DOI: 10.1002/cssc.201100379

Fibrous Nano-Silica (KCC-1)-Supported Palladium Catalyst: Suzuki Coupling Reactions Under Sustainable Conditions

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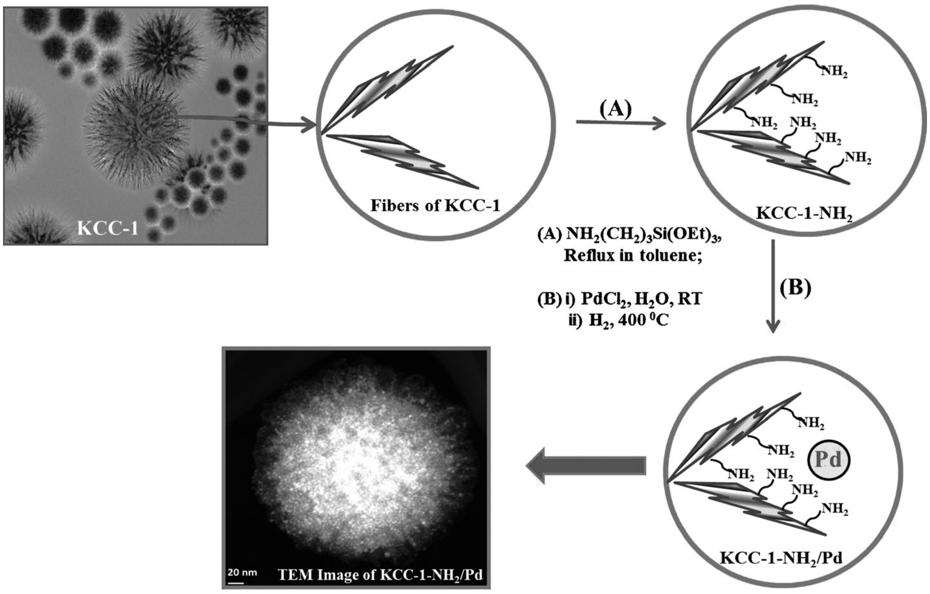
Since the discovery of the Ullmann reaction over a century ago, in 1901,[1] the transition-metal-catalyzed cross-coupling reaction has played an important role in the synthesis of C–C bonds.[2] In 1981, Suzuki discovered a novel Pd-catalyzed cross-coupling reaction of aryl boronic acids and aryl halides,[3] which has been applied widely[4–11] and for which he received the 2010 Nobel prize in chemistry. This reaction has become an extremely powerful process for the synthesis of biaryls, which have a diverse spectrum of applications, ranging from pharmaceuticals to materials science.[12–15]

Recently, the use of nanocatalysts has increased rapidly and has resulted in the development of several active and efficient nano-catalysts for various protocols.[16–20] These systems have several advantages over conventional catalysts, such as superior activity and improved stability. Combining metal nanoparticles with a support of choice provides a large field for the discovery of new, highly active nanocatalysts for important and challenging reactions, which also offer the additional advantage of recyclability. The preparation of Pd nanoparticles is usually based on the reduction of a metal salt in the presence of a reducing agent and a stabilizer. Many substrates, such as polymers,[21] dendrimers,[22] ionic liquids,[23] ordered mesoporous silica,[24] and carbon nanotubes,[25] have been used as stabilizers and supports for Pd nanoparticles. We recently reviewed these nano-catalysts for Suzuki coupling reactions[26] and observed that an extensive range of nano-catalyst systems was developed for this process in a short period of time. Although most of these nano-catalyst systems are active and usable, two main challenges still remain unresolved: 1) stable nano-catalysts that avoid activity loss from particle-size growth during the reaction caused by Ostwald ripening and 2) active nano-catalysts that use challenging, but economical chloroarenes as substrates.

