

A Practical Recycle of a Ligand-Free Palladium Catalyst for Heck Reactions

André H. M. de Vries,^{a,*} Floris J. Parlevliet,^a Lizette Schmieder-van de Vondervoort,^a John H. M. Mommers,^b Huub J. W. Henderickx,^b Monique A. M. Walet,^b Johannes G. de Vries^{a,*}

^a DSM Fine Chemicals-Advanced Synthesis & Catalysis, P.O. Box 18, 6160 MD Geleen, The Netherlands

Fax: (+31)-46-4767604, e-mail: andre.vries-de@dsm.com

^b DSM Research-Centre for Analysis & Technology, P.O. Box 18, 6160 MD Geleen, The Netherlands

Received: May 21, 2002; Accepted: July 18, 2002

Dedicated to Prof. Roger Sheldon on the occasion of his 60th birthday.

Abstract: Ligand-free palladium can be recovered almost quantitatively from Heck reaction mixtures by filtration after its deposition on a carrier such as silica or celite. Subsequently, it is re-activated to its original activity by adding a small amount of iodine or bromine prior to the next reaction cycle. The catalyst

results in excellent yields and selectivities, even for the less reactive aryl bromides. A catalytic cycle based on anionic palladium intermediates is proposed.

Keywords: catalyst recovery; Heck reaction; iodine; ligand-free; palladium; re-activation

Introduction

The number of highly (enantio)selective homogeneous catalysed transformations is growing rapidly,^[1] and the advantages of homogeneous catalysis in applications are broadly recognised.^[2] Initially, asymmetric hydrogenation appeared to be the most important reaction class,^[3] but in recent years aromatic substitution reactions and CO chemistry are rapidly gaining in importance. However, to date only a small percentage of fine chemicals are produced using homogeneous catalysis. This modest role is due to a whole range of critical factors from which the following ones are probably most decisive:

- i) The activity and stability of the catalyst.
- ii) The availability and cost of the catalyst and matching starting materials.
- iii) The short development time for a production process (a few months to 1 year) limiting the possibility to change complex synthetic routes.

Carbon-carbon bond forming reactions, such as the Heck reaction are used to some extent in fine chemical production.^[4] The wide functional group tolerance of these palladium-catalysed reactions allows their application at a late stage of total synthesis and eliminates the need for protecting groups.

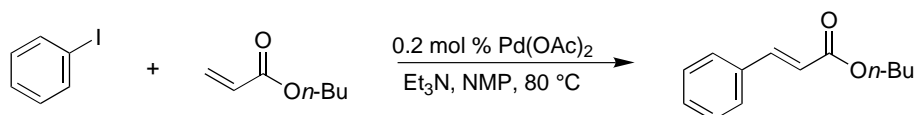
Heck chemistry is traditionally associated with the palladium-phosphine-catalysed reaction of aryl bromides or iodides with olefins presenting one of the simplest ways to obtain various substituted olefins.^[4,5]

Recently, a lot of effort has been put into the development of new, active and stable palladium catalysts such as palladacycles and other underligated single-phosphine systems.^[5] However, the use of phosphorus ligands in fine chemical processes is less desirable. They are usually unrecoverable and frequently hamper the isolation and purification of the desired product as well as the performance of consecutive catalytic steps of the total synthesis.

On the other hand, phosphine-free systems have shown excellent activities in Heck reactions.^[6] Successful ligand-free approaches have also been described when phase-transfer agents,^[7] aqueous systems,^[8] palladium nanoparticles^[9] or less usual leaving groups such as diazonium salts,^[10] acid chlorides^[11] or anhydrides^[12] are used.

Next to the activity of the catalyst, recovery and recycling of the expensive palladium is a major development issue. Several approaches based on biphasic liquid-liquid and polymer-supported systems have been reported but reactivity is often lower. Furthermore, due to the instability of the palladium complexes, leaching is a common problem.^[13]

Palladium-on-carbon-catalysed Heck reactions have been described and utilised in applied syntheses,^[13,14] but the true catalytically active species is arguably a leached soluble palladium complex.^[15] Recently, several palladium catalysts supported on various metal oxides, molecular sieves and zeolites have been separated from Heck reaction mixtures and re-used without any loss of activity.^[16]



Scheme 1.

