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Catalysis of C–C Cross-Coupling Reactions in Aqueous Solvent by Bis- and Tris(ferrocenyltriazolylmethyl)arene–β-Cyclodextrin-Stabilized Pd^0 Nanoparticles

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Keywords: Cyclodextrins / Nanoparticles / Palladium / Heterogeneous catalysis / C–C coupling / Click chemistry / Sandwich complexes

Mono-, bis-, and tris(4-ferrocenyl-1,2,3-triazolylmethyl)arene–β-cyclodextrin adducts have been used to prepare new Pd^0 nanoparticle (PdNP) catalysts for C–C cross-coupling reactions in EtOH/H_2O. The results show that these catalysts work well in Miyaura–Suzuki and Heck reactions with iodoarenes at 25 and 80 °C, respectively, with turnover numbers (TONs) of up to 31000 for standard Miyaura–Suzuki reactions of PhI when 10 ppm of the Pd catalyst (5 nm PdNPs) were used. The results show the benefit for PdNP catalysis of encapsulating hydrophobic catalytic systems between peripheral water-solubilizing cyclodextrins as bolamphiphile-like materials because the open monoferrocenyltriazolylmethylbenzene system shows a considerably reduced catalytic efficiency compared with bis- and tris(4-ferrocenyl-1,2,3-triazolylmethyl)arene–β-cyclodextrin adducts.

Introduction

Palladium is the most frequently used transition metal in catalysis,[1] especially for C–C cross-coupling reactions,[2] among which the Heck[3] and Miyaura–Suzuki[4] reactions are possibly the most useful. Metal nanoparticles (NPs) have appeared as a very promising approach to efficient catalysis under mild, environmentally benign conditions because of their large surface-to-volume ratio.[5] PdNPs[6] stabilized by polymers,[7] dendrimers,[8] or cyclodextrins (CDs)[9] have largely been used to catalyze C–C cross-coupling reactions in water, in particular the Miyaura–Suzuki,[10a,10b] Sonogashira,[10] and Heck reactions.[10a,10b] A recent review has summarized the applications of PdNPs as catalytic precursors in organic synthesis.[11]

Cyclodextrins,[12] a series of natural cyclic oligosaccharides composed of several D-glucopyranose residues joined by α-1,4 linkages, have commonly been used as supramolecular tools[13,14] in the synthesis and stabilization of transition-metal NPs for homogeneous,[10c,10d] heterogeneous,[14] or biphasic[15] catalysis. Indeed, cyclodextrins are a class of derivatives of choice in green chemistry[13] as a result of their hydrophilicity and their ability to encapsulate hydrophobic organic and organometallic substrates in their hydrophobic interior cavity. The hydrophilic hydroxy groups at the surface of cyclodextrins have often been modified by functional groups such as thiolates,[9] sulfobutyl ether,[16a] cholesterol,[16c] hydroxypropyl,[17a] alkyl, and poly(ethylene oxide) chains.[18] These functionalities have been used to stabilize catalytically active nanoparticles[13] as well as for applications in self-assembly[19a] and drug delivery.[19b] The hydrophobic interior cavity of CDs permits their use as hosts to accommodate a wide range of organic or lipophilic guest molecules.[16] The main driving forces of the host–guest inclusion complexes are indeed hydrophobic and van der Waals interactions, the release of CD ring strain, changes in solvent surface tensions, and hydrogen bonding with CD hydroxy groups.[20]

The inclusion of ferrocene by β-cyclodextrin was first described in 1975.[21] The stability of ferrocene and the ferrocenyl (Fc) group in aqueous and aerobic media, the accessibility of a large variety of derivatives, the lack of toxicity, and favorable redox recognition[22] and electrochemical properties[23] have made ferrocene and its derivatives very popular molecules for biological applications as sensors and drugs involving conjugation with biomolecules. Ferrocene and Fc derivatives are well known to be good guests for β-CD, forming relatively stable 1:1 complexes in water by the penetration of Fc into the internal hydrophobic cavity of the β-CD host.[9,24] Therefore stable and hydrophilic β-CD–Fc host–guest assemblies have been used to prepare and stabilize metal NPs for catalysis in aqueous solvents.[18] Kaifer and co-workers showed that the catalytic activity of

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β-CD-modified PdNPs could be tuned through host–guest binding interactions.[9] These authors used β-CD-capped PdNPs for the catalysis of the Miyaura–Suzuki reaction.[25] Xue et al. prepared β-CD-capped PdNPs to catalyze Sonogashira reactions.[10c,10d] Senra and co-workers used hydroxypropyl α-CD-capped PdNPs for efficient C–C coupling in water.[17] Monflier and co-workers have chemically modified CDs to generate carbon-supported RuNPs for application in gas-phase hydrogenation.[26]

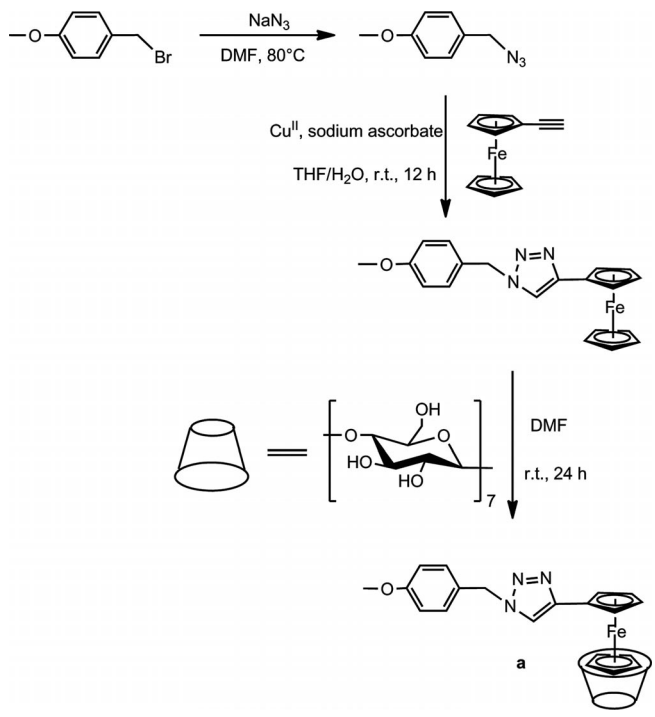
Our research group has stabilized PdNPs,[27] PtNPs,[28] and AuNPs[29] by the coordination of Pd^{II}, Pt^{II}, and Au^{III} with the 1,2,3-triazolyl heterocyclic ligands of "click" dendrimers[27–29] and polymers[30] followed by reduction to the metal(0) species. In the case of PdNPs, this procedure has been applied to the catalysis of olefin hydrogenation and Miyaura–Suzuki reactions.[27,28,30] When these nanomaterials were functionalized by sulfonate groups, the reactions could also be performed in aqueous media containing ethanol.[30] We are now examining more simple, rather small "clicked" molecules containing ferrocenyl-1,2,3-triazolyl groups. The idea was two-fold: 1) To use the triazolyl groups as ligands again for Pd^{II}, which would also involve a weak stabilization of the PdNPs formed by the reduction of Pd^{II}, and 2) to use the ferrocenyl groups to form host–guest complexes with β-CD that would solubilize the catalytic materials in an aqueous medium.

