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Synthesis of unsymmetrical pincer CNN palladium complex of 8-dimethylamino-3-ferrocenylmethyl-3-azabicyclo[3.2.1]octane and its catalytic activity in the Suzuki reaction

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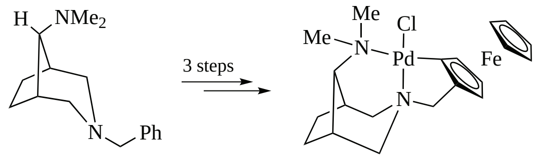
New bicyclic unsymmetrical CNN palladium 5,6-membered pincer complex was synthesized from 3-ferrocenylmethyl-8-dimethylamino-3-azabicyclo[3.2.1]octane by its direct cyclopalladation with Li_2PdCl_4 or Na_2PdCl_4 and sodium acetate in MeOH. The obtained complex exhibited high catalytic activity in the Suzuki cross-coupling between aryl bromides and phenylboronic acid.



Catalyst for the Suzuki reaction

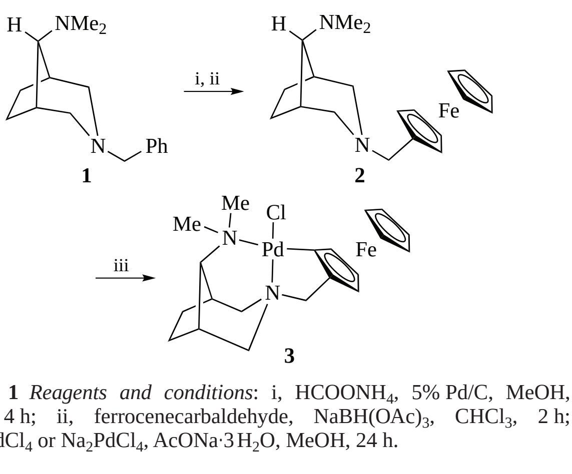
Keywords: unsymmetrical pincer complexes, palladium complexes, ferrocene, bicyclic ligand precursor, Suzuki reaction.

Cyclopalladated pincer complexes have been intensively investigated in recent years mainly due to their high stability, possibility of structural modification and significant catalytic activities in organometallic catalysis. They are found to be effective catalysts for the allylation of aldehydes and imines, Diels–Alder, Friedel–Crafts, cross-coupling (Heck, Suzuki, Sonogashira) and other reactions.[1–6] Among the plethora of palladium pincer CNN complexes that have been already synthesized, only a few examples of ferrocene CNN palladacycles have been reported[7–12] and their catalytic properties in the cross-coupling reactions were studied, to our knowledge, only in respect of two of them.[11,12] More of that, heterometallic complexes of transition metals including Pd with the ferrocenyl unit incorporated in the scaffold are currently under intense investigation as potential antitumoral[13–15] and antimalarial[16,17] agents.

In most of known CNN unsymmetrical pincer complexes at least one of coordinating nitrogen atoms has a double or aromatic bond with carbon, that is, sp^2-hybridized one. In this work, we describe the synthesis of new bicyclic palladium CNN pincer complex based on the 3-azabicyclo[3.2.l]octane structure (Scheme 1) where the metal atom is coordinated with two sp^3-hybridized N atoms and examination of its catalytic activity in the Suzuki cross-coupling reactions of aryl halides with phenylboronic acid.

The unsymmetrical CNN pincer ligand precursor **2** was prepared from known[18] 3-benzyl-8-dimethylamino-3-azabicyclo[3.2.1]octane **1** (see Scheme 1). The cleavage of *N*-benzyl group using palladium on activated charcoal as a catalyst and ammonium formate as a hydrogen source and the subsequent reductive amination with ferrocenecarbaldehyde and sodium triacetoxyborohydride followed by column chromatography on Al_2O_3 afforded a 58% yield of **2**. The palladium pincer 5,6-membered complex **3** was prepared by direct cyclopalladation of the ligand precursor with Li_2PdCl_4 or Na_2PdCl_4 and sodium acetate trihydrate in MeOH in 86–87% yields. The structure of **3** was determined using NMR, IR, EI-MS spectral data, elemental analysis and X-ray single-crystal diffraction. The assignment of the signals in ^1H and ^{13}C NMR spectra has been performed using 2D COSY, HMQC and HMBC techniques.

The NMR spectrum data of complex **3** are consistent with *ortho*-metallation of ferrocene ring. The set of proton signals in the ferrocene region with an intensity of 2 : 5 : 2 in the ^1H NMR spectrum of ligand precursor **2** have changed to a set of 1 : 1 : 5 : 1 in the spectrum of complex **3**, confirming the occurrence of metallation. In the ^{13}C NMR spectrum of complex **3**, the resonance of the new quaternary aromatic carbon (C–Pd) is observed at 91.4 ppm, which is consistent with previously published data for other ferrocene cyclopalladated complexes.[11,19] The resonance of another aromatic quaternary carbon (C–C) in complex **3** is shifted downfield in comparison with that for starting ligand precursor ($\Delta\delta$ = 10 ppm) as it was noted for other bicyclic pincer complexes.[18,20] The structure of palladacycle **3**



Scheme 1 *Reagents and conditions*: i, $HCOONH_4$, 5% Pd/C, MeOH, reflux, 4 h; ii, ferrocenecarbaldehyde, $NaBH(OAc)_3$, $CHCl_3$, 2 h; iii, Li_2PdCl_4 or Na_2PdCl_4, $AcONa \cdot 3H_2O$, MeOH, 24 h.

