Highly Active Palladium/Activated Carbon Catalysts for Heck Reactions: Correlation of Activity, Catalyst Properties, and Pd Leaching

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Dedicated to Professor Bernhard Lücke on the occasion of his 65th birthday

Abstract: A variety of palladium on activated carbon catalysts differing in Pd dispersion, Pd distribution, Pd oxidation state, and water content were tested in Heck reactions of aryl bromides with olefins. The optimization of the catalyst (structure – activity relationship) and reaction conditions (temperature, solvent, base, and Pd loading) allowed Pd/C catalysts with very high activity for Heck reactions of unactivated bromobenzene (turnover number (TON) ≈ 18000, turnover frequency (TOF) up to 9000, Pd concentrations down to 0.005 mol%) to be developed. High Pd dispersion, low degree of reduction, sufficient content of water, and uniform Pd impregnation are criteria for the most active system. The catalysts combine high activity and selectivity under ambient conditions (air and moisture), easy separation (filtration), and quantitative recovery of palladium. Determination of Pd in solution after and during the reaction, and catalyst characterization before and after the reaction (transmission electron microscopy (TEM), X-ray diffraction (XRD)), indicate dissolution/reprecipitation of palladium during the reaction. The Pd concentration in solution is highest at the beginning of the reaction and is a minimum (< 1 ppm) at the end of the reaction. Palladium leaching correlates significantly with the reaction parameters.

Keywords: carbon · C–C coupling · heterogeneous catalysis · palladium

Introduction

The olefination of aryl halides (Heck reaction), one of the most important C–C coupling reactions in organic synthesis,[1] is mostly catalyzed by palladium complexes in homogeneous solution. Important advantages of this reaction are the broad availability of aryl bromides and chlorides and the tolerance of the reaction for a wide variety of functional groups. In the last few years, the development of new highly active Pd complexes even allowed the activation and conversion of aryl chlorides, which are far less reactive than bromides and iodides, to a considerable extent.[2, 3] In terms of economical feasibility of C–C coupling reactions, this is good progress since aryl chlorides are much cheaper than bromides or iodides. However, homogeneous catalysts require ligands (usually phosphanes) which may be difficult to handle (e.g., air-sensitive phosphanes), and removal of the catalyst from the product is difficult. This applies to the ligand as well as the expensive precious metal. To the best of our knowledge, only a few experiments have been reported that deal with the separation of Pd from the reaction mixture.[4]

The problem of catalyst separation and Pd recovery has been addressed by immobilization of Pd catalysts (polymer-supported Pd catalysts[5]) and by using heterogeneous Pd catalysts[6] (Pd on activated carbon,[7] Pd on metal oxides,[8] and Pd on zeolites[9]). However, these systems do not reach the high activities of homogeneous catalysts. In addition supported Pd catalysts (mainly Pd/C) often cause unwanted dehalogenation of the haloaromatic compounds,[7h] convert interesting aryl bromides only in certain cases[8f, 8i, 8j] (only one paper deals with aryl chlorides[9c]), and often suffer from substantial Pd leaching (e.g., 14% of Pd is leached from Pd/C[10]). Since the use of supported Pd catalysts is motivated by the ease of catalyst separation, Pd leaching is the most important issue.

Arai et al. have recently published work on Pd/C-catalyzed Heck reactions[7h] in which aryl iodides could be activated easily by the employed Pd/C catalysts; however, low activities and dehalogenation were observed for aryl bromides. Besides Heck coupling,[7] promising results on Pd/C-catalyzed Suzuki

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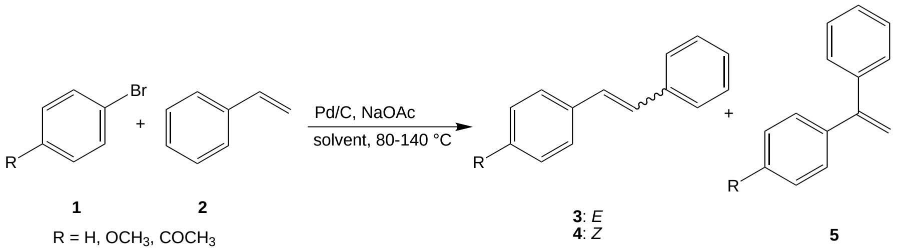
cross-coupling reactions were reported recently.[11] Here the attractive aryl chlorides could be coupled with various phenyl boronic acids.



Scheme 1. Heck coupling of bromoarenes with styrene.

Although the catalytic performance of the catalysts in the Heck reaction was studied thoroughly in the above-mentioned papers, little or no attention was paid to the influence of the catalyst properties (e.g., Pd dispersion, degree of Pd reduction, or preparation method). Other issues neglected so far are Pd leaching and the parameters that affect this undesirable loss of precious metal. Palladium leaching is also relevant to the mechanism of Pd/C-catalyzed Heck couplings. Several papers discuss mechanistic aspects of Pd/C-catalyzed Heck couplings, and it is still unclear whether the reaction takes place on the solid Pd surface[12] or the true catalyst is dissolved Pd that has been leached from Pd/C, which acts simply as a Pd reservoir.[5b, 7i, 13]

Herein we describe the first study of how Pd/C catalyst properties affect activity in the Pd/C-catalyzed Heck reaction. Knowledge of the structure–activity relationship and optimization of the reaction parameters for this heterogeneous system allowed the development of a Pd/activated carbon catalyst that exhibits the highest activity of heterogeneous catalysts reported up to now for the Heck reaction of aryl bromides with olefins. In addition we describe for the first time the parameters that influence Pd leaching during the reaction and show that redeposition of Pd occurs. These findings allowed the Pd concentration in solution after the reaction to be lowered to 1 ppm and provided new insights into the mechanism of Pd/C-catalyzed Heck reactions.

Results

Correlation of catalyst structure and activity: Due to the lack of information about catalyst structure–activity relationships for Pd/C systems in C–C coupling reactions, we studied a variety of different Pd on activated carbon systems. Twelve Pd/C catalysts were tested in the Heck coupling of bromobenzene and styrene as a model reaction for unactivated bromoarenes (Scheme 1, R = H). All Pd on activated carbon catalysts contained 5 wt% palladium and were characterized by a high (but variable) Pd dispersion (no thermal pretreatment). In addition to their Pd dispersion (average Pd crystallite size) the catalysts differed in the degree of reduction of Pd, water content (**D** for dry catalysts: ca. 5 wt% water; **W** for wet catalysts: ca. 50–60 wt% water), and Pd distribution (uniformly impregnated or eggshell catalysts). The degree of reduction is defined as the amount of Pd^0 relative to the total amount of Pd (Pd^{2+} and Pd^0) on the catalyst. The properties of the catalysts are summarized in Table 1.