The shapes of the molecular materials with two or three ferrocenyl termini were designed with a view to form bolamphiphile-like[31] materials upon terminal β-CD encapsulation. The syntheses of these materials and their catalytic activities in Miyaura–Suzuki and Heck reactions in EtOH/H_2O (1:1) are described herein.

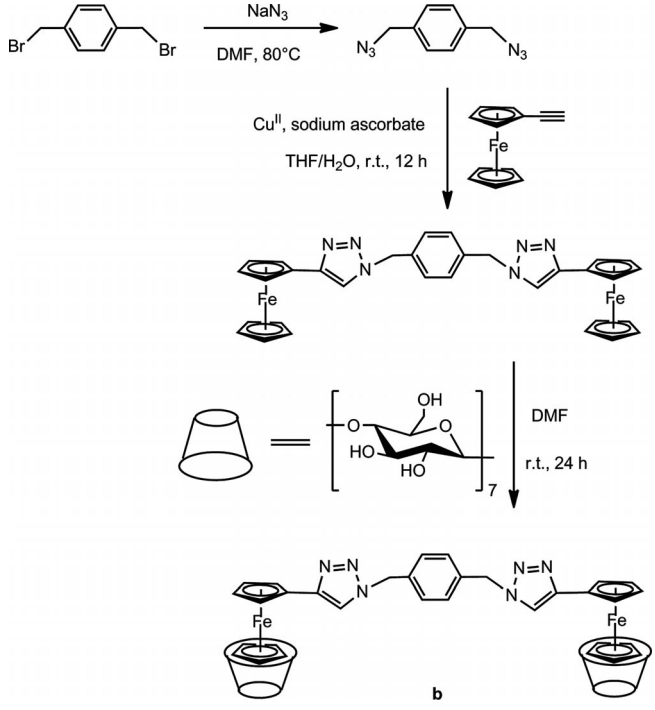
Result and Discussion

Preparation of the Ferrocenyl-1,2,3-triazolylmethyl–β-Cyclodextrin Derivatives

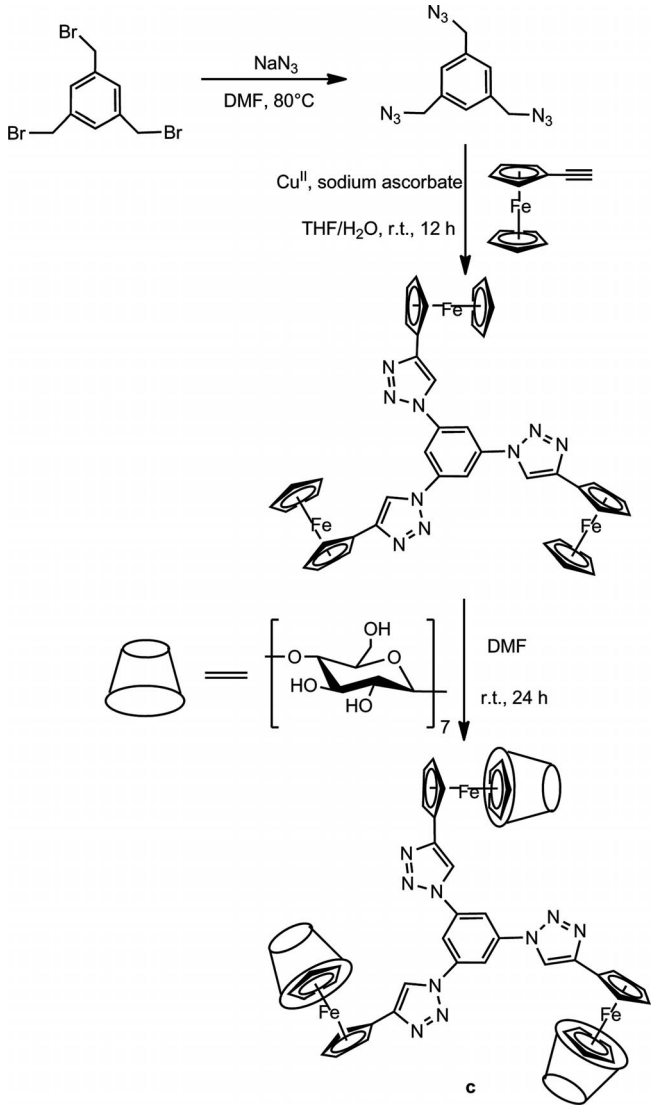
We synthesized three (ferrocenyl-1,2,3-triazolylmethyl)arene derivatives by the reactions of mono-, 1,4-bis-, and 1,3,5-tris(azidomethyl)benzene derivatives and ethynylferrocene according to the copper-catalyzed alkyne azide (CuAAC) "click" reaction.[32] Then, each of these compounds was dissolved together with a slight excess of β-cyclodextrin per ferrocenyl group (β-CD/Fc = 1.1) in DMF and the orange mixtures were stirred at room temperature for 24 h to ensure encapsulation of the peripheral ferrocenyl groups by β-cyclodextrins.[25] After removing the DMF solvent from this orange solution, pale-yellow powders of (ferrocenyl-1,2,3-triazolylmethyl)arene–β-CD derivatives were obtained (Schemes 1–3). The excess β-CD was removed by washing with dichloromethane (DCM). The 1:1 ferrocenyltriazole/β-CD stoichiometry was proven by integration of the corresponding ^1H NMR signals (see the Supporting Information) to contain equal amounts of ferrocenyl groups and β-CD. These compounds are soluble in water, unlike the starting (ferrocenyl-1,2,3-triazolylmethyl)arene derivatives.



Scheme 1. Synthesis of 4-methoxy-1-(4-ferrocenyl-1,2,3-triazolylmethyl)benzene–β-cyclodextrin (**a**).



Scheme 2. Synthesis of *p*-bis(4-ferrocenyl-1,2,3-triazolylmethyl)benzene–β-cyclodextrin (**b**).



Scheme 3. Synthesis of 1,3,5-tris(4-ferrocenyl-1,2,3-triazolylmethyl)benzene–β-cyclodextrin (**c**).

Preparation and Characterization of the New Supported PdNP Catalysts

The supported PdNP materials were prepared in water at room temperature under nitrogen by adding the brown-orange aqueous solution of $K_2[PdCl_4]$ (1 mg/mL) dropwise to an aqueous solution of β-CD-encapsulated ferrocenylarene derivative followed by reduction using $NaBH_4$ under vigorous stirring. The orange solution turned black, which indicated the formation of PdNPs (Scheme 4). These freshly prepared PdNP materials were used for the catalysis of C–C coupling reactions. Characterization by TEM (see the Supporting Information, pp. S8–S9) revealed the formation of small PdNPs of the order of 5–6 nm in addition to large aggregates. The PdNPs also slowly decomposed to Pd black, which is not catalytically active at room temp. The observation of aggregates by TEM is thus presumably an intermediate stage in the formation of Pd black. Thus, the catalyst could not be recycled after workup. The only way to reuse the catalyst was to reload the initial medium with substrates, which leads to a slight decrease in catalytic activity (see below). Although this is a drawback, these catalysts are efficient when used fresh (or reloaded) in extremely small amounts (see below).

