

On the Involvement of Palladium Nanoparticles in the Heck and Suzuki Reactions

Dmitry Tselikhovsky,^[a] Inna Popov,^[b] Vitaly Gutkin,^[b] Alina Rozin,^[a]
Azariya Shvartsman,^[a] and Jochanan Blum*^[a]

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We describe two different pathways by which palladium-catalyzed Heck and Suzuki coupling reactions take place. When sol–gel entrapped palladium acetate was used as a catalyst, the reactions proceed by the formation of metallic nanoparticles. Such particles were already formed during the immobilization of the palladium salt. Upon application of palladium derivatives of proline, tyrosine, or alanine, either in their homogeneous or in their sol–gel entrapped version, no Pd⁰ particles could be detected, even when the couplings were carried out in boiling mesitylene (161 °C) or during pro-

longed reaction periods (48 h). The reactions in the presence of the amino acid derivatives proceeded at a higher rate than those by the entrapped palladium acetate. The existence of palladium nanoparticles was investigated with the aid of high-resolution scanning transmission electron microscopy equipped with energy dispersive X-ray spectroscopy, as well as by X-ray photoelectron spectroscopy.

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Introduction

The wide application of palladium-catalyzed Heck and Suzuki reactions in academic studies and in the industry^[1] piqued the interest of many researchers in the characterization, the mechanisms, and the reaction intermediates involved in these processes.^[2] On the basis of experiments from various laboratories, de Vries reported in his critical review^[2f] that “*in all Heck reactions at high temperature, certainly above 120 °C, the palladium catalyst, irrespectively of the nature of its precursor, is rapidly reduced to Pd⁰ which has a strong tendency to form soluble colloids.*” Although this statement is certainly correct for many cases, we observed that it is not a general rule. Some nanoparticle-free couplings were found to take place even between 120 and 160 °C and may proceed at a higher rate than those in which colloidal palladium is formed. Unlike the catalytic systems that involve metallic nanoparticles,^[3] the nanoparticle-free systems do not require the presence of any stabilizer.

Results and Discussion

Transmission electron microscopy (TEM) images clearly show the formation of nanoparticles of palladium during

the physical entrapment of palladium acetate within hydrophobized silica sol–gel.^[4] A typical TEM image is shown in Figure 1A. Dark contrast of heavy dense crystalline Pd nanoparticles is seen on the image. The formation of the sol–gel entrapped nanoparticles is also associated with the darkening of the sol–gel matrix. The existence of most of the metal particles as Pd⁰ has been confirmed by X-ray photoelectron spectroscopy (XPS), which shows distinguished binding energy peaks (BE) of Pd 3d_{5/2} and 3d_{3/2} at 335.58 and 340.84 eV, respectively^[5] (Figure 2A). The shapes of these peaks may suggest the presence of small amounts (up to 10%) of Pd^{II} species. After the use of the catalyst in the Heck coupling reaction shown in Scheme 1 (R = H; X = Br) at 80 °C under the conditions described in our previous paper^[4] no significant changes in either the micrograph or the XPS spectrum could be observed. The appearance of the nanoparticles also did not change when the aqueous solvent was replaced by an organic medium (heptane, benzene, toluene, mesitylene). However, when the entrapped palladium acetate (**1**) was replaced by sol–gel entrapped *Z*-bis(L-prolinato)palladium(II) (**2**),^[6] *Z*-bis(L-tyrosinato)palladium(II) (**3**),^[7] or *Z*-bis(L-alaninato)palladium(II) (**4**),^[8] the catalyst did not form nanoparticles in detectable amounts during their entrapment within the ceramic matrix or during the coupling process (see Experimental Section). Unlike the reactions by Pd(OAc)₂ that could be performed in an aqueous medium under microemulsion/sol–gel transport (EST) conditions,^[4] the coupling by the palladium derivatives of the amino acids had to be conducted in benzene (or in other hydrocarbons), because the immobilized palladium compounds leach readily into

[a] Institute of Chemistry, The Hebrew University, Jerusalem 91904, Israel
Fax: +972-2-6513832
E-mail: jblum@chem.ch.huji.ac.il

