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Competing Reaction Method for Identification of Fast and Slow Steps of Catalytic Cycles: Application to Heck and Suzuki Reactions

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Abstract—A method for identification of fast and slow steps of catalytic cycles is suggested. This method provides reliable data for reactions conducted at an unsteady-state catalyst concentration. It has been used in the determination of the rate-determining step in the Heck reaction of aryl bromides and in the Suzuki reaction of aryl bromides and aryl iodides. The data obtained by this method are in agreement with the data obtained by other methods, including kinetic isotope effect measurements.

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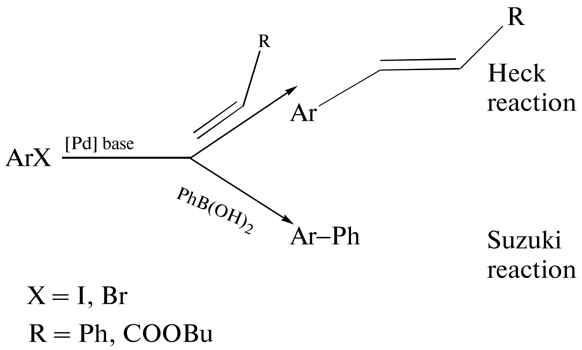
Standard procedures used to identify the rate-determining step of a chemical reaction, which are based on determination of the partial orders of the reaction with respect to the reactants, may yield erroneous data for catalytic processes [1]. This is due to active catalyst formation and deactivation processes taking place, which can lead to the variability of the catalyst concentration and thus can affect the apparent values of the partial orders of the reaction in a complicated way. In this case, the optimum methods are those whose results are independent of the concentration of the active catalyst. The conventional competing reaction method might seem appropriate in this case for the reason that, as determined by this method, the relative reactivities of the substrates competing for the catalyst are independent of the catalyst concentration. This method has indeed been widely employed in identifying rate-determining steps, including those of Heck reactions [2–8] and Suzuki reactions [9–11]. However, it is fundamentally incorrect to directly use relative substrate reactivities, which are conventionally measured in the competing reaction method, in identification of rate determining steps. This is due to the fact that the reaction step determining the relative reactivities of the substrates in the "competition" experiment does not necessarily coincide with the rate-determining step. This circumstance was noted by other authors [12] and was discussed in detail in our earlier work [13]. The approach suggested in that work [13] actually allows one to use results of competition experiments, namely, the absolute rates of the competing reactions. However, this approach requires that these rates be compared with the results of conventional, noncompetitive experiments. In addition, this approach allows the reactants involved in fast and slow reaction steps to be unambiguously identified, but it cannot clarify the issue of whether these steps are inside the catalytic cycle or are part of the active catalyst formation–deactivation process. For example, in the identification of the rate-determining step of the Heck reaction of aryl bromides in the presence of ligand-free catalytic systems, model experiments and kinetic measurements for the catalytic reaction demonstrated that the reaction rate is determined by a step involving the substrate [13]. However, this step does not belong to the catalytic cycle, but is involved in the formation of the active catalyst. The issue of what reaction step determines the rate of the catalytic cycle thus remained unclear. This posed the problem of distinguishing the steps of a catalytic cycle from the steps of catalyst formation and deactivation because of the direct involvement of the substrate in the latter. This is typical of the coupling of aryl halides with nucleophilic compounds and of some other catalytic reactions.

Here, we suggest a method making it possible to unambiguously identify fast and slow steps of catalytic cycles irrespective of the complexity of catalyst conversions (catalyst formation, deactivation, and regeneration) and irrespective of how strongly these processes affect the rate of the catalytic reaction. This method has been tested in the Heck reaction of aryl iodides, whose rate-determining step was reliably identified earlier, and has been used to identify the rate-limiting steps of the catalytic cycles for the Heck reaction of aryl bromides and for the Suzuki reaction of aryl bromides and aryl iodides in the presence of ligand-free and phosphine-containing catalytic systems (Scheme 1).



Scheme 1.