Catalysis of the C–C Cross-Coupling Reactions

Miyaura–Suzuki Reactions

Comparison of Various Reactants

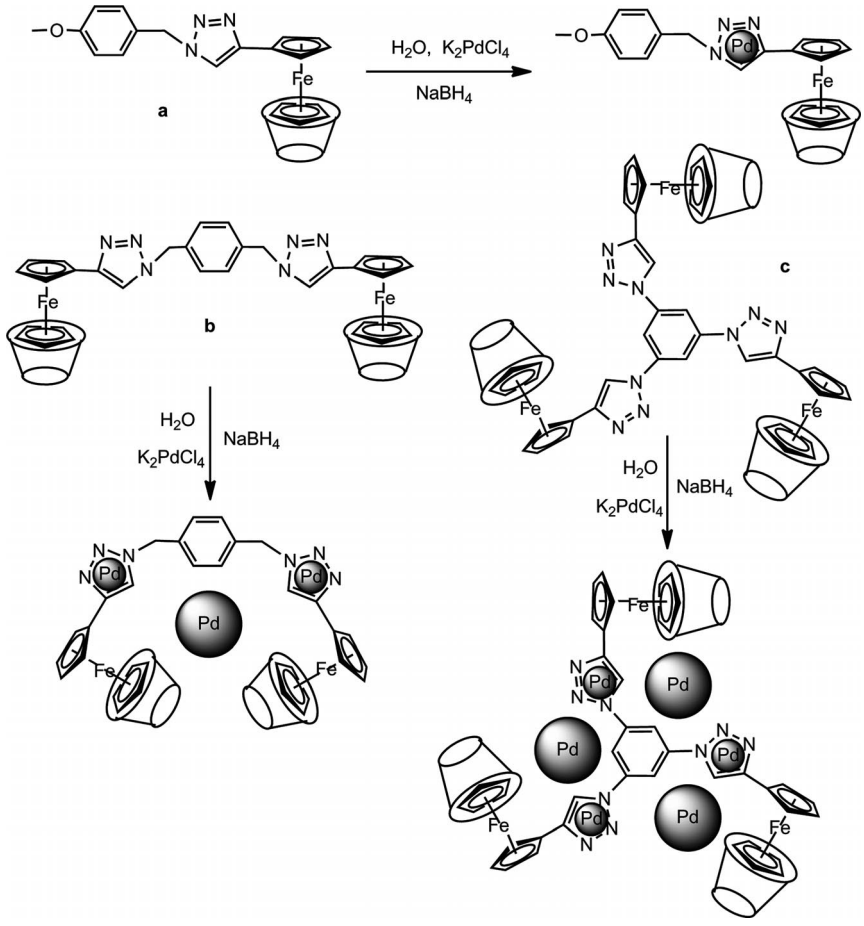
Two iodoarenes (iodobenzene and 4-iodoanisole) and bromobenzene were used in Miyaura–Suzuki reactions with four boronic acids (see Table 1 and Table 2). The catalytic reaction of iodobenzene worked much better than with bromobenzene, as expected. Comparison of various haloarenes revealed that the catalytic reaction was less efficient when the arene was substituted by electron-donating groups, such as methoxy. This is expected because classically the oxidative addition step from Pd^{II} is slowed in the presence of such a substituent. Thus, in the reactions of iodobenzene with various boronic acids, the Miyaura–Suzuki reaction worked well even with a very small quantity of Pd (0.001 mol-%, i.e., 10 ppm), but in the case of 4-iodoanisole, a higher load of catalyst was needed to obtain a quantitative yield. In the case of bromobenzene, the yield was 54% at 25 °C after 72 h (Table 1, entry 14).

Influence of the Amount of Solvent on the Catalytic Efficiency

Intriguingly, the amount of solvent in the system played an important role in the catalysis. When 1 mol-% of Pd per haloarene was used with $c(Pd) = 2.8 \times 10^{-4}$ mol/L, the yield of the Miyaura–Suzuki reaction was 76%. When the system was diluted to $c(Pd) = 1.4 \times 10^{-4}$ mol/L, 99% of the product was obtained (Table 2, entry 1). With $c(Pd) = 1.4 \times 10^{-4}$ mol/L and 0.1 mol-% of Pd/haloarene, the yield was 99.5%. In the case of 0.01 mol-% Pd/haloarene (reaction carried out for 48 h at room temp.), if $c(Pd) = 1.4 \times 10^{-5}$ mol/L, the yield was 10%, but with $c(Pd) = 2.8 \times 10^{-5}$ mol/L, the yield was 98.4% (Table 2, entry 3). In the case of 0.001% Pd/haloarene (reaction carried out for 72 h at room temp.), $c(Pd) = 0.93 \times 10^{-5}$, 0.7×10^{-5}, or 0.28×10^{-5}mol/L, the yields were 2.7, 19.4, or 3.4%, respectively (Table 2, entry 4). Thus, it appears that the yields increase upon dilution to a rather large extent.

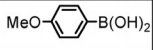
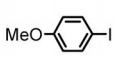
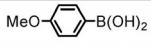
Study of the Air Sensitivity and Catalysis in Water without Co-Solvent

To examine the air sensitivity of the triazolylferrocenyl–CD-stabilized Pd catalyst, the reaction (Table 1, entry 2) was also performed in air under the same conditions for comparison; the yield was 91.4%, which is a little lower than that under nitrogen (99%). This means that the catalytic system is not very sensitive to air during the Miyaura–Suzuki reactions. The same reaction was chosen to carry out the reaction in pure water and the yield was 8%, much



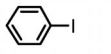
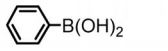
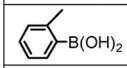
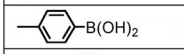
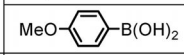
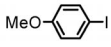
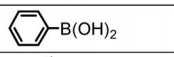
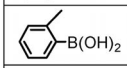
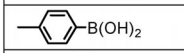
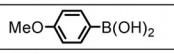
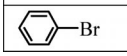
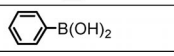
Scheme 4. Preparation of PdNP materials with **a**, **b**, and **c**. The positioning and numbers of the PdNPs shown in the scheme are arbitrary.

Table 1. Results of the Miyaura–Suzuki reactions catalyzed by the PdNP catalyst supported by the bis-triazolylferrocenyl–CD (**b**).

Haloarene[a]	Arylboronic acid	Entry	*c*(Pd) (mol/L)	% Pd[b]	*T* (°C)	*t* (h)	Yield[c] (%)	TON
		1	1.39×10^{-4}	1	25	24	98	98
		2	1.39×10^{-4}	0.1	25	24	99	990
		3	2.78×10^{-5}	0.01	25	48	99	9900
		4	6.95×10^{-6}	0.001	25	72	31	31000
		5	2.78×10^{-5}	0.01	25	48	98	9800
		6	2.78×10^{-5}	0.01	25	48	74	7400
		7	0.7×10^{-4}	0.1	25	24	90	900
		8	1.39×10^{-5}	0.1	25	48	35	350
		9	1.39×10^{-4}	1	25	24	100	100
		10	1.39×10^{-4}	1	25	24	100	100
		11	1.39×10^{-4}	1	25	24	80	80
		12	1.39×10^{-4}	1	25	24	100	100
		14	4.63×10^{-4}	1	25	72	54	54

[a] In the case of iodoarene substrates, the mol ratio was $n_{\text{iodoarene}}/n_{\text{boronic acid}}/n_{K_3PO_4}$ = 1:1.5:2. In the case of bromoarene substrates, the mol ratio was $n_{\text{bromoarene}}/n_{\text{boronic acid}}/n_{K_3PO_4}$ = 1:3:6. The reaction was carried out in EtOH/H_2O (1:1). [b] Mol ratio of Pd per haloarene. [c] GC yield.

