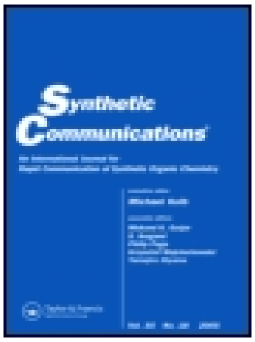


Taylor & Francis
Taylor & Francis Group

Synthetic Communications

An International Journal for Rapid Communication of Synthetic Organic Chemistry

ISSN: 0039-7911 (Print) 1532-2432 (Online) Journal homepage: https://www.tandfonline.com/loi/lsyc20

Microwave assisted cross-coupling reactions using palladium nanoparticles in aqueous media

Kalyan Dhara, Bibudha Parasar, Avinash J. Patil & Jyotirmayee Dash

To cite this article: Kalyan Dhara, Bibudha Parasar, Avinash J. Patil & Jyotirmayee Dash (2019): Microwave assisted cross-coupling reactions using palladium nanoparticles in aqueous media, Synthetic Communications, DOI: 10.1080/00397911.2019.1576203

To link to this article: https://doi.org/10.1080/00397911.2019.1576203

SYNTHETIC COMMUNICATIONS®
https://doi.org/10.1080/00397911.2019.1576203

Taylor & Francis
Taylor & Francis Group

Microwave assisted cross-coupling reactions using palladium nanoparticles in aqueous media

Kalyan Dhara[a], Bibudha Parasar[a], Avinash J. Patil[b], and Jyotirmayee Dash[a]

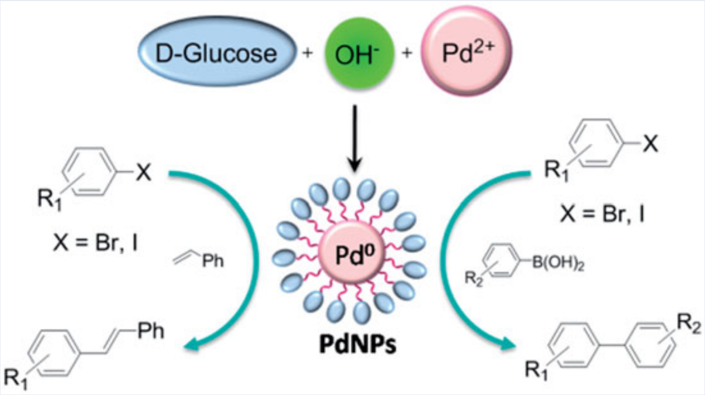
[a]Department of Organic Chemistry, Indian Association for the Cultivation of Science, Kolkata, India;
[b]Centre for Organized Matter Chemistry, University of Bristol, Bristol, UK

ABSTRACT
Glucose stabilized palladium nanoparticles (PdNPs) have been prepared and the application of NPs in catalyzing both Suzuki and Heck reactions has been explored in aqueous media under microwave conditions. Both electron-rich and electron-deficient aryl halides can be coupled with a variety of boronic acids and styrene to access a wide variety of biaryl compounds and substituted alkenes in good to excellent yields. The catalyst can be recycled and reused four times with minimally affecting the morphology and efficiency of the nanoparticles. A plausible reaction mechanism has been proposed.

ARTICLE HISTORY
Received 14 December 2018

KEYWORDS
Glucose; Heck coupling; palladium nanoparticle; recycling; Suzuki coupling

GRAPHICAL ABSTRACT



Introduction

In the past few decades, the major focus of catalysis has been shifted towards the development of sustainable synthetic reactions that can generate bio-friendly by-products and waste materials without compromising on yield. The persisting problem for industrial scale synthesis of drug molecules, pesticides etc. is the disposal of organic solvents, and therefore, efforts have been pursued to use eco-friendly alternative solvents; mainly water. Water has always been avoided as a solvent of choice due to the poor solubility

---

CONTACT Jyotirmayee Dash ocjd@iacs.res.in School of Chemical Sciences, Indian Association for the Cultivation of Science, 2B Raja S C Mullick Road, Kolkata 700032, India.

Supplemental data for this article is available online at on the publisher's website.

of reactants as well as the labile nature of reagents in aqueous media. In recent years, there is significant interest in developing metal-catalyzed organic transformations in aqueous media.[1] Increasing evidence further suggests that water, with its high dielectric constant, is an ideal solvent for microwave-based synthesis[2–4] that can also be carried out at a higher temperature.

