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"Click" Dendrimer-Stabilized Palladium Nanoparticles as a Green Catalyst Down to Parts per Million for Efficient C−C Cross-Coupling Reactions and Reduction of 4-Nitrophenol

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This article is dedicated to our distinguished colleague and friend Professor Marius Andruh on the occasion of his 60th birthday.

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Abstract: The concept of the nanoreactor valuably contributes to catalytic applications of supramolecular chemistry. Therewith molecular engineering may lead to organic transformations that minimize the amount of metal catalyst to reach the efficiency of enzymatic catalysis. The design of the dendritic nanoreactor proposed here involves hydrophilic triethylene glycol (TEG) termini for solubilization in water and water/ethanol mixed solvents combined with a hydrophobic dendritic interior containing 1,2,3-triazole ligands that provide smooth stabilization of very small (1 to 2 nm) palladium nanoparticles (PdNPs). The PdNPs stabilized in such nanoreactors are extraordinarily active in water/ethanol (1/1) for the catalysis of various carbon-carbon coupling reactions (Suzuki–Miyaura, Heck and Sonogashira) of aryl halides down to sub-ppm levels for the Suzuki–Miyaura coupling of aryl iodides and aryl bromides. The reduction of 4-nitrophenol to 4-aminophenol in water also gives very impressive results. The difference of reactivity between the two distinct dendrimers with, respectively, 27 (G0) and 81 (G1) TEG termini is assigned to the difference of PdNP core size, the smaller G0 PdNP core being more reactive than the G1 PdNP core (1.4 *vs.* 2.7 nm), which is also in agreement with the leaching mechanism.

Keywords: C−C coupling; dendrimers; green chemistry; nanoreactors; palladium nanoparticles (PdNPs)

Introduction

Nanoparticle catalysis has been shown to be a valuable approach to green processes, because it does not involve polluting ligands.[1] In particular, palladium nanoparticles (PdNPs) are one of the most remarkable examples of efficient catalysts for the formation of carbon-carbon bonds.[2] Dendrimers such as PAMAM and PPI are good catalytic supports that are widely used for active metal nanoparticle stabilization. Crooks' group has pioneered catalysis by PAMAM-encapsulated PdNPs[3] and these PdNPs as well as various other polymer- and inorganic substrate-stabilized PdNPs are good catalysts for carbon-carbon bond formation reactions.[1,4] Aryl cross-coupling reactions (Suzuki–Miyaura,[5] Sonogashira,[6] and Heck[1b,6c,7] reactions) have indeed become powerful synthetic methods for preparing biaryl compounds, such as, *inter alia*, natural products, pharmaceuticals and polymers. These cross-coupling reactions also allow a high degree of tolerance for a variety of functional groups. Another important issue is the use of minimum amounts of catalysts, because metal contamination tolerated in organic products does not exceed a few ppm. Along this line only few authors have reported PdNPs that can be active with 10^{-3} Pd mol%.[2,5f,i,j,8] In this context, the stabilization of active PdNPs by "click" dendrimers terminated by triethylene glycol groups has been proposed. These PdNPs seem to be sufficiently stabilized by the triazolyl groups to avoid aggregation and are at the same time labile enough to catalyze the Suzuki–Miyaura reaction of various bromoarenes in an aqueous solvent. The advantage of PEG termini is that PdNPs can be synthesized in water by reduction of K_2PdCl_4 using $NaBH_4$,[8f] which leads to a better activity than that

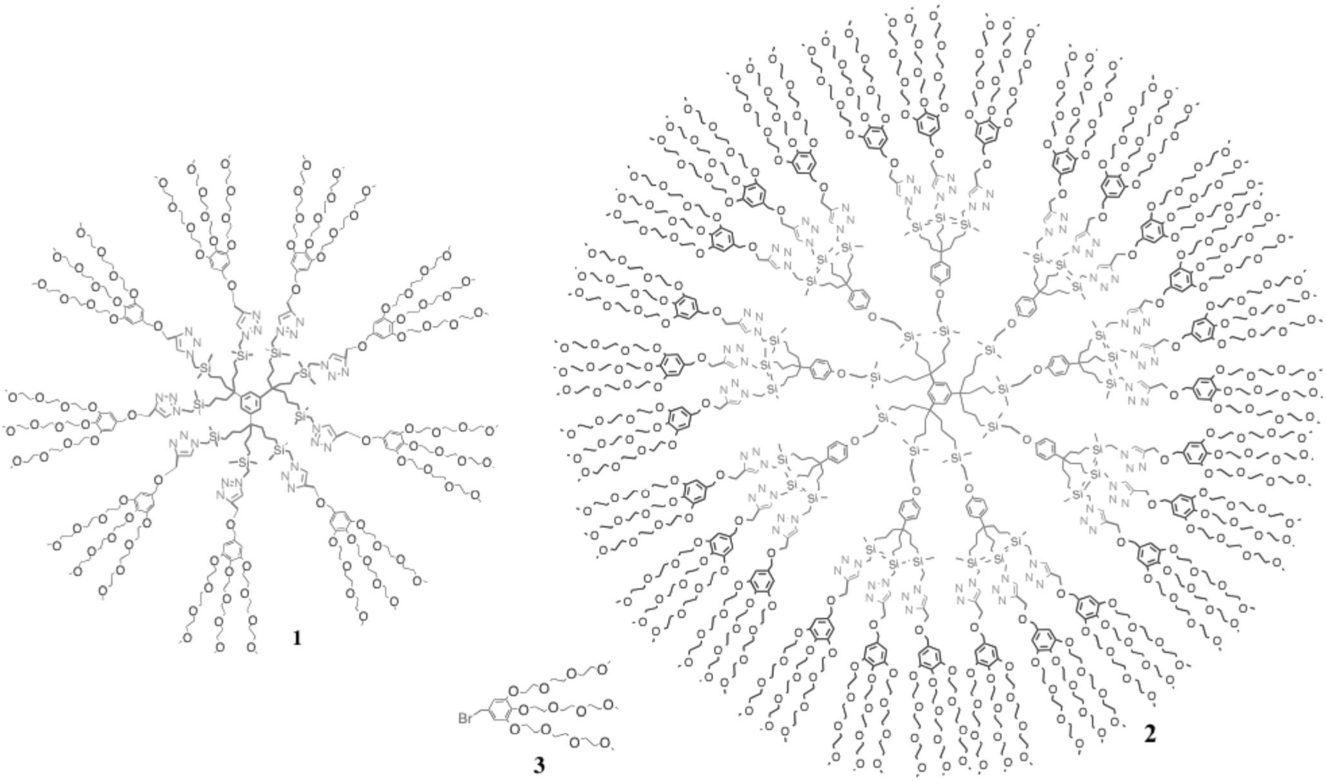


Figure 1. G0-27 TEG **1** dendrimer, G1-81 TEG **2** dendrimer and dendron TEG **3**.

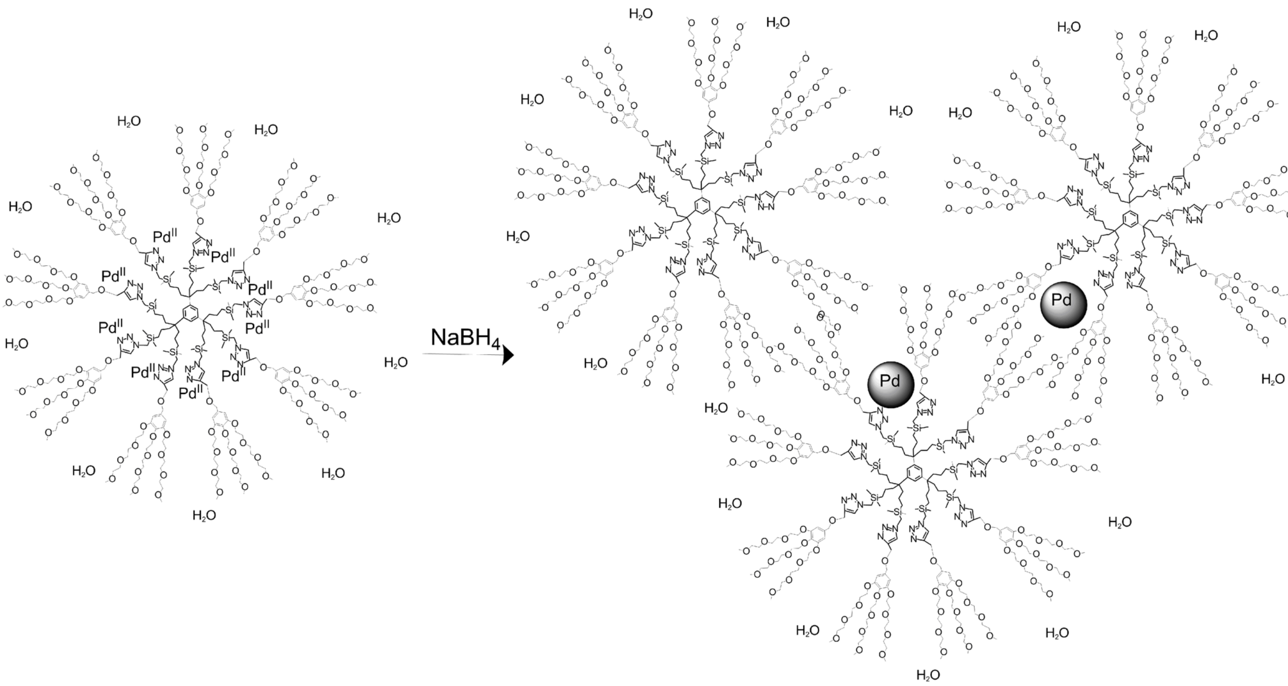
previously observed upon dendrimer stabilization of PdNPs.[8a]