Influence of Pd dispersion and degree of *reduction*: The catalytic results summarized in Table 2 illustrate that all parameters investigated are of importance for the activity in

Table 2. Catalytic activities of twelve different Pd/C catalysts (Table 1): Heck coupling of bromobenzene with styrene (Scheme 1, R = H).[a]

Entry	Catalyst	Conversion[b] [%]	Yield **3**[b] [%]	Yield **4**[b] [%]	Yield **5**[b] [%]	Pd-Leaching [%][c]
1	**1D**	46	41	0	4	0.3
2	**2D**	61	54	1	5	1.9
3	**3D**	48	43	0	4	0.4
4	**4D**	51	45	0	5	0.6
5	**5D**	70	62	1	6	2.7
6	**6D**	60	55	1	4	1.7
7	**1W**	88	80	1	7	0.6
8	**2W**	59	54	1	4	3.0
9	**3W**	92	84	1	7	0.4
10	**4W**	82	75	1	6	1.9
11	**5W**	79	71	1	7	2.2
12	**6W**	78	70	1	6	2.2

[a] Reaction conditions: bromobenzene, styrene, NaOAc, 1.0 mol% Pd, *N,N*-dimethylacetamide (DMAc); $T = 140\,^\circ C$ and $t = 20$ h. [b] Conversion of bromobenzene and yields of products **3**–**5** from GLC analysis. [c] Amount of palladium in solution/total amount of palladium in the reaction mixture.

Table 1. Properties of the 5 wt% Pd/C catalysts.

Catalyst	Pd distribution	Impregnation depth [nm]	Average crystallite size [nm]	Reduction degree[a] [%]	CO (chemisorption) [mL g^{-1} catalyst]	Pd dispersion[b]
1 D/W	eggshell	50–100	4.79	50	2.89	23
2 D/W	eggshell	50–150	4.07	55	2.50	27
3 D/W	uniform	–	3.07	0	1.97	36
4 D/W	eggshell	100–300	5.04	0	2.14	22
5 D/W	uniform	–	3.96	0	2.90	28
6 D/W	uniform	–	4.44	25	2.11	25

[a] Number of palladium atoms in oxidation state 0/total number of palladium atoms, detected by temperature-programmed reduction (TPR) measurements. [b] Calculated from CO (chemisorption) for a Pd/CO ratio of 1:1. Assumption that CO adsorbs on Pd^0 only. Accordingly, the comparison of Pd dispersion values calculated from CO measurements of non-reduced and reduced catalysts can lead to misinterpretation.

the Heck reaction. All catalysts show bromobenzene conversions of between 45 and 90 % and high selectivities for (*E*)-stilbene (≥ 90 %); no dehalogenation of bromobenzene occurred in any experiment.

A first tentative correlation gives the following catalyst features for high activity (Table 2): high Pd dispersion (**3**), low degree of Pd reduction (**3**–**5**), high water content (> 50 %, **W** series), and uniform Pd impregnation (Table 1, columns 2 and 3). In summary, catalyst **3W**, which combines all requirements listed above, is the most active.

Influence of the Pd loading: The influence of the Pd loading on activated carbon was investigated for catalyst **3W** with 1, 5, and 10 wt % Pd. Under identical reaction conditions and with identical amounts (relative to bromobenzene) of Pd in the reaction mixture the catalyst with 5 wt % Pd showed the highest activity (92 % conversion in the coupling of bromobenzene with styrene). The catalyst with 10 wt % palladium had almost the same activity (90 % conversion), but that with 1 wt % Pd had much lower activity (41 % conversion). This effect can be understood by the following experiment: addition of pure activated carbon (four times the amount of the catalyst) to the most active catalyst **3W** with 5 wt % palladium decreases the conversion to 45 %. This decrease in conversion could be interpreted, for example, by increased adsorption of starting materials and/or products on the carbon support.

Effect of thermal treatment: To provide support for the correlation between Pd dispersion, degree of reduction, and activity, catalyst **3W** was heated in different N_2 and N_2/H_2 atmospheres. As expected, the dispersion of the Pd/C catalyst decreased with increasing temperature, as illustrated by the decreasing amount of CO chemisorbed on the Pd surface (Table 3). The higher the treatment temperature, the lower the dispersion, and hence the lower the catalytic activity in the Heck reaction (Table 3, entries 2–7). Catalysts treated at 700 °C had no catalytic activity (Table 3, entries 4 and 7). This confirms the correlation between Pd dispersion and catalytic activity described above and in the recent literature.[8i, 8j] There was no influence of the atmosphere in which thermal treatment was performed (N_2 or N_2/H_2) on the catalytic activity of the Pd/C catalysts (e.g., Table 3, entries 2 and 5). In addition, thermal treatment is accompanied by increased Pd reduction and loss of water, and this also reduces the catalytic activity (Table 3, entry 8, added for comparison). This illustrates the mutual interdependence of the parameters Pd dispersion, Pd oxidation state, and water content with regard to catalytic activity.

Correlation of reaction parameters with activity and Pd leaching: After the selection of the best catalysts with optimized properties, the influence of the reaction parameters on activity and selectivity were studied in detail. In addition, we were interested in the Pd concentration in solution after separation of the solid catalyst at the end of the reaction as a function of these reaction parameters. Since the optimization of the reaction conditions included several parameters, and in order to recognize interactions between parameters, design of experiments (DoE), was used and the results of 294 experiments were evaluated by statistical software (Statgraphics 3.1).

After each experiment the Pd in solution was determined after removal of the solid catalyst by filtration at 110–120 °C. Because flame atomic absorption spectroscopy (AAS) was not precise enough for palladium analysis in this concentration range (the detection limit is too high) inductively coupled plasma optical emission spectroscopy (ICP-OES) and mass spectrometry (ICP-MS) were used. The Pd content in solution (leaching) after the reaction was between 0.3 and 3.0 % of the total amount of palladium (2.7–22.5 µg Pd per gram of catalysis solution). To a first approximation, the Pd leaching could not be correlated with the properties of the twelve different Pd/C catalysts described above. There is, however, a strong correlation with the reaction parameters (see below).

