

Suzuki reaction: mechanistic multiplicity versus exclusive homogeneous or exclusive heterogeneous catalysis

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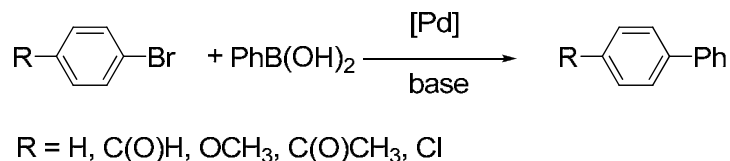
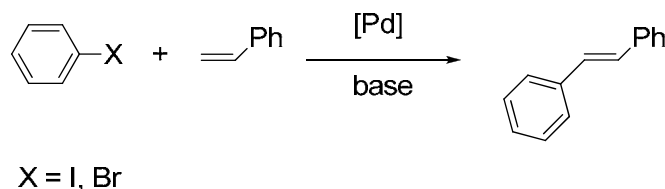
Abstract

Comparative studies of the kinetics and selectivity of the Suzuki and Heck reactions, the modified tests on homogeneity-heterogeneity and an implementation of the solid-phase variant of the Suzuki reaction indicate a substantial contribution of the heterogeneous mechanism to the Suzuki reaction catalysis which is in contrast to the Heck reaction. The contributions of molecular complexes, colloidal Pd and the larger-sized particles to Suzuki catalysis depend on the nature of the catalyst precursor, the solvent and the temperature of the reaction. It has been established that these contributions change significantly during the reaction as well.

Keywords: Suzuki reaction, Heck reaction, mechanism, palladium

Introduction

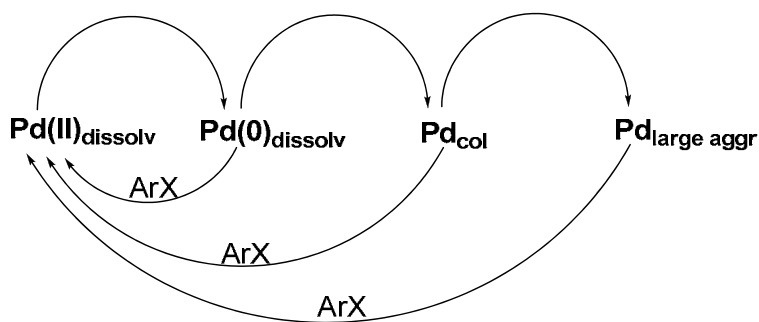
One of the most useful cross-coupling reactions between aryl halides and different reagents (alkenes, alkynes, amines, metallorganic compounds) has been the Suzuki–Miyaura reaction¹ that attracts the greatest attention of investigators (Scheme 1). Now it is quite clear that there is no consensus on the nature of the catalysis of this reaction (see review² published in 2006 and references cited therein). Analysis of the literature for the last two years indicates that some researchers advance the hypothesis of a homogeneous catalysis mechanism³⁻¹¹ while the others suggest a heterogeneous mechanism.¹²⁻¹⁸ It is worth mentioning that the most convincing evidence is for the homogeneous mechanism of the Suzuki reaction.^{3-5,10,11} But mechanistic studies of the reactions never provide absolute unequivocal evidence for any mechanism and it makes judging only possible about the relative probability; a set of different experimental approaches (as wide as possible) to perform the mechanistic research. In this work a new approach to the Suzuki reaction was applied for the first time: i.e. comparative studies of the Suzuki reaction and the Heck reaction (Scheme 2).

**Scheme 1.** Suzuki reaction.**Scheme 2.** Heck reaction.

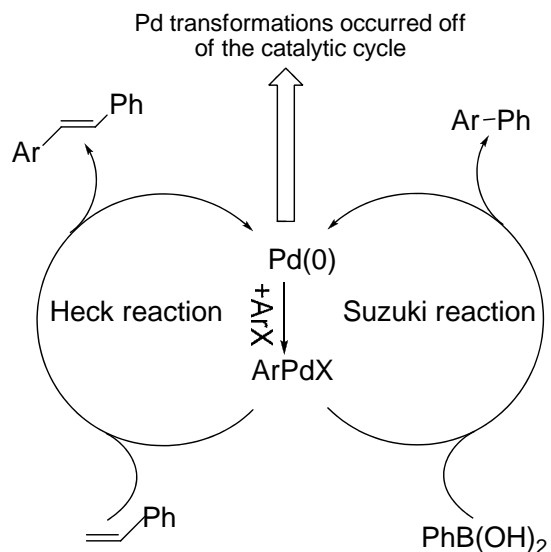
The nature of the Heck reaction catalysis was discussed since the end of the 90ths.^{2,19-27} In the reviews published in 2006^{2,21,22,28} the authors came to the conclusion on the higher probability of exclusive homogeneous catalysis and all of them proposed the same forms of catalyst existing in the course of the reaction (Scheme 3): Pd(0) and Pd(II) dissolved molecular complexes, colloidal Pd in the solution and/or on a support and larger-sized metallic Pd particles. It has been assumed that these catalyst forms interconvert during the reaction and aryl halide plays the most important role in these transformations (Scheme 3). The possibility of the Suzuki and Heck reaction comparative studies is determined by the absence of any experimental facts denying the usage for the Suzuki reaction of the catalyst transformation scheme elaborated earlier for the Heck reaction. These two reactions are related indeed. According to the commonly accepted point of view, the catalytic cycles of the Suzuki and Heck reactions proceed via the stage of an aryl halide oxidative addition to Pd(0) compounds giving rise to σ -arylpalladium intermediates (Scheme 4). The other intermediates of the Heck and Suzuki catalytic cycles appearing after oxidative addition stage do not directly participate in Pd transformations that occur off of the catalytic cycle (Scheme 3). So, it might be expected that the changes of the Pd transformation mechanism out of the catalytic cycle (Scheme 3) in the Suzuki reaction should occur only under the specific influence of arylboronic acid. There is the experimental evidence of such an influence in El-Sayed's work^{29,30} indicating an additive stabilization of Pd-colloidal particles by the arylboronic acid molecules that can be taken into account on subsequent examination of the comparative experiment results.

