Polymetallic magnetic palladium catalysts for the Suzuki reaction in aqueous media

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A mechanochemical method for the synthesis of Pd—Fe—Co—Ni ferromagnetic composites was developed. The composites are highly efficient catalysts for the Suzuki reaction in aqueous media. They can be easily removed with an external magnet and reused without losing catalytic activity.

**Key words:** palladium, Pd—Fe—Co—Ni composites, Suzuki reaction, aqueous media.

Catalytic cross-coupling of organic halides with organoelement compounds, olefins, and terminal acetylenes is widely used in fine organic synthesis as the most versatile route to functionalized biaryls, arylated olefins, acetylenes, and their heterocyclic analogs.[1—3] Numerous ongoing studies in this field are aimed to design novel efficient homogeneous and heterogeneous catalysts.[4—8] Among the variety of currently known heterogeneous catalysts, of particular interest are bimetallic (Pd/M) and polymetallic catalysts characterized by the synergy between the electron density transfer from the more electropositive metal (M = Fe, Co, Ni) to Pd, which allows one to design active catalysts with low content of the expensive palladium.[9] Problems and advances in heterogeneous catalysis by bi- and polymetallic nanoparticles composed of transition metal atoms have been comprehensively analyzed recently.[10,11]

This work was carried out in a continuation of our studies[12—24] on the synthesis of novel highly efficient heterogeneous catalysts for the Suzuki reaction in aqueous media.[25] The key point of our strategy was to prepare Pd-doped polymetallic nanocomposites composed of a mono- or polymetallic core based on active metals (Al, Zn, Fe, Ni, Co) and a protective shell made of inert metals (Cu, Ag, Ru, Au, Pd). Such a shell improves the stability of the activating metals in the high-temperature catalysis in aqueous media.

The iron group metals chosen to design polymetallic composites have a rather high activation ability in the M—Pd pair and exhibit the properties of ferromagnetics. The active metal core was composed of iron, cobalt, and nickel taken in the same atomic ratio (2.38 : 2.24 : 1) as in the well-known Alnico alloys used in production of permanent magnets. A thorough choice of the chemical composition of the polymetallic composites, stabilizing ligands, solvents, and other reactants revealed that reduction of a mixture of iron, cobalt, nickel, and palladium

salts with sodium borohydride in water or methanol results in Pd—Fe—Co—Ni composites possessing no magnetic properties. Solvent-free mechanochemical activation[26] of powder mixtures under affords ferromagnetic composites. In this work, we used additional modifiers, *viz.*, chitosan (Ch) hydrochloride and sodium carboxymethyl cellulose (Na—CMC), to mechanochemically synthesize the following composites: Pd—Fe—Co—Ni (**1**), Pd—Fe—Co—Ni—Ch (**2**) and Pd—Fe—Co—Ni—(Na—CMC) (**3**), Pd—Fe—Co—Ni@Pd (**4**), Pd—Fe—Co—Ni—Ch@Pd (**5**), and Pd—Fe—Co—Ni—(Na—CMC)@Pd (**6**). The forma-

Scheme 1

Pd—Fe—Co—Ni-composite

Pd—Fe—Co—Ni@Pd-composite
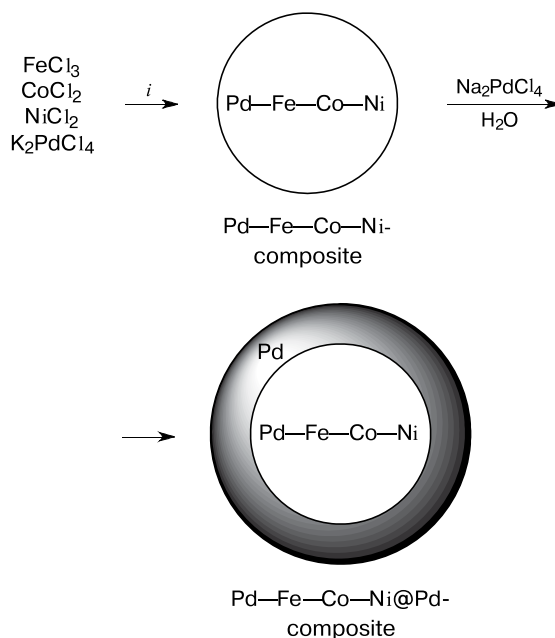
Reactants and conditions. *i*. NaBH$_4$, mechanochemical activation.

tion of polymetallic magnetic composites coated with palladium protective shell is outlined in Scheme 1 taking the synthesis of **4** as an example. According to atomic absorption analysis (AAA) data, the composites **1—3** and **4—6** contain ~0.5 and ~2 mmol of Pd per gram of the composite, respectively.

