

Palladium metal catalysts in Heck C–C coupling reactions

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Abstract

This review is devoted to the application of palladium metal catalysts to the Heck reaction (arylation or vinylation of alkenes with aryl or vinyl halides and pseudohalides). The number of relevant articles published in recent years shows steadily increasing interest in this field. A brief outline of the historical development of heterogeneous catalysis as applied to the Heck reaction is given (Section 2). Both supported metal catalysts (Section 3) and stabilized colloidal palladium catalysts (Section 4) are included. Heterogeneous catalysts supported over different kinds of supports (carbon, inorganic oxides, molecular sieves, polymeric materials, etc.) are reviewed under separate headings. Particular attention is paid to the metal leaching and the nature of catalysis, two tightly connected problems which appear to be still controversial (Section 5). Some perspectives are shortly discussed in the final section (Section 6). © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Metal palladium catalysts; Heck reaction; Heterogeneous catalysts

1. Introduction

The arylation and vinylation of alkenes with aryl or vinyl halides was discovered independently by Heck [1] and Mizoroki et al. [2] about 30 years ago and it is nowadays known universally as the Heck reaction (HR). This reaction, which brings about the formation of new C–C bonds (Scheme 1), is generally

catalyzed in solution by palladium species generated from either Pd(0) compounds, such as $[\text{Pd}(\text{PPh}_3)_4]$ and $[\text{Pd}_2(\text{dba})_3]$, or Pd(II) salts, such as the acetate and the chloride.

One out of several bases, both organic and inorganic (e.g. tertiary amines, alkali acetates, carbonates, phosphates), can be used to neutralize the acid (HX) ensuing from the formal exchange of a hydrogen atom with an aryl or vinyl group.

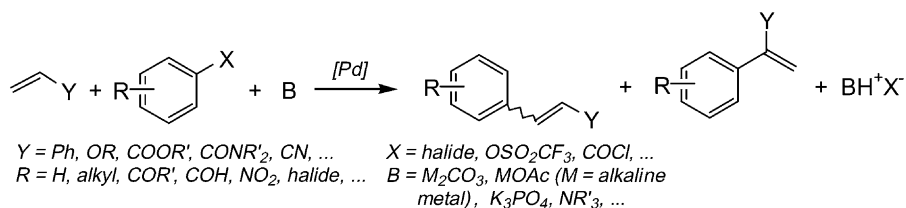
One of the major drawbacks of the early homogeneous systems was the precipitation of palladium black, which limited the lifetime of the active species. It was soon discovered that the addition of phosphines [3] greatly improved the stability of the catalytic system, although a large amount of the ligand inhibited the reaction. Later investigation demonstrated that heterocyclic carbenes [4] are suitable as well. Several palladacyclic compounds [5] also showed improved lifetimes and allowed, either on their own or with the aid of promoters, to sustain

Abbreviations: dba, dibenzylidenacetone; DMA, *N,N*-dimethylacetamide; DMF, *N,N*-dimethylformamide; ESCA, electron spectroscopy for chemical analysis; HR, Heck reaction; HETHR, heterogeneous HR; HOMHR, homogeneous HR; NEM, *N*-ethylmorpholine; NMM, *N*-methylmorpholine; NMP, *N*-methylpyrrolidone; PVP, poly-*N*-vinylpyrrolidone; SMSI, strong metal–support interaction; TEM, transmission electron microscopy; THF, tetrahydrofuran; TON, turnover number; TOF, turnover frequency; XRD, X-ray diffraction

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Scheme 1.

the reaction for millions of cycles [6,7]. A wide range of functional groups, both in the alkene and in the halide, is compatible with Heck coupling, which also tolerates the presence of water. In many instances, the addition of small amounts of water proved to be beneficial, leading to improved yields or reaction rates.

After a period of declining interest the huge synthetic potential of the HR (Heck reaction) was recognized and it started again to be thoroughly investigated. As the result of still continuing research efforts, its scope was greatly expanded [8] and light was shed on its mechanism [9], although it is still matter of debate whether the Pd(0)/Pd(II) or the Pd(II)/Pd(IV) redox couple is involved in the catalytic cycle [10]. As a matter of fact, the HR is considered nowadays one of the most versatile and useful tools in modern organic synthesis (see [11] for a very recent comprehensive review on this subject).

Although HR is very attractive also for industrial applications, according to the open literature the synthesis of an intermediate of the Prosulfuron[®] sulfonyl urea [12] is apparently the only homogeneous Heck reaction (HOMHR) currently practiced in the industry. The loss of the catalyst (most frequently needed in the 0.1–1% mol/mol range), which usually cannot be recovered, and the need of aryl iodides or bromides as starting materials are the major drawbacks that have prevented a more extensive exploitation of this reaction so far.

The loss of the catalyst could perhaps be tolerated if the cheaper and much more readily available aryl chlorides could be employed as starting materials. Under this respect, a homogeneous system, based on $[Pd_2(dba)_3]$ and $P(t-Bu)_3$, was recently reported to promote Heck couplings between a number of alkenes and aryl chlorides (both activated and inactivated) [13] and seems to have potential for general applicability.

However, as $P(t-Bu)_3$ is easily oxidized by air, the reaction must be carried out under inert atmosphere, which strongly reduces the appeal of this method.

In principle, heterogeneous catalysis could help in solving some of the problems which have prevented the technical applications of the HR so far. First of all, the catalyst could be easily recovered from the reaction mixture. Secondly, the heterogeneous catalyst could be recycled, provided it does not deactivate too quickly under duty. Third, palladium would be already present as metal crystallites dispersed onto the solid support, so that the precipitation of palladium black should not occur, unless it is not released in the liquid phase in soluble forms (HR takes place in liquid phase, hence any heterogeneous catalysis is bound to operate under solid–liquid conditions). As shown below, the question of metal losses is of the utmost importance in heterogeneous Heck reaction (HETHR). More generally, metal leaching is potentially a major problem in every reaction where solid–liquid heterogeneous catalysis is employed.

This paper aims at providing an overview of the state-of-the-art in heterogeneous catalysis as applied to Heck chemistry. A review on this subject appeared quite recently [14], but in fact its scope was rather narrow and we believe that a broader review, including also catalysis by soluble palladium nanoclusters and colloids, would be greatly appreciated. The field of stabilized metal colloids or nanoclusters has been continuously expanding since the beginning of the 1990s [15,16] and their catalytic applications have attracted considerable attention [17]. Of course, these materials are not heterogeneous in the usual sense, but the dimensions of the metal particles (some nanometers or tens of nanometers for palladium stabilized clusters) are not far from those of metal crystallites in classical heterogeneous catalysts. This resemblance makes

their catalytic action more similar to that of metal crystallites than that of homogeneous catalysts, although they are not affected by the presence of the support.

Palladium complexes anchored to solid supports (heterogenized homogeneous catalysts, hybrid catalysts) will not be included in this review, with the exception of the very few cases where they were employed as precursors of palladium metal catalysts. We have also not included in this review C–C couplings over heterogeneous catalysts different from HR. Highlights on this field, still extremely limited (the pertaining literature amounts to a few papers), can be found in the contribution to this volume by Blaser et al. [18].

2. Historical background

The first reports on the employment of heterogeneous catalysts for the HR followed its discovery pretty soon. Interestingly, very early experimental data suggested that palladium black, which could be formed in situ by reduction of Pd(II) precursors, was a crucial intermediate in homogeneous Heck catalysis [19,20]. Mizoroki, who independently of Heck discovered palladium catalyzed coupling reactions, reported that palladium black displayed a high catalytic activity in the arylation of ethene, propene, styrene and methylcinnamate with iodobenzene. However, he also observed that the catalytic activity was independent of the amount of palladium black and that arylation in benzene consumed exclusively iodobenzene. From these findings he judged that the catalytic coupling was not taking place directly on the metal surface, i.e. he came to the interesting conclusion that palladium black was not the actual catalyst, but rather a reservoir of active soluble zerovalent palladium species. In the same year Julia et al. reported their results on HETHR catalyzed by palladium on carbon [21,22]. These authors focused their attention on the coupling of styrene with aromatic chlorides, rather than iodides and bromides. They investigated on the effects of a number of parameters and obtained yields around 50% in the most favorable cases (very few, anyway).

After these very early reports, research on HETHR apparently subsided: only a few, scattered papers on this topic had been published up to the end of the 1980s [23–26]. This was the result of a number of circumstances. On one hand, the research in

homogenous Heck chemistry was also setting its pace in those years; on the other, the concept of heterogeneous catalysis as applied to fine chemistry was not popular yet. In fact, it started to grow important only at the end of the 1980s [27]. Since 1988 papers on HETHR have appeared rather regularly, and in the second half of the 1990s their number was relatively high, although not great in absolute terms. The most extensive and systematic pieces of research on HETHR were made by Hallberg and co-workers [25,26], Augustine and O'Leary [28,29], Zhuangyu and co-workers [30–33], Ying and co-workers [34,35], Arai et al. [36–38] and Köhler and co-workers [39,40]. Hallberg and Zhuangyu had a well-defined synthetic target, β -arylvinylethers (precursors of arylacetaldehydes), while Augustine, Ying, Arai and Köhler aimed their work at obtaining more basic information on the action of their catalysts. So far, Ying and Köhler are the only authors to report on tailor-made palladium catalysts supported onto molecular sieves. Other papers are apparently the outcome of preliminary screenings [23,24,41,42] and, in a few others, HR was simply employed as an attractive test for catalytic activity of new materials [43,44]. Finally, it appeared recently that HETHR was exploited for the multiton synthesis of octylmethoxycinnamate [45], an UV-B absorber commonly used in the manufacture of sunscreens. This process appears to be the only industrial application of HETHR reported in the open literature to date.

As for metal nanoclusters catalysis, the earliest reports [46–48] were limited to the recognition of the catalytic activity of palladium nanoclusters in the HR. In 1997 Antonietti et al. investigated for the first time on the structure–activity relationship for palladium colloids in block co-polymer micelles [49]. Quite recently, one of us [50] reported on the first example of palladium particles dispersed onto microgels, which are active in Heck catalysis. This kind of material, of which only very few examples existed before [51,52], can be considered in between colloidal and supported palladium particles. In fact, microgels are *intramolecularly* cross-linked polymers. Therefore, in contrast with polymeric resins, which are insoluble due to *intermolecular* cross-linking, they are soluble in a number of organic solvents, depending on their chemical structure. In this respect the microgels are more similar to linear polymers, but the

intramolecular cross-linking imparts to them better mechanical properties.

One point of utmost importance in HETHR is whether catalysis is truly heterogenous or not. As outlined above, Mizoroki collected evidence against true heterogenous catalysis. This point was more or less briefly touched in a few papers and it represented the central issue in the work of Zhao et al. [36–38], Schmidt and Mametova [53] and ourselves [54]. Köhler and co-workers also paid great attention to this issue [39,40], but Augustine and O’Leary were the first to have addressed this problem directly [28,29].

3. Supported palladium catalysts

3.1. Carbon

Palladium on carbon is one of the most frequently investigated catalysts: in several papers it is even the only one considered by the authors. This is not surprising at all, as palladium on carbon is a well-established hydrogenation catalyst, readily available from many commercial sources. Palladium on carbon proved active for Heck coupling under several different conditions. A selection of the results obtained with this kind of catalyst is presented in Table 1. These data show that carbon supported catalysts do not differ significantly in activity from homogenous ones: the proportion of the metal to the limiting reagent, the reaction temperatures, times and yields are comparable to those observed for homogenous catalysts. One of the most interesting results is the relatively high yield in stilbene from the reaction of chlorobenzene with styrene reported by Julia et al. (Eq. (1) and Table 1, nos. 1–4). In pure methanol at 120°C (the reaction was carried out in an autoclave under pressure) stilbene was afforded in 62% yield (82% conversion of styrene), without any added phosphine. In this connection the authors showed that under these conditions added triphenylphosphine was an inhibitor rather than a promoter.

Comparable results were obtained at atmospheric pressure using either ethylene glycol or a 1/2 (v/v) methanol/ethylene glycol mixture as the solvent. However, the reaction was very specific: low yields were reported for the other solvents and substituted chloroaryls (but 4-nitrochlorobenzene) investigated. In his investigation of the HR between 4-nitrohalobenzenes and vinylmethylether (Scheme 2), Hallberg tried to couple the chloroderivative under the same conditions employed by Julia. In his case the reaction was unsuccessful and he indicated the addition of ethylene glycol to the vinylic double bond (faster than the coupling) as the possible cause of the failure. In contrast, when chlorine was substituted for by bromine, the reaction took place with yields as high as those reported in Table 1 (nos. 5–7). Hallberg screened a number of solvents and he found that toluene and *p*-xylene were the most effective for 4-nitrobromobenzene and benzoylchlorides, respectively. In the case investigated by Hallberg, who aimed at the synthesis of arylacetaldehyde derivatives, also regio-selectivity had to be taken into account. Thus, in order to improve the β/α selectivity he moved from the classical HR with halobenzenes to the Blaser–Spencer variation, where an aroyl chloride is the alkene partner [55].

