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C,N-Palladacycle based on *N,N*-dimethyl-*N*-(diphenylmethyl)amine as an effective phosphine-free (pre)catalyst for the Suzuki–Miyaura cross-coupling

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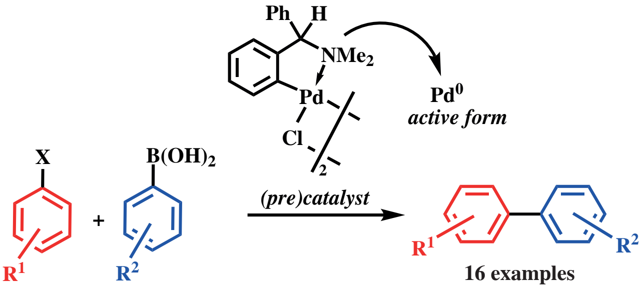
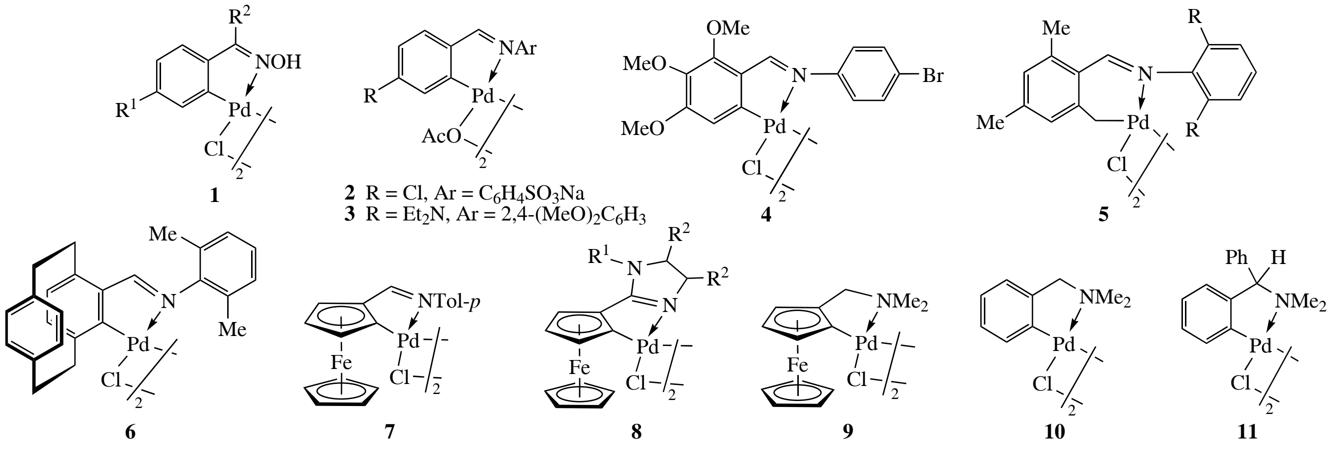
Phosphine-free cyclopalladated binuclear complex based on *N*,*N*-dimethyl-*N*-(diphenylmethyl)amine shows high catalytic efficiency for the Suzuki–Miyaura reaction of aryl halides with arylboronic acids under mild conditions. The catalytic process for the coupling is proved by dynamic light scattering analysis to proceed on Pd^0 nanoparticles. Palladium nanoparticles protected by tetrabutylammonium bromide and polyvinylpyrrolidone exhibit lower activities for the coupling reactions than those generated *in situ* without additives.



Keywords: binuclear C,N-palladacycle, Suzuki–Miyaura cross-coupling, phosphine-free catalysts, palladium nanoparticles, aryl halides, biaryls.