EXPERIMENTAL

The reactions were carried out in *N*,*N*-dimethylformamide in a magnetically stirred vessel under an argon atmosphere. The reaction mixture was sampled at intervals and was analyzed by GLC (HP-4890 chromatograph, flame-ionization detector, 15-m-long HP-5 capillary column, naphthalene as the internal standard, programmed heating of the oven from 100 to 250°C). The substrate conversion rate was estimated from the difference between the substrate concentrations in successive samples of the reaction mixture. When carrying out the competing reactions of styrene and styrene-d_8, the reaction mixture samples were additionally analyzed on a Shimadzu QP2010 Plus GC-MS system (Equity 5 column, helium as the carrier gas, electron impact ionization, electron energy of 70 eV, m/z scanning between 40 and 350, programmed heating between 110 and 250°C, injection port temperature of 250°C, interface and ion source temperature of 200°C). Styrene isotopomers were quantified as the relative intensities of the chromatographic peaks corresponding to m/z 104 and 112 using response factors determined by chromatographing reference solutions of styrene and styrene-d_8.

Solvents and reactants were purified using standard procedures.

Heck and Suzuki Reactions

A mixture of the alkene or phenylboric acid (10 mmol) and naphthalene (1 mmol) as the internal standard, dissolved in 10 mL of DMF, was placed in a reactor containing NaOAc (13 mmol) and $PdCl_2$ or 4% Pd/C (0.16 mmol in terms of Pd). The reaction was conducted at 140°C, and the reaction mixture was sampled at intervals for GLC analysis.

Table 1. Calculated rate constants of the rate-determining steps in Eq. (1) for Suzuki reactions of aryl bromides

Aryl bromide	k_S, L mol^{-1} min^{-1}
p-Bromoanisole	6.01
Bromobenzene	9.50
p-Bromochlorobenzene	14.70
p-Bromoacetophenone	15.88
p-Bromonitrobenzene	17.76
p-Bromobenzaldehyde	23.20

Competition Experiments

Competition experiments involving two aryl halides or two alkenes (1 : 1) were carried out in the same way as the above procedures. The amounts of substrates used in these experiments are specified in the corresponding figures.

Calculation of Rate Constants

Kinetic parameters of the Suzuki reaction of aryl bromides (Table 1) were calculated by minimizing the sum of squared deviations between the calculated and observed reaction rates (Table 2) by standard nonlinear function minimization methods (Microsoft Excel 2002, Solver add-in). The initial rates measured in competition experiments on equimolar amounts of aryl halides and phenylboric acid were used in these calculations. Integral kinetic relationships involving the rate constants thus obtained were simulated using the Gepasi 6.10 program.

RESULTS AND DISCUSSION

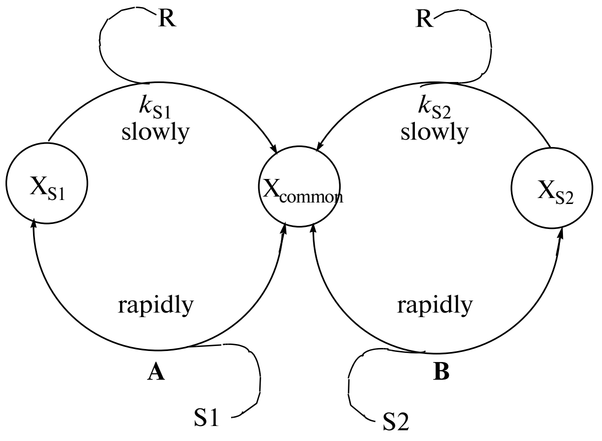
Theory

The fundamental distinction between our approach and the conventional competing reaction method is that we analyze integral disappearance curves for the competing substrates or integral accumulation curves for the respective products, not the initial reactivities of the substrates. Consider the simplest reaction scheme for two competing substrates (S1 and S2) and a common reactant (R) (Scheme 2). Two radically different variants of catalyst distributions between the intermediates during the reaction are possible here.