Table 2. Results of the Miyaura–Suzuki reactions catalyzed by the PdNP catalyst supported by the tris-ferrocenyl–CD material (**c**).

Haloarene[a]	Arylboronic acid	Entry	*c*(Pd) (mol/L)	% Pd[b]	*T* (°C)	*t* (h)	Yield[c] (%)	TON
		1	1.4×10^{-4}	1	25	24	99	99
		2	1.4×10^{-4}	0.1	25	24	99	990
		3	2.8×10^{-5}	0.01	25	48	98	9800
		4	0.7×10^{-5}	0.001	25	72	19	19000
		5	2.8×10^{-5}	0.01	25	48	96	9600
		6	2.8×10^{-5}	0.01	25	48	93	9300
		7	1.4×10^{-4}	0.1	25	24	91	910
		8	1.4×10^{-4}	1	25	24	99.7	99.7
		9	1.4×10^{-4}	1	25	24	95	95
		10	1.4×10^{-4}	1	25	24	99	99
		11	1.4×10^{-4}	1	25	24	99	99
		12	4.63×10^{-4}	2	25	72	100[d]	50

[a] In the case of iodoarene substrates, the mol ratio was $n_{iodoarene}/n_{boronic\ acid}/n_{K_3PO_4}$ = 1:1.5:2. In the case of bromoarene substrates, the mol ratio was $n_{bromoarene}/n_{boronic\ acid}/n_{K_3PO_4}$ = 1:3:6. The reaction was carried out in EtOH/H_2O (1:1). [b] Mol ratio of Pd per haloarene. [c] GC yield. [d] The result obtained with a mol ratio of Pd/CD = 2. All the other results were obtained with a mol ratio of Pd/CD = 1.

lower than in EtOH/H_2O (1:1); with the solvent ratio EtOH/H_2O (1:4), the yield was 73%. The reactants are soluble in EtOH and the homogeneous catalysis could be carried out much more easily in EtOH/H_2O than when the reactants are not soluble (H_2O only). In conclusion, the best conditions for the catalysis are in EtOH/H_2O (1:1) at room temp. under N_2.

Study of the Role of Triazolylferrocenyl–Cyclodextrin Complexes in the Catalytic Efficiency

To determine whether the (ferrocenyl-1,2,3-triazolylmethyl)arene–β-cyclodextrin plays a role in the efficiency of the palladium catalysis, an aqueous solution containing only $K_2[PdCl_4]$ was treated directly with $NaBH_4$ and the classic reaction of Table 1, entry 1, was carried out under nitrogen in EtOH/H_2O (1:1) at room temp. for 24 h. A 13% yield of product was obtained, much lower than that obtained with the triazolylferrocenyl–cyclodextrin complex (98%; Table 1, entry 1). Thus, the triazolylferrocenyl–cyclodextrin complex plays an important role in stabilizing PdNPs in the catalysis. It is probable that, as usual,[7] the heteroatoms (in this case, those of the triazolyl groups of the support) play the role of weak supramolecular stabilizers of the PdNP material. Note that the possibility of stabilization of PdNPs by π interaction between the ligand and the metallic (PdNP) surface has been suggested.[33]

Study of the Activity of the Catalyst upon Recharging the Substrates

To study the activity of the PdNP catalyst, the reaction in Table 2, entry 1 was taken as an example. After each 24 h, the Schlenk flask was recharged with reactants (this procedure was carried out twice) and the yield was reduced from 99% for the first run to 88% for the second run, and to 79% for the third run. Thus, after two recycles, the PdNP catalyst is somewhat less active.

Study of the Molar Relationship Between the Triazolylferrocenyl–β-CD Complex and Palladium

The PdNP catalysts were always prepared with a stoichiometric (1:1) amount of triazolylferrocenyl–CD per Pd atom before the catalysis. When the mol ratio of Pd/CD was increased to two (by decreasing the amount of CD), however, some interesting results were obtained. The reaction in Table 2, entry 12, is an example in which 2 mol-% Pd/bromobenzene was used for catalysis. With the mol ratio n_{Pd}/n_{CD} = 2, the yield was 100%, much higher than that obtained with n_{Pd}/n_{CD} = 1 (yield 27%). This result is the reverse of that noted as an unpublished result by Senra and co-workers.[17] When the mol ratio n_{CD}/n_{Pd} = 2 was used for the same reaction, the product was obtained in a yield of 18%.

*Comparison of the Catalytic Efficiency of the Mono-, Bis-, and Tris(ferrocenyl-1,2,3-triazolylmethyl)benzene–β-Cyclodextrins **a**, **b** and **c***

On the basis of the catalytic results presented in Tables 1 and 2 there is no significant difference between **b** and **c**, but **a** is not as effective as the two other supports. When the PdNP catalyst for the Miyaura–Suzuki reaction (entries 1 and 9 of Table 2 are taken as examples) was prepared with **a**, the yields were 54 and 68%, respectively, which is much lower than in the presence of **b** (98 and 100%, respectively) and **c** (99 and 95%, respectively). How does the ferrocenyl–β-CD support stabilize the PdNP catalyst? In the cases of **b** and **c**, there are two and three branches, respectively, that

Table 3. Heck reactions catalyzed by PdNPs stabilized by **b**.

Haloarene[a]		Entry	*t* (h)	*T* (°C)	Yield[b] (%)	TON
		1	24	80	99.4[c]	99.4
		2	24	80	92.5[c]	92.5

[a] 1% of Pd per haloarene; molar ratio: $n_{haloarene}/n_{styrene}/n_{K_2CO_3}$ = 1:3:6. [b] GC yield. [c] Result obtained for a Pd/CD molar ratio of 2.

Table 4. Heck reactions catalyzed by PdNPs stabilized by **c**.

Haloarene[a]		Entry	*t* (h)	*T* (°C)	Yield[b] (%)	TON
		1	24	80	79	79
			48	80	91	91
		2	24	80	70.8	70.8
			48	80	91	91

[a] 1% of Pd per haloarene; molar ratio: $n_{halogeno-arene}/n_{styrene}/n_{K_2CO_3}$ = 1:3:6. [b] GC yield.

can encapsulate the PdNP catalyst and reactants, whereas **a** has only one β-CD end (Scheme 4). This indicates that the catalytic reaction takes place between the β-CD termini and the support framework.

Heck Reaction

The Heck reactions between styrene and haloarenes were also catalyzed by 1% PdNP stabilized by **b** and **c**; the results are shown in Table 3 and Table 4. The results were obtained with Pd/CD molar ratios of 2 and 1, respectively. In the case of **b**, the yield was much more sensitive to the Pd/CD ratio than in the case of **c**, for example, in the reaction in Table 3, entry 1, the yield was 0% with a molar ratio of Pd/CD of 1. This dramatic difference in yield might possibly be caused by the fact that the ferrocenyl encapsulation by β-CD could be somewhat reversible at 80 °C and that the free β-CD in turn would then encapsulate the Pd catalyst, leading to inhibition.

