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Application of the ferrocene-containing chelated palladacycles as catalysts in the Suzuki reaction

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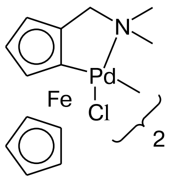
Two ferrocene-containing chelated palladacycles with the bi- and tridentate (C,N) and (C,N,N) ligands were used as catalysts in the Suzuki reaction. Both compounds were shown to be efficient catalysts.

Key words: Suzuki reaction, ferrocene-containing chelated palladacycles, catalysts.

In the previous report,[1] we have presented the results of investigation of the ferrocene-containing palladacycles **1** and **2** as catalysts in the Heck reaction. One of them, *viz.*, palladacycle **2** with tridentate ligand of the (C,N,N) type, is an efficient catalyst for this reaction in contrast to bispalladacycle **1** with the chelate node of the (C,N) type, which was unstable under drastic conditions (DMF, 140 °C).



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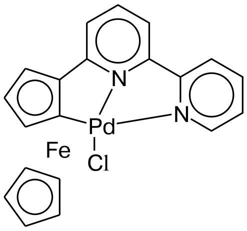

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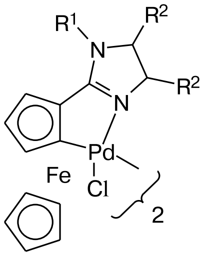
In the present work, we studied the possibility of application of compounds **1** and **2** as catalysts in the Suzuki reaction. It has been established earlier[2] that the structurally similar compounds **3** catalyze successfully the reaction of aryl halides with arylboronic acids even under mild conditions, *viz.*, in aqueous methanol at room temperature in the presence of K_2CO_3 and tetrabutylammonium bromide.



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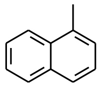
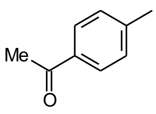
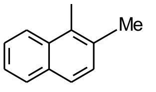
In addition, it has recently been shown[3] on the example of the reaction of 4-bromotoluene with phenylboronic acid that palladium complex **1** with the bidentate (C,N) ligand also catalyzes successfully the Suzuki reaction under the above-mentioned conditions and, moreover, it exhibits catalytic properties not only at room temperature, but also at 0 °C.

In order to confirm these results and broaden the range of compounds under study, we performed a series of experiments related to the reaction of phenylboronic acid (**4**) with aryl halides **5—10** in the presence of one of the palladium complexes, *i.e.*, **1** or **2**, and K_2CO_3 (Scheme 1, Table 1).

Scheme 1

4 **5—10** **11—16**

Reagents and conditions: **1** or **2**, K_2CO_3, MeOH, H_2O, 21 °C or 55 °C.

Compound	Ar	Compound	Ar
5, **11**	4-MeOC$_6$H$_4$	**8**, **14**	Ph
6, **12**	4-MeC$_6$H$_4$	**9**, **15**	
7, **13**	 Me, O	**10**, **16**	 Me

The conditions used in Refs 2 and 3 (aqueous methanol, room temperature, and K_2CO_3 as a base) were taken as a basis. However, we decided to perform the reaction

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Table 1. Reaction of phenylboronic acid (**4**) with aryl bromides **5—10** in the presence of catalysts **1** and **2**[a]

Entry	ArBr	Catalyst	T/°C	τ/h	Product	Yield (%)
1	4-$MeOC_6H_4Br$ (**5**)	**1**	21	0.5	**11**	95
2	4-MeC_6H_4Br (**6**)	**1**	21	0.5	**12**	95
3	4-$MeC(O)C_6H_4Br$ (**7**)	**1**	21	0.5	**13**	89
4	PhBr (**8**)	**1**	21	0.5	**14**	97
5	1-Br-naphthalene (**9**)	**1**	21	0.5	**15**	—[b]
6	1-Br-naphthalene (**9**)	**1**	21	48	**15**	76[c]
7	1-Br-naphthalene (**9**)	**1**	55	0.5	**15**	92
8	1-Br-2-Me-naphthalene (**10**)	**1**	55	15	**16**	44
9	4-$MeOC_6H_4Br$ (**5**)	**2**	55	5	**11**	88
10	4-MeC_6H_4Br (**6**)	**2**	55	5	**12**	70
11	4-$MeC(O)C_6H_4Br$ (**7**)	**2**	55	5	**13**	97
12	PhBr (**8**)	**2**	55	5	**14**	89
13	1-Br-naphthalene (**9**)	**2**	55	5	**15**	89
14	1-Br-2-Me-naphthalene (**10**)	**2**	55	5	**16**	70