We now report the optimized synthesis and full characterization of "click" dendrimer-stabilized PdNPs and their activity in very low amounts for cross carbon-carbon coupling reactions (Miyaura–Suzuki, Sonogashira and Heck) in "green" media such as water/ethanol (1/1) and for the reduction of 4-nitrophenol to 4-aminophenol in the presence of $NaBH_4$ in water. The latter reaction is also useful because 4-aminophenol is a potential industrial intermediate in the manufacture of many analgesic and antipyretic drugs, anticorrosion lubricants, and hair dying agents.[9]

Results and Discussion

Synthesis and Characterization of the PdNP Catalysts

The water-soluble "click" dendrimers of 0th (G0) and 1st generation (G1), compounds **1** and **2** respectively, have been previously synthesized[8f,10] and are represented in Figure 1. They contain 9 (G0) and 27 (G1) 1,2,3-triazolyl groups linking the dendritic core to Percec-type dendrons[11] and, respectively, 27 and 81 triethylene glycol (TEG) termini. The dendrimer-Pd(II) complexes are synthesized in water by adding to the dendrimer one equiv. K_2PdCl_4 per dendritic triazole group (the optimized stoichiometry towards further PdNP catalysis). The nature of the Pd(II) complexation sites in the dendrimer has been examined by UV-vis. spectroscopy, when K_2PdCl_4 is added to it. In the UV-vis. spectrum of K_2PdCl_4 alone, two characteristic bands are present at 208 nm and at 235 nm. When the UV-vis. spectra are recorded with the G0-TEG dendrimer **1** as a blank, a new band clearly appears at 217 nm upon mixing the aqueous solution of K_2PdCl_4 with that of **1** (after stirring for 5 min) (Figure 2). On the other hand, when Pd(II) is in the presence of the terminal TEG dendron **3** (no dendrimer core and no triazole ring, Figure 1), no band appears. The band observed at 217 nm when K_2PdCl_4 is added to the dendrimer in water has been assigned to a ligand-to-metal charge-transfer (LMCT) transition of Pd(II). It is associated to the complexation of the metal ions to the interior triazole of **1**. In Crooks' reports, a band at 225 nm has already been associated to the complexation of Pd(II) to the interior tertiary amine of the PAMAM dendrimer.[3a,c] The UV-vis. spectrum of the mixture of K_2PdCl_4 and **3** does not correspond to the UV-vis. spectrum of the mixture of K_2PdCl_4 with **1**. In particular, no band is observed at 217 nm in the mixture of K_2PdCl_4 with **3**. These experiments show the intradendritic complexation of Pd(II) at the triazole sites of **1**, and they also indicate that there is no strong Pd(II) complexation of the terminal TEG groups. The importance of the triazolyl



(1)

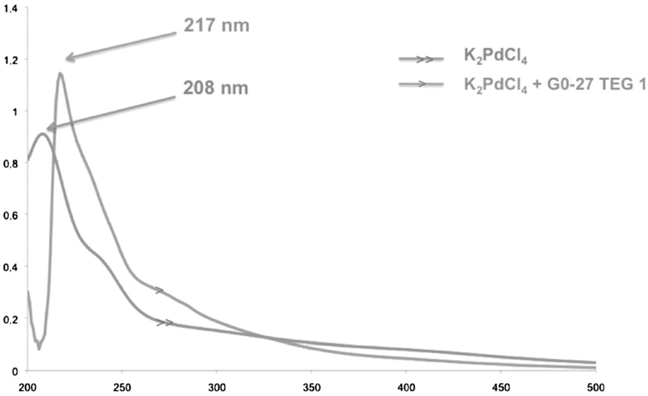


Figure 2. UV-vis spectrum of K_2PdCl_4 alone (one strong absorption band is observed at 208 nm) and UV-vis spectrum of Pd(II) complexed with the interior triazolyl groups of **1** (new absorption band at 217 nm). The UV-vis spectrum of complexed Pd(II) has been recorded with a solution of **1** alone as blank.

group in the stabilization of NPs has also been shown in former works during the synthesis/stabilization of AuNPs by various polyethylene glycol (PEG)-terminated dendrimers. When a dendrimer does not contain triazole groups, the AuNPs that are formed are very large (around 20 nm), whereas with a dendrimer containing triazole groups, smaller AuNPs are formed (around 4 nm).[12a] This clear distinction demonstrates the key role of triazole groups in the dendrimer for the stabilization of small (active) PdNPs. In the ^{1}H NMR spectrum, a shift of the triazolyl proton is observed upon adding 1, 5, and 9 equivalents of K_2PdCl_4 per G0 dendrimer **1** (7.85 ppm, 7.93 ppm, 7.96 ppm), and the peak becomes broader when Pd(II) is added, which confirms the presence of an interaction between the triazole group and Pd(II).

The reduction of Pd(II) (1 equiv. per triazolyl group) to Pd(0) is carried out in water using 10 equiv. $NaBH_4$ per Pd [Eq. (1)] in the case of PdNP stabilized by several equiv. of **1**). Dialysis is carried out in order to remove excess $NaBH_4$ and eventually purify the PdNPs from any Pd derivatives. It is not indispensable, however, because the results in catalysis are similar with and without dialysis. It is known that $NaBH_4$ inhibits catalytic activity by formation of borides at the particle surface,[8a] but this is not the case in aqueous media, because the borohydride is then fully hydrolyzed. When dialysis is applied during 1 day, ICP-OES analysis indicates that the Pd loading in the PdNPs is 96% of starting Pd.[8f] This result shows that 96% of the starting Pd is converted to PdNPs and they are stabilized by dendrimers. The polydispersities of these PdNPs shown by DLS are good, and the TEM and HRTEM images reveal that the PdNPs are very small, 1.4 ± 0.7 nm in **1** and 2.7 ± 1.0 nm in **2**, that is, of optimal size for their use in catalysis (Figure 3). The average number of Pd atoms in the G0-TEG-dendrimer **1** PdNPs is around 100 (with a large proportion on edges and corners) and that for G1-TEG **2** PdNPs is around 1000. Thus, although there are only 9 Pd(II) per G0-TEG dendrimer **1** and 27 Pd(II) per G1-TEG dendrimer **2**, the number of Pd atoms in the dendrimer-stabilized PdNPs is considerably larger than the number of Pd(II) ion precursors in each dendrimer. This means that the large majority of the dendrimer molecules do not contain a PdNP, and there is

