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Metal nanoparticles as efficient catalysts for organic reactions*

Brindaban C. Ranu‡, Kalicharan Chattopadhyay, Laksmikanta Adak, Amit Saha, Sukalyan Bhadra, Raju Dey, and Debasree Saha

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata 700032, India

Abstract: Pd(0) nanoparticles have been demonstrated to be very efficient catalysts for C–C bond-forming reactions. These include coupling of *vicinal*-diiodoalkenes and acrylic esters and nitriles leading to the stereoselective synthesis of 2-alkene-4-yn-esters and nitriles, allylation of active methylene compounds by allyl acetate, and Hiyama cross-coupling of aryl iodides with arylsilanes. Cu(0) nanoparticles catalyze aryl-sulfur bond formation, accomplishing the synthesis of functionalized aryl sulfides and aryl- and vinyl dithiocarbamates. Cu nanoparticles have also been used for the chemoselective reduction of aromatic nitro compounds.

Keywords: catalysis; copper; green chemistry; nanoparticles; palladium.

INTRODUCTION

The last decade has witnessed tremendous growth in the field of nanoscience and nanotechnology. The easy accessibility to nanoparticles has prompted investigations on their applications in catalysis. Several reports showed an amazing level of their performance as catalysts in terms of selectivity, reactivity, and improved yields of products [1]. In addition, the high surface-to-volume ratio of nanoparticles provides a larger number of active sites per unit area compared to their heterogeneous counterparts. Thus, in recent times interest in nanoparticles catalysis has increased considerably because of their high efficiency under environmentally benign reaction conditions [2]. As a part of our interest in this area, we initiated an investigation to explore the potential of metal nanoparticles for C–C and C–S bond formations. We report here several applications of Pd and Cu nanoparticles for useful organic reactions.

RESULTS AND DISCUSSION

Pd(0) nanoparticle-catalyzed synthesis of conjugated 1,3-en-yne derivatives by Heck coupling

The 1,3-enyne unit is of considerable interest in organic synthesis as these moieties are present in many naturally occurring and biologically active molecules [3]. Only a limited number of procedures for the synthesis of conjugated enynes have been developed. One of the most prevalent protocols was Pd–Cu-catalyzed coupling between an alkyne or an organometallic alkyne and a vinyl halide [4,5]. Pd-cat-

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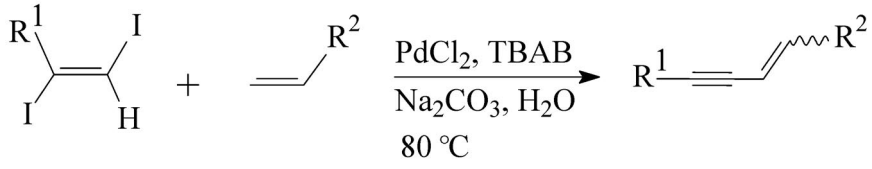
‡Corresponding author

alyzed oxidative alkynylation of alkenes has also been demonstrated to produce enynes [6b,c]. Another alternative approach involved Cu-catalyzed coupling of alkynes or alkyne derivatives with vinyl iodides [7]. However, these methods suffer from some limitations such as preparation of an organometallic alkyne and stereodefined vinyl halide through lengthy procedures, poor functional group tolerance, and undesired side products, resulting in low yields. We now report a new route involving a simple reaction of *vic*-diiodo-alkenes with an activated alkene catalyzed by Pd(0) nanoparticles in water (Scheme 1).



R^1 = aryl, alkyl

R^2 = CO_2Me, CO_2Bu, CN

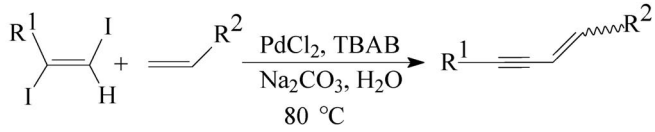
Scheme 1

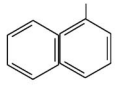
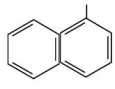
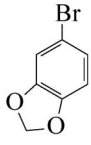
The experimental procedure is very convenient. A simple reaction of *vic*-diiodo alkene and conjugated alkene in the presence of $PdCl_2$/TBAB/Na_2CO_3/H_2O system provided the product. The Pd(0) nanoparticles were produced in situ from this reagent system. The formation of Pd nanoparticles was detected by us from analysis of the reaction mixture by transmission electron microscopy (TEM) and energy-dispersive X-ray spectroscopy (EDS). The TEM image showed the Pd nanoparticles with a size of 2–6 nm. The slurry of Pd nanoparticles in water was recycled for two runs without any loss of efficiency. After two runs, reactivity decreases possibly due to agglomerization of nanoparticles on each exposure.