The dramatic difference in the influence of the Pd/CD ratio on the catalytic efficiency between the Miyaura–Suzuki and Heck reactions is presumably due to the large differences in reaction temperatures and mechanisms.

Mechanistic Discussion

The finding of the dramatic increase in yield in the Heck reactions upon decreasing the amount of β-CD parallels that disclosed above for the Miyaura–Suzuki reaction. It is remarkable because it signifies that CD inhibits the catalysis. Because the major function of β-CD is the encapsulation of a rather small species, this catalyst inhibition could mean that the active Pd catalyst is such a small species, that is, a Pd atom or a small cluster of two or three (or very few) ligand-free atoms. This is in line with "homeopathic catalysis", a term first used by Beletskaya and Cheprakov for Heck reactions catalyzed by a minute amount of Pd catalyst.[34–36] We also noted in the study the influence of the amount of Pd catalyst; the yield increases when the catalyst concentration decreases. This negative influence of the precatalyst concentration again argues in favor of this "homeopathic mechanism". A mechanism for the Heck catalysis at high temperature for such a catalytically active Pd catalyst in very small amounts was proposed by de Vries in which atoms leached by a large PdNP precatalyst are caught by the mother PdNP all the more efficiently as the PdNP concentration increases.[2d,36] We have already encountered this situation in dendrimer-stabilized or -encapsulated PdNPs. It is of interest here to note that the triazolyl of the PdNPs is stabilized even with wheel-shaped (pre-dendritic) ferrocenyltriazolyl materials such as **c** and in the bolamphiphile-type[31] compound **b**. The limit has been disclosed here in reducing the scale and branching level of the support, as we note that the catalytic results obtained when only one ferrocenyltriazolyl group is present in the supporting structure **a** are far from being as good as with **b** and **c**.

Conclusions

Three (ferrocenyl-1,2,3-triazolylmethyl)arene–β-cyclodextrin derivatives served as simple supports for the preparation and stabilization of PdNPs. These supported PdNPs catalyze the Miyaura–Suzuki and Heck C–C cross-coupling reactions of iodoarenes, but the bis- and tris-cyclodextrin systems produce much better pre-catalysts than when only one ferrocenyltriazolyl–β-CD branch is present in the support material. This very important difference shows the efficiency of encapsulation of a hydrophobic catalytic system with two or three peripheral water-solubilizing cyclodextrin caps, whereas the open system **a** does not work as well. Although the best catalysts (**b** and **c**) are extremely active with very high TONs at 25 °C with iodoarenes, the other haloarenes are much more difficult or impossible to activate, as is usual with PdNPs under mild conditions.

These very efficient catalysts can be reloaded with substrates, resulting in a slight, progressive decrease in yield.

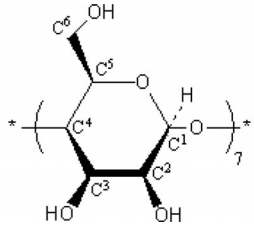
The catalysts cannot be recycled, however, because their amounts in the catalytic reactions are extremely low and also because of the slow formation of Pd black, which is essentially inactive at room temp.

Comparison with molecular catalysts indicates that such PdNP catalysts can be used in considerably smaller amounts than all the molecular catalysts in the Miyaura–Suzuki reactions at room temp., but they are less robust and less efficient than the best molecular catalysts with bromoarenes and chloroarene at high temperatures.

An increase in the catalytic TON of the Miyaura–Suzuki reaction of iodobenzene at 25 °C upon decreasing the amount of PdNP precatalyst used, high efficiency with 10 ppm PdNP in the Miyaura–Suzuki coupling reaction between PhI and $PhB(OH)_2$ under ambient conditions, and inhibition of catalysis by excess β-CD favor the homeopathic mechanism of de Vries in which leaching atoms from the mother precatalyst PdNPs are the active catalysts.[2d]

Experimental Section

General Data: All the solvents (THF, ethanol, and DMF) and chemicals were used as received. ^1H NMR spectra were recorded at 25 °C with a Bruker AC 200 or 300 (200 or 300 MHz) spectrometer. The ^{13}C NMR spectra were obtained in the pulsed FT mode at 50 or 75 MHz with a Bruker AC 200 or 300 spectrometer. All the chemical shifts are reported in parts per million (δ, ppm) with reference to Me_4Si (TMS) for the ^1H and ^{13}C NMR spectra. The IR spectra were recorded with an ATI Mattson Genesis series FT-IR spectrophotometer. The UV absorption and emission spectra were measured with a Perkin–Elmer Lambda 19 UV/Vis spectrometer and Hitachi F-2500 fluorescence spectrophotometer, respectively. Gas chromatography data were recorded on a Hewlett–Packard 5890 Series II gas chromatograph equipped with a Stabilwax (Crossband Carbowax-PEG) column and a flame ionization detector. Helium was used as the carrier gas for all substrates. The injector and detector temperatures were 240 °C. The elemental analyses were performed by the Center of Microanalyses of the CNRS at Lyon Villeurbanne, France. Azidomethylbenzene, *p*-bis(azidomethyl)benzene, and 1,3,5-tris(azidomethyl)benzene were synthesized as in ref.[32] as well as the corresponding "clicked" 4-ferrocenyl-1,2,3-triazolylmethylarene derivatives (see the Supporting Information).



4-Methoxy-1-(4-ferrocenyl-1,2,3-triazolylmethyl)benzene–β-Cyclodextrin: The procedure in reference[10c] was carried out with the following slight small changes. A DMF solution (5 mL) of 4-methoxy-1-(ferrocenyl-1,2,3-triazolylmethyl)benzene (40 mg, 0.107 mmol) was added to a DMF solution (5 mL) of β-CD (132 mg, 0.11 mmol) in a Schlenk flask at room temperature. After stirring for 24 h, the solvent was removed under vacuum and the crude product, 4-methoxy-1-(ferrocenyl-1,2,3-triazolylmethyl)benzene–β-CD (**a**) was isolated and washed with DCM (5 × 20 mL) to yield 0.140 g (87% yield)of the product. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 8.17 (s, 1 H, C*H* of triazole),7.31, 7.0 (d, 4 H, C*H* of Ar), 5.75, 5.73, 5.69 (d, 14 H, C*H* of CD), 5.52 (s, 2 H, Ar-CH_2), 4.84, 4.46 (d and t, 14 H, C*H* of CD), 4.72, 4.30, 4.03 (t, 9 H, C*H* of Cp), 3.75, 3.34 (m, C*H* of CD) ppm. ^{13}C NMR ([D$_6$]-DMSO, 75 MHz): δ = 159.6 (C_q of Ar), 146.0 (C_q of triazole), 129.8 (CH of triazole), 127.7 (C_q of Ar), 114.6 (CH of Ar), 102.4, 82.0 (C-1, C-4 of CD), 76.5 (C_q of Cp), 73.5, 72.9, 72.5 (C-2, C-3, C-5 of CD), 69.7, 68.7, 66.8 (CH of Cp), 60.4 (C-6 of CD), 56.5 (*C*H$_3$O-Ar), 55.6 (*C*H$_2$-triazole) ppm. $C_{171}H_{249}Fe_3N_9O_{105}$ (4278.39): calcd. C 49.37, H 5.95; found C 45.93, H 6.1. Mineral impurities are most probably included.

