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PII: S0022-328X(18)30239-0

DOI: 10.1016/j.jorganchem.2018.04.009

Reference: JOM 20401

To appear in: Journal of Organometallic Chemistry

Received Date: 19 February 2018

Revised Date: 1 April 2018

Accepted Date: 8 April 2018

Please cite this article as: B. Ghanbari, L. Shahhoseini, H. Hosseini, M. Bagherzadeh, A. Owczarzak, M. Kubicki, Synthesis of Pd(II) large dinuclear macrocyclic complex tethered through two dipyridinebridged aza-crowns as an efficient copper- and phosphine-free Sonogashira catalytic reaction, *Journal of Organometallic Chemistry* (2018), doi: 10.1016/j.jorganchem.2018.04.009.

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Synthesis of Pd(II) Large Dinuclear Macrocyclic Complex Tethered Through two Dipyridine-Bridged aza-Crowns as an Efficient Copper- and Phosphine-Free Sonogashira Catalytic Reaction

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Abstract

For the first time the new 32-membered macrocyclic dinuclear palladium complex of two aza-crown macrocycles, bearing two pyridine arms, $Pd_2L_2Cl_4$ was synthesized and characterized by elemental analysis, IR, NMR spectroscopy and single crystal X-ray diffraction methods. $Pd_2L_2Cl_4$ was investigated as a moisture/air-stable catalyst for Sonogashira cross-coupling reaction in the absence of copper and phosphine ligand in DMSO. Thermal stability, possible occurrence of tandem reactions, promoted catalytic performance as well as synergistic effects are of advantageous features of $Pd_2L_2Cl_4$. By employing Taguchi method, optimum conditions (110 °C, 6h, KOAc, 2 mol% cat.) were determined. Moreover, the homogenous catalyst represented good reusability up to four cycles. Comparing the catalytic activity of several other previously reported Pd(II) dinuclear complexes, $Pd_2L_2Cl_4$ enjoys the advantages of short time of reaction and thermal stability.

Keywords: dinuclear, macrocyclic, Sonogashira, palladium.

1. Introduction

Due to the applicability in the formation of carbon–carbon bonds, alkynylation *via* Sonogashira cross-coupling is one of the key reactions in organic synthesis ^[1–4]. Moreover, Pd(II) complexes are exceedingly effective and eminent catalysts applicable in the syntheses of the polyfunctional alkynes by combination of the corresponding alkynes and aryl halides, whereby the development of new catalysts is of vital research interest ^[5–9].

Historically, Sonogashira employed [PdCl₂(PPh₃)₂] for alkynylation reaction along with Cu(I) salt as co-catalyst in the presence of diethylamine as base and solvent in inert atmosphere ^[10]. The catalytic reaction suffers from two drawbacks. Firstly, the formation of a diyne due to the oxidative coupling of terminal acetylene (also known as Glaser–Hay type reaction) resulted in unwanted byproducts ^[11]. Again, owing to humidity and air sensitivity of phosphine ligands, researchers are encouraged to look for new alternative ligands to eliminate the necessity for inert condition in this catalytic reaction by developing copper- and phosphine-free Pd(II) catalysts ^[12–21].

Development of macrocyclic dinuclear Pd(II) (MDP) complexes are of significant research interests which had high contribution on development of new catalysts in modern synthetic organic chemistry ^[20,22]. Basically, MDP catalysts enjoy from two main features as having two metal cores and encompassing of the metal ions within the cyclic structure. From a mechanistic point of view, the presence of two metal cores in MDP catalysts results in synergistic effects which consecutively give rise to possible occurrence of tandem reactions ^[23]. Hence, these catalysts exhibit better catalytic activity and selectivity together with higher efficiencies in comparison with corresponding monometallic catalysts ^[24]. Another distinctive feature of MDP catalysts is their thermal stability which leads to the catalytic reactions at temperatures above 100°C.

The coordination chemistry of bridging ligands anchored with pyridine side arms has been shown to have prominent complex ability towards transition metal ions, leading to the formation of coordination polymers ^[25,26], coordination spheres ^[27–29], notable collection of macrocycles as well as interlocked molecules potentially applicable in formation of molecular machines ^[30]. In 1993, Fujita reported bis(4-pyridyl)-substituted ligands as new flexible dinuclear macrocyclic ligands to form *cis*-enthylenediamine Pd(II) complexes ^[31]. Later, he also published several reports on a group of functional macrocyclic complexes ^[32,33]. Since pyridine and pyrimidine moieties demonstrated appropriate complexation properties for Pd(II) cation, they were reputed as the suitable catalytic candidates for Sonogashira coupling reactions. In the meantime, the dipyrimidyl-Pd(II) complexes were employed in the copper-free coupling of different halobenzene with phenylacetylene using N-butylamine as base in THF solvent at 65 °C ^[34]. Recently, we reported ^[35] the synthesis of a tecton L (Scheme 1) constructed from aza-crown

macrocycle decorated with two pyridine side arms, capable to yield several new 1D coordination polymers (CPs) with Mn(II), Ni(II), Cu(II), Cd(II) and Pb(II) cations.

