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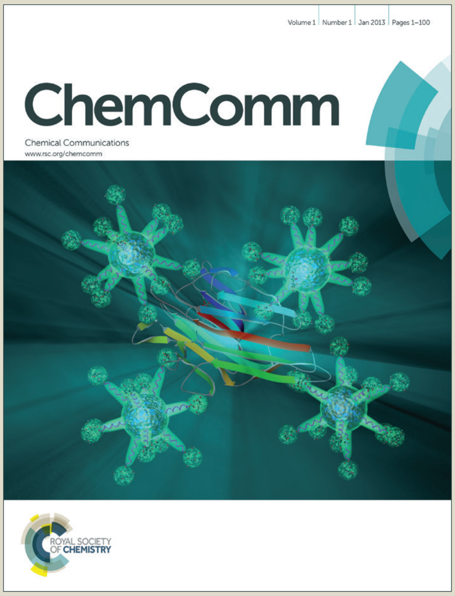

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Aggregates of Hetero-oligophenylene Derivative as Reactors for the Generation of Palladium Nanoparticles: A Potential Catalyst in Sonogashira Coupling Reaction under Aerial Conditions

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The utilization of Pd nanoparticles stabilized by aggregates of hetero-oligophenylene derivative 3 as excellent catalyst in copper/amine free Sonogashira coupling reactions under aerial conditions at room temperature has been demonstrated.

Palladium catalyzed Sonogashira coupling reaction is a well-established method for the synthesis of aryl alkynes which are important building blocks for the preparation of natural products, pharmaceutical ingredients, electronic materials and agrochemicals.[1] Under conventional conditions of Sonogashira coupling reaction, alkynylation of expensive aryl iodide/bromide is carried out in the presence of copper and palladium salts. Though these reactions have high synthetic utility yet the requirement of expensive, unrecoverable, toxic reagents in the reaction mixture and formation of moisture/air sensitive copper-acetylide species[2] preclude the wide use of Sonogashira coupling in industry. To overcome these limitations, new approaches have been developed for carrying out C-C coupling reactions using metal acetylides and excess of amine[3] instead of copper salts. However, utilization of excess of amine (even as solvent) in these copper-free reaction conditions actually decreased the economic and environmental advantage of the methodology. Furthermore, most of these reported catalytic systems work efficiently only in the presence of activated alkynes or aryl iodide/bromide. During the last few years, enormous efforts have been made to use aryl chlorides[4] in copper free Sonogashira coupling reactions using highly active palladium catalyst. However, these reactions suffer from various limitations such as high temperature and excess amount of aryl chlorides (in some cases five folds) to get the target compound in considerable yields. Therefore, development of an efficient catalytic system for carrying out Sonogashira coupling reaction using unactivated substrates under environmentally benign conditions without the need for any measures for exclusion of air/moisture still remains a challenge.

Our research interests involve development of fluorescent supramolecular aggregates for the reductant free preparation of metal nanoparticles which have further been utilized in various organic transformations.[5a-b] Recently, we used aggregates of pentacenequinone derivative **6** having pyridine groups as reactors and stabilizers for the preparation of palladium nanoparticles.[5b] In continuation of this work, we were then interested in developing palladium based efficient catalytic system for carrying out Sonogashira coupling under mild conditions. Keeping this in mind, we have designed and synthesized heteroligophenylene derivative **3** having amino and pyridine groups. Nonplanar heteroligophenylene moiety is the scaffold of our choice due to its self-assembly behaviour. We envisaged that the presence of electron rich hetero-oligophenylene scaffold could influence the catalytic activity and stability of *in situ* generated metal NPs in the Sonogashira coupling involving unactivated substrates. Pyridine and amino group were incorporated to enhance the affinity of derivative **3** towards palladium ions.[5b,7] As expected derivative **3** formed fluorescent aggregates in mixed aqueous media which exhibited sensitive response towards Pd^{2+} ions and during the sensing process aggregates of derivative **3** served as reactors, stabilizers and shape directing agents for the preparation of Pd NPs. The work being presented in this manuscript shows the tuning of shape of the *in situ* generated Pd NPs by changing the number/topology of binding units in the host molecule. To our pleasure, *in situ* generated Pd NPs exhibited high catalytic efficiency and stability in Sonogashira coupling reaction involving aryl iodides and furnished the desired products in high yields under aerial conditions at room temperature. Isolation of the product from the catalytic reaction was very easy as all the products were isolated by simple extraction with organic solvent followed by recrystallization. Interestingly, the catalytic activity of Pd NPs is quite impressive in the catalytic reactions involving aryl chlorides and even when extended to deactivated electron rich

