

The Mechanism of the Palladium Hydride β -Elimination Step in the Heck Reaction

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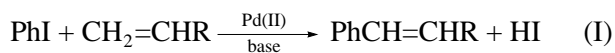
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Abstract—The kinetics of competitive phenylation of alkenes with iodobenzene over palladium complexes (the Heck reaction) was studied. The effect of one alkene on the arylation rate of another alkene conflicts with the conventional mechanism of the Heck reaction in which the arylated alkene is formed through the unimolecular step of palladium hydride β -elimination. Based on experimental data obtained, another mechanism is proposed in which a reaction product is formed through the transfer of palladium hydride to the initial alkene molecule.

INTRODUCTION

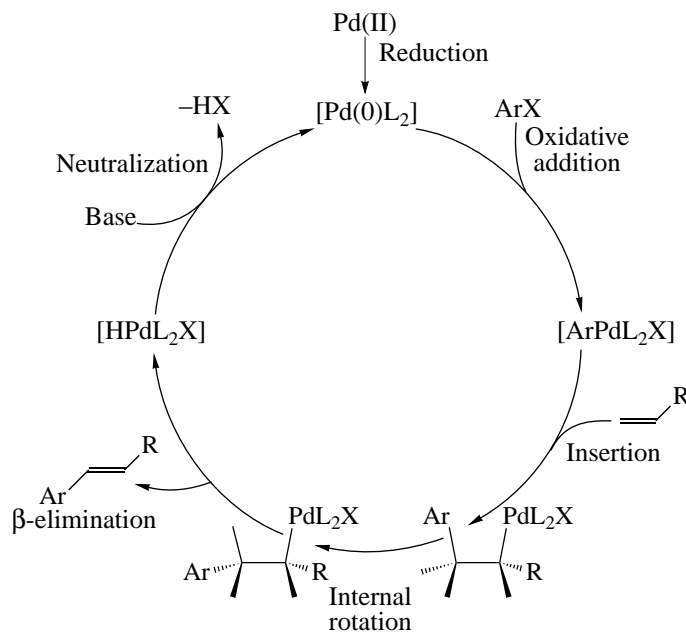
Due to the huge synthetic potential of alkene arylation, the Heck reaction



is increasingly attracting the attention of researchers [1, 2]. However, kinetic methods have not been extensively applied to this process and without them the reliability of the reaction mechanism cannot be judged seriously [3].

The conventional catalytic cycle for reaction (I) [1, 2] includes the following key steps typical of metal-complex catalysis: oxidative addition of aryl halide to a Pd(0) complex, alkene insertion into the Pd–C bond, and palladium hydride β -elimination (Scheme 1).

By measuring the isotope effect in reaction (I), we found [4] that the rate-determining step should include the dissociation of the C–H bond. Within the framework of the conventional mechanism of the Heck reaction (Scheme 1), such a step is the β -elimination of palladium hydride. However, based on the nonzero partial orders in alkene, we suggested [4] the possible involvement of the alkene molecule in the rate-determining reaction. In this work, new experimental data are presented that contradict the conventional mechanism of the Heck reaction and agree with the hypothesis put forward in [4]. This enabled us to propose a new mechanism of the step of palladium hydride β -elimination.



Scheme 1.