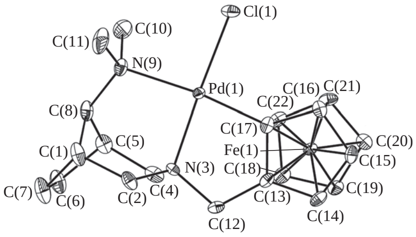


Figure 1 General view of the one of independent molecules of complex **3** in representations of atoms by thermal ellipsoids (p = 50%).

confirmed by X-ray single-crystal diffraction is shown in Figure 1.[†]

The palladium pincer complex **3** was tested as the precatalyst in the Suzuki cross-coupling reactions of phenylboronic acid with several aryl bromides in MeOH/H_2O for 5 h at 55 °C with K_2CO_3 as a base (Scheme 2). All experiments were conducted under the conditions similar to those we used earlier in studies of the catalytic activity of other CN or CNN palladium complexes. This allowed us to compare the results obtained in this and previous works. In the reaction of 4-bromoanisole **4a** with phenylboronic acid, the yield of 4-methoxybiphenyl **5a** turned out to be close to quantitative with the catalyst loads of 0.5 and 0.1 mol%, and the yield dropped with the catalyst load of 0.05 mol% (Table 1, entries 1–3). Subsequent reactions of other aryl bromides **4b**–**e** with phenylboronic acid with the catalyst load of 0.1 mol% lead to the corresponding biphenyls **5b**–**e** in high yields (entries 4–7). Close results were obtained during the study of the interaction of the same aryl bromides **4a**–**e** with phenylboronic acid under the same conditions using analogous CNN bicyclic pincer complex which contained phenyl unit instead of ferrocenyl one.[18] Therefore, it seems that the presence of a ferrocene moiety does not exert a noticeable effect on the catalytic activity of complex **3** in cross-coupling reactions. Nevertheless, bicyclic CNN Pd complex **3** with two sp^3-hybridized N atoms seems to be slightly more active catalyst for Suzuki cross-coupling than NCN pincer cyclopalladates with two sp^2-hybridized N atoms reported previously,[21,22] considering the slightly higher yield of the product under milder conditions in our case.

$$\underset{\textbf{4a–e}}{\text{ArBr}} + \text{PhB(OH)}_2 \xrightarrow{\text{i}} \underset{\textbf{5a–e}}{\text{Ar–Ph}}$$

a Ar = 4-MeOC$_6$H$_4$
b Ar = 4-MeC$_6$H$_4$
c Ar = 4-MeC(O)C$_6$H$_4$
d Ar = Ph
e Ar = 1-naphthyl

Scheme 2 *Reagents and conditions*: i, K_2CO_3, catalyst **3**, MeOH/H_2O (2 : 1), 55 °C, 5 h.

Table 1 The Suzuki cross-coupling between aryl bromides and phenylboronic acid catalyzed by complex **3**.

Entry	Aryl bromide		Catalyst load (mol%)	Product	Yield (%)[a]
	Ar	Code			
1	4-MeOC$_6$H$_4$	**4a**	0.5	**5a**	99
2	4-MeOC$_6$H$_4$	**4a**	0.1	**5a**	97
3	4-MeOC$_6$H$_4$	**4a**	0.05	**5a**	66
4	4-MeC$_6$H$_4$	**4b**	0.1	**5b**	94
5	4-MeC(O)C$_6$H$_4$	**4c**	0.1	**5c**	99
6	Ph	**4d**	0.1	**5d**	96
7	1-naphthyl	**4e**	0.1	**5e**	91
8[b]	4-MeOC$_6$H$_4$	**4a**	0.1	**5a**	90

[a] Isolated yields after column chromatography. [b] Na_2PdCl_4 was used instead of **3**.

It should be noted that trace amounts of palladium black are formed in the course of all studied reactions with complex **3**. Formation and interconversion of different palladium species during the catalytic process is a general feature of palladacyclic catalytic systems that do not contain phosphorus atom.[23,24] In the control experiment using Na_2PdCl_4 as a catalyst instead of **3** (see Table 1, entry 8), formation of noticeable amount of palladium black was observed (*cf*. ref. 25 indicating the instability of Na_2PdCl_4 in catalytic reactions).

In conclusion, new unsymmetrical pincer CNN 5,6-membered palladium complex based on the 3-azabicyclo[3.2.1]octane frame and containing ferrocene unit has been synthesized. The obtained complex appeared to be the efficient catalyst in some Suzuki cross-coupling reactions of aryl bromides.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2022.05.012.

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[†] *Crystal data for* **3**. $C_{20}H_{27}ClFeN_2Pd$ (M_r = 493.13), triclinic, space group $P\bar{1}$, a = 8.6005(13), b = 11.2153(17) and c = 19.128(3) Å, α = 86.644(3)°, β = 89.970(3)°, γ = 80.835(3)°, V = 1818.3(5) Å^3, Z = 2 (Z' = 1). The 14734 reflections were collected at 120(2) K using a Bruker APEX II diffractometer (MoK$_\alpha$ radiation, λ = 0.71073 Å, θ_{max} = 29°) and 9627 independent ones were used in further refinement. The structure was solved by direct methods and refined by the full-matrix least-squares technique against F^2 in the anisotropic-isotropic approximation with SHELXT and refined anisotropically for all non-hydrogen atoms with SHELXL. All hydrogen atoms were placed in geometrically calculated positions and refined within a riding model. A refinement with 9627 reflections and 456 parameters converged to ωR_2 = 0.1350 and R_1 = 0.0514 for 7521 reflections with $I > 2\sigma(I)$.

CCDC 2109389 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

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