Except for this case, all available experimental data confirm the similarity between Pd transformations occurring off of the catalytic cycle of the Suzuki and Heck reactions. For instance, Pd leaching under aryl halide action found earlier for the Heck reaction should theoretically (based on scheme 3) occur in the Suzuki reaction. Numerous confirmations of this were, indeed, found,^{4,7,10,31,32} moreover the correlation between the activity and the amount of Pd dissolved was observed in the Suzuki reaction^{10,31} as well as in the Heck reaction.²¹

However, from the previous discussion of the Heck chemistry, it can be concluded that distinguishing between true homogeneous catalysis from heterogeneous catalysis in the Suzuki reaction is undoubtedly a very complicated task. Unfortunately, the results of the conventional tests on reaction homogeneity-heterogeneity³³ are ambiguous due to the interconversions of different catalyst forms (Scheme 3). It can be associated with both varying Pd distribution between different forms during the reaction and the possible compensating effect of the catalytic system which responds (similar to Le Chatelier's principle) to the removal of one of the catalyst forms (for example filtration of solid catalyst or introduction of selective poison for soluble catalytic species) used in the tests. In addition the most complicated case when both homogeneous and heterogeneous catalysis take place simultaneously is very difficult to distinguish. Note this possibility was distinctly formulated only once in recently published work.³⁴ The contribution of both homogeneous and heterogeneous catalysis in the total substrate conversion might differ essentially at different reaction times. So, validity of the experimental data interpretation becomes dependent on the reaction time when one of the catalyst forms is separated during the test procedure. The same problems appear when relationships between the catalyst amount and the activity applied for distinguishing homogeneous catalysis from heterogeneous are analyzed.^{3,28,35} The results might differ essentially depending on both the manner and the time chosen for the measurement of the catalyst activity (initial, overall or maximal activity over a certain period of time).



Scheme 3. Pd transformations occurring off of the catalytic cycle in the course of the Heck reaction.



Scheme 4. The similarity between catalytic cycles of Suzuki and Heck reactions.

In this work we have attempted to interpret obtained experimental data taking into account all problems described above. For this purpose the corresponding kinetic experiments, modified tests on homogeneity-heterogeneity, studies of selectivity as well as a solid-phase variants of the Suzuki reaction were performed.

Results and Discussion

Comparative kinetic studies of the Suzuki and Heck reactions

It has been established that the performance of the Suzuki and Heck reactions under the same conditions at 140°C in DMF led to essentially different product yields. Figure 1 indicates that the main reason is the distinction between lifetime of the catalytic systems. Much more remarkable distinctions between the Suzuki and Heck reactions were observed at ambient conditions (22°C). There were no traces of product at all when the Heck reaction was performed, while the Suzuki reaction occurred smoothly and using NaOH as a base and an ethanol-H₂O mixture as solvent, the catalytic activity was so high that the reaction was completed in 40-60 min (Table 1).

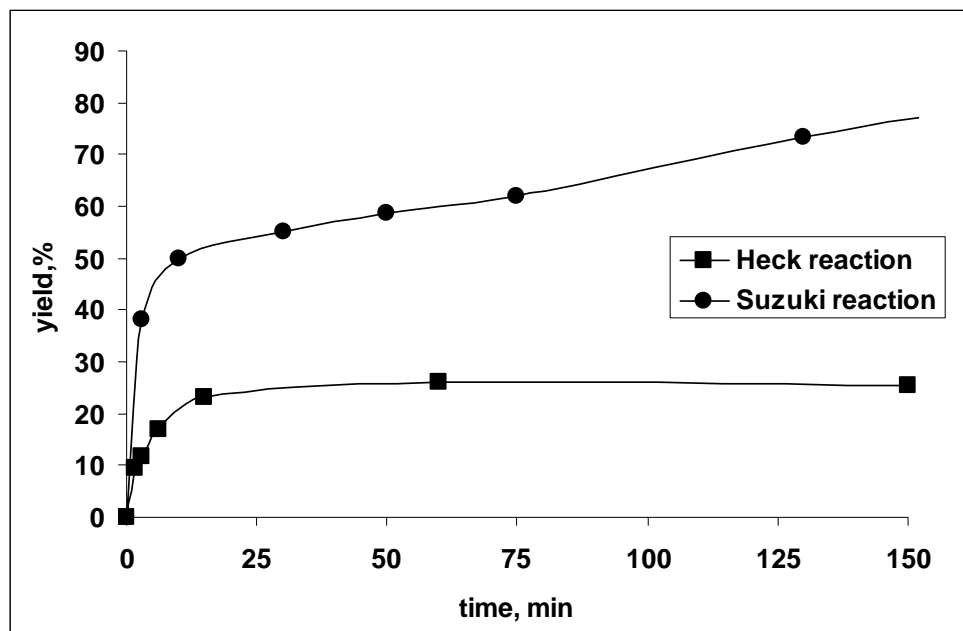


Figure 1. Yield vs. time diagram of the Suzuki and Heck reactions (Scheme 1, 2) at 140°C. Reaction conditions: bromobenzene (5 mmol), styrene or PhB(OH)₂ (5 mmol), sodium acetate(6.5 mmol), naphthalene (1 mmol) as internal standard, DMF (5 mL) as solvent and PdCl₂ (0.08mmol).

Table 1. Suzuki and Heck reactions at 22 °C

	Yield,% (DMF-H ₂ O, NaOAc)	Yield,% (Ethanol-H ₂ O, NaOH)
Suzuki reaction	74 ^[a]	80 ^b
Heck reaction	0 ^[a]	0 ^a

^areaction time 48 h. ^breaction time 1 h.

According to the conventional concept, the problems of the Heck reaction with non-activated arylating agents (like PhBr) are conditioned by the low rate of their oxidative addition to Pd(0) that leads to fast Pd agglomeration resulting in the formation of nonactive solid catalyst forms. Available examples of the Heck reaction performed at room temperature with the active alkenyl nonafluorobutanesulfonates (instead of aryl halides) in the presence of ligand-free catalytic systems³⁶ make the alternative explanations, which suppose a considerable challenge to the stages with alkene participation, less credible. In such a case, the longer catalyst lifetime and a higher yield at 140°C as well as the effective proceeding of the Suzuki reaction at room temperature in comparison with the Heck reaction, make a conclusion on the possible catalytic activity of the formed Pd aggregates, which are not able (according to the accepted viewpoint) to exhibit the catalytic activity in the Heck reaction, possible.