EXPERIMENTAL

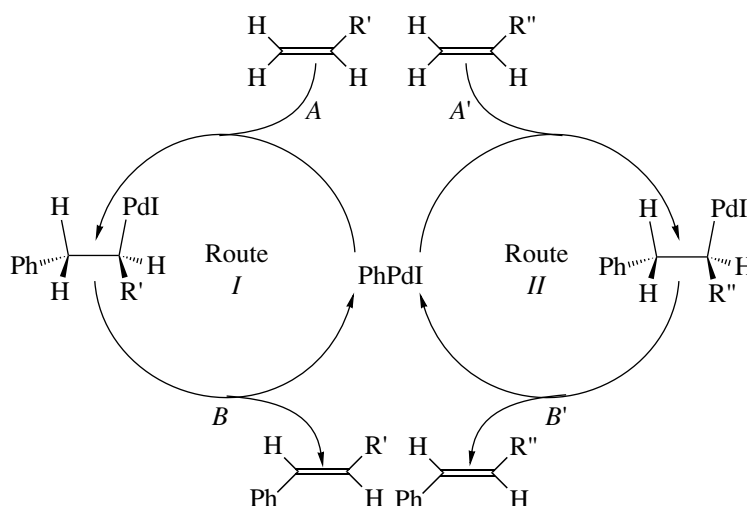
A standard run on the competitive phenylation of various alkenes was carried out at 60°C by mixing two alkenes (10 mmol each), PhI (10 mmol), NaOOCCH₃ (13 mmol), and PdCl₂ (0.16 mmol) in 10 ml of DMF. Phenylation of individual alkenes was performed similarly. In some runs, NBU₃ (13 mmol) or a mixture of NaOAc (11.2 mmol) + NBU₃ (1.8 mmol) were used as bases. The sampled probes were analyzed by GLC (HP-4890 chromatograph, 15% MePh-siloxane, 15 m, 100–200°C).

The reaction rates were determined by graphic differentiation of the stationary segments of the kinetic curves for accumulation of the alkene phenylation products. The time it took to reaching the stationary

regime was at most 1 min with 3–5% conversion of the reactants. The parameters of equations were calculated by the nonlinear least-squares methods using the program STATISTIKA for Windows. The reagents and solvents were purified by standard procedures.

RESULTS AND DISCUSSION

To elucidate the mechanism of the rate-determining step, we used the method of competitive reactions, which we applied previously to study the mechanism of reaction (I) [4]. Let us consider the scheme of phenylation of an alkene mixture consisting of two reaction routes (Scheme 2).



Scheme 2.

As shown in [5], the oxidative addition step in phenylation with aryl iodides occurs rather rapidly, and the Pd(0) concentration is negligible in the course of reaction. Therefore, the sequence of steps in Scheme 2 begins with the competitive irreversible insertion of two alkenes A, A'. Taking into account the relatively slow steps of palladium hydride β -elimination (B, B', Scheme 2), the rate equations for the competitive phenylation routes for two alkenes under quasi-steady-state approximation for the concentrations of intermediates can be presented as follows [4]:

$$w_{S1} = \frac{Lk_{S1}^{el}k_{S2}^{el}[Pd]_{\Sigma}}{Lk_{S2}^{el} + k_{S1}^{el}}; \quad w_{S2} = \frac{k_{S1}^{el}k_{S2}^{el}[Pd]_{\Sigma}}{Lk_{S2}^{el} + k_{S1}^{el}}, \quad (1)$$

where w_{S1} and w_{S2} are the rates of the phenylation routes for the substrates S1 and S2; k_{S1}^{el} and k_{S2}^{el} are the rate constants for the elimination steps (B, B', Scheme 2); $[Pd]_{\Sigma}$ is

the total palladium concentration in the reaction; and L is the reaction selectivity determined according to Scheme 2 as the ratio of insertion rates for the competing alkenes:

$$L = k_{S1}^{ins}/k_{S2}^{ins}. \quad (2)$$

Here k_{S1}^{ins} and k_{S2}^{ins} are the rate constants of the insertion steps (A and A' in Scheme 2) and [S1] and [S2] are the concentrations of alkenes. The validity of Eq. (2) is confirmed by the linear relationship between the w_{S1}/w_{S2} rate ratio (according to Eqs. (1), it should be equal to L) and the ratio of the concentrations of the arylating alkenes (Fig. 1).

If the suggestion that alkene participates in β -elimination [4] is true, then, in the case of competitive arylation of two alkenes, the effect of one alkene on the rate of elimination step in the reaction pathway for the second alkene might be possible. In this case, the

