Cite this: *INEOS OPEN*, **2023**, *6 (5)*, 126–137
DOI: 10.32931/io2321r

Received 6 April 2024,
Accepted 24 May 2024

http://ineosopen.org

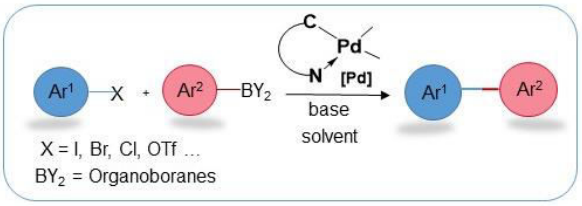
CATALYTIC ACTIVITY OF *C,N*-PALLADACYCLES IN THE SUZUKI–MIYAURA REACTION

M. P. Timerkaeva[a,b] and O. N. Gorunova*[a]

[a] *Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, ul. Vavilova 28, str. 1, Moscow, 119334 Russia*
[b] *Department of Chemistry and Technology of Biomedical Drugs, Mendeleev University of Chemical Technology of Russia, Miusskaya pl. 9, Moscow, 125047 Russia*

Abstract

Owing to the high thermal, oxidative and hydrolytic stability, as well as the ease of structural modification, cyclopalladated complexes (CPCs) have enormous potential in a wide range of chemical reactions and processes. This review highlights the examples of the successful application of azapalladacycles based on various *N*-donor ligands as the (pre)catalysts for the Suzuki–Miyaura cross-coupling.



Key words: *C,N*-palladacycles, catalysis, cross-coupling, Suzuki–Miyaura reaction.

1. Introduction

Cross-coupling reactions are one of the most popular methods for constructing C–C bonds and play a huge role in organic synthesis. They are actively used to obtain the analogs of natural compounds, drugs, and agrochemicals [1–5]. It is no coincidence that the 2010 Nobel Prize in Chemistry was jointly awarded to Richard F. Heck, Ei-ichi Negishi, and Akira Suzuki for palladium-catalyzed cross-couplings in organic synthesis [6]. The most popular reaction owing to the synthetic availability and stability of the substrates, namely, arylboronic acids, tolerance towards a large number of functional groups, low toxicity of the reagents and by-products (in contrast to the Stille reaction), predominantly low temperatures (unlike the Heck reaction), a wide scope of substrates, and a minimal amount of the resulting by-products is the Suzuki–Miyaura cross-coupling (SM). For example, the *bis*-heterocyclic and biphenyl moieties in the popular antihypertensive drugs telmisartan [7] and valsartan [8] were introduced into the molecules using the Suzuki–Miyaura reaction. The same reaction was used to synthesize abemaciclib [9], a drug for the treatment of breast cancer, and atanazavir, a drug for the treatment of infection caused by the human immunodeficiency virus (HIV) [10].

CPCs are a class of organometallic compounds that contain at least one covalent Pd–C bond stabilized by an additional coordination bond with a heterodonor (N, S, O, P). Due to their thermal and oxidative stability, as well as ample opportunities for structural modification, these compounds have enormous potential in a wide variety of chemical reactions and processes.

CPCs act as the key intermediates in heterodonor-directed C–H functionalization of organic substrates, display luminescent and liquid crystalline properties [11], exhibit a broad scope of biological activity, including antiparasitic [12], antibacterial and antioxidant [13], antifungal and antimicrobial [14, 15], and antimalarial [16] properties, as well as high antitumor activity [17–20]. Optically active CPCs are used as the matrices for the resolution of racemic substrates capable of coordinating with the palladium atom [11], as well as the catalysts in enantioselective catalysis [21].

Traditionally, commercially available reagents such as $Pd(OAc)_2$ and $Pd(PPh_3)_4$ are used as the catalysts in cross-couplings, which are quite effective catalysts in the presence of *P*- and *N*-donor ligands. However, the unique catalytic activity of phosphapalladacycles in cross-couplings, discovered in 1995 by Herman, opened a new page in achiral homogeneous catalysis [22–24]. Since then, the catalytic activity of dozens of new types of palladacycles has been studied, but interest in this field is only growing [24, 25]. The success and efficiency of cross-coupling reactions largely depend on the catalytic system in use, so even small changes in the catalyst structure can lead to increased activity and selectivity, and, as a result, to economic benefits.

Recently, there has been increased interest in the use of palladacycles based on *N*-donor ligands as the catalysts for cross-couplings. This is stipulated by the much higher stability of the nitrogen-containing ligands compared to the *P*-donor counterparts, as well as their lower cost and toxicity [26].

The goal of this review was to analyze the modern data on the catalytic activity of *C,N*-palladacycles in the Suzuki–Miyaura cross-coupling, focusing on the publications from 2017 to 2023. The earlier reports on the use of azapalladacycles as cross-coupling (pre)catalysts, including enantioselective modifications, were summarized in other reviews [21, 24, 27–31].

2. *C,N*-Palladacylces based on amines

Nowadays, amine-based palladacycles comprise a broad group of CPCs, consisting mainly of the complexes with an sp^2-metalated carbon atom [30]. Aminate CPCs, owing to their high catalytic activity, are currently extensively used in various C–C bond forming reactions, including the Heck, Suzuki-Miyaura and Sonogashira cross-couplings [24, 25]. It should be noted that the catalytic activity of mononuclear derivatives has been

mainly explored, while the dimers themselves are practically not used as the (pre)catalysts.

Karami *et al.* [26] demonstrated the effectiveness of a series of *C,N*-palladacycles **1**–**4** (Fig. 1) based on secondary amines in the SM reaction between aryl bromides and $PhB(OH)_2$.

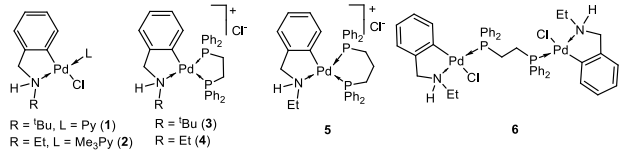
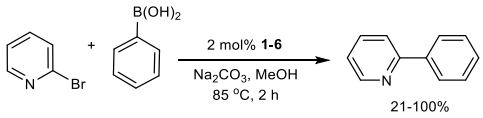


Figure 1. Derivatives of benzylaminate *C,N*-palladacycles.

In the cross-coupling of bromobenzene with $PhB(OH)_2$, the mononuclear derivatives with both monodentate pyridine ligands (**1**, **2**) and bidentately bound diphosphines (**3**–**5**) showed high catalytic activity: the product yields were 100% and 86–92%, respectively [26]. However, in the case of coordinating substrates, such as 2-bromopyridine, a stronger contrast was observed (Scheme 1). When the reaction was catalyzed by mononuclear complexes **1**, **2**, the coupling product was formed in a quantitative yield, while in the case of cationic complexes **3**–**5** featuring bidentately bound diphosphines 1,2-bis(diphenylphosphino)ethane (*dppe*) and 1,3-bis(diphenylphosphino)propane (*dppp*), the yield of the target product appeared to be significantly lower (21–30%).



Scheme 1. Suzuki–Miyaura cross-coupling between 2-bromopyridine and $PhB(OH)_2$.

A comparison of the catalytic performance of phosphine derivatives **3** and **5** revealed that complex **3** exhibits slightly higher activity than its less sterically hindered analog. Thus, the yields of the coupling product in the reaction of bromobenzene with $PhB(OH)_2$ catalyzed by these complexes were 93% and 86%, respectively. The authors noted that CPC **6** bearing the bridging diphosphine ligand exhibits considerably higher catalytic activity than its counterpart **5** containing the same but bidentately coordinated ligand: when 2-bromopyridine reacted with $PhB(OH)_2$, the product yield was 75 % and 30% in the case of azapalladacycles **6** and **5**, respectively [26]. However, this comparison is not exactly correct, since the molecule of complex **6** contains two palladium atoms, and the authors did not take this into account when calculating the catalyst loadings.

Poly(ethylene glycol) (PEG), an unconventional solvent for the SM cross-coupling, was used to study the catalytic activity of CPC **7** (Fig. 2) based on primary benzylamine with a bidentate coordinated *P,O*-ligand *dppmo* (*dppmo* = $Ph_2P(CH_2)P(O)Ph_2$) [32].

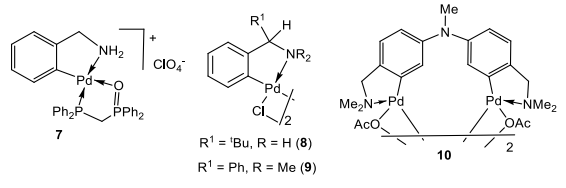
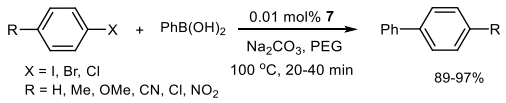


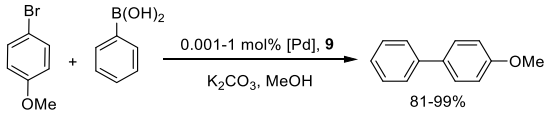
Figure 2. Derivatives of benzylaminate *C,N*-palladacycles.

A number of aryl iodides and aryl bromides reacted effectively with $PhB(OH)_2$ at the catalyst loading of 0.01 mol % over a short period of time (20–40 min), although the reactions were performed at elevated temperatures. In all cases, the products were obtained in high yields (89–97%). Furthermore, complex **7** turned out to be effective even in the cross-coupling of aryl chlorides. The yields of the coupling products in this case ranged within 89–92% (Scheme 2).



Scheme 2. Suzuki–Miyaura reaction catalyzed by complex **7**.

Recently, our research group demonstrated the high catalytic activity of benzylaminate dimeric *C,N*-palladacycles in the Suzuki–Miyaura reaction between aryl bromides and $PhB(OH)_2$ under mild conditions [33]. It should be noted that this is one of the rare examples of the application of dimers as (pre)catalysts for this process. The highest catalytic activity at 0.1 mol % [Pd] was observed in the case of dimer **8**, bearing a *tert*-butyl substituent at the α-carbon atom and a primary amino group, and complex **9**, containing a phenyl moiety and a tertiary amino group (Fig. 2, Scheme 3). As the concentration of (pre)catalyst **9** was reduced to to 0.01 mol % [Pd], the efficiency of the process was maintained by increasing the reaction temperature (up to 65 °C). In this case, the coupling product was formed in 94% yield in 2 h. Moreover, dimer **9** catalyzed the reaction even at the lower loadings (up to 0.001 mol %), but the formation of 4-methoxybiphenyl in a high yield (81%) requires a longer time and heating (15 h at 65 °C).