According to scanning electron microscopy (SEM) and EDX spectroscopy data, composites **1—6** are charac-
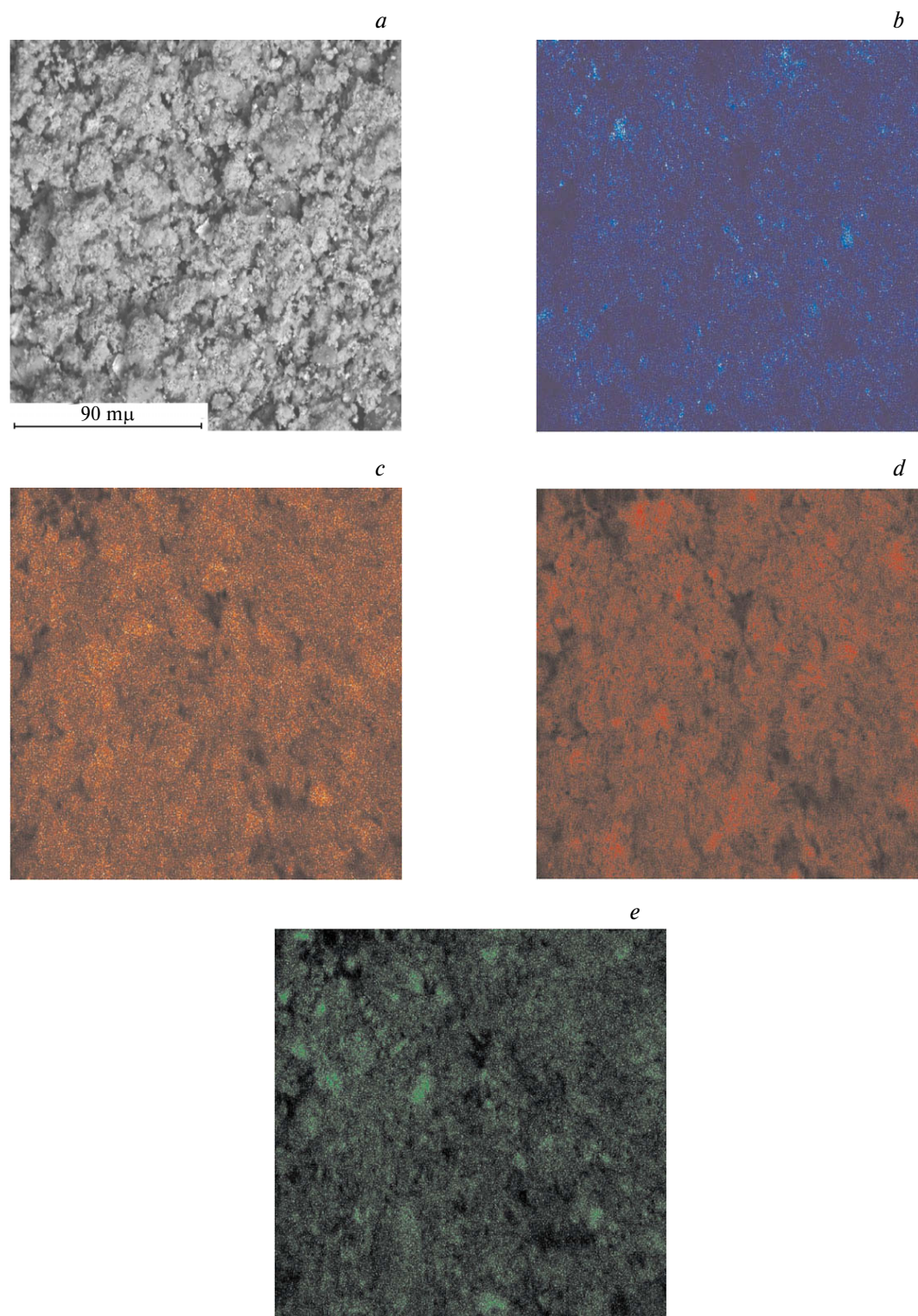
a

b

90 mμ

c

d

e

Fig. 1. SEM images (length scale 90 μm) of Pd—Fe—Co—Ni composite (*a*) and the element distribution maps for palladium (*b*), iron (*c*), cobalt (*d*), and nickel (*e*).

terized by a uniform distribution of palladium, iron, cobalt, nickel, and the modifier (if any). Figure 1 presents the SEM images of the composite **4** and the element distribution maps. As can be seen, palladium is uniformly distributed over the entire catalyst surface.