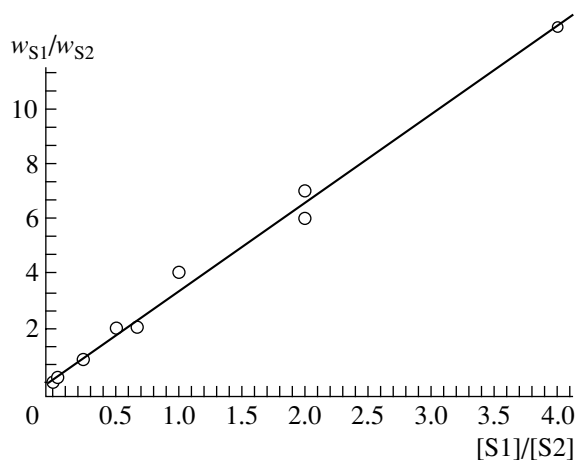


Fig. 1. Plot for the selectivity (w_{S1}/w_{S2}) of competitive phenylation of styrene and methyl methacrylate vs. the ratio of their concentrations $[S1]/[S2]$.

experimental relationships between the arylation rate for one alkene and the concentration of the second alkene should be different from those that follow from Eqs. (1) based on the inferred unimolecularity of β -eliminations (B and B' , Scheme 2). In line with Eqs. (1), the dependence of the phenylation rate of one alkene (w_{S1}) on the concentration of the second alkene ($[S2]$) should only be governed by changes in the selectivity of the insertion steps (A and A' , Scheme 2, parameter L in Eqs. (1)). With a constant concentration of one alkene (for instance, $[S1]$), this relationship will be as follows:

$$w_{S1} = \frac{a_1}{a_2 + a_3[S2]}, \quad (3)$$

$$\text{where } a_1 = \frac{k_{S1}^{\text{ins}}[S1]}{k_{S2}^{\text{ins}}} k_{S1}^{\text{el}} k_{S2}^{\text{el}} [\text{Pd}]_{\Sigma}, \quad a_2 = \frac{k_{S1}^{\text{ins}}[S1]}{k_{S2}^{\text{ins}}} k_{S2}^{\text{el}},$$

$$a_3 = k_{S1}^{\text{el}}.$$

This relationship can be obtained by calculation using the rate constants of the elimination steps found in [4] and parameter L for the competitive phenylation of styrene (ST) and methyl methacrylate (MMA) (Fig. 2, curve 1). However, the experimental plot for the ST phenylation rate vs. MMA concentration in the competitive runs (Fig. 2, curve 2) differed considerably from that expected according to Eq. (3). The existence of an extremum on the plot obtained agrees with the mutual influence of alkenes in the catalytic cycle of reaction (I) and can be explained by the involvement of alkene in the relatively slow step of the catalytic cycle. According to the data of measuring the isotopic effect [4], this step should also be accompanied by the dissociation of the C–H bond in the initial alkene.

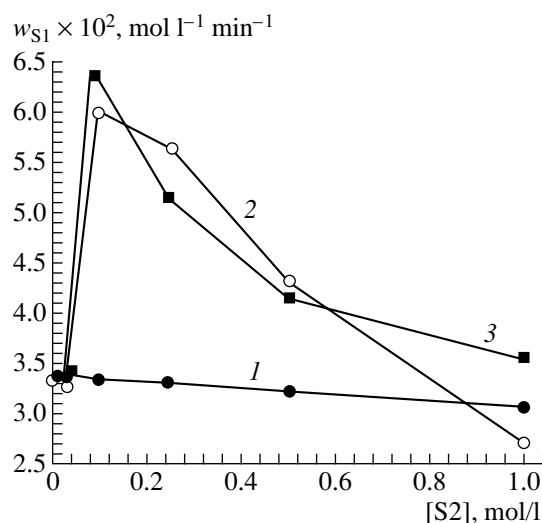


Fig. 2. Plot for the rate of ST phenylation (w_{S1}) vs. MMA concentration $[S2]$ at $[ST] = 1$ mol/l: (1) calculation by Eqs. (1), (2) experiment, (3) calculation by Eq. (4).

The mutual influence of alkenes is confirmed by the results of a series of runs with simultaneous variation of the ST and MMA concentrations (Fig. 3). As expected, the region of the maximal rates practically passes along a diagonal between the regions of high concentrations of both alkenes. In these regions, one alkene starts to dominate in the reaction, and the cross-effect of the second alkene decreases.