Scheme 3. Suzuki–Miyaura reaction catalyzed by complex **9**.

CPCs containing four palladium centers are rarely used in catalysis. However, the advantage of multinuclear complexes is the presence of multiple catalytically active metal centers in a relatively small organic ligand. Thus, tetranuclear cyclopalladated (pre)catalyst **10** (Fig. 2) at a loading of only 0.0002 mol % showed high efficiency in the reaction between 4-bromoacetophenone and $PhB(OH)_2$, affording the target product in 97% yield. The authors suggested that during the reaction, these tetranuclear palladium(II) complexes disintegrate into two halves, and the resulting binuclear fragments are capable of generating catalytically active forms of palladium at both ends of the resulting molecules [34].

Recently, the collection of aromatic bidentate *P*-donor ligands used in the Suzuki–Miyaura cross-coupling was expanded by two new sterically hindered phosphines, namely, HandaPhos [35] and EvanPhos [36]. The use of these ligands ensures a significant reduction of the concentration of a palladium catalyst, as well as the reactions under conditions of aqueous micellar catalysis. An environmentally benign surfactant (TPGS-750-M), a diester consisting of racemic α-tocopherol, MPEG-750, and succinic acid, was used to form nanomicelles.

The mononuclear palladacyclic derivatives based on 2-phenylaniline (the so-called Buchwald catalyst) containing the bulky phosphine ligand HandaPhos (Fig. 3) were tested in the SM cross-coupling of various aryl bromides [37].

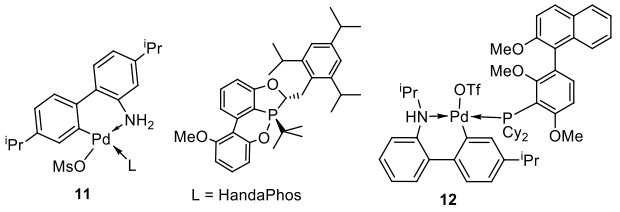
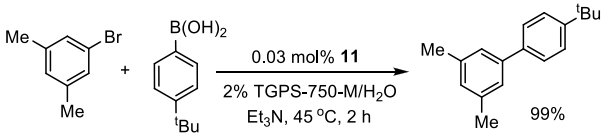


Figure 3. Phosphine derivatives of the *C,N*-palladacycle based on 2-phenylaniline.

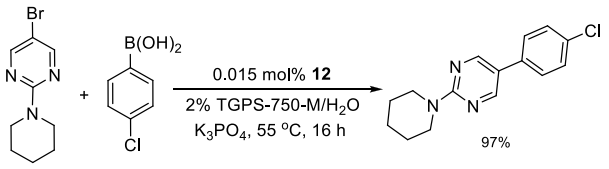
Diisopropyl-substituted phosphine complex **11** appeared to be the most effective catalyst. In the SM reaction of bulky 5-bromo-*meta*-xylene and 4-*tert*-butylphenylboronic acid under mild conditions, with the low catalyst loading, an excellent product yield of 99% was achieved (Scheme 4).



Scheme 4. SM reaction between 5-bromo-*meta*-xylene and 4-*tert*-butylphenylboronic acid.

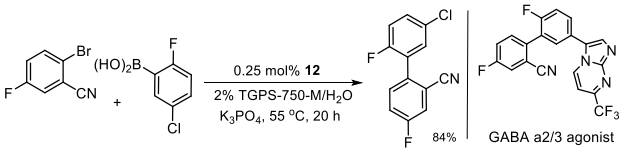
The effectiveness of catalyst **11** was demonstrated on a great variety of aryl halides containing both electron-donating and electron-withdrawing groups. In addition, the substrates and arylboronic acids based on heterocycles, the substrates with protecting groups and polyaromatic compounds were involved in the reaction. Using CPC **11** as the (pre)catalyst, a multi-stage one-pot synthesis of the fungicide boscalid as well as drugs anacetrapib, sonidegib, and valsartan was accomplished. The main drawback of this approach, according to the authors, is the laborious synthesis of HandaPhos [35].

Later, the same researchers obtained a series of new mononuclear *C,N*-palladacycles based on biphenylamines with another more accessible monophosphine ligand EvanPhos [38]. In the reaction between substituted 5-bromopyrimidine and 4-chlorophenylboronic acid, catalyst **12** (Fig. 3), containing an isopropyl group both in one of the phenyl rings and on the nitrogen atom (Scheme 5), was found to be the most effective complex.



Scheme 5. SM reaction catalyzed by *C,N*-palladacycle **12**.

The effectiveness of complex **12** at low concentrations under conditions of aqueous micellar catalysis was demonstrated on a large number of the examples. Thus, it successfully catalyzes the coupling of the substrates containing various functional groups (esters, nitriles, aldehydes, amides, amines, nitro compounds, and carbamates), thiophene-based halides, alkenes and alkynes. A series of heteroaryl chlorides were also reacted, and in each case the coupling product was obtained in good yield. In addition, the possibility of using complex **12** for the synthesis of drugs was shown. Using this catalyst, for example, intermediates for the synthesis of valsartan, sonidegib, anacetrapib, anticancer agents, and an agonist of α2- and α3-GABA receptors were obtained in high yields (83–93%) (Scheme 6).



Scheme 6. Synthesis of an intermediate of an agonist of α2-, α3-GABA receptors.

In recent years, reactions performed under microfluidic conditions have become very popular [39]. Sieber *et al.* [40] successfully used this approach for the Suzuki–Miyaura cross-coupling between 2-chloropyridine and arylboronic acid catalyzed by palladacycle **13** (Fig. 4, Scheme 7).

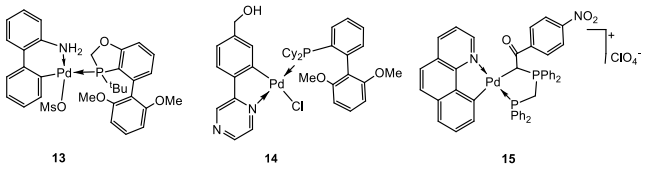
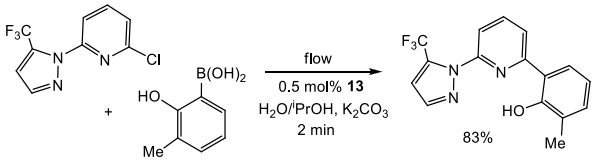


Figure 4. Phosphine derivatives of *C,N*-palladacycles.

The authors noted that performing the reactions in a microreactor ensures an increase in the yield of the target product, a reduction in the reaction time, scaling up to gram quantities, and avoiding the catalyst deactivation, which is observed in traditional catalysis.

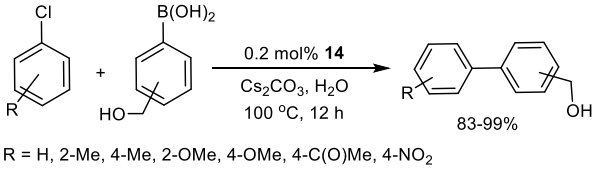


Scheme 7. SM reaction under microfluidic conditions catalyzed by palladacycle **13**.

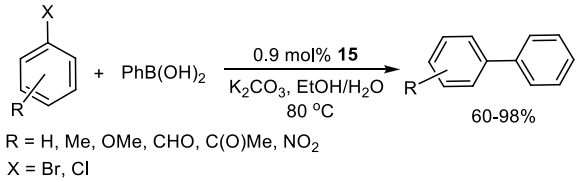
One aspect of expanding the application of the Suzuki–Miyaura reaction is the search for conditions that allow the use of inexpensive and readily available aryl chlorides as substrates as well as water as an ecologically friendly solvent. The water-soluble arylpyrazine palladacycle **14** (Fig. 4) with the bulky phosphine auxiliary SPhos was suggested as an effective catalyst for the SM reaction of aryl chlorides [41]. In the reaction of aryl chlorides containing both electron-donating and electron-withdrawing substituents with (hydroxymethylphenyl)boronic acid catalyzed by complex **14,** the coupling products were formed in high yields of 88–99% (Scheme 8). The catalyst loading was only 0.2 mol % at that.

Benzo[h]quinolinate palladacycle **15** (Fig. 4) stabilized with a phosphine ylide ligand exhibited high catalytic activity in the

cross-coupling of various aryl halides with $PhB(OH)_2$ [42]. As it was expected, the use of aryl bromides as substrates enabled the production of the target biphenyls in high yields (89–98%) over a short period of time (10–25 min), albeit upon heating (Scheme 9). On passing to aryl chlorides, the reaction time increased (40–60 mins) and the yields of the target products decreased (60–80%).



Scheme 8. SM reaction catalyzed by azapalladacycle **14**.



Scheme 9. SM reaction catalyzed by azapalladacycle **15**.

Firinci [43] showed high catalytic activity of three CPCs **16**–**18** based on 2-phenylpyridine containing a barbiturate ligand in the SM cross-coupling (Fig. 5). Thus, the reactions of 4-bromotoluene with $PhB(OH)_2$ promoted by 1 mol % of catalysts **16**–**18** afforded the final products in 1–4 h in good yields of 76–99%. When 4-bromoacetophenone was used as a substrate, the reaction time was halved.

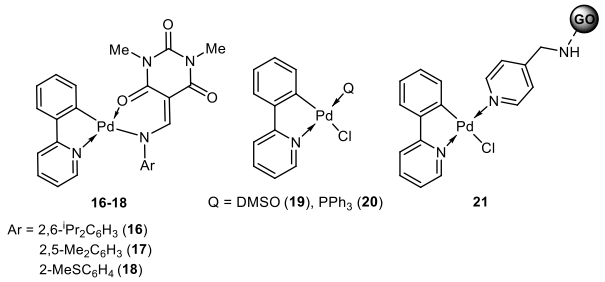


Figure 5. *C,N*-Palladacycles based on 2-phenylpyridine.

The catalytic properties of aminate *C,N*-palladacycles can be improved by complex depositing on a polymer substrate. The latter can be graphene oxide [44]. A two-dimensional structure with huge surface area as well as the presence of chemically active sites for functionalization make it a promising carrier for nanoparticles and complexes.