Several structurally diverse *vic*-diiodoalkenes underwent reactions with conjugated alkenes such as acrylic ester and nitriles catalyzed by in situ prepared Pd(0) nanoparticles in water to produce the corresponding 1,3-enyne esters and nitriles in good yields. The results are summarized in Table 1. The substituents on the aromatic ring of the diiodo alkenes did not have any appreciable effect on the reaction. Both aryl- and alkyl-substituted alkenes participated in this reaction. However, the reaction of dibromoalkenes in place of diiodoalkenes produced relatively low yields (30–40 %). This method is compatible with a variety of substituents such as OMe, Cl, Br, methylenedioxy. Significantly, coupling with acrylic esters always provided (*E*)-isomers exclusively, whereas acrylonitriles pushed the reaction to give (*Z*)-alkenes in high selectivity. This type of high selectivity with CO_2R compared to relatively small group CN is well addressed in Heck coupling.

The mechanism of this reaction has also been investigated. Two alternative routes (a and b) as outlined in Scheme 2 have been considered. In route a, the (*E*)-diiodoalkene is proposed to undergo elimination of HI to form iodoalkyne which then couples with conjugated alkene in Heck fashion catalyzed by Pd(0) to form the enyne. The route b proposes the initial formation of an iodopalladium complex **1** via Heck coupling with conjugated alkene followed by β-elimination to form the hydridopalladium halide π complex **2** which may give rise to two isomers **A** and **B** by hydridopalladium halide elimination. Now, the isomer **A** may lead to the product by syn elimination of HI and on the other hand, **B** may produce the enyne through E-2 type elimination. On theoretical calculation it was found that **A** is energetically favorable by .03 kcal/mol compared to **B**. Thus, the formation of product through intermediate **A** is predicted.