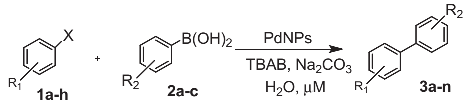
The Suzuki coupling[5–9] is one of the most commonly used C–C bond forming reactions for the construction of biaryl compounds.[10] These coupling reactions have also been optimized in aqueous media[11] using nanoparticle-based catalysts. Colloidal nanoparticle-based catalysts provide a platform to carry out reactions with high efficiency and catalyst reusability.[12] Given their large surface area, they provide an abundance of local reaction centers that could result in high turnover numbers (TON). With a water-soluble ligand/stabilizing agent, they can further be tuned to facilitate organic reactions in water.[13,14]

In this context, we herein report glucose stabilized palladium nanoparticles for cross-coupling reactions. We anticipated that the presence of five hydroxyl groups in glucose would efficiently chelate palladium nanoparticles as well as render high aqueous solubility of the palladium catalyst. Liu et al. described the catalytic ability of starch-based palladium nanoparticle (PdNP) to catalyze Suzuki–Miyaura coupling.[15] In their report, the particle size increased over successive recycling of the catalyst and the activity went down to 20% after 6th cycle. The decrease in yield was possibly due to the agglomeration of the nanoparticles. We envisaged that ligand might be useful to prevent the aggregation and retain the catalytic efficiency of the nanoparticles. Starch, being polymeric has a higher propensity to interact with other particles in a cooperative manner facilitating agglomeration. However, strategic use of a high binding monomer may prevent such a side reaction, and retain the property and catalytic activity of nanoparticles.[16,17] Herein, we report the catalytic activity of D-glucose stabilized Pd nanoparticles for the Suzuki and Heck cross-coupling reactions.

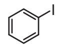
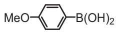
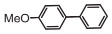
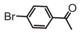
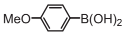
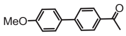
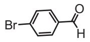
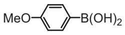
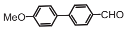
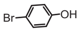
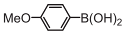
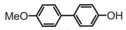
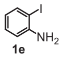
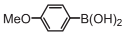
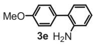
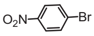
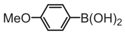
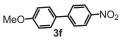
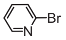
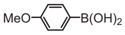
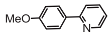
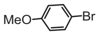
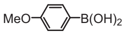
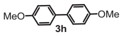
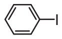
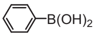
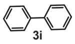
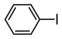
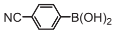
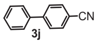
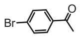
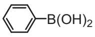
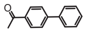
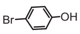
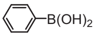
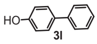
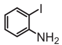
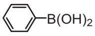
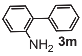
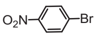
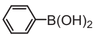
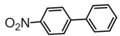
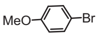
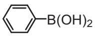
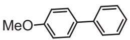
Results and discussion

We have performed the Suzuki reaction with freshly prepared Pd nanoparticles stabilized by D-glucose in neat water using microwave heating.[18–23] We first examined the catalytic efficiency of our synthesized glucose stabilized palladium nanoparticles by exploring the cross-coupling of iodobenzene **1a** with 4-methoxy phenylboronic acid **2a** in the presence of 5 mol % PdNPs, Na_2CO_3 as a base and tetrabutylammonium bromide to give the corresponding product **3a** in 95% yield (Table 1, entry 1).[22] Notably, under microwave conditions, the reaction underwent complete conversion within 5 min. The optimized reaction conditions were further applied for the cross-coupling of both electron-rich and electron-deficient aryl halides **1a**–**1n** with 4-methoxy phenylboronic acid **2a**, phenylboronic acid **2b**, and 4-cyano phenylboronic acid **2c** to obtain the corresponding products **3a**–**3n** in good to excellent yields with comparable reaction rate (Table 1). Next, electron-deficient aryl halides 4-bromoacetophenone **1b**, 4-bromo benzaldehyde **1c** and 4-bromo nitrobenzene **1f** were used to cross-couple with electron-rich 4-methoxy phenylboronic acid **2a** and the corresponding products **3b**, **3c,** and **3f** were obtained in 69–76% (Table 1, entries 2, 3, and 6). Subsequently, electron-rich aryl

Table 1. Suzuki couplings under microwave conditions in aqueous media[a].