Here we would like to present a practical method to recycle, and re-activate a ligand-free palladium catalyst for Heck reactions using the merits of both homogeneous and heterogeneous catalysis i.e., high activity and easy recovery, respectively.

Results and Discussion

By now the general acceptance is that none of the steps in the Heck catalytic cycle requires the presence of a strongly bound (phosphine) ligand in the coordination shell of palladium.^[5a] The most serious drawback of homogeneous ligand-free palladium catalysis is that deactivation of the instable palladium species occurs, mainly caused by the formation of inactive palladium(0) sediments. Tuning of the reaction conditions could in principle lead to highly active ligand-free palladium caught in the catalytic cycle, converting all aryl compound present prior to its precipitation to palladium black.

In order to find those conditions for the ligand-free Heck reaction of iodobenzene and *n*-butyl acrylate we investigated at 80 °C several combinations of solvents (NMP, DMF, DMA, DMSO, and acetonitrile), bases (K₂CO₃ and Et₃N) and palladium precursors [PdCl₂ and Pd(OAc)₂]. The reaction procedure using NMP, Et₃N, and Pd(OAc)₂ proceeded remarkably faster and more selectively (conversion and selectivity to the *trans*-cinnamate are both > 99%, Scheme 1) than those that utilised other combinations.^[17]

In addition, all combinations invariably led to precipitation of palladium, whether full conversion of iodobenzene was reached or not.

To get a more economical procedure we focused our investigation on the recovery and re-use of the precipitated catalyst. Recovery of the precipitated palladium(0) after the reaction performed as described in Scheme 1, followed by re-use in the same reaction showed that the activity had greatly diminished. As this might well be due to the reduced surface area of the catalyst the effect of deposition on carrier materials, like silica, or celite was studied. The use of these materials resulted in almost quantitative precipitation of the palladium (only ppb concentrations of palladium in the filtrate, ICP-MS) and facilitated the separation from the reaction mixture. No palladium precipitation on the glass tube wall was observed. However, the activity of these grey materials in the test reaction of Scheme 1 was still more than 10 times less on average than the original



Figure 1. TEM picture of palladium (black circles) deposited on silica from Heck reaction.

Pd(OAc)₂. Analysis with TEM (transmission electron microscopy) revealed that the deposited palladium on the carrier materials is in the form of fairly large crystalline clusters with a size of 40–100 nm (Figure 1).

At this stage we envisioned that the only manner in which the palladium could be restored to its original activity would be to oxidise it back to its monomeric form.

Therefore, several different oxidising agents and salts (as a solution in NMP) were added to the precipitated palladium on celite prior to the reagents and base necessary for the test reaction. This screening of suitable re-activators was performed in a fully automated synthesiser by using a reactor block equipped with a filter (8 vessels). In this manner we examined several different re-activators in 3 successive runs of the test reaction.

In the first run all vessels were filled with the same reagents including $\text{Pd}(\text{OAc})_2$ and celite, obviously giving the same results: >98% conversion, >98% selectivity to the *trans* product after 60 minutes (see Table 1, entries 1–8). The vessels were cooled, and the reaction mixtures were separated from the precipitated palladium on celite by filtration. The residues were washed with methyl *t*-butyl ether (MTBE) and filtered to exclude any residual homogeneous palladium. The resulting grey materials were treated with the different additives dissolved in NMP before the next Heck reaction was performed (Run 2, see Table 1, entries 1–8). Remarkably, I_2 and Br_2 were able to dissolve the precipitated palladium and led to full restoration of the original activity of $\text{Pd}(\text{OAc})_2$, while other additives, such as HOAc , LiI , and HI did not result in a catalytic activity to the same extent.^[18] When no re-activator or stronger oxidants (HNO_3 , H_2O_2 , NaIO_4) were used, hardly any Heck product was formed in the successive runs.