Palladacycle **21** immobilized on graphene oxide in the reaction of aryl bromides with $PhB(OH)_2$ under mild conditions (toluene, K_2CO_3, 20 °C, ~0.001 mol %) showed catalytic activity comparable with that of homogeneous analogs **19** and **20** and provided the target products in good yields (70–90%) (Fig. 5). At the same time, its efficiency in the cross-coupling of aryl chlorides was significantly higher than that of palladacycles **19** and **20**. For example, in the reaction of chlorobenzene with $PhB(OH)_2$ catalyzed by complex **21** under mild conditions, the coupling product was formed in 67% yield in just 45 min, whereas in the presence of complexes **19** and **20**, the reaction time reached 2–3 h. An obvious advantage of heterogeneous catalyst **21** immobilized on the graphene substrate is the ease of its separation from the reaction mixture as well as the possibility of recycling.

Recent decades have witness the growth in the popularity of *C,N*-palladacycles bearing an additional *N*-heterocyclic carbene ligand in the SM reaction. Carbenes constitute a class of ecologically friendly ligands with unique electronic and steric properties [45, 46]. A series of *C,N*-palladacycles based on 2-phenylpyridine **21**–**23** [47] and tertiary benzylamines **24**–**26** [47], **27** [48] with *N*-butyl-substituted *N*-heterocyclic carbenes as auxiliary ligands (Fig. 6) were tested in the SM cross-coupling.

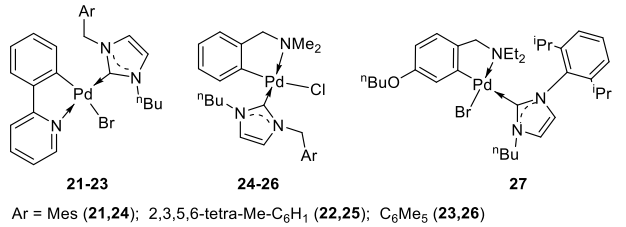
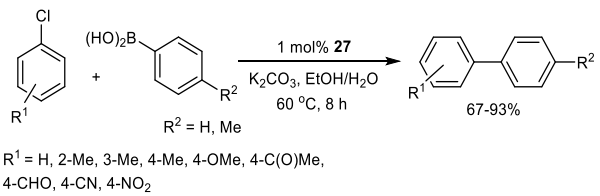


Figure 6. Mononuclear carbene derivatives of *C,N*-palladacycles.

All the complexes (at 1 mol % loading) showed high performance in the SM reaction. Palladacycles **24**–**26** appeared to be slightly less active than catalysts **21**–**23**: in the reaction of 4-bromotoluene with phenylboronic acid, the yields of the coupling products were 63–92% and 93–99%, respectively. It should be noted that the activity of the complexes increased slightly with the increasing number of methyl groups in the benzyl carbene substituent. In addition, complexes **23** and **26** were tested in the SM reaction of aryl chlorides. Thus, in the coupling between 4-chloroacetophenone and $PhB(OH)_2$ catalyzed by these palladacycles, the target products were obtained in moderate yields of 43% and 45%, respectively. The authors indicated that catalysts **21**–**26** with an *n*-butyl substituent are more efficient than the previously described related complexes containing methyl groups [49].

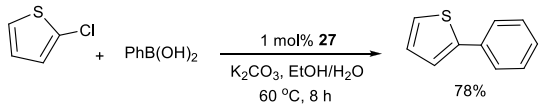
Chinese scientists demonstrated high catalytic activity of mononuclear derivative **27**, a benzylaminate palladacycle with an alkoxy-*N*-heterocyclic carbene ligand, in the SM cross-coupling with various aryl chlorides (Fig. 6, Scheme 10) [48].



Scheme 10. SM reaction of aryl chlorides catalyzed by palladacycle **27**.

Substituents in aryl chlorides (OMe, CHO, C(O)Me, CN, and NO_2) have virtually no effect on the yields of the reaction products (71–93%). In addition, heteroaryl chlorides, for example, 3-chlorothiophene, also entered the SM reaction catalyzed by complex **27**, forming the coupling products in good yields (Scheme 11).

The same research group compared the catalytic activity of CPC **28**, featuring a rigidly fixed aliphatic spacer between the



Scheme 11. SM reaction between 3-chlorothiophene and $PhB(OH)_2$ catalyzed by palladacycle **27**.

imidazolium ligand and the palladated phenylene moiety, with its analog **29**, bearing more flexible alkyl substituents, in the SM cross-coupling of various aryl chlorides in an aqueous medium (Fig. 7) [50].

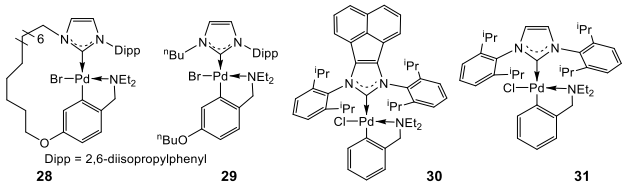
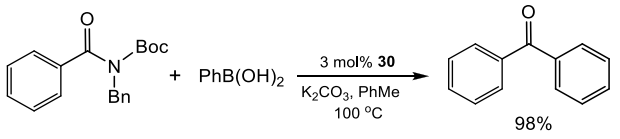


Figure 7. Mononuclear carbene derivatives of benzylaminate *C,N*-palladacycles.

In the model reactions of chlorobenzene with 4-methoxyphenylboronic acid acid under similar conditions (0.5 mol %, K_2CO_3, $EtOH/H_2O$, 50 °C, 6 h) in the presence of catalysts **28** and **29**, 4-methoxybiphenyl was obtained in 95% and 63% yield, respectively. Catalyst **28** exhibited high performance in the reactions with aryl halides, bearing both electron-donating and electron-withdrawing substituents, as well as with sterically loaded substrates and heterocycles. These results indicate that rigid complex **28** has better catalytic activity than its more flexible analog **29**, which should be taken into account when developing new potential catalysts.

Recently, the high catalytic activity of an acenaphthoimidazolylidene derivative of *C,N*-palladacycle **30** in the SM cross-coupling of inactive amides with various aryl-, alkyl-, and alkenylboronic acids was demonstrated to form the corresponding ketones in high yields [51]. Thus, benzylamide with *N*-Bn and electron-withdrawing bulky *N*-Boc groups in the reaction with $PhB(OH)_2$ catalyzed by CPC **30** was almost quantitatively converted into the corresponding ketone (Scheme 12):



Scheme 12. Synthesis of ketones using the SM reaction catalyzed by complex **30**.

The catalytic activity of complex **31** was significantly lower than that of catalyst **30**. For example, in the reaction between an inactive benzylamide with *N*-Ts/Bn substituents and $PhB(OH)_2$ in the presence of 3 mol % of the catalyst, the corresponding ketone was formed in 63% yield for palladacycle **30** and only 15% in the case of complex **31**. The authors explain this by the strong σ-donor and weak π-acceptor properties of acenaphthoimidazolylidene, as well as an increase in the size of the ligand π-ring in complex **30**.

3. Palladacycles based on oximes

Oximate palladacycles serve as efficient and versatile (pre)catalysts for a wide range of cross-couplings in air and at low catalyst loadings [29]. These palladacycles are highly stable to the action of oxygen air, moisture, as well as heat and can be obtained from inexpensive precursors.

The derivatives of the simplest oximate palladacycle with *P,P*-bidentately bound *dppp* **32** [52] and an unsymmetrical phosphorus ylide based on acetophenone **33** [53, 54], as well as complex **34** [55] bearing both a bridged and bidentate diphosphine *dppe* ligands were suggested as the catalysts for the SM coupling of aryl bromides with phenylboronic acid (Fig. 8).

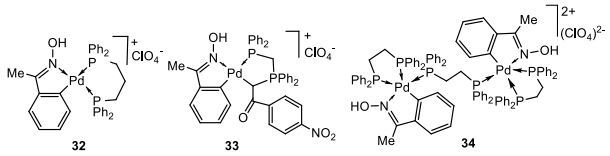
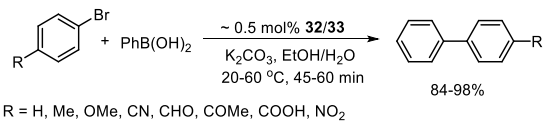


Figure 8. Derivatives of the oximate *C,N*-palladacycle with *P*-donor ligands.

It was shown that complexes **32** and **33** at ~0.5 mol % loading effectively promoted the cross-coupling of aryl bromides with $PhB(OH)_2$ under mild conditions, leading to substituted biaryls in high yields (Scheme 13).



Scheme 13. Catalytic activity of complexes **32** and **33** in the SM reaction.

The high catalytic activity was also observed in the case of binuclear oximate palladacycle **34** [55]. Thus, the reaction of 4-bromoanisole with $PhB(OH)_2$ catalyzed by 0.5 mol % [Pd] of complex **34** afforded the coupling product in 96% yield in 2 h.

The popularity of cross-coupling catalysts based on oximate palladacycles immobilized on various supports, such as SiO_2, ionic liquids, resins, and polymer substrates, is stipulated by the ease of separation and the possibility of catalyst recycling [29, 56–59]. However, significant disadvantages of such systems are an increase in the temperature and duration of the process, as well as the presence of an induction period, since the precatalyst slowly converts to an active form. This problem was solved by performing the reactions under microwave irradiation [60].

Thus, trialkoxy-substituted oximate palladacycle **35** (Fig. 9) immobilized on a polymer substrate in the reaction of aryl bromides with $PhB(OH)_2$ at a loading of 1 mol % provided biaryl products in high yields (96–99%) in just 30 min (Scheme 14). However, in the reactions of the corresponding aryl chlorides, a considerable decrease in the yields of the target products was observed (20–53%). When comparing the kinetic profiles of the cross-coupling between *para*-bromoanisole and $PhB(OH)_2$ under heating and microwave irradiation, a significant decrease in the induction period from 20 to 3 min was detected and the reaction with microwave activation

completed in 20 min. Moreover, catalyst **35** was reused in five consecutive cycles without any loss in the catalytic activity with excellent coupling yields (>94%).