In a continuation of our search for green and sustainable nano-catalytic protocols,[27–34] we herein report novel Pd-nano-catalysts supported on our recently discovered high-surface-area silica exhibiting a unique fibrous morphology (KCC-1).[27,28] We discovered that the high surface area of KCC-1 is attributable to fibers and not pores, which dramatically increases its accessibility.[27] We believe that this unique property will be very useful for the design of silica-supported catalysts, for which the accessibility of active sites can be increased significantly. After demonstrating the validity of this concept for the hydro-metathesis of olefins by using a KCC-1/TaH catalyst system,[28] we designed highly disperse Pd-nanoparticles supported on fibers of KCC-1 to examine the advantages of fibrous KCC-1 as a catalyst support in Suzuki coupling reactions.

The first step in accomplishing this catalyst design was the functionalization of KCC-1 with amino groups, which could then act as pseudo chelators or ligands to control the metal leaching during the reaction. Functionalization was achieved by post-synthetic modification of the fibers of KCC-1 by reaction with 3-aminopropyltriethoxysilane (Scheme 1) to produce KCC-1-NH_2.



Scheme 1. Synthesis of KCC-1-NH_2/Pd nano-catalysts (only two fibers are shown for clarity).

Nano-composite KCC-1-NH_2 was then characterized by using solid-state ^{29}Si and ^{13}C cross-polarization magic-angle-spinning (CP-MAS) NMR spectroscopy. The ^{29}Si CP-MAS NMR spectrum (Figure 1 a) shows two strong characteristic signals at $\delta = -99.7$ and -109.2 ppm that can be assigned to the Q3 and Q4

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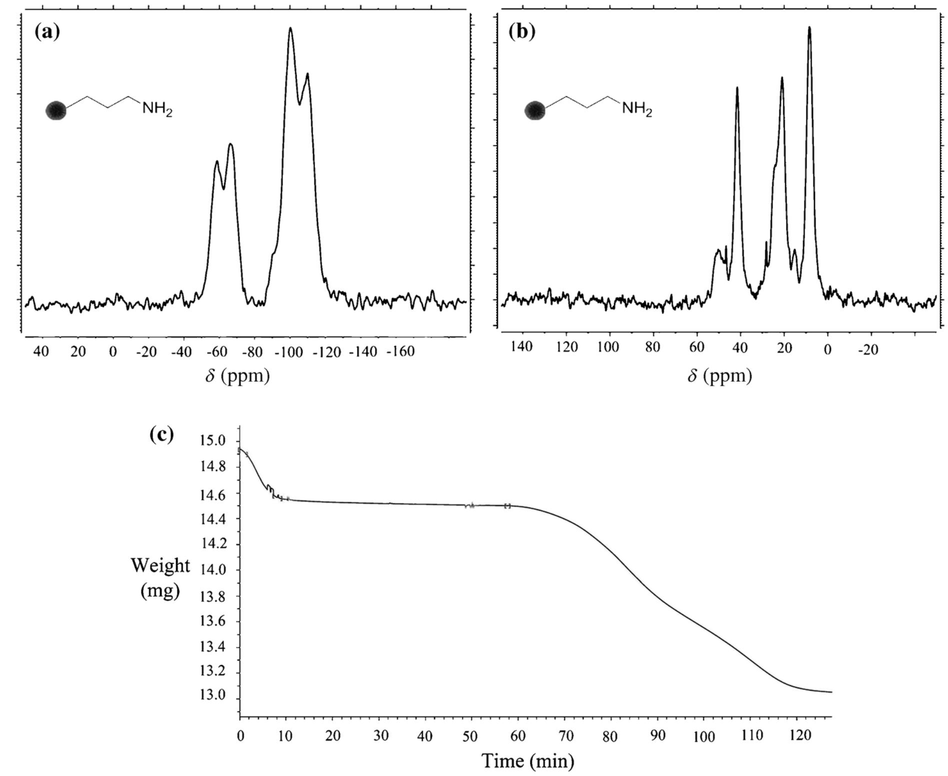


Figure 1. a) ^{29}Si CP-MAS NMR spectrum, b) ^{13}C CP-MAS NMR spectrum, and c) TGA spectrum of KCC-1-NH_2.