Therefore addition of only 2 mol equivalents of I_2 (or Br_2) dissolved in NMP to the recovered palladium precipitated on celite (or silica), followed by stirring at RT for a few minutes to dissolve the palladium prior to the following Heck reaction run, has led to the development of a very practical recycle of palladium, reducing the costs of the catalyst significantly. By using this mode 8 successive runs of the test reaction were performed manually in normal glass equipment without significant losses in activity.^[19]

The re-activation with I_2 of the precipitated palladium was also successful in the Heck reaction of iodobenzene with styrene giving the same performance as in run 1. Yields and selectivities found with this catalyst are comparable with those found for other catalytic systems (entry 9). Ligand-free Heck reactions on the less reactive aryl bromides are hardly known.^[5a,15b,16a,16c] Thus, we were delighted to see that by carefully adjusting the conditions, the coupling of 3-bromopyridine and *n*-butyl acrylate proceeded smoothly without any added ligand.^[20] Moreover, the I_2 re-activation mode is also applicable (entry 10). Activities and selectivities of this recyclable palladium catalyst are, for both the iodobenzene and 3-bromopyridine, comparable with the recently reported supported ligand-free systems.^[16]

Mechanistic Considerations

When the solution obtained after stirring with I_2 was separated from the silica (or celite), the solution showed high rates in the Heck reaction, but the silica was not active. Stirring of the precipitated palladium on silica with only NMP and testing the solution in the Heck reaction showed almost no activity. In an independent experiment we showed that commercial palladium black could also be dissolved using I_2 in NMP, and that

this solution was active in the Heck reaction. The combination of silica and iodine in the absence of palladium but otherwise equal conditions did not show any activity in the Heck reaction.

All these experiments are confirming the assumption that the precipitated palladium is oxidised back to $\text{Pd}(\text{II})$ by I_2 (or Br_2),^[21] which is then reduced again in the next Heck reaction to form the highly active palladium(0) species, see Figure 2.

On the molecular level very little is known about the catalytic cycle of these ligand-free Heck reactions. Extensive research has been performed on the use of anionic palladium phosphine catalysts in the Heck reaction.^[22] We thus attempted to gain more information about the ligand-free systems by the use of negative ion electron spray MS. The Heck reaction of Scheme 1 was followed over time and the anionic palladium complexes were recorded. Most striking observations are the presence of a unique palladium(0) species, $[(\text{H}_2\text{O})\text{PdOAc}]^-$, at low conversion and the palladium(II) species, $[\text{ArPdI}_2]^-$ and $[\text{PdI}_3]^-$, at higher conversion (>5%).^[23] Therefore we propose the mechanism depicted in Figure 3 based on the assumption that $[\text{PdI}_3]^-$, or its dimer $[\text{Pd}_2\text{I}_6]^{2-}$, is in equilibrium with the highly active PdI^- (or a dimer/cluster thereof). More details of this study will be published elsewhere as it is outside the scope of this paper.

In summary, we reported in this work a highly practical, cost-effective and robust solution for performing Heck reactions, combining the advances of heterogeneous and homogeneous catalysis. The precipitated palladium sediments can easily be recovered by filtration, and re-activated (“homogenised”) by addition of I_2 or Br_2 . The re-activated palladium catalyst is homogeneous in character, most likely as a mononuclear anionic species, although the presence of nanoparticles cannot be excluded.^[9] Scale-up studies using this ligand-free mode of Heck reactions are under investigations in our laboratories.

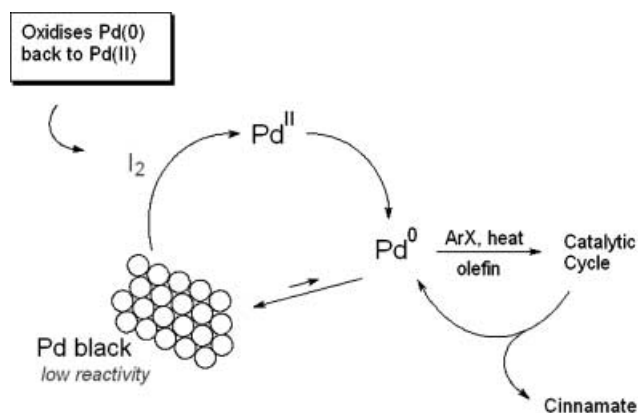
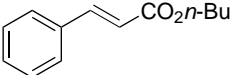
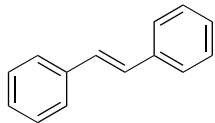
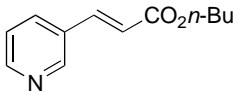


Figure 2. A practical catalyst recycle for ligand-free Heck reactions.