[a] Reaction conditions: $PhB(OH)_2$ (3 mmol), ArBr (2 mmol), K_2CO_3 (4 mmol), catalyst **1** or **2** (0.5 mol.%), MeOH (8—12 mL), and water (4 mL). [b] According to the data from TLC, the reaction mixture contains trace amounts of product **15**. [c] MeOH (8 mL), water (4 mL), and toluene (4 mL).

without a phase-transfer catalyst, since, in our opinion, all components of the reaction mixture are sufficiently well-soluble in aqueous methanol. Under these conditions, the reaction of phenylboronic acid (**4**) with the sterically unhindered aryl halides **5—8** (see Table 1, Entries *1—4*) proceeds very fast in the presence of palladacycle **1**. The biaryl poorly soluble in methanol precipitated abundantly from the reaction mixture even 1 min after the reaction started and TLC (Silufol, hexane—chloroform, 9 : 1) indicated the absence of the starting aryl halides in the reaction mixture 10 min after the reaction started. After 30 min, the reaction mixtures were worked-up and chromatographed to give the corresponding biaryls in high yields.

When going to more sterically hindered halides of the naphthalene series, the reaction slowed down. For example, 30 min after begining of the reaction of phenylboronic acid (**4**) with 1-bromonaphthalene (**9**) under the above-mentioned conditions, the reaction mixture contained only small amount of the corresponding biaryl according to the data from TLC (see Table 1, Entry *5*). In addition, the starting naphthyl halides are poorly soluble in aqueous methanol. After addition of toluene to the reaction mixture and increase in the reaction time to 2 days, 1-bromonaphthalene (**9**) affords biaryl **15** in a good yield at room temperature (see Table 1, Entry *6*). When increasing the temperature to 55 °C, the reaction occurs in 30 min almost quantitatively (see Table 1, Entry *7*). The sterically more hindered 1-bromo-2-methylnaphthalene (**10**) forms biaryl **16** in a low yield even upon heating for 15 h (see Table 1, Entry *8*).

In subsequent experiments, we used palladacycle **2** with the tridentate (C,N,N) ligand as the catalyst. It was found that phenylboronic acid (**4**) does not react with aryl bromides in the presence of catalyst **2** at room temperature and no expected product was observed (TLC) even after 1 day. Also, no formation of biaryls occurs when passing from K_2CO_3 to CsF. However, when increasing the temperature to 55 °C, the reaction was over in 5 h to give high yields of products (see Table 1, Entries *9—14*). It should be noted that, in the presence of catalyst **2**, the very sterically hindered 1-bromo-2-methylnaphthalene (**10**) forms biaryl **16** with a noticeably better yield than in the reaction using catalyst **1** (see Table 1, *cf.* Entries *8* and *14*).

The obtained results allow one to conclude that both ferrocene-containing palladacycles studied can be used as catalysts in the Suzuki reaction. The binuclear palladacycle **1** is efficient at room temperature, whereas the best results for the palladium complex **2** with the tridentate (C,N,N) ligand were obtained upon heating. Earlier[1], we suggested that catalyst **2** acts according to the associative mechanism with increase in the coordination number of palladium. It is likely that the formation of this intermediate requires overcoming of a comparatively high-energy barrier, which explains the necessity for heating in order that palladacycle **2** showed its catalytic properties.

