotonation of alkynes in the presence of triethylamine, followed by a *trans–cis* isomerization step and a reductive elimination of the dialkyne to generate the Pd(0) active catalyst (Scheme 3). NHCs are known to be stronger s donors than phosphine ligands and their transition metal complexes are more stable than the phosphine-based analogues, this despite the fact that they are less prone to p back-bonding from transition metal ions.[62,63] In light of these facts, the higher catalytic activity of **3a**, relative to the literature-reported palladium/phosphine systems, may be rationalized in several ways. On the one hand, in terms of the higher stability of both the pre-catalyst (NHC)Pd(II)(Py)Br_2 and the proposed active species (NHC)Pd(0)(Py), in



SCHEME 3 Plausible mechanism for carbonylative Sonogashira coupling reaction catalysed by Pd–NHC–Py complex

comparison with their phosphine-based counterparts. On the other hand, both the oxidative addition and substitution steps are likely to be enhanced by the more electron-rich species (NHC)Pd(0)(Py) and (NHC)Pd(II)(Py)(RCO)(I), respectively, compared to their phosphine-based analogues in the case of $Pd(PPh_3)_2Cl_2$-catalysed reactions. Accordingly, the inductive effect of 2-methylpropyl substituent in **3a**, leading to a more electron-rich palladium centre relative to the benzyl group in **3b**, is likely at the origin of the higher activity of the former. Aryl iodide is then added to Pd(0) in the oxidative addition step to form the palladium(II) intermediate ArPdLPyI (**V**). This step is followed by CO insertion into the Ar—Pd bond to form the acyl Pd intermediate (**VI**). Substitution of the iodide by the acetylide (**VII**), *trans–cis* isomerization (**VIII**) followed by reductive elimination yield the carbonylative Sonogashira product with the subsequent regeneration of the Pd(0) catalyst.[40,42]

4 | CONCLUSIONS

New NHC–Py ligands and new Pd–NHC–Py complexes (**3a** and **3b**) have been successfully synthesized and characterized using various analytical and spectroscopic techniques including single-crystal X-ray diffraction. The catalytic activities of the new complexes **3a** and **3b** were investigated in the carbonylative Sonogashira coupling reactions of various aryl iodides with arylalkynes and alkylalkynes including dialkynes. Excellent isolated yields of the expected alkynones were obtained for aryl iodides with both arylalkynes and alkylalkynes and very good yields were achieved for the carbonylative coupling of aryl diiodide with arylalkynes. Worth noting is the synthesis of a new compound, 1,1′-benzene-1,4-diylbis(4,4-dimethylpent-2-yn-1-one), from the carbonylative Sonogashira coupling reaction of 1,4-diiodobenzene with 4,4-dimethylpent-2-yne using the new catalytic system based on complex **3a**.

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REFERENCES

[1] A. S. Karpov, E. Merkul, F. Rominger, T. J. Müller, *Angew. Chem. Int. Ed.* **2005**, *44*, 6951.

[2] J. D. Kirkham, S. J. Edeson, S. Stokes, J. P. Harrity, *Org. Lett.* **2012**, *14*, 5354.

[3] M. S. Mohamed Ahmed, K. Kobayashi, A. Mori, *Org. Lett.* **2005**, *7*, 4487.

[4] A. Arcadi, M. Aschi, F. Marinelli, M. Verdecchia, *Tetrahedron* **2008**, *64*, 5354.

[5] C. G. Lee, K. Y. Lee, S. Lee, J. N. Kim, *Tetrahedron* **2005**, *61*, 493.

[6] P. Bannwarth, A. Valleix, D. Grée, R. Grée, *J. Org. Chem.* **2009**, *74*, 4646.

[7] E. Awuah, A. Capretta, *Org. Lett.* **2009**, *11*, 3210.

[8] Z. She, D. Niu, L. Chen, M. A. Gunawan, X. Shanja, W. H. Hersh, Y. Chen, *J. Org. Chem.* **2012**, *77*, 3627.