Table 2. Experimental and calculated rates of competing and noncompeting Suzuki reactions

S1	S2	r_{S1+S2}[a], 10^2 mol L^{-1} min^{-1}		r_{S1}[b], 10^2 mol L^{-1} min^{-1}		r_{S2}[b], 10^2mol L^{-1} min^{-1}		L[c]	
		exp	calc	exp	calc	exp	calc	exp	calc
Bromobenzene	*p*-Bromoanisole	12.1	15.4	15.0	14.5	9.1	8.9	15.1	15.0
Bromobenzene	*p*-bromoacetophenone	17.0	17.3	15.0	14.5	24.4	20.8	3.0	3.0
Bromobenzene	*p*-bromobenzaldehyde	34.6	30.8	15.0	14.5	34.7	36.9	0.2	0.19
p-Bromochlorobenzene	*p*-bromonitrobenzene	30.2	29.1	23.4	23.4	26.5	27.7	0.04	0.04
p-Bromoanisole	*p*-bromoacetophenone	21.9	24.9	9.1	8.9	24.4	20.8	0.2	0.19

[a] Total rate of the competing reactions.
[b] Rate of the noncompeting reaction of the substrate S1 or S2.
[c] Ratio of the conversion rate of the substrate S1 to that of the substrate S2 in the competition experiment.



Scheme 2.

In variant 1, most of the catalyst is in the intermediates X_{S1} and X_{S2}. This will be the case if steps **A** and **B** are fast and irreversible or, alternatively, fast and reversible, with the corresponding quasi-equilibrium shifted to the intermediates X_{S1} and X_{S2}.

In variant 2, most of the catalyst is in the intermediate X_{common}. This will be the case if steps A and B are slow and irreversible or, alternatively, fast and reversible, with the quasi-equilibrium shifted to the intermediate X_{common}.

It was demonstrated [13] that, irrespective of whether the first steps of the catalytic cycles (**A** and **B**) are reversible or irreversible, the substrate conversion rates in variant 1, in which the intermediates X_{S1} and X_{S2} are dominant, are described by the following equations:

$$r_{S1}^{comp} = \frac{L\frac{[S1]}{[S2]}k_{S1}k_{S2}[R][Cat]_{\Sigma}}{L\frac{[S1]}{[S2]}k_{S2} + k_{S1}},\qquad r_{S2}^{comp} = \frac{k_{S1}k_{S2}[R][Cat]_{\Sigma}}{L\frac{[S1]}{[S2]}k_{S2} + k_{S1}}, \tag{1}$$

where the parameter L is the rate constant or equilibrium constant ratio for steps **A** and **B** (Scheme 2) [13]. Under the assumption that the substrate S1 is more reactive than S2, the [S1]/[S2] ratio will decrease during the process. According to Eq. (1), this will lead to an increase in the S2 conversion rate and to a decrease in the S1 conversion rate. This is due to the fact that the catalyst passes from X_{S1} into X_{S2} as S1 is consumed. In the case of substrates differing markedly in reactivity, the catalyst will pass from X_{S1} into X_{S2} practically at the instant the substrate S1 disappears entirely and this will cause an abrupt increase in the S2 conversion rate. In order to verify this inference, we calculated, by numerical integration of the rate equations for the reaction steps presented in Scheme 2, the integral S1 and S2 disappearance curves and the time dependence of the S2 conversion rate (Fig. 1). In this calculation, we used the rate constant and L values determined by simultaneous analysis of the competing and noncompeting Suzuki reactions of phenylboric acid (R) with bromobenzene (S1) and *p*-bromoanisole (S2) (Tables 1, 2). The S2 conversion rate peaks at the point in time at which the substrate S1 is entirely converted (Fig. 1), and the integral curve of the substrate S2 indicates an acceleration of the reaction. The subsequent decrease in the reaction rate is caused by the decreasing concentration of the common reactant R.

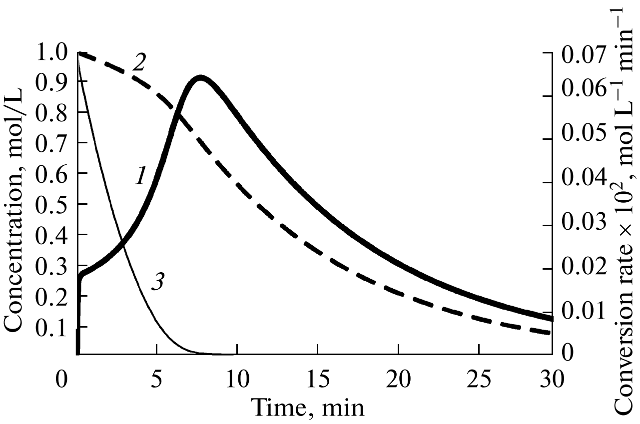


Fig. 1. Simulated kinetics of the conversion of the competing substrates in the reaction presented in Scheme 2 (k_{S1} = 9.5 L mol^{-1} min^{-1}, k_{S2} = 6.0 L mol^{-1} min^{-1}, L = 15): (*1*) S2 conversion rate, (*2*) [S2], and (*3*) [S1].