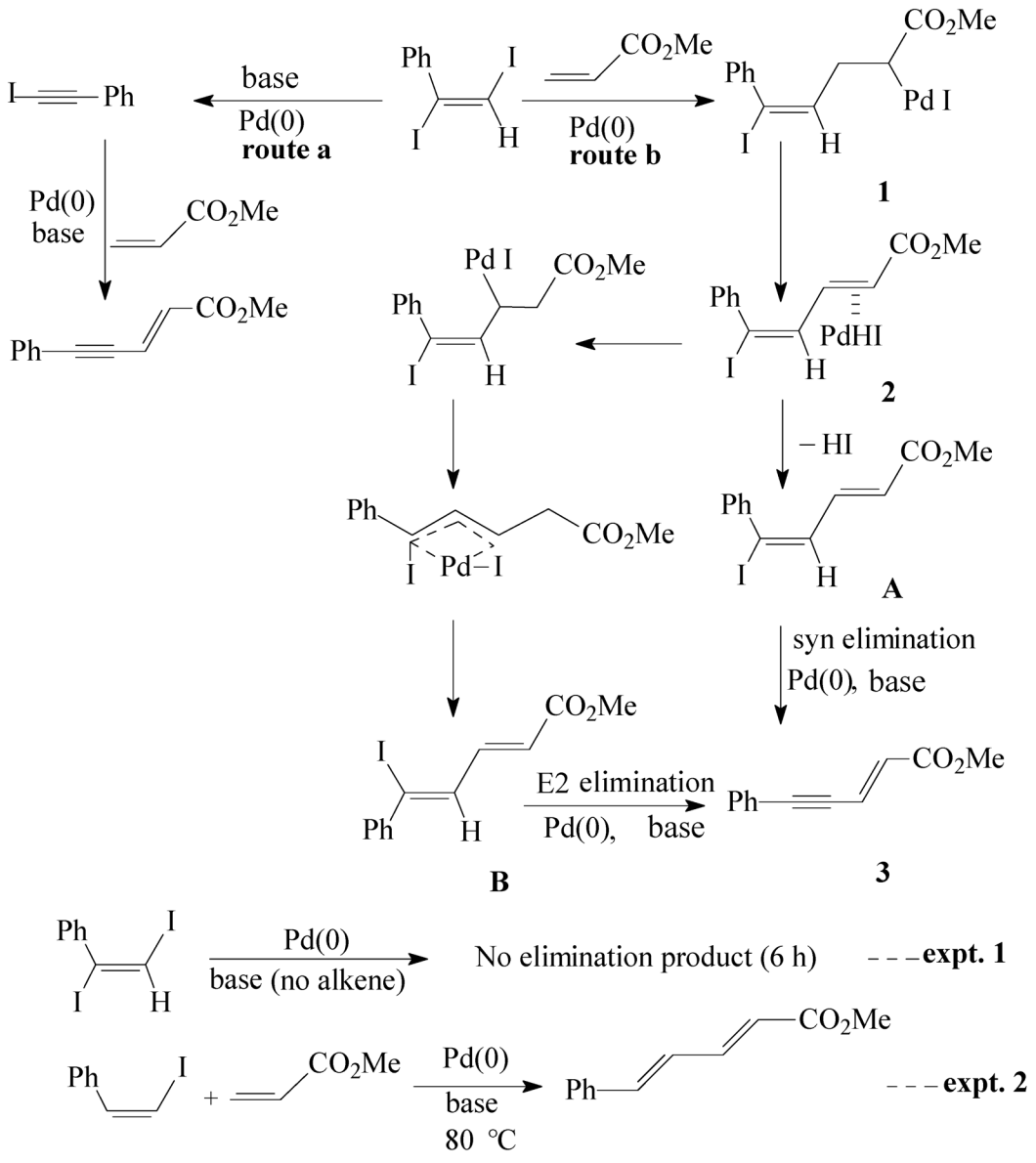
Table 1 Cross-coupling reaction of diiodo compounds with activated alkenes.



entry	R^1	R^2	time (h)	yield (%)[a]	*E*:*Z*
1	C_6H_5	CO_2Me	6	82	100:00
2	C_6H_5	CO_2Bu	7	78	100:00
3	C_6H_5	CN	6.5	72	10:90
4	*p*-Me- C_6H_4	CO_2Me	6	78	100:00
5	*p*-Me- C_6H_4	CN	6	72	20:80
6	*p*-Cl-C_6H_5	CO_2Me	6.5	72	100:00
7	*p*-Cl-C_6H_5	CN	7	70	5:95
8	*m*-Br-C_6H_5	CO_2Me	12	68[b]	100:00
9	*m*-OMe-C_6H_5	CO_2Me	6.5	80	100:00
10		CO_2Me	6.5	78	100:00
11		CO_2Bu	7	74	100:00
12		CO_2Me	9.5	65[b]	100:00
13	*n*-C_4H_9	CO_2Me	26	78	100:00
14	*n*-C_6H_{13}	CO_2Bu	24	72	100:00

[a] Yields refer to those of pure isolated products characterized by IR , ^1H, ^{13}C NMR spectroscopic data.

[b] Reaction was carried out under sonication.



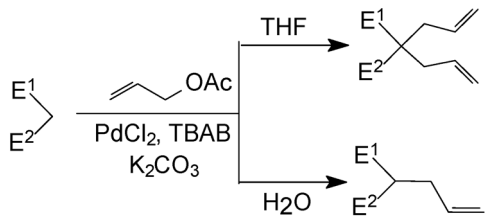
Scheme 2 Possible mechanism of the coupling reaction.

To check the feasibility of route a, a blank experiment with the starting diiodoalkene under identical experimental conditions without conjugated alkene was carried out and significantly, no iodoalkyne as predicted in route a was obtained (expt. 1). Thus, route a was not considered. On the other hand, a reaction of *cis*-diiodostyrene with the same conjugated alkene under identical reaction conditions produced the corresponding 1,3-diene (expt. 2). This certainly supports route b.

