Russian Chemical Bulletin, International Edition, Vol. 62, No. 3, pp. 657—660, March, 2013

Palladium nanoparticles stabilized by sterically hindered phosphonium salts as Suzuki cross-coupling catalysts*

V. V. Ermolaev, D. M. Arkhipova, L. Sh. Nigmatullina, I. Kh. Rizvanov, V. A. Milyukov,★ and O. G. Sinyashin

A. E. Arbuzov Institute of Organic and Physical Chemistry,
Kazan Research Center, Russian Academy of Sciences,
8 ul. Akad. Arbuzova, 420088 Kazan, Russian Federation.
E-mail: miluykov@iopc.ru

Palladium nanoparticles with an average size of 2.5±0.5 nm formed from palladium acetate in the presence of tri-*tert*-butyl(decyl)phosphonium tetrafluoroborate without an additional reducing agent exhibit high activity as a catalyst for the Suzuki cross-coupling reaction involving bromo- and chloroarenes under mild conditions.

Key words: palladium nanoparticles, bromoarenes, catalysis, cross-coupling, arylboronic acids.

The cross-coupling between aryl halides and arylboronic acids discovered by A. Suzuki[1] in 1979 is one of the most demanded and efficient methods for the formation of C—C bond between aryl fragments.[2—4] According to the commonly accepted mechanism, the reaction proceeds *via* three stages: oxidative addition of aryl halide to palladium(0), transmetallation, and reductive elimination of the product. The palladium(0) complexes with phosphine ligands are used most frequently as catalysts of the process.[5] The variation of the phosphine ligand structure makes it possible to "tune" the catalyst activity and to make even poorly reactive chloroarenes to react.[6]

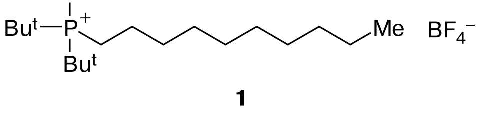
A substantial limitation for wide use of the Suzuki cross-coupling in practice is complicated recovery of the catalysts based on molecular palladium(0) complexes and high cost of phosphine ligands and palladium(0) compounds.

One of the most promising processing of the Suzuki cross-coupling is the use of nanosized palladium particles as catalysts. I. P. Beletskaya pioneered in demonstrating the possibility to carry it out in the "ligand-free" version[7—9]; however, in these works the authors did not mention the possibility of formation of palladium nanoparticles. This approach was successfully used for the synthesis of functional biaryls,[10] but the necessity to use a significant amount of palladium acetate (up to 5 mol.%) and impossibility to recover the catalyst impede the use of this method in daily practice.

The methods based on using colloidal solutions of palladium nanoparticles are very popular.[11,12] Polymers,[13,14] dendrimers,[15] and surfactants[16] act as stabilizers of palladium nanoparticles. Ionic liquids as stabilizers of palladium nanoparticles are of most interest, since they have low vapor pressure and are immiscible with the most organic solvents, which provides, on the one hand, easy catalyst recovery and, on the other hand, the entire correspondence to principles of green chemistry.

Presently, imidazolium salts (in which the carbene complex with palladium acts as a catalyst),[17,18] tetrabutylammonium salts,[19] and other nitrogen-containing salts[20,21] are most popular as stabilizers of palladium nanoparticles. These stabilizing agents are unstable under basic conditions because of the acidic proton, which restricts their application in the reactions involving strong nucleophiles.[22] Therefore, phosphonium salts that are resistant towards strong nucleophiles are interesting as potential stabilizers of palladium nanoparticles. However, only two examples for the stabilization of palladium nanoparticles by trihexyl(tetradecyl)phosphonium salts are described to date.[23,24] The influence of the phosphonium cation structure on the size and morphology of palladium nanoparticles and their catalytic activity remains unclear.

In this report, we present the data on the possibility of using the phosphonium salt with the sterically hindered cation, *viz.*, tri-*tert*-butyl(decyl)phosphonium tetrafluoroborate[25] (**1**), for the stabilization of palladium nanoparticles and applying the obtained system as a catalyst for the Suzuki cross-coupling involving bromo- and chloroarenes.



1

---

*Dedicated to the Academician of the Russian Academy of Sciences I. P. Beletskaya on the occasion of her anniversary.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 3, pp. 0656—0659, March, 2013.