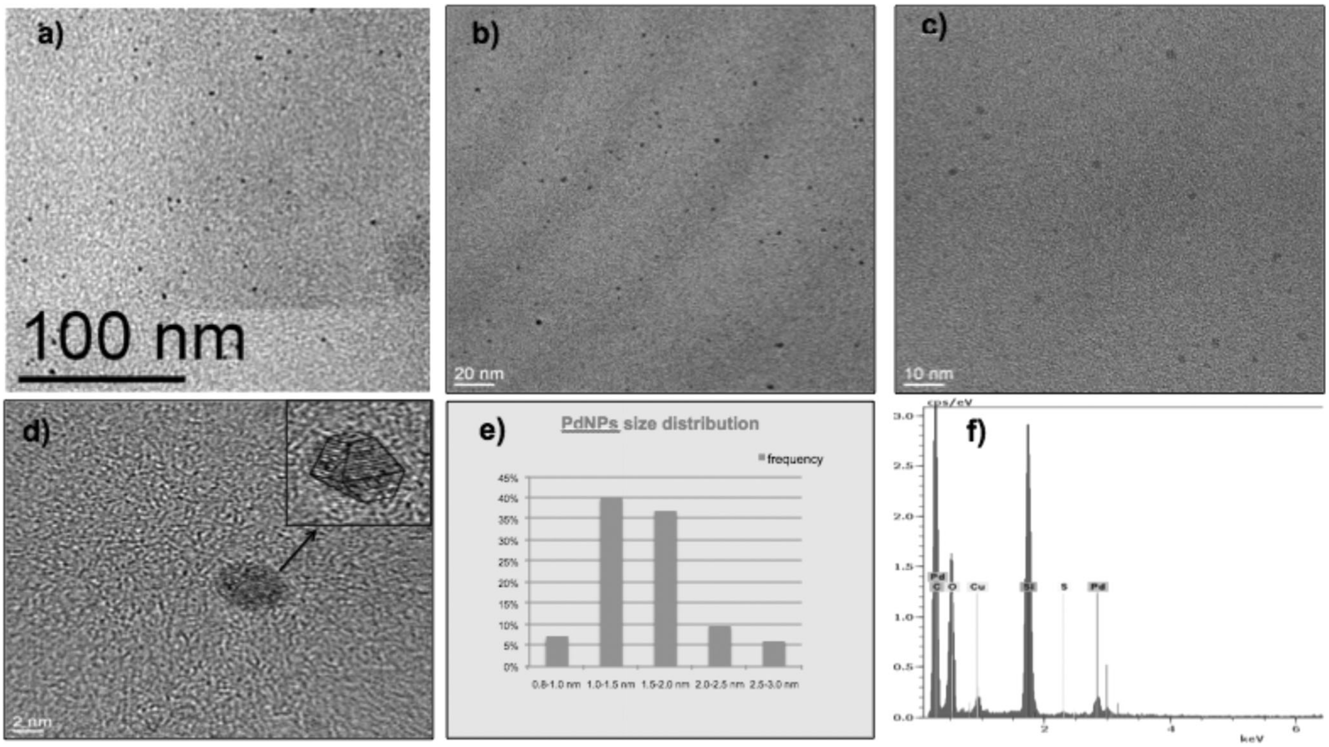


Figure 3. TEM HR-TEM of PdNPs stabilized by **1**. **a**) TEM of PdNPs stabilized by **1**. **b**) and **c**) HR-TEM of PdNPs stabilized by **1** with, respectively, 20 nm and 10 nm bar scales. **d**) PdNPs stabilized by **1** with a 2 nm bar scale, a truncated bipyramid is observed. **e**) PdNPs distribution (624 PdNPs). **f**) EDX of this system, indicating the presence of Pd in NP observed by HR-TEM.

thus an interdendritic contribution to the strong PdNP stabilization, specifically with **1** that has a relatively small size. That several dendrimers (11 small G0-TEG dendrimer molecules **1**) are necessary to stabilize a single PdNP is a situation that is in sharp contrast with the one previously encountered with ferrocenyl-terminated click dendrimers for which the number of Pd atoms in the PdNP matched that of Pd(II) precursors in each dendrimer.[8a] This contrast is due to the TEG termini of the present "click" dendrimer family. The hydrodynamic diameters of the TEG dendrimers determined by DOSY NMR and DLS are 5.5 ± 0.2 nm and 9 nm, respectively, for **1** and 13.2 ± 0.2 nm and 16 nm, respectively, for **2**. The actual size is best reflected by the DOSY NMR values, and it is expected that the DLS values take into account the water solvation around the dendrimers that increases the apparent dendrimer size. These DLS values are much larger than what is expected for a single dendrimer, which means that a number of dendrimers aggregate in water to form a supramolecular assembly of dendrimers. The aggregation of TEG dendrimers is facilitated by TEG-terminated dendrimers that interpenetrate one another because of the supramolecular forces attracting the TEG tethers among one another. What is remarkable is that, when the PdNPs are formed, the DLS size value considerably increases for G0 from 9 to 31 whereas it only increases from 16 nm to 18 nm for G1 (Figure 4). This strongly argues in favor of a full encapsulation of the stabilized PdNPs for the large dendrimer G1 that undergoes a modest size change upon PdNP formation and, on the opposite side, for an assembly of small dendrimers G0 stabilizing a PdNP. Note that the PdNPs stabilized by the TEG dendrimers are stable under air for several months without any sign of aggregation and that the size determined by TEM and the catalytic activity (*vide infra*) remain the same after such prolonged periods of time. It turns out that such an assembly of TEG dendrimers is ideal for the stabilization of a single PdNP. Thus, although dendrimer-stabilized NPs have been reported earlier,[6,8b,a,12] one is dealing here with a new type of stabilization of PdNPs by dendrimers that is specifically due to the combination between 1,2,3-triazole and TEG at the dendrimer periphery. The other interests of TEG moieties are the biocompatibility and the compatibility with both hydrophobic substrates and hydrophilic media.

Catalytic Experiments

The catalytic activity of the PdNPs has been investigated for three different C−C cross-coupling reactions: the Suzuki–Miyaura, Sonogashira and Heck

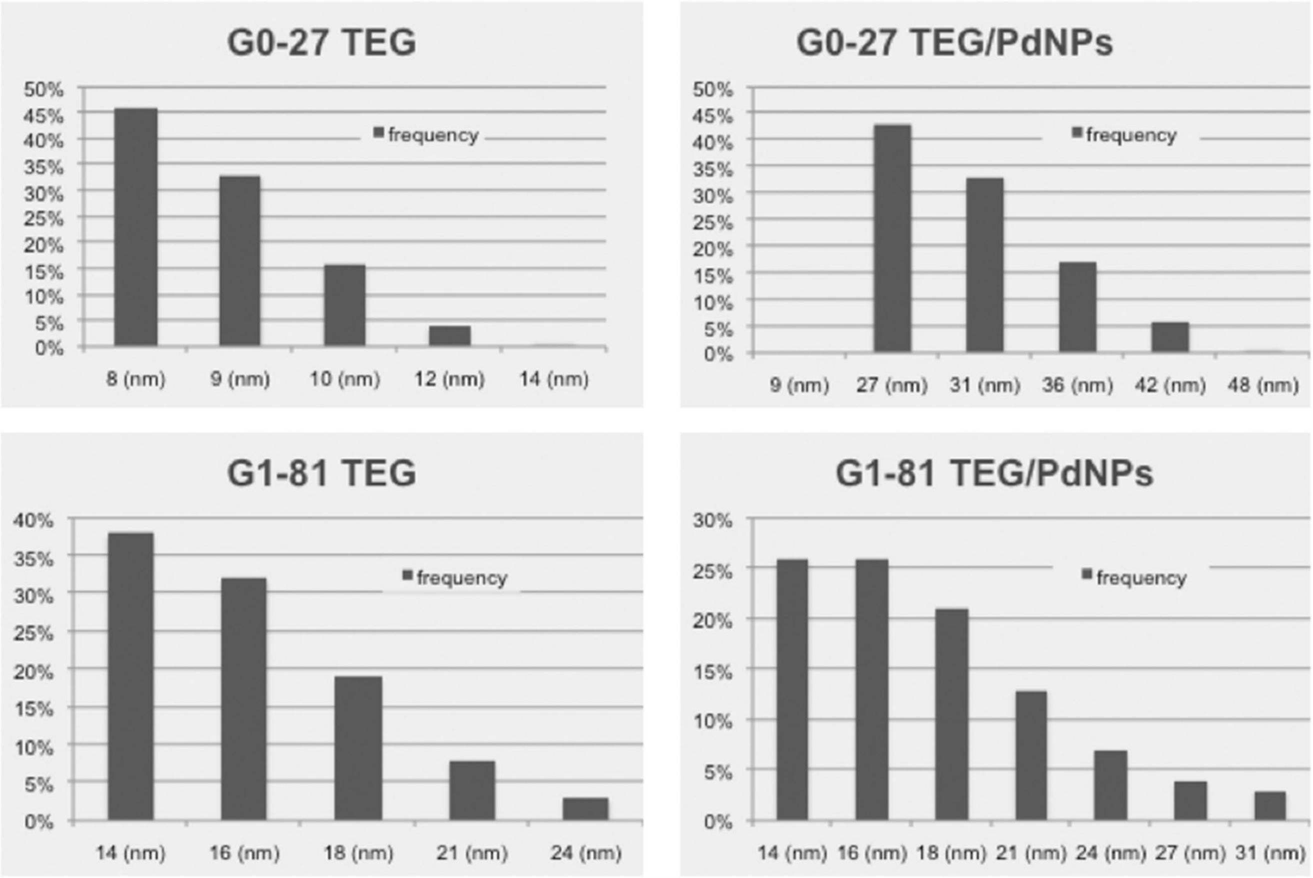
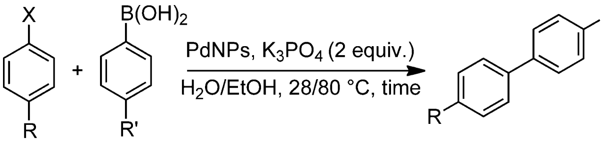


Figure 4. Dynamic light scattering (DLS) of dendrimers alone and dendrimer assemblies in the presence of PdNPs. **a**) DLS distribution of G0-27 TEG, **1**, alone. The average DLS size is 9 nm. **b**) DLS distribution of G0-27 TEG, **1**, with PdNPs. The average DLS size is 31 nm, no assemblage has been observed before 27 nm. **c**) DLS distribution of G1-81 TEG, **2**, alone. The average DLS size is 16 nm. **d**) DLS distribution of G1-81 TEG, **2**, with PdNPs. The average DLS size is 18 nm.

cross-coupling reactions and for the reduction of 4-nitrophenol to 4-aminophenol.