In conclusion, the present protocol using in situ prepared Pd(0) nanoparticles provides a very convenient and efficient methodology for a one-pot synthesis of conjugated en-yne compounds from *vic*-diiodoalkenes [8]. The significant improvements offered by this procedure are operational simplicity, excellent stereoselectivity, general applicability, high isolated yields of products and reaction in aqueous medium avoiding hazardous organic solvents.

Pd(0) nanoparticle-catalyzed Tsuji–Trost reaction

The Tsuji–Trost reaction, i.e., allylic substitution of active methylene compounds, has been less studied, and, only recently, Pd and Co nanoparticles immobilized on silica [9a], montmorillonite entrapped sub-nano-ordered Pd clusters [9b], and Pd nanoparticle stabilized by an asymmetric diphosphite [9c] were reported. Allylation of amines [9d] and phenols [9e] by Pd nanoparticles was also demonstrated. We report here a novel ligand-free protocol for allylic substitution of active methylene compounds by allyl acetate and its derivatives (Tsuji–Trost reaction), catalyzed by Pd(0) nanoparticles. The reaction in tetrahydrofuran (THF) leads to bisallylation in one stroke, whereas highly selective monoallylation by allyl acetate takes place in H_2O (Scheme 3).



Scheme 3

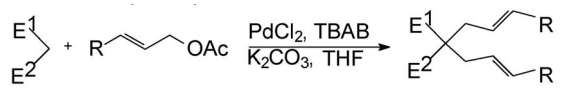
The experimental procedure is very simple. A one-pot reaction of active methylene compound and allyl acetate in the presence of the $PdCl_2$/TBAB/K_2CO_3 system in refluxing THF provided the product. The formation of Pd(0) nanoparticles in situ from this reagent system was detected by us from the analysis of the reaction mixture by TEM and EDS. The size of Pd nanoparticles was found to be 5–8 nm. In the absence of Pd nanoparticles, no reaction was initiated.

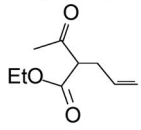
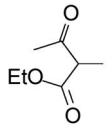
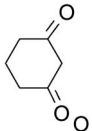
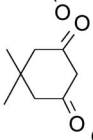
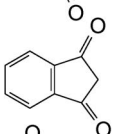
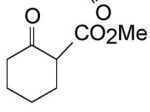
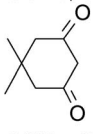
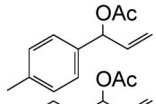
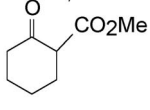
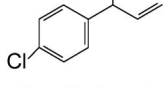
Several structurally diverse active methylene compounds underwent allylation by allyl acetate or its derivatives by in situ generated Pd(0) nanoparticles in THF to produce the corresponding allylated products in high yields. The results are summarized in Table 2.

As evident from the results, all reactions produced bisallylated products under these conditions. The participating active methylene compounds were acyclic and cyclic 1,3-diketones, 1,3-keto esters, 1,3-diester, and allylic agents used were allyl acetate, crotyl acetate, cinnamyl acetate, and its derivatives. The careful monitoring of the progress of the reaction by thin-layer chromatography (TLC) and ^{1}H NMR at intermediate stages indicated the presence of monoallylated compound in the range of 5–7 % together with the starting material and bisallylated compound. It was also found that allylation of monoallyl ethyl acetoacetate by this procedure was complete within 1.5 h (entry 4, Table 2) compared to 7 h required for bisallylation starting from ethyl acetoacetate (entry 2, Table 2). This indicates that bisallylation is much faster than the monoallylation step, restricting accumulation of monoallylated compound in the reaction mixture.

The reactions were very clean, and bisallylated products were the only isolable compounds. The bisallylated compounds are very useful synthons. THF was found to be the solvent of choice for the formation of bisallylated products in comparison with reaction results with other solvents. Pd(0) nanoparticles were formed from the reduction of $PdCl_2$ by the alkene moiety of allyl acetate. The slurry of Pd nanoparticles remaining after extraction of product was evaporated under vacuum to leave a dust of residue, which showed the presence of metallic Pd by XRD. This solid was equally effective for three subsequent runs without any loss of efficiency.