Another important distinction between the Suzuki and the Heck reactions in the presence of heterogeneous Pd/C as a catalyst precursor has been found. The availability of an induction period at the starting phase of the process²¹ is characteristic for the Heck reaction. It has unequivocally been established earlier that in the Heck reaction an induction period correlates with Pd leaching. It follows from figure 2 that an induction period in the Suzuki reaction was either absent or considerably shorter than in the Heck reaction under the same conditions. Formally this indicates either the catalytic activity of initial heterogeneous Pd/C or much faster Pd leaching in the Suzuki reaction than in the Heck reaction. Note that an induction period is not observed even when the temperature of the Suzuki reaction decreased from 140° to 22°C (the Suzuki reaction time profile at 22°C is presented in Supplementary materials).

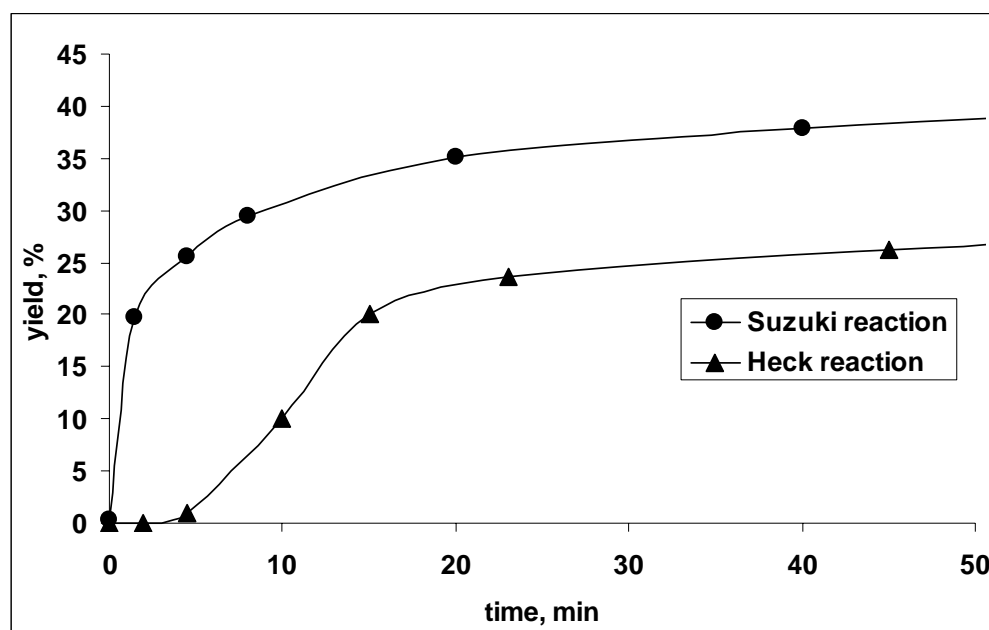


Figure 2. Yield vs. time diagram of the Suzuki and Heck reactions (Scheme 1, 2) with 4%-Pd(0)/C as catalyst precursor at 140 °C. Reaction conditions: bromobenzene (5 mmol), styrene or PhB(OH)₂ (5 mmol), sodium acetate(6.5 mmol), naphthalene (1 mmol) as internal standard, DMF (5 mL) as solvent and 4%-Pd(0)/C (0.08mmol of Pd).

The formation of Pd anionic complexes ($[\text{PdI}_4]^{2-}$, $[\text{Pd}_2\text{I}_6]^{2-}$) was observed earlier in the Heck reaction with aryl iodides.³⁷⁻⁴⁰ It was recently shown by UV-vis spectroscopic studies that in the Heck reaction with non-activated aryl bromides the considerable Pd quantity (up to 70% of the total metal amount) also transformed to the oxidized form $[\text{PdBr}_4]^{2-}$.⁴¹ Using the same approach to the Suzuki reaction the characteristic absorption of $[\text{PdBr}_4]^{2-}$ (335-340 nm) in spectra of reaction solution was not observed. However, the absorption was found in the area of 360 nm, and its intensity passed through the maximum in the course of reaction (Figure 3). The performance of the Suzuki reaction at room temperature was accompanied by an appearance of

the same absorption band which was stable during 68 hours of the reaction. It was noteworthy that a shoulder at 360 nm was observed as well when the Suzuki reaction was performed using Pd/C as catalyst precursor (Figure 4). According to experimental results,^{4,42} and the theoretical calculations based on Mi's theory,⁴³ the absorption at 360 nm is associated with the surface plasmon resonance of Pd nanoparticles. GC and UV monitoring of the Suzuki reaction performed simultaneously, indicated that a disappearance of both the catalytic activity and the absorption at 360 nm occurred practically at the same time (Figure 3). The latter can be explained by the participation of the "soluble" nanoparticles in catalysis (i.e. heterogeneous catalysis on the surface of the nanoparticles).

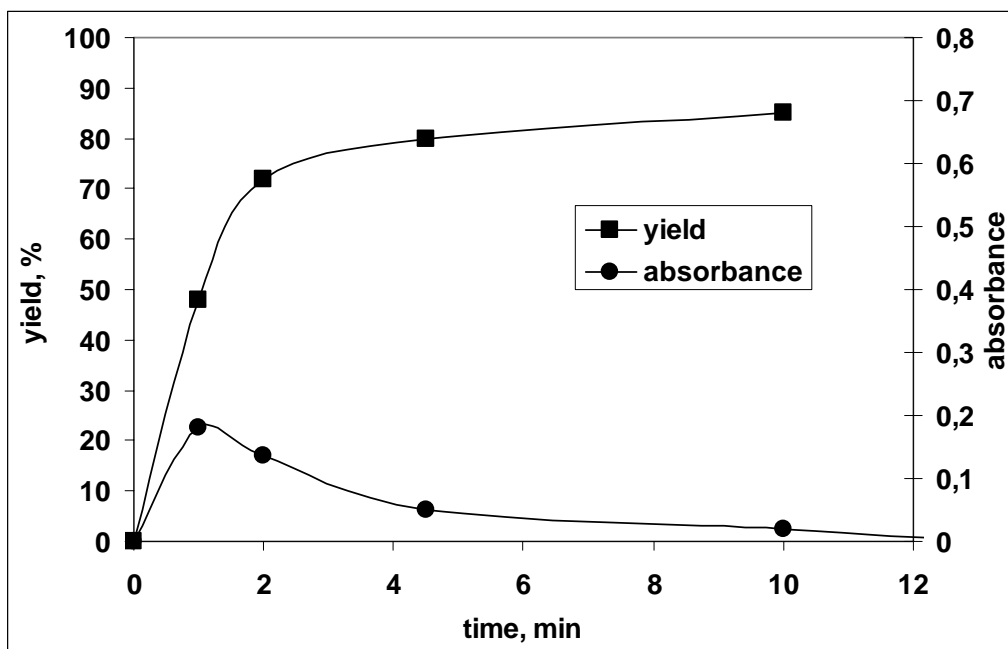


Figure 3. Temporal dependencies of the yield of biphenyl (GC) and absorbance at 360 nm (UV) during the Suzuki reaction (Scheme 1) at 140 °C. Reaction conditions: bromobenzene (5 mmol), PhB(OH)₂ (5 mmol), sodium acetate(6.5 mmol), naphthalene (1 mmol) as internal standard, DMF-H₂O (5 mL) as solvent and PdCl₂ (0.08mmol).