[b] Center for Nanoscience and Nanotechnology, The Hebrew University, Jerusalem 91904, Israel

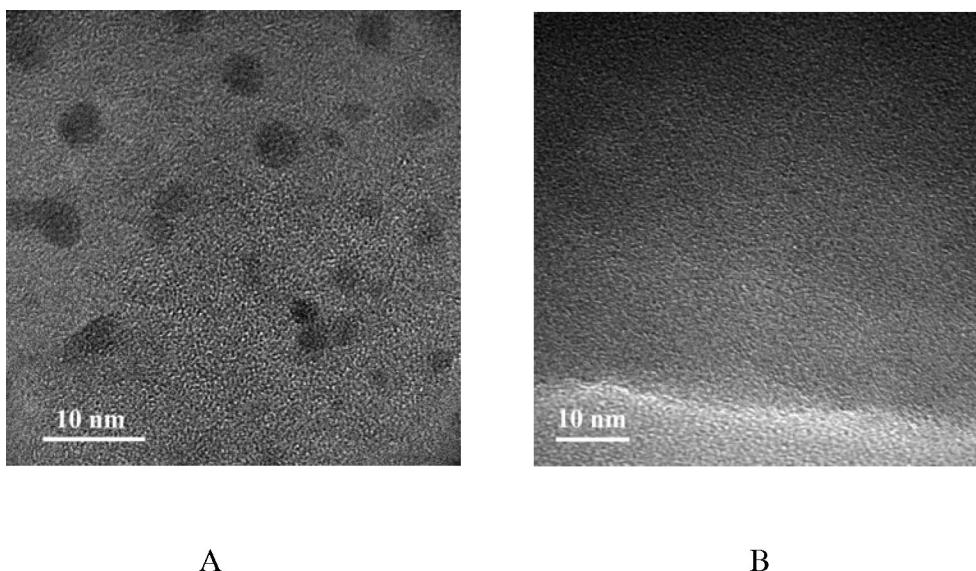
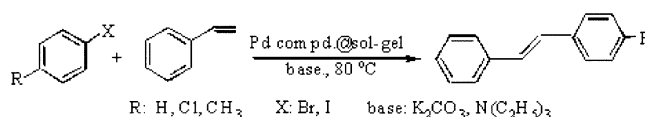


Figure 1. TEM images of the sol-gel support after the reaction of bromobenzene, styrene, and triethylamine in benzene (A) in the presence of entrapped palladium acetate (**1**) and (B) in the presence of entrapped palladium prolinates (**2**).

water. In contrast to the $\text{Pd}(\text{OAc})_2$ -catalyzed couplings, the color of the reaction mixtures by the amino acid derivatives remains pale yellow throughout the entire reaction period. Upon searching for any changes that might have occurred during the entrapment of **2**, **3**, and **4** we recorded the ^{13}C NMR spectra before and after the engagement processes. For example, the 125 MHz ^{13}C NMR of palladium prolinates (**2**) in D_2O consisted of resonance peaks at $\delta = 24.67$, 24.78, 29.44, 29.89, 50.14, 52.70, 63.63, 65.04, 186.50, 188.18 ppm. This spectrum is reduced to five signals at $\delta = 23.78$, 28.75, 51.64, 64.18, 184.71 ppm when the solvent-free solid-state NMR spectrum was recorded (owing to the diminished resolution). This spectrum resembles closely the solid-state spectrum of the sol-gel entrapped compound at $\delta = 24.05$, 29.54, 50.76, 63.80, 187.86 ppm.



Scheme 1.

161 °C. Likewise, we carried out couplings for an extended reaction period (48 h). The TEM images of the used catalysts in all these experiments were free of the dark TEM spots characteristic of palladium nanoparticles such as those formed when $\text{Pd}(\text{OAc})_2$ was used as catalyst [cf. e.g., the transmission electron micrographs of sol-gel entrapped $\text{Pd}(\text{OAc})_2$ shown as Figure 1A and that of sol-gel entrapped **2** shown as Figure 1B]. The only significant features in the micrographs of the palladium prolinates catalyzed Heck reactions were those of the pore entrances of ca. 2–4.5 nm. Numerous STEM and XPS analyses were carried out with the attempt to locate possible clusters of Pd^0 , but no such clusters were found. In contrast, the XPS studies clearly indicated the presence of $\text{Pd}^{\text{II}}\text{--O}$ species with BE of $\text{Pd } 3d_{5/2}$ of 336.83 and $\text{Pd } 3d_{3/2}$ of 342.09 eV.^[9] Attempts to find evidence for the presence of Pd^{IV} species^[10] did not give positive results.