***p*-Bis(4-ferrocenyl-1,2,3-triazolylmethyl)benzene–β-Cyclodextrin:** The above procedure was extended to *p*-bis(4-ferrocenyl-1,2,3-triazolylmethyl)benzene (30 mg, 0.049 mmol) and β-CD (123 mg, 0.108 mmol) to synthesize *p*-bis(4-ferrocenyl-1,2,3-triazolylmethyl)-benzene–β-CD (**b**). A pale-yellow powder was obtained (131 mg, 93% yield). ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 8.21 (s, 2 H, CH of triazole),7.31 (s, 4 H, CH of Ar), 5.76, 5.74, 5.69 (d, 28 H, CH of CD) 5.59 (s, 4 H, Ar-CH_2), 4.83, 4.47 (d and t, 28 H, CH of CD), 4.70, 4.29, 4.01 (t, 18 H, CH of Cp), 3.63, 3.37 (m, CH of CD) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 146.2 (C_q of triazole), 136.6 (C_q of Ar), 128.6 (CH of triazole), 121.2 (CH of Ar), 102.4, 82.0 (C-1, C-4 of CD), 76.3 (C_q of Cp), 73.5, 72.9, 72.5 (C-2, C-3, C-5 of CD), 69.7, 68.8, 66.8 (CH of Cp), 60.4 (C-6 of CD), 52.9 (*C*H$_2$-triazole) ppm. $C_{116}H_{168}Fe_2N_6O_{70}$ (2878.30): calcd. C 48.41, H 5.88; found C 46.7, H 5.96.

1,3,5-Tris(4-ferrocenyl-1,2,3-triazolylmethyl)benzene–β-Cyclodextrin: The above procedure was extended to 1,3,5-tris(4-ferrocenyl-1,2,3-triazolylmethyl)benzene (50 mg, 0.057 mmol) and β-CD (214 mg, 0.189 mmol) to synthesize 1,3,5-tris(4-ferrocenyl-1,2,3-triazolylmethyl)benzene–β-CD as 230 mg (0.054 mmol, 94% yield) of a pale-yellow powder. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 8.13 (s, 3 H, CH of triazole), 7.20 (s, 3 H, CH of Ar), 5.71, 5.68, 5.65 (d, 42 H, CH of CD), 5.57 (s, 6 H, Ar-CH_2), 4.81, 4.42 (d and t, 42 H, CH of CD), 4.66, 4.27, 4.0 (t, 27 H, CH of Cp), 3.62, 3.31 (m, CH of CD) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 146.2 (C_q of triazole), 137.9 (C_q of Ar), 127.3 (CH of triazole), 121.2 (CH of Ar), 102.4, 82.0 (C-1, C-4 of CD), 76.3 (C_q of Cp), 73.5, 72.9, 72.5 (C-2, C-3, C-5 of CD), 69.7, 68.7, 66.8 (CH of Cp), 60.4 (C-6 of CD), 55.4 (*C*H$_2$-triazole) ppm. $C_{171}H_{249}Fe_3N_9O_{105}$ (4278.39): calcd. C 48.0, H 5.9; found C 46.1, H 6.3.

Preparation of the PdNPs for Catalysis: A yellow solution (2.5 mL) of *p*-bis(4-ferrocenyl-1,2,3-triazolylmethyl)benzene–β-CD (2 mg, 6.95×10^{-4} mmol, 1 equiv.) in EtOH was introduced into a Schlenk flask and then a brown-orange aqueous solution (2.5 mL) of $K_2[PdCl_4]$ (0.45 mg, 13.9×10^{-4} mmol, 2 equiv.) was added dropwise. After stirring for 10 min, $NaBH_4$ (0.1 mg, 27.8×10^{-4} mmol, 4 equiv.) in water (0.01 mL) was added under vigorous stirring and the orange solution turned to the black of PdNPs (Scheme 4).

Miyaura–Suzuki Reactions: In a Schlenk flask containing freshly prepared PdNPs, tribasic potassium phosphate (2 equiv.), phenylboronic acid (1.5 equiv.), haloarene (1 equiv.), and a solution of water/ethanol (1:1, v/v) were successively added. The suspension was stirred under nitrogen. After the reaction time, the reaction mixture was extracted twice with DCM (all the reactants and final product were soluble in DCM) and the organic phase was dried with Na_2SO_4 and filtered through silica gel to remove the black Pd solid before analysis by gas chromatography.

Heck Reactions: In a Schlenk flask containing freshly prepared PdNPs, potassium carbonate (6 equiv.), styrene (3 equiv.), haloar-

ene (1 equiv.), and a solution of water/ethanol (1:1, v/v) were successively added. The suspension was stirred under nitrogen at 80 or 100 °C. After the given reaction time, the reaction mixture was extracted twice with DCM (all reactants and final products were soluble in DCM) and the organic phase was dried with Na_2SO_4 and filtered through silica gel to remove the black PdNPs before analysis by gas chromatography.

Supporting Information (see footnote on the first page of this article): Syntheses of the known precursors, ^1H and ^{13}C NMR spectra of the known ferrocenyl precursors and new products, and the UV/Vis spectra and TEM pictures of the PdNPs.

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[1] a) R. F. Heck, *Palladium Reagents in Organic Synthesis*, Academic Press, New York, **1985**; b) B. Cornils, W. A. Herrmann (Eds.), *Applied Homogeneous Catalysis in Organometallic Chemistry*, Wiley-VCH, Weinheim, Germany, **1996**, vol. 1 and 2; c) D. Astruc, *Organometallic Chemistry and Catalysis*, Springer, Heidelberg, Germany, **2007**, chapter 19.

[2] a) F. Diederich, P. J. Stang (Eds.), *Metal-catalyzed Cross-coupling Reactions*, Wiley-VCH, Weinheim, Germany, **1998**; b) J. Grunes, J. Zhu, G. A. Somorjai, *Chem. Commun.* **2003**, 2257–2260; c) A. de Meijere, F. Diederich (Eds.), *Metal-catalyzed Cross Coupling Reactions*, Wiley-VCH, Weinheim, Germany, **2004**; d) J. G. de Vries, *Dalton Trans.* **2006**, 421–429; e) N. T. S. Phan, M. van der Sluys, C. J. Jones, *Adv. Synth. Catal.* **2006**, *348*, 609–679; f) D. Astruc, *Anal. Bioanal. Chem.* **2011**, *399*, 1811–1815.

[3] R. F. Heck, *Acc. Chem. Res.* **1979**, *12*, 146–151; A. B. Dounay, L. E. Overman, *Chem. Rev.* **2003**, *103*, 2945–2964.

[4] a) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457–2483; b) J. Hassan, M. Sévignon, C. Gozzi, E. Schulz, M. Lemaire, *Chem. Rev.* **2002**, *102*, 1359–1469; c) A. Suzuki, in: *Modern Arene Chemistry* (Ed.: D. Astruc), Wiley-VCH, Weinheim, **2002**, pp. 53–106.