Reaction temperature: The most active catalysts **3W** and **4W** (Table 2) were used for these investigations. These Pd/C catalysts were tested at different reaction temperatures in the coupling of *p*-bromoacetophenone (Table 4, entries 1–4) and bromobenzene with styrene (Table 4, entries 5–10). The catalytic runs were performed with only 0.1 mol % palladium (instead of 1.0 mol %) relative to the bromoarene.

As expected, activated bromoarenes such as *p*-bromoacetophenone can be converted at lower temperatures than unactivated ones (Table 4, entries 2 and 7). At reaction temperatures as low as 80 °C, *p*-bromoacetophenone can be

Table 3. Thermally treated catalysts in Heck coupling of bromobenzene with styrene (Scheme 1, R = H).[a]

Entry	Pretreatment temperature [°C]	Pretreatment atmosphere	CO_{ads}[b] [mL g^{-1} cat]	Conversion[c] [%]	Yield **3**[c] [%]	Yield **4**[c] [%]	Yield **5**[c] [%]	Pd-Leaching [%][d]
1	**3W**	–	1.97	94	84	1	8	0.3
2	300	N_2	2.26	57	51	0	5	0.5
3	500	N_2	1.02	12	10	0	1	0.5
4	700	N_2	0.22	1	1	0	0	0.4
5	300	$N_2 + H_2$	1.79	58	52	0	5	0.7
6	500	$N_2 + H_2$	0.85	13	11	0	1	0.5
7	700	$N_2 + H_2$	0.16	4	3	0	0	0.9
8	**3D**	–	1.97	42	38	0	3	0.3

[a] Reaction conditions: bromobenzene, styrene, NaOAc, 1.0 mol % Pd, DMAc; $T = 140$ °C and $t = 20$ h. [b] The comparison of Pd dispersion values calculated from CO measurements of nonreduced and reduced catalysts can lead to misinterpretation, because CO adsorbs on Pd^0 only. [c] Conversion of bromobenzene and yields of products **3**–**5** from GLC analysis. [d] Amount of palladium in solution/total amount of palladium in the reaction mixture.

Table 4. Catalysis at different reaction temperatures: Heck coupling of *p*-bromoacetophenone or bromobenzene with styrene (Scheme 1; R = $COCH_3$, H).[a]

Entry	R	Catalyst	Temperature [°C]	Conversion[b] [%]	Yield **3**[b] [%]	Yield **4**[b] [%]	Yield **5**[b] [%]	Pd-Leaching [%][c]	Pd in solution [ppm][d]
1	$COCH_3$	**3W**	60	6	6	0	0	0.5	0.3
2	$COCH_3$	**3W**	80	95	91	0	4	26.3	19.7
3	$COCH_3$	**3W**	100	100	95	0	5	1.1	0.8
4	$COCH_3$	**3W**	120	100	95	0	5	1.0	0.8
5	H	**3W**	120	79	71	1	6	1.1	0.9
6	H	**4W**	120	58	51	1	5	7.8	6.1
7	H	**3W**	140	86	77	1	7	1.6	1.3
8	H	**4W**	140	69	61	1	6	4.0	3.1
9	H	**3W**	160	80	73	1	6	0.7	0.5
10	H	**4W**	160	61	55	1	4	4.2	3.3

[a] Reaction conditions: bromoarene, styrene, NaOAc, 0.1 mol% Pd (**3W** or **4W**), DMAc; $T = 60–160$ °C and $t = 20$ h. [b] Conversion of bromoarenes and yields of products **3**–**5** from GLC analysis. [c] Amount of palladium in solution/total amount of palladium in the reaction mixture. [d] Palladium in solution μg per g of solution.

converted almost quantitatively. The catalytic activity in the coupling of the unactivated bromobenzene is highest at 140 °C (Table 4, entries 7 and 8). As expected, the activity of the Pd/C catalyst is lower at 120 °C, but also at higher temperatures (Table 4, entries 5, 6, 9, and 10). The lower catalytic activity at 160 °C might result from the instability of the catalytically active Pd species in solution at such a temperature (see below and refs. [5b, 7i, 13]).

The palladium concentration in solution (leaching) also depends on the reaction temperature. This is illustrated for the coupling of bromobenzene and styrene with catalyst **4W** (Table 4, entries 6, 8 and 10) and **3W** (Table 4, entries 5, 7 and 9). Catalyst **3W** is not only more active than **4W** under identical reaction conditions, but also exhibits less Pd leaching (Table 2, entries 9 and 10).

The most pronounced influence of the reaction temperature on the Pd concentration in solution is found in the Heck reaction of *p*-bromoacetophenone and styrene with catalyst **3W**. At 60 °C no catalytic activity and almost no Pd (0.5%) was found in solution (Table 4, entry 1) after the reaction was finished. Quantitative conversion of *p*-bromoacetophenone was obtained at 80 °C and higher temperatures (Table 4, entries 2–4). Here the Pd leaching increased significantly to 26% of the total Pd content at 80 °C, but astonishingly decreased again to about 1.0% of the total palladium content at 100 and 120 °C.

Effect of the solvent: The influence of the solvent on catalytic activity and Pd leaching was studied in the coupling of *p*-bromoacetophenone and styrene with catalyst **3W** (Table 5). The catalytic activity in *N*-methylpyrrolidone (NMP) was higher than in *N,N*-dimethylacetamide (DMAc) (Table 5, entries 1 and 3). In toluene, acetonitrile, THF, and 1,4-dioxane the catalytic activity at 80 °C was very low. For the reaction of bromobenzene with styrene in NMP quantitative conversion was found at 140 °C after 20 h, while in DMAc only 86% conversion was achieved. This is in line with the results found for *p*-bromoacetophenone.

The solvent also affects palladium leaching. For more precise determination of the effect of solvent on palladium leaching, conditions favoring palladium leaching (80 °C) were applied in the coupling of *p*-bromoacetophenone and styrene (Table 5, entries 1–6). Both NMP and DMAc resulted in high Pd dissolution from the support: 22% for NMP and 26% for DMAc. Very low Pd leaching (1.2–1.5%) was found with toluene, THF, and 1,4-dioxane. This is accompanied by low catalytic activity in these solvents. This could be an indication that Pd in solution is the catalytically active species under the conditions used.