Whereas free amino acids such as proline, tyrosine, and alanine react readily with $\text{Pd}(\text{OAc})_2$ according to Schemes 2 and 3, the disubstituted *N,N*-dimethylglycine (DMG) cannot form an analogous palladium compound. Thus, in the experiments of Reetz et al.^[11] the formation of the active palladium nanoparticles, which presumably were stabilized by DMG, result from the existing $\text{Pd}(\text{OAc})_2$.

In analogy to the Heck reactions, the sol-gel entrapped $\text{Pd}(\text{OAc})_2$ (**1**) and palladium prolinates **2** promote the Suzuki cross couplings shown in Scheme 4. Here too, the $\text{Pd}(\text{OAc})_2$ ^[4] and $\text{Pd}(\text{OAc})_2/\text{DMG}$ were found to generate palladium nanoparticles, whereas in the reactions catalyzed by

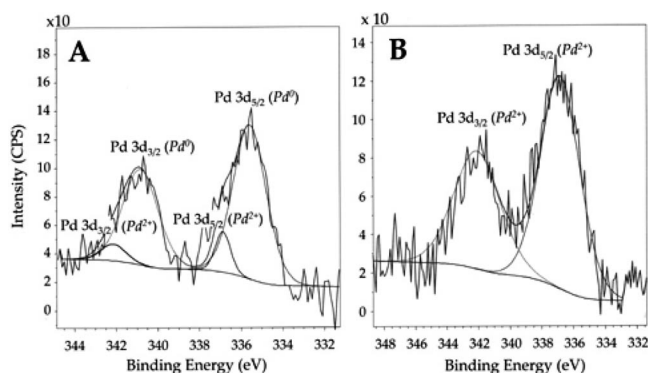
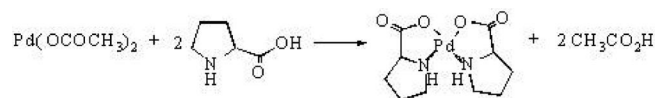
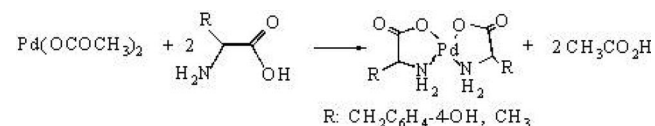


Figure 2. Palladium $3d_{5/2}$ and $3d_{3/2}$ profiles (A) obtained after Heck reaction in the presence of entrapped **1**; (B) obtained after the reaction in the presence of entrapped **2**.

Because it has been claimed that all palladium complexes formed during the Heck reaction decompose above 120 °C to give Pd^0 particles,^[21] we performed the coupling both under homogeneous and under heterogeneous conditions (with sol-gel entrapped catalyst) in boiling mesitylene at

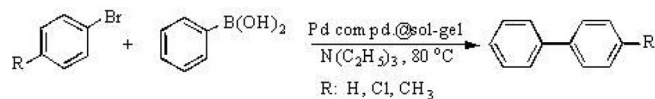


Scheme 2.



Scheme 3.

2 (irrespective if the complex was in its homogeneous or immobilized version) no Pd⁰ species could be detected. The results of some Heck and Suzuki coupling reactions by one of the amino acid derivatives are summarized in Table 1, which indicates that in analogy to the reaction promoted by immobilized Pd(OAc)₂^[4] the substitution of the aromatic bromide with an electron-donating methyl group has an inhibition effect on both the Heck and the Suzuki couplings, under the present conditions. However, also the reactions described in entries 3 and 7 (Table 1) can be brought to completion when the time is extended to 24 h. It is notable that although many Heck and Suzuki reactions are often accompanied under homogeneous conditions by side products,^[12,13] no 1,1-diarylethylenes are formed in entries 1–4 and no biphenyl (homocoupling product) is obtained in entries 6 and 7.