[5] a) M. T. Reetz, W. Helbig, S. A. Quaiser, in: *Active Metals: Preparation, Characterizations, Applications* (Ed.: A. Fürstner), VCH, Weinheim, Germany, **1996**, p. 279; A. Roucoux, J. Schulz, H. Patin, *Chem. Rev.* **2002**, *102*, 3757–3778; b) H. Bönnemann, R. Richards, *Synth. Methods Organomet. Inorg. Chem.* **2002**, *10*, 209; c) M. Moreno-Mañas, R. Pleixats, *Acc. Chem. Res.* **2003**, *36*, 638–643; d) D. Astruc, F. Lu, J. Ruiz, D. Astruc, *Angew. Chem.* **2005**, *117*, 8062; *Angew. Chem. Int. Ed.* **2005**, *44*, 7852–7872; e) D. Astruc, *Inorg. Chem.* **2007**, *46*, 1884–1894; f) D. Astruc (Ed.), *Nanoparticles and Catalysis*, Wiley-VCH, Weinheim, Germany, **2008**.

[6] a) L. D. Rapino, F. F. Nord, *J. Am. Chem. Soc.* **1941**, *63*, 2745; b) L. D. Rapino, F. F. Nord, *J. Am. Chem. Soc.* **1941**, *63*, 3268; c) K. E. Kavanagh, F. F. Nord, *J. Am. Chem. Soc.* **1943**, *65*, 2121–2125; d) P. Li, L. Wang, H. Li, *Tetrahedron* **2005**, *61*, 8633–8640; e) J. Athilakshmi, S. Ramanathan, D. K. Chand, *Tetrahedron Lett.* **2008**, *49*, 5286–5288; f) M. B. Thathagar, P. J. Kooyman, R. Boerleider, E. Jansen, C. J. Elsevier, G. Rothenberg, *Adv. Synth. Catal.* **2005**, *347*, 1965–1968; g) M. B. Thathagar, J. E. Elshof, G. Rothenberg, *Angew. Chem.* **2006**, *118*, 2952; *Angew. Chem. Int. Ed.* **2006**, *45*, 2886–2890; h) I.-K. Park, H. A. Recum, S. Jiang, S. H. Pun, *Langmuir* **2006**, *22*, 8478–8484; i) A. V. Gaikwad, G. Rothenberg, *Phys. Chem. Chem. Phys.* **2006**, *8*, 3669–3675.

[7] a) M. V. Seregina, L. M. Bronstein, O. A. Platonova, D. M. Chernyshov, P. M. Valetsky, J. Hartmann, E. A. Wenz, *Chem. Mater.* **1997**, *9*, 923–931; b) T. Yonezawa, N. Toshima, *Polymer-Stabilized Metal Nanoparticles: Preparation, Characterization and Applications*, in: *Advanced Functional Molecules and Polymers* (Ed.: H. S. Nalwa), OPA, Amsterdam, **2001**, vol. 2, pp. 65–86; c) L. M. Bronstein, in: *Encyclopedia of Nanoscience and Nanotechnology* (Ed.: H. S. Nalwa), American Scientific Publishers, Los Angeles, **2004**, vol. 7; d) C. Ornelas, A. K. Diallo, J. Ruiz, D. Astruc, *Adv. Synth. Catal.* **2009**, *351*, 2147–2154; e) A. Ohtaka, Y. Tamaki, Y. Igawa, K. Egami, O. Shimomura, R. Nomura, *Tetrahedron* **2010**, *66*, 5642–5646; f) T. Teratani, A. Ohtaka, T. Kawashima, O. Shimomura, R. Nomura, *Synlett* **2010**, *15*, 2271–2274.

[8] a) R. M. Crooks, M. Zhao, L. Sun, V. Chechik, L. K. Yeung, *Acc. Chem. Res.* **2001**, *34*, 181–190; b) L. Sun, R. M. Crooks, V. Chechik, *Chem. Commun.* **2001**, 359–360; c) E. H. Rahim, F. S. Kamounah, J. Frederiksen, J. B. Christensen, *Nano Lett.* **2001**, *1*, 499–501; d) T. Imaoka, H. Horiguchi, K. Yamamoto, *J. Am. Chem. Soc.* **2003**, *125*, 340–341; e) R. W. J. Scott, O. M. Wilson, R. M. Crooks, *J. Phys. Chem. B* **2005**, *109*, 692–704.

[9] J. Liu, J. Alvarez, W. Ong, E. Román, A. E. Kaifer, *Langmuir* **2001**, *17*, 6762–6764.

[10] a) E. H. Rahim, F. S. Kamounah, J. Frederiksen, J. B. Christensen, *Nano Lett.* **2001**, *1*, 499–501; b) G. Blay, I. Fernandez, A. Monlen, M. C. Muñoz, J. R. Pedro, C. Vila, *Adv. Synth. Catal.* **2009**, *351*, 2433–2440; c) C. Xue, K. Palaniappan, G. Arumugam, S. A. Hackney, J. Liu, H. Liu, *Catal. Lett.* **2007**, *116*, 94–100; d) T. Matsue, D. H. Evans, T. Osa, N. Kobayashi, *J. Am. Chem. Soc.* **1985**, *107*, 3411–3417; e) P. Li, L. Wang, H. Li, *Tetrahedron* **2005**, *61*, 8633–8640.

[11] I. Favier, D. Madec, E. Teuma, M. Gómez, *Curr. Org. Chem.* **2011**, *15*, 3127–3174.

[12] J. Szejtli, *Chem. Rev.* **1998**, *98*, 1743–1754; M. V. Rekharsky, Y. Inoue, *Chem. Rev.* **1998**, *98*, 1875–1918.

[13] F. Hapiot, S. Tilloy, E. Monflier, *Chem. Rev.* **2006**, *106*, 767–781.

[14] a) F. Hapiot, A. Ponchel, S. Tilloy, E. Monflier, *C. R. Chim.* **2011**, *14*, 149–166; b) F. Wyrwalskia, B. Légera, C. Lancelota, A. Roucoux, E. Monflier, A. Ponchel, *Applied Catalysis A: General* **2011**, *391*, 334–341.

[15] L. Yin, J. Liebscher, *Chem. Rev.* **2007**, *107*, 133–173.

[16] a) F. Shang, J. D. Glennon, J. H. T. Luong, *J. Phys. Chem. C* **2008**, *112*, 20258–20263; b) A. Harada, M. Okada, J. Li, M. Kamachi, *Macromolecules* **1995**, *28*, 8406–8411; c) F. Manakker, M. Pot, T. Vermonden, C. F. Nostrum, W. E. Hennink, *Macromolecules* **2008**, *41*, 1766–1773; d) L. C. Cesteros, C. A. Ramírez, A. Peciña, I. Katime, *Macromol. Chem. Phys.* **2007**, *208*, 1764–1772; e) L. X. Song, L. Bai, M. X. Xu, J. He, S. Z. Pan, *Coord. Chem. Rev.* **2009**, *253*, 1276–1284; f) J. Wu, H. He, C. Gao, *Macromolecules* **2010**, *43*, 2252–2260.