The Suzuki–Miyaura reactions were conducted in H_2O/EtOH (1/1), a green solvent, (as the two other C–C cross-coupling reactions) with three boronic acids and iodo-, bromo- and chloroarenes [Eq. (2)].



(2)

X = I, Br, Cl
R = H, CH_3, OCH_3, NO_2, CHO, NH_2
R' = H, CH_3, OCH_3

In the case of the reaction of iodobenzene with various boronic acids, the Suzuki–Miyaura reaction worked well even with a very small quantity of Pd (PdNPs stabilized by **1**), down to 3×10^{-5} mol%, that is, 0.3 ppm Pd in 80% yield (turnover number TON = 2.7×10^6; turnover frequency TOF = $2.8 \times 10^4\ h^{-1}$, entry 6). The effect of electron-releasing groups on phenylboronic acid and iodobenzene was examined, and the results are gathered in Table 1. The G0-PdNPs are still active after 96 h of reaction at 28 °C. Homocoupling between two iodobenzene molecules, that is, Ulmann-type coupling, is also catalyzed by the G0-PdNP, and at 28 °C it does not occur in the absence of PdNPs. With 0.1 mol% of these efficient PdNPs, the homocoupling yield is 20% in 24 h under the conditions of the reactions in Table 1, but lower amounts of G0-PdNPs give 0% yield of biphenyl, the homocoupling product, whereas a quantitative Suzuki–Miyaura coupling yield is obtained (with 1 ppm of Pd, for example). In the absence of iodoarene, no biphenyl is produced either in the presence of phenylboronic acid with 0.1% G0-PdNPs. This shows that the G0-PdNP-catalyzed cross-coupling reaction of iodobenzene occurs with complete selectivity. The reactions were also performed in air under the same conditions as those of entry 3 for comparison, and the yield was 98%, which is similar to that obtained

Table 1. Isolated yields and TONs for the catalysis by G0 PdNPs of the Suzuki–Miyaura coupling reactions between iodoarenes [p-RC$_6$H$_4$I] and arylboronic acids [p-R′C$_6$H$_4$B(OH)$_2$].[a]

R	R′	Entry	Pd [%]	Time [h]	Yield[d] [%]	TON
H	H	1[b]	0.1	6	86	860
		2[b]	0.1	12	99	990
		3	0.01	12	99	9900
		4	0.001	15	99	99000
		5	0.0001	96	92	920000
		6[b]	0.00003	120	80	2700000
	OMe	7	0.1	12	99	990
		8	0.01	15	96	9600
		9	0.001	84	99	99000
		10	0.0001	84	33	330000
	CH$_3$	11	0.1	12	99	990
		12	0.01	15	96	9600
		13	0.001	84	82	82000
		14	0.0001	84	66	640000
CH$_3$O	H	15[b]	0.1	15	99	990
		16	0.01	15	92	9200
		17[b]	0.001	84	14	14000
		18[c]	0.001	12	99	99000
I	H	19[b]	0.1	15	80	800
		20[b]	0.1	24	99	990
		21[b]	0.01	24	43	4300

[a] Each reaction is conducted with 0.1 mmol iodoarene p-RC$_6$H$_4$I, 0.15 mmol of arylboronic acid p-RC$_6$H$_4$B(OH$_2$), 0.2 mmol of K$_3$PO$_4$ in EtOH/H$_2$O 1 mL/1 mL at 28 °C.

[b] Each reaction is conducted with 1 mmol iodoarene p-RC$_6$H$_4$I, 1.5 mmol of arylboronic acid p-RC$_6$H$_4$B(OH$_2$), 2 mmol of K$_3$PO$_4$ in EtOH/H$_2$O 10 mL/10 mL at 28 °C.

[c] Standard conditions, but at 80 °C instead of 2 °C.

[d] Isolated yield.

under nitrogen. This means that the catalytic G0-PdNPs are not sensitive to air during the Suzuki–Miyaura reactions at 28 °C during 12 h. The water solution of PdNPs can also be re-used. For instance, with 0.1 mol% Pd, the PdNPs can be recycled more than four times without decrease of reactivity, the yield remaining at 98% for the reaction between iodobenzene and phenyl boronic acid for 15 h at 28 °C. TEM analyses show that the PdNPs are larger after the reaction (8 ± 1 nm) than before (1.4 nm ± 0.7 nm) but their sizes examined by TEM no longer increase after further catalytic runs. The catalytic activity with recycled PdNPs is the same with iodobenzene for G0-27 TEG under these conditions. At low PdNP concentration (1–5 ppm) with bromoarenes when the G0 PdNP size increased as indicated above, the catalytic activity decreased (*vide infra*). When the PdNPs are in very low amount, the recycling is very difficult to carry out. Another advantage of this system is that it is very simple to recycle the dendrimer alone without any decomposition, its recovery being quantitative.

The G0-PdNP catalyst is extremely active and efficient for the Suzuki–Miyaura coupling reactions of bromoarenes. At 80 °C, the reaction between 1,4-bromonitrobenzene and phenylboronic acid with only 0.3 ppm of Pd reaches a TON of 2.7×10^6 after 2.5 days (TOF $= 4.5 \times 10^4$ h^{-1}, entry 39). With only 1 ppm of Pd from the G0-PdNP catalyst, the cross-coupling of phenylboronic acid with bromobenzene is quantitative (TON $= 0.99 \times 10^6$; TOF $= 1.65 \times 10^4$ h^{-1}, entry 25), and the yield is 63% for 1,4-bromoanisole (TON $= 0.63 \times 10^6$; TOF $= 1.05 \times 10^4$ h^{-1}, entry 30). These reactions are not observed in the absence of catalyst with any studied substrate. The results of the Suzuki–Miyaura reactions of bromoarenes are gathered in Table 2. In conclusion for bromoarenes, the TONs are very impressive at 80 °C, sometimes even larger than 10^6. Interestingly, catalysis of cross-cou-

Table 2. Isolated yields and TONs for the catalysis by G0 PdNPs of the Suzuki–Miyaura reactions beween bromarenes [p-RC$_6$H$_4$Br] and phenylboronic acid.[a]

R	Entry	Pd [%]	Time [h]	Yield[e] [%]	TON
H	22	0.1	15	99	990
	23[c]	0.1	96	66	660
	24	0.01	24	99	9900
	25[b,d]	0.0001	60	99	990000
CH$_3$O	26	0.1	15	94	940
	27	0.01	24	99	9900
	28	0.001	24	60	60000
	29	0.001	48	99	99000
	30	0.0001	60	63	630000
NH$_2$	31	0.1	15	96	960
	32	0.01	24	31	3100
	33	0.01	48	40	4000
NO$_2$	34	0.1	15	99	990
	35[c]	0.1	240	80	800
	36	0.001	24	87	87000
	37	0.001	36	98	98000
	38[d]	0.0001	60	91	910000
	39[b]	0.00003	60	82	2700000
CH$_3$	40	0.1	24	99	990
	41	0.001	48	99	99000
	42	0.0001	48	46	460000
CHO	43	0.1	24	99	990
	44	0.01	24	80	8000
	45	0.001	24	20	20000

[a] Each reaction is conducted with 1 mmol bromoarene, [p-RC$_6$H$_4$Br] in 0.05 M as final concentration, 1.5 mmol of phenylboronic acid and 2 equiv. K$_3$PO$_4$ in EtOH/H$_2$O (10 mL/10 mL) at 80 °C.