The catalytic activity and the possibility to reactivate the magnetic polymetallic composites **1—6** (1 mol.% Pd) was studied on a model reaction between 4-methoxyphenylboronic acid and 3-bromobenzoic acid carried out in aqueous methanol (1 : 1) and in water (Scheme 2). For comparison, we also tested monometallic Pd black (**7**) prepared by mechanochemical reduction of Na_2PdCl_4 with sodium borohydride as described above. The model reactions were carried out in air at the boiling points of the solvents in the presence of K_2CO_3 as the base for 10 min (this parameter was not optimized). Catalysts **1—6** were separated from the reaction mixtures using an external magnet, while Pd black (**7**) was separated by centrifugation followed by rinsing with water and ethanol. The results obtained are presented in Table 1. It follows that

the activity of the catalysts in water and in aqueous methanol is very high and remains almost unchanged after five recycles. The preparative-scale yield of the reaction product (^{1}H NMR analytical yield was quantitative) in the presence of catalyst **4** was 98% (Table 1, cycles *2* and *3*). A comparable catalytic activity was reported for magnetic catalysts based on maghemite nanoparticles (γ-Fe_2O_3—Pd, 2 mol.% Pd, DMF—H_2O, 110 °C, 90—120 min, product yield 60—95%) and amino acid modified magnetite nanoparticles (Fe_3O_4@L-Tyrosine—Pd, 0.35 mol.% Pd, H_2O, 100 °C, 20—120 min, 75—99%; Fe_3O_4@L-Lysine—Pd, 0.08 mol.% Pd, H_2O, 100 °C, 30—110 min, 87—97%).[27—29]

High catalytic activity of the Pd—Fe—Co—Ni composites prepared in this work seems to be due to the very small size of the polymetallic particles, which allows a large proportion of palladium, as a constituent of the composite, to participate in the catalytic process. One can assume that the solution contains a "cocktail" of palladium compounds that catalyze the process under study.[30] An atomic absorption spectroscopy analysis of the reaction mixtures after completion of the process revealed no palladium in the solution at the sensitivity level of the method (~1 ppm). It follows that only a small proportion of the supported palladium participates in catalysis through reversible transition in solution and therefore the catalyst remains stable and active after a number of recycles. It should be noted that the monometallic catalyst **7** (Pd black) also exhibits high catalytic activity; however, the required amount of palladium is tenfold larger (10 mol.% Pd).

The potential of the new polymetallic catalysts was demonstrated taking the synthesis of 2-amino-4′-chloro-

Scheme 2
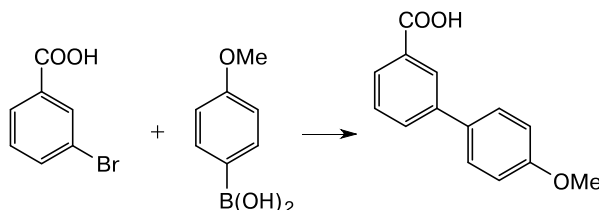
Reactants and conditions. *i*. Pd (1 mol.%), K_2CO_3, 70—100 °C, 10 min.

Table 1. Catalytic activity of polymetallic composites in the reaction of 3-bromobenzoic acid with 4-methoxyphenylboronic acid[a]

| Catalyst	Product yield[b] at different number of recycles in MeOH—H_2O/H_2O (%)				
	1	*2*	*3*	*4*	*5*
Pd—Fe—Co—Ni (**1**)	93/96	92/94	95/95	93/96	91/93
Pd—Fe—Co—Ni—Ch (**2**)	95/97	93/95	94/95	96/94	93/96
Pd—Fe—Co—Ni—(Na-CMC) (**3**)	96/95	94/96	93/97	92/94	93/95
Pd—Fe—Co—Ni@Pd (**4**)	94/97	95/100[c]	100[c]/98	96/96	96/97
Pd—Fe—Co—Ni—Ch@Pd (**5**)	97/98	96/97	94/96	96/98	95/98
Pd—Fe—Co—Ni—(Na-CMC)@Pd (**6**)	95/97	94/98	96/96	97/96	94/95
Pd-black (**7**)	91/96	94/95	96/95	94/97	93/94