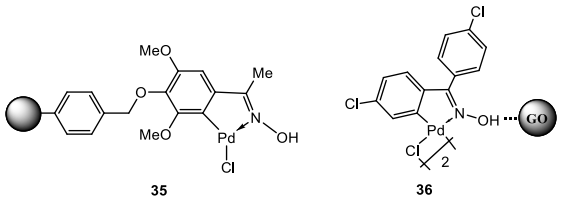
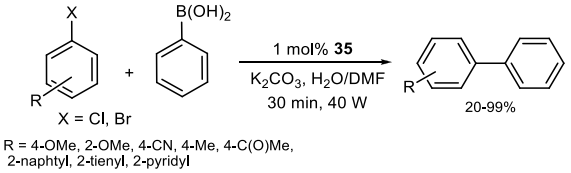


Figure 9. Heterogeneous oximate *C,N*-palladacycles.



Scheme 14. Catalytic activity of complex **35** in the SM reaction.

The high catalytic activity in the Suzuki–Miyaura reaction was demonstrated by oximate palladacycle **36** immobilized on graphene oxide (Fig. 9). The cross-coupling of aryl bromides was carried out in water at room temperature and at catalyst loadings reduced to 0.002 mol % [Pd] [61]. Catalyst **36** can be recovered and reused with loss in the catalytic activity after the second cycle due to metal oxidation and agglomeration processes.

4. *C,N*-Palladacycles based on imines

Iminate CPCs are known to be effective catalysts for cross-coupling reactions [27, 30]. Like most palladacycles, they can potentially be converted to a wide range of functional derivatives.

Babahan *et al.* [62] studied the catalytic activity in the SM reaction of a series of iminate *C,N*-palladacycles: μ-acetate dimers **37** and **38** and their mononuclear derivatives with carbene ligands **39**–**44** (Fig. 10).

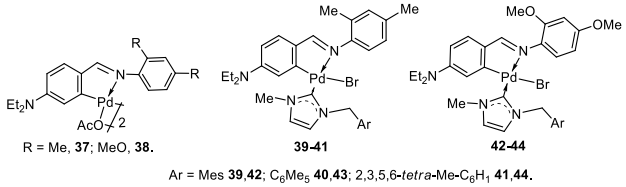
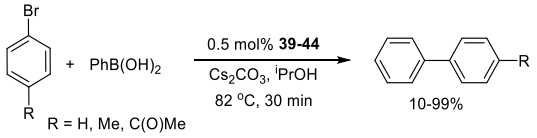


Figure 10. Dimeric iminate *C,N*-palladacycles and their derivatives with carbene ligands.

The catalytic activity of these complexes in the SM reaction between aryl bromides and $PhB(OH)_2$ was shown to depend on the structures of both the substrate and the catalyst itself (Scheme 15).



Scheme 15. Catalytic activity of complexes **39**–**44** in the SM reaction.

For example, in the case of electron-neutral bromobenzene, the yields of the coupling products were 48–98%. As expected, 4-bromoacetophenone was more reactive, while the reactions between electron-rich 4-bromotoluene and $PhB(OH)_2$ resulted in the coupling products in poor to moderate yields (10–45%). When comparing the catalytic activity of CPCs **37**–**44**, it was found that acetate-bridged dimers **37** and **38** were more active than carbene-containing mononuclear derivatives **39**–**44**. Thus, in the reaction of bromobenzene with $PhB(OH)_2$ catalyzed by complexes **37** and **38**, the product yields were 98% in each case, while in the case of complexes **39**–**44**, they ranged within 48–98%. Dimer **37** appeared to be the most active catalyst in the Suzuki–Miyaura reaction (98–99% yields in all three reactions).

A large series of iminate *C,N*-palladacycles were studied as the catalysts for the Suzuki–Miyaura cross-coupling by Bermúdez-Puente *et al.* [63]. The presence of methoxy substituents in the phenylene ring increased the solubility of these palladacycles, allowing catalysis to be carried out in an aqueous medium.

Dimers **45**–**50** as well as their derivatives with bipyridine **51**, **52**, 1,10-phenanthroline **53**, **54**, triphenylphosphine **55**, **56**, acetylacetonate **57**, **58**, and complexes with bridged **59**, **60** and chelating diphosphine **61**, **62** (Fig. 11) were tested in the model SM cross-coupling between 4-bromoacetophenone and $PhB(OH)_2$ at room temperature and 80 °C (Scheme 16) [63].

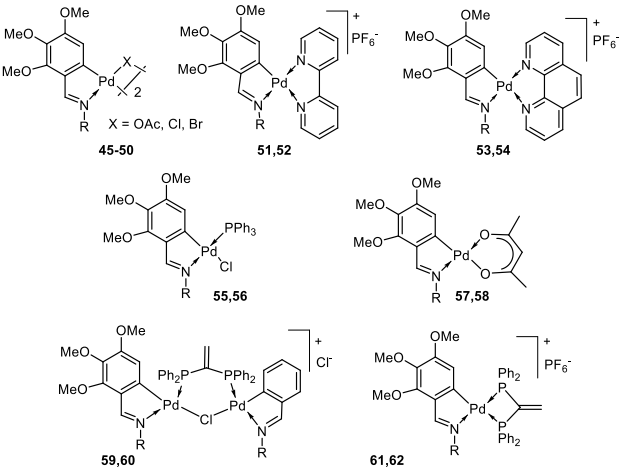
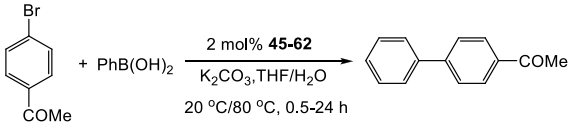


Figure 11. Iminate C,N-palladacycles **45**–**62**.

In the presence of 2 mol % of the catalyst, the product was obtained in most cases (Scheme 16) in >80% yields.



Scheme 16. Catalytic activity of iminate *C,N*-palladacycles **45**–**62** in the SM reaction.

The derivatives of azapalladacycles with a 1,10-phenanthroline ligand (complexes **53**, **54**) showed low performance. Catalysis was found to be possible only at elevated temperatures (80 °C), and the product yields were only 20% and 33%. In the case of the SM reactions catalyzed by palladacyclic derivatives with bipyridine **51**, **52**, heating and a long time (24

h) were required to obtain good yields of the substituted biphenyl (100% and 66%).

It should be noted that when dimers **48**–**50** and mononuclear triphenylphosphine adducts **55**, **56** were used as the catalysts, high yields of the coupling products (80–100%) were observed both at room temperature and upon heating.

Bermúdez-Puente *et al.* [63] studied the catalytic activity of (μ)-chloride dimer **49** in more detail due to its stability and ease of synthesis. In the reactions of aryl bromides with both activating (-CHO, -C(O)Me) and deactivating (-OMe) substituents catalyzed by complex **49** under mild conditions, the product yield was 100%. The reaction with *para*-chloroacetophenone took longer to complete (24 h, 98%), but the reaction with aryl chloride containing a deactivating (-OMe) substituent afforded the target product in only 13% yield.

For catalysts **59**, **60** bearing a bridged diphosphine ligand, high yields of the target products (95–99%) were achieved at room temperature, but the reaction time increased to 24 h. Heating to 80 °C allowed for reducing the reaction time to 5 h. Complexes with a bidentate coordinated diphosphine **61**, **62** and acetylacetonate **57**, **58** were also effective at elevated temperatures (90–95%).

Cyclopalladated iminate dimers **63**–**65** as well as their triphenylphosphine derivatives **66**–**68** (Fig. 12) were used as the catalysts for modifying nucleosides, which are classified as bioactive molecules [64]. The functionalized nucleosides are widely used as biological or fluorescent probes as well as in antiviral and antitumor therapy [65, 66].

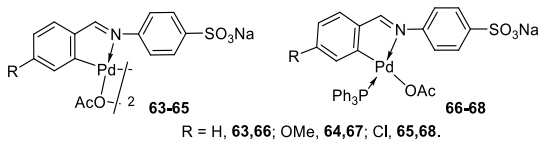
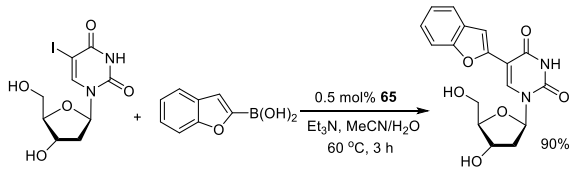


Figure 12. Iminate *C,N*-palladacycles **63**–**68**.

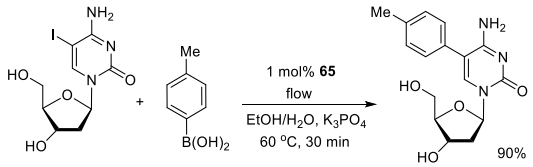
In the cross-coupling of 5-iodo-2'-deoxyuridine with benzofuran-2-boronic acid in an aqueous medium (Scheme 17), dimers **63**–**65** showed higher catalytic activity than their phosphine derivatives **66**–**68**: the product yields ranged within 81–90% and 72–83%, respectively. Complex **65** showed the best performance, presumably due to the better solubility compared to dimers **63** and **64**.



Scheme 17. Microfluidic synthesis of a substituted deoxyuridine catalyzed by complex **65**.

The coupling of 5-iodo-2'-deoxyuridine with a series of substituted arylboronic acids in the presence of 0.5 mol % of complex **65** was also explored and shown to provide the biaryl products in good yields (68–87%). Only in the case of bulk phenanthreneboronic acid, a decrease in the product yield to 48% was observed.

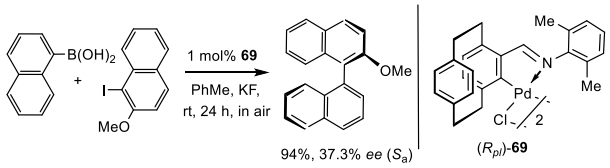
Recently, the same research group developed the conditions for modifying substituted pyrimidine nucleosides by the SM reaction catalyzed by palladacycle **65** under microfluidic conditions [68]. One of the main obstacles in flow synthesis is the non-homogeneity of reaction mixtures, which can lead to the system blockage; however, the good solubility of dimer **65** in an aqueous medium allowed for avoiding this problem. Thus, the cross-coupling between 5-iodo-2'-deoxycytidine and 3-methoxyphenylboronic acid under traditional conditions of the SM reactions (1 mol %, $EtOH/H_2O$, K_3PO_4, 60 °C, 24 h, N_2) provided, along with the target biaryl (76%), the product of dehalogenation (14%), and in the absence of an inert atmosphere the reaction did not proceed at all. When passing to the flow catalytic cross-coupling of 5-iodo-2'-deoxycytidine with 3-methoxyphenylboronic acid, the reaction proceeded selectively to form only the target product in high yield in just 30 min (Scheme 18).