Table 2 Allylation of active methylene compounds by allyl acetate catalyzed by Pd(0) nanoparticles in THF.

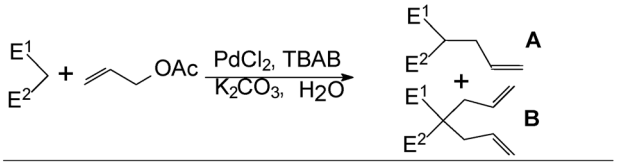


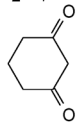
entry	E^1, E^2	R	time (h)	yield (%)[a]
1	COMe, COMe	H	6	82
2	COMe, CO_2Et	H	7	88
3	CO_2Et, CO_2Et	H	12	75
4		H	1.5	85
5		H	1.5	90
6		H	7	87
7		H	6	88
8		H	6.5	85
9		H	5	70
10	COMe, COMe	Me	9	75[b]
11	COMe, CO_2Me	Me	9.5	72[b]
12	COMe, COMe	Ph	10	85
13	COMe, CO_2Et	Ph	11	81
14		Ph	9	76
15	COMe, COMe		11	72
16			7	78

[a] Yields refer to those of purified products characterized by IR, ^1H and ^{13}C NMR spectroscopic data. [b] Mixture of *E* and *Z* isomers (90:10 by ^1H NMR)

Interestingly, when the reaction was carried out in H_2O, monoallylation took place selectively. The results are reported in Table 3. The reaction proceeded successfully only with allyl acetate; cinnamyl acetate and crotyl acetate failed to produce any allylated product. However, the selectivity was quite high; only in one example (entry 2, Table 3), 20 % of the bisallylated product was formed out of four types of substrates.

Table 3 Allylation of active methylene compounds by allyl acetate catalyzed by Pd(0) nanoparticles in H_2O.

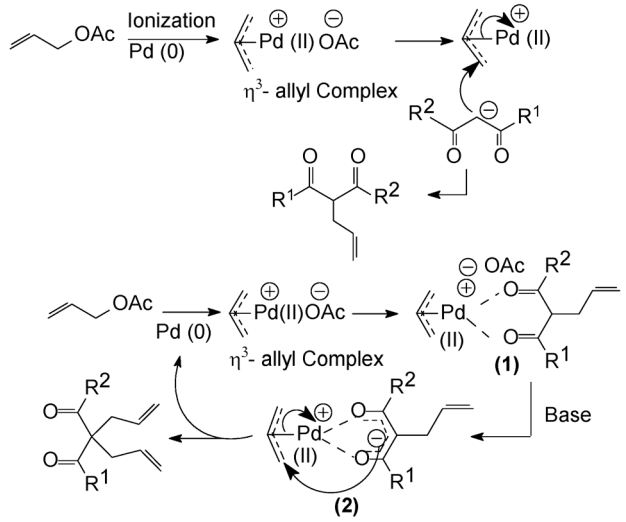


entry	E^1, E^2	time (h)	**A**:**B**	yield (%)[a]
1	COMe, COMe	9	100:00	86
2	COMe, CO_2Et	8	80:20	72
3	CO_2Et, CO_2Et	12	100:00	75
4		7	100:00	70

[a] Yields refer to those of purified products characterized by IR, ^1H and ^{13}C NMR spectroscopic data.

Analysis of results of allylation of all substrates included in Tables 2 and 3 revealed that the additions were highly regioselective. When allyl acetate was used, terminal alkenes were produced (entries 1–9, Table 2 and entries 1–4, Table 3), whereas substituted allyl acetates provided internal alkenes (entries 10–16, Table 2). We speculate that Pd(0) nanoparticles combine with allyl acetate to form a η^3-allyl-Pd(II)-complex **1** which then reacts with an active methylene compound to give an intermediate **2**, which provides the corresponding product by addition to the less-substituted carbon end (Scheme 4). The difference in reactivity of active methylene compounds in H_2O and THF leading to mono- and bisallylation, respectively, may be explained by the fact that H_2O hydrates the Pd(II) in the complex **1**, weakening the coordination of Pd with C=O, thereby decreasing the acidity at the methine center to go for further allylation. However, in nonaqueous medium having no such effect bisallylation is favored. THF was found to be the best solvent toward bisallylation as mentioned earlier. However, it is not clear to us why the monoallylation in water is successful only for allyl acetate and fails for other acetates. The steric factor may have a role.