As it can be seen from the data of Table 1, the best regio-selectivity was achieved in a HOMHR using $[\text{Pd}(\text{OAc})_2]$ as the catalyst precursor and starting from 4-nitrobenzoylchloride, although the overall yields in coupling derivatives was actually lower in comparison with a HETHR over Pd/C starting from 4-nitrobromobenzene. Also in these couplings, both homogeneous and heterogeneous, PPh_3 completely inhibited the reaction.

The results of Hallberg and co-workers inspired the work of Augustine and O’Leary, who tested a number of heterogeneous palladium catalysts in the same reaction. They substantially confirmed Hallberg’s findings and, in addition, identified some previously unknown side-products (Scheme 3). The heterogeneous catalyst was indeed less regio-selective than the

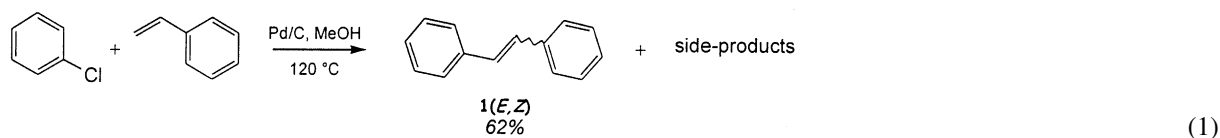


Table 1
Selected Heck reactions over Pd/C

Sl. no.	Catalyst, %Pd (w/w)	ArX	Alkene	Base	ArX/alkene/base/Pd (mol/mol/mol/mol)	Solvent	T (°C)	Time (h)	Yield (%)	Selectivity		Reference
										Regio ^a	Stereo ^b	
1	Pd/C, 5%	Iodobenzene	Methylacrylate	Na ₂ CO ₃	1/10/1/0.47	Methanol	150 ^c	4	70	–	–	[21]
2	Pd/C, 5%	Chlorobenzene	Styrene	Na ₂ CO ₃	1/10/1/0.47	Methanol	120 ^c	4	62	–	–	[22]
3	Pd/C, 5%	Chlorobenzene	Styrene	Na ₂ CO ₃	1/10/1/0.5	Ethylene glycol	120	4	55	–	–	[22]
4	Pd/C, 5%	Chlorobenzene	Styrene	Na ₂ CO ₃	1/10/1/0.5	Methanol/ethylene glycol (1/2, v/v)	100	24	46	–	–	[22]
5	Pd/C, 5%	4-Nitrobromobenzene	Vinylmethyl ether	NEt ₃	1/1.6/1.2/5 × 10 ⁻³	Toluene	120 ^c	16	80	6.3	–	[25]
6	Pd/C, 10%	4-Nitrobenzoylchloride	Vinylbutyl ether	NEM	1/1.5/2/3 × 10 ⁻²	Toluene	Reflux	8	68	–	–	[26]
7	[Pd(OAc) ₂]	4-Nitrobenzoylchloride	Vinylbutyl ether	NEM	1/2/1.2/1 × 10 ⁻²	<i>p</i> -Xylene	Reflux	3	75	10	–	[26]
8	Pd/C, 5%	4-Nitrobenzoylchloride	Vinylbutyl ether	NEt ₃	1/2/1.2/1 × 10 ⁻²	Dioxane	100	4	73	10	–	[28]
9	[Pd(OAc) ₂]	4-Nitrobenzoylchloride	Vinylbutyl ether	NEt ₃	1/2/1.2/1 × 10 ⁻²	Dioxane	100	4	57	56	–	[28]
10	Pd/C, 5%	<i>p</i> -Anisidyl diazonium tetrafluoroborate	Ethylacrylate	None	1/-/0/1 × 10 ⁻²	Ethanol	40–60	–	98	–	–	[56]
11	Pd/C _{Gr} , 33%	Iodobenzene	Ethylacrylate	NBu ₃	1/2/1.2/0.07	None	100	6	87	–	>100	[24]
12	Pd/C _{Gr} , 33%	Iodobenzene	Styrene	NBu ₃	1/2/1.2/0.07	None	100	5	92	–	>10	[24]
13	Pd/C _{Gr} , 37%	Iodobenzene	Styrene	K ₂ CO ₃	2/1/4/3.5 × 10 ^{-2 e}	DMF	100	95	82	–	–	[44]
14	Pd/C _{Gr} , 17%	Iodobenzene	Ethylacrylate	NBu ₃	1/1.2/1.3/4 × 10 ⁻²	DMA	80	–	76	–	–	[57]
15	Pd/C, 5%	Iodobenzene	Acrylonitrile	NEt ₃	1/1/1/1 × 10 ^{-2 f}	Acetonitrile	140	14	62	–	3.3	[60]
16	Pd/C, 5%	Bromobenzene	Styrene	NaOAc	1/1.5/1.2/1 × 10 ⁻³	DMA	140	20	84	–	96	[39]

^a β/α molar ratio.

^b E/Z molar ratio for β-derivatives.

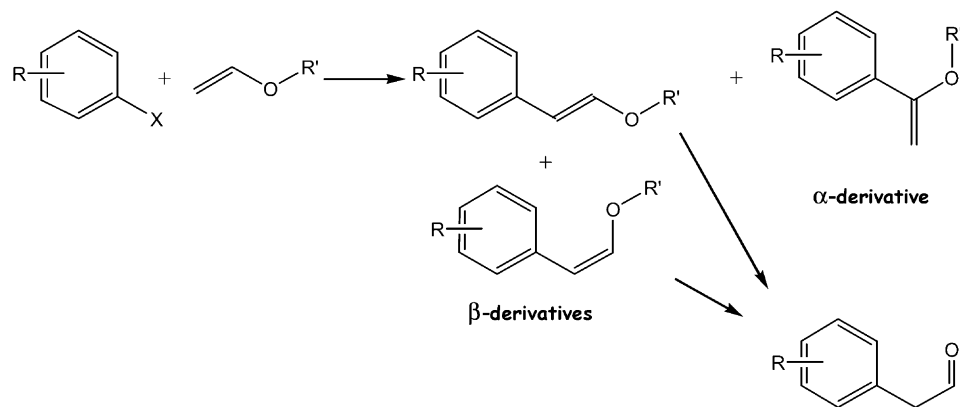
^c Under pressure.

^d (2 + 3)/(4 + 6), see Scheme 3.

^e NBu₄Br (1/1 vs. PhI) was also added.

^f PPh₃ (3/1 vs. Pd) was also added.

^g Stilbene/1,1-diphenylethene (mol/mol).

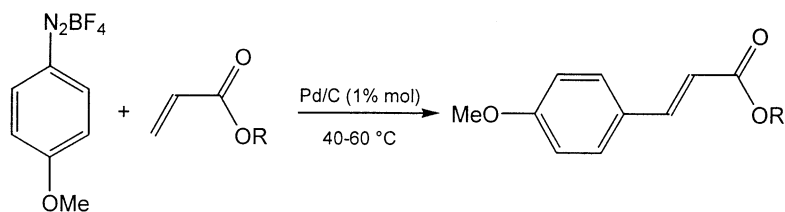


Scheme 2.

homogenous system based on $[\text{Pd}(\text{OAc})_2]$, although Augustine managed to achieve β/α molar ratios close to 10 over Pd/C in comparison with 6 obtained by Hallberg. Moreover, Augustine also managed to make the heterogenous catalyst as active as the homogenous one by simply using a more polar solvent (dioxane instead of toluene or xylene) which prevented the fouling of the catalyst by triethylammonium chloride (Table 1, nos. 8 and 9). Finally, he observed again that

versus 40%, respectively). These results were the starting point of further work concerning palladium heterogenous catalysts supported by inorganic oxides (see Section 3.2).

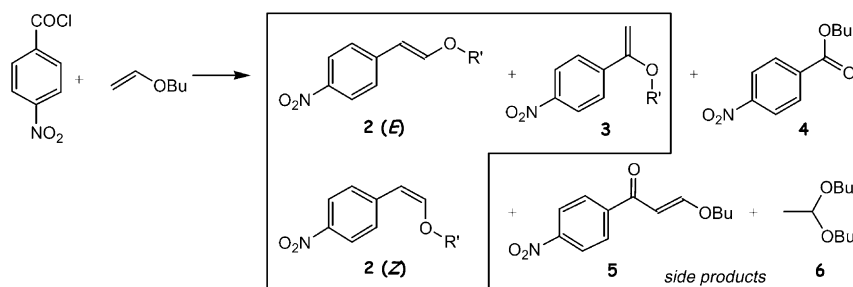
Palladium on carbon was also employed by Beller and Külhein as the catalyst for the reported first HETHR involving 4-methoxyphenyldiazonium (*p*-anisidyldiazonium) tetrafluoroborate [56] (Eq. (2) and Table 1, no. 10).



(2)

the heterogeneous catalyst was more chemoselective than the homogenous one (ca. 16% of by-products

According to them, this could be the alternative route to classical condensation for the synthesis of



Scheme 3.

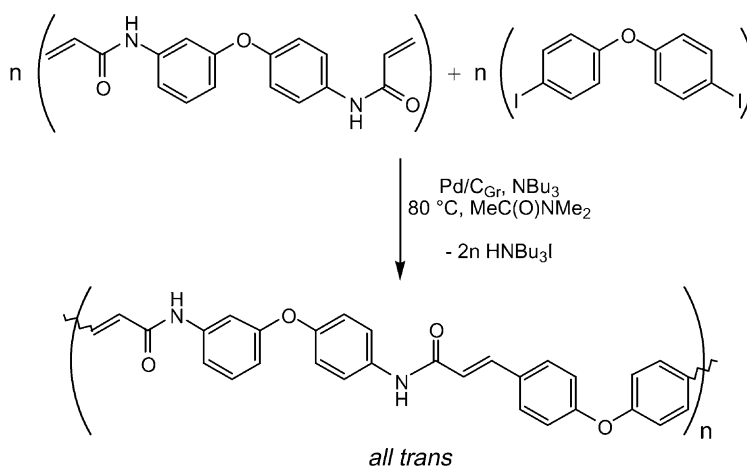
substituted cinnamic esters, which are industrially important UV absorbers. In their work, the authors pointed out that this starting materials allowed to carry out the reaction without any added bases and/or promoter. On the other hand, they recalled that aryl-diazonium salts usually require a higher catalyst amount in comparison to halides, but this problem could be circumvented by recycling the heterogeneous catalyst. In polar protic solvents like methanol and ethanol excellent yields were obtained in the methyl or ethyl ester of the 3-(4-methoxyphenyl)propenoic acid (methyl- or ethylmethoxycinnamate), but in the first recycle the yield did not exceed 31%.

Pd/C is employed in the coupling of 4-methoxybromobenzene with octylacrylate for the industrial production of octylmethoxycinnamate, a common UV absorber utilized in the manufacture of sunscreen lotions [14,45]. To the best of our knowledge, this is the only industrial application of HETHR ever reported in the open literature and the second if also HOMHR (see Section 1) is included. Highlights on this subject are given also by Blaser et al. in their contribution to this volume [18].

Graphite was taken into account as carbonaceous support in addition to activated carbon. Umami Ronchi and his co-workers reported that a Pd catalyst obtained by reduction of Pd(II) salts with potassium graphite (C₈K) [23] was active in a number of catalytic reactions, including HR [24]. However, the reaction required a relatively high amount of

palladium (7% molar of the metal versus the aromatic halide) and worked only with iodobenzene — bromobenzene did not react, even at 130°C (Table 1, nos. 11 and 12). These results suggest that this kind of catalyst is not particularly active, as the possible consequence of the relatively low dispersion of the metal (i.e. large size of the crystallites). The same procedure was used years later by Jikei et al. to prepare a Pd/C_{Gr} which was employed in a polycondensation reaction between a diacrylate and a diiodide (Scheme 4) [57].

In the model reaction between ethylacrylate and iodobenzene (Table 1, no. 14), Kakimoto found that the Pd/C_{Gr} catalyst was much more active than a Pd/C catalyst. Although the source and the “history” of the latter was not specified, the authors found that the crystallite size was smaller in the former and attributed its superior activity to this circumstance. The effect of a number of experimental parameters (base, solvent, starting molar ratio of the comonomers) on the molecular weight and its distribution was also investigated. Moreover, the authors compared the heterogeneous catalyst with the classical homogenous system based on [Pd(OAc)₂]/P(*o*-tolyl)₃. The characterization of the polymers obtained under heterogeneous and homogeneous conditions revealed that they possessed the same chemical structure. However, the product obtained over the heterogeneous catalyst was featured by a narrower molecular weight distribution and contained much smaller amounts of metallic palladium. As the metal contamination can be explained only by



Scheme 4.

take-up of palladium from the solution, it is a strong evidence of palladium leaching, although the authors were not apparently concerned with this problem.