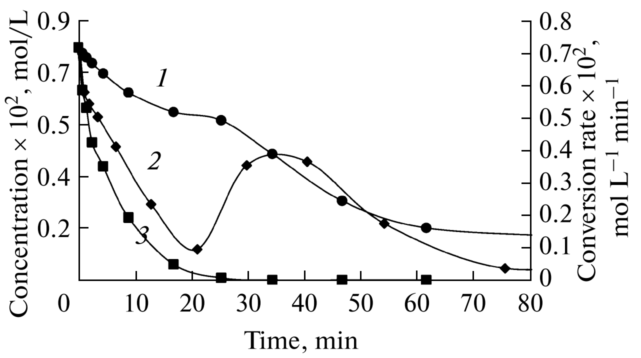


Fig. 2. Conversion of the competing aryl iodides in their reaction with styrene in the presence of Pd/C: (*1*) [*p*-iodotoluene], (*2*) *p*-iodotoluene conversion rate, and (*3*) [*p*-iodoacetophenone].

When the catalyst distribution variant 2 takes place, in which the dominant intermediate is X_{common}, this species will also dominate after the complete conversion of the more reactive substrate and this will have no effect on the integral disappearance curve of the substrate S2. Therefore, the acceleration of the reaction is evidence that the proportion of the catalyst in the common intermediate with which the competing substrates react is small and that the steps in which the substrates are involved are fast. This conclusion is true irrespective of whether these steps are reversible or practically irreversible. The absence of acceleration would mean that the common intermediate of the two catalytic cycles is dominant in catalyst distribution. This may be due to its involvement in slow steps of the catalytic cycles or in fast quasi-equilibrium steps in which the equilibrium is shifted to the dominant intermediate reacting with the substrates. Thus, the appearance/absence of acceleration in the disappearance curve of the less active substrate at the point of the complete conversion of the more active substrate is a kinetic feature making it possible to estimate the proportion of the intermediate common for the two competing reactions and to test whether the competing substrates are involved in a fast or slow step of the catalytic cycle.

Since the acceleration effect depends only on the relative amount of the catalyst in the common intermediate of the two competing reaction, the proportion of this intermediate can be estimated using this approach not only for the simplest mechanism presented in Scheme 2, but also for reactions with any number of intermediates in the catalytic cycle. Moreover, because two substrates with similar properties will likely be converted on the same type of catalyst (i.e., via a common intermediate), the share of the common intermediate of the competing reactions in catalyst distribution will be deducible even if the nature of the common intermediate and the complete catalytic cycle mechanism are unknown. Note also that the acceleration effect is independent of the absolute concentration of the active catalyst ($[Cat]_\Sigma$ in Eq. (1)). This effect will also be observed in the case of any changes in $[Cat]_\Sigma$ associated with the catalyst formation–deactivation kinetics. Nevertheless, in this approach it is better to carry out a series of experiments differing, e.g., in the nature or concentration of the catalyst precursor and/or competing substrates. This will rule out casual temporal coincidence between the total conversion of the more reactive substrate and the catalytic system activation or deactivation. This will also rule out any change in the contributions from different catalysts into conversion in the case of the reaction occurring simultaneously on different types of active species.

Testing the Method in the Heck Reaction of Aryl Iodides in the Presence of Ligand-Free Catalytic Systems

Use of aryl iodides as substrates made it possible to avoid the strong effect of catalyst deactivation on the reaction kinetics, so the slowest step of this reaction can be considered to be reliably identified [13–15]. Undoubtedly, aryl iodides, which are the most reactive aryl halides, are involved in the fast step of the catalytic cycle. In this case, according to the above analysis, the disappearance curve of one of the competing substrates would indicate acceleration. This acceleration was indeed clearly observed in the competition between *p*-iodoacetophenone and *p*-iodotoluene in their reaction with styrene in the presence of Pd/C as the heterogeneous precursor of the catalyst (Fig. 2). Similar acceleration was also observed in the presence of $PdCl_2$ as the homogeneous precursor of the catalyst and in the competition between other aryl iodides (*p*-acetophenone, *p*-iodoanisole, and iodobenzene).