Cross-coupling reactions represent one of the most popular methods for the C–C bond formation.[1–6] Among them, the Suzuki–Miyaura reaction is of great practical importance due to its tolerance to various functional groups, low organoborane toxicity, and availability of substrates.[7–11] For the past 30 years cyclopalladated complexes (CPCs) have been successfully used as effective (pre)catalysts for the Suzuki–Miyaura reaction.[12–16] P-Donor ligands are often used as additional ligands in such systems, the role of which in the catalysis of cross-coupling is well known.[16–20] On the other hand, the application of phosphine ligands requires, as a rule, an inert atmosphere, additional costs associated with their synthesis; their toxicity is also well known. From this point of view, the search for catalytic systems devoid of these disadvantages remains an actual objective. Binuclear C,N-palladacycles can serve as a successful alternative since they are resistant to moisture and atmospheric oxygen and are readily available from a large number of N-donor ligands. Their high catalytic activity in the Suzuki–Miyaura reaction is well known. While oximate **1**[21] and iminate dimers **2**–**5**[22–26] are effective (pre)catalysts for the standard version of this reaction, C,N-palladacycle **6**[27] has shown particular efficiency in asymmetric Suzuki–Miyaura coupling. Binuclear CPCs with a ferrocene backbone **7**,[28] **8**[29] and **9**[30] also were highly effective in the Suzuki–Miyaura cross-coupling (Figure 1).

We have recently shown that the catalytic activity of commercially available dimer **10** based on *N*-benzyl-*N*,*N*-dimethylamine in the Suzuki–Miyaura reaction is comparable to that of its numerous derivatives.[31] The related study[32] on catalytic activity of a series of benzylaminate binuclear α-C-substituted azapalladacycles revealed that binuclear CPC **11** based on *N*,*N*-dimethyl-*N*-(diphenylmethyl)amine proved to be the most effective (pre)catalyst in this series.



1

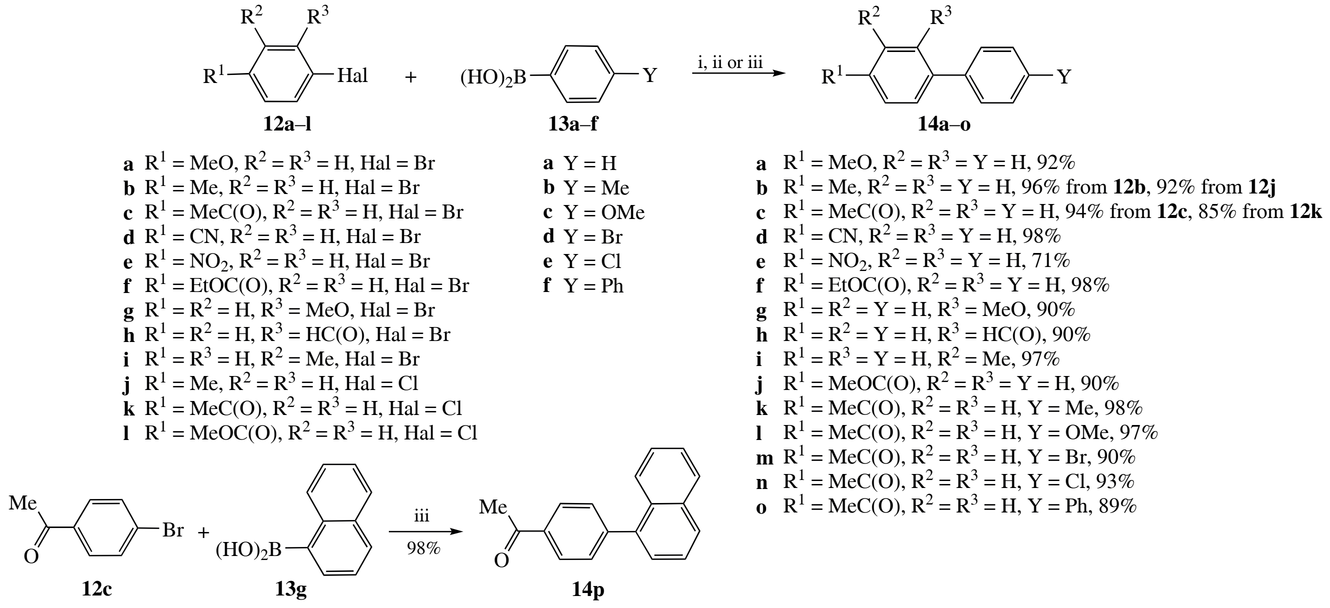
2 R = Cl, Ar = $C_6H_4SO_3Na$
3 R = Et_2N, Ar = 2,4-$(MeO)_2C_6H_3$

4

5

6 **7** **8** **9** **10** **11**

Figure 1 Known binuclear C,N-palladacycles as (pre)catalysts for the Suzuki–Miyaura reaction.