A different Pd/C_{Gr} material (of the “graphimet” type) was recently reported to be active as a heterogeneous Heck catalyst [44] (Table 1, no. 14). The catalyst contained “flat” palladium particles (width/thickness ratio = 24–70) sandwiched between the graphite layers of the support. No metal particles were detected on the external surface of the support in the fresh catalyst, as well as after two catalytic runs. Therefore, the authors suggested that the reaction took place in the interlayer space of graphite, but, as direct evidence was admittedly lacking, they did not rule out the possibility of homogeneous catalysis by leached species.

3.2. Metal oxides

The first paper on heterogeneous Heck catalysis over palladium supported onto an inorganic oxide was published by Kaneda et al. in 1990 [41]. They reported thereby the activation of chlorobenzene in the coupling with styrene in methanol at 150°C (Table 2, no. 1) using Na₂CO₃ as the base. This is one of the rare examples of activation of an aromatic chloride in a HR over a heterogeneous catalyst. The authors claimed that methanol was unique in allowing the reaction to proceed. Also in the case of Julia with Pd/C [21,22] a polar protic solvent (methanol or ethylene glycol) was necessary to achieve substantial reaction yields with chlorobenzene. Other alkali carbonates (Li, K) or other catalysts were much less effective. Interestingly, phosphine were found to strongly inhibit the reaction. The authors attributed the high activity of their MgO supported catalysts to the transfer of electron density from the very basic support to the metal. This would make the metal surface more readily oxidizable and therefore more reactive towards the halide. Such electron transfer was invoked for Pd/MgO catalysts employed in gas phase reactions of hydrocarbons, like the aromatization of alkanes [58]. It was argued that these processes were favored by a SMSI (strong metal–support interaction) which protected the metal crystallites from sintering and yielded an electron rich metal surface, with modified adsorption/desorption properties.

In their investigation on the HETHR of butylvinylether with 4-nitrohalobenzenes (Scheme 3), Augustine and O’Leary took into consideration a number of

oxide-based catalysts [28,29] in addition to Pd/C (see Section 3.1). They studied three palladium catalysts, Pd/SiO₂ 1.22% (w/w), Pd/γ-Al₂O₃ 6.06% (w/w) and Pd/MgO 1% (w/w), which were prepared in their laboratories. They also tested a platinum and a rhodium catalyst, both based on γ-Al₂O₃, but these yielded only side-products (4–6, Scheme 3, Section 3.1). Augustine and O’Leary initially found that whereas Pd/γ-Al₂O₃ was practically as active as Pd/C, Pd/SiO₂ was somewhat less efficient (Table 2, nos. 2–4). The chemoselectivity of the HR was slightly better for the Pd/C catalyst, but the effect of the support on regio-selectivity was negligible. The authors varied also other experimental parameters (nature of the solvent, amount and basicity of the tertiary amine, nature of the halide), but only small effects on the β/α selectivity, if any, were observed. However, they later discovered that the support effects on the regio-selectivity depended on the *para*-ring substitution (Fig. 1). Thus, in the couplings of benzoylchloride and 4-methylbenzoylchloride the regio-selectivity was reversed on passing from the most basic support (MgO, prevalence of the α-isomer) to the most acidic one (SiO₂, prevalence of β-isomers).

Augustine and O’Leary reported also some experimental reaction rate data (Fig. 2).¹ Support effects were observed only in the coupling of 4-nitrobenzoylchloride that was relatively slow over Pd/MgO in comparison with both Pd/SiO₂ and Pd/Al₂O₃. By contrast, for 4-bromotoluene and

¹ These data deserve some comments. In heterogeneous catalysis diffusion can be rate controlling and in this case the experimental rate reflects how fast reagents (products) are transported from (to) their phase to (from) the catalytic site and not the intrinsic rate of the chemical reaction. Moreover, the local concentration at the active site can be affected by the thermodynamic affinity of the intervening species towards the support. In liquid–solid heterogeneous catalysis this is complicated also by the presence of the solvent. This kind of partition effects has been recently established for heterogeneous molecular sieve catalysts [59]. In the second place, we are under the impression that the reported data are the average TOFs over the whole reaction time span (mol products/mol Pd/overall reaction time), which do not allow a fully reliable evaluation of the activity of the catalysts. In fact, small values could reflect high deactivation rates instead of an intrinsically low activity. Finally, these data seem in contrast with those reported by the same authors in [28]. The rate data of Fig. 2 (from Table 1 of [29]) for the coupling of 4-nitrobenzoylchloride indicate that Pd/SiO₂ is more effective than Pd/γ-Al₂O₃, the data of Table 2 (from Table 1 of [28]) support the opposite conclusion.

Table 2
Selected Heck reactions over palladium supported onto inorganic oxides

Sl. no.	Catalyst, %Pd (w/w)	ArX	Alkene	Base	ArX/alkene/base/Pd (mol/mol/mol/mol)	Solvent	T (°C)	Time (h)	Yield (%)	Selectivity		Reference
										Regio ^a	Stereo ^b	
1	Pd/MgO	Chlorobenzene	Styrene	Na ₂ CO ₃	7/1/0.33/2 × 10 ⁻⁴	None	150	5	32	–	42	[41]
2	Pd/C, 5%	4-Nitrobenzoylchloride	Vinylbutylether	NEt ₃	1/2/1.2/2.5 × 10 ⁻³	Dioxane	100	4	77	10	–	4.8 ^c [28]
3	Pd/Al ₂ O ₃ , 6.06%	4-Nitrobenzoylchloride	Vinylbutylether	NEt ₃	1/2/1.2/2.5 × 10 ⁻³	Dioxane	100	4	71	10	–	3.9 ^c [28]
4	Pd/SiO ₂ , 1.22%	4-Nitrobenzoylchloride	Vinylbutylether	NEt ₃	1/2/1.2/2.5 × 10 ⁻³	Dioxane	100	4	51	10	–	3.2 ^c [28]
5	Pd/Al ₂ O ₃ , 5%	Iodobenzene	Acrylonitrile	NEt ₃	1/1/1/1 × 10 ^{-2 d}	Acetonitrile	140	14	72	–	3.3	20 ^e [60]
6	Pd/MgO, 5%	Iodobenzene	Acrylonitrile	NEt ₃	1/1/1/1 × 10 ^{-2 d}	Acetonitrile	140	14	78	–	3.5	10 ^e [60]
7	Pd/MgO, 4.9%	Bromobenzene	Styrene	NaOAc	1/1.5/1.2/1 × 10 ⁻³	DMA	140	20	36.5	12.5	–	112 ^e [39]
8	Pd/ZnO, 4.5%	Bromobenzene	Styrene	NaOAc	1/1.5/1.2/1 × 10 ⁻³	DMA	140	20	33.3	11.8	–	101 ^e [39]
9	Pd/TiO ₂ , 4.3%	Bromobenzene	Styrene	NaOAc	1/1.5/1.2/1 × 10 ⁻³	DMA	140	20	41.2	12.7	–	95 ^e [40]
10	Pd/ZrO ₂ , 5.5%	Bromobenzene	Styrene	NaOAc	1/1.5/1.2/1 × 10 ⁻³	DMA	140	20	49.1	12.3	–	112 ^e [39]
11	Pd/SiO ₂ , 4.3%	Bromobenzene	Styrene	NaOAc	1/1.5/1.2/1 × 10 ⁻³	DMA	140	20	8.2	12.7	–	75 ^e [39]

^a β/α molar ratio.

^b E/Z molar ratio for β-derivatives.

^c (2 + 3)/(4 + 6), see Scheme 3.

^d PPh₃ (3/1 vs. Pd) was also added.

^e β-Monoarylated/β,β-diarylated derivatives molar ratio.

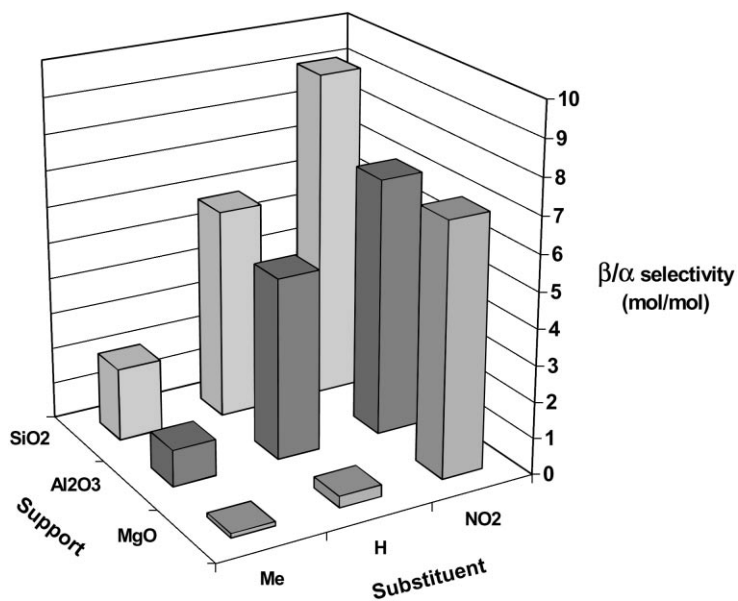


Fig. 1. Regio-selectivity in the coupling of 4-substituted benzoylchlorides with *n*-butylvinylether over palladium supported by inorganic oxides after Augustine et al. [29] (NEM as the base, other conditions as in Table 2, nos. 2–4).

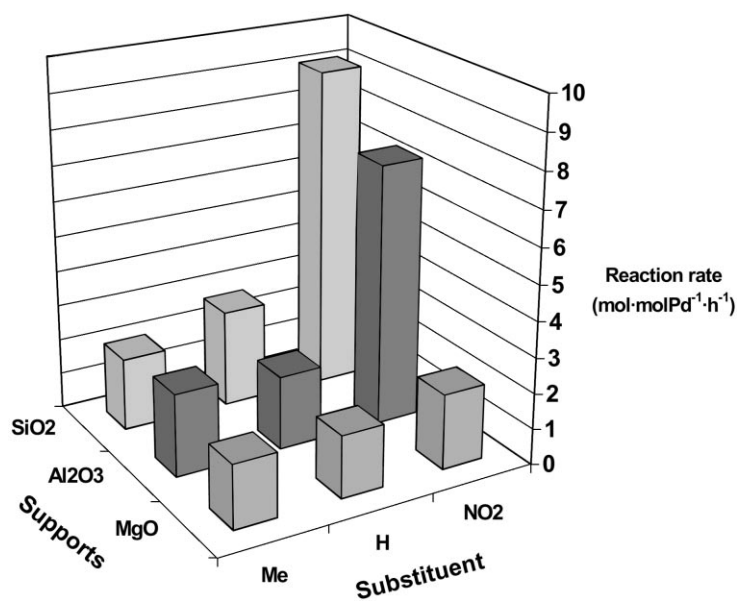
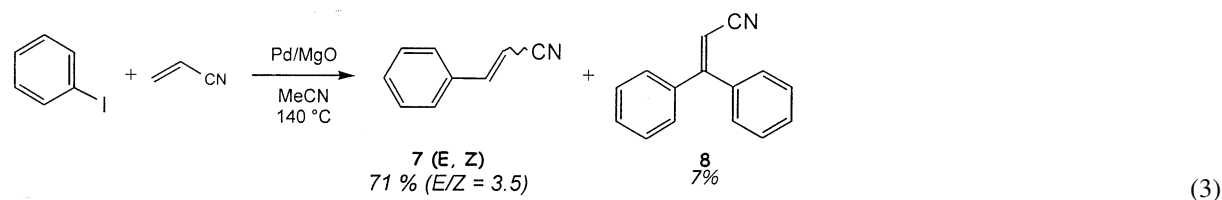


Fig. 2. Average rate in the coupling of 4-substituted benzoylchlorides with *n*-butylvinylether over palladium supported by inorganic oxides after Augustine et al. [29] (NEM as the base, other conditions as in Table 2, nos. 2–4).

bromobenzene the support nature did not affect the coupling rates.

Augustine and O'Leary were probably the first to address explicitly the heterogeneity/homogeneity dilemma in connection with Heck chemistry over supported palladium catalysts. This subject will be dealt with in Section 5 and it is anticipated here that these authors came to the conclusion that in their experiments catalysis was truly heterogeneous. In this connection they proposed that highly coordinative unsaturated palladium atoms (i.e. corner atoms of the metal crystallites or adatoms) were the active sites.

Some catalysts supported onto MgO were investigated also by Wali and co-workers and compared to palladium on carbon and on γ -alumina [60,61]. In his investigation Wali used $[\text{Pd}(\text{acac})_2]$ for the preparation of the MgO supported catalyst (impregnation and H_2 -reduction at 60°C) and as a homogenous reference catalyst for the coupling of acrylonitrile with iodobenzene (Eq. (3)).