[a] Reaction conditions: Ar—Br (1 mmol), $ArB(OH)_2$ (1.2 mmol), K_2CO_3 (2.5 mmol), catalyst amount: 20 (**1—3**), 5 (**4—6**), or 10 mg (**7**), solvent (5 mL), 10-min reflux; temperature: 70 °C (MeOH—H_2O) and 100 °C (H_2O).
[b] Product yields according to ^{1}H NMR data obtained using 1,1,2,2-tetrachloroethane (1 mmol) as internal reference.
[c] Preparative-scale yields were 98%.

biphenyl (Scheme 3), a key intermediate of the synthesis of a modern fungicide Boscalid® [2-chloro-*N*-(4′-chloro-diphenyl-2-yl)nicotinamide],[31] as an example.

Scheme 3
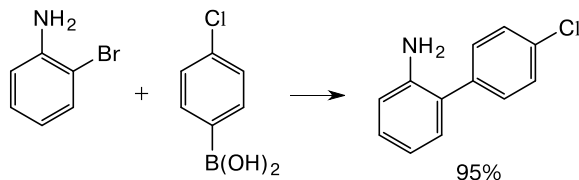
Reactants and conditions. *i.* **4** (1 mol.%), Bu₄NBr (1 mol.%), K₂CO₃, H₂O, 100 °C, 15 min.

Summing up, magnetic polymetallic composites Pd—Fe—Co—Ni prepared by the mechanochemical method demonstrate very high catalytic activity and can be used many times since no visible loss of activity was observed after five recycles. They allow one to carry out catalysis not only in aqueous organic media, but also under solvent-free conditions in non-inert atmosphere. The isolation and purification of the reaction products developed in this work makes it possible to reduce the amount of organic solvents used, which is of importance from the standpoint of environmental safety and protection. The results of our experiments on catalysis in aqueous media can be used in the design of "green" technologies of fine organic synthesis.

Experimental

Commercially available reactants and solvents (Aldrich, Acros Organics, and Merck) were used as purchased. Chitosan hydrochloride (poly(1,4-*b*-D-glucopyranosamine) hydrochloride), $(C_6H_{11}NO_4 \cdot HCl)_n$, OOO Bioprogress, Russia) was used as modifier.

The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance II 400 spectrometer (Bruker BioSpin GmbH, Germany) operating at 400 and 100 MHz, respectively, in DMSO-d_6 or CDCl₃. The chemical shifts were determined relative to the residual signals of DMSO-d_6 (δ 2.50 for ^1H and δ 40.1 for ^{13}C) or CDCl₃ (δ 7.26 for ^1H and δ 77.2 for ^{13}C). Mass spectra were recorded on an Agilent 6890N instrument (Agilent Technologies, USA) equipped with an Agilent HP-5ms capillary column (30 m×0.25 mm×0.25 μm) and an Agilent 5975C inert MSD detector (electron impact ionization, electron energy 70 eV, injector temperature +250 °C). The elemental analyses were performed with an Elementar vario MICRO cube C,H,N,S instrument (Germany). The content of palladium in the polymetallic composites and in the products of cross-coupling reactions was determined by atomic absorption analysis on an Akvilon MGA-915 spectrometer (Lumex, Russia). The microstructure of the composites was studied by scanning electron microscopy

(SEM) on a Zeiss LEO EVO 50 XVP electron microscope equipped with an Oxford Instruments EDX INCA Energy 350 analyzer (Leo/Zeiss, Germany). The course of reactions was monitored by thin-layer chromatography (TLC) on Merck Silica gel 60 F₂₅₄ plates. Melting points were determined using a Kofler plate.