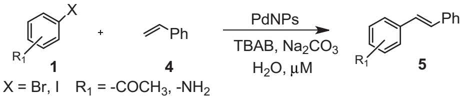


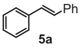
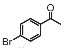
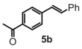
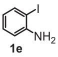
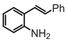
X = Br, I R$_2$ = -OMe, -H, -CN
R$_1$ = -COCH$_3$, -CHO, -OH, -NH$_2$, -NO$_2$, -OMe

Entry	ArX, **1**	Ar^{1}B(OH)$_2$, **2**	Ar-Ar^1, **3**	Yield (%)
1	 **1a**	 **2a**	 **3a**	95%
2	 **1b**	 **2a**	 **3b**	76%
3	 **1c**	 **2a**	 **3c**	69%
4	 **1d**	 **2a**	 **3d**	52%
5	 **1e**	 **2a**	 **3e**	88%
6	 **1f**	 **2a**	 **3f**	70%
7	 **1g**	 **2a**	 **3g**	54%
8	 **1h**	 **2a**	 **3h**	82%
9	 **1a**	 **2b**	 **3i**	93%
10	 **1a**	 **2c**	 **3j**	91%
11	 **1b**	 **2b**	 **3k**	88%
12	 **1d**	 **2b**	 **3l**	92%
13	 **1e**	 **2b**	 **3m**	93%
14	 **1f**	 **2b**	 **3n**	73%
15	 **1h**	 **2b**	 **3a**	89%

[a] Aryl halides (1.0 mmol), boronic acid (1.0 mmol), Na$_2$CO$_3$ (3 mmol), TBAB (1.0 mmol), 5 mol% water soluble glucose stabilized Pd (0) nanoparticles as catalyst, 2 mL water, microwave, 150 °C, 5 min.

Table 2. Heck couplings under Microwave conditions in aqueous media[a].



Entry	ArX, **1**	Product, **5**	Yield (%)
1	 **1a**	 **5a**	74%
2	 **1b**	 **5b**	47%
3	 **1e**	 **5c**	45%

[a]Aryl halides (1.0 mmol), Styrene (1.0 mmol), Na_2CO_3 (3 mmol), TBAB (1.0 mmol), 5 mol% water soluble glucose stabilized Pd (0) nanoparticles as catalyst, 2 mL water, microwave, 150 °C, 5 min.

halides and electron-rich boronic acids were examined for this coupling reaction. The catalytic system also proved to be highly efficient for electron-rich aryl halides. When the efficiency of the coupling reaction with electron-rich 4-bromo phenol **1d** was tested, the product was obtained in 52% yield (Table 1, entry 4).

However, the reaction with electron-rich aryl halides 4-bromoanisole **1h** and 2-iodoaniline **1e** underwent a coupling reaction with 4-methoxy phenylboronic acid **2a** using this protocol to afford corresponding products **3e** and **3h** in good yields (Table 1, entries 5 and 8). Aromatic heterocyclic halide, 2-bromopyridine **1g** also underwent reaction with 4-methoxy phenylboronic acid **2a** smoothly to give the desired product **3g** in 54% yield (Table 1, entry 7). We subsequently compared the reactivity of all the aryl halides with 4-methoxyphenylboronic acid **2a**. It can be easily realized that, aryl bromides bearing electron withdrawing group decreases the reaction yield (Table 1, entries 2, 3, and 6) whereas the presence of amino group in the *ortho* position and hydroxy group in the *para* position resulted in high yield for phenyl boronic acid (Table 1, entries 12 and 13). 4-Hydroxy bromobenzene **1d** and 2-iodoaniline **1e** reacted with phenylboronic acid **2b** to afford the corresponding products **3l** and **3m** in 92–93% (Table 1, entries 12 and 13). Electron-deficient 4-cyanophenylboronic acid **2c** also reacted with iodobenzene **1a** to give the corresponding product **3j** in 91% yield (Table 1, entry 10). Electron-deficient aryl halides 4-bromoacetophenone **1b** and 4-bromo nitrobenzene **1f** were also efficiently reacted with phenylboronic acid **2b** to afford the coupling products **3k** and **3n** in 88% and 73%, respectively (Table 1, entries 11 and 14). The coupling reaction of iodobenzene **1a** and 4-bromoanisole **1h** were performed with phenylboronic acid **2b**. The corresponding products **3i** and **3a** were isolated in synthetically useful yields (Table 1, entries 9 and 15).