Scheme 4.

Whereas the amino acid palladium catalysts are insoluble in many organic solvents, they can be entrapped within silica sol-gel matrices, and they then react in aromatic hydrocarbons without any detectable leaching of the catalyst. After each reaction, the catalyst-containing ceramic material was filtered off, and the filtrate was analyzed for palladium by ICP. The filtrates were also tested for residual catalytic

activity (before and after concentration). No palladium species and no catalytic activity could be traced. Sol-gel entrapped **2**, **3**, and **4** proved recyclable. For example, in a series of experiments with bromobenzene and styrene in the presence of sol-gel entrapped **2** at 80 °C for 4 h the yields in each of the first six runs was quantitative (>99% by GC analysis). We recall that recycling of the catalyst was also possible in reactions by entrapped Pd(OAc)₂ that forms metallic nanoparticles^[4] (see, however, ref.^[2f]).

Although we did not perform systematic kinetic studies, we compared under identical experimental conditions the initial rates of the coupling of iodobenzene with styrene in a DMF/benzene (2:5) mixture in the presence of one of the entrapped catalysts **1–4** at 80 °C. The corresponding rates are listed in Table 2. The faster coupling rates by the palladium derivatives of the amino acids as compared with the rate observed with the entrapped Pd(OAc)₂ catalyst, is responsible for the fact that in all coupling experiments performed, the yields obtained by **2–4** were higher than those by **1** (see Table 2).

Table 2. Comparison between the efficiencies of entrapped palladium catalysts **1–4** in the Heck coupling of iodobenzene and styrene.^[a]

Entry	Catalyst	10 ⁵ Initial rate (mol L ⁻¹ s ⁻¹)	Yield after 1 h (%)
1	1	17.5	52
2	2	48.9	99 ^[b]
3	3	20.8	62
4	4	23.9	70.6

[a] Reaction conditions: iodobenzene (1.34 mmol), styrene (1.34 mmol), triethylamine (2 mmol), entrapped palladium catalyst (0.027 mmol), DMF (2 mL), and dry benzene (5 mL); 80 °C, 1 h. [b] 72.5% after 30 min.

At this stage we have no sound explanation for the higher efficiency of the nanoparticle-free systems, despite earlier observations that stabilized nanoparticles are usually the more active ones.^[2g,14]

In order to test whether the catalytic activity of the palladium amino acid derivatives results from undetectable “homeopathic” amounts of metallic nanoparticles,^[2f] we gradually reduced the molar ratio of palladium/bromobenzene in the Heck and Suzuki couplings of entries 1 and 5 in

Table 1. *cis*-Bis(L-prolinato)palladium-catalyzed Heck and Suzuki coupling reactions of some bromoarenes under comparable conditions.^[a]

Entry	Bromoarene	Arylation reagent	Product (yield after 1.5 h, %) ^[b]
1	C ₆ H ₅ Br	C ₆ H ₅ CH=CH ₂	(<i>E</i>)-C ₆ H ₅ CH=CHC ₆ H ₅ (71)
2	4-ClC ₆ H ₄ Br	C ₆ H ₅ CH=CH ₂	(<i>E</i>)-4-ClC ₆ H ₄ CH=CHC ₆ H ₅ (44)
3	4-CH ₃ C ₆ H ₄ Br	C ₆ H ₅ CH=CH ₂	(<i>E</i>)-4-CH ₃ C ₆ H ₄ CH=CHC ₆ H ₅ (18.5)
4	C ₆ H ₅ Br	C ₆ H ₅ CH=CH ₂	(<i>E</i>)-C ₆ H ₅ CH=CHC ₆ H ₅ (72)
5	C ₆ H ₅ Br	C ₆ H ₅ B(OH) ₂	(C ₆ H ₅) ₂ (84)
6	4-ClC ₆ H ₄ Br	C ₆ H ₅ B(OH) ₂	4-ClC ₆ H ₄ C ₆ H ₅ (54)
7	4-CH ₃ C ₆ H ₄ Br	C ₆ H ₅ B(OH) ₂	4-CH ₃ C ₆ H ₄ C ₆ H ₅ (27)