Thus, the results provided by this method are in full agreement with earlier data [13–15]. Therefore, this

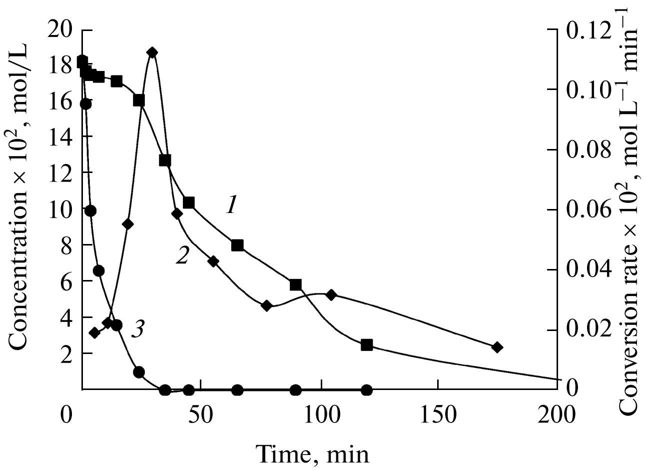


Fig. 3. Conversion of the competing aryl bromides in their reaction with styrene in the presence of Pd/C: (*1*) [*p*-bromochlorobenzene], (*2*) *p*-bromochlorobenzene conversion rate, and (*3*) [*p*-bromobenzaldehyde].

method is applicable to reactions whose rate-determining step remains unidentified because of the strong effect of catalyst formation and deactivation processes.

Heck Reaction of Aryl Bromides in the Presence of Ligand-Free Catalytic Systems

The assumption that aryl bromides, unlike their more reactive iodide analogues, are involved in the rate-determining step of the catalytic cycle of the Heck reaction was long unchallenged [5, 16–19]. However, there are experimental observations that cast doubt on this hypothesis [13]. We think that the acceleration observed in the disappearance curve of the less reactive substrate in the reaction of styrene with competing *p*-bromobenzaldehyde and *p*-bromochlorobenzene in the presence of Pd/C (Fig. 3) is the first direct evidence that the aryl bromides participate not in the slow step of the catalytic step of the Heck reaction, but in the rapid one.

After this fact was established, it was necessary to carry out additional experiments for identification of the slow step. As in the case of aryl iodides [13, 14], in order to verify the hypothesis that the slow step is C–H bond breaking, we measured, under the same conditions, the bromobenzene conversion rate in three independent experiments, specifically, in the reactions of bromobenzene with styrene and deuterated styrene alone and in the competing reactions of bromobenzene with equimolar amounts of styrene and styrene-d_8. The conversion rates were determined to be 0.138, 0.065, and 0.088 L mol^{-1} min^{-1}, respectively. According to GC-MS data, the relative reactivities of styrene and styrene-d_8 in the competition experiment were equal. The value of the kinetic isotope effect (KIE) can be determined by simultaneous analysis of reaction rate data from competition and non-competition experiments using Eq. (1) [13]. The KIE values derived from reaction rate data of three independent experiments (2.12, 2.14, and 2.10) are smaller than the corresponding value for the reactions of iodobenzene (3.0) [13]. This may be due to the lower sensitivity of the reaction of bromobenzene to the rate of the slow step. At the same time, the KIE values for bromobenzene are practically equal to the KIE value reported for the stoichiometric β-hydride elimination reaction on palladium (2.28) [20], which is included in the conventional catalytic cycle of the Heck reaction. Thus, the KIE data suggest that the slowest step of the catalytic cycle of the reactions of styrene with aryl bromides is C–H bond breaking. Therefore, although the aryl bromides are less reactive than the aryl iodides, the nature of the slow step of the catalytic cycle is the same for both groups of compounds.