sites corresponding to silica substructures with different degrees of condensation. A weak Q2 signal at $\delta = -90.2$ ppm is also observed. The signals at $\delta = -57.3$ and -66.8 ppm are characteristic for the T2 and T3 sites of $RSiO_3$ units of as-synthesized nano-composite KCC-1-NH_2, indicating the covalent attachment of organic molecules to silica. To confirm that the aminopropyl group is attached to KCC-1, a ^{13}C CP-MAS experiment was performed. The resultant spectrum (Figure 1 b) has signals at $\delta = 8.4$, 21, and 41.5 ppm corresponding to the three carbon atoms of the aminopropyl group, confirming the presence of this organic functionality. To calculate the amount of amino group loading, thermogravimetric analysis (TGA; Figure 1 c) of the KCC-1-NH_2 silica spheres was performed under an inert atmosphere. After an initial weight loss attributable to water and moisture up to 110 °C, the nano-composite was relatively stable up to 350 °C; from 350–650 °C, a 10.5 % weight loss was observed, which could be attributed to the loss of covalently bound aminopropyl groups.

The as-synthesized KCC-1-NH_2 composite was then treated with $PdCl_2$, followed by the reduction of Pd^{II} to Pd^0 by using a hydrogen reduction method, to produce the KCC-1-NH_2/Pd nanocatalyst (Scheme 1). TEM images of this catalyst revealed that the fibers of KCC-1 were fully loaded with well-dispersed Pd nanoparticles with an average size range of 1–5 nm (Figure 2). Inductively coupled plasma coupled with atomic absorption spectroscopy (ICP-AAS) was used for elemental analysis, and the results revealed a 6.3 % concentration of Pd in the as-synthesized catalyst system.

Next, we evaluated this nano-composite (KCC-1-NH_2/Pd) as a heterogeneous catalyst in Suzuki coupling reactions (Scheme 2). Initial trials were performed to optimize the reaction conditions for the coupling reaction of bromobenzene and phenylboronic acid. After screening a range of usual inorganic and organic bases and exploring the scope of various solvents, this nano-catalyst was found to be most active in a water–ethanol mixture used as a solvent with potassium phosphate as a base. Using these optimized reaction conditions, the efficiency of the catalyst system was studied for the Suzuki coupling reaction of various aryl halides and aryl boronic acids (Table 1).

Clearly, KCC-1-NH_2/Pd is an active and efficient catalyst for coupling a range of aryl iodides and bromides with several aryl boronic acids, producing the corresponding biaryl compounds in good to excellent yields (Table 1). Although aryl halides with various functional groups efficiently couple with a range of boronic acids (Entries 1–13), our attempts to use 2-furanboronic acid (entry 14) resulted in no product formation, which may be attributable to the substrate's instability in water. However, a phenylboronic acid with a sensitive 1,3-dioxolane ring underwent the Suzuki coupling

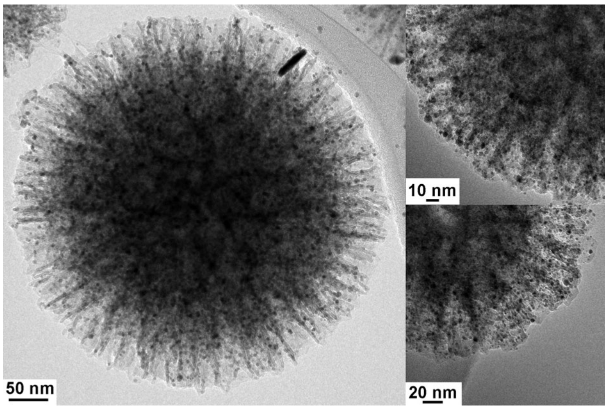
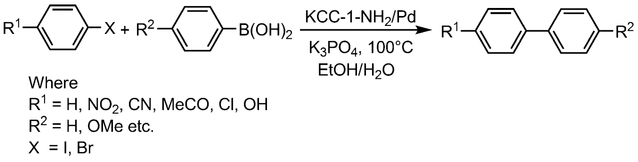
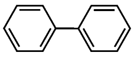
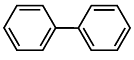
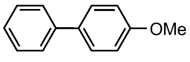
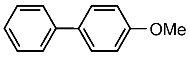
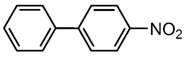
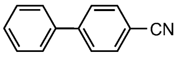
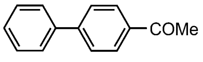
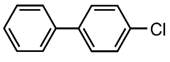
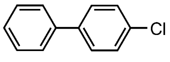
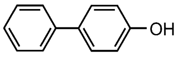
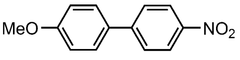
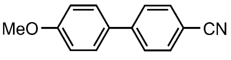
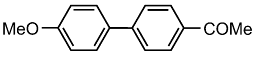
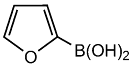
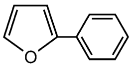
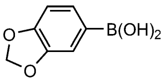
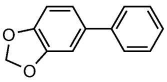