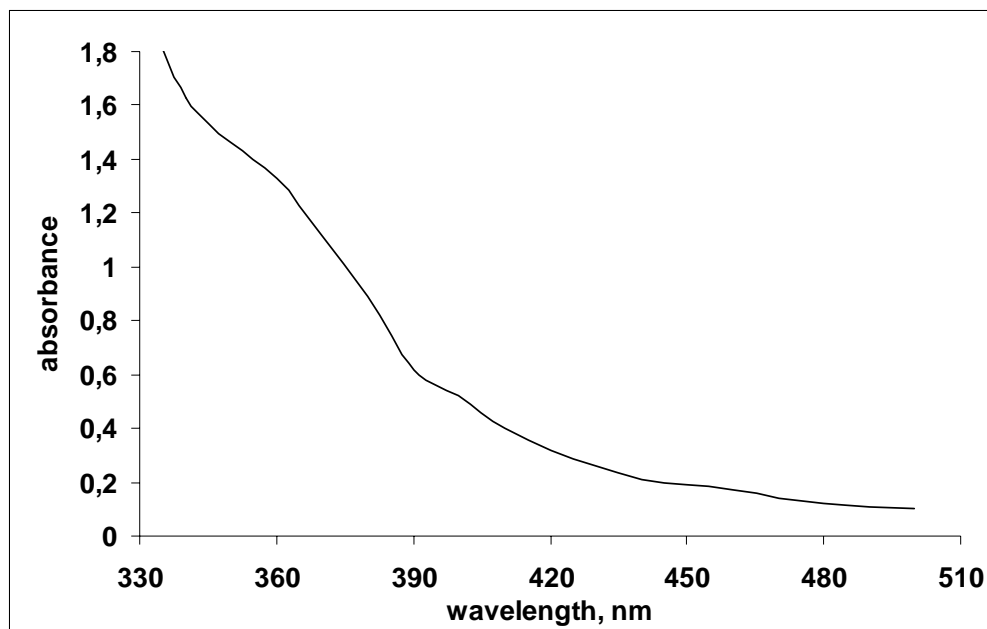


Figure 4. The UV-spectrum of the Suzuki reaction solution with 4%-Pd(0)/C as catalyst precursor at 22°C (reaction time 140 h). Reaction conditions: bromobenzene (5 mmol), PhB(OH)₂ (5 mmol), sodium acetate(6.5 mmol) DMF-H₂O (5 mL) as solvent and 4%-Pd(0)/C (0.08mmol of Pd).

In our opinion, according to the results presented in this section, some doubts are rising on the exclusive homogeneous catalysis of the Suzuki reaction postulated by analogy with the Heck reaction. It is worth assuming that at least the Suzuki reaction partially proceeds on the surface of colloidal Pd or on larger Pd particles formed in the course of the reaction.

The Suzuki and Heck reaction tests on homogeneity-heterogeneity

The authors supporting the opposite hypotheses on the catalysis nature of the Heck and Suzuki reactions have used the test results as evidence for their conclusions.^{4-8,15-18} The principle of most tests is the withdrawal of one of the catalyst forms from the reaction by any chemical or physical manipulation followed by measurement of the catalytic activity. But the most difficult situation might appear when catalyst forms (for instance dissolved and solid) are able to interconvert directly during the catalytic reaction. Then the removal of any catalytic form, irrespective of its role in catalysis, leads undoubtedly to changes of the catalytic activity due to redistribution of the catalyst between its form and therefore to the possibility of incorrect interpretation of the test results. As mentioned above, the interconversion of Pd species in the coupling reactions of aryl halides is the established fact (Scheme 3) and we believe that just that has caused contradictory test results reported by different authors.

In the case when all of the catalyst forms contribute significantly to the catalyst distribution and the fast interconversion of these forms are implemented, two limiting cases of the reaction response to the removal of one of the catalyst forms are theoretically possible:

- the removal of the active catalyst form causes a significant decrease of the catalytic activity with its subsequent gradual increase;
- the removal of the non-active catalyst form leads to the gradual decrease of the activity.

However, since the processes of the interconversion are usually multistage and therefore they are of complicated kinetics, another reaction response is also possible.

The general way to overcome these difficulties might be a withdrawal of one of the catalyst forms as fast as possible and the mandatory fixation of the temporal dependence of the response of reaction kinetics (e.g. the rate and/or selectivity, but not yield!).⁴⁴ In doing so, it is necessary to strive not to break the reaction conditions (at least these conditions should be controlled). By following these recommendations, a researcher has a chance to observe the true response of the catalytic system to the test procedure. Such an approach is close to a “response method”,⁴⁵ when the responses of a reaction system to perturbations of several kinds are studied.