Table 1. Re-activation and re-use of the palladium catalyst (0.5 mol %) in ligand-free Heck reactions.^[a]

Entry	ArX	Olefin	Temp. [°C]	Base	Product	Re-activator ^[b]	Time [h]	Run 1 Conv. ^[c] [%]	Yield ^[c] [%]	Time [h]	Run 2 Conv. ^[c] [%]	Yield ^[c] [%]	Time [h]	Run 3 Conv. ^[c] [%]	Yield ^[c] [%]
1	Iodo benzene	<i>n</i> -butyl acrylate	80	Et ₃ N		I ₂	1	98	98	1	100	99	1	99	99
2	"	"	"	"	"	Br ₂	1	99	99	1	99	99	1	100	98
3	"	"	"	"	"	NaIO ₄	1	99	98	1	10	10	1	8	2
4	"	"	"	"	"	H ₂ O ₂	1	100	99	1	19	2	1	11	2
5	"	"	"	"	"	LiI	1	98	98	1	65	70	1	63	57
6	"	"	"	"	"	HOAc	1	99	99	1	38	41	1	23	17
7	"	"	"	"	"	HI	1	100	99	1	80	81	1	60	56
8	"	"	"	"	"	–	1	99	99	1	15	9	1	5	1
9 ^[d]	Iodo benzene	styrene	120	Et ₃ N		I ₂	3	98	94	3	97	92			
10 ^[e]	3-bromo pyridine	<i>n</i> -butyl acrylate	130	NaOAc		I ₂	4	95	85	4	92	83			

^[a] All experiments were performed under a nitrogen atmosphere in the ASW 2000 of ChemspeedTM, a fully automated synthesiser, unless stated otherwise. Sequence of the procedure: Heck reaction run 1 (amount of reagents and additives: 2.0 mmol of aryl compound, 2.8 mmol of olefin, 0.01 mmol of Pd(OAc)₂, 2.5 mmol of base, 25 mg of celite, and 3 mL of NMP), cooling to RT, filtration, washing of the solids with MTBE (3 mL), filtration, addition of the oxidant/additive (0.02 mmol in 1 mL of NMP) to the solid grey material (palladium deposited on celite), Heck reaction run 2 (2.0 mmol aryl compound, 2.8 mmol of olefin, 2.5 mmol of base, 2 mL of NMP), followed by another cycle starting with cooling to RT.

^[b] Added just before Heck reaction run 2, and just before run 3. Two mol equivalents of re-activator with respect to the amount of palladium.

^[c] Determined by GC using dihexyl ether as internal standard.

^[d] Performed manually in a 10-mL round-bottom flask. Amount of reagents and additives: 5.0 mmol of iodobenzene, 5.5 mmol of styrene, 0.0125 mmol of Pd(OAc)₂ (0.25 mol %), 5.5 mmol of Et₃N, 35 mg of celite, and 5 mL of NMP. No MTBE wash between the 2 runs.

^[e] Performed manually in a 50-mL Schlenk vessel. Amount of reagents and additives: 16.8 mmol of 3-bromopyridine, 30 mmol of *n*-butyl acrylate, 0.057 mmol of Pd(OAc)₂ (0.3 mol %), 25.6 mmol of NaOAc, 400 mg of celite, and 30 mL of NMP.