According to the accepted mechanism of the Heck reaction, the alkene inserts into the Pd–Ar bond in the σ-aryl complex, thus being involved in a step showing no KIE [13]. This is in agreement with the fact that styrene and styrene-d_8 are equally reactive in the competition experiment. Therefore, in order to make an ultimate conclusion as to the nature of the slow step, it was necessary to ascertain that alkenes, like aryl bromides, are involved in fast steps of the catalytic cycles. For this purpose, we carried out an experiment in which the competing substrates were two alkenes (*n*-butyl acrylate and styrene) and the common reactant was *p*-bromochlorobenzene. An acceleration of the reaction of styrene, the less reactive substrate, was observed in this experiment. This provided evidence that the alkenes are involved in fast steps, which is consistent with the above conclusion that the slow step is C–H bond breaking.

Heck Reaction of Aryl Bromides in the Presence of Phosphine-Containing Catalytic Systems

Passage from the ligand-free catalytic systems to systems containing phosphine ligands, which are frequently used in practice, may be accompanied by changes in the ratios of reaction step rates. For this reason, we conducted competition experiments using a $PdCl_2$-based catalytic system containing two equivalents of triphenylphosphine. For the competing reactions of *p*-bromobenzaldehyde and *p*-bromochlorobenzene with styrene, we observed well-pronounced acceleration in the conversion of the less reactive substrate (Fig. 4). This fact is unambiguous evidence that the aryl bromides are involved in the fast step of the catalytic cycle, as in the case of the ligand-free catalytic systems. However, the bromobenzene conversion rates in three independent experiments, specifically, in its reactions with styrene and styrene-d_8 and its competing reactions with a styrene + styrene-d_8 mixture were observed to be equal. This indicated that there is no KIE in the presence of this catalytic system, as dis-

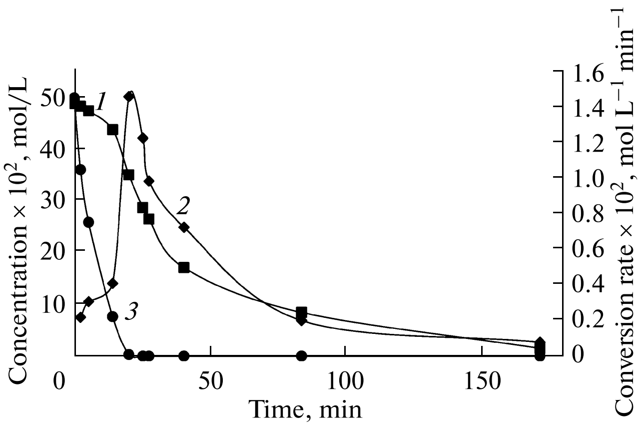


Fig. 4. Conversion of the competing aryl bromides in their reaction with styrene in the presence of the catalytic system $PdCl_2$–$2PPh_3$: (*1*) [*p*-bromochlorobenzene], (*2*) *p*-bromochlorobenzene conversion rate, and (*3*) [*p*-bromobenzaldehyde].

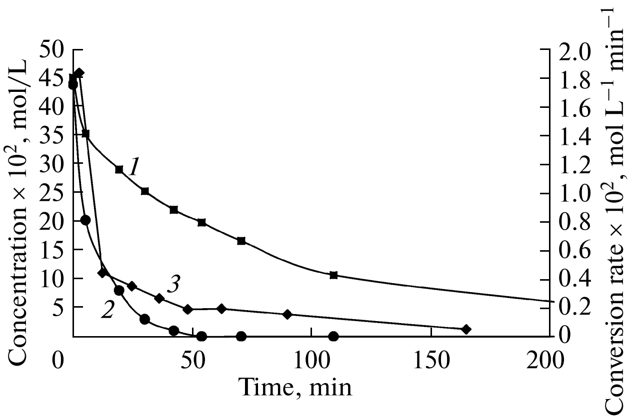


Fig. 5. Conversion of the competing alkenes in their reaction with bromobenzene in the presence of the catalytic system $PdCl_2$–$2PPh_3$: (*1*) [styrene], (*2*) styrene conversion rate, and (*3*) [butyl acrylate].

tinct from the above ligand-free system. Note that the introduction of triphenylphosphine does not change the KIE value in the same reactions of iodobenzene [21], indicating that the rate-determining step remained the same—dissociation of the C–H bond. Thus, the introduction of triphenylphosphine into the reactions of the aryl bromides (as distinct from aryl iodides) changes the rate-determining step of the process.