Scheme 18. Microfluidic synthesis of a substituted deoxycytidine catalyzed by complex **65**.

Hence, a series of aryl-substituted nucleosides was obtained in high yields (74–90%), independent of the substituents in the arylboronic acid or the nucleophilicity of the reagents in use. The main advantages of this approach include a considerable reduction in the reaction time, the absence of an inert atmosphere, the possibility of scaling, high yields of the coupling products, and the ease of isolating the reaction products without recourse to column chromatography.

The catalytic activity and enantioselectivity of the non-metallocene planar chiral iminate *C,N*-palladacycle (R_{pl})-**69** was evaluated in the model atroposelective reaction of 1-naphthylboronic acid with 2-methoxynaphthyl-1-iodide [69] (Scheme 19).



Scheme 19. Atroposelective SM reaction catalyzed by *C,N*-palladacycle (R_{pl})-**69**.

Under mild conditions, 2-methoxy-1,1'-binaphthyl was formed in high yield and with moderate enantioselectivity. An increase in the catalyst loading to 5 mol % and reaction time led to an increase in the enantiomeric purity of the target binaphthyl to 53% *ee*. It should be noted that this reaction is one of the rare examples of the application of the enantioselective Suzuki–Miyaura cross-coupling catalyzed by palladacycles.

5. Unsymmetrical pincer CPCs

Pincer palladacycles comprise a class of complexes containing at least one Pd–C bond and two intramolecular coordination bonds with heteroatoms [70]. They are the objects

of intensive research owing to the high stability, the possibility of structural modification, and the prominent catalytic activity [71].

Unsymmetrical pincer palladacycle **70** (Fig. 13), containing a hybrid *C,N,N*-tridentate ligand based on a hydrazone and a thiazolyl group, was tested in the reaction of aryl halides with various arylboronic acids in water under IR irradiation [72].

The reaction between 4-bromoanisole and $PhB(OH)_2$ catalyzed by palladacycle **70** afforded the target product in 45% yield in 60 min; the addition of TBAB to the reaction mixture led to an increase in the biaryl yield to 90% (Scheme 20).

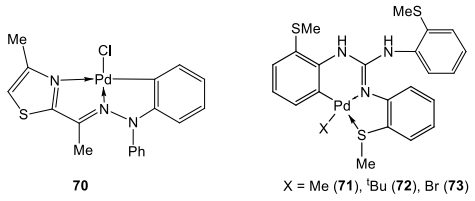
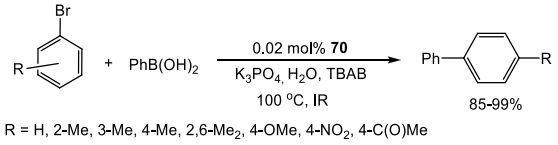


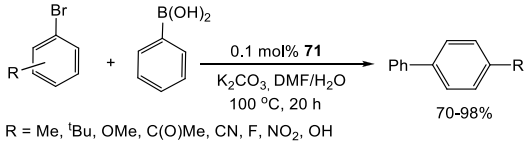
Figure 13. Pincer-type *C,N,N*-palladacycles **70**–**73**.



Scheme 20. Catalytic activity of complex **70** in the SM reaction.

Further studies on the catalytic activity of palladacycle **70** showed that aryl bromides with both electron-withdrawing and electron-donating groups can react with $PhB(OH)_2$ in a short period of time (30–90 min) to form the coupling products in high yields (90–96%). In the reactions with sterically hindered substrates, such as 3-bromotoluene, 2-bromotoluene, 2-bromo-1,3-dimethylbenzene, high yields (85–93%) of the corresponding coupling products were achieved by increasing the process duration. Heterocyclic substrates such as 2-bromopyridine, 3-bromopyridine, 2-bromothiophene were also introduced into the SM reaction to form the corresponding biaryls in moderate yields (50–60%), although over longer reaction times. Various arylboronic acids featuring methyl, methoxy, nitro, and trifluoromethyl substituents successfully reacted with 4-bromoanisole with high product yields (70–95%). The reactions with aryl chlorides required a higher catalyst loading (0.1 mol %). While excellent yields (95%) were obtained with activated aryl chlorides, deactivated substrates such as 4-chlorotoluene and 4-chloroanisole afforded low yields (10% and 15%, respectively) [72].

Unusual unsymmetrical *C,N,S*-pincer complexes **71**–**73** based on *N,N′,N″*-tris(2-thioanisyl)guanidine, containing a nucleophilic SMe group in the ligand (Fig. 13), were tested in the Suzuki–Miyaura reaction [73]. It was shown that palladacycles **71** and **72** with alkoxy anions showed higher catalytic performance than bromide analog **73**: in the model reaction between *para*-bromoanisole and $PhB(OH)_2$, when the catalyst loadings were 0.1 mol %, the cross-coupling product was formed in 95–98% and 81%, respectively. Subsequently, complex **71**, as the most active one, was tested in the reaction of various aryl bromides with $PhB(OH)_2$ under similar conditions (Scheme 21).



Scheme 21. Catalytic activity of complex **71** in the SM reaction.

The corresponding cross-coupling products were formed in 65–98% yields. The best result was achieved in the reaction with *para*-bromoacetophenone (98%), while the worst result—with *para*-(4-bromophenyl)acetophenone (65%). CPC **71** was also tested in the coupling of *para*-bromoanisole with a series of substituted arylboronic acids. Depending on the structure of the boron reagent, the product yields ranged within 63–92%.

Unsymmetrical 5,6-membered *C,N,N*-pincer complexes based on bicyclo[3.3.1]nonane and bicyclo[3,2.1]octane, featuring a phenylene (**74**, **75**) [70] or ferrocenyl (**76** [74], **77** [75]) backbone, showed high catalytic activity in the cross-coupling of aryl bromides with $PhB(OH)_2$ (Fig. 14).

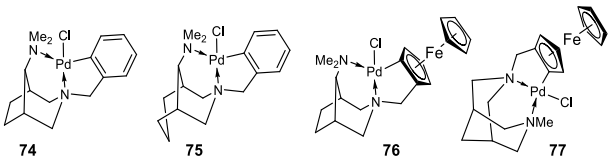
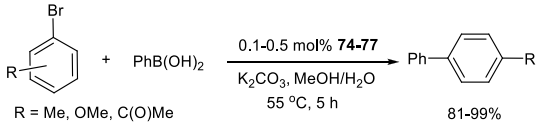


Figure 14. Unsymmetrical 5,6-membered *C,N,N*-palladacycles.

In all reactions catalyzed by (pre)catalysts **74**–**77** (0.1–0.5 mol %), the corresponding biaryls (R = Me, OMe, C(O)Me) were formed in high yields of 81–99% (Scheme 22). Using the reaction of 4-bromoanisole with $PhB(OH)_2$ as an example, it was shown that a reduction in the catalyst loading to 0.05 mol % leads to a significant decrease in the yields of the target products to 9–13%.



Scheme 22. Catalytic activity of complexes **74**–**77** in the SM reaction.

Bulygina *et al.* [70] stated that pincer CPCs **74** and **75** with two sp^3-hybridized nitrogen atoms are slightly more active catalysts for this reaction than unsymmetrical *C,N,N*-palladacycles with two sp^2-hybridized nitrogen atoms [76]. It should be noted that complex **77** was also effective at room temperature (74–90%) [75]. The authors conclude that neither the presence of the ferrocenyl moiety nor the different structures of the bicyclic ligand have a noticeable effect on the catalytic activity of complexes **74**–**77**.

6. *C,N*-Palladacycles based on ferrocenes

Active (pre)catalysts for the Suzuki–Miyaura, Heck, Sonogashira, and Buchwald–Hartwig reactions are not only the complexes in which the Pd atom is bound with an aromatic ring, but also the bimetallic derivatives in which Pd is attached to an organometallic moiety, in particular, a ferrocenyl core. The known ferrocenyl palladacycles based on tertiary amines [77,

78], quinolone [79], Schiff bases [80], 3-pyridyl bromide [81, 82], pyridazine [83], pyrimidine [84], and other ligands are effective catalysts for the SM reaction.

In a recent work, Bulygina *et al.* [85] studied the catalytic activity of new six-membered *C,N*-palladacycles based on 1-*N*-ferrocenylmethylindazole **78**–**85** in the SM reaction (Fig. 15).

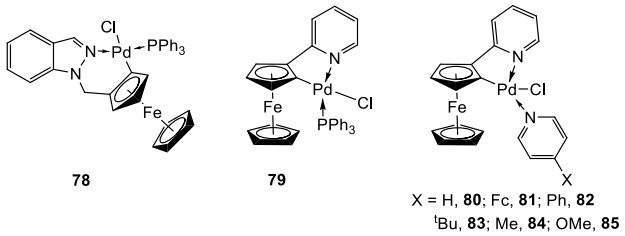
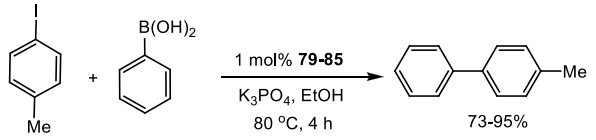


Figure 15. Ferrocene-based *C,N*-palladacycles.

The reaction of 4-bromoanisole with $PhB(OH)_2$ in the presence of catalyst **78** at room temperature (0.1 mol %, K_2CO_3, $MeOH/H_2O$, 5 h) afforded the coupling product in 77% yield. Under the same conditions, the coupling of $PhB(OH)_2$ with 4-bromotoluene resulted in the target biaryl only in moderate yield (69%), while analogous reaction with 4-bromoacetophenone, as expected, led to the corresponding product in high yield (92%). When the reaction temperature was raised to 55 °C, all three aryl bromides were converted to the corresponding biaryls in high yields (89–95%). The results of the investigations on the catalytic activity of complex **78** are comparable with the data for other ferrocenyl CPCs reported in the literature [83, 86–88].