The usage of a DMF-H₂O mixture as a solvent considerably increased the rate and conversion in the Suzuki reaction at 140^oC with Pd/C as catalyst precursor. Therefore DMF-H₂O was used in subsequent experiments with filtration. When fast filtration was performed in the special two-compartment reactor (filtration time was ~1 min)⁴⁴ we have obtained data indicating that the reaction rate before and after the filtration procedure remained practically unchanged in the Suzuki reaction (Figure 5). Similar results were obtained earlier for the Heck reaction.⁴⁴

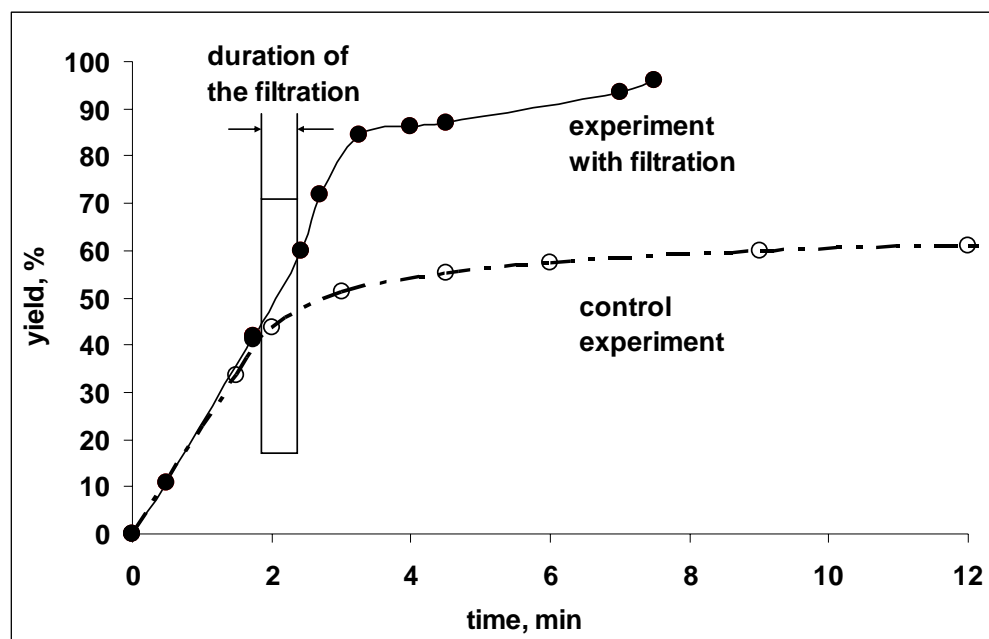


Figure 5. Yield vs. time diagram of the Suzuki reaction (Scheme 1) with fast filtration (control experiment without filtration is shown by the dashed curve, the duration of filtration is indicated

by the marked area) at 140°C. Reaction conditions: bromobenzene (5 mmol), PhB(OH)₂ (5 mmol), sodium acetate(6.5 mmol), naphthalene (1 mmol) as internal standard, DMF-H₂O (5 mL) as solvent and 4%-Pd(0)/C (0.08mmol of Pd). Fast filtration was applied at 1.8 min.

Such a test result is strong evidence⁴⁶ that a solid form of the catalyst (removed by filtration) is not responsible for the activity. However this test does not allow to distinguish between true homogeneous catalysis from “soluble” Pd nanoparticle heterogeneous catalysis. All the same, in our opinion, the hypothesis for nanocatalysis in the Suzuki reaction in the DMF-H₂O mixture might be considered more probable since Pd nanoparticles were not only found experimentally but their lifetime correlated with the catalyst lifetime (Figure 3).

After filtration, the further control over the reaction makes it possible to observe the response of the Suzuki catalytic system (Figure 5). In the Heck reaction after the withdrawal of the solid catalyst⁴⁴ the second limiting case of the theoretically expected reaction response has been observed. The catalytic activity dropped in comparison with the control experiment (without filtration) in some time. A number of similar effects using hot filtration procedures are described in the literature.^{5,7,26,47} Pd black particles were visually observed after 7 minutes after filtration.⁴⁴ The formation of Pd black particles was indicative of the redistribution between catalyst forms after the solid phase separation. In contrast, the catalytic system in the Suzuki reaction after the filtration was more stable in comparison to the control experiment that allowed obtaining a higher conversion (Figure 5). Note that the higher catalyst activity after hot filtration was also observed earlier in Heck reaction.⁴⁸

The different behavior of the catalytic systems after the withdrawal of the catalyst points to a different nature of the true catalytic species of these reactions. Actually, an aggregation of Pd(0) complexes, unstable in the solution during the Heck reaction, is a negative process leading to catalyst deactivation, while in the Suzuki reaction such a process might be the process of the active catalyst formation. The filtration allows avoiding the adsorption of the formed nanoparticles to the activated carbon. The adsorption might cause a decrease of the accessible surface of particles and therefore a decrease of their catalytic activity.

The possibility of the Suzuki reaction proceeding at room temperature in a DMF-H₂O mixture allowed us to apply another procedure of the fast separation of the solid phase without interfering with the reaction conditions via centrifugation of the reaction mixture. One half of the reaction mixture from the first reactor was subjected to centrifugation and then placed into the second reactor. The reaction proceeding in both reactors did not practically differ from the other (See Supplementary materials). This was compelling evidence that a solid form of the catalyst (removed by centrifugation) is not responsible for the activity as well as it was at 140°C.

As it was mentioned, the highest activity was observed when the Suzuki reaction was performed in a ethanol-H₂O mixture in the presence of NaOH as a base and PdCl₂ as catalyst precursor. Noteworthy, the color of the reaction mixture changed very fast (~30 seconds) from light brown to black and then to gray even at room temperature and the Pd-black formation was visually observed. Interestingly, in such a case after the Pd-black separation by centrifugation,

the solution was absolutely colorless and the UV-spectrum did not contain signs of the plasmon resonance or light scattering from Pd particles. It points to the predominant contribution of the catalyst solid phase to the Pd distribution at relatively low temperatures. Such a shift in the Pd distribution with a lowering temperature was expected due to the retardation of the stages responsible for Pd preservation in the solution. It implies with the aryl halide oxidative addition to Pd(0) molecular complexes and the metallic Pd dissolution (Scheme 3). The latter is most likely to proceed through the same stage.⁴⁹ Note that the Pd agglomeration rate is less sensitive to lowering the temperature due to the low activation energy in comparison with the rate of conventional chemical reactions.

It is very important in our opinion that just under these conditions the positive result of the test using centrifugation has been observed which is indicative of the catalytic activity of the solid catalyst (Figure 6). Undoubtedly, the very fast deactivation of the homogeneous catalyst or nanocatalyst following shortly after the solid phase separation can not be ruled out. However centrifugation allows to reduce the time of the solid catalyst separation under a few seconds (decantation procedure) without any change in reaction conditions. Therefore a full termination of the reaction after centrifugation provides a good reason for the conclusion on a dominant role of heterogeneous catalysis in the Suzuki reaction performed in an ethanol-H₂O mixture.

