Suzuki–Miyaura Reaction in Water, Catalyzed by Palladium Nanoparticles Stabilized by Pluronic F68 Triblock Copolymer

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Received November 8, 2010

Abstract—Palladium nanoparticles stabilized by Pluronic F68 triblock copolymer effectively catalyzed Suzuki–Miyaura reaction in water. The reactions with water-soluble aryl iodides and aryl bromides containing electron-withdrawing or electron-donating substituent occurred at room temperature. The catalytic efficiency was found to depend on the size of palladium nanoparticles and their morphology.

DOI: 10.1134/S1070428011040014

Reactions leading to formation of new carboncarbon bonds, such as Suzuki-Miyaura and Mizuroki-Heck reactions, are very important for organic synthesis, and they permanently attract researchers' attention, especially if these reactions are carried out in water as the most accessible and ecologically safe solvent. It was proposed to catalyze such reactions in aqueous medium by metal nanoparticles, in particular by palladium nanoparticles stabilized by micelles formed by surfactants and amphiphilic block copolymers [1]. Examples of the latter are micelles containing polystyrene-b-poly(ethylene oxide) (PS-PEO) [2], poly-(ethylene oxide)-b-poly(2-vinylpyridine) (PEO-P2VP) [3], polystyrene-b-poly(4-vinylpyridine) (PS-P4VP) [1, 4, 5], and poly(ethylene oxide)-b-poly(isopropylene oxide)-b-poly(ethylene oxide) (PEO-PPO-PEO) [6]. To ensure efficient recycling of the catalyst, PS-P4VP micelles were immobilized on polystyrene-bpoly(methyl methacrylate) microspheres [5].

We previously showed that palladium nanoparticles (PdNPs) stabilized by PS–PEO and cetylpyridinium chloride (CPC) micelles [2] efficiently catalyzed Suzuki–Miyaura reactions with water-soluble reagents in water [7]. We now propose to stabilize PdNPs with the aid of accessible Pluronic F68 triblock copolymer (PEO₇₆–PPO₃₀–PEO₇₆). Among triblock copolymers studied previously [Pluronic PL64 (PEO₁₃–PPO₃₀–PEO₁₃), Pluronic P103 (PEO₁₇–PPO₆₀–PEO₁₇), Pluronic P123 (PEO₁₉–PEO₁₉), and Pluronic F108 (PEO₁₃₂–PPO₅₀–PEO₁₃₂)], only Pluronic P123 was used as PdNPs stabilizer in Suzuki–Miyaura reactions [6]. However, the catalytic activity of PdNPs was

determined only in dimethylformamide. Pluronic F68 is characterized by an intermediate length of PEO fragments among the above triblock copolymers. It is fairly hydrophilic and convenient for studying Suzuki– Miyaura reactions in water.

The catalyst stabilized by Pluronic F68 was prepared according to the procedure described previously for the catalyst with Pluronic P123 [6], by reduction of Na₂PdCl₄ in the presence of Pluronic F68. According to the transmission electron microscopy (TEM) data, the obtained catalyst contained mainly cubooctahedral PdNPs with an average diameter of 5.4 nm and relatively low dispersion (Fig. 1). The position of reflexes (111, 200, and 220) in the electron diffraction pattern indicated crystalline nature of PdNPs [6, 8–11].

We examined Suzuki-Miyaura reactions of phenylboronic acid PhB(OH)₂ with water-soluble aryl iodides and aryl bromides containing an electron-withdrawing (m-COOH) or electron-donating substituent (p-OH) in water in the presence of potassium hydroxide as base (Scheme 1). The catalyst showed a high efficiency, and the reaction occurred at room temperature in the presence of an optimal amount of KOH (5 equiv). At a palladium concentration of 1 mol %, the reaction with *m*-iodobenzoic acid was almost complete in 0.5 h (Table 1, run no. 1), and with *m*-bromobenzoic acid, in 10 h (Table 1, run no. 6). In the reaction with *p*-iodophenol, the conversion attained 95% in 4 h (run no. 8), whereas the conversion of *p*-bromophenol was only 60% even in 24 h (run no. 10). The reactions were selective, and the yield approached the conversion of the initial aryl halide. Biphenyl was formed as by-



Fig. 1. (a) Transmission electron micrograph of palladium nanoparticles and (b) their size distribution.