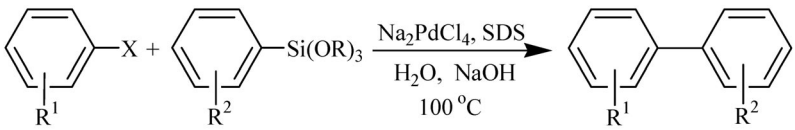
In conclusion, the present protocol using an in situ prepared Pd(0) nanoparticle provides a convenient and efficient procedure for allylation of active methylene compounds by allyl acetate [10]. The significant improvements offered by this procedure are operational simplicity, achievement of selective mono- or bisallylation in H_2O or THF, respectively, high regioselectivity in formation of products, high isolated yields, and reusibility of catalyst.



Scheme 4 Possible mechanism of mono-allylation in water and bisallylation in THF.

Pd(0) nanoparticle-catalyzed Hiyama coupling

The Pd-catalyzed cross-coupling reaction to produce unsymmetrical biaryls is a useful protocol in organic synthesis and has wide applications in the synthesis of polymers, agrochemicals, and pharmaceutical intermediates [11]. The most frequently employed methods to perform this coupling reaction are Stille [12], Suzuki-Miyaura [13], and Hiyama [14] reactions. In spite of comparable excellent yields, high stereoselectivities and superior functional group tolerance, the use of toxic tin reagents in Stille couplings, and difficulties in the preparation and purification of Suzuki boron reagents are disadvantages. The ease of preparation and low toxicity of organosilane reagents made the Hiyama coupling more attractive. Thus, several methods have been developed for this transformation using various Pd catalysts in the presence of a ligand and fluoride derivatives [15]. We report here a one-pot fluoride-free Hiyama coupling of aryl bromides with arylsilanes using Pd(0) nanoparticles, prepared in situ from Na_2PdCl_4/SDS (sodium dodecyl sulfate) in water (Scheme 5).



Scheme 5

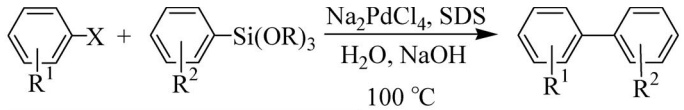
The experimental procedure is very simple. A mixture of aryl bromide and aryl siloxane in water was stirred at 100 °C (oil bath temperature) in the presence of a catalytic amount of Na_2PdCl_4, SDS, and NaOH (3 M) for the required period of time. Standard work-up provided the product. Two surfactants, SDS and SDBS (sodium dodecylbenzene sulfonate) were investigated. SDS gave better yields and is also less expensive and easily available. The base, NaOH, was found to be the best compared to Na_2CO_3, $NaHCO_3$, KOH, and NaOAc.

To determine the active catalytic species in this reaction, an extract from the reaction of 4-bromoanisole and phenyltrimethoxysilane after 3 min, when analyzed by UV (H_2O) spectroscopy, did not show the presence of a Pd(II) peak. However, the TEM image and EDS confirmed the presence of Pd

nanoparticles (3–6 nm). It is suggested that SDS served as the reductant as well as stabilizer in the formation of Pd nanoparticles.

Several substituted aryl bromides underwent cross-coupling with phenyltrimethoxysilanes using this procedure to produce the corresponding biaryl derivatives. The results are summarized in Table 4. Trace amounts (2–5 %) of dimeric products of arylsiloxane coupling were removed during the purification process. The reaction was uniform irrespective of the nature of the substituents (electron-withdrawing or -donating) on the aromatic ring. A wide range of substituents which included CHO, OMe, NO_2, COMe, F, and Cl were compatible with this procedure. As shown in Table 4, this procedure provides high chemoselectivity in reactions with other halo-substituted aryl compounds. Only bromo- and iodo- derivatives (entries 15–18, Table 4) participated in the reaction, leaving chloro- and fluoro groups (entries 11 and 12, Table 4) unaffected. Interestingly, aldehydes (entries 6 and 10, Table 4) did not undergo metal-catalyzed nucleophilic addition with the aryltrimethoxysilane.