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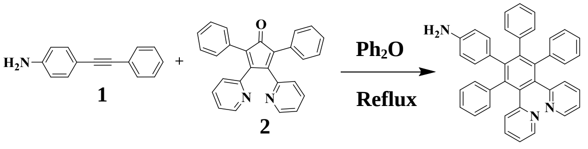
aryl chloride. Various methods have been reported for the generation of Pd Nps. However, most of these methods suffer from several limitations of requiring longer reaction times, high temperature, presence of reducing agents and additives. In contrast, the method being reported in the present manuscript for the preparation of Pd NPs at room temperature is fast, facile and free of reducing agent, which makes this method better than the other methods reported in the literature (Table S1, ESI†). Additionally, the catalytic efficiency of *in situ* generated Pd NPs utilized for Sonogashira reaction is better than the other reported systems (Table S2, ESI†). To the best of our knowledge, these *in situ* generated Pd NPs serve as one of the best catalytic systems for carrying out copper and amine free Sonogashira cross coupling reactions at room temperature in mixed aqueous media under aerial conditions.

Heteroligophenylene derivative **3** was synthesized *via* Diels–Alder reaction of 4-phenylethynyl-phenylamine[8] with 2,5-diphenyl-3,4-di(pyridin-2-yl)cyclopenta-2,4-dienone[9] in diphenylether at 240°C in 78% yield. The structure of derivative **3** was confirmed from its spectroscopic and analytical data (Fig. S1-S3, ESI†).



3 (78%)

Scheme 1. Synthesis of derivative **3**.

The UV-vis spectrum of compound **3** in EtOH exhibits an absorption band at 236 nm with a shoulder band at 270 nm due to π-π* and n-π* transitions. Upon addition of water (70% volume fractions) to the EtOH solution of compound **3**, the absorption band at 236 nm is red shifted to 240 nm (Fig. S4(A), ESI†). The fluorescence spectrum of compound **3** in EtOH exhibits dual emission peaks at 430 nm and 435 nm when excited at 270 nm. Upon addition of water (70% volume fractions) to the EtOH solution of compound **3**, the emission band at 435 nm is red shifted to 440 nm (Fig. S4(B), ESI†). Thus, the UV-vis and fluorescence studies suggest the formation of J-type assemblies in case of derivative **3**. The temperature-dependent UV-vis studies of derivative **3** in H_2O/EtOH (7:3) solvent mixture and the concentration-dependent ^1H NMR studies of derivative **3** in $CDCl_3$ support the formation of J-type assemblies (Fig. S5 and S6, ESI†). The transmission electron microscopy (TEM) image of compound **3** in the solvent mixture of H_2O/EtOH (v/v, 7:3) shows the presence of aggregates having flake like morphology (Fig. S7, ESI†). The DLS studies also indicate the formation of aggregates having an average diameter in the range of 900 nm (Fig. S8, ESI†).The solution of aggregates is visibly transparent and stable at room temperature for several weeks.

The presence of amino and pyridine moieties prompted us to evaluate the binding behaviour of aggregates of derivative **3** toward different metal ions such as Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, Co^{2+}, Pb^{2+}, Zn^{2+}, Ni^{2+}, Pd^{2+} , Cd^{2+}, Ag^{+}, Au^{3+}, Ba^{2+}, Mg^{2+}, K^{+}, Na^{+} and Li^{+} as their perchlorates/chloride salts by UV-Vis and fluorescence studies (Fig. S9, ESI†). Upon addition of Pd^{2+} ions (2 equiv.) to the solution of derivative **3** (5 μM) in H_2O/EtOH (v/v, 7:3), an increase in the absorbance over the entire spectral range fro 250 to 600 nm was observed (Fig. S10(A), ESI†). In th fluorescence spectrum, the quenching of the emission wa observed upon addition of Pd^{2+} ions (2 equiv.) to the solutio of aggregates of derivative **3** in mixed aqueous medi (H_2O/EtOH, v/v, 7:3) (Fig. 1(A)). Aggregates of derivative **3** also displayed chromogenic behaviour towards Pd^{2+} ions with a colour change from colourless to brown that is clearly visible to naked eye (Fig. S10(B), ESI†). The time resolved fluorescence studies of derivative **3** in the presence of palladium ions suggest the static quenching (Fig. S11(B), ESI†). Therefore, we have calculated the Stern Volmer constant (3.8×10^5 M^{-1}) from the linear plotting which was observed a lower concentrations of Pd^{2+} ions (upto 2.5 μM) added to th solution of aggregates of derivative **3**. (Fig. S11(A),ESI†).[10] Th detection limit of aggregates **3** for Pd^{2+} ions was found to b 6.83 x 10^{-7} M (Fig. S12, ESI†).