Table 1. Suzuki–Miyaura reaction of phenylboronic acid with aryl halides in water in the presence of palladium nanoparticles stabilized by Pluronic F68 block copolymer micelles^a

Run no.	Aryl halide (ArX)	Time, h	Yield, ^b %	Conversion of ArX, ^b %
1	<i>m</i> -Iodobenzoic acid	0.5	93	98
2 ^c		0.5	69	75
3		1	95	98
4 ^d		1	72	80
5 ^e		4	85 [7]	89
6	<i>m</i> -Bromobenzoic acid	10	93	98
7	p-Iodophenol	1	30	44
8		4	86	95
9 ^e		4	68 [7]	91
10	<i>p</i> -Bromophenol	24	49	60

- ^a Reaction conditions: 0.075 mmol of ArX, 0.09 mmol of PhB(OH)₂, 0.38 mmol of KOH, 1 mol % of Pd, 0.25 ml of water; temperature 20°C.
- ^b According to the GLC data; biphenyl was also formed as byproduct, yield 5–12%.
- ^c In the presence of 0.5 mol % of Pd.
- ^d KOH, 0.23 mmol.
- ^e In the presence of palladium nanoparticles stabilized by PS– PEO/CPC micelles [7].



Hlg = I, Br; R = *m*-COOH (**a**), *p*-HO (**b**).

product (5–12%) via oxidation of phenylboronic acid with atmospheric oxygen [12]. It should be emphasized that the examined reactions in water occurred very easily at room temperature. By contrast, analogous reactions catalyzed by Pluronic P123-stabilized palladium species in DMF required heating at 90°C over a period of 8 h to attain quantitative yield of cross-coupling products [6]. Presumably, the difference in the reaction conditions is related primarily to good solubility of KOH in water and poor solubility of Cs₂CO₃ in DMF.

The catalyst stabilized by Pluronic F68 was more active than that based on palladium nanoparticles stabilized by PS-PEO/CPC micelles [7]. In the first case, the reaction with m-iodobenzoic acid was complete in 30 min at room temperature (Table 1, run no. 1), whereas in the second case as long reaction time as 4 h was insufficient to complete the process. Even stronger difference in the activity of the above catalysts was observed in the reaction with p-iodophenol. The reaction in water in the presence of PdNPs stabilized by Pluronic F68 was complete in 4 h at room temperature (see above), while the reaction with the same substrate, catalyzed by 3.5-nm palladium nanoparticles with a surface coated by 46% with perthiolated β -cyclodextrin, in aqueous acetonitrile (1:1) was not complete even on heating for 2 h under reflux [13].

Using the reaction of PhB(OH)₂ with *m*-iodobenzoic acid in water as model process, we examined the effect of the size of PdNPs and their morphology on the catalytic activity. Apart from cubooctahedral catalyst with a particle size of 5.4 nm, we prepared other catalysts which contained mainly the following types of palladium nanoparticles: (a) trigonal, palladium concentration ~70%, particle size ~25 nm [8]; (b) hexagonal, ~90%, 10–20 nm [8]; (c) cubooctahedral, ~90%, 8–10 nm [9]; and (d) cubooctahedral, >90%, 1.7 nm [2]. The reactions were carried out under similar conditions in the presence of the same amount of Pluronic F68 (Table 2). The results showed that at 20°C small cubooctahedal PdNPs with a size of 1.7 or 5.4 nm (Table 2; run nos. 9, 10), regardless of their morphology, were more active than larger PdNPs with a size of 8–25 nm (Table 2; run nos. 1, 4). High catalytic activity of small palladium particles is generally rationalized in terms of developed metal surface and a larger number of defects in the crystal lattice.