Influence of inert-gas atmosphere: Most homogeneously catalyzed Heck reactions were studied under inert conditions (argon atmosphere).[2] For the Pd/C catalysts investigated here, almost no influence of the atmosphere over the reaction mixture on catalytic activity was observed. However, a significant difference in Pd leaching was observed when argon or air was used (Table 6). Without exclusion of air, about 26% of the total amount of palladium was lost from catalyst **3W** and found in solution, as opposed to 1.1% under an argon atmosphere (Table 6, entries 1 and 3). The same was

Table 5. Variation of the solvent: Heck coupling of *p*-bromoacetophenone with styrene (Scheme 1, R = $COCH_3$).[a]

Entry	Solvent	Conversion[b] [%]	Yield **3**[b] [%]	Yield **4**[b] [%]	Yield **5**[b] [%]	Pd-Leaching [%][c]	Pd in solution [ppm][d]
1	DMAc	94	90	0	3	26.0	19.5
2	toluene	0	0	0	0	1.4	1.1
3	NMP	100	95	0	4	22.0	16.4
4	acetonitrile	3	3	0	0	6.4	4.9
5	THF	3	3	0	0	1.5	1.1
6	1,4-dioxane	4	3	0	0	1.2	0.9

[a] Reaction conditions: *p*-bromoacetophenone, styrene, NaOAc, 0.1 mol% Pd (**3W**); $T = 80$ °C and $t = 20$ h. [b] Conversion of *p*-bromoacetophenone and yields of products **3**–**5** from GLC analysis. [c] Amount of palladium in solution/total amount of palladium in the reaction mixture. [d] Palladium in solution μg per g of solution.

Table 6. Influence of atmosphere on activity and Pd leaching in Heck coupling of *p*-bromoacetophenone with styrene (Scheme 1, R = $COCH_3$).[a]

Entry	Catalyst	Atmosphere	Conversion [%]	Yield **3**[b] [%]	Yield **4**[b] [%]	Yield **5**[b] [%]	Pd-Leaching [%][c]	Pd in solution [ppm][d]
1	**3W**	Ar	100	94	0	5	1.1	0.8
2	**4W**	Ar	98	90	0	5	5.0	3.8
3	**3W**	air	100	94	0	5	26.3	20.0
4	**4W**	air	94	88	0	5	30.2	22.7

[a] Reaction conditions: *p*-bromoacetophenone, styrene, NaOAc, 0.1 mol% Pd (**3W** or **4W**), DMAc; $T = 100\,^{\circ}C$ and $t = 20$ h. [b] Conversion of *p*-bromoacetophenone and yields of products **3**–**5** from GLC analysis. [c] Amount of palladium in solution/total amount of palladium in the reaction mixture. [d] Palladium in solution µg per g of solution.

found for catalyst **4W** under the same conditions (Table 6, entries 2 and 4).

Statistical methods (design of experiments; DoEs): An extensive series of experiments was performed by varying the following parameters: reaction temperature, solvent, catalyst concentration, base, and type of filter used for catalyst separation. For these investigations fractional factorial designs such as 2^{5-1} (16 experiments) and 2^{4-1} (8 experiments) were selected for the DoE.[14] In each experiment the catalytic activity (conversion) and palladium content in solution after filtration were determined, so that both response variables could be studied with statistical methods. After processing the data statistically, it could be unambiguously shown that the reaction temperature and the solvent have dominant effects both on activity and Pd leaching (see also Tables 4 and 5). This is illustrated by the Pareto diagrams[14] in Figure 1. In addition, a significant correlation of the catalytic activity and the base was found: Higher activities were obtained with sodium acetate than with other bases such as amines. In the reaction of bromobenzene and styrene, conversions of up to 98% were obtained with sodium acetate, but only 36% with tributylamine under identical reaction conditions (catalyst **3W**, NMP, 140 °C, 20 h, 0.1 mol% Pd). A slight additional increase in activity was found when sodium acetate and an amine were used simultaneously (see also refs.[7h, 7j]). The palladium concentration (ca. 0.1 mol% relative to the bromoarene) is not a limiting factor for high activity. It could be reduced to 0.005 mol% without loss of activity.

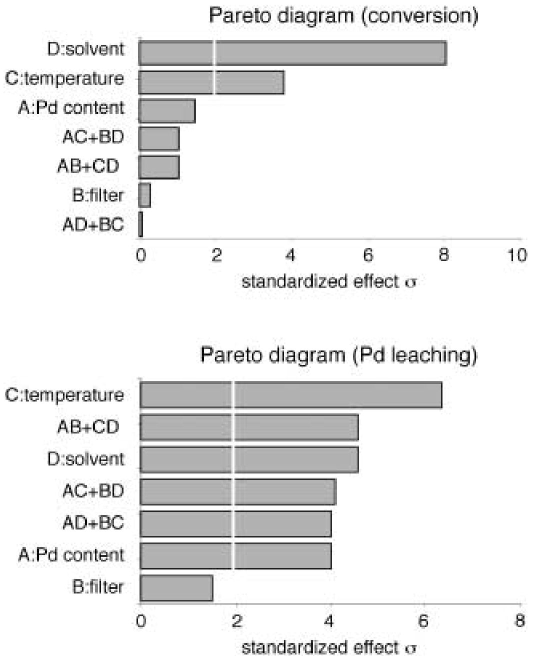


Figure 1. Pareto diagrams for conversion (top) and Pd leaching (bottom) for the reaction of bromobenzene with styrene, illustrating the dominating influence of chosen reaction parameters (2^{4-1} factorial design: $T = 80$ or 100 °C, Pd content = 0.1 or 0.2 mol%, solvent = NMP or DMAc).

The palladium concentration in solution was not affected by the type of filter used for catalyst separation. This is connected with the excellent filterability of the carbon support used (optimized particle size distribution, attrition resistance, morphology).

Activity under optimized reaction conditions: Analysis and evaluation of the results discussed above lead to the following optimum reaction conditions for the Heck reaction with catalysis by Pd/C: 140 °C for unactivated bromoarenes (Table 4), NMP as solvent (Table 5), and sodium acetate as base. The high catalytic activity of the Pd/C catalysts allowed the palladium concentration to be decreased to 0.01 mol%. An argon atmosphere helps to decrease the Pd leaching while maintaining the high activity. The most active Pd/C catalyst **3W** should be used without thermal treatment (Table 2).

