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Role of Catalyst Deactivation and Regeneration in the Heck Reaction Involving Unactivated Aryl Bromides

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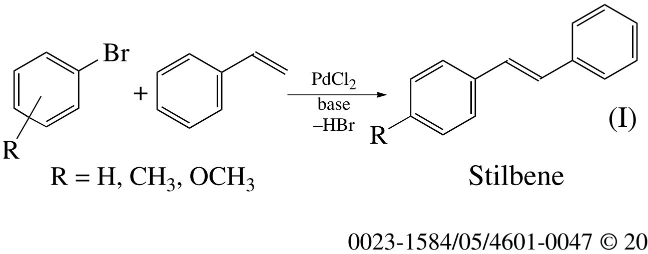
Abstract—Excess aryl halide and a reducing agent admixture extend the lifetime of a catalyst in the Heck reaction. In the presence of a simple catalytic system without any ligands, the reaction between an unactivated aryl bromide and styrene in dimethyl formamide yields a stoichiometric amount of the product when the starting mixture contains 0.04–1.6 mol % $PdCl_2$, 18% HCOONa, 112% AcONa, and a sixfold excess of the aryl bromide (with respect to the initial amount of styrene). It is possible to raise the turnover number of the catalyst by conducting the reaction in several successive runs without regenerating or separating the catalyst. The data obtained confirm the earlier hypothesis that colloidal palladium particles formed during the reaction serve as a main “reservoir” accumulating catalytically active, homogeneous Pd(0) complexes.

The Heck reaction is a promising method for obtaining substituted alkenes [1, 2]. At present, researchers are seeking catalytic systems capable of activating aryl bromides, which are more readily available but less reactive than iodides. Such a catalytic system would make the Heck reaction commercially feasible [1]. The insufficiently high catalytic activity is mainly due to the low reactivity of the aryl bromide in oxidative addition to the Pd(0) complex (Scheme 1). This causes catalyst withdrawal from the main catalytic cycle through the aggregation of Pd(0) particles. Note that aryl bromides differ considerably in their reactivity in the Heck reaction. Substrates having strong acceptor groups in the aromatic ring are comparable in reactivity with aryl iodides [1]. In the case of unactivated aryl bromides with donor substituents, of special interest are catalytic systems that contain no ligands (e.g., phosphines, which are conventionally used in this reaction). There have already been reports on phosphine-free catalytic systems capable of involving unactivated aryl bromides in the Heck reaction [3, 4]. In those cases, heterogeneous supported palladium catalysts were used as precursors. The only homogeneous catalytic system is described by Reetz *et al.* [5]. However, tetraphenylphosphonium and dimethylglycine were employed in place of phosphine in that study. Here, we report the first ligand-free catalytic system capable of effectively catalyzing the reaction of unactivated aryl bromides with styrene in air:



(I)

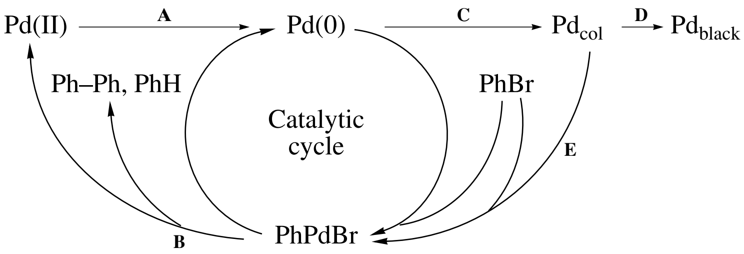
EXPERIMENTAL

Styrene was arylated in a magnetically stirred vessel at 140°C. To dimethyl formamide (10 ml) were added styrene (10 mmol), PhBr (60 mmol), NaOOCH (1.8 mmol), NaOAc (11.2 mmol), naphthalene (2 mmol) as the internal standard, and $PdCl_2$ (0.16 mmol or 1.6 mol % with respect to styrene) or the corresponding amount of the 5% Pd/C catalyst (IKB-3-20). Analysis of the products was carried out in the temperature-programmed mode between 100 and 250°C using an HP 4890 gas–liquid chromatograph with a flame-ionization detector and an HP-5 15-m-long capillary column (Hewlett-Packard). Reaction rates were determined by graphical differentiation of the linear portions of concentration-versus-time curves.

RESULTS AND DISCUSSION

Scheme 1 presents the main processes responsible for catalyst deactivation and regeneration in the Heck reaction. The interrelation of the rates of these processes and the rate of the main catalytic cycle plays the key role in arylation by nonreactive aryl halides. Pd(II) reduction to Pd(0) (Scheme 1, process **A**) is necessary throughout the reaction, not only at its initial stage, because of the permanent reduction of the aryl bromide to Ph–Ph and PhH (Scheme 1, process **B**). As a result, even at 130°C, most of the palladium in the reaction between iodobenzene and styrene is in the oxidized state [6]. However, this problem can be eliminated by adding a small amount of a reducing agent, e.g., sodium formate, to the system, as in the case of the reaction with aryl iodides [7].