[9] C. L. Taylor, Y. Bolshan, *J. Vis. Exp.* **2015**, *9*, 52401.

[10] A. Zapf, M. Beller, *Topics Catal.* **2002**, *19*, 101.

[11] X. F. Wu, H. Neumann, M. Beller, *Chem. Soc. Rev.* **2011**, *40*, 4986.

[12] J. B. Peng, X. Qi, X. F. Wu, *Synlett* **2017**, *28*, 175.

[13] C. Shen, X. F. Wu, *Chem. A Eur. J.* **2017**, *23*, 2973.

[14] X. F. Wu, H. Neumann, M. Beller, *Chem. Rev.* **2013**, *113*, 1.

[15] J. B. Peng, F. P. Wu, C. L. Li, X. Qi, X.-F. Wu, *Eur. J. Org. Chem.* **2017**, *1434*.

[16] Y. Wang, X. Yang, J. Yu, *RSC Adv.* **2017**, *7*, 31850.

[17] F.-P. Wu, J. B. Peng, X. Qi, X. F. Wu, *Cat. Sci. Technol.* **2017**, *7*, 4924.

[18] P. Gautam, B. M. Bhanage, *Chemistry Select* **2016**, *1*, 5463.

[19] G. Martra, *Appl. Catal. A* **2014**, *80*, 1.

[20] X. Qi, L. B. Jiang, C. L. Li, R. Li, X. F. Wu, *Chem. Asian J.* **2015**, *10*, 1870.

[21] W. Li, X. F. Wu, *Org. Biomol. Chem.* **2015**, *13*, 5090.

[22] X.-F. Wu, H. Neumann, M. Beller, *Chem. A Eur. J.* **2010**, *16*, 12104.

[23] S. Perrone, F. Bona, L. Troisi, *Tetrahedron* **2011**, *67*, 7386.

[24] T. Kobayashi, M. Tanaka, *J. Chem. Soc. Chem. Commun.* **1981**, *333*.

[25] S.-K. Kang, H.-C. Ryu, Y.-T. Hong, *J. Chem. Soc. Perkin Trans.* **2001**, *1*, 736.

[26] X.-F. Wu, H. Neumann, M. Beller, *Org. Biomol. Chem.* **2011**, *9*, 8003.

[27] M. T. Rahman, T. Fukuyama, N. Kamata, M. Sato, I. Ryu, *Chem. Commun.* **2006**, *2236*.

[28] M. S. M. Ahmed, A. Mori, *Org. Lett.* **2003**, *5*, 3057.

[29] B. Liang, M. W. Huang, Z. J. You, Z. C. Xiong, K. Lu, R. Fathi, J. H. Chen, Z. Yang, *J. Org. Chem.* **2005**, *70*, 6097.

[30] B. M. O'Keefe, N. Simmons, S. F. Martin, *Org. Lett.* **2008**, *10*, 5301.

[31] P. J. Tambade, Y. P. Patil, N. S. Nandurkar, B. M. Bhanage, *Synlett* **2008**, 886.

[32] A. Park, K. Park, Y. Kim, S. Lee, *Org. Lett.* **2011**, *13*, 944.

[33] A. Brennführer, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2009**, *48*, 4114.

[34] J. H. Liu, J. Chen, W. Sun, C. G. Xia, *Cuihua Xuebao* **2010**, *1*, 31.

[35] S. T. Gadge, B. M. Bhanage, *RSC Adv.* **2014**, *4*, 10367.

[36] X.-F. Wu, B. Sundararaju, H. Neumann, P. H. Dixneuf, M. Beller, *Chem. A Eur. J.* **2011**, *17*, 106.

[37] C. Bai, S. Jian, X. Yao, Y. Li, *Sci. Technol.* **2014**, *4*, 3261.

[38] Y. Wang, J. H. Liu, C. G. Xia, *Tetrahedron Lett.* **2011**, *52*, 1587.