Scheme 1 is here

In the course of preparation more new CPs, however, we strikingly found that **L** was capable to produce a new MDP in the presence of Pd(II) (Scheme 1), instead. To the best of our knowledge, no report on the synthesis nor catalytic activity of MDP complexes cyclized through aza-crown macrocycle linkers has been reported before. Thus, we undertook the synthesis, full characterization and catalytic activity of the new large 32-membered MDP complex, $Pd_2L_2Cl_4$, comprising two aza-crown macrocycles bearing two pyridine linkers, coordinating Pd(II) in the *trans* form (Scheme 1).

2. Results and discussion

2.1. Syntheses and characterizations

The macrocyclic ligand **L** was synthesized^[35] through the reaction of the precursor macrocycle **1** with two equivalents of 4-(chloromethyl) pyridine hydrochloride in the present of potassium carbonate and potassium iodide in DMF as solvent (Scheme 1). The purity of the sample was checked by employing ¹H and ¹³C{¹H}NMR spectroscopy (Fig. S1).

The dinuclear complex, $Pd_2L_2Cl_4$, was quantitatively prepared by admixing of L and bis(acetonitrile) dichloropalladium(II) in DMF (see also Scheme 1).

2.2. Single Crystal X-ray Diffraction Studies

Some appropriate crystals of $Pd_2L_2Cl_4$ applicable in X-ray crystallography were obtained by slow layering of L on DMF solution of bis(acetonitrile)dichloropalladium(II) complex without stirring and keeping the solution at room temperature for several days. Some selected crystallographic data for $Pd_2L_2Cl_4$ complex were summarized in Table S1.

The molecular structure of $Pd_2L_2Cl_4$ was shown in Figure 1, together with the pertinent atomic notations.

Figure 1 is here

The dimeric complex molecule is C_i -symmetrical (it lies across the inversion center in the space group $P2_1/n$; in consequence, the asymmetric unit for $Pd_2L_2Cl_4$ encompasses one macrocyclic ligand (L), two Cl atoms and one Pd(II) center together with three DMF molecules (Figure 1b). Table S1 and Figure 1b show some selected bond lengths and angles for $Pd_2L_2Cl_4$ complex. The crystal structure of $Pd_2L_2Cl_4$ exhibited a dinuclear architecture, resembling a rhombus having two Pd(II) centers on each parallel sides, whereby bridged via two flexible L units. Pd atoms were coordinated with two nitrogen donors of the pyridyl side arms on L alongside two chlorine atoms that brought about a square planar geometry about the Pd(II) metal center (see also the bond angles for the abovementioned square planer geometry in Table S2). The resulted $Pd_2L_2Cl_4$ complex demonstrated a *trans* stereochemistry, i.e. *trans*- $[Pd_2(\mu-L)_2Cl_4]$ Meanwhile, the macrocycle moieties on $Pd_2L_2Cl_4$ accepted drawn-out chair conformations. The molecular dimensions of $Pd_2L_2Cl_4$ were ~13.7 × 5.6 Å, whereas two Pd(II) atoms were separated from each other by ~5.41Å. Three molecules of DMF were situated on one side of the aromatic ring (Figure S2) and connected through CH...O type hydrogen bonding interactions between C(10)–H(10A), C(27)-H(27) of $Pd_2L_2Cl_4$ and O(1A), O(1B) of DMF with a distance of 2.56, 2.48 Å (Table S3). Additionally, C–H^{...}Cg (π ring) interactions are perceptible between C(1C)–H(1C) of DMF and Cg(3) of Pd₂L₂Cl₄ through a distance of 2.93 Å (Figure S2). Moreover, some selected weak interaction data were collected in Table S3.

2.3. Thermal experiments and FTIR spectra of $Pd_2L_2Cl_4$

Thermogravimetric behavior of $Pd_2L_2Cl_4$ complex was surveyed under a nitrogen atmosphere in the temperature range of 25-900°C. TGA and DTGA curves are exhibited in Figure S3.

Figure S3 addressed a typical weight loss up to 1.5% at ~200 °C, corresponding to the evaporation of the entrapped solvent molecules within the crystal structure. Immediately, $Pd_2L_2Cl_4$ commenced to decompose at about >225 °C and continuously lose weight to achieve balance at 744°C. As a final point, amount of the residual was found ~15% corresponding to 2 mol of Pd per one mole of $Pd_2L_2Cl_4$.

The FTIR spectra of L and $Pd_2L_2Cl_4$ complex were run in the spectral range of 400-4000 cm⁻¹. The spectra accompanied by the probable assignments for the main bands belong to various functional groups were shown in Figure 2.