[a] Reaction conditions for entries 1–3: bromoarene (1.34 mmol), styrene (1.34 mmol), *cis*-bis(prolinato)palladium (0.0134 mmol) entrapped within silica sol-gel [from tetramethoxysilane (3.6 mL), MeOH (2.4 mL), and H₂O (2 mL)], Et₃N (1.62 mg, 1.61 mmol), and benzene (10 mL), 78 °C; conditions for entries 5–7: the same as for entries 1–3 but instead styrene phenylboronic acid (1.34 mmol) was used; conditions for entry 4: the reaction was performed without sol-gel material in a microemulsion that contained sodium dodecyl sulfate (3.3 wt.-%), BuOH (6.6 wt.-%), H₂O (89.3 wt.-%), and Et₃N was replaced by K₂CO₃. [b] By extending the reaction time to 4 h, entries 1, 2, 4, 5, and 6 afforded quantitative yields and entries 3 and 7 afforded 48.5 and 71% yield, respectively. In order to obtain quantitative yield in entries 3 and 7 the reactions were conducted for 24 h.

Table 1 from 1:10² to 1:10⁴ and found that the yields also decreased gradually. Below 1:10³ hardly any reaction took place during the first 20 h.

Conclusions

Although our experiments indicate clearly the formation of palladium nanoparticles during the entrapment of Pd(OAc)₂ within silica sol–gel matrices, as well as during the application of the heterogeneous salt in the Heck and Suzuki coupling reactions, we found no proof for the generation of metallic particles in the presence of the amino acid derivatives **2–4**. As no Pd⁰ nanoparticles were found even after conducting the coupling reactions in the presence of **2–4** at 160 °C or after extending the reaction time to 48 h, we assume that the reaction by **1** proceeds by a different pathway than by the entrapped palladium amino acid derivatives. It is possible that despite the fact that XPS analysis was unable to detect the presence of unstable Pd^{IV} species, the faster nanoparticle-free processes take place through a catalytic cycle that includes Pd^{II} and Pd^{IV} species [but not Pd⁰] as suggested, for example, by Herrmann et al. and by Shaw.^[2a,15]

Finally, we wish to draw attention to the existence of a combined catalyst system composed of sol–gel entrapped [Rh(cod)Cl]₂ and Na[HRu₃(CO)₁₁] that promotes the hydrogenation of methylated arenes with the formation of metallic nanoparticles at 80 °C, but that takes place without their intermediary at 20 °C.^[16]

Experimental Section

General: ¹H and ¹³C NMR spectra were recorded with either a Bruker DRX-400 or a Bruker Avance II-500 instrument in CDCl₃. Infrared spectra were obtained with a Bruker Vector 22-FRIT spectrometer. Mass spectral measurements were performed with a Hewlett–Packard model 4989 Å mass spectrometer equipped with an HP model 5890 series II gas chromatograph. ICP-MS analyses were performed with a Perkin–Elmer model ELAN DRC II instrument. A Micrometrics ASAP 2020 instrument was used for BET-N₂ and BJH-N₂ surface area and pore diameter measurements of the sol–gel matrices. Gas chromatographic separations were performed with a Hewlett–Packard model Agilent, 4890D, by using either a 15 m long capillary column packed with bonded and crosslinked (5% phenyl)methyl polysiloxane (HP-5) or a 30 m long column packed with Carbowax 20 m-poly(ethylene glycol) in fused silica (Supelco 25301-U). XPS measurements were performed with a Kratos Axis Ultra X-ray photoelectron spectrometer. Spectra were acquired with monochromated Al-K_α (1486.7 eV) X-ray source with 0° take-off angle. The pressure in the test chamber was maintained at 1.5 × 10^{−9} Torr during the acquisition process. High-resolution XPS scans were collected for Pd 3d and C 1s peaks with pass energy 20 eV. The XPS binding energy was calibrated with respect to the peak position of C 1s as 285.0 eV. Data analysis was performed with Vision processing data reduction software (Kratos Analytical Ltd.) and CasaXPS (Casa Software Ltd.). Transmission electron microscopy was done with Scanning Transmission Electron Microscope (STEM) Tecnai G² F20 (FEI Company, USA) operated at 200 kV and equipped with EDAX-EDS for identification of ele-