For gaining further evidence in favor of the change of the rate-determining step, it was necessary to verify the hypothesis that this step involves the alkene. For this purpose, we carried out an experiment in which the competing substrates were two alkenes (*n*-butyl acrylate and styrene) and the common reactant was bromobenzene (Fig. 5). As follows from the data of this experiment, there was no acceleration of the conversion of the less reactive substrate. The same result was obtained for the reactions of these alkenes with *p*-bromochlorobenzene. Therefore, in view of the accepted mechanism of the catalytic cycle of the Heck reaction [21], the greater part of the catalyst in this case is in the form of palladium σ-aryl complexes reacting with the alkenes. The rate-determining step may be the reaction of these complexes with the alkenes, which yields the corresponding π-complexes. Alternatively, the quasi-equilibrium in this reaction is shifted to the free alkene and σ-aryl complex and the overall reaction rate is limited by the subsequent intramolecular insertion of the alkene into the Pd–Ar bond. Both deductions are in agreement with the results of NMR monitoring of the reactions of aryl bromides: no alkene π-complexes were detected under the same conditions [22]. A considerable proportion of palladium was identified as σ-aryl complexes. This finding is in full agreement with the absence of acceleration in the case of two competing alkenes (Fig. 5).

Suzuki Reaction of Aryl Iodides and Aryl Bromides in the Presence of Ligand-Free Catalytic Systems

The mechanism of the Suzuki reaction is currently understood much more poorly than the mechanism of the Heck reaction. There have been contradictory hypotheses as to the rate-determining steps of the Suzuki catalytic cycle [9–11, 23–33]. The authors of all of these works ignored the possible effect of the nonstationarity of the concentration of the active catalyst.

We established that, for the competing reactions of iodobenzene and *p*-iodoacetophenone with phenylboric acid in the presence of Pd/C as the catalyst precursor, the iodobenzene disappearance curve indicates acceleration at the point of the complete conversion of *p*-iodoacetophenone, the more reactive competitor (Fig. 6). Similar effects were observed in the competition between *p*-iodoacetophenone and *p*-iodotoluene, including in the presence of $PdCl_2$. The Suzuki reaction of aryl bromides also shows an increase in the conversion rate of the less active substrate. For example, this was observed for the bromobenzene–*p*-bromoacetophenone competing pair (Fig. 7). Acceleration took place in the reactions of *p*-bromoanisole and *p*-bromochlorobenzene with *p*-bromoacetophenone and *p*-bromobenzaldehyde, respectively, both in the presence of Pd/C and in the presence of $PdCl_2$. These results unambiguously indicate that the aryl iodides and aryl bromides are involved in the fast steps of the catalytic cycle of the Suzuki reaction. There is no doubt that the replacement of aryl iodides with less reactive aryl bromides does not change the rate determining step of the catalytic cycle.

This inference is consistent with the simultaneous analysis of the reaction rates in competition and noncompetition experiments on various aryl bromides (11 independent experiments) using Eq. (1). It was assumed in this analysis that the catalytic cycle of the

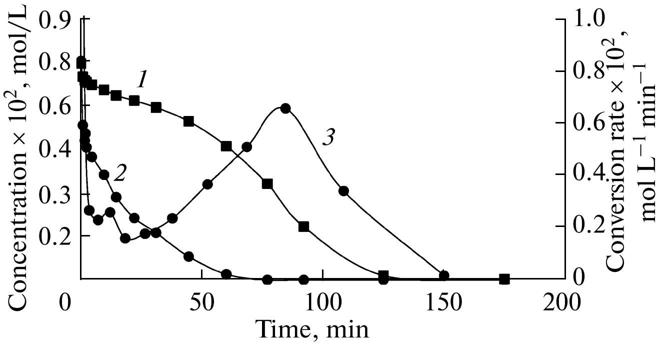


Fig. 6. Conversion of the competing aryl iodides in their reaction with phenylboric acid in the presence of Pd/C: (*1*) iodobenzene], (*2*) [*p*-iodoacetophenone], and (*3*) iodobenzene conversion rate.