a R^1 = MeO, $R^2 = R^3$ = H, Hal = Br
b R^1 = Me, $R^2 = R^3$ = H, Hal = Br
c R^1 = MeC(O), $R^2 = R^3$ = H, Hal = Br
d R^1 = CN, $R^2 = R^3$ = H, Hal = Br
e R^1 = NO_2, $R^2 = R^3$ = H, Hal = Br
f R^1 = EtOC(O), $R^2 = R^3$ = H, Hal = Br
g $R^1 = R^2$ = H, R^3 = MeO, Hal = Br
h $R^1 = R^2$ = H, R^3 = HC(O), Hal = Br
i $R^1 = R^3$ = H, R^2 = Me, Hal = Br
j R^1 = Me, $R^2 = R^3$ = H, Hal = Cl
k R^1 = MeC(O), $R^2 = R^3$ = H, Hal = Cl
l R^1 = MeOC(O), $R^2 = R^3$ = H, Hal = Cl

a Y = H
b Y = Me
c Y = OMe
d Y = Br
e Y = Cl
f Y = Ph

a R^1 = MeO, $R^2 = R^3$ = Y = H, 92%
b R^1 = Me, $R^2 = R^3$ = Y = H, 96% from **12b**, 92% from **12j**
c R^1 = MeC(O), $R^2 = R^3$ = Y = H, 94% from **12c**, 85% from **12k**
d R^1 = CN, $R^2 = R^3$ = Y = H, 98%
e R^1 = NO_2, $R^2 = R^3$ = Y = H, 71%
f R^1 = EtOC(O), $R^2 = R^3$ = Y = H, 98%
g $R^1 = R^2$ = Y = H, R^3 = MeO, 90%
h $R^1 = R^2$ = Y = H, R^3 = HC(O), 90%
i $R^1 = R^3$ = Y = H, R^2 = Me, 97%
j R^1 = MeOC(O), $R^2 = R^3$ = Y = H, 90%
k R^1 = MeC(O), $R^2 = R^3$ = H, Y = Me, 98%
l R^1 = MeC(O), $R^2 = R^3$ = H, Y = OMe, 97%
m R^1 = MeC(O), $R^2 = R^3$ = H, Y = Br, 90%
n R^1 = MeC(O), $R^2 = R^3$ = H, Y = Cl, 93%
o R^1 = MeC(O), $R^2 = R^3$ = H, Y = Ph, 89%

Scheme 1 *Reagents and conditions*: i, cat. **11**, 0.1 mol% [Pd], KF, MeOH, 20 °C, 5 h (for **12a–i**); ii, cat. **11**, 1 mol% [Pd], KF, MeOH, 65 °C, 1 h (for **12j–l**); iii, cat. **11**, 0.1 mol% [Pd], KF, MeOH, 65 °C, 2 h (for **12c** and **14k–p**).

In this communication, we expanded the use of C,N-palladacycle based on *N*,*N*-dimethyl-*N*-(diphenylmethyl)amine in phosphine-free catalysis for the Suzuki–Miyaura reaction toward other aryl halogenides and also conducted additional studies to establish the nature of the active particles. Dimer **11** was synthesized in high yield by the described method[33] by reacting palladium acetate with *N*,*N*-dimethyl-*N*-(diphenylmethyl)amine. In the test reaction between model 4-bromoanizole **12a** and phenylboronic acid **13a** when (pre)catalyst **11** was loaded in 0.1 mol% [Pd] amount, the target biaryl **14a** was formed in 98% yield under mild conditions (Scheme 1). When reducing the catalyst loading to 0.01 mol% [Pd], the efficiency of the process could be maintained by raising the temperature to 65 °C.[32]

The limits of the applicability of binuclear complex **11** as a catalyst were estimated in the Suzuki–Miyaura reaction of a variety of aryl bromides **12a–i** (with both electron-acceptor and electron-donor substituents) with phenylboronic acid **13a** (see Scheme 1). We chose KF because the reactions are known to be faster in the presence of this base.[34,35] At room temperature, the target products **14a–i** were obtained in high yields of 71–98%.