Results and Discussion

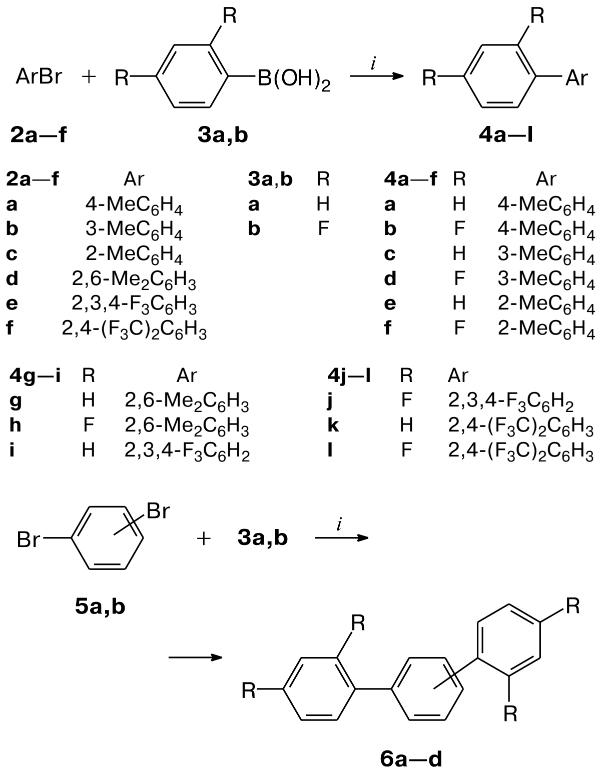
Palladium nanoparticles were obtained by the reduction of palladium acetate in the presence of phosphonium salt. There are two possible routes for the reduction of palladium(II) to palladium(0): decomposition of palladium acetate at 70—80 °C and reduction with phenylboronic acid affording biphenyl as the homocoupling product. The obtained nanoassociates were characterized by transmission electron microscopy (Fig. 1).

In this case, both individual nanoparticles with a complicated shape and small aggregates are observed. The average size of the prepared palladium nanoparticles stabilized by salt **1** is 2.5±0.5 nm, which is comparable with the sizes of the palladium nanoparticles obtained in the presence of trihexyl(tetradecyl)phosphonium salts (7±2 nm and 3.5±1 nm).[23,24]

The system based on the palladium nanoparticles stabilized by phosphonium salt **1** exhibits good activity as the catalyst for the Suzuki cross-coupling of bromoarenes **2** with phenylboronic acid **3a** (Scheme 1, Table 1). Note that the process takes place under mild conditions (30 °C) in the presence of 1 mol.% catalyst, and the yields of the isolated products are 57—92%. The activity of this catalytic system is comparable[26] with the "reference" catalyst $Pd(OAc)_2$—PBu^t_3. The formation of a small amount (2—3%) of the homocoupling product of phenylboronic acid is observed.

The high conversion of bromoarenes in the Suzuki cross-coupling in the presence of palladium nanoparticles stabilized by salt **1** is also observed when 2,4-difluorophenylboronic acid (**3b**) is used (see Scheme 1 and Table 1).

Scheme 1



2a—f	Ar
a	4-MeC_6H_4
b	3-MeC_6H_4
c	2-MeC_6H_4
d	2,6-$Me_2C_6H_3$
e	2,3,4-$F_3C_6H_3$
f	2,4-$(F_3C)_2C_6H_3$

3a,b	R
a	H
b	F

4a—f	R	Ar
a	H	4-MeC_6H_4
b	F	4-MeC_6H_4
c	H	3-MeC_6H_4
d	F	3-MeC_6H_4
e	H	2-MeC_6H_4
f	F	2-MeC_6H_4

4g—i	R	Ar
g	H	2,6-$Me_2C_6H_3$
h	F	2,6-$Me_2C_6H_3$
i	H	2,3,4-$F_3C_6H_2$

4j—l	R	Ar
j	F	2,3,4-$F_3C_6H_2$
k	H	2,4-$(F_3C)_2C_6H_3$
l	F	2,4-$(F_3C)_2C_6H_3$

1,3-disubstituted: **5a**, **6a**,**b**; 1,4-disubstituted: **5b**, **6c**,**d**.
R = H (**6a,c**), R = F (**6b,d**)

Reagents and conditions: *i*. nano-Pd, **1**, Cs_2CO_3, toluene, 30 °C, 12 h.