Under these optimized reaction conditions, unactivated bromoarenes such as bromobenzene, and even deactivated bromoarenes such as *p*-bromoanisole, could be converted almost quantitatively within 2 h (Table 7, entries 3 and 6). The Pd content could be drastically decreased to 0.005 mol% (1 µmol Pd for 20 mmol bromobenzene) in the coupling of bromobenzene and styrene (Table 7, entry 5). This extremely high catalytic activity is reflected by turnover numbers (TONs) of up to 18000 and turnover frequencies (TOFs) of up to 9000 h^{-1} for this reaction. Even with very low Pd loadings of 0.005–0.01 mol% Pd, all bromoarenes studied here could be coupled almost quantitatively within 2–6 h (Table 7, entries 1, 3, and 9) with high selectivity (> 90%) for the *E* products. In the presence of air (no purging with argon), bromobenzene can be converted almost quantitatively within 3 h with a Pd loading of only 0.01 mol%. The TON and TOF for this reaction were 9600 and 3200 h^{-1}, respectively (Table 7, entry 4).

Pd leaching and catalyst evolution during the reaction: *Activity and leaching as a function of time*: All determinations of the Pd concentration in solution described above were performed after filtration of the solid catalyst from the hot reaction mixture at the end of the reaction. However, to gain insight into how the catalytic reaction proceeds on the atomic

Table 7. Optimized reaction conditions: Heck coupling of different bromoarenes with styrene (Scheme 1).[a]

Entry	R	Catalyst [mol % Pd]	Solvent	*t* [h]	*T* [°C]	Conversion[b] [%]	Yield **3**[b] [%]	Yield **4**[b] [%]	Yield **5**[b] [%]	TON[c] [h⁻¹]	TOF[d] [h⁻¹]
1	$COCH_3$	0.01	NMP	4	140	96	90	0	5	9500	2375
2	H	0.01	NMP	1	140	73	65	1	5	7100	7100
3	H	0.01	NMP	2	140	97	87	1	7	9500	4750
4[e]	H	0.01	NMP	3	140	97	88	1	7	9600	3200
5[f]	H	0.005	NMP	2	140	90	82	1	7	18000	9000
6	OCH_3	0.10	NMP	2	140	92	80	1	9	900	450
7	OCH_3	0.02	NMP	2	140	72	63	0	7	3500	1750
8	OCH_3	0.02	DMAc	2	140	62	53	0	6	2950	1475
9	OCH_3	0.01	NMP	6	140	95	85	1	9	9500	1583

[a] Reaction conditions: bromoarene, styrene, NaOAc, 0.005–0.10 mol % Pd (**3W**), NMP or DMAc; $T = 80-140$ °C. [b] Conversion of the bromoarenes and yields of the products **3**–**5** from GLC analysis. [c] TON = moles of coupling products (all isomers)/moles of Pd. [d] TOF = moles of coupling products (all isomers)/moles of Pd per hour. [e] Without exclusion of air and moisture (no purging with argon). [f] 20 mmol bromobenzene, 30 mmol styrene, 24 mmol NaOAc, 20 mL solvent.

level it is important to determine the Pd concentration in solution during the reaction at a given time and to correlate it with the catalytic activity.

Therefore, 25 samples of the reaction mixture were taken during the reaction of bromobenzene and styrene and analyzed by GLC and ICP-OES or ICP-MS (to ensure higher accuracy in this experiment, 1.0 mol % Pd was used). Figure 2 shows that the palladium concentration in solution was highest at the beginning of the reaction and had dropped to 1 ppm when the reaction was complete. During the reaction the conversion decreased with decreasing Pd concentration in solution. The conversion–time behavior observed is expected for the Heck reaction, regardless of the Pd concentration in solution. The apparent relationship between conversion and Pd concentration could be understood, for example, by the influence of the concentration of starting materials (potential ligands) on Pd leaching.

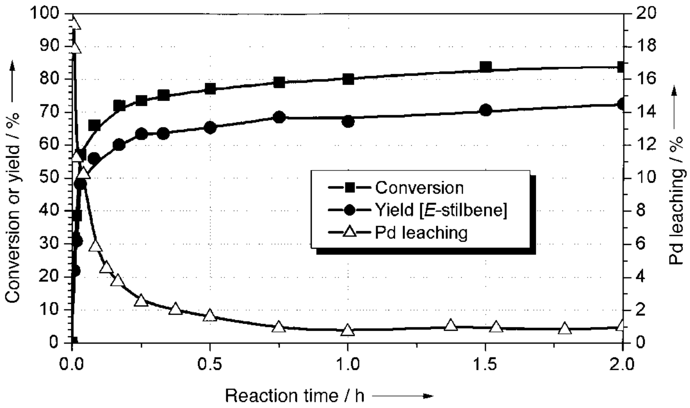


Figure 2. Investigation of activity and Pd leaching as a function of time: heterogeneous Heck coupling of bromobenzene with styrene (Scheme 1); reaction conditions: bromobenzene (200 mmol), styrene (300 mmol), sodium acetate (240 mmol), 1.0 mol % Pd, catalyst **3W**, DMAc (200 mL), $T = 140$ °C.

Catalyst evolution: As stated above, the reaction is accompanied by a Pd dissolution/precipitation process.[7i] This catalyst evolution is also reflected by transmission electron microscopy (TEM) investigations of catalyst **3W** before and after the reaction (Figure 3). The fresh catalyst **3W** (Figure 3, top) clearly exhibits a higher Pd dispersion and more uniform distribution than the catalyst (Figure 3, bottom) after Heck coupling of bromobenzene and styrene under standard reaction conditions (DMAc, sodium acetate, 140 °C, 20 h). The used catalyst was washed with dichloromethane and water before TEM investigations. The average Pd crystallite size has increased by one order of magnitude from 2.4 nm to 23 nm. The TEM images indicate the agglomeration of small primary Pd crystallites to large "grapes" (Figure 3). In addition, Figure 4 shows that Pd precipitation occurs on the outer activated carbon grains only. This destroys the uniform