For another pair of substrates, ST and methacrylate (MA), the experimental plots for the rates vs. alkene concentrations can be described without accepting the hypothesis about the cross-effect of alkenes. The relationship calculated using Eq. (3), that is, not taking into account the alkene cross-effect, was in good agreement with the experimental data (Fig. 4). The rate constants of the elimination steps and the value of the L parameter for the reactions of ST and MA were also taken from [4].

If we assume that the relationship between the rate of the rate-determining step and the alkene concentration in the “noncompetitive” runs can be approximated by the power function $w_{S1} = k_{S1}[S1]^{n_1}[\text{Pd}]_{\Sigma}$ in which the product $k_{S1}[S1]^{n_1}$ can be treated as the effective constant k_{S1}^{el} in Eq. (1), then, in the case of two alkenes, the cross-effect of the second alkene on the rate of the slow step in the phenylation pathway of the first alkene can be expressed as $k_{S1}'[S2]^{n_1}[\text{Pd}]_{\Sigma}$. Similarly, the cross-effect of the first alkene on the phenylation rate of the second substrate can be represented as $k_{S2}'[S1]^{n_2}[\text{Pd}]_{\Sigma}$. In this case, the equation for the phenylation rate of the first substrate (Eq. (1)) transforms into Eq. (4).

$$w_{S1} = \frac{L' \frac{[S1]}{[S2]} (k_{S1}[S1]^{n_1} + k'_{S1}[S2]^{n_1}) (k_{S2}[S2]^{n_2} + k'_{S2}[S1]^{n_2}) [Pd]_{\Sigma}}{L' \frac{[S1]}{[S2]} (k_{S2}[S2]^{n_2} + k'_{S2}[S1]^{n_2}) + (k_{S1}[S1]^{n_1} + k'_{S1}[S2]^{n_1})}, \quad (4)$$

where $L' = k_{S1}^{ins}/k_{S2}^{ins}$.

Depending on the values of parameters, such a function may have a maximum (as in Fig. 2) or a minimum or may not have an extremum at all (as in Fig. 4). For example, for the above pair ST + MMA, Eq. (4) well described the existence of an extremum on the experimental plot for the rate (Fig. 2, curve 3) at $k'_{S1} = 0.40$, $n_1' = -0.83$, and $n_2' = 0$, which characterize the MMA effect on the rate of ST arylation, and vice versa. The values of the rate constants k_{S1} , k_{S2} , and L' were again taken from [4]. The calculated values of n_1 and n_2 were close to 0 and 1, respectively, and this is in agreement with the found reaction orders in ST and MMA in the noncompetitive runs.

Hence, according to Eq. (4), the significance of the cross-effects is governed by a number of factors: the values of effective rate constants, the orders of steps, and the alkene concentrations. Therefore, the extent of the cross-effect may be different for each pair of substrates.

The results for the competitive arylation of ST in pairs with propyl acrylate (PA), vinyl butyl ether (VBE), ethylene (ET), and propylene (PR) (see table) confirm the above conclusion. The significance of the cross-effect can be evaluated by the degree of coincidence of the k_{S1}^{el}/k_{S2}^{el} values presented in the table, which were calculated by three methods for each pair of the substrates under the assumption that the reaction rate of the elimination step is independent of the alkene concentration:

$$\frac{k_{S1}^{el}}{k_{S2}^{el}} = \frac{w_{S1}}{w_{S2}}, \quad (5)$$

$$\frac{k_{S1}^{el}}{k_{S2}^{el}} = \frac{w_{S1}}{w_{S1} + w_{S2}} (L + 1) - L, \quad (6)$$

$$\frac{k_{S1}^{el}}{k_{S2}^{el}} = \frac{L}{\frac{w_{S2}}{w_{S1} + w_{S2}} (L + 1) - 1}. \quad (7)$$

Equation (5) is obtained by dividing one of the rate equations (8) by another for the uncompetitive phenylation of two alkenes. The simplicity of Eqs. (8) is due to the fact that β -elimination is the slowest step (Scheme 1):

$$w_{S1} = k_{S1}^{el} [Pd]_{\Sigma}; \quad r_{S2} = k_{S2}^{el} [Pd]_{\Sigma}. \quad (8)$$

Equations (6) and (7) are obtained by dividing one of Eqs. (8) by the sum of Eqs. (1). They also allow one to calculate k_{S1}^{el}/k_{S2}^{el} by using not only the experimental values of the phenylation rates of individual alkenes but also the rate in the corresponding competitive experiment ($w_{S1} + w_{S2}$).