To further explore the scope of our proposed methodology, we have performed the Heck coupling[24–26] of different aryl halides with styrene. Applying the conditions established for the Suzuki coupling, Heck coupling was carried out and the results are summarized in Table 2. Both electron withdrawing (*p*-bromoacetophenone **1b**) and electron donating groups bearing aryl halides (2-iodoaniline **1e**) reacted with styrene **4**

Table 3. Reusability of the glucose stabilized palladium nanoparticle for Suzuki and Heck coupling reaction[a].

Recycle Number	1	2	3	4
Yield for Suzuki reaction	95%	85%	79%	70%
Yield for Heck reaction	74%	65%	63%	60%

[a]All reactions are carried out under optimized condition.

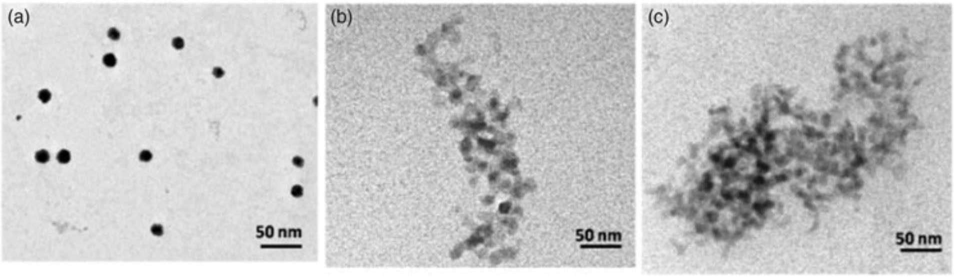


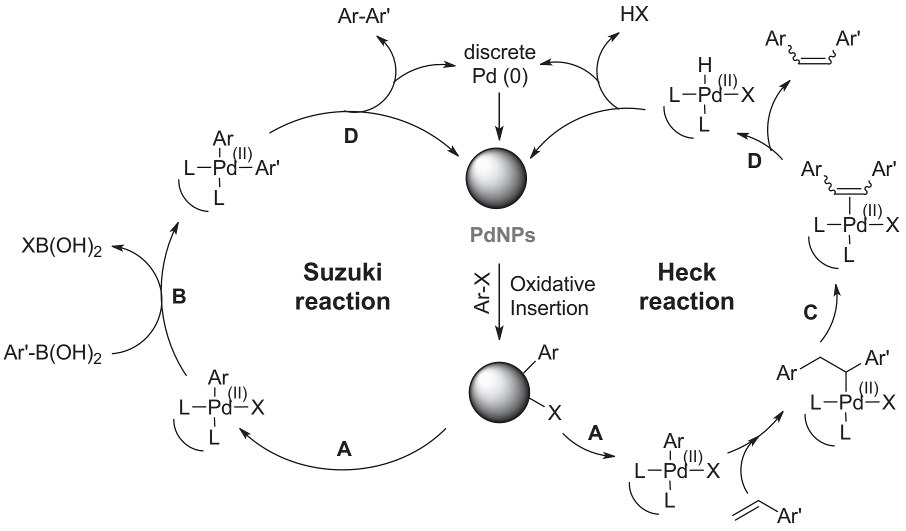
Figure 1. TEM images of PdNPs freshly prepared (a), after 1st cycle (b), after 4th cycle (c).

to afford the corresponding products in comparable yields whereas iodobenzene **1a** reacted with styrene **4** to generate the compound **5a** in 74% yield.

Recycling of catalyst

Catalysts with durable lifetime and recyclability are highly desirable traits in industrial scale synthesis. Keeping the broad applications in mind, catalytic recycling efficiency of PdNPs was investigated for both Suzuki and Heck coupling reactions. The reaction between iodobenzene **1a** and 4-methoxyphenyl boronic acid **2a** was chosen as the model reaction for Suzuki coupling and that between iodobenzene **1a** and styrene **4** was considered as the model reaction for Heck coupling reaction, to assess the efficiency of the catalysis after successive reusability. In a typical procedure, both the reactions were carried out under optimized conditions using glucose stabilized palladium nanoparticles. After each catalytic cycle, the aqueous part was washed with diethyl ether, and then the colloidal aqueous part was used in the subsequent catalytic reaction. The catalyst remained active up to four consecutive cycles for both the reactions, albeit with a gradual decrease in efficiency over repeated use (Table 3). Notably, the catalytic efficiency in 4th reuse was still higher than that observed in the starch stabilized PdNP observed earlier.[15,27]