mental composition. Initial powders were dispersed in ethanol and dropped onto a standard 400 mesh carbon coated copper TEM grid. The various bromo- and iodoarenes, styrene, tetramethoxysilane, palladium acetate, sodium dodecyl sulfate, B-phenylboronic acid, L-alanine, L-tyrosine, L-proline, N,N-dimethylglycine, 1,1'-(1E)-1,2-ethenediylbis(benzene), 1-methyl-4-[(1E)-2-phenylethenyl]benzene, 1-chloro-4-[(1E)-2-phenylethenyl]benzene, and biphenyl were obtained from commercial sources. 4-Methyl-1,1'-biphenyl,^[4] 4-chloro-1,1'-biphenyl,^[4] Z-bis(L-prolinato)palladium,^[6] Z-bis(L-tyrosinato)palladium,^[7] and Z-(L-alaninato)palladium^[8] were prepared according to literature procedures.

Entrapment of **2**, **3** and **4** within Sol–gel Matrices

Method A: A solution of tetramethoxysilane (3.6 mL) in triply distilled water (TDW, 2 mL) was stirred magnetically with a solution of palladium acetate (30 mg, 0.134 mmol) in dichloromethane (1 mL), and with a solution of the amino acid (0.67 mmol) in MeOH (2.4 mL). Usually 4–5 drops of MeOH was added to obtain a clear transparent solution. After ca. 10 h gelation was complete. The pale-yellow gel was aged for 24 h and then dried under 0.5 Torr at 80 °C for 24 h, washed with MeOH (20 mL), sonicated with dichloromethane (20 mL), and dried again until constant weight was achieved.

Method B: A mixture of a solution of palladium acetate (400 mg, 1.78 mmol) in dichloromethane (5 mL) and the amino acid (8.9 mmol) in MeOH (5 mL) was agitated in an open-glass vessel for 30 min at room temperature. The pale-yellow powder was filtered and recrystallized from MeOH, added to a mixture of tetramethoxysilane (48 mL) and TDW (27 mL), awaited gelation, and worked up as described above. The palladium content of the entrapped complexes was determined by ICP. The palladium-entrapped sol–gel material was heated at reflux for 24 h in dry benzene, cooled, and filtered. The concentrated filtrate was then subjected to TEM analysis, which indicated in all cases the absence of palladium nanoparticles.

General Procedure for the Heck and Suzuki Cross-Coupling Reactions by Sol–gel Entrapped **2–4:** The sol–gel entrapped catalyst (**2**, **3**, or **4**, 0.0134 mmol) and the organic substrates (0.67–1.34 mmol of each of them), triethylamine (2.6 mmol), and benzene (7 mL) were placed in a glass pressure tube. The mixture was agitated at 80 °C for the desired length of time. After cooling the reaction mixture to room temperature the ceramic material was filtered off, extracted with diethyl ether (2 × 50 mL), dried at 80 °C under 1 Torr, and analyzed by ICP for leached palladium. Under the above conditions no leaching could be detected and the recovered immobilized catalyst could be used without further workup in the next run. The organic solutions were concentrated, and the residues were either separated by column chromatography or analyzed by GC, GC–MS, and NMR spectroscopy. The physical data of the products were compared with those of authentic samples.

Comparative experiments were also performed (a) in DMF/benzene (2:5) without the ceramic support and (b) in a microemulsion (without sol–gel material) prepared from sodium dodecyl sulfate (≈3 wt.-%), *n*-propanol (≈7 wt.-%), the aromatic substrates (1.34 mmol of each, ≈1 wt.-%), and water (≈89 wt.-%). Reactions in aqueous media were carried out usually in the presence of K₂CO₃ rather than in the presence of triethylamine.