[b] Same conditions but in EtOH/H$_2$O (5 mL/5 mL), C[RC$_6$H$_4$Br] = 0.1 M.

[c] Standard conditions but at 28 °C instead of 80 °C.

[d] The reaction is also conducted on a larger scale (10 g of p-RC$_6$H$_4$Br), leading to similar isolated yields.

[e] Isolated yield.

Table 3. Comparison of Suzuki–Miyaura reactions of bromoarenes catalyzed by various PdNP catalysts from the literature [Eq. (3)].[a]

R[ref]	Catalyst	Temp. [°C]	TON	TOF [h^{-1}]
4-H[13a]	PSSA-co-MA-Pd(0)	100	99	5940
4-OMe[13b]	Pd-SDS	100	38	456
4-OMe[8e]	Pd-PVP (MTPs)	100	1680	1680
4-Me[13c]	Pd-PEG	25	90	45
4-NO_2[13d]	Pd-1/FSG	100	990	123
4-OMe[6a]	Fe_3O_4-Pd	50	144	12
4-OMe[13e]	pEVPBr-Pd	90	340	38
4-OMe[13f]	Pd-PS	100	50	10
4-COMe[13g]	HAP-Pd(0)	100	139	23
4-OMe[13h]	$PdCl_2(py)_2$@SHS	60	4681	14050
4-COMe[5i]	Pd/IL	120	970	970
4-OMe[5j]	Pd-MEPI	100	24250	8083
4-COMe[5f]	Pd-salt	90	4250	1062
4-OMe[13i]	Pd@PNIPAM	90	300	30
4-Me[13j]	$Pd_x([PW_{11}O_{39}]^{7-})_y$	80	89	7
4-OMe[13k]	Pd-block-co-poly	90	310	31
4-COMe[8c]	Pd-G3-p3	80	85000	2125
4-OMe[8c]	Pd-G3-p3	80	82	10
4-H[4l]	Pd@CNPCs	50	982	327
4-Me[13l]	PS-PdONPs	80	59	59
4-Me[4n]	Pd-TiO_2	80	115	29
4-OMe[13m]	Pd@PMO-IL	75	475	95
4-NH_2[13n]	Pd-XH-15-SBA	90	96	7
4-OMe[13o]	Pd^{2+}-G0	80	386	99
4-Me[13p]	$Pd(^0)/Al_2O_3$-ZrO_2	60	45	12
4-OMe[5i]	$Pd(OAc)_2$/L	100	19600	2800
4-OMe[13q]	$Pd(OAc)_2$/CNC-pincer	100	1000	500
4-H[5g]	Pd/Y Zeolite	100	13×10^6	8.7×10^6

[a] The reactions have been conducted with various catalysts at various temperatures in aqueous solvents (the comparison is limited to representative PdNP catalysts that are used in aqueous solvents).

pling between bromobenzene and phenylboronic acid at 80 °C at relatively high concentrations such as 0.1 mol% Pd is relatively slow, that is, the yield is 20% after 2 h, 50% after 6 h, and 15 h are required for completion (entry 22). Thus diluting the catalyst 1000 times to the ppm level leads to only a period of time four times longer to reach completion (entry 25). This in favor of the leaching mechanism along with capture of the reactive leached atoms by the mother PdNP, an inhibition phenomenon that increases as the catalyst concentration increases.

Recycling experiments using the G0-PdNPs for which the TEM shows a size of 8 nm after the first run give a 78% yield of coupling between bromoanisole and phenylboronic acid at 80 °C (2.5 days) when 5 ppm Pd of the G0-PdNPs are used, which shows that the activity has decreased compared to the initial run, due to the increased size. Concerning the G1-PdNP catalyst, reactions under the same conditions as in Table 2, (80 °C, 2.5 days) between bromoarenes and phenylboronic acid using 1 ppm Pd give yields of 20% with bromobenzene, 27% with bromoanisole and 39% with 1,4-bromonitrobenzene.

The catalytic efficiency of G1-PdNPs is lower than that of the G0-PdNPs, which is taken into account by the fact that the G1-PdNPs are larger than the G0-PdNPs. This also is in accord with a leaching mechanism. Thus PdNPs stabilized by **2** will not be used for the other reactions.

With chloroarenes, the results with G0-PdNPs are less impressive than with the other haloarenes, because high temperatures (> 100 °C) are required to activate chloroarenes under these conditions, and at such temperatures these PdNPs aggregate more rapidly than activation of the reactions. For instance, in the case of 1,4-chloronitrobenzene, 0.1% Pd from G0-PdNPs at 90 °C for 2.5 days using KOH gives a 55% yield. Bromoarenes are often less expensive than chloroarenes, however, which is never the case for iodoarenes.

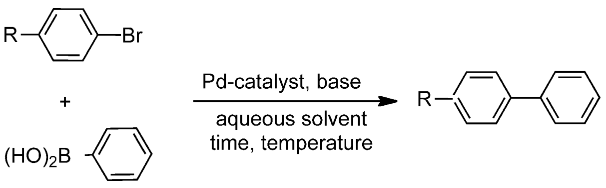
Some recent literature results are summarized in Table 3. These results concern the activity of PdNPs systems (various stabilizers) in the Suzuki–Miyaura cross-coupling reactions.

The G0-27 TEG-PdNPs catalyst is, to the best of our knowledge, one of the most active catalysts

Table 4. Comparison between various dendrimers for the stabilization of PdNPs.

Dendrimer	PdNP size	Solvent used for the synthesis	Storage	Air stable	Iodobenzene TON, **TOF**	Bromobenzene TON, **TOF**
G0-9 Fc	2.8 nm	$CHCl_3$/MeOH	no	no	540000, **1042 h^{-1}**	265, **15 h^{-1}**
*G1-27 Fc	1.3 nm	$CHCl_3$/MeOH	no	no	5200, **363 h^{-1}**	–
G0-9 biFc	–	–	–	–	–	–
G1-27 biFc	*in situ*	$CHCl_3$/MeOH	no	no	5300, **221 h^{-1}**	–
G0-9 SO_3^-	2.3 nm	H_2O	no	no	9200, **1533 h^{-1}**	10000, **8700 h^{-1}**
G1-27 SO_3^-	2.8 nm	H_2O	no	no	9400, **1567 h^{-1}**	–
G0-27 TEG **1**	1.4 nm	H_2O	yes	yes	2700000, **28000 h^{-1}**	990000, **16000 h^{-1}**

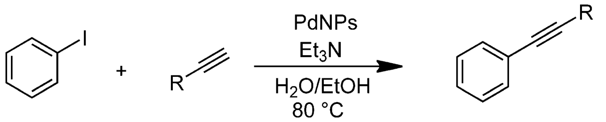
known for Suzuki–Miyaura coupling of bromoarenes [Eq. (3)]. The Suzuki–Miyaura reaction of bromoarenes should be of interest for industrial applications (multi-gram scale reactions have been carried out without decreases of yield and TONs). The use of a very low amount of catalyst will lead to lower costs and lower toxicity.



(3)

PdNPs stabilized by dendrimers have been previously reported with various triazolyl termini. First PdNPs were stabilized by dendrimer-containing triazolylferrocenes (Fc)[8a] (G0-9 Fc, G1-27 Fe) or biferrocenes[12f] (G0-9 biFc, G1-27 biFc). These dendrimers were not soluble in water, thus only PdNPs synthesized in the mixed solvent $CHCl_3$/MeOH were appropriate. The solution of PdNPs had to be kept under N_2 and fresh PdNPs used for catalysis. Concerning PdNPs stabilized by dendrimers containing triazolylsulfonated termini,[8b] the PdNPs synthesis is the same as that used for the synthesis of PdNPs stabilized by G0-27 TEG and G1-81 TEG, thus the comparison is more suitable. Table 4 shows a comparison of all the PdNPs stabilized by the present dendrimers The Suzuki–Miyaura cross-coupling reactions with PdNPs that are stabilized by ferrocenyl- and biferrocenyl-terminated dendrimers are not as favorable, and these reactions are carried out in $CHCl_3$/MeOH. Moreover, the PdNPs are less stable than in this present case. PdNPs stabilized by G1-27 Fc have sizes that are similar to those of PdNPs stabilized by G0-27 TEG, but the activity is completely different; no activity is observed with bromobenzene. Significant comparisons with G0-9 SO_3^- and G1-27 SO_3^- indicate that the PdNPs are a little larger than PdNPs stabilized by the TEG dendrimers, which shows the important role of the TEG termini of the dendrimers **1** and **2**. The activity in the Suzuki–Miyaura reaction is also lower with the PdNPs stabilized by the sulfonated dendrimers. The stabilities of the PdNPs stabilized by **1** and **2** are far better that those observed earlier, with a possible storage of the present catalyst without strain for months.