The catalytic properties of triphenylphosphine complex **79** and a series of pyridine analogs **80**–**85** derived from *C,N*-palladacycle based on 2-ferrocenylpyridine were assessed in the SM reaction between 4-iodotoluene and phenylboronic acid (Fig. 14, Scheme 23) [89]. In the reaction performed in air, most of pyridine complexes **80**–**85** appeared to be more effective (82–95%) than triphenylphosphine counterpart **79** (73%). However, in an inert atmosphere, the catalytic activity of complex **79** increased and the product yield reached 91%.



Scheme 23. Catalytic activity of complexes **79**–**85** in the SM reaction.

The authors noted that there is a linear correlation between the pKa value of the auxiliary pyridine ligands in complexes **80**–**85** and the yields of the coupling products. Complex **81**, containing the strongest electron-donating ligand (X = Fc), afforded the lowest product yield (68%). In contrast, the highest product yield (95%) was observed in the reaction with CPC **80** bearing the weakest electron-donating auxiliary ligand (X = H).

7. Miscellaneous *C,N*-palladacycles

Recently, the catalytic activity in the Suzuki–Miyaura reaction of a series of *C,N*-palladacyclic derivatives based on phenyl- and naphthyloxazolines containing acenaphthoimidazol-2-ylidene as an auxiliary ligand was studied [90].

The most active (pre)catalyst was complex **86** with a bulky *tert*-butyl substituent at the fourth position of an oxazoline ring (Fig. 16). A wide range of (hetero)aryl bromides and (hetero)arylboronic acids were introduced into the SM reaction catalyzed by complex **86** to form biaryls in high yields (77–99%), albeit under severe temperature conditions. The biaryls containing polycyclic aromatic hydrocarbons, such as phenanthrene, anthracene, pyrene, and acridine, were also obtained in high yields (85–98%). Thus, the reaction of methoxy-substituted bromoquinoline with phenanthrenylboronic acid in the presence of complex **86** leads to a coupling product in high yield (Scheme 24).

A large series of ternaphthalenes and diarylanthracenes were synthesized in high yields *via* the SM reaction catalyzed by complex **86**. The advantages of this system include the use of equimolar amounts of organoboron compounds and aryl bromides, since an excess of the boron reagent is usually used in these reactions.

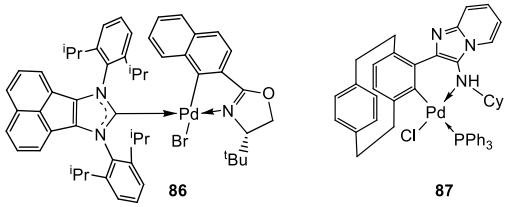
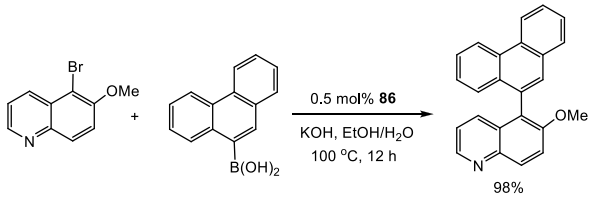
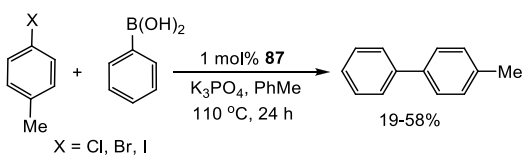


Figure 16. Naphthyloxazoline and paracyclophane-based *C,N*-palladacycles.



Scheme 24. Catalytic activity of complex **86** in the SM reaction.

C,N-Palladacycle **87** featuring a paracyclophane backbone (Fig. 16) containing a 3-aminoimidazole moiety and triphenylphosphine as an additional ligand showed low catalytic activity in the SM cross-coupling [91]. Thus, in the SM reaction between various 4-halotoluenes and $PhB(OH)_2$ (Scheme 25), even at high temperatures, the coupling products were obtained in moderate yields (19–58%), depending on the nature of the halogen. As expected, the highest yield was achieved in the reaction with 4-iodotoluene (58%).



Scheme 25. Catalytic activity of complex **87** in the SM reaction.

The catalytic activity of both tetranuclear CPCs **88**–**90** based on thiosemicarbazone and their derivatives with bis(diphenylphosphino)methane (*dppm*) **91**–**96** (Fig. 17) was studied in the reaction of 4-bromoacetophenone with $PhB(OH)_2$ (Scheme 26) [92].

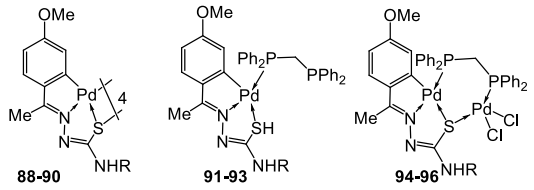
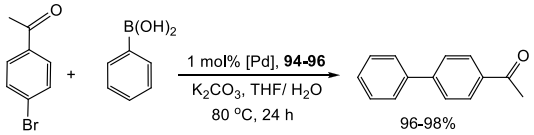


Figure 17. Thiosemicarbazone-based *C,N*-palladacycles.

The best conversions (96–98%) were achieved using binuclear CPCs **94**–**96**. Under similar conditions, complexes **88**–**90** and **91**–**93** exhibited low catalytic activity (conversions 0–18% and 12–22%, respectively).



Scheme 26. Catalytic activity of complexes **94**–**96** in the SM reaction.

In contrast to the mentioned reports [47, 48, 50, 90], which described the catalytic activity of *C,N*-palladacycles with monodentate auxiliary carbene ligands, Fizia *et al*. [45] presented the results of testing in the Suzuki-Miyaura reaction of cyclopalladated carbene derivatives containing a pyrimidine backbone. Thus, mononuclear pyridine derivatives **97**–**100** (Fig. 18) exhibited high catalytic activity in the cross-coupling of aryl chlorides with arylboronic acids. In the case of aryl chlorides with electron-withdrawing substituents, high yields of the coupling products were achieved: for example, in the reaction of 4-chloroacetophenone with $PhB(OH)_2$ (1 mol %, K_3PO_4, ^{i}PrOH/H_2O, 90 °C, 30 min), the product yields were 96–99%. In the case of aryl chlorides containing electron-donating substituents (-OMe), the reaction efficiency decreased markedly (39–53%). The yields drop significantly when sterically hindered arylboronic acids were introduced into the reaction. For example, in the reaction of 2-naphthylboronic acid with 4-methoxychlorobenzene, the yields of the coupling products were only 24–39%.

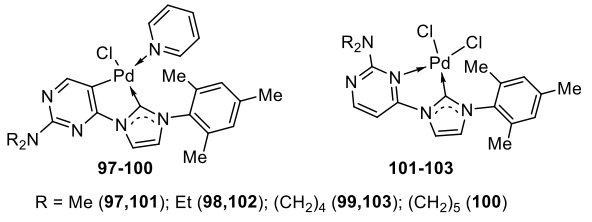


Figure 18. Cyclopalladated carbenes.

The catalytic activity of *C,N*-palladacycles **101**–**103** under similar conditions (1 mol %, K_3PO_4, ^{i}PrOH/H_2O, 90 °C, 30 min) appeared to be extremely low: the yields of the coupling products were only 6–9%.

8. Conclusions

Hence, this literature survey provides information on the catalytic activity of various structural types of *C,N*-palladacycles in the Suzuki–Miyaura cross-coupling.

The analysis of the reported data showed that azapalladacycles are effective catalysts for the Suzuki–Miyaura reaction. CPCs exhibit high catalytic activity not only in the reactions of aryl iodides and aryl bromides with arylboronic acids, but also in the case of cheap and available aryl chlorides. In addition, the number of non-traditional halides (heterocycles, nucleosides) used in the reaction is increasing. It was also shown that the catalytic performance of CPCs depends on the metal surrounding and can vary depending on the nature of the auxiliary ligand and anion. Of particular note is a gradual transition from the model reactions to the synthesis of biologically relevant biaryls.

The main trends in recent years in the Suzuki–Miyaura cross-coupling with azapalladacycles are the following ones: a reduction in the catalyst loading and reaction temperature, a transition to an aqueous medium and other more environmentally benign solvents, the structural modification of palladacyclic catalysts by the immobilization on polymer substrates, which facilitates the process of their separation from the reaction mixture, and the use of IR and microwave activation as well as microfluidic technologies.

Abbreviations

Aryl (Ar)
Suzuki–Miyaura reaction (the SM reaction)
cyclopalladated complex (CPC)
tert-butyl (^{t}Bu)
pyridine (Py)
2,4,6-trimethylpyridine (Me_3Py)
ethyl (Et)
1,2-bis(diphenylphosphino)ethane (*dppe*)
1,3-bis(diphenylphosphino)propane (*dppp*)
poly(ethylene glycol) (PEG)
1,1-bis(diphenylphosphino)methane monoxide (*dppmo*)
methyl (Me)
phenyl (Ph)
methanesulfonyl (Ms)
triflate (Tf)
isopropyl (^{i}Pr)
cyclohexyl (Cy)
(2*S*,3*S*)-4-(2,6-dimethoxyphenyl)-3-(2-methyl-2-propanyl)-2-(2,4,6-triisopropylbenzyl)-2,3-dihydro-1,3-benzoxaphosphole (HandaPhos)
dicyclohexyl-[2,6-dimethoxy-3-(2-methoxynaphthalen-1-yl)phenyl]phosphane (EvanPhos)
methoxypoly(ethylene glycol)-750 (MPEG-750)
γ-aminobutyric acid (GABA)
dicyclohexylphosphino-2',6'-dimethoxybiphenyl (SPhos)
dimethylsulfoxide (DMSO)
graphene oxide (GO)
n-butyl (^{n}Bu)
benzyl (Bn)
tert-butoxycarbonyl (Boc)
tosyl (Ts)
N,N-dimethylformamide (DMF)
acetyl (Ac)
mesityl (Mes)
tetrahydrofuran (THF)
tetrabutylammonium bromide (TBAB)
infrared radiation (IR)
ferrocenyl (Fc)
1,1-bis(diphenylphosphino)methane (*dppm*)

Acknowledgements

This work was supported by the Ministry of Science and Higher Education of the Russian Federation (agreement no. 075-00277-24-00).