Large palladium particles catalyzed the model reaction only on heating (Table 2; run nos. 3, 6, 8). However, at 80°C PdNPs catalyzed the reaction so effectively that it was almost complete in 5 h, regardless of the catalyst morphology. Nevertheless, we succeeded in detecting the effect of morphology of PdNPs on their catalytic activity at an intermediate temperature, 60°C (Table 2; run nos. 2, 5, 7). As follows from the results of run nos. 2 and 5 (Table 2), hexagonal PdNPs are less active (yield 3.6% in 5 h) than trigonal (29% in 5 h), though the latter are larger than hexagonal particles. On the other hand, the catalytic activity of cubooctahedral PdNPs remains as high as at 80°C (Table 2, run no. 7); presumably, this is related to their lower size as compared to PdNPs of the other type. This factor complicates analysis of the effect of morphology of PdNPs on the catalytic activity.

Obviously, under the examined conditions trigonal PdNPs are more active in the Suzuki–Miyaura reaction than hexagonal PdNPs with a similar size. The activity of PdNPs is determined by the relative free energy which depends on the number of palladium atoms on the edges and apices of the corresponding nanoparticles [14, 15]. An indirect support in favor of higher free energy of trigonal PdNPs is the fact that palladium leaching (in the presence of O_2 and FeCl₃) is accompanied by transformation of trigonal palladium particles into thermodynamically more stable hexagonal [8] or cubooctahedral species [9].

The catalytic activity of PdNPs in the Suzuki– Miyaura reaction depends not only on their initial size and morphology but also on their transformations during the process. As we showed previously [7], Suzuki–Miyaura reaction is accompanied by change of the size of PdNPs, and increase in the size of PdNPs is accompanied by "crunching." There are published data, according to which the size of palladium particles in Suzuki–Miyaura reactions and related processes with participation of aryl halides decreases [16, 17] or increases [7, 18]. For example, in the reaction of phenylboronic acid with *m*-iodobenzoic acid catalyzed

Table 2. Suzuki–Miyaura reaction of phenylboronic acid with *m*-iodobenzoic acid in water, catalyzed by palladium nanoparticles with different morphologies^a

Run no.	Morphology of PdNPs	Pd, mol %	<i>T</i> , ℃	Time, h	Yield, ^b %
1	Trigonal	2	20	4	3.5
2		1	60	5	29
3		1	80	5	98
4	Hexagonal	2	20	4	<3.5
5		1	60	5	3.6
6		1	80	5	91
7	Cubooctahedral		60	5	92
8		1	80	5	95
9°			20	0.5	93
10 ^d			20	4	85

^a Reaction conditions: 0.075 mmol of ArX, 0.09 mmol of PhB(OH)₂, 0.38 mmol of KOH, 0.25 ml of water, 30 mg (3.6 μmol, 4.8 equiv) of Pluronic F68.

^b GLC data.

^c Palladium nanoparticles were prepared in water in the presence of Pluronic F68; particle size 5.4 nm.

by PS–PEO/CPC-stabilized PdNPs, palladium particles with a size of 1.7 nm after the first cycle are converted into particles with a size of 1.9 nm and agglomerates with a size of 2.4–3.1 nm; the latter are characterized by a definite structure, and they consist of small particles [7].

In the Suzuki–Miyaura reaction catalyzed by PdNPs stabilized by Pluronic F68 micelles we observed decrease of the size of PdNPs from 5.4 to 4.3 nm. The size of PdNPs also decreased from 5.4 to 4.1 nm in the absence of PhB(OH)₂, i.e., as a result of reaction of PdNPs with *m*-iodobenzoic acid. On the other hand, in the presence of *p*- and *o*-iodobenzoic acids, the size of PdNPs increased from 5.4 to 6.3 and 9.2 nm, respectively.