At the same time, the conversion of chloroarenes **7a—f**, under the same conditions, depends considerably on the

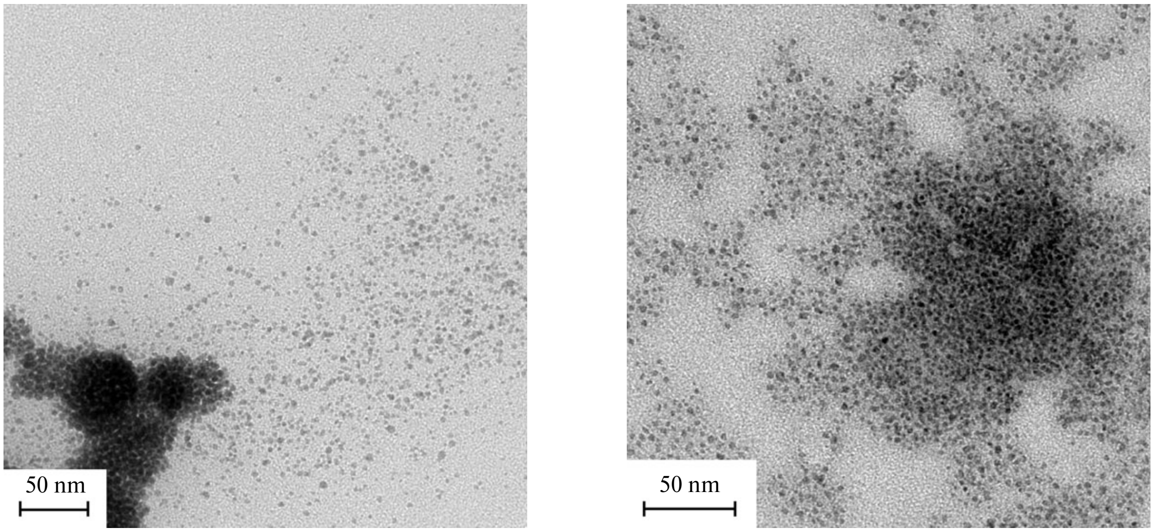


Fig. 1. TEM images of palladium nanoparticles obtained by reduction in the presence of tri-*tert*-butyl(decyl)phosphonium tetrafluoroborate (**1**).

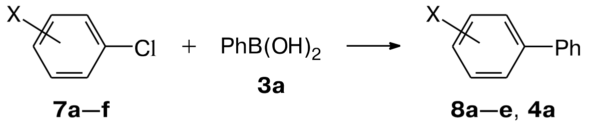
Table 1. Conversions of the starting bromoarenes **2a—f** and **5a**,**b** and the yields of products **4a—l** and **6a—d** in the Suzuki cross-coupling between bromoarenes and arylboronic acids catalyzed by the $Pd(OAc)_2$—**1** (I) and $Pd(OAc)_2$—PBu^t (II) systems

Bromoarene	Conversion of bromoarene (yield of product) (%)					
	$PhB(OH)_2$ (**3a**)			$2,4\text{-}F_2C_6H_3B(OH)_2$ (**3b**)		
	Product	I	II	Product	I	II
2a	**4a**	99 (92)	99	**4b**	99 (91)	88
2b	**4c**	99 (88)	77	**4d**	87 (82)	76
2c	**4e**	93 (85)	91	**4f**	83 (74)	62
2d	**4g**	61 (57)	93	**4h**	54 (42)	93
2e	**4i**	86 (77)	99	**4j**	83 (69)	99
2f	**4k**	93 (90)	94	**4l**	46 (39)	99
5a	**6a**	84 (77)	35	**6b**	73 (65)	72
5b	**6c**	69 (57)	94	**6d**	83 (72)	9

Note. Reaction conditions: bromoarene (2 mmoles), boronic acid (2.3 mmoles, 15% excess), Cs_2CO_3 (2.3 mmoles), toluene (5 mL), $Pd(OAc)_2$ (0.02 mmole, 1 mol.%), phosphonium salt **1** or $PdBu^t_3$ (1 mmole), 30 °C, 12 h (the yields of isolated products are given).

substituent in the substrate (Scheme 2). So, the conversion of activated chloroarenes with electron-withdrawing substituents **7a—c** ranges from 60 to 70%, while it is only 11% in the case of deactivated 4-chlorotoluene (**7f**).

Scheme 2



X	7a—f	Product	Conversion of chloroarene **7** (%)
4-MeC(O)	**7a**	**8a**	63
4-MeOC(O)	**7b**	**8b**	68
2-MeOC(O)	**7c**	**8c**	54
$4\text{-}O_2N$	**7d**	**8d**	40
4-CN	**7e**	**8e**	75
4-Me	**7f**	**4a**	11

Reagents and conditions: nano-Pd, **1**, Cs_2CO_3, toluene, 30 °C, 12 h.