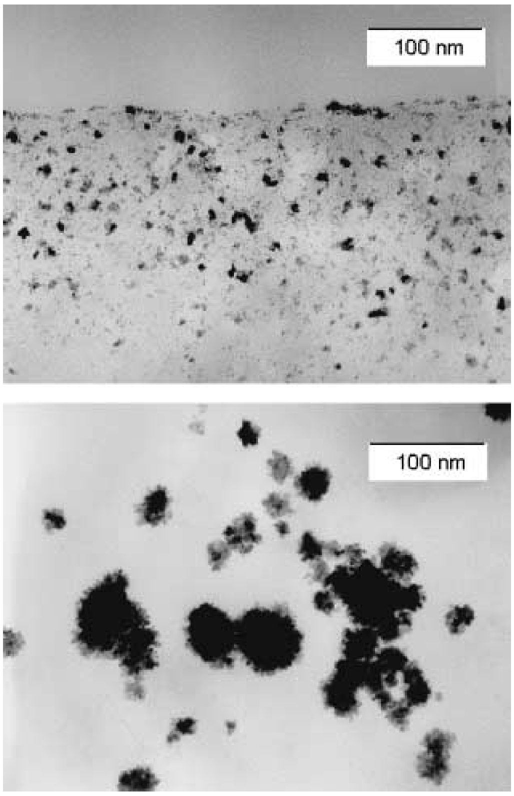


Figure 3. Transmission electron micrographs (magnification 1:400000) of catalyst **3W** before Heck coupling of bromobenzene with styrene (top) and after the Heck reaction (bottom). Reaction conditions: bromobenzene (10 mmol), styrene (15 mmol), sodium acetate (12 mmol), 1.0 mol % Pd, DMAc (10 mL), $T = 140$ °C, reaction time 20 h.

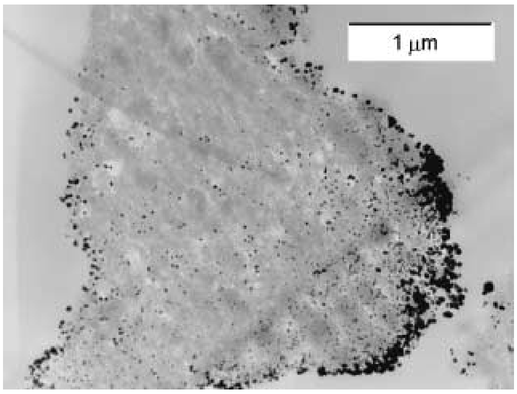


Figure 4. Transmission electron micrograph of Pd/C catalyst **3W** after the Heck reaction (magnification 1:50000). Reaction conditions: bromobenzene (10 mmol), styrene (15 mmol), sodium acetate (12 mmol), 1.0 mol% Pd, DMAc (10 mL), $T = 140$ °C, reaction time 20 h.

Pd distribution of the fresh catalyst and leads to an eggshell catalyst.

In addition, the increase in the lattice constants of the Pd crystallites precipitated at the end of the reaction ($a = 395$ pm for the used catalyst versus $a = 388$ pm for the fresh catalyst) found by X-ray diffraction (XRD) indicate the incorporation of impurities (e.g., carbon) into the Pd lattice during precipitation.

Recycling and re-use of the catalysts: The dramatic decrease in Pd dispersion during the reaction should lead to a significant decrease in catalytic activity when the catalyst is re-used in Heck reactions. This was indeed found in recycling studies with catalyst **3W** in Heck couplings of bromobenzene with styrene (Table 8). The conversion after 6 h with recycled catalyst that was washed with dichloromethane is roughly 50% of that with fresh **3W** (Table 8, entry 2). A second recycling (Table 8, entry 3) of the Pd/C catalyst decreases the reaction rate further, and conversion was very low (4% after 6 h). For higher or almost complete conversions 20 h or more is necessary. Table 8 additionally illustrates that the activity of the recycled catalysts is significantly influenced by the washing procedure applied. Washing with dichloromethane and water (necessary to remove sodium bromide or excess base) further reduces the catalytic activity compared to washing with dichloromethane (Table 8, entries 4 and 5). Thus, the extremely high activity of the catalyst system is only found in the first run if very low Pd concentrations are used. Used catalysts exhibit low activities comparable to other (fresh) heterogeneous systems.[7h] However, easy and quantitative separation of the Pd/C catalyst allows effective recovery of the noble metal.

Discussion and Conclusion

A variety of Pd/C catalysts with different properties were studied in Heck reactions of aryl bromides with olefins. The activity of the catalysts strongly depends on the palladium dispersion, the Pd oxidation state in the fresh catalyst, the water content (wet or dried catalysts), and the conditions of catalyst preparation (impregnation method, pretreatment conditions). For example, Pd on the same activated carbon support can be a nearly inactive catalyst or have the highest activity reported so far for heterogeneous systems for the conversion of aryl bromides (Table 9).

The strong effect of Pd dispersion (see Table 3) proposed earlier,[8i, 8j] but mostly ignored and never studied in detail, seems to be most easily understandable. Increasing Pd surface

Table 8. Re-use of Pd/C catalyst: Heck coupling of bromobenzene with styrene (Scheme 1, R = H).[a]

Entry	State	Catalyst washed with	Conversion[b] [%]	Yield **3**[b] [%]	Yield **4**[b] [%]	Yield **5**[b] [%]
1	new	–	92	84	1	7
2	1st re-use	dichloromethane	63	56	1	5
3	2nd re-use	dichloromethane	4	3	0	0
4	1st re-use	dichloromethane and water	27	25	0	2
5	2nd re-use	dichloromethane and water	2	1	0	0

[a] Reaction conditions: bromobenzene, styrene, NaOAc, 0.1 mol% Pd (**3W**), DMAc; $T = 140$ °C and $t = 6$ h. [b] Conversion of bromobenzene and yields of products **3**–**5** from GLC analysis.

Table 9. Comparison of activity and reaction conditions for heterogeneous and homogeneous catalysts in the Heck reaction of bromobenzene (Scheme 1, R = H) with styrene (or methyl arcylate[d]) published in the literature very recently.

Catalyst	Catalyst [mol% Pd][a]	T [°C]	t [h]	Yield **3**–**5** [%]	TON [b]	TOF [c] [h^{-1}]	Reference
Pd/mesoporous silica	0.1	170	48	39	390	8	[8f]
Polymer supported Pd carbenes	0.02	150	60	75	3750	63	[5a]
Pd/C[d]	> 1	160	12	< 20	≤ 20	2	[7h]
3W (E 105 CA/W 5% Pd)	0.005	140	2	90	18000	9000	this paper
Pd/zeolites	0.05	140	0.5	96	1920	3840	[9c]
Palladacycle	0.0001	130	72	29	290000	4028	[3a]
Pd carbenes	5	184	1	100	20	20	[3s]
Pd(OAc)$_2$	0.0009	130	96	85	94400	984	[3b]

[a] Moles of Pd/moles of bromobenzene. [b] Moles of coupling products (all isomers)/(moles of Pd). [c] TOF = moles of coupling products (all isomers)/moles of Pd per hour. [d] Reaction of bromobenzene and methyl acrylate. High selectivity (up to 80%) to undesired benzene (dehalogenation).