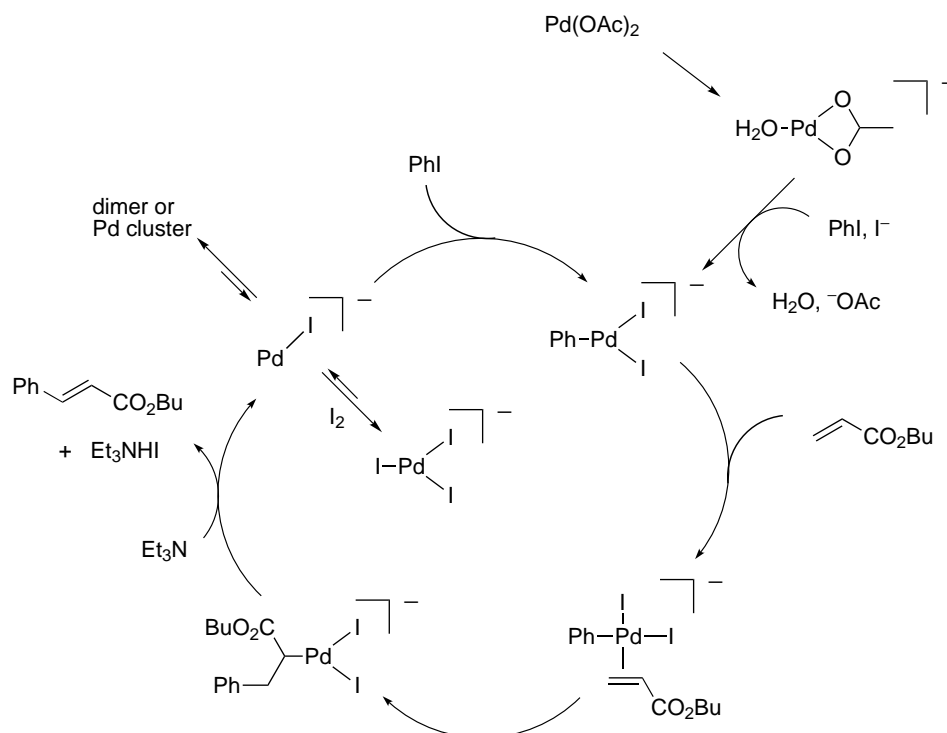


Figure 3. Proposed catalytic cycle of the ligand-free Heck reaction.

Experimental Section

Automated Screening of Suitable Re-activators, Typical Procedure

In an automated synthesis robot (ASW 2000, from Chem-speed™) 8 double jacketed reaction vessels each equipped with a glass sinter were installed. Each vessel was filled with 25 mg of celite, the vessels were closed and nitrogen gas was applied. To each vessel was added subsequently NMP (2.0 mL), iodobenzene (0.225 mL, 2.0 mmol), dihexyl ether (0.118 mL, 0.50 mmol, internal standard for GC), Et₃N (0.350 mL, 2.5 mmol) and 1.0 mL of a solution of Pd(OAc)₂ in NMP (0.01 M solution, 0.01 mmol of Pd(OAc)₂ in each vessel = 0.50 mol % compared to iodobenzene), by using the fully automated syringe of the robot. All vessels were vortexed (600 rpm) and heated up to 70 °C. *n*-Butyl acrylate (0.400 mL, 2.8 mmol) was added to all 8 vessels (*t* = 0) and the vessels were further heated to 80 °C. After 15, 30, 60, and 90 minutes a sample (0.1 mL) of every vessel was taken. The samples were diluted and analysed by GC. The vessels were cooled to room temperature and the reaction mixtures were filtered by applying a small vacuum. The grey solid residues (palladium deposited on celite) were washed with methyl *t*-butyl ether (MTBE, 3 mL) and the resulting mixture was filtered. To each individual vessel, containing the grey solid residues, the re-activator (0.02 mmol in 1 mL of NMP) was added and the reagents and additives necessary for the next Heck reaction run were added, leaving out the celite and the Pd(OAc)₂ solution. The re-activating cycle and a next Heck reaction run were repeated once more. The results of the analyses are shown in Table 1.

Typical Procedure for Successive Heck Reactions by Recovery and Re-activation of the Palladium Catalyst

A Schlenk flask was filled with Pd(OAc)₂ (10.5 mg, 0.047 mmol), celite (1 g) and NMP (25 mL). Nitrogen atmosphere was applied and the vessel was closed with a septum. The mixture was stirred and the following reagents were added successively by using syringes: Et₃N (3.05 g, 30 mmol), iodobenzene (5.2 g, 25.4 mmol) and dihexyl ether (internal standard for GC). The reaction mixture was heated to 70 °C, *n*-butyl acrylate (4.26 g, 33 mmol) was added (*t* = 0) and the mixture was further heated to 80 °C.

At certain time intervals aliquots were taken from the dark reaction mixture and analysed by GC. After 90 minutes the mixture was cooled to room temperature and transferred into a vessel suited for a centrifuge. (NB. This last handling and all the next handlings till the following Heck reaction were performed in air). The solid and liquid materials were separated by 2000 rpm for 3 minutes. The liquid phase was decanted. The solid residue was washed with a portion of MTBE (20 mL) and the solid material and the supernatant were separated again. The solid residue was transferred with a fresh portion of NMP (30 mL) into a clean Schlenk vessel and the Heck reaction was performed again, without adding celite and the palladium catalyst. Up to 8 successive runs were performed all giving similar conversion and yield (> 90%).