Corresponding author

* E-mail: olg111@yandex.ru. Tel: +7(499)135-5033 (O. N. Gorunova)

References

1. A.-T. Kal-Koshvandi, M. M. Heravi, T. Momeni, *Appl. Organomet. Chem.*, **2018**, *32*, e4210. DOI: 10.1002/aoc.4210
2. P. Devendar, R.-Y. Qu, W.-M. Kang, B. He, G.-F. Yang, *J. Agric. Food Chem.*, **2018**, *66*, 8914–8934. DOI: 10.1021/acs.jafc.8b03792
3. S. Tabassum, A. F. Zahoor, S. Ahmad, R. Noreen, S. G. Khan, H. Ahmad, *Mol. Diversity*, **2022**, *26*, 647–689. DOI: 10.1007/s11030-021-10195-6
4. B. S. Takale, F.-Y. Kong, R. R. Thakore, *Organics*, **2022**, *3*, 1–21. DOI: 10.3390/org3010001
5. M. J. Buskes, M.-J. Blanco, *Molecules*, **2020**, *25*, 3493. DOI: 10.3390/molecules25153493
6. Nobel Prizes 2010: Richard F. Heck, Ei-ichi Negishi, Akira Suzuki, *Angew. Chem., Int. Ed.*, **2010**, *49*, 8300. DOI: 10.1002/anie.201006286
7. A. D. Martin, A. R. Siamaki, K. Belecki, B. F. Gupton, *J. Org. Chem.*, **2015**, *80*, 1915–1919. DOI: 10.1021/jo5025333
8. C. Zhang, G. Zheng, L. Fang, Y. Li, *Synlett*, **2006**, *3*, 0475–0477. DOI: 10.1055/s-2006-926234
9. M. P. Carroll, H. Moloney, O. Gowran, A. O'Connor, E. M. Wilson, M. M. Murray, M. A. Pietz, D. P. Kjell, C. B. Held, M. O. Frederick, *Org. Process Res. Dev.*, **2019**, *23*, 2549–2555. DOI: 10.1021/acs.oprd.9b00347
10. C. Vijayalakshmi, M. G. Prasad, N. K. Katari, P. N. Reddy, *Lett. Org. Chem.*, **2020**, *17*, 68–72. DOI: 10.2174/1570178616666190514080155
11. *Palladacycles. Synthesis, Characterization and Application*, J. Dupont, M. Pfeffer (Eds.), Wiley, Weinheim, **2008**. DOI: 10.1002/9783527623211
12. C. S. Paladi, D. A. M. da Silva, P. D. Motta, D. M. Garcia, D. Teixeira, I. M. Longo-Maugéri, S. Katz, C. L. Barbiéri, *Front. Microbiol.*, **2017**, *8*, 333. DOI: 10.3389/fmicb.2017.00333
13. J. Albert, J. Granell, J. A. Durán, A. Lozano, A. Luque, A. Mate, J. Quirante, M. K. Khosa, C. Calvis, R. Messeguer, L. Baldomà, J. Badia, *J. Organomet. Chem.*, **2017**, *839*, 116–125. DOI: 10.1016/J.JORGANCHEM.2017.04.002
14. O. Zalevskaya, Y. Gur'eva, A. Kutchin, K. A. Hansford, *Antibiotics*, **2020**, *9*, 277. DOI: 10.3390/antibiotics9050277
15. O. A. Zalevskaya, Ya. A. Gur'eva, A. V. Kutchin, *Russ. Chem. Rev.*, **2023**, *92*, RCR5093. DOI: 10.59761/RCR5093
16. M. Adams, C. de Kock, P. J. Smith, K. Chibale, G. S. Smith, *J. Organomet. Chem.*, **2013**, *736*, 19–26. DOI: 10.1016/j.jorganchem.2013.02.024
17. M. N. Alam, F. Huq, *Coord. Chem. Rev.*, **2016**, *316*, 36–67. DOI: 10.1016/j.ccr.2016.02.001
18. V. A. Kozlov, D. V. Aleksanyan, S. G. Churusova, A. A. Spiridonov, E. Yu. Rybalkina, E. I. Gutsul, S. A. Aksenova, A. A. Korlyukov, A. S. Peregudov, Z. S. Klemenkova, *Int. J. Mol. Sci.*, **2023**, *24*, 17331. DOI: 10.3390/ijms242417331
19. A. van Niekerk, A. Blanckenberg, S. Kimani, S. Chakraborty, S. Prince, P. Chellan, S. Mapolie, *J. Inorg. Biochem.*, **2023**, *243*, 112191. DOI: 10.1016/j.jinorgbio.2023.112191
20. J. S. Bleloch, A. du Toit, L. Gibhard, S. Kimani, R. D. Ballim, M. Lee, A. Blanckenberg, S. Mapolie, L. Wiesner, B. Loos, S. Prince, *Cell Death Discovery*, **2019**, *5*, 60. DOI: 10.1038/s41420-019-0139-9
21. V. V. Dunina, O. N. Gorunova, P. A. Zykov, K. A. Kochetkov, *Russ. Chem. Rev.*, **2011**, *80*, 51–74. DOI: 10.1070/rc2011v080n01abeh004151
22. W. A. Herrmann, C. Brossmer, K. Öfele, C.-P. Reisinger, T. Priermeier, M. Beller, H. Fischer, *Angew. Chem., Int. Ed.*, **1995**, *34*, 1844–1848. DOI: 10.1002/anie.199518441
23. N. Hazari, P. R. Melvin, M. M. Beromi, *Nat. Rev. Chem.*, **2017**, *1*, 0025. DOI: 10.1038/s41570-017-0025
24. R. B. Bedford, in: *Palladacycles. Synthesis, Characterization and Applications*, J. Dupont, M. Pfeffer (Eds.), Wiley, Weinheim, **2008**, ch. 9, pp. 209–225. DOI: 10.1002/9783527623211.ch9
25. *Palladacycles: Catalysis and Beyond*, A. Kapdi, D. Maiti (Eds.), Elsevier, Amsterdam, **2019**. DOI: 10.1016/C2017-0-03671-6
26. K. Karami, M. Hosseini-Kharat, Z. Shirani-Sarmazeh, R. Zahedi-Nasab, C. Rizzoli, J. Lipkowski, *J. Coord. Chem.*, **2016**, *69*, 763–778. DOI: 10.1080/00958972.2016.1151876
27. A. Kumbhar, *J. Organomet. Chem.*, **2019**, *881*, 79–129. DOI: 10.1016/j.jorganchem.2018.09.020
28. J. Dupont, C. S. Consorti, J. Spencer, *Chem. Rev.*, **2005**, *105*, 2527–2572. DOI: 10.1021/cr030681r
29. C. Nájera, *ChemCatChem*, **2016**, *8*, 1865–1881. DOI: 10.1002/cctc.201600035
30. J. M. Vila, M. T. Pereira, F. Lucio-Martínez, F. Reigoza, in: *Palladacycles. Catalysis and Beyond*, A. Kapdi, D. Maiti (Eds.), Elsevier, Amsterdam, **2019**, ch. 1, pp. 1–20. DOI: 10.1016/B978-0-12-815505-9.00002-0
31. P. Das, W. Linert, *Coord. Chem. Rev.*, **2016**, *311*, 1–23. DOI: 10.1016/j.ccr.2015.11.010
32. A. Naghipour, M. Sayadi, A. Sedghi, S. J. Sabounchei, H. Babaee, B. Notash, *Inorg. Chim. Acta*, **2021**, *515*, 120039. DOI: 10.1016/j.ica.2020.120039
33. O. N. Gorunova, M. P. Timerkaeva, K. A. Kochetkov, V. V. Dunina, *Russ. Chem. Bull.*, **2024**, *73*, 733–737. DOI: 10.1007/s11172-024-4184-z
34. F. Puls, N. Richter, O. Kataeva, H.-J. Knoelker, *Chem. Eur. J.*, **2017**, *23*, 17576–17583. DOI: 10.1002/chem.201703926
35. S. Handa, M. P. Andersson, F. Gallou, J. Reilly, B. H. Lipshutz, *Angew. Chem., Int. Ed.*, **2016**, *55*, 4914–4918. DOI: 10.1002/anie.201510570
36. E. B. Landstrom, S. Handa, D. H. Aue, F. Gallou, B. H. Lipshutz, *Green Chem.*, **2018**, *20*, 3436–3443. DOI: 10.1039/C8GC01356J
37. B. S. Takale, R. R. Thakore, S. Handa, F. Gallou, J. Reilly, B. H. Lipshutz, *Chem. Sci.*, **2019**, *10*, 8825–8831. DOI: 10.1039/c9sc02528f
38. R. R. Thakore, B. S. Takale, F. Gallou, J. Reilly, B. H. Lipshutz, *ACS Catal.*, **2019**, *9*, 11647–11657. DOI: 10.1021/acscatal.9b04204
39. M. Trojanowicz, *Molecules*, **2020**, *25*, 1434. DOI: 10.3390/molecules25061434
40. J. D. Sieber, F. Buono, A. Brusoe, J.-N. Desrosiers, N. Haddad, J. C. Lorenz, Y. Xu, H. Wu, L. Zhang, Z. S. Han, F. Roschangar, J. J. Song, N. K. Yee, C. H. Senanayake, *J. Org. Chem.*, **2019**, *84*, 4926–4931. DOI: 10.1021/acs.joc.8b03040
41. X. Han, H.-M. Li, C. Xu, Z.-Q. Xiao, Z.-Q. Wang, W.-J. Fu, X.-Q. Hao, M.-P. Song, *Transition Met. Chem.*, **2016**, *41*, 403–411. DOI: 10.1007/s11243-016-0036-5
42. S. Samiee, F. E. Noorabadi, R. Azadi, *Polyhedron*, **2021**, *195*, 114973. DOI: 10.1016/j.poly.2020.114973
43. R. Firinci, *J. Mol. Struct.*, **2019**, *1195*, 246–251. DOI: 10.1016/j.molstruc.2019.05.129
44. R. H. Fath, S. J. Hoseini, *J. Organomet. Chem.*, **2017**, *828*, 16–23. DOI: 10.1016/j.jorganchem.2016.11.016
45. A. Fizia, M. Gaffga, J. Lang, Y. Sun, G. Niedner-Schatteburg, W. R. Thiel, *Chem. Eur. J.*, **2017**, *23*, 14563–14575. DOI: 10.1002/chem.201702877
46. P. Bellotti, M. Koy, M. N. Hopkinson, F. Glorius, *Nat. Rev. Chem.*, **2021**, *5*, 711–725. DOI: 10.1038/s41570-021-00321-1