The copper-free Sonogashira coupling is more difficult to carry out with PdNPs than the Suzuki–Miyaura reaction and has been investigated in the present study between iodobenzene and various terminal alkynes [Eq. (4)].



(4)

The reactions have been carried out in the same mixture of solvents as for the Suzuki–Miyaura reactions but the base Et_3N proved to be more efficient than KOH, K_2CO_3 or K_3PO_4. The results are reported in Table 5.

Remarkably, the Sonagashira coupling between iodobenzene and aromatic alkynes works without

Table 5. Sonogashira coupling between iodobenzene and different alkynes catalyzed by G0-27 TEG-PdNPs.[a]

R [Eq. (4)]	Entry	Pd [%]	Time [h]	Yield[c] [%]	TON, **TOF [h^{-1}]**
C_6H_5	46[b]	0.1	24	93	930, **38.75**
C_6H_5	47	0.01	24	90	9000, **375**
p-Br-C_6H_4	48	0.01	24	71	7100, **296**
p-NH_2-C_6H_4	49	0.01	24	75	7500, **312.5**
p-NH_2-C_6H_4	50	0.01	36	93	9300, **258.3**
C_5H_4N[d]	51	0.01	36	79	7900, **219.4**
p-CH_3-C_6H_4	52	0.01	24	90	9000, **375**

[a] Each reaction is conducted with 1 mmol iodobenzene, 1.2 mmol of alkyne and 3 equiv. Et_3N in EtOH/H_2O (1 mL/1 mL) at 80 °C.
[b] Same conditions but with 10/10 mL EtOH/H_2O.
[c] Isolated yield.
[d] Substrate = 3-ethynylpyridine.

Table 6. Examples of active PdNP catalysts in Sonogashira coupling between iodobenzene and phenylacetylene.

Catalyst[ref.]	Pd [mol%]	Solvent	Temp. [°C]	TON, **TOF [h^{-1}]**
Pd/Pectin[14a]	0.28	DMF	100	325, **433**
Pd/SiO_2@Fe_2O_3[14b]	1	DMF	100	95, **15.8**
Pd/NH_2-SiO_2[14c]	0.05	DMF	110	1960, **980**
Pd-$C_{binaphthyl}$[14d]	1	MeOH	90	91, **4.1**
Pd/carbene[14e]	4	DMF/H_2O	90	23.5, **7.8**
Pd/MOF-5[14f]	2.8	MeOH	80	35, **11.6**
Pd/PRGO[14g]	0.5	H_2O/EtOH	180 (*μw*)	184, **1104**
PS-PdONPs[13l]	1.5	H_2O	80	66, **11**

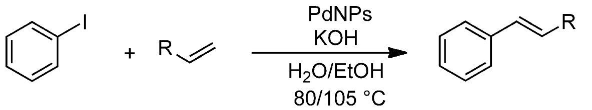
copper co-catalyst even with a low amount of Pd (i.e., 0.01% mol) leading to TONs up to 9300 and TOFs up to 375 h^{-1} (entry 47). These results are not as impressive as those obtained for the Suzuki–Miyaura reaction (the reaction does not work with bromobenzene instead of the iodobenzene nor with aliphatic alkynes instead of aromatic alkynes), but in the context of using as little metal as possible, they are of great interest. Let us compare the reaction between iodobenzene and phenylacetylene in the presence of PdNPs in various solvents with literature data (Table 6). The results obtained with the present PdNP catalyst are comparable with those obtained with other systems. The solvent used is safer than in most cases, and the temperature is modest. Even if the time of reaction is longer, the small amount of catalyst used in the present study is a serious advantage in the perspective of "green" chemistry.

Table 7. Heck reaction between iodobenzene and styrene or methyl acrylate.[a]

R	Entry	Pd [%]	Time [h]	Yield[f] [%]	TON, **TOF [h^{-1}]**
C_6H_5	53	0.1	14	73	730, **52**
C_6H_5	54	0.1	24	82	820, **34**
C_6H_5	55	0.1	24	50[b]	500, **20.8**
C_6H_5	56	0.1	24	66[c]	660, **27.5**
C_6H_5	57	0.1	24	8[d]	80, **3.3**
C_6H_5	58	0.3	24	90	300, **12.5**
C_6H_5	59	0.01	24	8[b]	800, **33**
$CH_3OC(O)$[e]	60	0.1	14	42	420, **30**
$CH_3OC(O)$[e]	61	0.1	14	0[g]	0, **0**
$CH_3OC(O)$	62	0.1	24	98	980, **40.8**
$CH_3OC(O)$	63	0.01	48	20	2000, **41.6**

[a] Each reaction has been conducted with 1 mmol iodobenzene, 1.5 mmol alkene and 3 equiv. KOH in EtOH/H_2O: 1/1 at 105 °C.
[b] Reaction conducted with K_3PO_4 (3 equiv.) as a base.
[c] Reaction conducted with K_2CO_3 (3 equiv.) as a base.
[d] Reaction conducted with Et_3N (3 equiv.) as a base.
[e] The reaction has been conducted at 80 °C.
[f] Isolated yield.
[g] Yield for the reaction in H_2O alone as solvent).

The Heck reaction between iodobenzene and styrene or methyl acrylate has been examined under the same conditions as the Suzuki–Miyaura and the Sonogashira reactions, that is, at 80 °C or 105 °C in H_2O/EtOH: 1/1 essentially with 0.1 % Pd [Eq. (5)], and the results are gathered in Table 7.



(5)

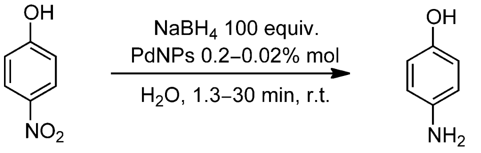
The reaction works well between iodobenzene and styrene, the best results being obtained using KOH as the base.

The reaction with methyl acrylate and iodobenzene leads to the corresponding phenylacrylic acid due to *in situ* saponification. Some destruction of the PdNPs and formation of Pd black precipitate are observed upon excessive heating. Moreover the reaction is not observed when bromobenzene is used instead of iodobenzene. With 0.01% PdNPs the yield is very low for this reaction (8%, entry 57; 20%, entry 63) due to complete precipitation of the PdNPs to Pd black. In water only as the solvent, the Heck reaction does not work with 0.1% Pd.

Seminal studies from the groups of Reetz,[2a] Beletskaya,[2b] and de Vries[2c,4d,e] led to the designation of "homeopathic" palladium catalysis for Heck and Suzuki–Miyaura reactions with aryl iodides and, in some cases, aryl bromides, and industrial large-scale applications have been developed with the term "homeopathic" indicating the use of extremely low amounts of catalyst.[2c]

The present results for the Heck reaction are not as impressive in comparison with the "homeopathic" studies of Beletskaya, Reetz, and de Vries (and others) but the term "homeopathic" could be assigned to the present results on the Suzuki–Miyaura and Sonogashira reactions.

The reduction of 4-nitrophenol (4-NP) to 4-aminophenol (4-AP) is another very quick and simple reaction that is catalyzed by these PdNPs stabilized by G0-27 TEG **1** [Eq. (6)].



(6)

4-AP is a potential industrial intermediate in manufacturing many analgesic and antipyretic drugs, anti-corrosion lubricants, and hair dying agents, thus efficient PdNP catalysis of 4-NP reduction is of great value. The high efficiency in the C–C cross-coupling reactions and the dependence of the rate of this catalysis on the nanoparticle size were encouraging factors to probe this reaction. A convenient aspect is the possibility of monitoring the progress of the reaction by UV-vis spectroscopy. Indeed, a typical peak at 400 nm is directly related to 4-NP (corresponding to 4-nitrophenate appearing in the presence of $NaBH_4$) and at 300 nm to the 4-AP. The disappearance of the yellow color of the solution is a sign of the reaction progress. The reduction of 4-NP has been carried out in the presence of excess of $NaBH_4$ (100 equiv.) as a "safe" source of H_2 and 0.2% mol of PdNPs in water. The progress of the reaction is connected to the concentration of 4-NP in water solution (Figure 5). When the solution is diluted (4 times) in order to conduct a kinetic monitoring of the reaction, it shows that it is complete in 400 seconds. The apparent rate constant k_{app} is directly obtained from the curve of $-\ln(C_t/C_0)$ *vs.* time by linear fit, $k_{app} = 0.004\ s^{-1}$.