Another unwanted process in the Heck reaction is the aggregation of catalytically active Pd(0) complexes



Scheme 1.

(Scheme 1, processes **C**, **D**) because of the low reactivity of PhBr. The formation of colloidal palladium (Pd$_{col}$) in the course of aggregation was observed in [8]. The significant role of colloidal palladium is demonstrated below. At this point, note that part of the aggregated palladium can return into the catalytic cycle through reaction with the aryl halide [9, 10] (Scheme 1, process **E**). This process includes oxidation of surface palladium by the aryl halide and the dissolution of the complex that has resulted from halide anion coordination [9, 10]. The competition between aggregation and the catalytic cycle suggests that raising the ArBr concentration will at least favor an increase in the current palladium concentration in the catalytic cycle.

This theoretical analysis has received complete experimental substantiation (Table 1). As would be expected, the catalytic system PdCl$_2$ + AcONa (Table 1, test 1) shows low activity in the reaction between styrene and bromobenzene. Adding sodium formate increases the reaction rate and does not change the stilbene yield (Table 1, test 2). At the same time, with a fourfold excess of bromobenzene, the stilbene yield is 41% (Table 1, test 3). With a sixfold excess of bromobenzene, it is possible to convert all of the styrene

Table 1. Effect of introducing a reducing agent and excess PhBr in reaction (I)

Test no.	Catalytic system	Styrene : PhBr	Time,[a] min	Reaction rate $\times 10^2$, mol l^{-1} min^{-1}	Ph–Ph and PhH yields,[b] %	Stilbene yield,[c] %
1	PdCl$_2$ + AcONa	1 : 1	45	2.1	1.0	26
2	PdCl$_2$ + AcONa + HCOONa	1 : 1	5	6.0	3.0	24
3	PdCl$_2$ + AcONa + HCOONa	1 : 4	15	4.2	1.0	41
4	PdCl$_2$ + AcONa + HCOONa	1 : 6	10	18	1.5	95
5	PdCl$_2$ + AcONa	1 : 6	80	5.2	1.3	94
6[d]	PdCl$_2$ + AcONa + HCOONa	1 : 6	180	1.0	0.7	95
7[e]	PdCl$_2$ + AcONa + HCOONa	1 : 6	50	14.0	1	96
8[f]	PdCl$_2$ + AcONa + HCOONa	1 : 6	180	2.0	0.8	93
9[g]	PdCl$_2$ + AcONa + HCOONa	1 : 6	180	1.5	0.2	70
10[g]	PdCl$_2$ + AcONa	1 : 6	180	0.6	–	8
11	Pd/C + AcONa + HCOONa	1 : 6	260	0.4	1.3	95
12	Pd/C + AcONa	1 : 1	180	0.1	1.0	12
13[g]	PdCl$_2$ + AcONa + HCOONa	1 : 1	60	1.4	1.0	10

Note: [a] Time after which the concentrations of the components remained constant.
[b] With respect to the initial amount of PhBr.
[c] Calculated with respect to the initial amount of styrene. The yield of 1,1-regioisomers never exceeded 3%.
[d] [PdCl$_2$] = 0.16 mol %.
[e] [PdCl$_2$] = 0.08 mol %.
[f] [PdCl$_2$] = 0.04 mol %.
[g] The reaction was conducted at 100°C.

Table 2. Styrene arylation with a sixfold excess of the arylating agent in the presence of a reducer

Test no.	ArBr	Time,[a] min	Reaction rate $\times 10^2$, mol l^{-1} min^{-1}	Ph–Ph and PhH yields,[b] %	Yield of the arylation product,[c] %
1	BrC_6H_5	10	18.0	1.5	95
2	1,4-Br,CH_3–C_6H_4	120	12.5	0.4	65
3	1,2-Br,CH_3–C_6H_4	60	12.0	1.0	55
4	1,4-Br,OCH_3–C_6H_4	210	9.8	7	95
5[d]	1,4-Br,OCH_3–C_6H_4	65	4.7	13	90

Note: [a] Time after which the concentrations of the components remained constant.
[b] With respect to the initial amount of ArBr.
[c] Calculated with respect to the initial amount of styrene. The yield of 1,1-regioisomers never exceeded 3%.
[d] The reaction was conducted at 100°C.

and obtain the stoichiometric amount of stilbene in 10 min without using any ligand (Table 1, test 4).