Transmission electron microscopy (TEM) images of the PdNPs were taken after successive recovery of the catalyst for both Suzuki and Heck reactions. The size of the freshly prepared glucose stabilized PdNPs was 10 nm (Fig. 1a). The TEM images recorded after the catalytic runs revealed that both size and morphology of the PdNPs remained same even after the fourth round of the catalytic cycle (Fig. 1b and c). However, comparison of the images of PdNPs recovered after the first and fourth round of catalysis revealed the increase in density of the aggregated clusters that were formed post reaction. This gradual decrease of the catalytic efficiency may be attributed to aggregation and formation of a supercluster of PdNPs over successive reuse of the



Scheme 1. Proposed mechanism of Suzuki and Heck reaction. **A**: chemical etching, **B**: transmetalation, **C**: β-hydride elimination, **D**: reductive elimination.

catalyst, which in turn may potentially have a critical effect on the catalytic efficiency. PdNPs were washed with organic solvents and that may alter or remove the glucose layer from the surface of the nanoparticles facilitating aggregation and decreasing the catalytic efficiency.

Proposed mechanism

We believe both Suzuki and Heck reactions are initiated with oxidative addition of aryl halide to the core of the palladium nanoparticles, involving both Pd (0) and Pd (II). Involvement of both the oxidation states along with an abundance of ionic species creates a corrosive environment[28–30] around the active site that finally lead to chemical etching of nanocluster to generate discrete Pd(II) catalytic center (Scheme 1). Our hypothesis is supported by the fact that the homocoupling byproduct has not been formed during the reaction. Suzuki reactions may further undergo transmetalation and reductive elimination to release biaryl **3** and Heck reactions may undergo β-hydride elimination followed by reductive elimination to generate substituted alkene **5** as the product. Along with the desired product, both the reactions also generate discrete Pd (0) species, which in turn is deposited back to Pd (0) nanocluster.[31] The palladium nanoparticles aggregated with repeated cycling of the catalyst as a result of a process similar to Ostwald ripening,[32] causing atomic rearrangement.

We believe, glucose being a monomer is a weaker ligand than starch and is less corrosive. Hence, glucose stabilized nanoparticle would exhibit aggregation at a slower rate. Given the dependence of reaction efficiency on the size of metal nanoparticles[33] and glucose being a softer ligand than starch, palladium nanoparticles stabilized by glucose would function better than the starch stabilized nanoparticles on the recovery and reuse of the catalyst.[34]

Experimental

General remarks

All experiments were carried out under an inert atmosphere of argon in flame-dried flasks. Solvents were dried using standard procedures reported in Perrin, D. D.; Armarego, W. L. F., Purification of Laboratory Chemicals, 3rd edition, Pergamon Press, Oxford, 1988. All starting materials were obtained from commercial suppliers and used as received. Products were purified by flash chromatography on silica gel (100–200 mesh, Merck). **^{1}H NMR** spectra were recorded at 500 MHz using Brüker ADVANCE 500 MHz (Bruker, Switzerland) and JEOL 400 MHz (JEOL, Japan) at 298 K. Signals are quoted as δ values in ppm using residual protonated solvent signals as internal standard ($CDCl_3$: δ 7.26 ppm). Data is reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet), and coupling constants (Hz). **^{13}C NMR** spectra were recorded on either a JEOL-400 (100 MHz) or a Brüker ADVANCE 500 MHz (125 MHz) with complete proton decoupling. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane with the solvent as the internal reference ($CDCl_3$: δ 77.16 ppm). **HRMS** analyses were performed with Q-TOF YA263 high resolution (Water Corporation, Australia) instruments by + ve mode electrospray ionization. All the reactions were carried out in a Biotage Microwave synthesis system (Initiator EXP. EU, Biotage Sweden AB).