A first screen of the catalysts (Table 1, no. 15 and Table 2, nos. 5 and 6) showed that they differed to some extent in the final yield at fixed reaction time (14 h). The highest overall yield was obtained with the Pd/MgO catalyst and therefore it was investigated in greater detail. It was found that the presence of PPh_3 ($\text{P/Pd} = 3$) is beneficial to the catalyst performance. The catalyst was recycled several times: at first turnover numbers apparently increased, then the

catalyst effectiveness started to decline. ESCA characterization of the materials gave interesting results. Electron binding energies for the Pd $3d_{5/2}$ are reported in Table 3. ESCA showed that the binding energy for palladium in MgO impregnated with $[\text{Pd}(\text{acac})_2]$ before reduction was lower in comparison to the pure metal complex. This is a clear evidence of electron transfer from the support to the Pd(II) centers, which highlights the basicity of the support. As expected, the palladium peaks were shifted to even lower binding energy values after reduction with H_2 (60°C , 4 h). However, some broadening towards higher binding energy values of the Pd $3d_{5/2}$ peak indicated that the reduction of palladium was not complete. The ESCA data obtained on spent materials are particularly interesting in that they demonstrate that the amount of supported Pd(II) relative to Pd(0) increased steadily after each run. Thus, in $[\text{Pd}(\text{acac})_2]/\text{MgO}$ practically no zerovalent palladium could be detected after one cycle, and the same was found for Pd/MgO after three

cycles. Some possible implication of these findings will be discussed in Section 5.

Another important piece of research on metal oxide-based catalysts as applied in HETHR was provided by Köhler and co-workers [39], who studied the coupling of bromobenzene with styrene over a number of 5% palladium (w/w) catalysts as a model reaction (Eq. (4)).

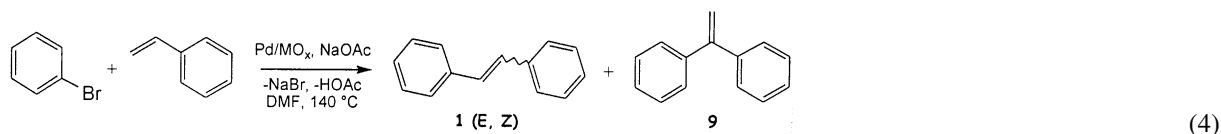
Table 3

Binding energies for the Pd $3d_{5/2}$ level in palladium catalysts supported over MgO after Wali et al. [60]

	[Pd(acac) ₂]	[Pd(acac) ₂]/MgO ^a		Pd/MgO ^a		
		0	1	0	1	3
BE, Pd $3d_{5/2}$ (eV)	338.3	336.6	337.1	335.4 ^b	335.2	336.4
		336.1 (sh)		336.9 (sh)		

^a 0 refers to the fresh catalyst, and 1 and 3 refer to the catalyst recovered after one and three catalytic runs, respectively.

^b The peak showed some broadening towards higher binding energies.



As shown in Table 1 (no. 12) and Table 2 (nos. 7–11), they found that under their standard conditions the catalyst effectiveness decreased in the order Pd/C > Pd/TiO₂ > Pd/ZrO₂ > Pd/MgO > Pd/ZnO > Pd/SiO₂. The finding that highly acidic supports like titania and zirconia gave the best yields in the series of oxide-based catalysts did not match the previous observation that palladium on MgO, a definitely basic support, seemed the most suitable for the coupling of aryl halides with alkenes with electron withdrawing substituents [41,60,61]. Therefore, Köhler tried to correlate his results to other parameters and focused his attention on the specific palladium surface area (i.e. its dispersion). All the catalysts, apart Pd/C, which was commercial, were prepared by an impregnation/H₂-reduction procedure similar to that employed by Wali et al. [60]. Different reduction temperatures were applied in order to get some control over the specific palladium surface area and the resulting catalytic activity. For Pd/MgO the data seemed in agreement with a decrease in the catalyst effectiveness with increasing reduction temperature, but for Pd/TiO₂ a reversed relationship was observed up to a reduction temperature of 400°C. In the case of Pd/MgO the dependence of catalyst effectiveness on reduction temperature was attributed to the decrease of the metal surface (i.e. increasing of particle size) with increasing reduction temperatures. By contrast, SMSI were indicated as responsible for the observed dependence of Pd/TiO₂ catalysts effectiveness on the reduction temperature. In fact, metal catalysts supported onto reducible oxides are subjected to SMSI, which are known to lower the adsorption capacity of the supported metals with no significant change in their specific surface areas [62–64].

3.3. Molecular sieves

Only two research group have reported so far on heterogeneous Heck catalysts based on molecular sieves. Ying and co-workers prepared and tested some palladium catalysts supported onto a niobium modified mesoporous silicalite (Nb-MCM-41) [34,35].

Mesoporous molecular sieves are crystalline materials structurally related to zeolites and featured by pores with diameters ranging from 1.5 to 10 nm. Nb-MCM-41 could be silanized after the synthesis in order to block the hydroxyl groups present on the intracrystalline surface of the material. Palladium was introduced by means of either impregnation or metal organic chemical vapor deposition (MOCVD), followed by metal reduction with hydrogen. MOCVD on the non silanized Nb-MCM-41 yielded a catalyst with metal surface area as high as 140 m²/g. XRD characterization showed that the crystalline structure was practically unchanged with respect to the support: only the pore size was slightly smaller than in the support, as the consequence of the palladium deposition.

The performance of the non silanized catalyst is illustrated by the data in Table 4 (nos. 1–7). The catalyst is very effective for the coupling of bromoaryls with *para*-electron withdrawing ring substituents (–NO₂, –COCH₃), but not so much with bromobenzene. Only small amounts of coupling products were observed with chlorobenzene. A reaction time profile showed that there was an induction time of 5 min before the reaction started, which was attributed to the period of catalyst heating. However, about 20 min were required before the highest apparent reaction rate was reached. A catalyst sample recovered after duty showed evidence of structural damage of the support (TEM) and of restructuring of the polydispersed metal phase. Characteristic XRD peaks of palladium, not present in the powder spectrum of the fresh catalyst, were detected in the spectrum of the recovered solid. This finding indicates that the crystallite size increased during the reaction. Palladium particles of average diameter of 15 nm were observed in TEM microphotographs of the recovered material. No data were reported on catalyst recycling, but it was found that about 5% of the metal was lost and that some carbon deposited onto the catalyst.

Djakovitch and Köhler have studied a series of palladium catalysts obtained by ion-exchanging Na- or H-zeolites (Mordenite, Y) with [Pd(NH₃)₄]Cl₂ [40]

Table 4
Selected Heck reactions over palladium supported by molecular sieves

Sl. no.	Catalyst, %Pd (w/w)	ArX	Alkene	Base	ArX/alkene/base/Pd (mol/mol/mol/mol)	Solvent	T (°C)	Time (h)	Yield (%)	Selectivity		Reference
										Regio ^a	Stereo ^b	
1	Pd/Nb-MCM-41 ^a	Bromobenzene	Styrene	NEt ₃	1/1.2/1.1/1 × 10 ⁻³	DMA	170	48	32	–	99	[29]
2	Pd/Nb-MCM-41 ^a	Bromobenzene	Butylacrylate	NEt ₃	1/1.2/1.1/1 × 10 ⁻³	DMA	170	48	62	–	99	[29]
3	Pd/Nb-MCM-41 ^a	Chlorobenzene	Butylacrylate	NEt ₃	1/1.2/1.1/1 × 10 ⁻³	DMA	170	32	6.4	–	99	[29]
4	Pd/Nb-MCM-41 ^a	4-Nitrobromobenzene	Styrene	NEt ₃	1/1.2/1.1/1 × 10 ⁻³	DMA	170	1/3	97	–	24	[29]
5	Pd/Nb-MCM-41 ^a	4-Bromoacetophenone	Styrene	NEt ₃	1/1.2/1.1/1 × 10 ⁻³	DMA	170	3/4	97	–	19	[29]
6	Pd/Nb-MCM-41 ^a	4-Nitrobromobenzene	Butylacrylate	NEt ₃	1/1.2/1.1/1 × 10 ⁻³	DMA	170	1/4	99	–	99	[29]
7	Pd/Nb-MCM-41 ^a	4-Bromoacetophenone	Butylacrylate	NEt ₃	1/1.2/1.1/1 × 10 ⁻³	DMA	170	2/5	99	–	99	[29]
8	Pd(O)/Na-Mor, 7%	4-Fluorobromobenzene	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	89	10	24	[40]
9	Pd(O)/Na-Mor, 7%	4-Nitrobromobenzene	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	96	–	–	[40]
10	Pd(O)/Na-Mor, 7%	4-Bromoacetophenone	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	86	–	–	[40]
11	Pd(O)/Na-Mor, 7%	Bromobenzene	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	32	–	–	[40]
12	Pd(II)/Na-Mor, 7%	4-Fluorobromobenzene	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	92	10	92	[40]
13	Pd(II)/Na-Mor, 7%	4-Nitrobromobenzene	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	94	–	–	[40]
14	Pd(II)/Na-Mor, 7%	4-Bromoacetophenone	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	86	–	–	[40]
15	Pd(II)/Na-Mor, 7%	Bromobenzene	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	72	–	–	[40]
16	Pd(II)/H-Mor, 7%	4-Fluorobromobenzene	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	91	–	–	[40]
17	Pd(II)/HY, 7% ^c	4-Fluorobromobenzene	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	92	–	–	[40]
18	Pd(II)/HY, 7% ^d	4-Fluorobromobenzene	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	93	–	–	[40]
19	Pd(II)/HY, 7% ^e	4-Fluorobromobenzene	Styrene	NaOAc	1/1.5/1.5/2 × 10 ⁻³	DMA	140	20	92	–	–	[40]

^a β/α molar ratio.

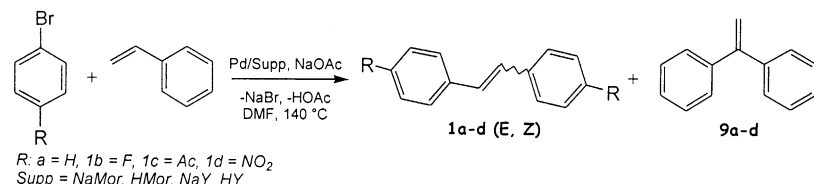
^b E/Z molar ratio for β-derivatives.

^c Si/Al = 9.4.

^d Si/Al = 24.

^e Si/Al = 50.

(Table 4, nos. 8–19). The exchanged materials were calcined in dioxygen at 500°C and then used as such or after reduction of Pd(II) to Pd(0) under dihydrogen at 350°C. The performances of the reduced and unreduced catalysts in term of yields and product distribution are similar for the HR of styrene with 4-substituted bromobenzenes (nitro, acetyl and fluoro derivatives, Eq. (5)).



(5)

The apparent reaction rate was slightly higher with Pd(II) catalysts, in spite of the induction time required for the reduction in situ of the metal. This finding was attributed to the smaller size of the palladium crystallites generated in situ with respect to those obtained upon pre-hydrogenation of the catalyst. These catalysts, however, were not particularly active: reaction times exceeding 24 h were required for complete reaction. The catalysts generally showed reduced effectiveness upon recycling. However, in the second run over Pd(0)/H-Mor, the yield of the coupling of bromobenzene was roughly two times larger than in the first cycle. This finding was attributed to the re-dispersion of the metal throughout the support, leading to smaller crystallite sizes. This conclusion is in contrast with the evidence of the growth of metal particle sizes during the reaction presented by Ying and co-workers in their work on Nb-MCM-41 supported catalysts. Djakovitch and Köhler did not measure the crystallite size in their recovered catalysts, hence only a tentative explanation can be given of these discrepancies. In particular, the higher reaction temperature employed by Ying et al. (170 versus 140°C) could account for the palladium sintering which they observed. Moreover, they also reported that the Nb-MCM-41 support underwent structural damage, which could have diminished the protection against metal agglomeration. The performance of the catalysts was found to be independent of the acidity of the support, at least in the first run. The catalysts supported by either HY zeolites with different Si/Al ratios (9.4, 24 and 50) or mordenite gave results quite comparable to one another.

3.4. Polymeric materials

Polymeric materials have been relatively widely used for the immobilization of homogenous Heck catalysts onto a solid support (see [65] for a very recent example). Hybrid Heck catalysis, however, is outside the scope of this review and we will consider here

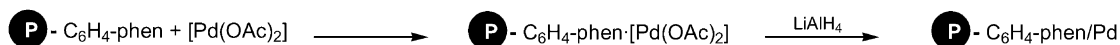
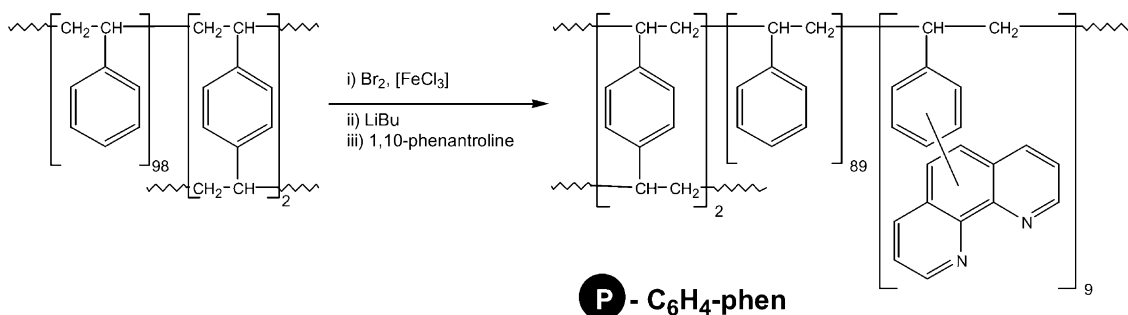
only those cases where the polymer-immobilized palladium complexes were transformed into supported metal particles prior to the reaction.