Complex **11** was also examined as (pre)catalyst in the Suzuki–Miyaura coupling of less reactive, but affordable aryl chlorides **12j–l** (see Scheme 1). The target products **14b**,**c**,**j** were formed in high yields (85–92%) from substrates having either electron-acceptor (COMe, CO_2Me) **12k**,**l** or electron-donating (Me) **12j** groups, however the processing was performed at 65 °C for 1 h. Also, in the reaction of methyl 4-chlorobenzoate **12l** with $PhB(OH)_2$ **13a** the product **14j** was formed in high yield (89%) at room temperature, although within 9 h. It should be noted that the cross-coupling of methyl 4-chlorobenzoate **12l** with $PhB(OH)_2$ **13a** in the presence of K_3PO_4 or K_2CO_3 in EtOH was accompanied by complete hydrolysis of the ester to produce salts of the corresponding carboxylic acid. A similar matter occurred for the reaction of methyl 4-bromobenzoate with $PhB(OH)_2$ in the presence of K_3PO_4.[36]

To further extend the scope of application of binuclear (pre)-catalyst **11** (0.1 mol% [Pd], KF, MeOH, 20 °C), a diverse arylboronic acids **13b–g** were tested. In the case of 4-bromoacetophenone **12c**, the yields of products **14k–p** were moderate (33–85%). However, these yields were essentially improved (89–98%) when the reaction temperature was raised to 65 °C (see Scheme 1, conditions iii).

The efficiency of dimer **11** as a (pre)catalyst was compared with that of other phosphine-free palladacycles and $Pd(OAc)_2$ using a cross-coupling of 4-bromoacetophenone with phenylboronic acid (see Online Supplementary Materials, Table S1).

In almost all reactions catalyzed by palladacycle **11**, a color change in the reaction mixture from colorless to brownish was observed, which indicated the *in situ* formation of Pd^0 nanoparticles, presumably *via* the reduction of Pd^{II} centers with the organoboron reagent (phenylboronic acid) under basic conditions, a well-documented pathway in Pd-catalyzed cross-coupling reactions.

Several mechanistic studies were performed to understand the nature of the active particles formed from dimer **11** during the catalysis between 4-bromoacetophenone **12c** and $PhB(OH)_2$ **13a** as the reactants (0.1 mol% [Pd], KF, MeOH, 20 °C, 3 h). The mercury test is often used to evaluate the mechanism of cross-coupling, however in cases of palladacycles it is inapplicable without control experiments. We have previously established that when Hg^0 was added to the Suzuki–Miyaura reaction mixture catalyzed by iminate binuclear C,N-palladacycle, instead of palladium amalgamation or adsorption on its surface the redox transmetalation was observed with the formation of organomercuric chlorides.[27,37] Later, it was shown that the interaction of various aza- and phosphapalladacycles with metallic mercury also led to the formation of organomercuric chlorides during redox transmetalation.[38,39]

Sulfides are effective poisons for various metal catalysts due to their strong and preferred binding to the metal center compared to other ligands.[40–42] When an excess of carbon disulfide CS_2 was added to the catalytic system, we observed a complete inhibition of the reaction between **12c** and **13a**. We also tested the effect of nanoparticle stabilizers such as tetrabutylammonium bromide (Bu_4NBr) and polyvinylpyrrolidone (PVP). When 1 equiv. (relative to substrate) of Bu_4NBr was added, the conversion dropped to 7%, while at 0.1 equiv., the reaction proceeded with 55% conversion. In contrast, 0.1 equiv. of PVP completely inhibited the reaction (0% conversion). This strong inhibitory effect suggests that a large excess of stabilizer can block the catalyst active sites, with PVP showing particularly pronounced deactivation. The catalysis proceeds in the absence of additives with 57% conversion. Palladium(0) nanoparticles with a diameter of ~2 nm were detected in the reaction mixture by dynamic light scattering.

In conclusion, binuclear C,N-palladacycle **11** is a universal and highly effective (pre)catalyst in the Suzuki–Miyaura reaction for a wide range of aryl halides and arylboronic acids. The main advantages of this phosphine-free dimer include no need for inert atmosphere, low catalyst loads, and mild conditions. Mechanical tests confirmed the formation of Pd^0 nanoparticles in the reaction mixture.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.71267/mencom.7836.

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