Thus, the catalytic system based on palladium nanoparticles stabilized by phosphonium salt **1** is highly active in the cross-coupling of bromoarenes and activated chloroarenes, providing high conversion under mild conditions.

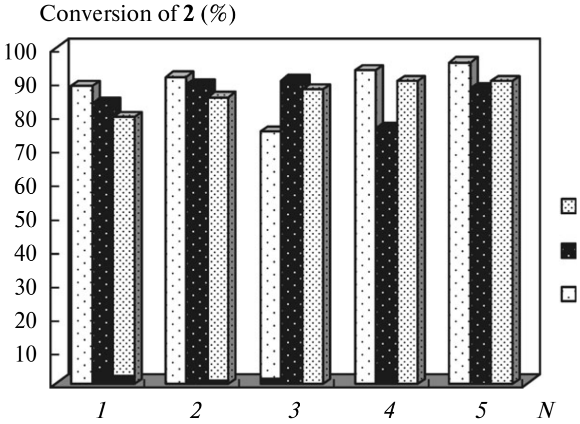


Fig. 2. Activity of the $Pd(OAc)_2$—**1** catalytic system in the cross-coupling of bromotoluenes **2a—c** and phenylboronic acid **3a**; *N* is the number of catalytic cycles.

The palladium nanoparticles stabilized by phosphonium salt **1** can readily be isolated from the reaction mixture and recycled without loss of activity. For this purpose, we developed the following procedure: after the solvent was removed, a mixture of hexane and water was added to the dry residue to form a three-layer system. The upper layer (organic phase) of this three-layer system contains the reaction products and haloarenes (if any), the medium layer contains phosphonium salt **1** and palladium nanoparticles, and the bottom layer (inorganic phase) is an aqueous solution of inorganic salts. The medium layer was separated, washed with a mixture of water and hexane (twice), and used in the subsequent catalytic cycles. The results obtained in five catalytic cycles are shown in Fig. 2.

Additional experiments were carried out to determine the dependence of the conversion of bromoarenes on the nature of the phosphonium cation. The results are presented in Table 2. The control experiment in the absence of phosphonium salts revealed that the salt is important for the stabilization of catalytic particles in the course of the reaction. In addition, the conversion of bromotoluenes in the Suzuki cross-coupling depends substantially on the cation structure of the phosphonium salt. For example, 93% conversion is observed in the coupling between 2-bromotoluene (**2c**) and phenylboronic acid (**3a**) in the presence of salt **1**, while the conversion is only 23% under the same conditions in the case of less sterically hindered phosphonium salt, *viz.*, tributyl(decyl)phosphonium tetrafluoroborate.

To conclude, it was found in this work that the cross-coupling of bromo- and chloroarenes with phenylboronic

Table 2. Conversion (%) of bromotoluenes **2a—c** in the reaction with phenylboronic acid **3a** *vs* structure of the cation of phosphonium salt

Phosphonium salt	Bromoarene		
	2a	**2b**	**2c**
$[Bu^t_3PC_{10}H_{21}]^+BF_4^-$ (**1**)	100	100	93
$[Bu_3PC_{10}H_{21}]^+BF_4^-$	85	27	23
Without phosphonium salt	34	0	0

acid can occur under mild conditions using palladium nanoparticles stabilized by the phosphonium salts containing sterically hindered cation, *viz.*, tri-*tert*-butyl(decyl)phosphonium tetrafluoroborate (**1**). The prepared catalytic system is characterized by high activity, which makes it possible to carry out the Suzuki cross-coupling involving bromoarenes and activated chloroarenes under mild conditions with high conversions.

Experimental

All procedures associated with the preparation of the starting reagents, syntheses, and isolation of products were carried out under argon using a standard Schlenk technique. The conversion of bromo- and chloroarenes was evaluated by gas chromatography coupled with mass spectrometry on a DFS instrument (Thermo-Scientific, USA), injector temperature 280 °C, MS-5 column (30 m, 0.25 mm, 0.25 μm). TEM images of the catalyst surface before and after the reaction were obtained using a PHILIPS/FEI CM20 transmission electron microscope. The particle size distribution was determined on a Veeco MultiMode V scanning probing microscope using the intermittent-contact atomic force method.