0947-6539/02/0803-0628 $ 17.50+.50/0

area (decreasing Pd crystallite size) is expected to increase the activity in a heterogeneous reaction. However, an increased surface area could also promote the dissolution of Pd into the solvent (leaching), and these aspects must be included in a discussion of the mechanism (see below). Nevertheless, different Pd dispersion, catalyst preparation, and pretreatment conditions may explain the differences in the catalytic activity of the various Pd/C catalysts reported in the literature[7h] in comparison to the high activity of catalyst **3W**. The low activity of Pd/C for the activation of aryl bromides reported by Arai et al.[7h] can thus be expected from the drastic pretreatment conditions (reduction of Pd/C at 350 °C). The influence of the Pd oxidation state (0 or +2) can be interpreted in the context of Pd dispersion as well: Each thermal treatment under a gaseous atmosphere (hydrogen, inert gas, air) to produce Pd^0, which is generally accepted as the active state,[2] is connected with a decrease in Pd dispersion (Table 3). Clearly, the in situ reduction of Pd^{II} under Heck reaction conditions leads to the best catalysts with the highest dispersion. The presence of water (see Table 3, entries 1 and 8) possibly prevents the precipitation of sodium bromide or base near the reaction center(s). The tolerance of water in the reaction mixture is an interesting advantage of these catalysts. They can be used without exclusion of air in undried solvents (Table 6 and Table 7, entry 4). Uniformly impregnated Pd/C catalysts show higher activities than eggshell catalysts. This underlines that diffusion limitations, which were never indicated in any experiment performed in this work, do not play a role. However, it also supports the hypothesis that leached Pd is the active species, for which the solid (fresh) Pd/C catalyst acts as a reservoir that delivers catalytically active Pd species into solution. This is favored by a uniform distribution of Pd over the activated carbon support.

The optimization of catalyst and reaction parameters allowed the development of a high-performance catalyst for the reaction of bromoarenes with olefins that exceeds the activity of any heterogeneous palladium catalysts reported in the literature by at least an order of magnitude (Table 9). No dehalogenation of bromoarenes occurred in any experiment, in contrast to the results of Arai et al.[7h] who observed up to 80 % formation of benzene by dehalogenation. Bromobenzene can be converted to 90 % in 2 h with catalyst concentrations of only 0.005 mol % Pd. Turnover numbers (TON) of up to 18000 and turnover frequencies (TOF) of up to 9000 h^{-1} are obtained (Table 7, entry 5). Even deactivated bromoarenes (*p*-bromoanisole) can be coupled with yields of up to 95 % (Table 7, entries 6–9). *p*-Bromoacetophenone can be converted completely even at temperatures as low as 80 °C (Table 5, entry 3). Similarly high TONs are only reached by the highly active Pd/zeolite systems reported recently.[9c] Even without exclusion of air/moisture (no purging with argon) bromobenzene can be converted within 3 h at catalyst concentrations of only 0.01 mol % palladium (Table 7, entry 4). The selectivities for the main coupling products are generally 90 % or more. The catalysts combine all important demands for practical application: high activity and selectivity without exclusion of air and moisture, extremely low Pd concentrations (0.005–0.1 mol %), easy and complete separation from the product mixture, easy and quantitative recovery of palladium, and commercial availability.

However, the TONs are still clearly lower than those of the best homogeneous catalyst systems for the activation of aryl bromides[2] (Table 9). However, even the best of them do not reach the TOF of the Pd/C system **3W** (Table 9). This shows that the reaction rate of the Pd/C system can be even higher than that of homogeneous systems. The activity at the beginning of the reaction seems to be extremely high before deactivation of the catalyst occurs. The Pd/C catalyst possibly represents an excellent reservoir for active palladium species in solution (see below). However, in contrast to the homogeneous catalysts listed in Table 9, aryl chlorides can only be converted to a very low extent under the conditions investigated for catalyst **3W**. Nevertheless, the optimized Pd/C catalyst presented here can be regarded as an important step towards surprisingly simple systems that meet the needs of synthetic organic chemists, and towards the commercial application of heterogeneous catalysts in C–C coupling reactions.

The approach described above gave new information about the role of different palladium species (solid particles, complexes, or clusters) in this complex reaction. However, for a deeper understanding it is necessary to answer the main question of these solid–liquid reactions: Does palladium act as heterogeneous catalyst or are Pd complexes or colloids in solution the catalytically active species in the Heck reaction? Extensive studies of the Pd content in solution after separation of the catalyst from the reaction mixture but also during the reaction were therefore performed.

The palladium concentration in solution is the highest at the beginning of the reaction (Figure 2), but drops to less than a few parts per million after completion of the reaction. Under optimized reaction conditions with 0.01 mol % Pd the palladium concentration in solution can be minimized to 0.3–2.3 ppm by simply filtering the hot reaction mixture. The Pd concentration in solution correlates with the progress of the reaction, the nature of the starting materials and products, the temperature, the solvent, the base and the atmosphere (argon or air). Lower temperatures, higher concentrations of the bromoarenes, and strong coordinating ability of the bromoarenes towards palladium (*p*-bromoacetophenone)[15] clearly increase Pd leaching. Higher temperatures seem to favor precipitation (Table 4, entries 2–4). While these effects are easy to rationalize, the influence of the atmosphere (air, argon) remains subject of speculation (Table 6). Oxidic Pd species, the content of which should be higher in the presence of air, are perhaps more easily leached than Pd^0.

The experimental results, in particular the direct correlation of conversion and concentration of palladium in solution (Figure 2), indicate a quasihomogeneous reaction mechanism, that is, Pd complexes[7i, 13a, 13c] or colloidal particles[12b, 13b] are the active species in solution, as was already proposed earlier. A distinction between these two kinds of Pd species is not possible on the basis of our results. Although there are still several inconsistencies, the present investigations are in good agreement with the detailed studies on this subject by Arai et al.,[7i], Biffis et al.,[5b] and Shmidt et al.[13a, 13c] The claim that classical homogeneously catalyzed Heck reactions and Pd/C-catalyzed Heck reactions proceed by a similar mechanism is supported by the identical selectivity. According to Arai et al.[7h] who used Pd on activated carbon (thermally treated at 200–350 °C) as catalyst, a heterogeneous mechanism (Pd surface reaction) would lead to dehalogenation (at higher temperatures), whereas the coupling reaction is supposed to be catalyzed by Pd leached into solution. In their experiments Pd/C almost exclusively gave benzene as product. At present, however, we would not generalize these ideas for all heterogeneously catalyzed Heck reactions.