Figure 2 is here

In the spectra, weaker bands at 2850-3000 cm⁻¹ were assigned to sp³ C–H bond stretching modes, whereas the respective band at 3050 cm⁻¹ was attributed to sp² C-H stretching. Meanwhile, the band at ~1412 cm⁻¹ was assigned to the stretching vibration of the pyridine ring ^[36] in ligand L, wherein this band was shifted to 1443 cm⁻¹ in the Pd₂L₂Cl₄ comparing to L spectra (Figure 2). The ring breathing band of the pyridine moieties ^[37,38] was found at shifted from ~991 cm⁻¹ in L to the above mentioned band in Pd₂L₂Cl₄. Moreover, thanks to the coordination of Pd(II) with pyridine side arms, the C=C and C=N bonds shifted from 1595 cm⁻¹ ^[39] in L to new bands at 1610 and 1662 cm⁻¹. Owing to coordination of Pd(II) with N atoms of pyridine ring in Pd₂L₂Cl₄ determined by single crystal X-ray diffraction, it would be reasonable to assume that the observed blue shift in the stretching vibration of the pyridine ring from 1412

(in **L**) to 1443 cm⁻¹ (Pd₂**L**₂Cl₄) was another supportive indication on the coordination of Pd(II) with the pyridine moieties in **L**.

2.4. ¹H NMR study of Pd₂L₂Cl₄ in DMSO-d₆

The ¹H NMR spectra of $Pd_2L_2Cl_4$ and L were displayed in Figure 3 alongside the assignment of the protons in L.

Figure 3 is here

The aliphatic region of the spectrum exhibited five signals, three of which were composed of singlets (at 3.48 ppm for H_c , 3.56 ppm for H_d and 4.39 ppm for H_e) and the other two signals were a triplet at 2.42 ppm and a quintet 1.59 ppm assigned to H_b and H_a , respectively. Moreover, the other five signals were assigned to the aromatic protons at 6.9 ppm for H_h , 7.1 ppm for H_j , 7.22 ppm for H_g , 7.26 ppm for H_i and 8.43 ppm for H_f in DMSO-d₆. Comparing remarkable downfield chemical shifts for the protons in $Pd_2L_2Cl_4$ with the parent free ligand indicated on the stability of $Pd_2L_2Cl_4$ in the DMSO (Table 1).

Table 1 is here

Some practical features of $Pd_2L_2Cl_4$ as air/moisture and thermal stability together with potential existence of promoted synergistic effects and possible occurrence of tandem reactions for N-donor pyridine ligands ^[40] as well as the large ring system encouraged us to explore the employment of $Pd_2L_2Cl_4$ in popular Sonogashira catalytic cross-coupling reaction.

2.5. Catalytic activity

Hereinafter, the study on catalytic activity of $Pd_2L_2Cl_4$ in Sonogashira coupling reaction were executed under phosphine- and copper-free and aerobic condition, owing to the rich chemistry of Pd(II) complexes. For this purpose, the copper-free catalytic reaction of iodo benzene (0.6 equiv.) with phenyl acetylene (1 equiv.) was employed as the model reaction. DMSO was employed as the solvent because of the solubility of the reaction components as well as its high boiling point. Primarily, in order to determine the optimum reaction conditions for the synthesis of 1,2-diphenyl acetylene, the impacts of various parameters (e.g., type of the solvent and base as well as the reaction time) were considered. The results for choosing of appropriate solvent alongside with the reaction time in this reaction were summarized in Table 2.

Table 2 is here

A series of the experiments were proceeded to assess the effect of some common bases viz. KOAc, NaOAc, KOH and NEt₃. The results together with the catalyst amount were tabulated in Table 3, whereas the best efficiency was found for KOAc.

Table 3 is here

2.5.1. Determination of the optimal conditions by using Taguchi method

In order to acquire sufficient and pertinent data to understand the science behind a scientific phenomenon, Taguchi has established a technique based on "orthogonal arrays" experiments. By employing this method to engineering experiments ^[41], the number of "variance" in the process

could be considerably reduced, giving rise to reducing the number of the experiments needed to attain "optimum settings" for critical parameters.

Herein, we applied the Taguchi approach to optimize conditions and to select the most influential parameters on conversion of the phenylacetylene to diphenylacetylene. In our experiments, Taguchi's orthogonal array table was set up by choosing four parameters at three levels for each of them (Table S4).

By this condition, the number of arrangements will be 3^4 =81, whereby employing Taguchi method the number of the required experiments is reduces to nine. The Taguchi's L₉ design together with the results for the corresponding measurements were summarized in Table S5 (each experiment was repetitively performed three times).

One of the most important parameters is S/N ratio in Taguchi method (see also Table S5) in which S (signal) and N (noise) signify the desirable and undesirable characteristic output values, respectively. Although, the S/N ratios in Table S5 are different according to the type of characteristics, but the greater S/N ratio is the more desirable one. In the case that bigger characteristics are required, the S/N ratio is defined by the Eq (1).^[42]

$$\frac{s}{N} = -10 \log_{10} \left[\frac{\sum_{i=1}^{n} \left(\frac{1}{y_{i}^{2}} \right)}{n} \right] \qquad \text{Eq (1)}$$

In the Eq (1), y_i signifies the result of the experiment and *n* is the replication number of the experiment. Table S5 represents the S/N ratio for diphenylacetylene conversion calculated by using Eq. (1).