Enlargement of PdNPs both during Suzuki– Miyaura reaction and in reaction with aryl halide in the absence of PhB(OH)₂ is the result of known process involving growth of some species at the expense of dissolution of other smaller species that are more catalytically active (Ostwald ripening process). Initial PdNPs decrease in size due to partial dissolution by the action of reagents or oxygen. Here, aryl halide can act as palladium carrier via leaching of palladium from

^d In the presence of palladium nanoparticles stabilized by PS– PEO/CPC micelles [7]; particle size 1.7 nm.



Fig. 2. Transmission electron micrograph of (a) agglomerated palladium nanoparticles and (b) globule under strong magnification.

small PdNPs with formation of ArPdX species (direct oxidative addition; for analysis of published data and experimental proofs, see [19]). The reverse reaction, reductive elimination of palladium from ArPdX occurs on the surface of larger PdNPs; as a result, the size of PdNPs increases [7].



Fig. 3. Transmission electron micrograph of palladium nanoparticles after repeated use as catalyst in Suzuki–Miyaura reaction.

The size of PdNPs can also increase through agglomeration of initial palladium particles to form large spherical particles. Examination of the latter by TEM showed that they consist of smaller particles. Spherical agglomerates can be formed during the synthesis of PdNPs [10, 20]. We were the first to observe their formation in water from 5.4-nm palladium particles in the presence of 1.2 equiv of m-iodobenzoic acid and 3 equiv of KOH. After 3 h, initial PdNPs are converted into globules with a size of ~50 nm (Fig. 2). These globules should be considered to be intermediate species between the initial palladium particles (Fig. 1) and very large aggregates which are formed after repeated use of the catalyst, e.g., when the next cycle is initiated after loading of new portions of the reactants without preliminary isolation of the product (Fig. 3). It should be noted that such aggregates consist of palladium particles with a size fairly similar to the size of initial PdNPs, which are stuck together.

Thus Pluronic F68 triblock copolymer is an effective stabilizer for palladium nanoparticles which catalyze Suzuki–Miyaura reactions in water. The activity of this catalytic system is sufficient to ensure successful reaction at room temperature not only for watersoluble aryl iodides containing an electron-withdrawing or electron-donating substituent but also for the corresponding aryl bromides. The catalytic activity was found to depend on the size of palladium nanoparticles and their morphology. In particular, the most active under the examined conditions were trigonal PdNPs. The catalytic activity can change during the process as a result of transformations of the catalyst.

EXPERIMENTAL

The reaction mixtures were analyzed by GLC on a Kristalyuks 4000M chromatograph equipped with a flame-ionization detector (Chrompack CP-Sil 8 CB capillary column, 25 m×0.25 mm; oven temperature programming from 120 to 300°C at a rate of 25 deg× min⁻¹; injector and detector temperature 310°C). Transmission electron microscopic studies were performed using a Carl Zeiss LEO912 AB Omega microscope.

Commercially available (Lancaster, Aldrich) aryl halides, phenylboronic acid, block copolymers, poly-(N-vinylpyrrolidin-2-one) (M 55000), and calibration standard for GLC were used without additional purification. In the synthesis of palladium nanoparticles with different morphologies, the reactants were supplied with the aid of an ABU12 autoburette with a TTT1c titrator (Radiometer).

General procedure for Suzuki–Miyaura reaction. A glass 5-ml test tube equipped with a magnetic stirrer was charged with 0.075 mmol of the corresponding aryl halide, 0.09 mmol of phenylboronic acid, 0.38 mmol of potassium hydroxide, and 0.25 ml of water. The catalyst (0.1 ml of a solution containing a required amount of palladium) was added with the aid of a chromatographic syringe, and this moment was taken as the reaction start. When the reaction was complete, the mixture was diluted with 2 ml of a saturated aqueous solution of sodium chloride, 5–7 µl of hexadecane $C_{16}H_{34}$ (internal standard) was added, and the mixture was extracted with methylene chloride (3 × 2 ml). The extract was dried over anhydrous sodium sulfate and analyzed by GLC.