Synthesis of Pd—Fe—Co—Ni composites (general procedure). A mixture of crystal hydrates FeCl₂·4H₂O (2 mmol), CoCl₂·6H₂O (1.84 mmol), NiCl₂·6H₂O (0.82 mmol), and K₂PdCl₄ (0.126 mmol) was thoroughly ground in an agate mortar for 5 min. Then, NaBH₄ (15 mmol) was added, and the mixture was ground for an additional 5 min until the formation of homogeneous black powder that was transferred to a flask filled with argon. Water (5 mL) was added to the composite thus prepared to decompose excess NaBH₄, and then the composite was washed with the following argon-presaturated solvents: water (5×3 mL), acetone (3×5 mL), and diethyl ether (3×3 mL). The composite was separated using an external magnet and dried in a desiccator over CaCl₂ in argon atmosphere at room temperature for 10 h. The yield of the composite **1** was 0.275 g (98%).

The modified composites Pd—Fe—Co—Ni—Ch (**2**) and Pd—Fe—Co—Ni—(Na—CMC) (**3**) were prepared analogously using chitosan hydrochloride (0.099 g, ~0.5 mmol) or sodium carboxymethyl cellulose Na—CMC (0.120 g, ~0.5 mmol) as additives in the salt grinding stage; the yields were almost quantitative, *viz.*, 0.353 g (~97%) and 0.392 g (~98%), respectively. Then, water (5 mL) and 0.1 *M* aqueous Na₂PdCl₄ (0.2 mmol) was added to 0.1 g of each composite **1—3**. The mixtures thus prepared were sonicated on a Skymen ultrasonic bath (P.R.China) for 1 min until disappearance of the red-brown color of Na₂PdCl₄, the composites were removed from the mother liquor using an external magnet and successively washed with water (4×2 mL), acetone (3×2 mL), and diethyl ether (2×2 mL) and then dried. The yields of the palladium-containing composites were as follows: 0.098 g (~90%) for Pd—Fe—Co—Ni@Pd (**4**), 0.099 g (~91%) for Pd—Fe—Co—Ni—Ch@Pd (**5**), and 0.102 g (~94%) for Pd—Fe—Co—Ni—(Na—CMC)@Pd (**6**). According to AAA data, the composites **1—3** and **4—6** contain ~0.5 and ~2 mmol of Pd per gram of the composite, respectively.

A sample of Pd black (**7**) was prepared by analogy from K₂PdCl₄ (1 mmol) and NaBH₄ (3 mmol). The yield was 0.102 g (~96%).

Suzuki reaction catalyzed by Pd—Fe—Co—Ni polymetallic composites (general procedure). To a mixture of arylboronic acid (1.20 mmol), aryl bromide (1.00 mmol), and K₂CO₃ (0.35 g, 2.50 mmol) in H₂O (or in 50% aqueous methanol, 5 mL in both cases), the catalyst 1 mol.% Pd (20 mg for samples **1—3** and 5 mg for samples **4—6**) or 10 mol.% Pd (10 mg of Pd black **7**) was added. Then, the mixture was transferred to a reactor equipped with a reflux condenser and heated on a silicone bath preheated to 120 °C (for the reactions in aqueous methanol) or 160 °C (for the reactions in water) under vigorous stirring for 10 min at the boiling point of the solvent (this parameter was not optimized). The course of the reactions was monitored by TLC (with hexane—Et₂O (3 : 1) mixture as eluent) using calibration solutions of the corresponding biaryl and aryl bromide taken in a molar ratio of 1 : 1 and 9 : 1, respectively. The product yields were determined by ^1H NMR using tetrachloroethane (1 mmol)

as internal reference. As the process completed, the reaction mixture was diluted with water (5 mL), the catalyst was removed using an external magnet, washed with water (3×2 mL) and ethanol (3×1 mL) and then reused. The reaction mass was heated and the slightly turbid hot mixture was filtered through two layers of filter paper on a Büchner funnel to separate a small amount of anisole formed as a result of partial protodeboronation of 4-methoxyphenylboronic acid. Then, ethanol (10—15% v/v) was added to the filtrate and the mixture was heated to ~50 °C and slowly acidified with 5% HCl to pH 2—3 under stirring. The precipitate was filtered off to obtain analytically pure samples of the cross-coupling products.