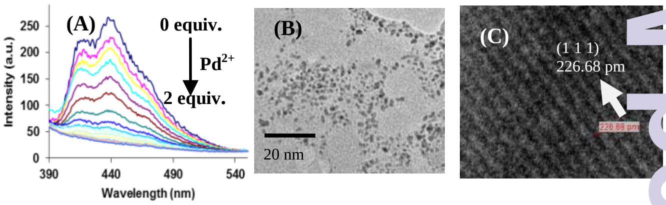


Fig. 1. (A) Changes in the fluorescence spectrum of derivative **3** (5 μM) upon addition of Pd^{2+} in H_2O/EtOH (7:3); λ_{ex} = 270 nm. (B) TEM image of the *in sit* generated Pd NPs of derivative **3**. (C) HR-TEM of the Pd NPs of derivative **3.**

The powder X-ray diffraction (XRD) studies of the precipitates obtained after the evaporation of solution mixture o compound **3** and Pd^{2+} ions in mixed aqueous medi (H_2O/EtOH, v/v, 7:3) showed the formation of crystal face cantered cubic (*fcc*) lattice of Pd(0) (Fig. S13, ESI†). The transmission electron microscopy (TEM) image of aggregates of derivative **3** in the presence of Pd(II) (1:1) ions showed the formation of spherical nanoparticles of average diameter in the range of 2 to 10 nm (Fig. S14, ESI†). On the basis of S measurements, an average diameter of 7 nm could be assigned to Pd NPs (Fig. S15, ESI†). When ratio of aggregates of derivative **3** to that Pd^{2+} ions was increased from 1:1 to 2: , nanorods of Pd NPs were observed while switching this ratio t 1:2 nanorods and nanospheres were observed (Fig. S16, ESI†) These studies suggest that by changing the amount o aggregates of derivative **3**, shape of Pd NPs could b controlled.

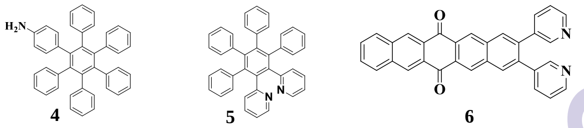
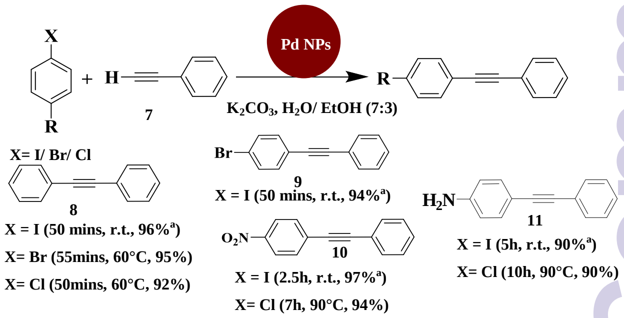


Fig. 2. Structures of derivatives **4**, **5** and **6**.

To get insight into the mechanism of formation of Pd NPs, we slowly evaporated the solution of aggregates of derivative containing Pd NPs. The precipitates were observed after two days which were filtered and washed with $CHCl_3$ and THF. The ^1H NMR spectrum of the residue so obtained after evaporation of the solvent showed the downfield shift of signals corresponding to aromatic protons (Fig. S18, ESI†). On the basis of above results, we suggest that upon addition of Pd ions to the solution of aggregates of derivative **3**, the palladium ions interact with nitrogen atoms of pyridyl moieties and that of amino group and get reduced to Pd(0). We believe that the aggregates of derivative **3** reduce Pd^{2+} ions to Pd(0) and during this process they themselves get oxidized. To confirm the oxidation of aggregates of derivative **3**, we carried out fluorescence studies of aggregates of derivative **3** in the presence of *tert*-butyl hydroperoxide a strong oxidizing agent. The fluorescence spectrum exhibited the quenching of the emission bands at 430 and 435 nm as was observed in the presence of Pd^{2+} ions (Fig. S19(A), ESI†). This result clearly indicates the reduction of Pd^{2+} ions to Pd(0) and oxidation of derivative **3**. We also carried out the UV-vis studies to confirm the reduction of Pd(II) to Pd(0) in the presence of compound **3** (Fig. S19(B), ESI†). The Pd(II) ions in mixed aqueous media (H_2O/EtOH, v/v, 7:3) exhibited a band at 420 nm. On addition of aggregates of derivative **3**, this band gradually disappeared, indicating the formation of Pd (0) nanoparticles.[11] Thus, aggregates of derivative **3** function as reactors and stabilizing agents for the preparation of Pd NPs at room temperature.