The authors thank Dr. S.S. Abramchuk for performing TEM studies. This study was performed under financial support by the Russian Foundation for Basic Research (project no. 08-03-00659 a) and by the Council for Grants at the President of the Russian Federation (project no. NSh-4668.2008.3).

REFERENCES

- Klingelhofer, S., Heitz, W., Greiner, A., Oestreich, S., Forster, S., and Antonietti, M., J. Am. Chem. Soc., 1997, vol. 119, p. 10116.
- Beletskaya, I.P., Kashin, A.N., Litvinov, A.E., Tyurin, V.S., Valetsky, P.M., and van Koten, G., Organometallics, 2006, vol. 25, p. 154.
- Semagina, N.V., Bykov, A.V., Sulman, E.M., Matveeva, V.G., Sidorov, S.N., Dubrovina, L.V., Valetsky, P.M., Kiselyova, O.I., Khokhlov, A.R., Stein, B., and Bronstein, L.M., *J. Mol. Catal. A*, 2004, vol. 208, p. 273.
- Seregina, M.V., Bronstein, L.M., Platonova, O.A., Chernyshov, D.M., Valetsky, P.M., Hartmann, J., Wenz, E., and Antonietti, M., *Chem. Mater.*, 1997, vol. 9, p. 923.

- Jiang, X., Wei, G., Zhang, W., Zhang, X., Zheng, P., Wen, F., and Shi, L., *J. Mol. Catal. A.*, 2007, vol. 277, p. 102.
- Piao, Y., Jang, Y., Shokouhimehr, M., Lee, I.S., and Hyeon, T., *Small*, 2007, vol. 3, p. 255.
- Beletskaya, I.P., Kashin, A.N., Khotina, I.A., and Khokhlov, A.R., Synlett, 2008, p. 1547.
- Xiong, Y., McLellan, J.M., Chen, J., Yin, Y., Li, Z.-Y., and Xia, Y., J. Am. Chem. Soc., 2005, vol. 127, p. 17118.
- Xiong, Y., Chen, J., Wiley, B., Xia, Y., Aloni, S., and Yin, Y., J. Am. Chem. Soc., 2005, vol. 127, p. 7332.
- Cong-Wen, X., Cheng-Min, S., Zhi-Chuan, X., Tian-Zhong, Y., and Hong-Jun, G., *Chin. Phys. B.*, 2008, vol. 17, p. 2066.
- 11. Sawoo, S., Srimani, D., Dutt, P., Lahiri, R., and Sarkar, A., *Tetrahedron*, 2009, vol. 65, p. 4367.
- 12. Moreno-Manas, M., Pajuelo, F., and Pleixats, R., J. Org. Chem., 1996, vol. 61, p. 2346.
- 13. Strimbu, L., Liu, J., and Kaifer, A.E., *Langmuir*, 2003, vol. 19, p. 483.
- 14. Le Bars, J., Specht, U., Bradley, J.S., and Blackmond, D.G., *Langmuir*, 1999, vol. 15, p. 7621.
- Li, Y., Boone, E., and El-Sayed, M.A., *Langmuir*, 2002, vol. 18, p. 4921.
- Yang, X., Fei, Z., Zhao, D., Ang, W.H., Li, Y., and Dyson, P.J., *Inorg. Chem.*, 2008, vol. 47, p. 3292.
- 17. Thathagar, M.B., Kooyman, P.J., Boerleider, R., Jansen, E., Elsevier, C.J., and Rothenberg, G., *Adv. Synth. Catal.*, 2005, vol. 347, p. 1965.
- Narayanan, R. and El-Sayed, M.A., J. Am. Chem. Soc., 2003, vol. 125, p. 8340.
- Gaikwad, A.V., Holuigue, A., Thathagar, M.B., ten Elshof, J.E., and Rothenberg, G., *Chem. Eur. J.*, 2007, vol. 13, p. 6908.
- 20. Athilakshmi, J., Ramanathan, S., and Chand, D.K., *Tetrahedron Lett.*, 2008, vol. 49, p. 5286.