Comparative studies of the Suzuki and Heck reaction selectivity

The investigation of the selectivity does not provide an answer to the quintessential question about the nature of the catalytically active species. But it allows to obtain unequivocal answers to the other important question whether the nature of the actual catalyst is unchanged using different catalyst precursors. Such an approach can be applied to comparative studies of homogeneous and heterogeneous catalyst precursors. In cases when the reaction occurs on the surface of metallic Pd or is subjected to molecular complexes in solution, the equal selectivity of the reaction is highly improbable. The selectivity of several homogeneous and heterogeneous catalysts used in the Heck reaction with the same substrate was studied earlier.⁵⁰ The employment of the substrate set under the conditions of competitive reactions should give much more information. The set of aryl halides with various substituents allowing the application of the Hammett equation formalism could be used. Similar studies using the Hammett equation for the Heck reaction were already carried out to compare just different homogeneous^{51,52} to homogeneous and heterogeneous catalyst precursors.⁴⁴ This approach was applied to the Suzuki reaction only once.⁵³ But the authors have apparently used non-competitive experiments for the construction of Hammett dependences that could lead to wrong results since different amounts of catalytically active species might be formed from different catalyst precursors.

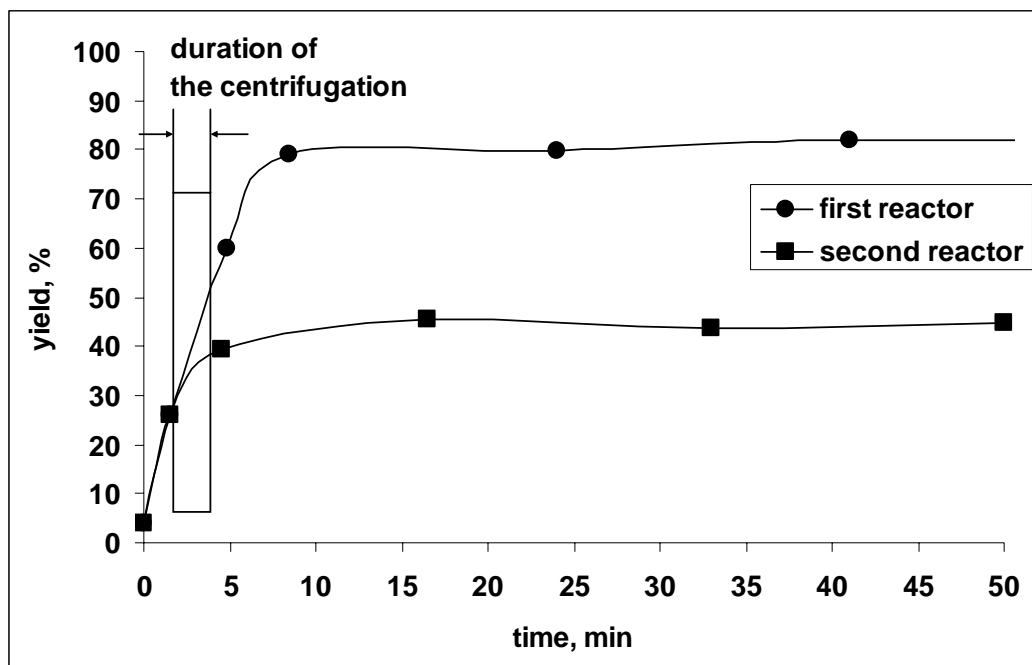


Figure 6. Yield vs. time diagram of the Suzuki reaction (Scheme 1) without (first reactor) and with (second reactor) centrifugation at 22°C (the duration of centrifugation is indicated by the marked area). Reaction conditions: bromobenzene (5 mmol), PhB(OH)₂ (5 mmol), sodium hydroxide(6.5 mmol), naphthalene (1 mmol) as internal standard, ethanol-H₂O (5 mL) as solvent and PdCl₂ (0.08mmol). Centrifugation was applied at 1.5 min.

As the formation of solid catalyst is most likely in the reactions with non-reactive aryl halides, several *p*-substituted aryl bromides were used in the experiments described below. Since the consumption rates of competitive substrates are different during reaction, the measurement of the reaction selectivity in such a kind of experiments is usually carried out at very low conversion to prevent the effect of a changeable ratio of the substrate concentrations. However we are interested in dependencies of the selectivity vs. reaction time to establish possible changes of the selectivity caused by Pd redistribution between different forms during the reaction. In this case the temporal control of the selectivity requires taking into account the changeable substrate concentrations. Therefore, we estimated the selectivity as follows (See Supplementary materials):

$$S_n^{ArBr} = \frac{(C_n^{ArBr} - C_{n+1}^{ArBr})}{C_n^{ArBr}} \frac{C_n^{PhBr}}{(C_n^{PhBr} - C_{n+1}^{PhBr})}$$

The magnitude of the selectivity is expected to be constant during the reaction providing the catalyst exists in a single catalytically active form irrespective of the amount of this form (See Supplementary materials). Thus a deviation from the constant value might be connected with a

change of the contributions of two or more catalyst forms of different selectivity into catalysis. The magnitudes of $\log(S_n^{ArBr})$ obtained at the certain reaction time ($t_{n+1}-t_n$) were used for construction of the Hammett plot. Calculated ρ value characterizes the sensitivity of the catalyst selectivity to a substituent in the aryl halide. The correlation coefficients of obtained dependencies were varied in the range 0.90-0.95.

From figure 7 it follows that ρ parameter vs. time dependence for the Suzuki reactions using PdCl_2 or Pd/C are varied fundamentally. In the reaction with Pd/C , ρ passed through a maximum while in the reaction with PdCl_2 , ρ decreased continuously.