Figure 2. TEM images of KCC-1-NH_2/Pd nano-catalysts.



Scheme 2. Suzuki coupling reactions using the KCC-1-NH_2/Pd nano-catalyst.

Table 1. Suzuki coupling reactions of aryl halides with aryl boronic acid using KCC-1-NH_2/Pd.[a]

Entry	X	R^1	R^2	Product	Yield[b] [%]
1	I	H	H		95
2	Br	H	H		86
3	I	H	MeO		94
4	Br	H	MeO		81
5	Br	NO_2	H		94
6	Br	CN	H		93
7	Br	MeCO	H		97
8	Br	Cl	H		81
9	Br	Cl	H		97[c]
10	Br	OH	H		77
11	Br	NO_2	MeO		95
12	Br	CN	MeO		88
13	Br	MeCO	MeO		92
14	Br	H			0
15	Br	H			95[d]

[a] Reaction conditions: aryl halide (1 equiv), arylboronic acid (1.5 equiv), and K_3PO_4 (3 equiv) were heated in 5 mL of 3:2 mixture of H_2O and Ethanol at 100 °C for 4 h in the presence of KCC-1-NH_2/Pd (0.5 mol% of Pd). [b] Yields determined by using GC. [c] *N*-Methyl-2-pyrrolidone was used as solvent at 140 °C. [d] The reaction was run for 6 h.

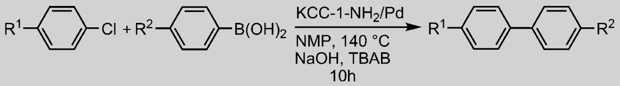
smoothly (entry 15), notably with the 1,3-dioxolane ring remaining intact.

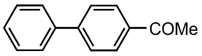
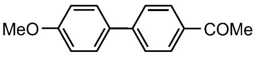
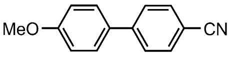
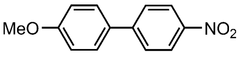
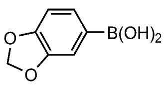
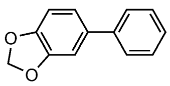
Although the catalyst was active for bromo- and iodoaryl compounds, our main objective was to design a nano-catalyst for the Suzuki coupling of challenging, but economical substrates, that is, aryl chlorides. In our initial attempts, we used the same optimized conditions as for the bromo and iodo aromatics, and the reactions proceeded under these conditions, but with lower conversions. Therefore, we optimized several reaction parameters, including the solvent, base, and reaction temperature, and finally found that the use of tetra-*n*-butylammonium bromide (TBAB) and changing the base from K_3PO_4 to NaOH was necessary to achieve good yields. Using these optimized conditions, we tested several aryl chlorides for Suzuki coupling reactions, which are summarized in Table 2.

Interestingly, KCC-1-NH_2/Pd was also active for a range of chloro aromatics with good to excellent yields. This is an additional and important attribute of this nano-catalyst protocol, as few heterogeneous catalyst systems show good activity toward aryl chlorides, which are sustainable substrates for Suzuki coupling reactions, under ligand-free conditions.[26]