This restricts this sub-field of HETHR to a handful of papers, most of which by a Chinese research group [30–33]. In fact, at the beginning of the 1990's, Zhuangyu and co-workers reported on the preparation of palladium catalysts supported onto modified polystyrene resins (Scheme 5).

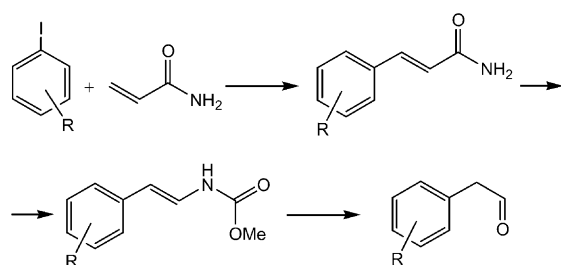
Their preliminary results showed that this kind of catalysts were as active as [Pd(OAc)₂] in a number of Heck couplings of iodobenzene (Table 5, nos. 1–7), if not somewhat superior. However, they also found that the catalysts underwent severe metal leaching (up to 74% of the metal was released into the liquid phase after three runs), which limited the catalyst lifetime. This was attributed to the metal coordination of NBU₃ that stabilized palladium in solution. The catalyst lifetime could be improved by using NaOAc as the base in *N,N*-dimethylformamide/water mixtures (2/1, v/v): under these conditions, up to six couplings of iodobenzene with styrene (and 10 for acrylamide) were carried out with the same catalyst batch with only a moderate decrease of the reaction yields. The reaction of bromobenzene under slightly harsher conditions gave an 80% yield of *trans*-stilbene, but the catalyst was completely deactivated (Table 5, nos. 5 and 6). No reaction was detected with chlorobenzene.

Zhuangyu and co-workers applied these catalysts to the synthesis of arylacetaldehydes according a pathway alternative to Hallberg's one (Scheme 6) [32].

Quite recently, Ding and Gin reported on the preparation of a heterogeneous catalyst supported onto a



Scheme 5.

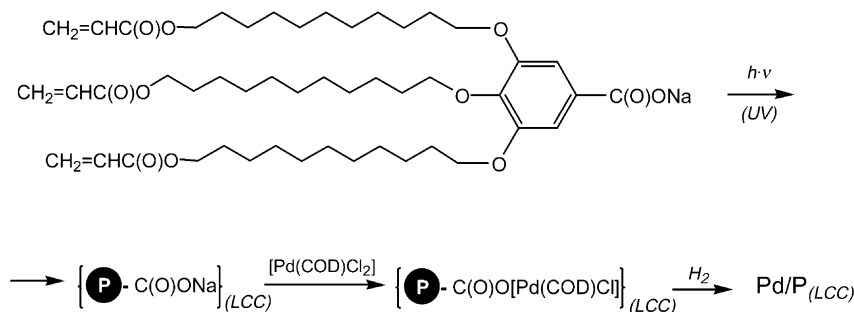


Scheme 6.

rather exotic polymeric material, which can be considered as a fully organic analogue of monodimensional molecular sieves [66]. In fact, due to the nature of the monomer employed (Scheme 7) and to the polymerization conditions, the support retained the same organized microstructure of the starting liquid crystalline

phase, featured by an array of parallel, essentially monodispersed, cylindrical pores. After exchanging the sodium ions of the hydrophilic heads in the monomeric units with [Pd(COD)Cl]⁺, nearly spherical palladium particles, with diameters ranging from 4 to 7 nm (TEM), were obtained upon treatment with H₂. However, the metal crystallites were larger than the original pores of the matrix, which suggested the collapse of the ordered microstructure of the support.

This catalyst is quite efficient in the HR of activated 4-substituted bromobenzenes, such as the nitro- and acetyl derivative, with either styrene or *n*-butylacrylate. Recycling experiments showed that the apparent loss of activity depended on the nature of the halide: it was negligible, if any, with 4-bromoacetophenone (Table 5, nos. 8 and 9), but it was quite appreciable for 4-nitrobromobenzene (Table 5, nos. 10 and 11). The performance with less



Scheme 7.

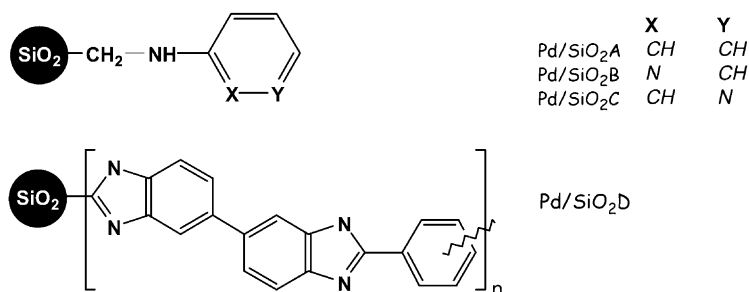
Table 5
Selected Heck reactions over palladium supported by insoluble organic polymers

Sl. no.	Catalyst, %Pd (w/w)	ArX	Alkene	Base	ArX/alkene/base/Pd (mol/mol/mol/mol)	Solvent	T (°C)	Time (h)	Yield (%)	Reference
1	P-C ₆ H ₄ -phen/Pd, 5.08%	Iodobenzene	Styrene	NBt ₃	1/1.1/1.1/3.2 × 10 ⁻³	None	100	4	90	[30]
2 ^a	P-C ₆ H ₄ -phen/Pd, 5.08%	Iodobenzene	Styrene	NBt ₃	1/1.1/1.1/3.2 × 10 ⁻³	None	100	4	53	[30]
3	P-C ₆ H ₄ -phen/Pd, 5.08%	Iodobenzene	Styrene	NaOAc	1/1.1/1.1/3.2 × 10 ⁻³	DMF/H ₂ O	130	4	89	[31]
4 ^b	P-C ₆ H ₄ -phen/Pd, 5.08%	Iodobenzene	Styrene	NaOAc	1/1.1/1.1/3.2 × 10 ⁻³	DMF/H ₂ O	130	4	72	[31]
5	P-C ₆ H ₄ -phen/Pd, 5.08%	Bromobenzene	Styrene	NaOAc	1/1.1/1.1/3.2 × 10 ⁻³	DMF/H ₂ O	130	5	80	[30]
6 ^c	P-C ₆ H ₄ -phen/Pd, 5.08%	Bromobenzene	Styrene	NaOAc	1/1.1/1.1/3.2 × 10 ⁻³	DMF/H ₂ O	130	5	Trace	[30]
7	P-C ₆ H ₄ -phen/Pd, 5.08%	Chlorobenzene	Styrene	NaOAc	1/1.1/1.1/3.2 × 10 ⁻³	DMF/H ₂ O	130	5	Trace	[30]
8	P _{LCC} /Pd, 8.3%	4-Nitrobromobenzene	Styrene	NEt ₃	1/1.3/1.4/8.6 × 10 ⁻⁴	DMF	80	2	100	[66]
9 ^c	P _{LCC} /Pd, 8.3%	4-Nitrobromobenzene	Styrene	NEt ₃	1/1.3/1.4/8.6 × 10 ⁻⁴	DMF	80	20	91	[66]
10	P _{LCC} /Pd, 8.3%	4-Bromoacetophenone	Styrene	NEt ₃	1/1.3/1.4/8.6 × 10 ⁻⁴	DMF	80	2	96	[66]
11 ^c	P _{LCC} /Pd, 8.3%	4-Bromoacetophenone	Styrene	NEt ₃	1/1.3/1.4/8.6 × 10 ⁻⁴	DMF	80	2	96	[66]
12	P _{LCC} /Pd, 8.3%	Bromobenzene	Styrene	NEt ₃	1/1.3/1.4/8.6 × 10 ⁻⁴	DMF	80	8	54	[66]
13	P _{LCC} /Pd, 8.3%	4-Bromoanisole	Styrene	NEt ₃	1/1.3/1.4/8.6 × 10 ⁻⁴	DMF	80	2	17	[66]
14	P _{LCC} /Pd, 8.3%	Chlorobenzene	Styrene	NEt ₃	1/1.3/1.4/8.6 × 10 ⁻⁴	DMF	80	24	<5	[66]

^a Second recycle of the batch from entry 1.

^b Fifth recycle of the batch from entry 3.

^c Recycle of the batch from the previous entry.



Scheme 8.

reactive aryl bromides and with chlorobenzene was much less satisfactory (Table 5, nos. 12–14).

3.5. Miscellaneous supports

Following the same procedure employed for the preparation of their polymer supported catalysts, Zhuangyu and co-workers reported also a number of palladium catalysts supported onto ligand-modified silica [33] (Scheme 8).

The comparison of catalysts Pd/SiO₂A–D in the coupling of iodobenzene with styrene (or acrylamide) showed that Pd/SiO₂D was the least efficient. Recycling experiments in the same reaction demonstrated that Pd/SiO₂C had the longest lifetime, with up to eleven consecutive runs with practically no decrease of the final yield in *E*-stilbene. The comparison of this catalyst with [Pd(OAc)₂] showed that the performances of the homogeneous and heterogeneous systems are close to each other. However, also these catalysts gave poor results with bromides: in fact no reaction was observed in the coupling of styrene with bromobenzene. This is even worse than with *P*-C₆H₄-phen/Pd, which at least allowed an 80% yield in the first catalytic run (Table 5, no. 5).

Palladium catalysts on BaSO₄ and CaCO₃ were also reported to be active in a few HETHR involving aryldiazonium salts [56,67]. In particular it was shown that Pd/CaCO₃ in the presence of additional CaCO₃ as the base was a convenient catalyst for Heck couplings of both electron-poor and electron-rich aryldiazonium with acrylic derivatives under mild, aerobic conditions. In contrast with Beller's findings [56], no transesterification of acrylic esters was reported in alcoholic solvents. However, it also

appeared that simple catalysis by [Pd(OAc)₂] in the presence of CaCO₃ was more efficient.

HETHR was considered by Strauss and co-workers for the preliminary screening of a palladium catalyst supported onto porous glass [43]. This catalyst was active in the coupling of iodobenzene or activated arylbromides with both alkenes and alkynes, also under microwave irradiation. However, the reported data were clearly not optimized and the intention of the authors was apparently only to check for activity.

Finally, a Pd²⁺/Cu²⁺ exchanged clay (montmorillonite K10) was tested as a heterogeneous Heck catalyst [42]. It was shown that the bimetallic catalyst was more efficient than the palladium and copper monometallic catalysts (also the latter was found to be active) in the coupling of methyl acrylate with iodobenzene and iodoanisole. It was also reported, but no data were given, that the catalyst could be reused three times with no loss of activity. Good yields could be obtained also with styrene, but they were only moderate to low with bromobenzene.

4. Palladium metal colloids

In the last 5 years, a significant number of reports on the use of palladium metal colloids as catalysts in Heck and related chemistry have appeared in the literature and the most recent investigation started to be focused to the correlations between the structure of such colloidal catalyst and their catalytic performance.

Beller et al. were the first to try Heck reactions with preformed palladium colloids as catalysts [46]. They used colloids prepared by Bönemann's method, i.e. via chemical reduction in the presence

of tetra-alkylammonium ions as stabilizers. Such colloids (1–6 nm sized according to the original work of Bönemann) turned out to be very active catalysts for the HR of activated aryl bromides with a number of olefins, at temperatures not lower than 130°C. However, the reaction failed to give appreciable yields with deactivated aryl bromides and chlorides. Furthermore, the palladium colloids were found to be unstable under the reaction conditions and had to be added slowly to the reaction mixture in order to hamper metal aggregation, leading eventually to the precipitation of inactive palladium black.

In the same year Reetz et al. reported twice on the application of colloidal palladium for the catalysis of C–C coupling reactions [47,48]. In one case, they used solutions of colloidal Pd in propylene carbonate. Such solutions can be prepared electrochemically as well as by thermal decomposition of simple palladium salts. Both methods yielded 8–10 nm colloids, which were stable for days even at 140–155°C in solution. However, they could not be isolated as they did not redissolve after precipitation. Their solutions, which had to be used as such, were active in the HR, giving appreciable yields even with aryl chlorides, although the selectivity to the Heck products was low. In addition, relatively harsh conditions involving high temperatures, long reaction times and high catalyst loadings (3.5 mol%) had to be applied. In another paper, Reetz et al. briefly described the use of a different kind of palladium colloids as catalysts for the Suzuki reaction. They utilized palladium as well as palladium/nickel colloids (2–3 nm in size) stabilized by tetra-alkylammonium ions, prepared by electrochemical reduction, as well as poly-*N*-vinyl-2-pyrrolidone (PVP)-stabilized colloids prepared by the method of Bradley (no indication was given on the size of this kind of colloids). Such colloids catalyzed the Suzuki reaction of phenylboronic acid with several aryl bromides or even chlorides at 100–120°C. Also in this case, large amounts of catalyst were needed (2–5 mol%) and the selectivity for the coupling products was often low. No mention was made of the stability of these colloidal catalyst systems. The same colloids were claimed to be efficient catalysts also for the HR, although only a single reaction example using iodobenzene was presented.