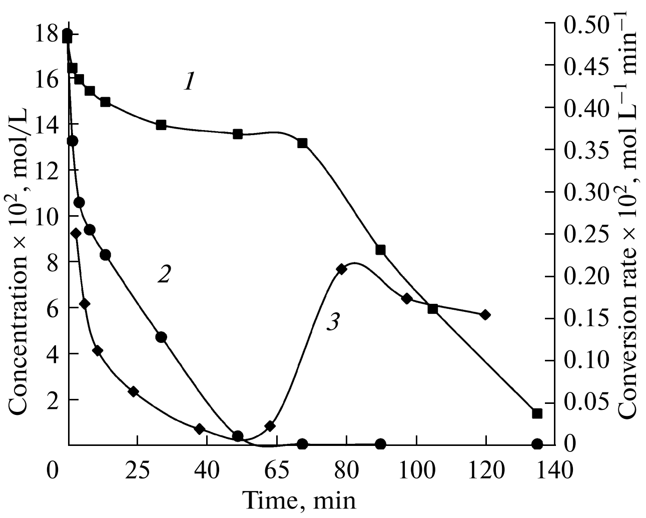


Fig. 7. Conversion of the competing aryl bromides in their reaction with phenylboric acid in the presence of Pd/C: (*1*) bromobenzene], (*2*) [*p*-bromoacetophenone], and (*3*) bromobenzene conversion rate.

Suzuki reaction is describable in terms of a two-step mechanism including rapid interaction between the catalyst and the aryl halide and the slow irreversible reaction of the resulting intermediate with arylboric acid (Scheme 2). Similar to what was done in our earlier study in which this approach was applied to the Heck reaction [13], we calculated kinetic parameters for six aryl bromides (Table 1) involved in five competition experiments by minimizing the sum of squared deviations between reaction rates and between relative reactivities (parameter L) determined experimentally and calculated via Eq. (1) (Table 2). The good agreement between the data calculated using Eq. (1) and the experimental data (Table 2) suggests that the aryl bromides are involved in the fast step of the reaction. The rate-determining step is likely the transmetalation reaction postulated for the catalytic cycle of the Suzuki reaction. The alternative hypothesis that the slow step is reductive Pd(0) elimination subsequent to transmetalation, which was suggested in a single work [24], seems far less likely because of the high reactivity of palladium compounds having two Pd–Ar bonds and because of the high stability of the resulting biaryl.

Thus, the approach suggested here—analysis of the integral disappearance curves of the competing substrates—can be used at least in qualitative estimation of the proportion of the catalytic cycle intermediate directly reacting with the competing substrates. The acceleration occurring in the disappearance curve of the less reactive substrate at the instant the more reactive substrate is entirely converted unambiguously indicates that only a small proportion of the catalyst is in the form of the common intermediate of the competing processes and that the competing substrates are involved in the fast reversible or irreversible steps of the catalytic cycles. The absence of acceleration in the conversion of the less reactive substrate is possible only when the greater part of the catalyst is in the form of the common intermediate and can be due to low rate of the steps involving the competing substrates. This approach enables one to successively test alternative hypotheses as to the sensitivity of the reaction rate to the rates of particular steps of the catalytic cycle that directly involve the substrates and reactants of the catalytic reaction.

Application of the above approach to the Heck and Suzuki reactions has provided convincing evidence that the catalytic cycle steps involving aryl halides proceed at a high rate. It is important that, in both reactions, rapid aryl halide activation is possible in the case of less reactive aryl bromides as well. The introduction of triphenylphosphine into the catalytic system changes the nature of the slowest step of the catalytic cycle of the Heck reaction of aryl bromides. But again, in this case the aryl bromide is involved in the fast step of the catalytic cycle and most likely rate-determining step is is the step involving the alkene.

Note that these conclusions have been formulated in spite of the strong effect of catalyst deactivation on the reactions of aryl bromides catalyzed by ligand-free systems. This catalyst deactivation showed itself as a marked decrease in the conversion rate of the less active substrate at the instant the more active substrate is entirely consumed. For example, bromobenzene conversion in the Suzuki reaction stopped almost completely in 70 min (Fig. 7). No such rapid decrease in the reaction rate was observed with more stable catalytic systems containing triphenylphosphine (Fig. 4) and in the reactions of aryl iodides in the presence of ligand-free catalytic systems (Figs. 2, 6). Nevertheless, it follows from our data that the progressive deactivation of the catalyst in the reactions of aryl bromides did not prevent the acceleration effect from being observed. Therefore, the approach presented here is applicable to reactions proceeding at a nonstationary catalyst concentration.

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