The rates calculated for the ST + PA pair (table, entry 2) were close to those for the ST + MA system (table, entry 1), for which the absence of significant cross-effects was mentioned above. This provides satisfactory coincidence for the ratios of rate constants of the elimination steps k_{S1}^{el}/k_{S2}^{el} (table, entries 1 and 2) obtained from Eqs. (5)–(7), that is, assuming that the elimination rate is independent of the alkene concentration. However, the ratios of the rate constants for other pairs of alkenes calculated by Eqs. (5)–(7) varied considerably even with the appearance of negative values. The total rate of competitive phenylation for the ST + ET and ST + PR pairs was higher than those of phenylation of individual alkenes (table, entries 4, 5). It is obvious that, in this case, Eqs. (1), unlike Eq. (4), cannot explain the increase in the competitive phenylation rate, and this leads to a substantial difference in the ratios of the rate constants of elimination calculated according to Eqs. (5)–(7) (table, entries 4, 5). An increase in the total reaction rate during competitive phenylation of these alkene pairs was found to be due to the acceleration of ST phenylation in the presence of ET and PR. A similar acceleration of VBE phenylation in the presence of ST was also observed for the ST + VBE pair (table, entry 3), although the total phenylation rate for the mixture was not higher than that in "uncompetitive" experiments. Hence, one can ascertain that for some combination of substrates (table, entries 3–5), as previously for the ST + MMA pair, Eqs. (1) are inadequate for the experiment. Then, one can suggest that the deviations found are due to the cross-effect of alkenes during competitive experiments because of their involvement in the slow steps of the competing routes.

The effect of the alkene concentration on the rate of stoichiometric β -elimination in the complexes of some metals has been known for a long time [6], but this phenomenon was never suggested for the Heck reaction. The most probable explanation for the above effect [7] is the possibility that a hydrogen transfer reaction to the molecule of an unsaturated substrate takes place, along with unimolecular metal hydride β -elimination. This mechanism of the direct involvement of alkene in the rate-determining step is confirmed by the fact found by the authors of [8] that the σ -alkyl complex formed in the insertion step was decomposed (Scheme 1) and the

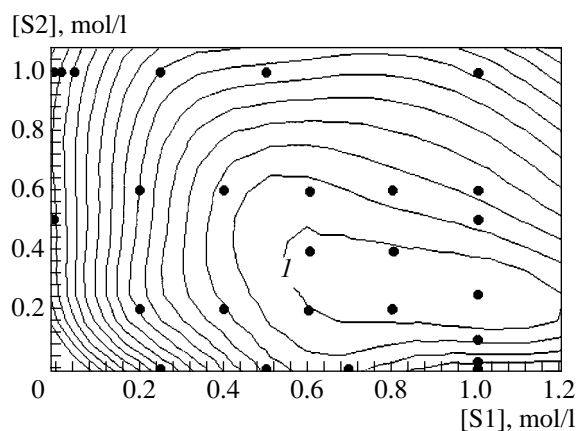


Fig. 3. Plot (plane projection) for the rate of ST phenylation (w_{S1}) vs. concentrations of ST ($[S1]$) and MMA ($[S2]$). The rate isolines shown by a step of $0.5 \times 10^{-2} \text{ mol l}^{-1} \text{ min}^{-1}$ are obtained by spline approximation of the experimental data. Iso-line 1 corresponds to the maximal rate $5.5 \times 10^{-2} \text{ mol l}^{-1} \text{ min}^{-1}$.