Preparation of glucose stabilized palladium nanoparticles

Reusable D-glucose stabilized Pd nanoparticles with controlled particle sizes were prepared using the procedure described by Xu and coworkers.[27,35]

Typical procedure for Suzuki–Miyaura coupling reaction

Biphenyl derivatives were prepared from cross-coupling of commercially available aryl halides and boronic acids using glucose stabilized Pd-nanoparticles (PdNPs), Na_2CO_3, TBAB in water under microwave irradiation at 150 °C for 5 min. In a 5 mL microwave vial Na_2CO_3 (3 equiv.) and TBAB (1 equiv.) were added to a suspension of aryl halide (1 equiv.) and boronic acid (1 equiv.) in 2 mL water. Then the mixture was degassed with N_2 for 5 min. Then a catalytic amount of PdNPs (5 mol %) was added and the resulting mixture was stirred at 150 °C in the microwave for 5 min. Then the reaction mixture was cooled and extracted with diethyl ether (3 × 20 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuum*. The crude residue was then purified by column chromatography on silica gel with ethyl acetate hexane (5/95 to 10/90) to provide compounds **3**.

Typical procedure for Heck coupling reaction

In a 5 mL microwave vial containing Na_2CO_3 (3 equiv.) and TBAB (1 equiv.), aryl halide (1 equiv.) and styrene (1 equiv.) were added in 2 mL water. Then the mixture was degassed with N_2 for 5 min in room temperature. Then 5 mol% glucose stabilized Pd nanoparticles (PdNPs) was added to it and stirred at 150 °C in the microwave for 5 min. Then the reaction mixture was cooled to room temperature and extracted with diethyl ether (3 × 20 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuum*. The crude residue was then purified by column chromatography on silica gel with ethyl acetate-hexane (5/95 to 10/90) to provide compounds **5**.

Conclusions

In conclusion, our results suggest that use of a monomeric ligand over polymeric may increase reaction efficiency by controlling aggregation of the nano-catalysts over successive use. As a proof of principle, we have synthesized glucose stabilized palladium nanoparticles and showcased its efficiency for Suzuki and Heck coupling reactions in aqueous media, with potential reusability of the catalyst and relatively minimal loss in activity. The exact mechanism of aggregation induced decrease in reaction efficiency is currently under investigation.

Funding

We thank the Department of Science and Technology, Ministry of Science and Technology (DST) and CSIR- India for research funding. KD thanks UGC for a research fellowship.

References

[1] Cornils, B.; Herrmann, W. A. *Aqueous-Phase Organometallic Catalysis, Concepts and Applications*; Wiley-VCH: Weinheim, **1998**.

[2] Dallinger, D.; Kappe, C. O. Microwave-Assisted Synthesis in Water as Solvent. *Chem. Rev.* **2007**, *107*, 2563–2591. DOI: 10.1021/cr0509410.

[3] Kappe, C. O. Microwave Dielectric Heating in Synthetic Organic Chemistry. *Chem. Soc. Rev.* **2008**, *37*, 1127–1139. DOI: 10.1039/B803001B.

[4] Högermeier, J.; Reißig, H.-U. First Comprehensive Investigation of Suzuki Couplings of Alkenyl Nonaflates with Aryl and Alkenyl Boronic Acid Derivatives by Using Classical Conditions and Microwave Heating. *Chem. Eur. J.* **2007**, *13*, 2410–2420. DOI: 10.1002/chem.200601394.

[5] Scheuermann, G. M.; Rumi, L.; Steurer, P.; Bannwarth, W.; MuLhaupt, R. Palladium Nanoparticles on Graphite Oxide and Its Functionalized Graphene Derivatives as Highly Active Catalysts for the Suzuki–Miyaura Coupling Reaction. *J. Am. Chem. Soc.* **2009**, *131*, 8262–8270. DOI: 10.1021/ja901105a.

[6] Chen, Y.; Wang, M.; Zhang, L.; Liu, Y.; Han, J. Poly (o-aminothiophenol)-Stabilized Pd Nanoparticles as Efficient Heterogenous Catalysts for Suzuki Cross-Coupling Reactions. *RSC Adv.* **2017**, *7*, 47104–47110. DOI: 10.1039/C7RA09947A.

[7] Qiu, L.; McCaffrey, R.; Jin, Y.; Gong, Y.; Hu, Y.; Sun, H.; Park, W.; Zhang, W. Cage-templated Synthesis of Highly Stable Palladium Nanoparticles and Their Catalytic Activities in Suzuki–Miyaura Coupling. *Chem. Sci.* **2018**, *9*, 676–680. DOI: 10.1039/C7SC03148C.