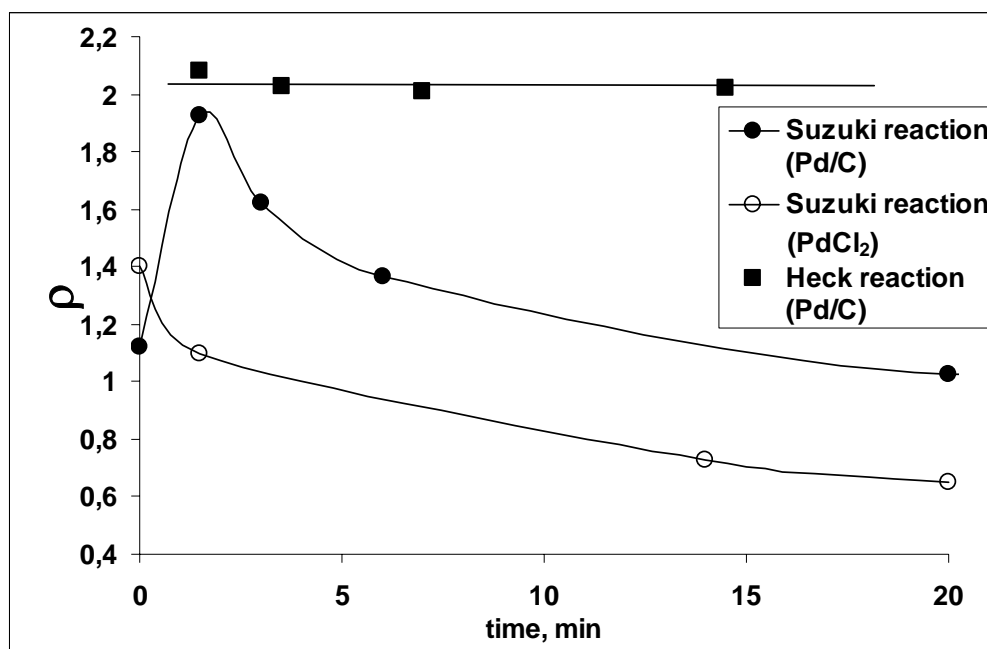


Figure 7. ρ vs. time diagram of the Suzuki and Heck reactions (Scheme 1, 2) with set of arylbromides at 140°C. Reaction conditions: Arylbromides (see experimental section), PhB(OH)_2 (5 mmol), sodium acetate(6.5 mmol), naphthalene (1 mmol) as internal standard, DMF (5 mL) as solvent and PdCl_2 or 4%-Pd/C (0.08mmol).

In Pd/C catalyzed Heck reactions under the same conditions ρ magnitudes were greater than 2 (Figure 7) which correlated with the data of other investigators for the Heck reaction with aryl bromides.^{51,54,55} The ρ parameters obtained in our work in different instances of the Suzuki competitive reaction for both PdCl_2 and Pd/C were less than 2 which was also consistent with the data of other researchers.^{56,57} A single exception is the work⁹ where the ρ magnitude for the Suzuki reaction was greater than 2 and practically concurred with the magnitude obtained for the Heck reaction.⁵⁸ Based on that, the authors came to a conclusion on the identity of catalytically active species in these reactions. But it is necessary to note that the possible changes of ρ during the reaction induce the ρ magnitude to be dependent on the method of the reaction rate

measurement. In addition a comparison of the ρ absolute magnitude in both Suzuki and Heck reactions will be only proper provided that the oxidative addition of aryl halides to Pd(0) occur as a practically irreversible stage. In that case ρ magnitude in the Suzuki and Heck reactions should be determined only by properties of the oxidative addition stage (See Supplementary materials). But an assumption of the irreversibility of the oxidative addition requires experimental evidence.

For the catalysis nature to be clarified, it is more important to know the trends of the changes of ρ magnitudes during the reaction rather than their absolute magnitudes. A practically invariable ρ magnitude was observed for the Heck reaction (Figure 7) that pointed to the domination of the single catalyst form viz. Pd dissolved molecular complexes according to the accepted viewpoint. The change of ρ magnitude in the course of the Suzuki reaction is indicative for the contribution of at least two catalyst forms of different selectivity. If it is considered that the high ρ magnitude in the Heck reaction is conditioned by the dominant contribution of homogeneous catalysis into total conversion, then the lower ρ magnitude in the Suzuki reaction might be connected with significant contribution of other catalyst forms including heterogeneous ones. On this basis, passing ρ through the maximum for the reaction with Pd/C (Figure 7) signifies just a temporary increase of the homogeneous catalysis contribution. That is in excellent agreement with assumptions made above of the catalytic activity of the initial Pd/C prevailing in the reaction beginning (low ρ), the formation of molecular complexes in the solution (maximal ρ) and the subsequent formation of colloidal Pd (low ρ). A decrease of the ρ magnitudes with time in the Suzuki reaction using reasonable amounts of dissolved PdCl₂ as a catalyst precursor might also be attributed to an increase of the heterogeneous catalysis contribution which occurs due to the formation of the Pd aggregates and a decrease of the molecular complexes fraction.

Thus the data obtained point to the existence of one or a few catalyst forms in the Suzuki reaction, the selectivity of which differs from the catalyst selectivity in the Heck reaction. The trends of the selectivity change correlate well with an assumption of the catalytic activity of Pd heterogeneous forms in Suzuki reaction based on the tests and kinetic studies described above.

The solid-phase Suzuki reaction

The implementation of a solid-phase version of the Suzuki reaction using only solid components under solvent-free conditions may be an important demonstration of the heterogeneous catalysis possibility. In the literature there are a few examples of the Suzuki reaction performed without solvent.⁵⁹⁻⁶³ But in all of these cases at least one liquid component was used. Therefore, we have attempted to perform the reaction between solid *p*-bromobenzaldehyde, phenylboronic acid, NaOH and PdCl₂ at room temperature. In 20 min after the components were mixed, a change of both the color and the consistence of the solid mixture was observed. In one hour, the color changed from light-brown to black. Analysis of the probes, being periodically taken up, showed the presence of the Suzuki reaction products. Product yield was increasing as reaction time increased (Figure 8).

As GC required dissolution of the solid samples of the reaction mixture it was necessary to exclude the possibility of the reaction product formation after solvent addition. Note that a monotone increase in yield of the reaction product with time is in itself contradictory to such an assumption. If a reaction proceeded as a liquid-phase reaction, the nature of the solvent would affect the reaction rate and consequently the GC results. So different solvents: toluene, aqueous DMF, aqueous ethanol and a mixture of toluene and styrene were used for an analysis of the solid probes taken in the same instance of time. Using the mixture of toluene and styrene (1:1) the liquid-phase reaction is particularly unlikely to proceed due to alkene capability (established by special experiments) to inhibit the Suzuki reaction completely at low temperature. Product yields were practically the same using toluene, aqueous DMF and a mixture of toluene and styrene. A somewhat higher product yield (8-10 % more) has been observed in aqueous ethanol which is a very effective medium for the Suzuki reaction at room temperature as noted above. In addition the product content in all of the liquid probes, being controlled several times, remained unchanged during 24 hours. Based of these data there is a good reason to believe that the Suzuki reaction products are formed, indeed, under solid-phase reaction conditions.