[39] M. Genelot, V. Dufaud, L. Djakovitch, *Synth. Catal.* **2013**, *355*, 2604.

[40] J. H. Liu, J. Chen, C. G. Xia, *J. Catal.* **2008**, *253*, 50.

[41] J. M. Liu, X. G. Peng, W. Sun, Y. W. Zhao, C. G. Xia, *Org. Lett.* **2008**, *10*, 3933.

[42] W. Y. Hao, J. C. Sha, S. R. Sheng, M. Z. Cai, *J. Mol. Catal. A* **2009**, *298*, 94.

[43] F. Rajabi, W. R. Thiel, *Adv. Synth. Catal.* **2014**, *356*, 1873.

[44] C. Zhang, J. Liu, C. Xia, *Org. Biomol. Chem.* **2014**, *12*, 9702.

[45] A. Chartoire, A. Boreux, A. R. Martin, S. P. Nolan, *RSC Adv.* **2013**, *3*, 3840.

[46] T. Wang, H. Xie, L. Liu, W. X. Zhao, *J. Org. Chem.* **2016**, *804*, 73.

[47] K. Natte, J. Chen, H. Neumann, M. Beller, X. Wu, *Biomol. Chem.* **2014**, *12*, 5590.

[48] A. Chartoire, X. Frogneux, S. P. Nolan, *Adv. Synth. Catal* **2012**, *354*, 1897.

[49] V. H. Nguyen, M. B. Ibrahim, W. W. Mansour, B. M. El Ali, H. V. Huynh, *Organometallics* **2017**, *36*, 2345.

[50] M. B. Ibrahim, B. El Ali, M. Fettouhi, L. Ouahab, *Appl. Organomet. Chem.* **2015**, *29*, 400.

[51] M. B. Ibrahim, S. M. S. Hussain, A. Fazal, M. Fettouhi, B. El Ali, *J. Coord. Chem.* **2015**, *68*, 432.

[52] S. M. S. Hussain, M. B. Ibrahim, A. Fazal, R. Suleiman, M. Fettouhi, B. El Ali, *Polyhedron* **2014**, *70*, 39.

[53] M. B. Ibrahim, R. Suleiman, M. Fettouhi, B. El Ali, *RSC Adv.* **2016**, *6*, 78826.

[54] Bruker, Smartm Saint, Bruker Axs Inc., Madison, WI, **2008**.

[55] G. M. Sheldrick, *SADABS, Program for Empirical Absorption Correction of Area Detector Data*, University of Gottingen, Germany **1996**.

[56] G. M. Sheldrick, *Acta Crystallogr.* **2008**, *64*, 112.

[57] Y.-C. Lin, H. H. Hsueh, S. Kanne, L.-K. Chang, F.-C. Liu, I. J. B. Lin, G.-H. Lee, S.-M. Peng, *Organometallics* **2013**, *32*, 3859.

[58] L. Ray, M. M. Shaikh, P. Ghosh, *Dalton Trans.* **2007**, *4546*.

[59] K. Y. Lee, M. J. Lee, J. N. Kim, *Tetrahedron* **2005**, *61*, 8705.

[60] C. Chowdhury, N. G. Kundu, *Tetrahedron* **1999**, *55*, 7011.

[61] Q. Wei, H. Deng, Y. Cai, J. W. Y. Lam, J. Li, J. Sun, M. Gao, A. Qin, N. Z. Tang, *Macromol. Rapid Commun.* **2012**, *33*, 1356.

[62] D. J. D. Wilson, S. A. Couchman, J. L. Dutton, *Inorg. Chem.* **2012**, *51*, 7657.

[63] J. Jover, N. Fey, M. Purdie, G. C. Lloyd-Jones, J. N. A. Harvey, *J. Mol. Catal. A* **2010**, *39*, 324.

[64] M. Bakherad, A. Keivanloo, B. Bahramian, S. Jajarmi, *Synlett* **2011**, *3*, 311.

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