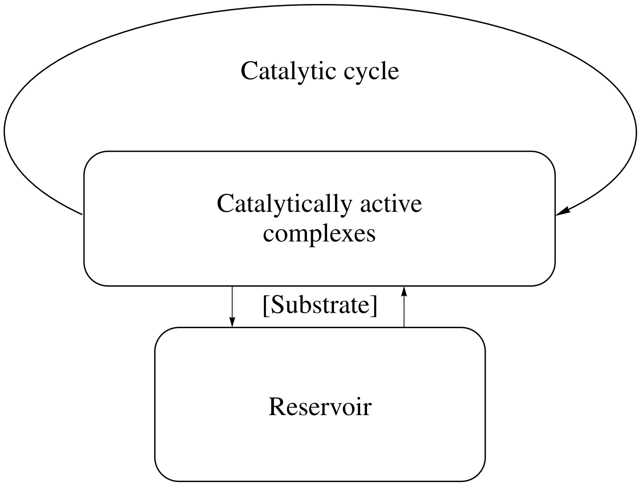
Addition of a reducing agent to a mixture with a high PhBr concentration or with equimolar amounts of the reactants raises the reaction rate (Table 1, tests 4, 5). This allows one to reduce the catalyst concentration from 1.6 to 0.04 mol % (Table 1, tests 6–8) and to conduct the reaction at a lower temperature of 100°C (Table 1, test 9). Note that the conventional temperature for the Heck reaction involving aryl bromides is ~140°C [1]. Tests 9 and 10 (Table 1) demonstrated that, at 100°C, a reducing agent is necessary for a high yield of the desired product. It is important that, with the heterogeneous catalyst 5% Pd/C, the stilbene yield again grows with increasing aryl bromide concentration (Table 1, tests 11, 12). The reaction with this catalyst can also be homogeneous because of the dissolution of palladium from the carbon surface [3, 4, 9–11].

Replacing bromobenzene with *o*-bromotoluene or *p*-bromotoluene, a less reactive compound, lowers the reaction rate (Table 2, tests 2, 3). The methoxyl radical is a stronger donor than the methyl group; as a consequence, *p*-bromoanisole is still less reactive than *p*-bromotoluene (Table 2, test 4). However, the product yield remains high with these reactants, even when the reaction temperature is decreased to 100°C (Table 2, test 5).

Comparing reaction rate data for the mixture containing equimolar amounts of the reactants and the mixture containing excess bromobenzene suggests that the increase in the stilbene yield cannot be explained only by the acceleration of the oxidative addition stage in the catalytic cycle and/or the increase in the turnover frequency in this cycle due to the increased current palladium concentration. This is clearly demonstrated by tests at 100°C: raising the amount of bromobenzene does not change the reaction rate and increases the product yield by a factor of 7 (Table 1, tests 9, 13). Thus, the increase in the product yield is due to the longer action of the catalyst. This effect of the increased substrate concentration may be due to the fact that most of the catalyst is in an inactive form capable of regeneration, forming a "reservoir" of catalytically active complexes. The regeneration of these complexes needs a substrate (Scheme 2). The role of such a substrate is played by aryl halide, which favors palladium dissolution [3, 4, 9–11]. A quasi-steady-state distribution of palladium between the reservoir and the catalytic cycle is established during the reaction. The palladium concentration in the catalytic cycle is very low, extending the lifetime of the catalyst (Scheme 2).

In view of the above, the observed behavior of the Heck reaction can be explained by the fact that Pd(0) aggregation (Scheme 1, process **C**) does take place in spite of the high bromobenzene concentration. However, owing to the competition between processes **E** and **F** (Scheme 1), raising the ArBr concentration suppresses irreversible aggregation (Scheme 1, process **D**) and takes most of the palladium to the intermediate state (reservoir) capable of regeneration (Scheme 1, processes **C**, **E**). Colloidal metal particles can well serve as a reservoir.

Scheme 1 demonstrates that, when the reaction is complete (all of the reducing agent and deficient alkene reacted), part of the palladium remains in the oxidized state in the solution (Scheme 1, process **B**). It is likely that, if the colloidal metal particles formed during the Heck reaction are stable both kinetically and thermodynamically, they will exist for some time after the reaction is complete. This would allow extra unsaturated substrate to be reacted, and the arylation method in question would, therefore, be even more practical. Adding a new portion of the styrene–bromobenzene (1 : 1) mixture before all of the styrene is reacted (when the styrene conversion is 80%) again yields a stoichiometric amount of stilbene (Table 3, test 1). After the first step was completed, the reaction mixtures was cooled to room temperature, and not only styrene and bromobenzene (liquid substances) but also a base and a reducing agent (solids) were added, the conversion of the reactants was again complete (Table 3, test 2). Furthermore, the reaction time in the second step was even



Scheme 2.