Acknowledgments

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- [1] For some leading reviews, see: a) F. Diederich, P. J. Stang (Eds.), *Metal Catalyzed Cross Coupling Reactions*, Wiley-VCH, Weinheim, **1997**; b) E. I. Neghishi, *Handbook of Organopalladium Chemistry for Organic Synthesis*, Wiley, Hoboken, N. J. **2002**; c) F. Alonso, I. P. Beletskaya, M. Yus, *Tetrahedron* **2005**, *61*, 11771–11835.
- [2] See, for example: a) B. L. Shaw, *New J. Chem.* **1998**, *22*, 77–79; b) C. Amatore, A. Jutand, *Acc. Chem. Res.* **2000**, *33*, 314–321; c) J. A. Widegren, R. G. Finke, *J. Mol. Catal. A* **2003**, *198*, 317–341; d) M. T. Reetz, J. G. de Vries, *Chem. Commun.* **2004**, 1559–1563; e) R. Narayanan, M. A. El-Sayad, *J. Phys. Chem. B* **2005**, *109*, 12663–12676; f) J. G. de Vries, *Dalton Trans.* **2006**, 421–429 and references cited therein; g) N. T. S. Phan, M. V. Der Sluys, C. W. Jones, *Adv. Synth. Catal.* **2006**, *348*, 609–679; h) A. V. Gaikward, A. Holuigue, M. B. Thathager, J. E. ten Elshof, G. Rothenberg, *Chem. Eur. J.* **2007**, *13*, 6908–6913; i) L. Durán-Pachón, G. Rothenberg, *Appl. Organomet. Chem.* **2008**, *22*, 288–299; j) D. Astruc (Ed.), *Nanoparticles and Catalysis*, Wiley-VCH, Weinheim, **2008**.
- [3] D. Astruc, F. Lu, J. R. Aranzaes, *Angew. Chem. Int. Ed.* **2005**, *44*, 7852–7872.
- [4] D. Tselikhovsky, J. Blum, *Eur. J. Org. Chem.* **2008**, 2417–2422.
- [5] a) V. I. Nefedov, Ya. V. Salyn, I. I. Moiseev, A. P. Sadovskii, A. S. Berenbljum, A. G. Knizhnik, S. L. Mund, *Inorg. Chim. Acta* **1979**, *35*, L343–L344; b) R. J. Bird, P. Swift, *J. Electron. Spect. Relat. Phenom.* **1980**, *21*, 227–240.
- [6] T. Ito, F. Marumo, Y. Saito, *Acta Crystallogr., Sect. B: Struct. Sci.* **1971**, *27*, 1062–1066.
- [7] M. Sabat, M. Jezawska, H. Kozlowski, *Inorg. Chim. Acta* **1979**, *37*, L511–L512.
- [8] V. I. Krovtsov, T. G. Nikiforova, *Russ. J. Electrochem.* **2002**, *38*, 972–980.
- [9] a) A. Tressaud, S. Khairoun, H. Touhara, N. Z. Watanabe, Z. *Anorg. Allg. Chem.* **1986**, *540*, 291–299; b) J. Z. Shyu, K. Otto, W. L. H. Watkins, G. W. Graham, R. K. Belitz, H. S. Gandhi, *J. Catal.* **1988**, *114*, 23–33.
- [10] K. S. Kim, A. F. Gossman, N. Winograd, *Anal. Chem.* **1974**, *46*, 197–200.
- [11] M. T. Reetz, E. Westermann, R. Lohmer, G. Lohmer, *Tetrahedron Lett.* **1998**, *39*, 8449–8452.
- [12] R. F. Heck, *Org. React.* **1982**, *27*, 345–390.
- [13] N. Miyaoura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457–2483.
- [14] A. H. M. de Vries, J. M. C. A. Mulders, J. H. M. Mommers, H. J. W. Henderickx, J. G. de Vries, *Org. Lett.* **2003**, *5*, 3285–3288.
- [15] W. A. Herrmann, C. Brossmer, K. Öfele, C. P. Reisinger, T. Priemeier, M. Beller, H. Fischer, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1844–1847.
- [16] R. Abu-Reziq, M. Shenglof, L. Penn, T. Cohen, J. Blum, *J. Mol. Catal. A* **2008**, *290*, 30–34.

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