[17] a) J. D. Senra, L. F. B. Malta, A. L. F. Souza, L. C. S. Aguiar, O. A. C. Antunes, *Adv. Synth. Catal.* **2008**, *350*, 2551–2558; b) J. D. Senra, L. F. B. Malta, M. E. H. M. Costa, R. C. Michel, L. C. S. Aguiar, A. B. C. Simas, O. A. C. Antunes, *Adv. Synth. Catal.* **2009**, *351*, 2411–2422.

[18] a) J. Liu, R. Xu, A. E. Kaifer, *Langmuir* **1998**, *14*, 7337–7339; b) J. Liu, W. Ong, E. Román, M. J. Lynn, A. E. Kaifer, *Langmuir* **2000**, *16*, 3000–3002; c) J. Liu, S. Mendoza, E. Román, M. J. Lynn, R. Xu, A. E. Kaifer, *J. Am. Chem. Soc.* **1999**, *121*, 4304–4305; d) N. Badi, P. Guégan, F.-X. Legrand, L. Leclercq, S. Tilloy, E. Monflier, *J. Mol. Catal. A* **2010**, *318*, 8–14.

[19] a) P. Gou, W. Zhu, Z. Shen, *Biomacromolecules* **2010**, *11*, 934–943; b) S. Salmaso, A. Semenzato, S. Bersani, P. Matricardi, F. Rossi, P. Caliceti, *Int. J. Pharm.* **2007**, *345*, 42–50.

[20] a) D. Harries, D. C. Rau, V. A. Parsegian, *J. Am. Chem. Soc.* **2005**, *127*, 2184–2190; b) F. Manakker, T. Vermonden, C. F. Nostrum, W. E. Hennink, *Biomacromolecules* **2009**, *10*, 3157–3175.

[21] B. Siegel, R. Breslow, *J. Am. Chem. Soc.* **1975**, *97*, 6869.

[22] a) P. D. Beer, *Acc. Chem. Res.* **1998**, *31*, 71–80; b) F.-S. Sharon, I. Turyan, D. Mandler, D. Avnir, S. Marx, *Langmuir* **2005**, *21*,

7842–7847; c) D. Astruc, C. Ornelas, J. Ruiz, *Acc. Chem. Res.* **2008**, *41*, 841–856.
[23] L. Cui, S. Gadde, W. Li, E. A. Kaifer, *Langmuir* **2009**, *25*, 13763–13769.
[24] a) J. A. Fernandes, S. Lima, S. S. Braga, P. Ribeiro-Claro, J. E. Rodriguez-Borges, C. Teixeira, M. Pillinger, J. J. C. Teixeira-Dias, S. I. J. Gonçalves, *J. Organomet. Chem.* **2005**, *690*, 4801–4808; b) O. Buriez, J. M. Heldt, E. Labbé, A. Vessières, G. Jaouen, C. Amatore, *Chem. Eur. J.* **2008**, *14*, 8195–8203; c) J. M. Casas-Solvas, E. Ortiz-Salmeron, I. Fernandez, L. Garcia-Fuentes, F. Santoyo-Gonzalez, A. Vargas-Berenguel, *Chem. Eur. J.* **2009**, *15*, 8146–8162.
[25] L. Strimbu, J. Liu, A. E. Kaifer, *Langmuir* **2003**, *19*, 483–485.
[26] M. Ferreira, H. Bricout, A. Sayede, A. Ponchel, S. Fourmentin, S. Tilloy, E. Monflier, *Adv. Synth. Catal.* **2008**, *350*, 609–618.
[27] a) C. Ornelas, J. Ruiz, E. Cloutet, S. Alves, D. Astruc, *Angew. Chem.* **2007**, *119*, 890; *Angew. Chem. Int. Ed.* **2007**, *46*, 872–877; b) C. Ornelas, L. Salmon, J. Ruiz, D. Astruc, *Chem. Commun.* **2007**, 4946–4948; c) A. Diallo, C. Ornelas, J. Ruiz, L. Salmon, D. Astruc, *Angew. Chem.* **2007**, *119*, 8798; *Angew. Chem. Int. Ed.* **2007**, *46*, 8644–8648; d) C. Ornelas, L. Salmon, J. Ruiz, D. Astruc, *Chem. Eur. J.* **2008**, *14*, 50–64.
[28] S. Gatard, L. Liang, L. Salmon, J. Ruiz, D. Astruc, S. Bouquillon, *Tetrahedron Lett.* **2011**, *52*, 1842–1846.
[29] a) E. Boisselier, A. K. Diallo, L. Salmon, J. Ruiz, D. Astruc, *Chem. Commun.* **2008**, 4819–4821; b) E. Boisselier, A. K. Diallo, L. Salmon, C. Ornelas, J. Ruiz, D. Astruc, *J. Am. Chem. Soc.* **2010**, *132*, 2729–2742; c) M.-C. Daniel, D. Astruc, *Chem. Rev.* **2004**, *104*, 293–346.
[30] a) C. Ornelas, J. Ruiz, L. Salmon, D. Astruc, *Adv. Synth. Catal.* **2008**, *350*, 837–845; b) C. Ornelas, A. K. Diallo, J. Ruiz, D. Astruc, *Adv. Synth. Catal.* **2009**, *351*, 2147–2154; c) D. Astruc, L. Liang, A. Rapakousiou, J. Ruiz, *Acc. Chem. Res.* **2012**. ASAP, DOI: 10.1021/ar200235m.
[31] Y. Chen, Y. Liu, R. Guo, *J. Colloid Interface Sci.* **2009**, *336*, 766–772.
[32] S. Badèche, J.-C. Daran, J. Ruiz, D. Astruc, *Inorg. Chem.* **2008**, *47*, 4903–4908.
[33] I. Favier, S. Massou, E. Teuma, K. Philippot, B. Chaudret, M. Gómez, *Chem. Commun.* **2008**, 3296–3298.
[34] I. P. Beletskaya, A. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009–3066.
[35] M. T. Reetz, E. Westermann, *Angew. Chem.* **2000**, *112*, 170; *Angew. Chem. Int. Ed.* **2000**, *39*, 165–168; M. T. Reetz, J. G. de Vries, *Chem. Commun.* **2004**, 1559–1563.
[36] J. G. de Vries, A. H. de Vries, *Eur. J. Org. Chem.* **2003**, 799–804.
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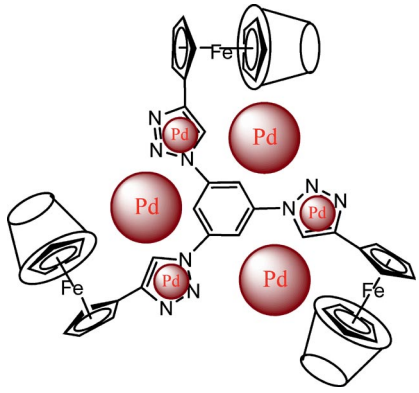
Pd Nanoparticle Catalysts

Water-soluble "clicked" assemblies containing two or three cyclodextrin-encapsulated ferrocenyl termini and 1,2,3-triazolyl internal ligands for Pd^{II} are precursors of stabilized Pd^0 nanoparticle precatalysts for efficient Miyaura–Suzuki and Heck reactions of iodobenzene in water/ethanol under mild conditions.



Keywords: Cyclodextrins / Nanoparticles / Palladium / Heterogeneous catalysis / C–C coupling / Click chemistry / Sandwich complexes