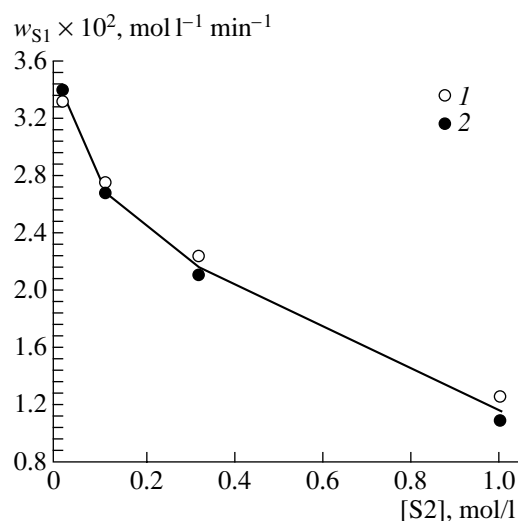
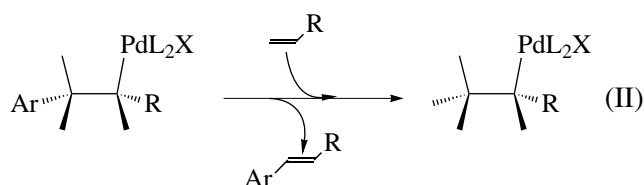


Fig. 4. Plot for the rate of ST phenylation (w_{S1}) vs. MA concentration ($[S2]$) with the ST concentration $[ST] = 1 \text{ mol/l}$ (1, experiment; 2, calculation by Eqs. (1)).

arylated product was only formed in the presence of excess initial alkene:



Note that the quantum chemical calculations of β -hydride elimination [9] showed that the activation

energy of the hydrogen transfer to coordinated alkene is lower than that of the β -hydride transfer to the metal.

Hence, the mutual influence of alkenes during competitive arylation observed experimentally indicates that the rate-determining step of the Heck reaction occurs not only through monomolecular mechanism (Scheme 3, step A) but also mediated with the alkene molecule (Scheme 3, step B). Note that this hypothesis does not rule out negative values of the effective orders with respect to reactants, which were observed in [4], when the hydrogen transfer to alkene, as was shown in

Rates of the competitive (w_{S1+S2})^a and uncompetitive (w_{S1} , w_{S2})^b phenylation of ST, PA, VBE, ET, and PR

No.	Substrate		Rate $\times 10^2$, $\text{mol l}^{-1} \text{ min}^{-1}$			Selectivity (L)	k_{S1}^{el}/k_{S2}^{el} , calculated from ratios:		
	S1	S2	w_{S1+S2}	w_{S1}	w_{S2}		$\frac{w_{S1}}{w_{S2}}$	$\frac{w_{S1}}{w_{S1+S2}}$	$\frac{w_{S2}}{w_{S1+S2}}$
1	ST	MA	4.0	3.4	5.0	0.91	0.68	0.71	0.66
2	ST	PA	5.7	3.4	5.8	0.12	0.59	0.55	0.85
3	ST ^c	VBE ^c	3.9	5.8	0.71	1.60	8.10	2.27	-3.04
4	ST ^d	ET ^d	29.5	22.5	14.0	2.00	1.61	0.29	0.21
5	ST ^d	PR ^d	28.6	22.5	7.2	7.00	3.13	-0.71	6.90

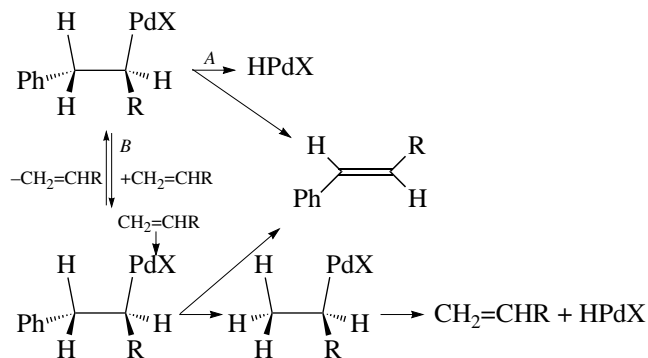
^a Total rate of phenylation of two substrates in the competitive experiment.

^b Rate of the substrate phenylation in the uncompetitive experiment.

^c NBu_3 as a base, 80°C .

^d $\text{NBu}_3 + \text{NaOAc}$ as bases, 80°C .

(II), is accompanied by the formation of relatively more stable σ -complexes.



Scheme 3.

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