Table S6 presented the mean S/N ratio calculated for each level of the parameters as well as the relative significance of each parameter which was shown in the last column of Table S6.

Moreover, Figure S4 exhibits the S/N response graph for diphenyl acetylene conversion.

The best operational settings for this catalytic reaction were found corresponding to A3, B3, C3 and D2 levels in Table S6. Accordingly, the best S/N ratio exhibited in Figure S4 established the optimal conditions as follow: the best temperature (A at level 3), catalyst content (B at level 3), the shortest reaction time (C at level 3) and the most efficient base (D at level 2) were 110 °C, 2 mol%, 8 h and KOAc, respectively. Incidentally, the reaction proceeding at temperatures above 110 °C makes the catalyst susceptible to solvolysis process and/or solvent decomposition, though, the reaction conversion was close to 100% at this temperature. In case of the reaction time, since >99% yields were obtained for the reaction times of 6 (C at level 2) and 8 (C at level 3) hours, the former reaction time was selected. Likewise, the catalyst value 2 mol% was chosen because of the conversion >99%.

2.5.2. Substrate scope for the Sonogashira cross-coupling reaction

In order to evaluate the applicability of $Pd_2L_2Cl_4$ in Sonogashira cross coupling reaction, the optimized conditions (i.e. with 2 mol% $Pd_2L_2Cl_4$, aryl halides (0.6 mmol), phenyl acetylene (1 mmol), KOAc (1.5 mmol), T = 110 °C, t = 6h and solvent = DMSO) were employed in the cross coupling reaction of phenyl acetylene with a number of aryl halides represented in Table 4 (entries 1–6).

Table 4 is here

The experimental results in Table 4 disclosed that the reaction of aryl bromide containing electron withdrawing substituents such as acetyl group (Table 4, entry 3 and 4) afforded the corresponding coupled products in high yields (based on GC yield). Furthermore, the employing 1-bromo naphthalene led to good reaction yield compared to aryl bromide (Table 4, entry 5 and 3). In the course of these experiments, aryl iodide exhibited much more reactivity than the corresponding aryl bromide (Table 4, entry 5 and 3). Meanwhile, the dinitro-substituted aryl chloride exhibited better reaction yield than aryl bromide (Table 4, entry 3 and 6). The catalytic reaction represented far better yield in the case of benzyl chloride (Table 4, entry 2).

The probability of Glaser homocoupling reactions was checked by applying phenyl acetylene as the only reagent in the catalytic reaction (see Table 4, entry 7), wherein no homocoupling product was obtained ^[43]. From the mechanistic point of view, Sonogashira reaction is generally involved in the formation of a Pd(0) species (e.g., by reductive elimination of the product from an Ar-Pd-C=C-Ar' intermediate) prior to the subsequent oxidative addition of Ar-X, regenerating Pd(II) species which is the key step in the catalytic cycle ^[44].

2.5.3. Reusability

The reusability of $Pd_2L_2Cl_4$ as the catalyst was explored and the results were summarized in Figure S5.

As evident from Figure S5, the accomplishment of the first cycle resulted 99% yield of the corresponding product while the yield was decreased progressively in subsequent cycles to 96%, 80% and finally 58% (Figure S5). More experimental studies are required in future to immobilize $Pd_2L_2Cl_4$ on the surface of a catalytic support to improve the reusability of the catalyst.

2.6. Comparison of $Pd_2L_2Cl_4$ with the other MDP catalysts There are several reports ^[20,45–55] in the literatures on the catalytic activity of the other MDP complexes in coupling reactions. Some of these examples are comparable with Pd₂L₂Cl₄ in terms of the overall yield as well as the reaction conditions in Table S7.

In order to explain the scope of $Pd_2L_2Cl_4$ application in catalytic cross-coupling reactions, several examples of MDP complexes are given in the Table S7. Considering Sonogashira crosscoupling reaction, Pd₂L₂Cl₄ exhibited higher yield of the product alongside with less reaction time, comparing with the complexes in the entries 13 and 14 in Table S7. $Pd_2L_2Cl_4$ was also superior to complex 11 in Table S7 regarding the time of reaction.

Some practical features of $Pd_2L_2Cl_4$ as air/moisture, thermal stability, good catalytic performance, promoted synergistic effects and possible occurrence of tandem reactions were attributed to the presence of N-donor pyridine ligands ^[40] as well as the large ring system.