Suzuki cross-coupling reaction (general procedure). A mixture of arylboronic acid (2.3 mmol), bromo- or chloroarene (2 mmol), Cs_2CO_3 (2.3 mmol), $Pd(OAc)_2$ (0.02 mmol), tri-*tert*-butyl(decyl)phosphonium tetrafluoroborate (**1**) (0.46 mmol), and toluene (5 mL) was placed in a Schlenk flask and vigorously stirred for 12 h at 30 °C. To isolate the products, the reaction mixture was filtered through Al_2O_3, the solvent was completely removed *in vacuo*, and the obtained solid powder was recrystallized from petroleum ether.

This work was financially supported by the Ministry of Education and Science of the Russian Federation (state contract no. 8451).

References

1. N. Miyaura, K. Yamada, A. Suzuki, *Tetrahedron Lett.*, 1979, **20**, 3437.
2. A. Balanta, C. Godard, C. Claver, *Chem. Soc. Rev.*, 2011, **40**, 4973.
3. K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem.*, *Int. Ed.*, 2005, **44**, 4442.
4. F. Alonso, I. P. Beletskaya, M. Yus, *Tetrahedron*, 2008, **64**, 3047.
5. N. Miyaura, A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457.
6. R. Martin, S. L. Buchwald, *Acc. Chem. Res.*, 2008, **41**, 1461.
7. N. A. Bumagin, V. V. Bykov, I. P. Beletskaya, *Bull. Acad. Sci. USSR, Div. Chem. Sci.* (*Engl. Transl.*), 1989, **38**, 2206 [*Izv. Akad. Nauk SSSR*, *Ser. Khim.*, 1989, 2394].
8. N. E. Bumagin, V. V. Bykov, I. P. Beletskaya, *Dokl. Akad. Nauk SSSR*, 1990, **315**, 1133 [*Dokl. Chem.* (*Engl. Transl.*), 1990, **315**, No. 5].
9. N. A. Bumagin, V. V. Bykov, I. P. Beletskaya, *Bull. Acad. Sci. USSR, Div. Chem. Sci.* (*Engl. Transl.*), 1990, **39**, 2426 [*Izv. Akad. Nauk SSSR*, 1990, 2672].
10. E. M. Campi, W. R. Jackson, S. M. Marcuccio, C. G. M. Naeslund, *Chem. Commun.*, 1994, 2395.
11. V. P. Ananikov, I. P. Beletskaya, *Organometallics*, 2012, **31**, 1595.
12. D. Astruc, F. Lu, J. R. Aranzaes, *Angew. Chem.*, *Int. Ed.*, 2005, **44**, 7852.
13. C. Ornelas, A. K. Diallo, J. Ruiz, D. Astruca, *Adv. Synth. Catal.*, 2009, **351**, 2147.
14. Y. Li, X. M. Hong, D. M. Collard, M. A. El-Sayed, *Org. Lett.*, 2000, **15**, 2385.
15. Y. Tsuji, T. Fujihara, *Inorg. Chem.*, 2007, **46**, 1895.
16. J. P. Hallett, T. Welton, *Chem. Rev.*, 2011, **111**, 3508.
17. L. D. Pachon, C. J. Elsevier, G. Rothenberg, *Adv. Synth. Catal.*, 2006, **348**, 1705.
18. C. Ye, J.-C. Xiao, B. Twamley, A. D. LaLonde, M. G. Norton, J. M. Shreeve, *Eur. J. Org. Chem.*, 2007, 5095.
19. V. Calo, A. Nacci, A. Monopoli, F. Montingelli, *J. Org. Chem.*, 2005, **70**, 6040.
20. J.-H. Cha, K.-S. Kim, H. Lee Korean, *J. Chem. Eng.*, 2009, **26**, 760.
21. M. T. Reetz, M. Winter, R. Breinbauer, T. Thurn-Albrecht, W. Vogel, *Chem. Eur. J.*, 2001, **7**, 1084.
22. L. Ford, F. Atefi, R. D. Singer, P. J. Scammells, *Eur. J. Org. Chem.*, 2011, 942.
23. A. Banerjee, R. Theron, R. W. J. Scott, *ChemSusChem*, 2012, **5**, 109.
24. H. A. Kalviri, F. M. Kerton, *Green Chem.*, 2011, **13**, 681.
25. V. Ermolaev, V. Miluykov, I. Rizvanov, D. Krivolapov, E. Zvereva, S. Katsyuba, O. Sinyashin, R. Schmutzler, *Dalton Trans.*, 2010, **39**, 5564.
26. A. F. Littke, G. C. Fu, *J. Am. Chem. Soc.*, 2001, **123**, 6989.

Received January 16, 2013;
in revised form February 26, 2013