Work-Up Procedure

After cooling, the reaction mixture was poured into water (150 mL) and extracted with toluene (2 times 80 mL). The collected organic layers were washed with water (3 times 125 mL), brine (150 mL), dried with Na₂SO₄, and filtered

through celite. The inorganic material was washed with toluene (100 mL) and the solvents were evaporated; yield: > 90%. ^1H and ^{13}C NMR are in full accordance with the literature.

Electron Spray MS

Negative ion electrospray (ESI) of reaction samples diluted to a 5% solution in acetonitrile were recorded using a PE SCIEX API150 single quadrupole mass spectrometer (Applied Biosystems/MDS SCIEX, Toronto, Ontario, Canada). The samples were introduced by direct infusion of the sample solution at $5\ \mu\text{L}\ \text{min}^{-1}$ with a syringe pump (Harvard Apparatus, Saint Laurent, Quebec, Canada). The spray capillary voltage was maintained at $-4\ \text{kV}$, while the defragmentation potential was set at $10\ \text{V}$. The quadrupole resolution was set to high resolution. Mass spectra were collected in full scan mode, scanning from $100\text{--}700\ \text{amu}$ in 40 seconds.

Acknowledgements

We thank the Dutch Ministry of Economic affairs for a subsidy under the EET program (EET grants: EETK97107 and EETK99104).