3. Experimental

3.1. Materials and instrumentations

The chemicals applied in this work were purchased from commercial suppliers. IR spectra were recorded on a FT-IR ABB Bomem MB-100 as KBr disks within the range of 400-4000 cm⁻¹. Thermogravimetric measurements were executed through thermogravimetry runs at a temperature ramp of 10 °C min⁻¹ up to 900°C under a continuous flow of dry nitrogen. The thermal analysis instrument was a METTLER/TOLEDO in the TG mode. Gas chromatography

(GC) analyses were accomplished on an Agilent Technologies 6890N, equipped with a 19, 019 J-413 HP-5, 5% phenyl methyl siloxane, capillary column (60.0 m ×250 μ m × 1.00 μ m). ¹H and ¹³C NMR spectra were run in CDCl₃ and DMSO-d₆ at room temperature on a Bruker-ARX500 instrument.

Diffraction data were collected at 120 (1) K, by the ω -scan technique on Agilent Technologies Xcalibur four-circle diffractometer with Eos CCD detector and graphite-monochromated MoK_a radiation (λ =0.71069 Å). The data were corrected for Lorentz-polarization as well as for absorption effects. The structures were resolved with SHELXT-2013 and refined with the full-matrix least-squares procedure on F² by SHELXL-2013. All non-hydrogen atoms were refined anisotropically, all hydrogen atoms were placed in idealized positions and refined as 'riding model' with isotropic displacement parameters set at 1.2 (1.5 for methyl groups) times U_{eq} of appropriate carrier atoms. Analysis of the structure and presentation of the results were carried out by PLATON software. Crystallographic data (excluding structure factors) for the structural analysis has been deposited with the Cambridge Crystallographic Data Centre, Nos. CCDC 1542745 (Pd₂L₂Cl₄·6DMF).

3.2. Synthesis of the precursor dialdehyde, 1 and L

The precursor dialdehyde as well as the macrocycle **1** were prepared according to the procedure illustrated in Scheme 1, employing previous reports ^[56,57]. The diaza-crown macrocycle bearing pyridine unit, **L** was also synthesized by employing a new method that was less complicated (Scheme 1) than the recently reported method ^[35] as follow: the parent macrocycle **1** (1.00 g) was dissolve in DMF (10 cm³), potassium carbonate (1.12 g) and potassium iodide (0.03 g) was added to the above solution. By stirring the mixture in the presence of 4-chloromethyl pyridine hydrochloride (0.5 g) for one week under N₂ atmosphere (without heating), a cream-colored precipitate was obtained after adding water (300 cm³). The solid was filtered and washed with distilled water prior to drying in air. The product was purified by recrystallization from acetonitrile. Yield: 35 mg, 57%, Anal. Calc. for C₃₁H₃₄N₄O₂: C, 75.28; H, 6.93; N, 11.33. Found: C, 75.4; H, 6.9; N, 11.2%. m. p. 165°C.

¹H NMR (500 MHz, CDCl₃, TMS) δ (ppm):1.64 (q, 2H, NCH₂CH₂CH₂N); 2.56 (t, 4H, NCH₂CH₂CH₂N); 3.49, 3.63 (s, 8H, ArCH₂, CH₂C₅H₄N); 4.38 (s, 4H, OCH₂CH₂O); 6.90-6.93,7.08-7.10, 7.25-7.28 (m, 8H, C₆H₄); 7.19, 8.47 (8H, C₅H₄N).

¹³C NMR (500 MHz, CDC1₃, TMS) δ (ppm): 24.55 (NCH₂CH₂CH₂N); 51.19 (NCH₂CH₂CH₂N); 52.73 (CH₂C₅H₄N); 56.53 (ArCH₂); 66.27 (OCH₂CH₂O); 110.73, 120.31, 123.59, 125.98, 128.58, 132.57, 149.52, 150.01, 157.19 (C₆H₄, C₅H₄N).

FT-IR (KBr, cm⁻¹) bands: 2798-3065 (m), 1595 (s), 1491 (s), 1445 (s),1412(w), 1373 (w), 1339(w), 1290(w), 1232(s), 1114(m), 1053(m), 990 (w), 936 (s), 835(w), 803(w), 763 (s), 616 (m), 489 (m).

3.3. Preparation of the dinuclearPd(II) complex

Bis(acetonitrile)dichloropalladium(II) was prepared by recrystallization of Pd(II) chloride in acetonitrile. Layering of a DMF solution (1 mL) of L (50 mg, 0.100 mmol) over an DMF solution (0.5 mL) of bis(acetonitrile)dichloropalladium(II) (16.5 mg, 0.130 mmol) in narrow tube

in room temperature for 1 weak, resulted single crystals of $Pd_2L_2Cl_4$. Yield: 40.8%. Elemental analysis (%) calculated for $C_{62}H_{68}Cl_4N_8O_4Pd_2$, 6(C_3H_7NO) (1115.141g/mol): C, 66.78, H, 6.15, N, 10.05; found C, 66.7, H, 5.93, N, 10.1.

¹H NMR (500 MHz, DMSO-d₆, TMS) δ (ppm): 1.70 (q, 2H, NCH₂CH₂CH₂N); 3.58, 3.72 (s, 8H, ArCH₂, CH₂C₅H₄N); 4.40 (s, 4H, OCH₂CH₂O); 6.96, 7.29, 7.32 (m, 8H, C₆H₄); 7.13, 8.80 (8H, C₅H₄N).