Analogous PVP-stabilized palladium colloids were recently reinvestigated by Li et al. as catalysts for

the Suzuki reaction of phenyl or 2-thiophenylboronic acids with different iodoarenes in ethanol/water at reflux [68]. The reactions could be generally accomplished with good yields after 12 h utilizing 0.3 mol% of catalyst. However, also in this case catalyst deactivation by agglomeration and precipitation of Pd black was observed. A simple linear correlation between the initial reaction rate and the concentration of Pd colloids in solution was established. The authors took this as an indication that the reaction occurs at the surface of the Pd nanoparticles.

In 1997, Antonietti et al. presented a systematic study on the use of palladium colloids stabilized by block copolymer micelles [49]. Such polymeric stabilizers are made out of diblock polymers with a hydrophobic block (polystyrene) as well as a hydrophilic one (poly-4-vinylpyridine). In suitable solvents (e.g. toluene), such polymers organize themselves in micelles with a hydrophilic core made out of the polyvinylpyridine segments and a hydrophobic shell built by the polystyrene segments. The hydrophilic core can be conveniently loaded with metal ions which give the metal colloids upon chemical reduction. Solution of micelle-stabilized palladium colloids in toluene obtained in this way were tested in Heck reactions at 140°C using tris(*n*-butyl)amine as the base. The metal colloids turned out to be remarkably stable under the reaction conditions: no formation of palladium black was observed. The reaction worked well with activated aryl bromides, but unsatisfactory results were obtained with deactivated aryl bromides and chlorides. In this respect, these colloids are comparable to those described by Beller et al., although the reaction rates were remarkably lower with respect to the latter. The remarkable effect of the micelle size and of the nature of the alkene on the apparent reaction rate suggested that it could be limited by mass transport phenomena. Palladium colloids of different sizes were also tested and a strong inverse correlation between the metal particle size and the catalytic activity was observed. The catalysts were claimed to be reusable without any loss of activity, but no details were given about the recycling procedure.

In another elegant study, Le Bars et al. have addressed the problem of the correlation of the colloid size with catalytic activity in greater detail [69]. They prepared a number of PVP-stabilized palladium colloids by controlled hydrogenation of a solution of

[Pd(dba)₂] in the presence of the polymer. The authors were able to prepare in this way metal colloids in the range 1.5–4 nm with narrow size distribution, highly active in the HR of 4-bromobenzaldehyde with *n*-butylacrylate at 140°C. The catalytic activity turned out to be significantly superior to simple homogeneous [Pd(dba)₂]. Remarkably, the initial reaction rate increased with decreasing particle size, but no simple direct correlation with the metal surface area was observed. On the contrary, a linear correlation was established with the number of defect sites on the surface of the colloids, from which it was concluded that they represented the active sites.

Yet another way of obtaining palladium colloids, active for the HR, was recently presented by Biffis [50]. It is based on the use of microgels (soluble cross-linked macromolecules), functionalized with a limited amount of sulfonic groups as stabilizers. After loading with palladium ions and subsequent chemical reduction, microgel-stabilized metal colloids (10–20 nm size) were obtained and isolated. At variance with Reetz's colloids, these materials could also be redispersed in suitable liquid media. They proved active catalysts for the HR of aryl iodides and activated aryl bromides at 140°C, but, as most other colloidal catalysts, they were ineffective with deactivated aryl bromides and chlorides. Although the colloids were stable under the reaction conditions employed, the apparent reaction rates were rather low, which is probably due to the relatively large size of the metal particles.

5. Metal leaching and the nature of catalysis

The problem of metal leaching from supported catalysts working under liquid–solid conditions is well known. It is, for instance, the major cause of deactivation of the Pd/C catalysts employed for the industrial hydrogenation of nitro compounds [71,72]. In this case, it is also well established that catalysis is truly heterogeneous, but this is not necessarily the case for every kind of palladium catalyzed reaction. Sheldon recently addressed the problem of the nature of catalysis in the presence of heterogeneous catalysts under liquid–solid conditions [73]. He illustrated “case histories” where such catalysts were just reservoirs of soluble, *active* species, generated under

reaction conditions by the chemical interaction of the catalyst with one or more of the components of the liquid phase. In this sense, he defined these catalysts as “Trojan horses”. Several researchers, including ourselves, have come to the conclusion that the supported palladium catalysts employed for HETHR belong to this class as well.

In this connection, there are at least three questions that must be answered: is there any palladium leaching in HETHR? If so, are the released species catalytically active? In this case, which is the minimum level of palladium leaching for appreciable catalytic activity in solution? All these aspects are extremely important for both the fundamental understanding of this reaction and its technological applications. A detailed knowledge of the nature of the active catalyst is essential for process optimization as well as for establishing intellectual property rights. Furthermore, a reliable estimation of the level of metal leaching is of the utmost importance in order to determine the economics of the process.

It is not trivial to give unambiguous answers to the questions listed above. In recent years simple catalytic systems based on homogeneous palladium complexes were reported to achieve TONs exceeding 10⁶ catalytic cycles per palladium atom in HR [6,7]. It is easy to calculate that in this case extremely low levels of metal leaching, probably hard to detect, would be compatible with appreciable activity in solution.² However, it must be pointed out that the homogeneous catalytic reactions with ppm or sub-ppm levels of palladium are usually slow or do not come to completion. In spite of this, when palladium metal is introduced in the reaction mixture — either as a supported catalyst or as a stabilized colloid — in the common 0.1–1% molar amount with respect to the limiting reagent, a “normal” reaction rate is observed quite frequently.

² Let us assume that an aryl halide (10 mmol) and an alkene (25 mmol) are coupled over a 1% (w/w) supported palladium catalyst (106 mg, 10⁻² mmol Pd), in 50 ml of solvent. The apparent TON calculated with respect to the total amount of palladium would equal 500 mol mol⁻¹ for a 50% final yield. However, if the reaction is actually homogeneously catalyzed by a highly active soluble species (let us assume a “true” TON of 5 × 10⁵ mol mol⁻¹, which can be obtained even using [Pd(OAc)₂] as the catalyst without any promoter [5]), only 10⁻⁵ mmol of palladium would be required in solution. This corresponds to roughly 20 ppb of the metal in solution and to the lowering of the palladium load in the recovered “heterogeneous” catalyst to 0.999% from the initial 1%.

This finding is compatible with the hypothesis of extensive metal leaching and homogeneous catalysis by soluble palladium species, but it does not imply that an appreciable concentration of palladium is to be found in solution at the end of the reaction, because the support can sometimes re-capture most of the dissolved metal, as it will be shown below.

In many reported investigations, the onset of HR is indeed accompanied by significant metal leaching from the heterogeneous catalyst. In spite of this, there are also claims of true heterogeneous catalysis, mostly based on apparent activity upon recycling and/or on support effects. This argument has already been criticized by Sheldon et al. [73]. In the specific case of HETHR, recycling may well be possible if enough metal remains on the support or if the support is able to re-capture leached metal species at the end of the reaction. Therefore, the observation that a catalyst maintains its activity upon recycling is not an unambiguous evidence of true heterogeneous catalysis, since the catalyst may continue to leach and re-capture appreciable levels of palladium through consecutive catalytic runs. On the other hand, the reported support effects appear to be fully compatible with a reaction mechanism based on the leaching of catalytically active species. In fact, in this case the catalytic activity should depend on the amount of leached palladium and both the extent and the rate of leaching are likely affected by the support nature. Furthermore, the leached palladium species could interact with the functional groups of the support surface, with possible effects on their electronic and steric features and therefore on their catalytic activity.

Mizoroki, as early as in 1973, was the first to collect some evidence that when palladium black was the starting catalytic material the reaction was actually promoted by soluble palladium species (see Section 2) [19,20]. However, it was only in 1992 that Augustine and O'Leary systematically addressed the problem of the real nature of catalysis in the presence of supported palladium catalysts. They stopped some of the catalytic experiments (with fresh catalysts) at relatively low conversion (around 20%) and after filtering away the Pd/C catalyst they heated again the filtrate and kept it at the reaction temperature for further 2 h. No change was observed in the filtrate composition. Accordingly, they concluded that their catalysts were truly heterogeneous. Unfortunately,

from their description it appears that whereas the reactions were carried out at 100°C, the catalyst was separated at room temperature. As Sheldon et al. pointed out [73], the quenching and re-heating procedure could bring about the deactivation of possibly active soluble species: therefore the findings reported by Augustine and O'Leary are not conclusive. This consideration is reinforced by the observations of Shmidt and Mametova [53], who studied the kinetics of the coupling of iodobenzene and styrene in DMF at 80°C, in the presence of NBu_3 over a 5% Pd/C catalyst. They found that the kinetic plot was not affected by the removal of the catalyst from the reaction mixture just after the attainment of the maximum apparent reaction rate. They also observed that substantial amounts of palladium were dissolved in the presence of the components of the reaction mixture under reaction-like conditions and suggested that this was due to the oxidative action of iodobenzene. In summary, Shmidt and Mametova came to conclusions just opposite to Augustine's. However, it should be pointed out that whereas Shmidt and Mametova employed an aryl iodide, Augustine and O'Leary used aroyl chlorides.

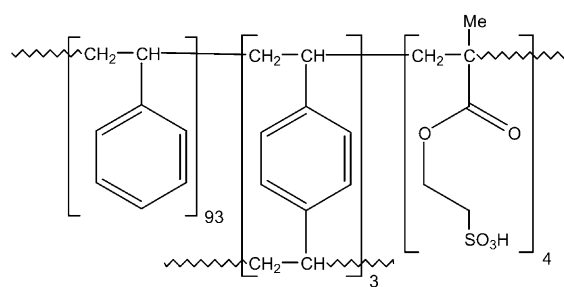
Like Shmidt and Mametova, Djakovitch and Köhler and their co-workers observed residual activity in the filtrate from the reactions over Pd/MgO and over Pd/HY. In the first case they reported that this residual activity was too little in comparison to that observed in the presence of the solid catalyst. In the second case, the residual activity was relatively high and it increased with increasing acidity of the supporting zeolite Y [39]. Djakovitch and Köhler also found that catalysts supported by H-mordenite did not release active species into solution. As mordenite has smaller pores than zeolite Y, they suggested that palladium soluble species were able to escape only from the latter support, but not from the former. Nevertheless, the catalytic performance was very similar for both the mordenite and zeolite Y-based catalysts, which suggests that the nature of catalysis is likely the same for both kind of catalysts, i.e. homogeneous. In the case of mordenite-based catalysts this would imply that the catalytic reaction takes place in the intracrystalline pores of the zeolite, where soluble palladium species are retained.

Arai and co-workers investigated thoroughly the leaching process and obtained very interesting results [36–38]. In the first place they observed that some

palladium catalysts, including a 10% Pd/C and a 1% Pd/SiO₂, underwent extensive leaching during the HR of iodobenzene and methylacrylate at 75°C, in the presence of NEt₃ in *N*-methylpyrrolidinone. They also found that the maximum apparent reaction rate was attained at maximum palladium concentration in solution, which was monitored during the reaction course. Finally, it was apparent that palladium re-precipitated onto the support at high conversion of iodobenzene. The extent of re-precipitation depended on several factors, including the nature of the base employed, the reaction temperature, the nature of the support. The highest recovery of supported palladium was achieved when Na₂CO₃ and NEt₃ were employed together (2.5/1, mol/mol). Palladium leaching at the end of the reaction (140°C) amounted to 4% for Pd/C (either Na₂CO₃ or NEt₃) and to 51% (NEt₃) or 76% (Na₂CO₃) for Pd/SiO₂, but it was limited to 2% (Pd/C) and 9% (Pd/SiO₂) with the mixed bases. Relatively high temperatures appeared to enhance and accelerate the re-precipitation of palladium. Thus, at 160°C the re-precipitation was practically quantitative just at the reaction end (30 min) in the case of Pd/C. At 110 and 90°C the reaction again ended in 30 min, but complete re-precipitation took 1 h at 110°C and was not achieved at 90°C even after 2 h. Carbon showed the highest affinity to palladium and turned out to be the most effective support for palladium re-precipitation. This was confirmed also in cross-transfer experiments [37]. When the coupling was carried out at 160°C with the Pd/C catalyst in the presence of bare SiO₂, 99 and 1% of palladium was found on the two solids, respectively, at the end of the reaction. On the contrary, when Pd/SiO₂ was employed as the catalyst in the presence of bare carbon, only 33% of palladium was left onto the original catalyst and the remainder was found on carbon. This is a rather impressive demonstration that palladium must undergo dissolution, as it can be transferred only through the liquid phase, and that palladium prefers by far to re-precipitate over carbon than over silica. The addition of water as co-solvent was found to favor the formation of large colloidal palladium particles, a few hundreds of nanometers in size [38]. These relatively large metal aggregates, which did not re-precipitate over the support, could be recovered, but they proved catalytically inactive in recycling experiments. In general, the dissolution/re-precipitation

process could account for the restructuring of the supported metallic phase (variations in the metal particle size, in the degree of metal crystallinity, etc.), which was observed in several instances. Arai et al. pointed out that re-precipitation can occur only towards the reaction end, i.e. when the aryl halide concentration in solution is considerably decreased. In other words, he observed that the halide is necessary to keep palladium in solution. In spite of this, he proposed that the metal is leached out in the form of some zerovalent palladium species, in contrast with the suggestion of Schmidt and Mametova that dissolution is brought about by oxidative attack of the halide over palladium particles. In this connection, we have collected quite recently sound evidence that the metal is released as Pd(II) [54]. We have investigated a commercial 1% Pd/Al₂O₃ catalyst and a tailor made 1% catalyst (Pd/PS) supported onto a basically polystyrene divinylbenzene resins (Scheme 9).