Finally, we studied the reaction of the sterically hindered 2-methylnaphthyl-1-boronic acid (**17**) with 4-bromoanisole (**5**) in the presence of the palladium complexes **1** and **2** (Scheme 2, Table 2).

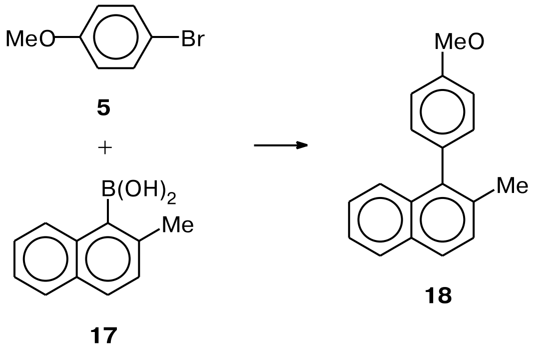
When performing the reaction in aqueous methanol in the presence of complex **1** and K_2CO_3 at room temperature, 2-methylnaphthalene that formed upon deboronation was the only reaction product after 5 h (see Table 2, Entry *1*). Under the conditions that are most favorable for the reaction of boronic acid **17** with aryl halides[4] (catalyst **1**, CsF, THF, 65 °C), we succeeded in isolating biaryl **18**

Table 2. Reaction of 2-methylnaphthyl-1-boronic acid (**17**) with 4-bromoanisole (**5**)

Entry	Molar ratio **17** : **5**	Base (mmol)	Catalyst (mol.%)	Solvent (*V*/mL)	*T*/°C	τ/h	Yield of compound **18** (%)
1	3 : 2	K_2CO_3 (4)	**1** (0.5)	MeOH (12), H_2O (4)	21	5	—*
2	1.4 : 0.8	CsF (3)	**1** (10)	THF (10)	65	7	24
3	1.2 : 0.8	CsF (2.4)	**2** (0.5)	Dioxane (10)	100	7	—*

* No product **18** was detected.

Scheme 2



in a yield of 24% after 7 h (see Table 2, Entry *2*). When passing to the heat-stable catalyst **2**, we replaced THF for higher-boiling dioxane.[5] However, there was no product **18** in the reaction mixture after 7 h of reaction (see Table 2, Entry *3*).

Experimental

^{1}H NMR spectra were obtained on a Bruker (300 MHz) instrument. Phenylboronic acid,[6] 1-bromo-2-methylnaphthalene,[7] 2-methylnaphthyl-1-boronic acid,[7] and catalysts **1** (see Ref. 8) and **2** (see Ref. 9) were synthesized according to the previously published procedures.

Reaction of phenylboronic acid (4) with aryl bromides 5—10 (general procedure). To a mixture of MeOH (8—12 mL) and water (4 mL), phenylboronic acid **4** (3 mmol), the corresponding aryl bromide (2 mmol), and K_2CO_3 (4 mmol) (and toluene (4 mL), see Table 1, Entry *6*) were added with stirring, the mixture was stirred for 5 min, and catalyst **1** or **2** (0.5 mol.%) was added. The reaction mixture was stirred at room temperature or 55 °C (see Table 1), diluted with water, extracted with diethyl ether, dried with Na_2SO_4, concentrated, and chromatographed on SiO_2 (hexane—$CHCl_3$, 9 : 1). The yields of the prepared biaryls **11—16** are given in Table 1.

Reaction of 2-methylnaphthyl-1-boronic acid (17) with 4-bromoanisole (5) (general procedure). A mixture of boronic acid **17**, 4-bromoanisole (**5**), catalyst **1** or **2**, a base, and a solvent was stirred at room temperature or with heating, diluted with water, extracted with diethyl ether, dried with Na_2SO_4, concentrated, and chromatographed on SiO_2 (hexane—$CHCl_3$, 9 : 1). The ratio of reagents, the bases and solvents used, the temperature and duration of the reaction, as well as the yields of biaryl **18** are given in Table 2.

All compounds prepared have been described earlier and were characterized by the comparison of their ^{1}H NMR spectra with those given in the literature.

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