In the absence of catalyst the reaction does not progress and the yellow color of the solution is retained after 1 hour. When only 10 equiv. of $NaBH_4$ are used, the reaction is complete in 30 min. When 4 times less water is used for the same quantity of substrate, the reduction is complete in 80 seconds, $k_{app} = 0.044\ s^{-1}$ (calculated with only 3 results because of the high reaction rate); see Figure 6 (moreover with 0.02% of PdNPs, the reaction is complete in 300 s). The reduction of 4-NP to 4-AP is successful at room temperature in water with a low amount of catalyst (0.2 mol% and 0.02 mol%).

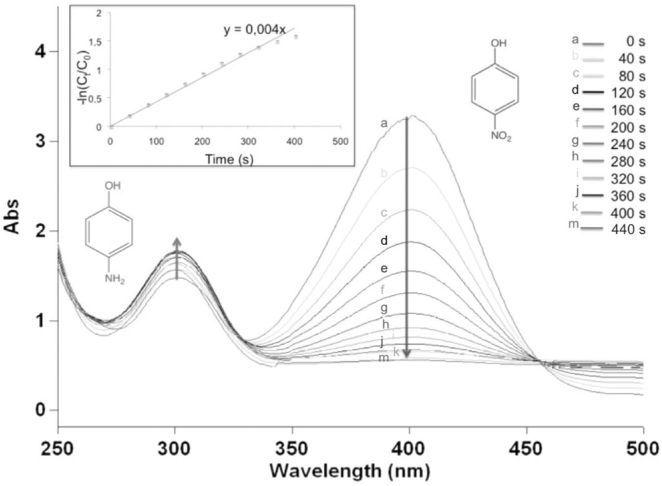


Figure 5. Kinetic study of 4-nitrophenol ($[4\text{-NP}] = 1.25\ 10^{-3}$ M) reduction by $NaBH_4$ in the presence of 0.2% mol of PdNP stabilized by G0-27 TEG using UV-vis. spectroscopy at 400 nm and plot of $-\ln(C_0/C_t)$ *vs.* time (s) for its disappearance (*left corner*). (The solution of the reaction has been directly used for the kinetic study.)

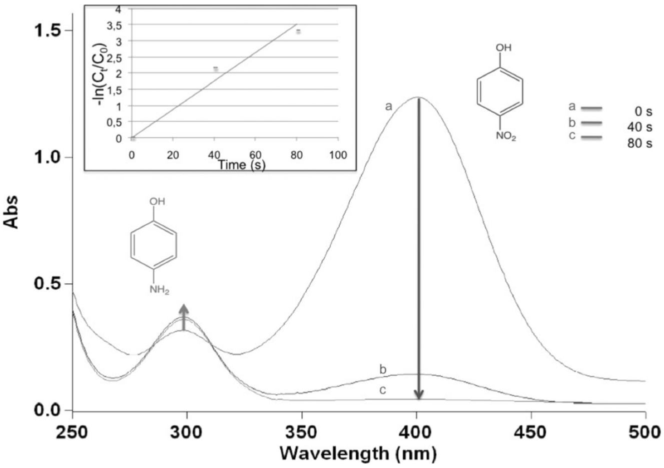


Figure 6. Kinetic study of the 4-nitrophenol ($[4\text{-NP}] = 5.0\ 10^{-3}$ M) reduction by $NaBH_4$ in the presence of 0.2% mol of PdNP stabilized by G0-27 TEG, using UV-vis. spectroscopy at 400 nm and plot of $-\ln(C_0/C_t)$ *vs.* time (s) for its disappearance (left corner). (The solution of the reaction is diluted 4 times before recording each run).

The k_{app} obtained during our study is among the best ones ever obtained, and the TOFs are impressive, as it was in the case for the Suzuki–Miyaura coupling. The comparative Table 8 concerns Pd catalyst systems.

Let us also compare with the investigation of another metal nanoparticle catalyst, gold nanoparticles (AuNPs, Table 9). A large variety of PdNPs and

Table 8. Some examples of PdNP systems used in the reduction of 4-NP.

Catalyst[ref.]	Pd [mol%]	$NaBH_4$ [equiv.]	k_{app} [s^{-1}]	TOF [h^{-1}]
CNT/PiHP/Pd[15a]	4	80	5×10^{-3}	300
Fe_3O_4/Pd[15b]	10	139	3.3×10^{-2}	300
PEDOT-PSS/Pd[15c]	77	excess	6.58×10^{-2}	13
SPB/Pd[15d]	0.36	100	4.41×10^{-3}	819
Microgels/Pd[15e]	2.1	100	1.5×10^{-3}	139
PPy/TiO_2[15f]	2.6	11	1.22×10^{-2}	326
SBA-15[15g]	100	1000	1.2×10^{-2}	6
@Pd/CeO_2[15h]	0.56	83	8×10^{-3}	1068
G0-27 TEG	0.2	100	4.0×10^{-3}	4500
G0-27 TEG	0.2	100	4.4×10^{-2}	22500

Table 9. Some examples of AuNP systems used in 4-NP reduction.

Catalyst support[ref.]	Au [mol%]	$NaBH_4$ [equiv.]	k_{app} [s^{-1}]	TOF [h^{-1}]
GO[16a]	2.6	23	1.9×10^{-1}	126
4,4-bpy[16b]	5	100	7.2×10^{-4}	19
PDDA/NCC[16c]	2.7	100	5.1×10^{-3}	212
Boehmite[16d]	270	100	1.7×10^{-3}	0.69
PANI[16e]	1.7	4.4	1.2×10^{-2}	570
GO/SiO_2[16f]	1.6	200	1.7×10^{-2}	1028
SNTs[16g]	27	42	1.1×10^{-2}	46
PNIPAP-b-P4VP[16h]	20	33	1.5×10^{-3}	16
PDMAEMA-PS[16i]	700	57	3.2×10^{-3}	1
Poly(DVP-co-AA)[16j]	0.37	37	6.0×10^{-3}	222
Chitosan[16k]	17	3	1.2×10^{-2}	50
CSNF[16l]	0.66	100	5.9×10^{-3}	563
PMMA[16m]	6.6	1500	7.2×10^{-3}	89
DMF[16n]	1	2000	3.0×10^{-3}	83
SiO_2[16o]	10.6	29	1.0×10^{-3}	14
PAMAM[16p]	1	17	2.0×10^{-3}	196
EGCG-CF[16q]	100	1320	2.4×10^{-3}	2
Biomass[16r]	5	66	4.6×10^{-4}	20
TWEEN/GO[16s]	62.5	23	4.2×10^{-3}	7
HPEI-IBAm[16t]	9.5	100	–	120
Graphene[16u]	43.4	71	3.2×10^{-3}	12
hydrogel ZnO[16v]	333	3000	2.4×10^{-3}	3
αCD[16w]	16.6	42	4.7×10^{-3}	34
Peptide[16x]	200	246	1.3×10^{-3}	7
PC/PEI/PAA[16y]	26.3	160	7.0×10^{-3}	33
MPFs[16z]	5	200	3.0×10^{-3}	80
SiO_2 @Au/CeO_2[15h]	5	83	1.3×10^{-2}	240

AuNPs stabilized by various supports (polymers, dendrimers, inorganic materials, organic materials and bio-molecules) has been used in the catalytic reduction of 4-NP. All the characteristic of these systems and their catalytic activities are indexed in Table 8 and Table 9.

This comparison shows the high efficiency of our system for this reaction. Even if the k_{app} is not the biggest (although it is nearly so), the amount of catalyst is the lowest and the TOF the largest disclosed one so far.

Conclusions

The TEGylated click dendrimer assemblies represent a new type of nanoreactors for PdNPs that provide stability and catalytic activity during several months without the strain of inert atmosphere. The TEG termini of the dendrimer tethers are responsible for this high degree of intradendritic PdNP stabilization, because they interact interdendritically to form large assemblies. The intradendritic PdNPs are loosely liganded by the 1,2,3-triazoles, which present an excellent compromise between stabilization and lability for an optimized catalytic activity. The catalytic activity of these PdNPs is exceptionally high with both iodoarene and bromoarene families, reaching TONs that are equal to or larger than 10^6 for both families in the Suzuki–Miyaura reactions. The catalyst **1**-PdNPs is so far, to the best of our knowledge, the most active one for the Suzuki–Miyaura reaction in terms of TONs for bromoarenes. The activity for the Sonogashira coupling is also very remarkable, because the Pd catalyst is copper-free and only 0.01% mol of Pd is used for this coupling, which is rarely used for this reaction (Table 5). The Heck coupling with these PdNPs gives positive results, but because of the instability of the PdNPs at high temperature (>100 °C), 0.1 mol% is used for this coupling, and no reaction is observed with less catalyst. The last reaction investigated during this work is the reduction of 4-nitrophenol. As it was in the case of the Suzuki–Miyaura coupling, the results are very impressive and never reached by other systems (Table 8 and Table 9). The amount of Pd is quite low (down to 0.02 mol%) and the TOFs are very high. All these reasons and especially the fact that very low amounts of Pd (down 0.3 ppm) are used, are in agreement with the principles of green chemistry.