Catalyst stability, heterogeneity, and leaching are important factors to evaluate the sustainability of the catalyst system. We conducted a recycling and leaching study for the KCC-1-NH_2/Pd catalyst system by using the Suzuki coupling of 4′-bromoacetophenone and phenylboronic acid as a test reaction. After completion of the first reaction to yield the corresponding biaryl, the catalyst was recovered, washed sequentially with ethanol and acetone, and finally dried under vacuum. Utilizing the used catalyst, the above test reaction was performed again under the same conditions with similar catalyst activity. We were able to reuse the catalyst for at least seven times with a negligible change in its activity (Table 3). Thus, the as-synthesized nanocatalyst showed excellent recyclability, and catalyst deterioration was not observed, confirming its high stability. Also, the Pd-metal concentration of the catalyst before and after the reaction was very similar, and no Pd was detected (by using ICP-MS analysis) in the isolated biaryl product. The reason for negligible leaching is the presence of the amino group on the surface of KCC-1 that acts as a pseudo ligand or chelating agent for the metal and thus prevents leaching to the reaction solvent.[31]

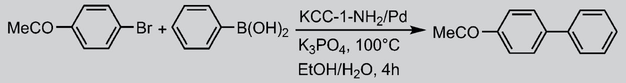
Table 2. Suzuki coupling reactions of chloroarenes using KCC-1-NH_2-Pd.[a]



Entry	R^1	R^2	Product	Yield[b] [%]
1	MeCO	H		94
2	MeCO	MeO		95
3	CN	MeO		93
4	NO_2	MeO		91
5	H			95

[a] Reaction conditions: aryl chloride (1 equiv), arylboronic acid (1.5 equiv), and NaOH (3 equiv) were heated in 5 mL *N*-Methyl-2-pyrrolidone (NMP) at 140 °C for 10 h in the presence of tetra-*n*-butylammonium bromide (0.1 equiv) and KCC-1-NH_2/Pd (2.5 mol% of Pd). [b] Yield determined by using GC.

Table 3. Recycling study of KCC-1-NH_2-Pd using the Suzuki coupling reaction of 4′-bromoacetophenone and phenylboronic acid.



Run	Yield [%]
1	97
2	95
3	96
4	94
5	93
6	95
7	90

Why does the KCC-1-NH_2/Pd nano-catalyst not deactivate even after several reactions? Restricted Ostwald ripening provides the explanation. The catalytic activity of nano-Pd depends on the size of the particles, and we observed that Pd-nanoparticles with sizes ranging from 1–5 nm are effective in catalyzing Suzuki coupling reactions. However, these nanoparticles generally lose their activity slowly during every reaction cycle. This loss in activity is a result of the nanoparticles growing larger in size through the Ostwald ripening process, in which small nanoparticles merge together to form larger nanoparticles.[35] In the case of the KCC-1-NH_2/Pd catalyst system, we observed no appreciable Ostwald ripening, and the particle size and distribution remained the same even after the reaction (Figure 3), which in turn maintained the catalytic activity. Ostwald ripening may be absent because most of the Pd-nanoparticles are present between two fibers of KCC-1 (where the maximum distance between two fibers is 5 nm), which implies that the nano-particles cannot grow larger than 5 nm in size because such a growth would be restricted by the fibers of KCC-1. Therefore, even after several reaction cycles, the size and distribution of Pd-nano-particles remains nearly the same (Figure 3), and thus, the system maintains nearly the same catalytic activity. These results clearly indicate the advantage of the fibrous nature of KCC-1.

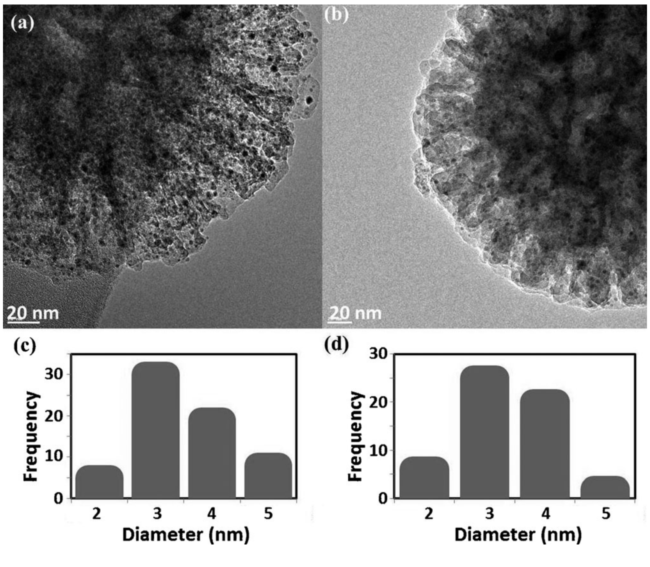


Figure 3. TEM images of KCC-1-NH_2/Pd nano-catalysts a) before reaction and b) after reaction. Particle size distribution c) before reaction and d) after reaction.