47. R. Firinci, G. M. Gü, A. G. Gökce, *Appl. Organomet. Chem.*, **2018**, *32*, e4109. DOI: 10.1002/aoc.4109
48. B. Zuo, H. Shao, E. Qu, Y. Ma, W. Li, M. Huang, Q. Deng, *ChemistrySelect*, **2021**, *6*, 10121–10126. DOI: 10.1002/slct.202102733
49. M. E. Günay, R. Gümüşada, N. Özdemir, M. Dinçer, B. Çetinkaya, *J. Organomet. Chem.*, **2009**, *694*, 2343–2349. DOI: 10.1016/j.jorganchem.2009.03.034
50. B. Zuo, Z. Lu, X. Wu, W. Fang, W. Li, M. Huang, D.-Y. Yang, Q. Deng, T. Tu, *Asian J. Org. Chem.*, **2021**, *10*, 3233–3236. DOI: 10.1002/ajoc.202100592
51. Q. Deng, Q. Zheng, B. Zuo, T. Tu, *Green Synth. Catal.*, **2020**, *1*, 75–78. DOI: 10.1016/j.gresc.2020.06.001
52. S. Samiee, A. Shiralinia, E. Hoveizi, R. W. Gable, *Inorg. Chim. Acta*, **2022**, *538*, 120964. DOI: 10.1016/j.ica.2022.120964
53. S. Samiee, A. Shiralinia, E. Hoveizi, R. W. Gable, *J. Organomet. Chem.*, **2019**, *900*, 120927. DOI: 10.1016/j.jorganchem.2019.120927
54. A. Shiralinia, S. Samiee, E. Hoveizi, *J. Coord. Chem.*, **2021**, *74*, 2542–2557. DOI: 10.1080/00958972.2021.1993206
55. S. Samiee, A. Shiralinia, E. Hoveizi, R. W. Gable, *Appl. Organomet. Chem.*, **2019**, *33*, e5098. DOI: 10.1002/aoc.5098
56. H.-J. Cho, S. Jung, S. Kong, S.-J. Park, S.-M. Lee, Y.-S. Lee, *Adv. Synth. Catal*., **2014**, *356*, 1056–1064. DOI: 10.1002/adsc.201300499
57. Y.-C. Yang, P. H. Toy, *Synlett*, **2014**, *25*, 1319–1324. DOI: 10.1055/s-0033-1341054
58. F. Ghahramani, Y. Mansoori, A. Bezaatpour, D. Esquivel, M. A. Navarro, *Catal. Surv. Asia*, **2023**, *27*, 232–245. DOI: 10.1007/s10563-023-09396-w
59. R. Wang, S. Li, J. Li, J. Wei, *Appl. Organomet. Chem*., **2019**, *33*, e5226. DOI: 10.1002/aoc.5226
60. S.-J. Park, H.-J. Cho, S.-M. Lee, Y.-S. Lee, *Tetrahedron Lett.*, **2017**, *58*, 2670–2674. DOI: 10.1016/j.tetlet.2017.05.080
61. M. Gómez-Martínez, A. Baeza, D. A. Alonso, *Catalysts*, **2017**, *7*, 94. DOI: 10.3390/catal7030094
62. I. Babahan, R. Firinci, N. Özdemir, M. E. Günay, *Inorg. Chim. Acta*, **2021**, *522*, 120360. DOI: 10.1016/j.ica.2021.120360
63. B. Bermúdez-Puente, L. A. Adrio, F. Lucio-Martínez, F. Reigosa, J. M. Ortigueira, J. M. Vila, *Molecules*, **2022**, *27*, 3146. DOI: 10.3390/molecules27103146
64. J. L. Serrano, L. García, J. Pérez, P. Lozano, J. Correia, S. Kori, A. R. Kapdi, Y. S. Sanghvi, *Organometallics*, **2020**, *39*, 4479–4490. DOI: 10.1021/acs.organomet.0c00580
65. J. L. Serrano, *Chem. Rec.*, **2022**, *22*, e202200179. DOI: 10.1002/tcr.202200179
66. *Fluorescent Analogs of Biomolecular Building Blocks: Design and Application*, M. Wilhelmsson, Y. Tor (Eds.), Wiley, Hoboken, **2016**.
67. G. Hervé, C. Len, *Sustain. Chem. Process*, **2015**, *3*, 3. DOI: 10.1186/s40508-015-0029-2
68. S. Gaware, S. Kori, J. L. Serrano, R. Dandela, S. Hilton, Y. S. Sanghvi, A. R. Kapdi, *J. Flow Chem.*, **2023**, *13*, 293–310. DOI: 10.1007/s41981-023-00265-1
69. O. N. Gorunova, Yu. K. Grishin, M. M. Ilyin, K. A. Kochetkov, A. V. Churakov, L. G. Kuz'mina, V. V. Dunina, *Russ. Chem. Bull.*, **2017**, *66*, 282–292. DOI: 10.1007/s11172-017-1729-4
70. L. A. Bulygina, N. S. Khrushcheva, K. A. Lyssenko, A. S. Peregudov, *J. Organomet. Chem.*, **2019**, *887*, 64–70. DOI: 10.1016/j.jorganchem.2019.02.017
71. *Pincer and Pincer-Type Complexes: Applications in Organic Synthesis and Catalysis*, K. J. Szabó, O. F. Wendt (Eds.), Wiley, Weinheim, **2014**. DOI: 10.1002/9783527681303
72. M. Camacho-Espinoza, A. Reyes-Deloso, R. A. Toscano, J. G. Penieres-Carrillo, J. G. López-Cortés, M. C. Ortega-Alfaro, F. Ortega-Jiménez, *New J. Chem.*, **2019**, *43*, 12967–12978. DOI: 10.1039/c9nj02977j
73. N. K. Sinha, N. Thirupathi, *ChemistrySelect*, **2022,** *7,* e202202778. DOI: 10.1002/slct.202202778
74. L. A. Bulygina, N. D. Kagramanov, N. S. Khrushcheva, K. A. Lyssenko, A. S. Peregudov, V. I. Sokolov, *J. Organomet. Chem.*, **2017**, *846*, 169–175. DOI: 10.1016/j.jorganchem.2017.06.009
75. L. A. Bulygina, N. S. Khrushcheva, K. A. Lyssenko, A. S. Peregudov, *Mendeleev Commun.*, **2022**, *32*, 331–333. DOI: 10.1016/j.mencom.2022.05.012
76. X.-Q. Hao, Y.-N. Wang, J.-R. Liu, K.-L. Wang, J.-F. Gong, M.-P. Song, *J. Organomet. Chem.*, **2010**, *695*, 82–89. DOI: 10.1016/j.jorganchem.2009.09.031
77. H. Qian, T. Zhang, Z. Yin, Q. Wang, Q. Yuan, R. Jiang, S. Yan, X. Zhao, *J. Organomet.* Chem., **2016**, *824*, 124–130. DOI: 10.1016/j.jorganchem.2016.10.006
78. O. N. Gorunova, P. A. Zykov, M. V. Livantsov, K. A. Kochetkov, Yu. K. Grishin, V. V. Dunina, *Russ. Chem. Bull*., **2010**, *59*, 1840–1842. DOI: 10.1007/s11172-010-0322-x
79. C. Xu, H.-M. Li, Z.-Q. Wang, W.-J. Fu, *Inorg. Chim. Acta.*, **2014**, *423*, 11–15. DOI: 10.1016/j.ica.2014.07.037
80. A. K. Sharma, H. Joshi, R. Bhaskar, S. Kumar, A. K. Singh, *Dalton Trans.*, **2017**, *46*, 2485–2496. DOI: 10.1039/c7dt00083a
81. H.-M. Li, C. Xu, L.-M. Duan, X.-H. Lou, Z.-Q. Wang, Z. Li, Y.-T. Fan, *Transition Met. Chem.*, **2013**, *38*, 313–318. DOI: 10.1007/s11243-013-9695-7
82. C. Xu, H.-M. Li, H. Liu, Z.-Q. Zhang, Z.-Q. Wang, W.-J. Fu, Y.-Q. Zhang, *Inorg. Chim. Acta.*, **2012**, *386*, 22–26. DOI: 10.1016/j.ica.2012.01.063
83. S.-Z. Bai, C. Xu, H.-M. Li, Z.-Q. Wang, W.-J. Fu, *Molecules*, **2012**, *17*, 5532–5543. DOI: 10.3390/molecules17055532
84. C. Xu, Z.-Q. Wang, Y.-P. Zhang, X.-M. Dong, X.-Q. Hao, W.-J. Fu, B.-M. Ji, M.-P. Song, *Eur. J. Inorg. Chem.*, **2011**, *31*, 4878–4888. DOI: 10.1002/ejic.201100617
85. L. A. Bulygina, N. S. Khrushcheva, K. A. Lyssenko, A. A. Anisimov, A. S. Peregudov, *Transition Met. Chem.*, **2022**, *47*, 39–46. DOI: 10.1007/s11243-021-00486-0
86. J. Ma, X. Cui, B. Zhang, M. Song, Y. Wu, *Tetrahedron*, **2007**, *63*, 5529–5538. DOI: 10.1016/j.tet.2007.04.022
87. B. Mu, T. Li, J. Li, Y. Wu, *J. Organomet. Chem.*, **2008**, *693*, 1243–1251. DOI: 10.1016/j.jorganchem.2008.01.012
88. C. Xu, J.-F. Gong, Y.-H. Zhang, Y. Zhu, Y.-J. Wu, *Aust. J. Chem.*, **2007**, *60*, 190–195. DOI: 10.1071/CH07014
89. L. Yan, L. Han, R. Xie, *J. Coord. Chem.*, **2019**, *72*, 2705–2721. DOI: 10.1080/00958972.2019.1662898
90. K. Wang, H. Yang, F. Bauer, B. Breit, W. Fang, *Chem. Eur. J.*, **2023**, *29*, e202300719. DOI: 10.1002/chem.202300719
91. M. Stahlberger, N. Schwarz, C. Zippel, J. Hohmann, M. Nieger, Z. Hassan, S. Bräse, *Chem. Eur. J.*, **2022**, *28*, e202103511. DOI: 10.1002/chem.202103511
92. M. Rúa-Sueiro, P. Munín-Cruz, S. Bermúdez-Fernández, J. M. Vila, *Chem. Proc.*, **2022**, *6*, 10. DOI: 10.3390/ECCS2021-11034

This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.