4′-Methoxy-[1,1′-biphenyl]-3-carboxylic acid. White crystalline powder (0.223 g, 98%), m.p. 203.4—204 °C (*cf.* 202—203 °C according to Ref. 32). Found (%): C, 73.69; H, 5.35. $C_{14}H_{12}O_3$. Calculated (%): C, 73.67; H, 5.30. ^1H NMR (400 MHz, DMSO-d_6, δ): 3.83 (s, 3 H, CH_3O); 7.05 (dd, 2 H, H(3′), H(5′), $J = 6.8$ Hz, $J = 2.1$ Hz); 7.56 (t, 1 H, H_{Ar}, $J = 7.7$ Hz); 7.66 (dd, 2 H, H(2′), H(6′), $J = 6.8$ Hz, $J = 2.1$ Hz); 7.83—7.94 (m, 2 H, H_{Ar}); 8.11 (dd, 1 H, H(4), $J = 7.8$ Hz, $J = 2.0$ Hz); 13.12 (br.s, 1 H, COOH). ^{13}C NMR (100 MHz, DMSO-d_6, δ): 54.3 (CH_3O), 114.0, 127.2, 127.4, 127.6, 128.5, 130.6, 131.0, 132.4, 141.0, 159.7, 168.5 (COOH).

2-Amino-4′-chlorobiphenyl. Following the general procedure, the reaction of 2-bromoaniline (1.72 g, 10 mmol) with 4-chlorophenylboronic acid (1.72 g, 11 mmol) in the presence of K_2CO_3 (3.45 g, 25 mmol) and Bu_4NBr (0.0322 g, 0.1 mmol, 1 mol.%) acting as the phase transfer carrier was carried out in H_2O (100 mL) in the presence of the Pd—Fe—Co—Ni@Pd composite (50 mg , 1 mol.% Pd). The reaction mixture was refluxed with stirring for 15 min; according to TLC data, this time was long enough for the reaction to complete. Then, the mixture was diluted with water (100 mL), heated to 100 °C and kept at this temperature for an additional 30 min, cooled to room temperature and filtered to separate the cross-coupling products and the catalyst. Hexane (50 mL) was added to the residue, the mixture was heated until complete dissolution of the reaction product and the catalyst (48 mg) was separated using an external magnet. The solution thus obtained was cooled at 2—3 °C for 3 h, the crystals that precipitated were filtered off and dried at room temperature in air for 12 h. White crystalline powder (1.94 g, 95%) was obtained, m.p. 48—49 °C (*cf.* 47—48 °C according to Ref. 33). Found (%): C, 70.69; H, 5.01; N, 6.84. $C_{12}H_{10}NCl$. Calculated (%): C, 70.77; H, 4.95; N, 6.88; Cl, 17.41. ^1H NMR (400 MHz, CDCl$_3$, δ): 3.63 (br.s, 2 H, NH_2); 6.78 (dd, 1 H, $J = 7.9$ Hz, $J = 1.0$ Hz); 6.85 (td, 1 H, $J = 7.6$ Hz, $J = 1.0$ Hz); 7.11 (dd, 1 H, $J = 7.6$ Hz, $J = 1.5$ Hz); 7.19 (td, 1 H, $J = 7.9$ Hz, $J = 1.0$ Hz); 7.38—7.46 (m, 4 H). ^{13}C NMR (100 MHz, CDCl$_3$, δ): 115.7, 118.7, 126.2, 128.8, 128.9, 130.3, 130.4, 133.0, 137.8, 143.4. Mass spectrum, *m/z* (*I* (%)): 205 [$^{37}Cl − M$]$^+$ (27), 204 (12), 203 [$^{35}Cl − M$]$^+$ (100), 202 (13), 169 (17), 168 (55), 167 (34), 166 (16), 83 (26).