¹³C NMR. The acquisition of the spectra was unsuccessful due to insufficient solubility of $Pd_2L_2Cl_4$ in any deuterated solvent.

FT-IR (KBr, cm⁻¹) bands: 2801-3027 (m), 1602(s), 1610 (s), 1495 (s), 1443 (s), 1378 (w), 1237(s), 1112 (m), 1057 (m), 936 (m), 814(w), 753 (s),615 (w), 508 (w).

3.4. General procedure for the Sonogashira cross-coupling reaction

A solution of phenyl acetylene (0.5 mmol), aryl halide (0.3 mmol), $Pd_2L_2Cl_4$ (2 mol%), 2 mL solvent and 1.5 mmol base was mixed and stirred under air atmosphere at 110°C for the fixed time. During the reaction proceeding, the consumption of starting material was checked by TLC. After elapsing of the chosen time, water (2 mL) was added to the reaction mixture, extracted with ethyl acetate (2 × 5 mL) (products and starting materials are soluble in ethyl acetate), dried over MgSO₄, and injected to the GC chromatography. All of compounds have been characterized by ¹H NMR spectra (Figure S3).

3.5. Reusability test

0.6 mmol iodo benzene was charged into a reaction vessel together with 1 mmol phenyl acetylene and 3 mmol KOAc in DMSO (2 ml). 2 mol% of $Pd_2L_2Cl_4$ was added to the abovementioned mixture at 110 °C. After 6 h the mixture was cooled to room temperature, wherein enough water was delivered to the flask to form a biphasic mixture for extraction with ethyl acetate (2 mL) for three times. After collecting of the organic phase aliquots (ethyl acetate), they were sampling for injection to the GC chromatography for more analysis. In order to recover, the remaining phase of the previous step, aqueous solution (DMSO+water) was washed with ethyl acetate for several times to accomplish thorough removal of the products as well as starting materials. The extracted DMSO solution was checked with GC chromatography to monitor the presence of any unreacted starting material. Finally, the aforesaid solution (DMSO+water) was evaporated and the remaining catalyst utilized as the next catalytic cycle under the same reaction conditions.

4. Conclusions

We successfully prepared and characterized a new dinuclear Pd(II) complex with pyridine-based aza-crown macrocyclic ligand. The X-ray analysis endorsed the presence of large macrocyclic structure for $Pd_2L_2Cl_4$ complex. Diagnosis of the complex by TGA reserved typical thermal stability up to 200 °C, whereas the application of $Pd_2L_2Cl_4$ in solution as a catalyst was permitted. Moreover, ¹H NMR and FTIR spectra concisely exhibited the persistence of the solid

state structure in DMSO-d₆. Thus, the complex showed strong performance as copper- and phosphine-free Sonogashira cross coupling reaction in aerobic condition between aryl halides and phenyl acetylene in DMSO. $Pd_2L_2Cl_4$ unveiled much better catalytic performance in Sonogashira cross-coupling reactions than several other previously reported Pd(II) dinuclear complexes which is attributed to the presence of N-donor ligands alongside with having the large ring system in the complex.

Acknowledgement

This work was supported by Research Office of Sharif University of Technology.