[8] Mäsing, F.; Nüsse, H.; Klingauf, J.; Studer, A. Visible-Light-Enabled Preparation of Palladium Nanoparticles and Application as Catalysts for Suzuki–Miyaura Coupling. *Org. Lett.* **2018**, *20*, 752–755. DOI: 10.1021/acs.orglett.7b03892.

[9] Miyaura, N.; Suzuki, A. Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds. *Chem. Rev.* **1995**, *95*, 2457–2483. DOI: 10.1021/cr00039a007.

[10] Maluenda, I.; Navarro, O. Recent Developments in the Suzuki–Miyaura Reaction: 2010–2014. *Molecules* **2015**, *20*, 7528–7557. DOI: 10.3390/molecules20057528.

[11] Schmidt, B.; Riemer, M. Suzuki–Miyaura Coupling of Halophenols and Phenol Boronic Acids: Systematic Investigation of Positional Isomer Effects and Conclusions for the Synthesis of Phytoalexins from Pyrinae. *J. Org. Chem.* **2014**, *79*, 4104–4118. DOI: 10.1021/jo500675a.

[12] Kumbhar, A.; Kamble, S.; Mane, A.; Jha, R.; Salunkhe, R. Modified Zeolite Immobilized Palladium for Ligand-free Suzuki–Miyaura Cross-coupling Reaction. *J. Organomet. Chem.* **2013**, *738*, 29–34. DOI: https://doi.org/10.1016/j.jorganchem.2013.03.031.

[13] Joshi, H.; Sharma, K. N.; Sharma, A. K.; Singh, A. K. Palladium–Phosphorus/Sulfur Nanoparticles (NPs) Decorated on Graphene Oxide: Synthesis Using the Same Precursor for NPs and Catalytic Applications in Suzuki–Miyaura Coupling. *Nanoscale* **2014**, *6*, 4588–4597. DOI: 10.1039/c3nr06586c.

[14] Bej, A.; Ghosh, K.; Sarkar, A.; Knight, D. W. Palladium Nanoparticles in the Catalysis of Coupling Reactions. *RSC Adv.* **2016**, *6*, 11446–11453. DOI: 10.1039/C5RA26304B.

[15] Liu, S.; Zhou, Q.; Jiang, H. Water Soluble Starch Stabilized Palladium Nanoparticle: Efficient Catalyst for Miyaura-Suzuki Coupling Reaction. *Chin. J. Chem.* **2010**, *28*, 589–593. DOI: https://doi.org/10.1002/cjoc.201090117.

[16] Wang, Y.; Sauer, D. R. Use of Polymer-Supported Pd Reagents for Rapid and Efficient Suzuki Reactions Using Microwave Heating. *Org. Lett.* **2004**, *6*, 2793–2796. DOI: 10.1021/ol048972p.

[17] Kabalka, G. W.; Pagni, R. M.; Wang, L.; Namboodiri, V.; Hair, C. M. Microwave-Assisted, Solventless Suzuki Coupling Reactions on Palladium-Doped Alumina. *Green Chem.* **2000**, *2*, 120–122. DOI: 10.1039/b001191f.

[18] Gong, Y.; He, W. Direct Synthesis of Unprotected 4-Aryl Phenylalanines via the Suzuki Reaction under Microwave Irradiation. *Org. Lett.* **2002**, *4*, 3803–3805. DOI: 10.1021/ol026587z.

[19] Namboodiri, V. V.; Varma, R. S. Microwave-accelerated Suzuki Cross-coupling Reaction in Polyethylene Glycol (PEG). *Green Chem.* **2001**, *3*, 146–148. DOI: 10.1039/b102337n.

[20] Zhang, W.; Chen, C. H.-T.; Lu, Y.; Nagashima, T. A Highly Efficient Microwave-Assisted Suzuki Coupling Reaction of Aryl Perfluorooctylsulfonates with Boronic Acids. *Org. Lett.* **2004**, *6*, 1473–1476. DOI: 10.1021/ol0496428.

[21] Shen, L.; Huang, S.; Nie, Y.; Lei, F. An Efficient Microwave-Assisted Suzuki Reaction Using a New Pyridine-Pyrazole/Pd(II) Species as Catalyst in Aqueous Media. *Molecules* **2013**, *18*, 1602–1612. DOI: 10.3390/molecules18021602.