References

1. A. Suzuki, *J. Organomet. Chem.*, 1999, **576**, 147.
2. *Metal-Catalyzed Cross-Coupling Reactions: monography*, Eds F. Diederich, P. J. Stang, Wiley—VCH, New York, 1998, 203 pp.
3. I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.*, 2000, **100**, 3009.
4. M. S. Denisov, M. V. Dmitriev, A. A. Gorbunov, V. A. Glushkov, *Russ. Chem. Bull.*, 2019, **68**, 2039.
5. S. B. Soliev, A. V. Astakhov, D. V. Pasyukov, V. M. Chernyshev, *Russ. Chem. Bull.*, 2020, **69**, 683.
6. A. V. Astakhov, S. B. Soliev, V. M. Chernyshev, *Russ. Chem. Bull.*, 2020, **69**, 2073.
7. L. Yin, J. Liebscher, *Chem. Rev.*, 2007, **107**, 133.
8. A. B. Shishmakov, Yu. V. Mikushina, L. A. Petrov, *Russ. Chem. Bull.*, 2019, **68**, 1451.
9. N. A. Bumagin, S. K. Petkevich, A. V. Kletskov, R. S. Alekseev, V. I. Potkin, *Chem. Heterocycl. Compd.* (*Engl. Transl.*), 2019, **55,** 508 [*Khimiya geterotsikl. soedineniy*, 2019, **55,** 508].
10. R. K. Rai, D. Tyagi, K. Guptaa, S. K. Singh, *Catal. Sci. Technol.*, 2016, **6**, 3341.
11. S. M. H. Chopani, S. Asadi, M. M. Heravi, *Curr. Org. Chem.*, 2020, **24**, 2216.
12. A. V. Kletskov, N. A. Bumagin, S. K. Petkevich, E. A. Dikusar, A. S. Lyakhov, L. S. Ivashkevich, I. A. Kolesnik, V. I. Potkin, *Inorg. Chem.*, 2020, **59**, 10384.
13. A. V. Kletskov, N. A. Bumagin, F. I. Zubkov, D. G. Grudinin, V. I. Potkin, *Synthesis*, 2020, **52,** 159.
14. N. A. Bumagin, V. I. Potkin, *Russ. Chem. Bull.*, 2016, **65**, 321.
15. N. A. Bumagin, *Catal. Commun.*, 2016, **79**, 17.
16. V. I. Potkin, N. A. Bumagin, S. K. Petkevich, A. S. Lyakhov, D. A. Rudakov, M. V. Livantsov, N. E. Golantsov, *Synthesis*, 2012, **44**, 151.
17. V. I. Sokolov, E. G. Rakov, N. A. Bumagin, M. G. Vinogradov, *Fullerenes, Nanotubes and Carbon Nanostructures*, 2010, **18**, 558.
18. N. A. Bumagin, D. A. Tsarev, *Tetrahedron Lett.*, 1998, **39**, 8155.
19. V. V. Bykov, N. A. Bumagin, *Russ. Chem. Bull.*, 1997, **46**, 1344.
20. N. A. Bumagin, V. V. Bykov, I. P. Beletskaya, *Bull. Acad. Sci. USSR, Div. Chem. Sci.* (*Engl. Transl.*), 1990, **39**, 2426.
21. N. A. Bumagin, Y. V. Gulevich, I. P Beletskaya, *J. Organomet. Chem.*, 1985, **285**, 415.
22. N. A. Bumagin, Y. V. Gulevich, I. P Beletskaya, *J. Organomet. Chem.*, 1985, **282**, 421.
23. N. A. Bumagin, I. O. Kalinovsky, A. B. Ponomarev, I. P. Beletskaya, *Dokl. Akad. Nauk SSSR* [*Dokl. Chem.*], 1982, **265**, 1138 (in Russian).
24. A. N. Kashin, I. G. Bumagina, N. A. Bumagin, V. N. Bakunin, I. P. Beletskaya, *Zh. Organ. Khimii* [*J. Org. Chem. USSR*], 1981, **17**, 905 (in Russian).
25. V. Polshettiwar, R. Luque, A. Fihri, M. Zhu, M. Bouhrara, J. M. Basset, *Chem. Rev.*, 2011, **111**, 3036.
26. A. S. Rogachev, *Russ. Chem. Rev.*, 2019, **88**, 875.

27. A. K. Rathi, M. B. Gawande, J. Pechousek, J. Tucek, C. Aparicio, M. Petr, O. Tomanec, R. Krikavova, Z. Travnicek, R. S. Varmac, R. Zboril, *Green Chem.*, 2016, **18**, 2363.
28. H. Xie, H. Liu, M. Wang, H. Pan, C. Gao, *Appl. Organometal. Chem.*, 2020. **34**, e5256.
29. M. A. Ashraf, Z. Liu, D. Zhang, A. Alimoradi, *Appl. Organometal. Chem.*, 2020. **34**, e5668.
30. D. B. Eremin, V. P. Ananikov, *Coord. Chem. Rev.*, 2017, **346**, 2.
31. C. Torborg, M. Beller, *Adv. Synth. Catal.*, 2009, **351**, 3027.
32. W. G. Dauben, M. Tanabe, *J. Am. Chem. Soc.*, 1953, **75**, 4969.
33. E. H. Huntress, M. K. Seikel, *J. Am. Chem. Soc.*, 1939, **61**, 816.