These results do not limit the practical advantages of the heterogeneous system studied, because the Pd is re-precipitated onto the support at the end of the reaction and can thus be recovered almost quantitatively from the product mixture (<1 ppm Pd in the reaction mixture after filtration). This re-precipitation process can be controlled by careful choice of the reaction parameters (at the end of the reaction), which could be deduced from a large number of catalytic experiments and by employing statistical methods (design of experiments). Unfortunately, the re-precipitation significantly changes the state of the palladium catalyst (Figure 3 and 4), decreases its activity, and making its re-use unattractive.

Experimental Section

Catalyst preparation: All catalysts were obtained by wet impregnation.[16] All catalysts were prepared with H_2PdCl_4 at a constant Pd loading of 5 wt %. The support material (BET specific surface area 1120 $m^2 g^{-1}$; mean grain size 23 μm) was first suspended in distilled water. Then an aqueous solution of the Pd compound was added. After impregnation and heating to 80 °C the suspension was adjusted to pH 10 by adding sodium hydroxide. After agitation Pd was reduced by adding formaldehyde (**2W**, **4W**, and **5W**) or hydrazine (**6W**). After further agitation the catalyst was collected by filtration and washed with distilled water. Catalysts **1W** and **3W** were collected by filtration immediately after the heating phase without reduction. The dry catalysts were prepared by drying an infrared dryer at 100 °C to constant weight.

General reaction procedures: The catalytic reactions were carried out in pressure tubes in air or under argon. All reactants and solvents were obtained from Aldrich/Fluka or Merck (grade p.a.) and were used as received without further purification or drying. The qualitative and quantitative analysis of the reactants and products was performed by GLC or GC-MS. Products were identified by comparison with authentic samples. Conversion and selectivity are represented by product distribution (relative area of GLC signals) and GLC yields (relative area of GLC signals referred to an internal standard calibrated to the corresponding pure compound, $\Delta_{rel} < \pm 10\%$). The term "activity" is used in a rather general sense, that is, the conversion during the total reaction time. Note, however, that the reaction time varies significantly and differences in catalyst deactivation characteristics may be relevant. Conversion/total reaction time values are thus not an accurate measure for a variety of experiments. However, the kinetic data shown in Figure 2 describe the activity accurately.

Procedures for catalytic tests: Bromoarene (10 mmol), styrene (1.562 g, 15 mmol), base (12 mmol; usually sodium acetate, 0.984 g), diethylene glycol *n*-butyl ether (0.500 g, as internal standard for GC analysis), and 0.01–1.0 mol % of Pd as heterogeneous catalyst (e.g., **3W**) were introduced into a pressure tube. Solvent (10 mL, usually NMP or DMAc) was added. For experiments with a Pd concentration of 0.005 mol %, bromobenzene (3.141 g, 20 mmol), styrene (3.124 g, 30 mmol), sodium acetate (1.968 g, 24 mmol), diethylene glycol *n*-butyl ether (1 g), and NMP (20 mL) were used. The mixture was optionally de-aerated by purging with argon for 5 min. The reactor was placed in a preheated oil bath at the reaction temperature (60–160 °C) with vigorous stirring of the reaction mixture. After the reaction was complete a small sample of the reaction mixture was collected for GLC analysis, and the remainder was separated by hot filtration (110–120 °C for a reaction temperature of 140 °C). A sample was taken from the filtrate for Pd analysis.

For time-resolved investigations of activity and Pd leaching, bromobenzene (31.408 g, 200 mmol), sodium acetate (19.690 g, 240 mmol), diethylene glycol *n*-butyl ether (10 g), and 1.0 mol % Pd (4.26 g **3W**) were introduced with DMAc (200 mL) into a three-necked flask (500 mL) equipped with a septum and a reflux condenser. After the mixture was de-aerated by purging with argon for 20 min, styrene (31.24 g, 300 mmol) was added. The reactor was placed in a pre-heated oil bath at the reaction temperature (140 °C) with vigorous stirring of the reaction mixture. From time to time samples (ca. 8 mL) of the reaction mixture were collected while the reaction was running, and the Pd content in solution was determined by GLC and ICP-OES or ICP-MS.

For re-use studies the Pd/C catalyst was washed twice with dichloromethane (2 × 10 mL) or washed twice with dichloromethane (2 × 10 mL) and subsequently purified water (2 × 10 mL) after hot filtration. The catalyst was dried at room temperature and then re-used in Heck coupling.

For the GLC analyses the sample (1 mL) taken from the reaction mixture before filtration was quenched with water (2 mL) in a test tube. This mixture was extracted with dichloromethane (2 mL), and the organic layer was filtered and dried over $MgSO_4$. The resulting dry organic layer was analyzed by GLC or GC-MS.

Investigation of Pd leaching: For the determination of the Pd content in solution, a maximum amount of the clear filtrate was collected for better and more precise Pd analysis (usually half of the reaction mixture, i.e., 4–5 mL). A defined amount of the clear filtrate was collected in a glass vessel immediately after hot filtration. After careful evaporation of the organic compounds, the sample was treated with aqua regia and diluted, and the solution was filtered and analyzed by ICP-OES or ICP-MS. For better accuracy, multiple analysis was performed for each sample.

Methods: Gas-liquid chromatography was performed on a HP 6890 series chromatograph equipped with a FID detector and a HP-1 column (cross-linked methylsiloxane, 30 m × 0.25 mm × 0.25 μm film thickness). GC-MS analysis was performed on a HP 5890 instrument with a HP 5970 mass detector and a HP-1 column.

The palladium content in solution was determined by ICP-OES on a Perkin Elmer Optima 3300 DV spectrograph and ICP-MS on a VG Elemental Plasmaquad 2+ spectrograph.

Transmission electron microscopy (TEM) was carried out on a Hitachi H 500 H microscope.

The XRD measurements were performed on a Stoe spectrometer with $Cu_{K\alpha}$ X-ray emission radiation.

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