To understand the influence of scaffold on morphology and catalytic activity of generated metal nanoparticles, we also synthesized heteroligophenylene derivatives **4**[8] and **5**[12] (Fig. 2). Interestingly, absorption and emission studies of both the derivatives suggest affinity of these molecules towards Pd^{2+} ions. The calculated Stern-Volmer constants of aggregates of derivatives **4** and **5** for Pd^{2+} ions were found to be 5×10^5 M^{-1} and 6×10^5 M^{-1}, respectively (Fig. S11(C)-(D), ESI†). The TEM image of derivative **4** in the presence of palladium ions showed the formation of nanospheres and nanocubes whereas the TEM image of derivative **5** showed the presence of nanorods as well as nanospheres (Fig. S17, ESI†). These studies suggest that presence of amino as well as pyridine groups in the heteroligophenylene scaffold is essential for generation of spherical NPs. We believe that aggregates of derivative **3** form a uniform layer around the metal ions and bind strongly with palladium ions which increases the rate of reduction for the preparation of Pd(0) nanoparticles. Thus, higher number of nanoparticles is available in this case which leads to uniform growth of nanoparticles in all directions resulting in the formation of spherical nanoparticles.

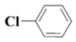
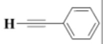
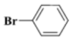
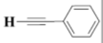
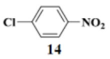
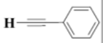
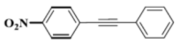
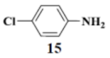
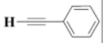
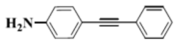
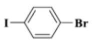
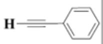
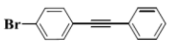
Having done all this, we were then interested in studying the catalytic efficiency of *in situ* generated Pd NPs in the Sonogashira coupling (Fig. S20, ESI†). For this, we selected aryl iodide and phenylacetylene as model substrates. We carried out the coupling reaction between aryl iodide and phenylacetylene using 1 mole % of *in situ* generated Pd NPs and K_2CO_3 as base (1 mM) in different solvents such as H_2O, EtOH and H_2O/EtOH (v/v, 7:3) solvent mixture and also under solvent free conditions (entries 1, 2, 3 and 4, table S3, ESI†). In all the cases reaction was complete within 50 mins at room temperature, whereas on increasing the temperature up to 60°C, the reaction completed within 10 minutes (entry 5, table S3, ESI†). Interestingly, the model reaction went smoothly to furnish the desired product under aerial conditions at room temperature. However, the model reaction carried out in DMF at 100°C, was complete in 50 minutes (entry 6, table S3, ESI†). Further, the model reaction between iodobenzene and phenylacetylene when carried out in toluene required higher reaction temperature and the product was obtained in relatively lower yield (entry 7, table S3, ESI†). These studies suggest that the polar protic media is more suitable for carrying out the Sonogashira coupling reactions. Furthermore, the model reaction remained unaffected by change in the amount of base (entries 8 and 9, table S3, ESI†). However, the same reaction when carried out in the absence of K_2CO_3, showed almost no conversion (entry 10, table S3, ESI†). Thus, basic medium is essential for carrying out these reactions. We also carried out the reaction between aryl iodide and phenylacetylene using aggregates of derivative **4** and **5** stabilized Pd NPs, respectively and in both cases reaction took longer time for completion and desired product was obtained in lower yields (entries 2 and 3, table S4, ESI†). The faster reaction rate observed in case of aggregates of derivative **3** stabilized Pd NPs may be attributed to the spherical shape of the nanoparticles and spherical shaped NPs provide large surface area for the reaction, consequently rate of reaction is increased. We also carried out the model reaction between aryl iodide and phenylacetylene using aggregates of pentacenequinone derivative **6** stabilized Pd NPs (entry 4, table S4, ESI†). Interestingly, the reaction was complete in 6 hours and the product was obtained in 68% yield. This study suggests that spherical Pd NPs stabilized by electron rich heteroligophenylene derivative **3** are more suitable for carrying out Sonogashira coupling. We also carried out the reaction between aryl iodide and phenylacetylene using 1 mole % of $PdCl_2$ in H_2O/EtOH (v/v, 7:3) solvent system in the absence of aggregates of derivative **3** (entry 5, table S4, ESI†). Under these conditions, the reacting substrates remained unchanged even after 15 hours. On the basis of these studies, we conclude that aggregates of derivative **3** stabilized NPs are promising catalysts for carrying out copper and amine free Sonogashira coupling reaction. For further studies, we selected H_2O/EtOH (v/v, 7:3) as the solvent mixture for carrying out various reactions (Scheme 2).