Conclusions

Fibrous high-surface-area nano-silica KCC-1 was functionalized with aminopropyl groups and was loaded with Pd nanoparticles by treating the functionalized surface with $PdCl_2$, followed by hydrogen reduction. TEM images revealed that fibers of KCC-1 were fully loaded with well-dispersed Pd nanoparticles (1–5 nm). The as-synthesized KCC-1-NH_2/Pd nanocatalyst was then evaluated for the Suzuki coupling of aromatic halides and was found to be active for the reaction of a range of aryl bromides and iodides with aryl boronic acids in good to excellent yields. Notably, the catalyst was also active for aryl chlorides, which are difficult, but more "sustainable substrates". The catalyst was easily recovered from the reaction mixture and was reused for a number of cycles with negligible change in the catalyst activity, confirming the heterogeneity and good stability of this catalyst system. TEM images of the fresh and used catalyst showed that the Pd nanoparticles supported on fibrous nano-silica remained unchanged, indicating no significant Ostwald ripening. Thus, the KCC-1-NH_2/Pd nanocatalyst synthesized by using a simple protocol displays superior activity for Suzuki coupling reactions even with challenging substrates like aryl chlorides under sustainable ligand-free conditions.

Experimental

Preparation of KCC-1-NH_2

In a 250 mL round-bottom flask, anhydrous toluene (150 mL), KCC-1 (12.00 g), and 3-aminopropyltriethoxysilane (APTS, 40 mL) were introduced successively. The mixture was refluxed for 48 h. The solution was filtered, the solid was washed with acetone and chloroform, and then the solid was dried overnight at 65 °C under vacuum to yield the KCC-1-NH_2 nano-composite.

Preparation of KCC-1-NH_2/Pd

A Schlenk flask was charged with of KCC-1-NH_2 (1 g), $PdCl_2$ (0.25 g), and deionized water (40 mL), and the mixture was then sonicated for 2 h. The obtained suspension was stirred at room temperature for 24 h. The solid collected by centrifugation was washed several times with water, ethanol, and acetone and dried overnight under vacuum at 65 °**C**. The reduction was performed in a fixed-bed continuous-flow reactor. The unreduced catalyst (200 mg) was placed in a stainless steel tabular reactor with a 9 mm internal diameter and then reduced in a stream of hydrogen (20 mL min^{-1}) at 400 °C for 15 h. The temperature in the reactor was controlled by using a PID temperature controller connected to a thermocouple placed inside the catalyst bed. The Pd content in the final material was determined by using ICP-elemental analysis to be 6.3 %.

Representative procedure for the KCC-1-NH_2/Pd-catalyzed Suzuki coupling reaction

Aryl halide (0.50 mmol), phenylboronic acid (0.75 mmol), K_3PO_4 (1.50 mmol), and KCC-1-NH_2/Pd (0.5 mol% Pd) were combined in a 50 mL Schlenk tube equipped with a magnetic stirrer. Then, a mixture of H_2O and ethanol ($v/v = 3{:}2$; 5 mL) was added; the reaction mixture was heated and stirred in the oil bath at 100 °C for 4 h, and the reaction was monitored by using GC–MS. After completion of the reaction, the mixture was extracted with dichloromethane (3×5 mL), and the combined dichloromethane phase was dried over anhydrous $MgSO_4$, filtered, and the organic solvent was evaporated under reduced pressure to yield the final biaryl product.

Acknowledgements

We thank the King Abdullah University of Science and Technology (KAUST) for financial and logistic support. Thanks are also due to Prof. Jean-Marie Basset, Director of the KAUST Catalysis Center (KCC), for his encouragement and support.

Keywords: amines · nanoparticles · palladium · supported catalysts · suzuki coupling reactions

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Received: July 19, 2011