Both catalysts were active in the HR of 4-bromoacetophenone with *n*-butylacrylate (Table 6), during which they underwent extensive leaching. In spite of the very low activity exhibited by both catalysts towards 4-chloroacetophenone, sensible metal leaching occurred also with this halide. In particular, for Pd/PS it was comparable to that observed with the bromide. The treatment of both catalysts with the reaction solvents, with solutions of the individual components (base, alkene, halide) or of mixtures thereof (Table 7) under reaction-like conditions showed that metal leaching did not occur in the absence of the halide. Furthermore, the presence of acetate ions was necessary to obtain metal dissolution with 4-chloroacetophenone. Pd/Al₂O₃ was apparently more resistant to leaching than Pd/PS. This could be



Scheme 9.

Table 6

Heck coupling of 4-haloacetophenones with butylacrylate over commercial Pd/Al₂O₃ and Pd/PS after Biffis et al. [54]^a

Sl. no.	Catalyst, %Pd (w/w)	ArX	Alkene	Base	ArX/alkene/base/Pd (mol/mol/mol/mol)	Solvent	T (°C)	Time (h)	Yield (%)	Pd leached (%)
1	Pd/Al ₂ O ₃ , 1%	4-Bromoacetophenone	Butylacrylate	NaOAc	1/1.7/1/1 × 10 ⁻³	DMA	120	3	97	79
2	Pd/Al ₂ O ₃ , 1%	4-Chloroacetophenone	Butylacrylate	NaOAc	1/1.7/1/1 × 10 ⁻³	DMA	120	3	5	22
3	Pd/PS, 1%	4-Bromoacetophenone	Butylacrylate	NaOAc	1/1.7/1/1 × 10 ⁻³	DMA	120	3	82	100
4	Pd/PS, 1%	4-Chloroacetophenone	Butylacrylate	NaOAc	1/1.7/1/1 × 10 ⁻³	DMA	120	3	6	92

^a Inert atmosphere (N₂), 25 ml DMA, 10 mmol ArX; the selectivity towards Heck products was always 100%.

attributed to a higher affinity of palladium metal for the inorganic support, due to stronger interactions with its surface, or to the superior ability of alumina to re-capture palladium from the solution. These tests were carried out with a ArX/Pd molar ratio equal to 10³ and therefore the halide was always present in large excess. According to Arai's results these conditions are unfavorable for metal re-precipitation and so the first explanation seems more appropriate. These results are in agreement with Shmidt and Mametova's hypothesis of the oxidative attack of the halide to the

metal crystallites, yielding directly Pd(II) in solution. Good coordinating agents for Pd(II), such as acetate ions, further stabilize these soluble species and favor dissolution. We have also demonstrated that these soluble species are catalytically active. After separation of the solid at the end of the treatment by filtration *at high temperature and under inert atmosphere* we added the missing components of the reaction mixture to the filtrate and carried out homogeneous catalytic runs without any promoter. Not only high yields of coupling products (Table 8) were obtained, but we

Table 7

Metal leaching from commercial Pd/Al₂O₃ and Pd/PS after Biffis et al. [54]^a

Sl. no.	Leaching agent(s)	Pd/PS	Pd/Al ₂ O ₃
1	DMA	0	0
2	DMA + NaOAc	0	0
3	DMA + NaOAc + butylacrylate	0	0
4	DMA + 4-bromoacetophenone	85	–
5	DMA + 4-bromoacetophenone + NaOAc	88	11
6	DMA + 4-chloroacetophenone	0	0
7	DMA + 4-chloroacetophenone + NaOAc	92	10
8	DMA + chlorobenzene	0	–
9	DMA + chlorobenzene + NaOAc	0	–

^a Inert atmosphere (N₂), 25 ml DMA, 10 mmol ArX, 18 h; other conditions as in Table 6.

Table 8

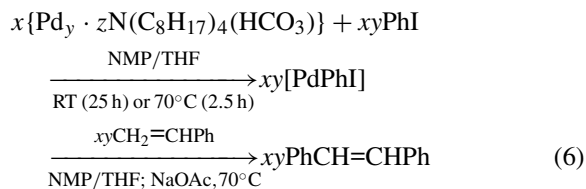
Catalytic activity of leached palladium species in the Heck coupling of 4-bromoacetophenone with butylacrylate after Biffis et al. [54]^a

Sl. no.	Pd source	Pd in solution (mmol)	Coupled aryl halide	Yield (%)
1	[Pd(OAc) ₂]	0.050	4-Bromoacetophenone	80
2	Pd/PS (from Table 7, no. 4)	0.088	4-Bromoacetophenone ^b	100
3	Pd/PS (from Table 7, no. 5)	0.085	4-Bromoacetophenone ^b	100
4	Pd/Al ₂ O ₃ (from Table 7, no. 4)	0.011	4-Bromoacetophenone ^b	83
5	Pd/Al ₂ O ₃ (from Table 7, no. 7)	0.020	4-Chloroacetophenone ^b	8
6	Pd/PS (from Table 7, no. 7)	0.092	4-Chloroacetophenone ^b + 4-bromoacetophenone ^c	95 ^d

^a Reaction conditions as in Table 6.^b Residue from leaching test.^c Added to the filtrate.^d Referred to the bromide.

also showed that the homogeneous catalyst was still appreciably active in a second homogeneous run. Interestingly, yields were invariably low in the case of 4-chloroacetophenone. This finding is in contrast with the high reactivity towards the chloride displayed by the metal in Pd/PS and provides additional support to the conclusion that the supported metal is not the real catalyst.

As mentioned above, metal colloids cannot undergo leaching as it is usually figured out for supported heterogeneous catalysts. However, the disaggregation (possibly oxidative) of the dissolved metal colloidal particles to mono- or oligonuclear metal species resembles the chemical process that causes leaching from supported metal catalysts. For instance, Reetz and Westermann observed that palladium colloids stabilized by tetraoctylammonium hydrogenocarbonate react with stoichiometric amounts of PhI in NMM/THF (1/1, v/v), to give quantitatively Pd(II) species [70], at both room temperature (25 h) and 70°C (2.5 h). The oxidation of Pd(0) to Pd(II), suggested by the color change of the solution from black to dark red, was confirmed by UV–VIS and NMR spectroscopy. Reetz and Westermann also showed that these soluble Pd(II) species react with styrene, in the presence of NaOAc, to afford stilbene quantitatively (Eq. (6)).

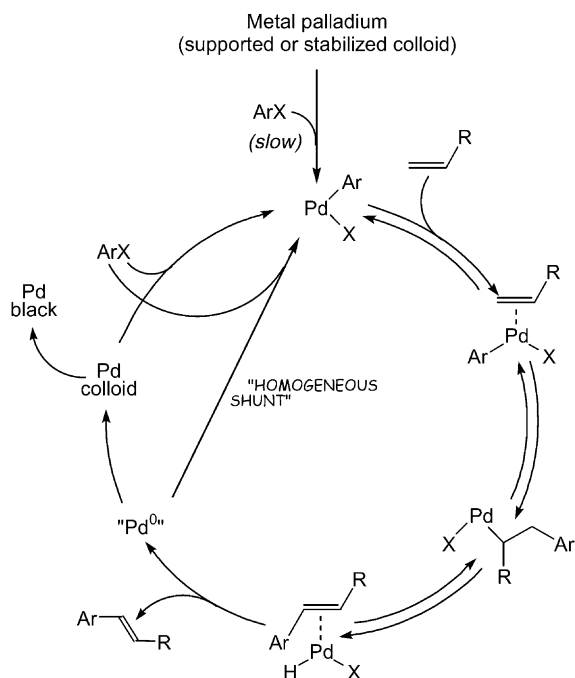


They argued that these results and the coincidence of the reaction onset with the appearance of colloidal palladium, sometimes reported in ligandless homogeneous Heck couplings, were a proof of the crucial role of colloidal palladium and concluded that, at least in those cases, “catalysis is likely to occur at defect sites, steps and kinks on the surface of the colloidal metal particles”. In our opinion this statement can be misleading, because it suggests that all or most of palladium was present as active colloidal particles during the catalytic reactions. As it was shown by Reetz and Westermann, palladium colloids are destroyed by *stoichiometric* amounts of the aryl halide. This implies that the survival or the accumulation of

colloidal metal is possible only if the attack of the aryl halide to the metal surface is relatively slow. This is certainly true at high conversion of the halide and is probably the reason for both the precipitation of palladium metal in not stabilized homogeneous systems and for the re-precipitation of palladium onto supports in heterogeneous systems, which are observed close to the reaction end. However, at low conversion the aryl halide is present in large excess in comparison to the total amount of palladium. Therefore, the survival of colloidal palladium under these conditions requires that its reaction with the halide is intrinsically slow, which is apparently not in agreement with the hypothesis that the activation of the halide on the metal surface is a step of the catalytic transformation.

In this connection, also Bradley came to the conclusion that Heck catalysis in the presence of his PVP-stabilized palladium colloids occurred at defective sites on the metal surface, since the initial reaction rates were directly proportional to their number on the particle surface, rather than to the total metal surface area or to the total amount of palladium introduced. However, these findings can be traced to the intermediacy of soluble palladium species too. In fact, the palladium atoms located at the defective sites are certainly the most reactive and it is likely that they are quickly brought in solution. This process would give soluble palladium species, in concentration proportional to the initial number of the defective sites, and palladium colloidal particles with a smoothed surface. This could explain the observed correlation if it is also assumed that the dissolved palladium species are catalytically active and the remainder of colloidal palladium is relatively little active or not active at all.

As a matter of fact, all these results can be reconciled with the hypothesis that palladium metal (either supported or in the form of stabilized colloids) is actually the precursor of a catalytic system involving dissolved species. After being formed in solution upon oxidative attack by the aryl halide to the metal particles, aryl-Pd(II) soluble species undergo insertion of the alkene into a Pd–Ar bond, thus giving the start to the catalytic cycle. Of course this does not rule out the possibility that colloidal palladium is formed from dissolved species, for instance after the reductive elimination of the coupling products and it cannot be ruled out a priori that it is involved into the catalytic



transformation, even though the results of Reetz and Westermann are not in agreement with this hypothesis.

A possible mechanistic pattern for Heck catalysis with metal palladium catalysts is illustrated in Scheme 10. The steps from $[PdArX]$ to $"Pd(0)"$ are just the same of the classical mechanism for HOMHR. Palladium colloids can be formed from $"Pd(0)"$, if this process is not too slow in comparison with the "homogeneous shunt", i.e. the direct oxidative addition of the aryl halide to the soluble zerovalent palladium complexes. If they are formed, they can either propagate the catalytic cycle or be transformed into inactive palladium black, thus contributing to the deactivation of the catalytic system, depending on the relative rates of the two processes.

6. Conclusions and perspectives

It is our opinion that the literature data presented in this review provide convincing evidence that in Heck reactions carried out with palladium metal catalysts, either supported or colloidal, the catalytic cycle is

sustained mainly by soluble species leached out from the starting solid material. Therefore, great care must be generally taken in evaluating the performance of "heterogeneous" Heck catalysts. On the other hand, the presence of homogeneous catalysis by leached palladium species does not necessarily imply that heterogeneous palladium metal catalysts are of no practical use for HR. Indeed, *controlled* metal leaching may represent an effective tool for the minimization of metal losses. The major advantages of supported palladium metal are the simplification of the work-up procedure and the possibility of facile recovery of the precious metal. In homogeneous HR this is usually not permitted by the work-up procedures and the precious metal is completely lost, but with supported palladium metal only leached palladium is lost at the end of the reaction and the remainder is easily removed. As it has been shown above, in some cases it is even possible to choose the support so that it can re-capture most of the leached palladium species. Another positive feature of these catalysts is that promoters like phosphines are generally not needed (in fact, they were reported to inhibit the catalytic reaction more often than not). This circumstance is particularly favorable, because side reactions involving phosphines usually prevent to carry out HR at relatively high temperatures. On the contrary, the high thermal stability of palladium metal catalysts makes it possible to use higher temperatures in HR, thus speeding up the reaction and allowing for the activation of unreactive aryl bromides and in some cases even of chlorides (see Section 3). Therefore, if the extent of metal leaching is limited the use of supported palladium metal can be economically viable, as it is demonstrated by the industrial synthesis of octyl-methoxycinnamate [45].