References and Notes

- [1] a) *Transition Metals for Organic Synthesis*, (Eds.: M. Beller, C. Bolm), Wiley, Weinheim, **1998**; b) *Comprehensive Asymmetric Catalysis*, (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**.
- [2] *Applied Homogeneous Catalysis with Organometallic Compounds*, (Eds.: B. Cornils, W. A. Herrmann), Wiley, Weinheim, **1996**.
- [3] H. U. Blaser, F. Spindler, M. Studer, *Appl. Cat. A*, **2001**, *221*, 119.
- [4] a) J. G. de Vries, *Can. J. Chem.* **2001**, *79*, 1086; b) C. E. Tucker, J. G. de Vries, *Topics in Catalysis* **2002**, *19*, 111.
- [5] a) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009; b) N. J. Whitcombe, K. K. (M.) Hii, S. E. Gibson, *Tetrahedron* **2001**, *57*, 7449.
- [6] a) W. A. Herrmann, M. Elison, J. Fischer, C. Köchler, G. R. J. Artus, *Angew. Chem. Int. Ed.* **1995**, *34*, 2371; b) M. T. Reetz, E. Westermann, R. Lohmer, G. Lohmer, *Tetrahedron Lett.* **1998**, *39*, 8449; c) M. Ohff, A. Ohff, D. Milstein *Chem. Commun.* **1999**, 357; d) A. S. Gruber, D. Zim, G. Ebeling, A. L. Monteiro, J. Dupont, *Org. Lett.* **2000**, *2*, 1287; e) D. A. Alonso, C. Nájera, M. C. Pacheco, *Org. Lett.* **2000**, *2*, 1823; f) I. P. Beletskaya, A. N. Kashin, N. B. Karlstedt, A. V. Mitin, A. V. Cheprakov, G. M. Kazankov, *J. Organomet. Chem.* **2001**, *622*, 89.
- [7] a) T. Jeffery, *Synthesis* **1987**, 70; b) T. Jeffery, *Tetrahedron* **1996**, *52*, 10113; c) T. Jeffery, in *Advances in Metal-Organic Chemistry*, (Ed.: L. S. Liebeskind), JAI Press, Greenwich, **1996**, Vol. 5 p. 153; d) C. Gürtler, S. L. Buchwald, *Chem. Eur. J.* **1999**, *5*, 3107.
- [8] a) N. A. Bumagin, P. G. More, I. P. Beletskaya, *J. Organomet. Chem.* **1989**, *371*, 397; b) N. A. Bumagin, V. V. Bykov, L. I. Sukhomlinova, T. P. Tolstaya, I. P. Beletskaya, *J. Organomet. Chem.* **1995**, *486*, 259; c) I. P. Beletskaya, *Pure Appl. Chem.* **1997**, *69*, 471.
- [9] a) M. T. Reetz, G. Lohmer, *Chem. Commun.* **1996**, 1921; b) M. Beller, H. Fischer, K. Kühlein, C.-P. Reisinger, W. A. Herrmann, *J. Organomet. Chem.* **1996**, *520*, 257; c) M. T. Reetz, E. Westermann, *Angew. Chem. Int. Ed.* **2000**, *39*, 165.
- [10] a) K. Kikukawa, K. Maemura, Y. Kiseki, F. Wada, T. Matsuda, *J. Org. Chem.* **1981**, *46*, 4885; b) S. Sengupta, S. Bhattacharya, *J. Chem. Soc. Perkin Trans. 1* **1993**, 1943; c) M. Beller, H. Fischer, K. Kühlein, *Tetrahedron Lett.* **1994**, *35*, 8773; d) M. Beller, K. Kühlein, *Synlett* **1995**, 441.
- [11] a) H. U. Blaser, A. Spencer, *J. Organomet. Chem.* **1982**, *233*, 267; b) A. Spencer, *J. Organomet. Chem.* **1983**, *247*, 117.
- [12] M. Stephan, A. J. J. M. Teunissen, G. K. M. Verzijl, J. G. de Vries, *Angew. Chem. Int. Ed.* **1998**, *37*, 662.
- [13] For a recent review on catalyst product separation techniques in Heck reactions, see: B. M. Bhanage, M. Arai, *Catalysis Reviews* **2001**, *43*, 315.
- [14] a) A. Eisenstadt, in *Catalysis of Organic Reactions*, (Ed.: F. E. Herkes), Chemical Industries, **1998**, p. 415; b) V. M. Wall, A. Eisenstadt, D. J. Ager, S. A. Laneman, *Platinum Metals Rev.* **1999**, *43*, 138. c) F. Zhao, B. M. Bhanage, M. Shirai, M. Arai, *Chem. Eur. J.* **2000**, *6*, 843 and references therein.
- [15] a) A. Biffis, M. Zecca, M. Basato, *Eur. J. Inorg. Chem.* **2001**, 1131; b) K. Köhler, R. G. Heidenreich, J. G. E. Krauter, J. Pietsch, *Chem. Eur. J.* **2002**, *8*, 622.
- [16] a) C. P. Mehnert, D. W. Weaver, J. Y. Ying, *J. Am. Chem. Soc.* **1998**, *120*, 12289; b) A. Wali, S. Muthukumar Pillai, V. Kaushik, S. Satish, *Appl. Catal. A* **1996**, *135*, 83; c) L. Djakovitch, K. Köhler, *J. Am. Chem. Soc.* **2001**, *123*, 5990.
- [17] Recently a similar ligand-free catalyst for the reaction between iodobenzene and methyl acrylate has been described using DMF, Et_3N , and $\text{Pd}(\text{OAc})_2$, but at $140\ ^\circ\text{C}$: M. Qadir, T. Möchel, K. K. (M.) Hii, *Tetrahedron* **2000**, *56*, 7975.
- [18] F. J. Parlevliet, A. H. M. de Vries, J. G. de Vries, (DSM nv), WO 02/00340, **2002**; *Chem. Abstr.* **2002**, 555436.
- [19] The separated reaction mixtures contained between 5–10 ppm palladium indicating a small level of leaching of the palladium (2–3% in every run).
- [20] A manuscript is in preparation describing our detailed study on ligand-free Heck reactions between a wide range of aryl bromides (activated, non-activated and de-activated) and several olefins (electron deficient and electron rich). Aryl chlorides were not reactive at all using this ligand-free palladium catalysts.
- [21] *Gmelins Handbuch der Anorganischen Chemie*, (Ed.: E. Pietsch), Verlag Chemie, Berlin, **1942**, system nummer 65, p. 288.
- [22] C. Amatore, A. Jutand, *Acc. Chem. Res.* **2000**, *33*, 314

[23] Recently similar palladium species were detected by using EXAFS in the phosphine-free Heck reaction between iodobenzene and 2-methylprop-2-en-1-ol: J.

Evans, L. O'Neill, V. L. Kambhampati, G. Rayner, S. Turin, A. Genge, A. J. Dent, T. Neisus, *J. Chem. Soc. Dalton Trans.* **2002**, 2207.