References

- [1] R. Chinchilla, C. Nájera, *Chem. Rev.* **2014**, *114*, 1783–1826.
- [2] D. Mc Cartney, P. J. Guiry, *Chem. Soc. Rev.* **2011**, *40*, 5122.
- [3] M. Punk, C. Merkley, K. Kennedy, J. B. Morgan, ACS Catal. 2016, 6, 4694–4698.
- [4] A. Petuker, C. Merten, U.-P. Apfel, Eur. J. Inorg. Chem. 2015, 2015, 2139–2144.
- [5] R. Chinchilla, C. Nájera, Chem. Soc. Rev. 2011, 40, 5084.
- [6] K. Yavuz, H. Küçükbay, Appl. Organomet. Chem. 2018, 32, 1–8.
- [7] Z. Mandegani, M. Asadi, Z. Asadi, Appl. Organomet. Chem. 2016, 30, 657–663.
- [8] A. R. Hajipour, Z. Tavangar-Rizi, Appl. Organomet. Chem. 2017, 31, 1–10.
- [9] M. Bakherad, Appl. Organomet. Chem. 2013, 27, 125–140.
- [10] K. Sonogashira, Y. Tohda, N. Hagihara, Tetrahedron Lett. 1975, 16, 4467–4470.
- [11] C. Glaser, *Chem. Ber* **1869**, *2*, 422–424.
- [12] P. Sharma, A. P. Singh, Catal. Sci. Technol. 2014, 4, 2978–2989.
- [13] C. Bai, S. Jian, X. Yao, Y. Li, J. Väyrynen, T. Salmi, D. Y. Murzin, Z. Yang, *Catal. Sci. Technol.* 2014, 4, 3261.
- [14] A. Dhakshinamoorthy, A. M. Asiri, H. Garcia, Chem. Soc. Rev. 2015, 44, 1922–1947.
- [15] A. John, S. Modak, M. Madasu, M. Katari, P. Ghosh, *Polyhedron* **2013**, *64*, 20–29.
- [16] M. Bakherad, A. Keivanloo, S. Samangooei, M. Omidian, J. Organomet. Chem. 2013, 740, 78–82.
- [17] A. Dewan, M. Sarmah, U. Bora, A. J. Thakur, *Tetrahedron Lett.* 2016, 57, 3760–3763.
- [18] S. K. Das, M. Sarmah, U. Bora, *Tetrahedron Lett.* 2017, 58, 2094–2097.
- [19] M. K. Kolli, N. M. Shaik, G. Chandrasekar, S. Chidara, R. B. Korupolu, New J. Chem. 2017, 41, 8187–8195.
- [20] L.-M. Zhang, H.-Y. Li, H.-X. Li, D. J. Young, Y. Wang, J.-P. Lang, *Inorg. Chem.* 2017, 56, 11230–11243.
- [21] J. N. Buckler, T. Meek, M. G. Banwell, P. D. Carr, J. Nat. Prod. 2017, 80, 2088–2093.
- [22] N. L. S. Yue, M. C. Jennings, R. J. Puddephatt, Polyhedron 2016, 108, 67–73.
- [23] Y.-B. Huang, J. Liang, X.-S. Wang, R. Cao, Chem. Soc. Rev. 2017, 46, 126–157.
- [24] D. C. Powers, T. Ritter, Acc. Chem. Res. 2012, 45, 840–850.
- [25] Q. Zha, C. Ding, X. Rui, Y. Xie, Cryst. Growth Des. 2013, 13, 4583–4590.
- [26] L. Fan, X. Zhang, Z. Sun, W. Zhang, Y. Ding, W. Fan, L. Sun, X. Zhao, H. Lei, *Cryst. Growth Des.* **2013**, *13*, 2462–2475.
- [27] K. Suzuki, K. Takao, S. Sato, M. Fujita, J. Am. Chem. Soc. 2010, 132, 2544–2545.
- [28] M. Yoneya, T. Yamaguchi, S. Sato, M. Fujita, J. Am. Chem. Soc. 2012, 134, 14401– 14407.

- [29] D. Fujita, Y. Ueda, S. Sato, N. Mizuno, T. Kumasaka, M. Fujita, *Nature* 2016, 540, 563– 566.
- [30] B. Linton, A. D. Hamilton, Chem. Rev. 1997, 97, 1669–1680.
- [31] M. Fujita, S. Nagao, M. Iida, K. Ogata, K. Ogura, J. Am. Chem. Soc. **1993**, 115, 1574–1576.
- [32] M. Fujita, Coord. Chem. Rev. 1996, 148, 249–264.
- [33] M. Fujita, Acc. Chem. Res. 1999, 32, 53–61.
- [34] M. R. Buchmeiser, T. Schareina, R. Kempe, K. Wurst, J. Organomet. Chem. 2001, 634, 39–46.
- [35] B. Ghanbari, L. Shahhoseini, A. Owczarzak, M. Kubicki, R. Kia, P. R. Raithby, *CrystEngComm* **2018**, *20*, 1783–1796.
- [36] S. Zhu, H. Hu, J. Hu, J. Li, F. Hu, Y. Wang, J. Mol. Struct. 2017, 1144, 191–198.
- [37] R. H. U. Borges, A. Abras, H. Beraldo, J. Braz. Chem. Soc. 1997, 8, 265–270.
- [38] G. V. Seguel, B. L. Rivas, P. Órdenes, J. Chil. Chem. Soc. 2015, 60, 3080–3082.
- [39] C. Giacomelli, F. C. Giacomelli, A. L. Santana, V. Schmidt, A. T. N. Pires, J. R. Bertolino, A. Spinelli, *J. Braz. Chem. Soc.* **2004**, *15*, 818–824.
- [40] G. Tseberlidis, D. Intrieri, A. Caselli, Eur. J. Inorg. Chem. 2017, 2017, 3589–3603.
- [41] J. L. Rosa, A. Robin, M. B. Silva, C. A. Baldan, M. P. Peres, J. Mater. Process. Technol. 2009, 209, 1181–1188.
- [42] S.-T. Kim, M.-S. Park, H.-M. Kim, Sensors Actuators B Chem. 2004, 102, 253–260.
- [43] F. Yang, X. Cui, Y. Li, J. Zhang, G. Ren, Y. Wu, Tetrahedron 2007, 63, 1963–1969.
- [44] B. E. Jaksic, J. Jiang, A. W. Fraser, M. C. Baird, Organometallics 2013, 32, 4192–4198.
- [45] T. Tsubomura, M. Chiba, S. Nagai, M. Ishihira, K. Matsumoto, T. Tsukuda, J. Organomet. Chem. 2011, 696, 3657–3661.
- [46] N. Dehury, N. Maity, S. K. Tripathy, J.-M. Basset, S. Patra, ACS Catal. 2016, 6, 5535– 5540.
- [47] G. Y. Li, G. Zheng, A. F. Noonan, J. Org. Chem. 2001, 66, 8677–8681.
- [48] J. Lasri, M. N. Kopylovich, M. F. C. Guedes da Silva, M. A. J. Charmier, A. J. L. Pombeiro, *Chem. - A Eur. J.* 2008, 14, 9312–9322.
- [49] N. M. Motsoane, I. A. Guzei, J. Darkwa, Zeitschrift für Naturforsch. B 2007, 62, 323–330.
- [50] S. Pal, W. S. Hwang, I. J. B. Lin, C. S. Lee, J. Mol. Catal. A Chem. 2007, 269, 197–203.
- [51] M. Guerrero, J. Pons, J. Ros, J. Organomet. Chem. 2010, 695, 1957–1960.
- [52] M. Navidi, B. Movassagh, Monatshefte für Chemie Chem. Mon. 2013, 144, 1363–1367.
- [53] S. Rau, K. Lamm, H. Görls, J. Schöffel, D. Walther, *J. Organomet. Chem.* **2004**, 689, 3582–3592.
- [54] B. J. Khairnar, S. Dey, V. K. Jain, B. M. Bhanage, *Tetrahedron Lett.* 2014, 55, 716–719.
- [55] M. Bagherzadeh, N. Mousavi, M. Zare, S. Jamali, A. Ellern, L. K. Woo, *Inorganica Chim.* Acta **2016**, 451, 227–232.
- [56] P. G. Grimsley, L. F. Lindoy, H. C. Lip, R. J. Smith, J. T. Baker, Aust. J. Chem. 1977, 30, 2095–2098.
- [57] L. G. Armstrong, L. F. Lindoy, *Inorg. Chem.* 1975, 14, 1322–1326.