[22] Leadbeater, N. E.; Marco, M. Ligand-Free Palladium Catalysis of the Suzuki Reaction in Water Using Microwave Heating. *Org. Lett.* **2002**, *4*, 2973–2976. DOI: 10.1021/ol0263907.

[23] Zhou, J.; Guo, X. M.; Tu, C. Z.; Li, X. Y.; Sun, H. J. Aqueous Suzuki Coupling Reaction Catalyzed by Water-Soluble Diimine/Pd(II) Systems. *J. Organomet. Chem* **2009**, *694*, 697–702. DOI: 10.1016/j.jorganchem.2008.11.060.

[24] Choudary, B. M.; Madhi, S.; Chowdari, N. S.; Kantam, M. L.; Sreedhar, B. Layered Double Hydroxide Supported Nanopalladium Catalyst for Heck-, Suzuki-, Sonogashira-, and Stille-Type Coupling Reactions of Chloroarenes. *J. Am. Chem. Soc.* **2002**, *124*, 14127–11413. DOI: 10.1021/ja026975w.

[25] Moreno-Mañas, M.; Pleixats, R.; Villarroya, S. Fluorous Phase Soluble Palladium Nanoparticles as Recoverable Catalysts for Suzuki Cross-Coupling and Heck Reactions. *Organometallics* **2001**, *20*, 4524–4528. DOI: 10.1021/om010442z.

[26] Calo, V.; Nacci, A.; Monopoli, A.; Detomaso, A.; Iliade, P. Pd Nanoparticle Catalyzed Heck Arylation of 1, 1-Disubstituted Alkenes in Ionic Liquids. Study on Factors Affecting the Regioselectivity of the Coupling Process. *Organometallics* **2003**, *22*, 4193–4197. DOI: 10.1021/om034020w.

[27] Xu, L.; Wu, X.-C.; Zhu, J.-J. Green Preparation and Catalytic Application of Pd Nanoparticles. *Nanotechnology* **2008**, *19*, 305603. DOI: https://doi.org/10.1088/0957-4484/19/30/305603.

[28] Liu, Y.; Khemtong, C.; Hu, J. Synthesis and Catalytic Activity of a Poly (*N, N*-dialkylcarbodiimide)/Palladium Nanoparticlecomposite: A Case in the Suzuki Coupling Reaction Using Microwave and Conventional Heating. *Chem. Commun.* **2004**, *2004*, 398–399. DOI: 10.1039/B313210M.

[29] Gedye, R.; Smith, F.; Westaway, K.; Ali, H.; Baldisera, L.; Laberge, L.; Rousell, J. The Use of Microwave Ovens for Rapid Organic Synthesis. *Tetrahedron Lett.* **1986**, *27*, 279–282. DOI: 10.1016/S0040-4039(00)83996-9.

[30] Zhang, A.; Neumeyer, J. L. Microwave-Promoted Pd-Catalyzed Cyanation of Aryl Triflates: A Fast and Versatile Access to 3-Cyano-3-desoxy-10-Ketomorphinans. *Org. Lett.* **2003**, *5*, 201–203. DOI: 10.1021/ol027256p.

[31] Hu, J.; Liu, Y. Pd Nanoparticle Aging and Its Implications in the Suzuki Cross-Coupling Reaction. *Langmuir* **2005**, *21*, 2121–2123. DOI: 10.1021/la0471902.

[32] Narayanan, R.; El-Sayed, M. A. Effect of Catalysis on the Stability of Metallic Nanoparticles: Suzuki Reaction Catalyzed by PVP-Palladium Nanoparticles. *J. Am. Chem. Soc.* **2003**, *125*, 8340–8347. DOI: 10.1021/ja035044x.

[33] Schmid, G. Large Clusters and Colloids. Metals in the Embryonic State. *Chem. Rev.* **1992**, *92*, 1709–1727. DOI: 10.1021/cr00016a002.

[34] Pérez-Lorenzo, M. Palladium Nanoparticles as Efficient Catalysts for Suzuki Cross-Coupling Reactions. *J. Phys. Chem. Lett.* **2012**, *3*, 167–174. DOI: 10.1021/jz2013984.

[35] Molńar, Á.; Papp, A. The Use of Polysaccharides and Derivatives in Palladium-Catalyzed Coupling Reactions. *Catal. Sci. Technol.* **2014**, *4*, 295–310. DOI: 10.1039/C3CY00699A.