Scheme 2. Sonogashira coupling of phenyl acetylene with various aryl halides catalyzed by *in situ* generated Pd(0) nanoparticles. [a]under aerial conditions.

To check the scope of substrates, we utilized the *in situ* generated Pd NPs as catalyst in coupling reaction between aryl iodide having electron donating/accepting moiety and phenylacetylene under aerial conditions (entries 1 and 2, table S5, ESI†). It was found that aryl iodide bearing electron-donating group provided slightly lower yield of the product. The *in situ* generated Pd NPs also showed high efficiency in the reaction for the preparation of symmetrically substituted alkyne (entry 3, table S5, ESI†). Moreover, 2-bromothiophene and 2-bromopyridine also furnished the corresponding products in excellent yields (entries 4 and 5, table S5, ESI†).

Table 1: Sonogashira coupling of phenylacetylene with various aryl halides catalyzed by *in situ* generated Pd(0) nanoparticles.

Entry	Halide	Alkyne	Product	Time	Temp. (°C)	Yield[b] (%)
1	 12	 7	 8	55 min	60	92
2	 13	 7	 8	50 min	60	95
3	 14	 7	 10	7 h	90	94
4	 15	 7	 11	10 h	90	90
5	 16	 7	 9	50 min	RT	94[a]

[a]under aerial conditions. [b]Isolated yields determined after recrystallization

To broaden the scope of Sonogashira coupling, we also carried out the reaction of aryl chloride and aryl bromide with phenylacetylene. To our pleasure, both the reactions went smoothly and desired products were obtained in excellent yields (entries 1 and 2, table 1). To check the scope of catalytic efficiency of Pd NPs with regard to chloride, we carried out the reaction between substituted aryl chlorides and phenyacetylene using 1 mole % of Pd NPs at 90°C (entries 3 and 4, table 1) and it was found that substituted aryl chlorides also furnished the desired products in high yields. Further, in the presence of *in situ* generated Pd NPs, 1-bromo-4-iodobenzene reacted with phenylacetylene to furnish 1-bromo-4-(phenylethynyl)benzene in 94% yield (entry 5, table 1). This result shows the high selectivity of Pd NPs in Sonogashira reaction. However, Sonogashira coupling involving aryl bromide/aryl chloride did not complete under aerial conditions.

Further, recyclability of Pd NP catalyst was also checked by monitoring the model reaction between aryl iodide and phenylacetylene. The product was separated from the reaction mixture by extracting with organic solvent and the catalyst was recovered in the aqueous layer which was used as such in the next cycle of the reaction. The product yield remained quantitative even after four cycles of the reaction. Thus, catalyst recycling was very facile since almost all the coupling products could be readily separated by simple extraction.

The efficiency of the *in situ* generated Pd NPs was tested for the reaction between iodobenzene and phenyl acetylene using various amounts of catalyst, down to 0.0003 mole % of Pd NPs (table S7, ESI†). This study indicate that the Pd NPs can also be utilized at such a low concentration (0.0003 mole %) to furnish the desired product in good yield (83%). Such an extremely low quantity of palladium has never been successfully used for Sonogashira coupling before the present study.

To evaluate the practical applicability of the *in situ* generated Pd NPs, we carried out the Sonogashira coupling reaction of dibromo perylenediisimide[13] with phenylacetylene (Scheme S2). Earlier the desired product[13] was obtained by Sonogashira coupling of dibromo perylenediisimide with phenylacetylene in the presence of light sensitive CuI, toxic triethylamine and carcinogenic THF in 82% yield. It took 14 h for completion of this reaction. We chose the desired derivative as a candidate due to its potential applications in the material[14] and supramolecular chemistry.[15] Interestingly, as shown in Scheme S2, in the presence of 1 mole % of *in situ* generated Pd NPs in H_2O/EtOH (7:3), the reaction was complete in 12 h and the product was obtained in 86% yield (Fig. S28, ESI†). This study demonstrates the practical utility of *in situ* generated Pd NPs for carrying out Sonogashira coupling reaction.

In conclusion, we designed and synthesized heteroligophenylene derivative **3** and aggregates of this derivative served as reactors, stabilizers and shape directing agents for the preparation of spherical Pd NPs. Furthermore, the *in situ* generated Pd NPs worked as excellent catalyst for carrying out copper and amine free Sonogashira coupling reactions involving activated/unactivated substrates under environmentally benign conditions.

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