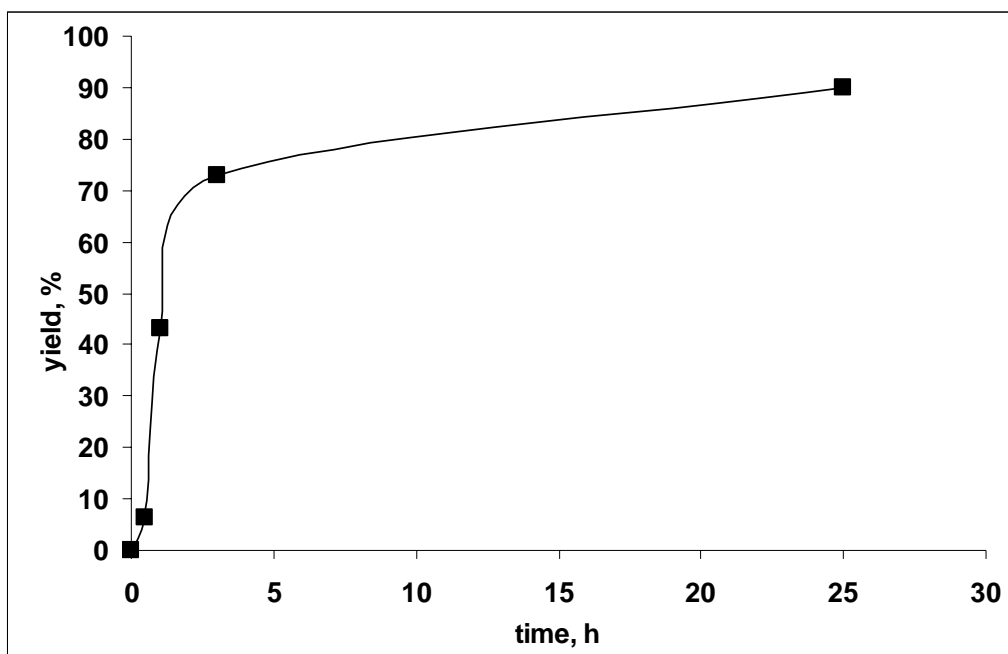


Figure 8. Yield vs. time diagram of the solid-phase Suzuki reaction (Scheme 1) between *p*-brombenzaldehyde and phenylboronic acid at 22°C. Reaction conditions: *p*-brombenzaldehyde (5 mmol), PhB(OH)₂ (5 mmol), sodium hydroxide(6.5 mmol), naphthalene (1 mmol) as internal standard and PdCl₂ (0.08mmol).

Conclusions

The combination of our experimental results - comparative kinetic studies of the Suzuki and Heck reactions; modified tests on homogeneity-heterogeneity, studies of the selectivity, implementation of solid-phase variant of the Suzuki reaction – indicates the significant contribution of a heterogeneous mechanism to the Suzuki reaction catalysis. The Suzuki reaction was found to occur more smoothly compared to the Heck reaction accompanied by quantitative product yields under mild conditions. It is associated with participation of heterogeneous catalyst forms such as colloidal Pd and larger-sized aggregates. The contributions of molecular complexes, colloidal Pd and the larger-sized aggregates to catalysis depend on the nature of the catalyst precursor, solvent and temperature. It has been established that these contributions change during the reaction as well.

So both concepts that are discussed in the literature to be exclusive homogeneous or exclusive heterogeneous catalysis of the Suzuki reaction are not consistent with the data obtained in this work. The possibility of the “soluble” Pd nanoparticle formation after Pd leaching from the surface of supported catalysts (Pd/C in this work) suggests that previous analysis of several experiments including results of three-phase tests and activity-Pd leaching relationships may need to be reinterpreted.

Experimental Section

General Procedures. All reactions were carried out under an air atmosphere. UV spectra (absorbance vs. wavelengths) were recorded on a Spekord-UV-VIS spectrophotometer. The samples of the reaction mixture after centrifugation (used for removal of solids) were placed into a quartz cuvette ($b=0.01$ cm) without additional dilution. The gas-liquid chromatograms were recorded on a chromatograph HP-4890 series equipped with a FID detector and a HP-5 column (cross-linked methylphenylsiloxane, 15 m x 0.53 mm x 1.5 μ m film thickness). The reactions were monitored by taking small samples for GC and UV analysis. Products were identified by comparison with the authentic samples. In all experiments benzene formed as byproduct (3-10%). The calibration curves for determining the yields of benzene and biphenyl were constructed by plotting the peak area vs. concentration of benzene and biphenyl standards. The consumption of bromobenzene at any reaction time coincided with the sum of biphenyl and benzene yields that indicated negligible effect of reductive and oxidative homocoupling of bromobenzene and phenyl boronic acid respectively.

The fast filtration of the reaction mixture was performed without interruption of the reaction using special glass two-compartment reactor.⁴⁴ The centrifugation was performed for 2 min; after that one half of a liquid phase was separated and introduced into another reactor. The rate of centrifugation (11500 rpm) allowed separating only large-sized particles from the solution.

Dissolved Pd (including “soluble” nanoparticles) remained in the solution. The control of reaction (GC) was performed in both reactors.

General procedure for catalytic runs

In comparative kinetic experiments bromobenzene (5 mmol), PdCl₂ or 4% Pd/C (0.08 mmol based on Pd), styrene (5 mmol) in Heck reaction or PhB(OH)₂ in Suzuki reaction, naphthalene (1 mmol) as internal standard for GC analysis, base (6.5 mmol) and 5 ml of solvent were introduced in a glass reactor fitted with a magnetic stirring bar and septum inlet. The reactor was placed into a pre-heated oil bath and the reaction mixture was stirred. NaOAc or NaOH were used as a base, and DMF, DMF-H₂O mixture (4:1) or ethanol-H₂O (4:1) were used as a solvents. The experiments were performed at 140° or 22°C.

General procedures for the comparative studies of the selectivity

In case of the competitive reactions with a set of aryl bromides the mixture of PhBr, 4-H(O)C-C₆H₄-Br, 4-MeO-C₆H₄-Br, 4-MeCO-C₆H₄-Br, 4-Cl-C₆H₄-Br (1 mmol of each) was used.

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