Tables

Table 1. ¹H NMR chemical shift assignments (δ in ppm) together with $\Delta\delta$ for the L and Pd₂L₂Cl₄ and their displacement in DMSO-d₆ at 25°C.

	H _a	H_{b}	H _c	H _d	H _e	H_{h}	H_i	H_j	H_{g}	$H_{\rm f}$
L	1.59	2.42	3.48	3.56	4.39	6.90	7.26	7.10	7.22	8.43
$Pd_2L_2Cl_4$	1.70	-	3.58	3.72	4.40	6.96	7.29	7.13	7.32	8.80
$\Delta\delta(ppm)$	0.11	-	0.08	0.16	0.01	0.06	0.03	0.03	0.10	0.37
$\Delta\delta$ (Hz)	55	-	40	80	5	30	15	15	50	185

Table 2. The effect of time and solvent in Sonogashira cross coupling reaction. $Pd_2L_2Cl_4$ KOAc 110 ⁰C solvent GC yield(%) Entry Solvent 3h 6h 12h 24h DMSO/H₂O 1 2 2 DMSO 60 >99 100 -3 H_2O _ _ _ _

Entry	base	GC yi	ield(%)	cat. amount	
		3h	6h	(mmol)	
1	KOAc	60	>99	0.01	
2	NaOAc	50	95	0.01	
3	KOH	63	80	0.01	
4	NEt ₃	40	87	0.01	
5	KOAc	75	>99	0.02	

Table 3. Effect of common base and catalyst amount in Sonogashira cross coupling iodo benzene (0.6 mmol), phenyl acetylene (1 mmol), base (3 mmol), T = $110 \text{ }^{\circ}\text{C}$ and solvent: DMSO.

Table 4. Sonogashira coupling reaction conditions of some	aryl
halides with phenyl acetylene in the presence of $Pd_2L_2Cl_4$.	





Scheme 1. The synthetic route for the preparation of L and $\text{Pd}_2L_2\text{Cl}_4$ complex.

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Figure 1. (a) The X-ray crystal structure of $Pd_2L_2Cl_4$, the solvent molecules are omitted for simplicity; (b) asymmetric unit of the complex; (thermal ellipsoid plot at 30%).



Figure 2. (a) FTIR spectra of L and the $Pd_2L_2Cl_4$ complex; (b) expanded region of the stretching vibrations of the complexed pyridine covering its band shifts to higher wavenumbers.



Figure 3. ¹H NMR spectra of L (top) and $Pd_2L_2Cl_4$ (bottom) (ca. 2×10^{-2} M) in DMSO-d₆ at 25°C.

Highlights

- A new large dinuclear macrocyclic Pd(II) complex was synthesized.
- The linker was made from aza-crown macrocycle bearing two pyridine moieties.
- The TGA exhibited thermal stability up to 200 °C.
- The complex showed strong performance as Sonogashira cross-coupling catalyst.
- The catalyst was moisture/air-stable, copper and phosphine free.