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**LETTERS
TO THE EDITOR**

Role of a Base in Suzuki–Miyaura Reaction

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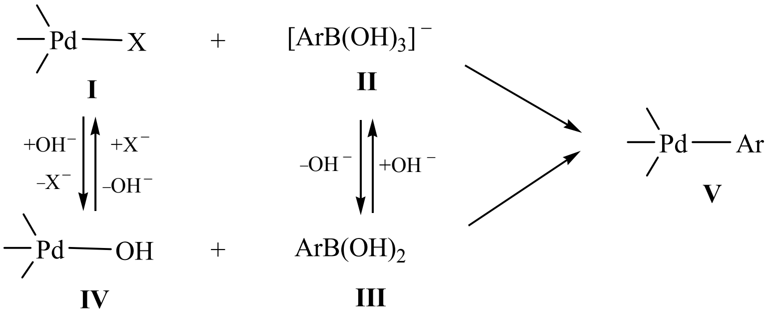
A specific feature of the reaction of aryl halides with arylboronic acids (Suzuki–Miyaura reaction) [1–3] actively investigated today among the family of catalytic cross-coupling processes is the mandatory presence of the base excess. However, its role in the reaction still remains ambiguous.[1]



X = I, Br.

The existing hypotheses about the base role are limited to two possible versions of the transmetallation stage in the catalytic Suzuki–Miyaura reaction. According to the first hypothesis, the transmetallation is possible only when the palladium compound **I** reacts with borate anions **II** formed *in situ* starting from arylboronic acid **III** and the base. The second version postulates that the transmetallation is possible only if the palladium intermediate **IV** involves the basic counterion originating from the present base.

The quantum-chemical modeling results [4–6] favor the first hypothesis. However, there are no experimental evidences. The main argument in favor of the borate anion **II** participating in the reaction is the experimental observation of their presence in the reaction mixture [7]. However, this reason is unacceptable, since the expected formation of borate anions **II** as a result of the reaction of a Lewis acid **III** with a base implies the existence of at least the equilibrium concentration of the starting arylboronic acid **III**. In addition, it does not exclude the equilibrium involving the base and palladium intermediates **I**, **IV**. It is important that the identification of the borate anions **II** or the corresponding palladium intermediate **IV**, involved into the relatively rapid equilibrium with the base, does not allow the estimation of their roles in the transmetallation stage. The only evidence may be the kinetic data.

In the present work the model experiments were carried out under kinetic control of the concentration of the parent Pd^{+2} compound. As one of the reactants we used a solution containing the preliminary prepared equilibrium mixture of NaOAc with $Pd(OAc)_2$ or $PhB(OH)_2$, which was mixed with a solution of $PhB(OH)_2$ or $Pd(OAc)_2$, respectively. The formation of compound **V** with Pd–Ar bond and its repeated participation in the transmetallation reaction led to the formation of biphenyl and Pd^0 as in the case of the oxidative version of the Suzuki–Miyaura reaction [8].

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[1] The Nobel lecture of prof. A. Suzuki, http://nobelprize.org/nobel_prizes/chemistry/laureates/2010/suzuki-lecture.html.

The rate of the reaction of $Pd(OAc)_2$ in the presence of various amounts of NaOAc (2, 5, and 10 eq per 1 eq of Pd) was found to be always 1.3–2 times higher than in the case of phenylboronic acid **III** and an equilibrium mixture of $Pd(OAc)_2$ and the base. These data indicate that the transmetallation stage involved not borate anion **II**, as assumed earlier [4–7], but a neutral molecule of the acid **III**. Note that it is in agreement with the recent research results on the isotopic distribution in the Suzuki–Miyaura reaction products [9].

On the other hand, it was found that the use of palladium complexes containing less basic anions instead $Pd(OAc)_2$ led to a significant decrease in the reaction rate, as follows: OAc > Br >> I. In this case no conversion in the system PdI_2–NaI–$PhB(OH)_2$ was observed even in the presence of a base. Special experiments showed that the iodide complexes of palladium were far superior in the stability than the corresponding acetate complexes [adding an equivalent amount of NaI was sufficient for the quantitative formation of Na_2PdI_4 from $Pd(OAc)_2$]. These results indicate the crucial role of the counterion in the palladium compound participating in the reaction with $PhB(OH)_2$, and they are consistent with the general theoretical view on the transmetallation reaction as the driving force [10].

Thus, the kinetic data indicate that a neutral molecule of phenylboronic acid and Pd compound containing a basic anion are involved into the transmetallation reaction. Consequently, the base plays a dualistic role in the Suzuki–Miyaura reaction: On the one hand, it participates in an undesirable process of borate anions formation, on the other hand, it provides for the formation of catalytic intermediates capable of transmetallation. This role of the base is consistent with the complex character of the influence of its nature and quantity on the catalytic activity [11].

Experimental procedure. A prepared solutions (5 ml, DMF: H_2O = 4:1) of 0.16 mmol of PdX_2 (X = OAc, I, Br, Cl) or 10 mmol of $PhB(OH)_2$ were mixed with the corresponding quantity of NaOAc in a temperature-controlled reactor (22°C). The equilibrium establishing in the initial solutions was monitored by UV and ^{11}B NMR spectroscopy [12]. The consumption of the Pd compound was controlled by the decrease in the intensity of the absorption spectrum (cell 0.1 cm, SF-2000, 320–600 nm) of the reaction samples (the samples were centrifuged to separate the Pd-black precipitate). Biphenyl, a product of oxidative homocoupling of $PhB(OH)_2$, was detected by GLC (HP-4890, DIF, column HP-5 15 m).

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