It is suggested that the reason for this exceptional catalytic activity of the dendritic nanorector **1** is the loose intradendritic stabilization of PdNPs by the triazole ligands combined with the interdendritic assembly provided by the TEG termini that better protects the PdNPs than a single dendrimer The small size of the PdNPs stabilized by **1** (1.4 ± 0.7 nm), with a truncated bipyramid shape, provides a higher proportion of reactive Pd atoms on the edges and summits than is the case for larger NPs. As a consequence, extremely high TONs are reached, because the catalytic activity is retained at extremely high substrate/catalyst ratios, which is compatible with a leaching mechanism with absence (or rarity) of quenching of the catalytically active species (presumably atoms) at high dilution. At relatively high PdNP concentration, the formation of Pd black that destroys the Pd precatalyst in conventional PdNP catalytic systems is suppressed here by the dendritic stabilization. Finally, these water-soluble dendrimers themselves are very stable and easy to recover whenever needed, and they are re-used many times without signs of decomposition.

Experimental Section

General Data

All the solvents (THF, EtOH, Et_3N) 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. All the chemical shifts are reported in parts per million (δ, ppm) with reference to Me_4Si (TMS) for the ^1H spectra. The UV-vis. absorption spectra were measured with Perkin–Elmer Lambda 19 UV-vis. The DLS measurements were made using a Malvern Zetasizer 3000 HSA instrument at 258 °C at an angle of 908.

Preparation of the PdNPs for Catalysis

Dendrimer **1** (2.59 mg, 3.6×10^{-4} mmol) was dissolved in 1.1 mL of water in a Schlenk flask, and an orange solution of K_2PdCl_4 (3.2×10^{-3} mmol in 1.1 mL water) was added to the solution of the dendrimer. 30 mL of water were then added, and the solution was stirred for 5 min. The concentration of Pd(II) is 0.1 mM. A 1 mL aqueous solution containing 3.2×10^{-2} mmol of $NaBH_4$ was added dropwise, provoking the formation of a brown/black color (see the Supporting Information) corresponding to the reduction of Pd(II) to Pd(0) and PdNP formation. Then, dialysis was conducted for 1 day in order to remove excess $NaBH_4$ and eventually purify the PdNPs from any Pd derivatives. Thereafter, ICP-OES analysis indicated that the Pd loading in the PdNPs solution is 96% of starting Pd. This solution was directly used for catalysis. 10 mL of this solution were used when 0.1 mol% Pd per mol substrate is needed for a reaction between 1 mmol of haloarene and 1.5 mmol of boronic acid, and 10 μL of this solution were used when 1 ppm Pd per mol substrate was needed (in the case of the Suzuki–Miyaura reaction).

General Procedure for Suzuki–Miyaura Catalysis

In a Schlenk flask containing tribasic potassium phosphate (2 equiv.), phenylboronic acid (1.5 equiv.), aryl halide (1 equiv.) and 10 mL of EtOH were successively added. Then the solution containing the dendrimer-stabilized PdNPs was added followed by addition of water in order to respect a volume ratio of H_2O/EtOH of 1/1 (when only water was used, the reaction did not work as well, because of the hydrophobicity of the substrates). The suspension was allowed to stir under N_2 or air (no yield difference). After the reaction time (see Table 1 and Table 2), the reaction mixture was extracted twice with Et_2O (all the reactants and final products are soluble in Et_2O), the organic phase was dried over Na_2SO_4, and the solvent was removed under vacuum. In parallel, the reaction was checked using TLC in only petroleum ether as eluent in nearly all the cases and ^1H NMR. Purification by flash chromatography column was conducted with silica gel as stationary phase and petroleum ether as mobile phase. Another procedure of purification consists in cooling the Schlenk flask at the end of the reaction. The product precipitated, and a simple filtration allowed collection of the product that was then washed with a cold solution of H_2O/EtOH. After each reaction, the Schlenk flask was washed with a solution of aqua regia (3 volumes of hydrochloric acid for 1 volume of nitric acid) in order to remove traces of Pd.

General Procedure for Sonogashira Catalysis

In a Schlenk flask containing triethylamine (3 equiv.), the alkyne (1.2 equiv.), iodobenzene (1 equiv.) and 1 mL of EtOH (volume ratio of H_2O/EtOH of 1/1) were successively added. Then the solution containing the dendrimer-stabilized PdNPs was added (1 mL). The suspension was allowed to stir under N_2 or air (no yield difference). After the reaction time (see Table 5), the reaction mixture was extracted twice with Et_2O (or CH_2Cl_2), the organic phase was dried over Na_2SO_4, and the solvent was removed under vacuum. In parallel, the reaction was checked using TLC in only petroleum ether as eluent and ^1H NMR. Purification by flash chromatography column was conducted with silica gel as stationary phase. After each reaction, the Schlenk flask was washed with a solution of aqua regia (3 volumes of hydrochloric acid for 1 volume of nitric acid) in order to remove traces of Pd.

General Procedure for Heck Catalysis

In a Schlenk flask containing the base (3 equiv.), the alkene (1.2 equiv.), iodobenzene (1 equiv.) and 10 mL of EtOH (volume ratio of H_2O/EtOH of 1/1) were successively added. Then the solution containing the dendrimer-stabilized PdNPs was added (10 mL). The suspension was allowed to stir under N_2 or air (no yield difference). After the reaction time (see Table 7), the reaction mixture was extracted twice with Et_2O (or CH_2Cl_2), the organic phase was dried over Na_2SO_4, and the solvent was removed under vacuum. In parallel, the reaction was checked using TLC in only petroleum ether as eluent in the 2 cases, and ^1H NMR. Purification by flash chromatography column was conducted with silica gel as stationary phase. After each reaction, the Schlenk flask was washed with a solution of aqua regia (3 volumes of hydrochloric acid for 1 volume of nitric acid) in order to remove traces of Pd.

General Procedure for the Reduction of 4-Nitrophenol

In a beaker, 7 mg of 4-nitrophenol (5.03×10^{-5} mol) were mixed with 195 mg of $NaBH_4$ (5.13×10^{-3} mol) in 20 mL of water. 1 mL of the PdNPs was added (0.2% mol), and the reaction was complete in 80 seconds. 0.5 mL of the total solution was diluted with 1.5 mL of water before the reaction started in order to follow its course by UV-vis. This diluted reaction mixture went to completion in 400 seconds.

PdNP Recycling Procedure

The recycling procedure was carried out 4 times for the Suzuki–Myiaura coupling between iodobenzene (1 mmol) and phenylboronic acid (1.5 mmol). The standard cross-coupling procedure was followed using 0.1% mol PdNPs (10 mL). 1 mL of the PdNP solution was kept before the reaction in order to measure the PdNP size by TEM. After the reaction, the products were extracted twice from the H_2O/EtOH solvent using Et_2O (the dendrimer **1** is not soluble in Et_2O, thus it remains in the aqueous phase with PdNPs). The organic solvent was dried, evaporated, and purification on a column was carried out. 1 mL of the 10 mL aqueous phase was retained for TEM analysis. The remaining solution (containing **1** and PdNPs recycled) was introduced into the following reaction mixture in which all the compounds (1 mmol halide, 1.5 mmol boronic acid, 2 mmol K_3PO_4, 9 mL EtOH) except Pd, have been introduced. This procedure was repeated three more times.

Alternatively, the PdNPs were recycled as follows. In order to investigate the efficiency of the re-used PdNPs, a classic Suzuki–Miyaura reaction was launched between iodobenzene and phenylboronic acid. When the reaction was finished, the solution contained biphenyl, the excess of phenylboronic acid, the base, H_2O/EtOH (10/10 mL) and PdNPs with a size of 8 nm. The preceding solution (100 μL) corresponding to 5 ppm of PdNPs for 1 mmol of substrate was used to catalyze a Suzuki–Miyaura reaction between bromoarenes and phenylboronic acid. The dendrimers alone **1** and **2** were easily quantitatively separated and recycled.

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