shorter than in the previous case. The key role of excess aryl bromide in maintaining the high activity of the catalytic system shows itself as follows: if the starting styrene-to-bromobenzene ratio is 2 : 7 (Table 3, test 3) or only styrene is introduced in the second step (Table 3, test 4), the product yield is markedly lower than that in the previous tests. At the same time, introducing a 2 : 2 mixture of styrene and PhBr in the second step of the reaction results in a stoichiometric yield of arylation products, although the reaction time is longer (Table 3, test 5). It is clear from tests 1–3 and 6 (Table 3) that a later introduction of the reactants is favorable. The reaction involving 1,4-Br,OCH_3–C_6H_4, which is less reactive than PhBr, also results in complete styrene conversion (Table 3, test 7). We have carried out four steps of the reaction, cooling the reaction mixture and adding the lacking reactants after each step. A decrease in catalytic activity is observed no sooner than in the fourth step.

The results of the experiments are in good agreement with the above hypothesis that the colloidal particles serve as an active catalyst reservoir. Furthermore, the tests in which the reaction was completely terminated and data available from the literature [3, 4, 9–11] suggest that aryl bromide is capable of regenerating not only colloidal catalysts but also systems consisting of large palladium aggregates.

Thus, introducing a reducing agent and excess aryl bromide in the Heck reaction produces a favorable effect on the ratio of the catalyst deactivation and regeneration rates and thereby allows the stoichiometric yield of the desired product to be attained and the reaction temperature to be reduced without using any ligand or inert atmosphere. The hypothesis that the colloidal palladium particles formed during the reaction are only the reservoirs of catalytically active Pd(0) complexes [8] has received first experimental substantiation. Therefore, colloidal palladium is outside the

Table 3. Styrene–bromobenzene (PhBr) reaction conducted in two steps

Test no.	Step no.	Total component concentrations, mol/l				Step duration, min	Stilbene yield[a], %
		PhBr	styrene	base	reducer		
1	1	6.0	1.0	2.24	0.195	4.0	80
	2	7.0	2.0	2.24	0.195	185	>99
2	1	6.0	1.0	2.24	0.195	45	93
	2[b]	7.0	2.0	4.48	0.39	130	>99
3	1	7.0	2.0	2.24	0.39	195	76
4	1	6.0	1.0	2.24	0.39	5	77
	2	6.0	2.0	2.24	0.39	243	>99
5	1	6.0	1.0	3.36	0.58	4	78
	2	8.0	3.0	3.36	0.58	226	>99
6	1	6.0	1.0	2.24	0.39	2	75
	2	7.0	2.0	2.24	0.39	236	>99
7	1[c]	6.0	1.0	2.24	0.39	6.0	96
	2[c]	1.0	1.0	2.24	0.39	140	92

Note: [a] Calculated with respect to the total amount of styrene introduced.
[b] Before this step, the reaction mixture was cooled.
[c] 1,4-Br,OCH_3–C_6H_4 was used in place of PhBr.

main catalytic cycle. The experimental procedure suggested here extends the lifetime of the catalyst: it allows several reaction cycles to be carried out without regenerating the catalyst and separating it out of the reaction mixture.

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REFERENCES

1. Whitcombe, N.J., King Luik (Mimi) Hii, and Gibson, S.E., *Tetrahedron*, 2001, vol. 57, no. 35, p. 7449.
2. Beletskaya, I.P. and Chepracov, A.V., *Chem. Rev.*, 2000, vol. 100, no. 8, p. 3009.
3. Kohler, K., Heidenreich, R.G., Krauter, J.G.E., and Pietsch, J., *Chem.—Eur. J.*, 2002, vol. 8, no. 3, p. 622.
4. Biffis, A., Zecca, M., and Basato, M., *Eur. J. Inorg. Chem.*, 2001, vol. 421, no. 5, p. 1131.
5. Reetz, M.T., Lohmer, G., and Schwickardi, R., *Angew. Chem., Int. Ed. Engl.,* 1998, vol. 37, no. 4, p. 481.
6. Shmidt, A.F., Mametova, L.V., Tkach, V.S., and Dmitrieva, T.V., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, no. 1, p. 208.
7. Shmidt, A.F., Halaiqa, A., Nindakova, L.O., and Skripina, O.S., *React. Kinet. Catal. Lett.*, 1999, vol. 67, no. 2, p. 301.
8. Reetz, M.T. and Westermann, E., *Angew. Chem.*, 2000, vol. 39, no. 1, p. 165.
9. Shmidt, A.F. and Mametova, L.V., *Kinet. Katal.*, 1996, vol. 37, no. 3, p. 431.
10. Shmidt, A.F., Smirnov, V.V., Starikova, O.V., and Elaev, A.V., *Kinet. Katal.*, 2001, vol. 42, p. 223.
11. Biffis, A., Zecca, M., and Basato, M., *J. Mol. Catal. A: Chem.*, 2001, vol. 173, nos. 1–2, p. 249.