In principle, recycling of the heterogeneous catalyst is also possible, as it has been demonstrated in a number of cases. However, efficient catalyst recycling is of course conditioned by the preservation of catalytic activity in the recovered material. Extensive metal leaching, metal phase restructuring (e.g. sintering), structural damage of the support, fouling by carbonaceous deposits were reported as possible causes of activity losses. In connection to catalyst fouling, this can also ensue from precipitation of salts, formed as by-products of the HR, if they are too little soluble in the reaction solvent. In this case deactivation is reversible, but thorough washing of

the catalyst is required for activity restoration and this could make recycling not practical from the viewpoint of both technical and laboratory applications. Moreover, in most cases knowledge on the exact nature of the re-precipitated palladium species as well as of the kind and degree of metal phase restructuring is lacking, and this prevents the meaningful comparison of the catalytic activity in the first and in the following catalytic cycles.

In conclusion, metal leaching, whatever be its mechanism, must be considered a necessary activation process in most HETHR, if not all. As highlighted above, no or very low apparent leaching at the end of the reaction does not imply that the metal remains on the support during the reaction. In fact, the ability of the supports to scavenge the metal at high aryl halide conversion must be taken into account. The observation that in the dissolution/re-precipitation process the palladium affinity is different from support to support is particularly interesting. In fact, the support tailoring could allow to control this process, i.e. the metal recovery from the solution. The different behavior observed by Köhler and co-workers for zeolite supported catalysts indicates that this should be possible to some extent. The support design could involve not only the physico-chemical properties of the material, like pore size in molecular sieves, but also its chemical features, like the kind and degree of functionalization. In this connection, a large array of functional groups able to coordinate and capture the leached palladium species can be relatively easily introduced into polymeric materials or onto modified silicas. The catalysts behaving in this way can be considered “hybrid” (not to be confused with homogeneous catalysts chemically bound to solid supports, which are generally referred to as hybrid [74]). We believe that these materials have potential for the development of useful “heterogeneous” Heck catalysts.

References

- [1] R.F. Heck, *Acc. Chem. Res.* 12 (1979) 146–151.
- [2] T. Mizoroki, K. Mori, A. Ozaki, *Bull. Chem. Soc. Jpn.* 44 (1971) 581.
- [3] H.A. Dieck, R.F. Heck, *J. Am. Chem. Soc.* 96 (1974) 1133–1136.
- [4] W.A. Herrmann, M. Ellison, J. Fisher, C. Köcher, G.R.J. Artus, *Angew. Chem. Int. Ed. Engl.* 34 (1995) 2371–2374.
- [5] W.A. Herrmann, C. Brossmer, C.P. Reisinger, T.-H. Riermeier, K. Öfele, M. Beller, *Chem. Eur. J.* 3 (1997) 1357–1364.
- [6] M. Ohff, A. Ohff, D. Milstein, *Chem. Commun.* (1999) 357–358.
- [7] F. Miyazaki, K. Yamaguchi, M. Shibasaki, *Tetrahedron Lett.* 40 (1999) 7379–7383.
- [8] A. de Meijere, F.E. Meyer, *Angew. Chem. Int. Ed. Engl.* 33 (1994) 2379–2411.
- [9] W. Cabri, I. Candiani, *Acc. Chem. Res.* 28 (1995) 2–7.
- [10] G.T. Crisp, *Chem. Soc. Rev.* 27 (1998) 427–436.
- [11] P. Beletskaya, A.V. Cheprakov, *Chem. Rev.* 100 (2000) 3009–3066.
- [12] P. Baumeister, W. Meyer, K. Örtle, G. Seifert, U. Siegrist, H. Steiner, *Chimia* 51 (1997) 144.
- [13] A.F. Littke, G.C. Fu, *J. Org. Chem.* 64 (1999) 10–11.
- [14] V.M. Wall, A. Eisenstadt, D.J. Ager, S.L. Laneman, *Plat. Met. Rev.* 43 (1999) 138–145.
- [15] G. Schmidt (Ed.), *Clusters and Colloids: From Theory to Application*, VCH, New York, 1994.
- [16] L.J. de Jongh (Ed.), *Physics and Chemistry of Metal Clusters Compounds*, Kluwer Academic Publishers, Dordrecht, 1994.
- [17] J.D. Aiken III, R.G. Finke, *J. Mol. Catal. A: Chem.* 145 (1999) 1–44.
- [18] H.-U. Blaser, A. Indolese, A. Schnyder, H. Steiner, M. Studer, *this issue*.
- [19] T. Mizoroki, K. Mori, A. Ozaki, *Bull. Chem. Soc. Jpn.* 44 (1971) 581.
- [20] K. Mori, T. Mizoroki, A. Ozaki, *Bull. Chem. Soc. Jpn.* 46 (1973) 1505–1508.
- [21] M. Julia, M. Duteil, *Bull. Soc. Chim. Fr.* (1973) 2790.
- [22] M. Julia, M. Duteil, C. Grad, E. Kuntz, *Bull. Soc. Chim. Fr.* (1973) 2791–2794.
- [23] D. Savoia, C. Trombini, A. Umami Ronchi, G. Verardo, *J. Chem. Soc., Chem. Commun.* (1981) 540–541.
- [24] D. Savoia, C. Trombini, A. Umami Ronchi, G. Verardo, *J. Chem. Soc., Chem. Commun.* (1981) 541–542.
- [25] A. Hallberg, L. Westfelt, *J. Chem. Soc., Perkin Trans. 1* (1984) 933–935.
- [26] C.-M. Andersson, A. Hallberg, *J. Org. Chem.* 53 (1988) 235–239.
- [27] M. Guisnet, J. Barrault, C. Bouchoule, D. Duprez, C. Montassier, G. Perot (Eds.), *Heterogeneous Catalysis and Fine Chemicals*, Elsevier, Amsterdam, 1988.
- [28] R.L. Augustine, S.T. O’Leary, *J. Mol. Catal.* 72 (1992) 229–242.
- [29] R.L. Augustine, S.T. O’Leary, *J. Mol. Catal. A: Chem.* 95 (1995) 277–285.
- [30] Z. Zhuangyu, H. Hongwen, K. Tsi-Yu, *React. Polym.* 9 (1988) 249–255.
- [31] Z. Zhuangyu, H. Hongwen, K. Tsi-Yu, *React. Polym.* 12 (1990) 229–235.
- [32] Z. Zhuangyu, P. Yi, H. Hongwen, K. Tsi-Yu, *Synthesis* (1991) 539–542.
- [33] P. Yi, Z. Zhuangyu, H. Hongwen, *J. Mol. Catal.* 62 (1990) 297–306.
- [34] C.P. Menhert, J.Y. Ying, *Chem. Commun.* (1997) 2215–2216.
- [35] C.P. Menhert, D.W. Weaver, J.Y. Ying, *J. Am. Chem. Soc.* 120 (1998) 12289–12296.

- [36] F. Zhao, B.M. Bhanage, M. Shirai, M. Arai, *Chem. Eur. J.* 6 (2000) 843–848.
- [37] F. Zhao, K. Murakami, M. Shirai, M. Arai, *J. Catal.* 194 (2000) 479–483.
- [38] F. Zhao, M. Shirai, M. Arai, *J. Mol. Catal. A: Chem.* 154 (2000) 39–44.
- [39] M. Wagner, K. Köhler, L. Djakovitch, S. Weinkauff, V. Hagen, M. Muhler, *Top. Catal.* 13 (2000) 319–326.
- [40] L. Djakovitch, K. Köhler, *J. Mol. Catal. A: Chem.* 142 (1999) 275–284.
- [41] K. Kaneda, M. Higuchi, T. Imanaka, *J. Mol. Catal.* 63 (1990) L33–L36.
- [42] R.K. Ramchandani, B.S. Uphade, M.P. Vinod, R.D. Wakharkar, V.R. Choudary, A. Sudalai, *Chem. Commun.* (1997) 2071–2072.
- [43] J. Li, A.W.-H. Mau, C.R. Strauss, *Chem. Commun.* (1997) 1275–1276.
- [44] J. Walter, J. Heiermann, G. Dyker, S. Hara, H. Shiiyama, *J. Catal.* 189 (2000) 449–455.
- [45] A. Eisenstadt, *Chem. Ind. (Dekker)* 75 (1998) 415–427.
- [46] M. Beller, H. Fischer, K. Kühlein, C.-P. Reisiger, W.A. Herrmann, *J. Organomet. Chem.* 520 (1996) 257–259.
- [47] M.T. Reetz, G. Lohmer, *Chem. Commun.* (1996) 1921–1922.
- [48] M.T. Reetz, R. Breinbauer, K. Wanninger, *Tetrahedron Lett.* 37 (1996) 4499–4502.
- [49] S. Klingelhöfer, W. Heitz, A. Greiner, S. Östereich, S. Förster, M. Antonietti, *J. Am. Chem. Soc.* 119 (1997) 10116–10120.
- [50] A. Biffis, *J. Mol. Catal. A: Chem.* 165 (2001) 303–307.
- [51] M. Antonietti, F. Gröhn, J. Hartmann, L. Bronstein, *Angew. Chem. Int. Ed.* 36 (1997) 2080–2083.
- [52] N.T. Whilton, B. Berton, L. Bronstein, H.-P. Hentze, M. Antonietti, *Adv. Mater.* 11 (1999) 1014–1018.
- [53] A.F. Schmidt, L.V. Mametova, *Kinet. Catal.* 37 (1996) 406–408.
- [54] A. Biffis, M. Zecca, M. Basato, *Eur. J. Inorg. Chem.* (2001) 1131–1133.
- [55] H.-U. Blaser, A. Spencer, *J. Organomet. Chem.* 233 (1982) 267.
- [56] M. Beller, K. Külhein, *Synlett* (1995) 441–442.
- [57] M. Jikei, Y. Ishida, Y. Seo, M.-A. Kakimoto, Y. Imai, *Macromolecules* 28 (1995) 7924–7928.
- [58] C. Dossi, A. Fusi, S. Recchia, M. Anghileri, R. Psaro, *Chem. Commun.* (1994) 1245.
- [59] G. Langhendries, D.E. van De Vos, G.V. Baron, P.A. Jacobs, *J. Catal.* 187 (1999) 153–163.
- [60] A. Wali, S.M. Pillai, V.S. Kaushik, S. Satish, *Appl. Catal. A: Gen.* 135 (1996) 83–93.
- [61] A. Wali, S.M. Pillai, S. Satish, *React. Kinet. Catal. Lett.* 60 (1997) 189–194.
- [62] C.N. Satterfield, *Heterogeneous Catalysis in Practice*, 2nd Edition, McGraw-Hill, New York, 1991, p. 139.
- [63] G.A. Somorjai, in: L.L. Hegedus (Ed.), *Catalyst Design, Progress and Perspectives*, Wiley, New York, 1987, p. 58.
- [64] A.T. Bell, in: L.L. Hegedus (Ed.), *Catalyst Design, Progress and Perspectives*, Wiley, New York, 1987, p. 118.
- [65] M. Nowtony, U. Hanefeld, H. von Konigsveld, T. Maschmeyer, *Chem. Commun.* (2000) 1877–1878.
- [66] J.H. Ding, D. L. Gin, *Chem. Mater.* 12 (2000) 22–24.
- [67] H. Brunner, N. Le Cousturier de Courcy, J.P. Genêt, *Tetrahedron Lett.* 40 (1999) 4815–4818.
- [68] Y. Li, M. Hong, D.M. Collard, M. El-Sayed, *Org. Lett.* 2 (2000) 2385–2388.
- [69] J. Le Bars, U. Specht, J.S. Bradley, D.G. Blackmond, *Langmuir* 15 (1999) 7621–7625.
- [70] M.T. Reetz, E. Westermann, *Angew. Chem. Int. Ed. Engl.* 39 (2000) 165–168.
- [71] P.N. Rylander, in: J.R. Anderson, M. Boudart (Eds.), *Catalysis — Science and Technology*, Vol. IV, Akademie Verlag, Berlin, 1983, p. 1.
- [72] A.J. Bird, D.T. Thomson, *Catalysis*, in: W.H. Jones (Ed.), *Organic Synthesis*, Academic Press, New York, 1980, p. 61.
- [73] R.A. Sheldon, M. Wallau, I.W.C.E. Arends, U. Schuchardt, *Acc. Chem. Res.* 31 (1998) 485–493.
- [74] G.W. Parshall, *Homogeneous Catalysis*, 1st Edition, Wiley, Chichester, 1980.