Table 4 Pd nanoparticle-catalyzed Hiyama cross-coupling of aryl bromides and iodides with arylsiloxanes.



Entry	R^1	R^2	R	Time (min)	Yield (%)[a]
1	H	H	Me	5	96
2	2-Me	H	Me	5	92
3	2-OMe	H	Me	5	90
4	3-Me	H	Me	5	86
5	3-OMe	H	Me	5	90
6	3-CHO	H	Me	5	88
7	4-Me	H	Me	5	94
8	4-OMe	H	Me	5	92
9	4-COMe	H	Me	5	95
10	4-CHO	H	Me	5	88
11	4-F	H	Me	5	92
12	4-Cl	H	Me	5	94
13	4-Me	4-Me	Et	6	80
14	3-OMe	4-Me	Et	6	80
15	3-NO_2	4-Me	Et	6	75
16	H	H	Me	5	94

(*continues on next page*)

Table 4 (*Continued*).

Entry	R^1	R^2	R	Time (min)	Yield (%)[a]
17	4-Me	H	Me	5	90
18	3-NO_2	H	Me	5	93

Entries 1-14, X = Br; 15-18, X = I.

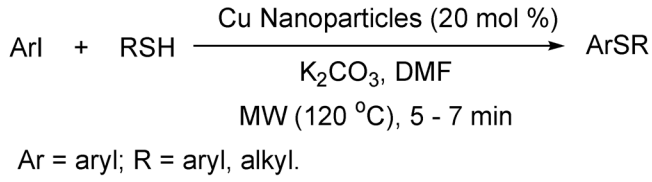
[a] Isolated yields of purified products (^{1}H and ^{13}C NMR)

In general, the reactions are clean and high yielding. All the products were obtained in high purities. The aqueous layer containing the catalyst after work-up, was recycled for three subsequent runs with only a gradual loss of efficiency. It is believed that the reaction proceeds through the usual pathway of the Pd-catalyzed Hiyama coupling. Sodium hydroxide works here as an alternative promoter to fluoride ions used in conventional procedures.

In conclusion, this procedure has a marked distinction from other Pd nanoparticle-catalyzed processes [15a,b], providing a one-pot, simple, and fast (5 min) operation compared to other multi-step and lengthy reactions [15a]. Other significant advantages offered by this procedure are mild reaction conditions, no requirement of phosphine or imine ligands or a fluoride source, and the reaction occurs in water. To the best of our knowledge, this is the fastest Hiyama coupling of aryl bromides with arylsilanes to afford biaryl derivatives using Pd catalysis [16].

Cu nanoparticle-catalyzed aryl-sulfur bond formation

The formation of aryl-sulfur bond is of much importance because of the prevalence of this bond in many molecules of pharmaceutical and material interest [17] and the utility of aryl sulfides as useful intermediates in organic synthesis. The classical method for the synthesis of aryl sulfides involved condensation of aryl halides with thiols requiring strongly basic and harsh reaction conditions. However, such methods are not desirable for molecules containing sensitive functional groups. The development of transition-metal-catalyzed coupling have overcome these difficulties to a great extent. A number of methods have been reported for the synthesis of aryl-aryl and aryl-alkyl sulfides using Pd [18], Cu [19], Co [20], and other metal catalysts. We report here a novel ligand-free protocol for the condensation of aryl iodides with thiols using nano Cu (20 mol %) under microwave irradiation in the presence of a base (Scheme 6).

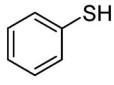
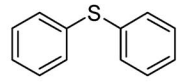
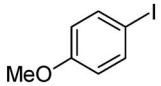
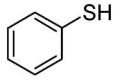
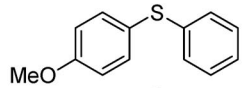
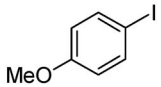
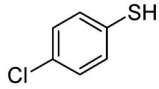
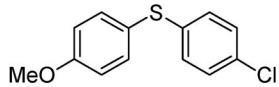
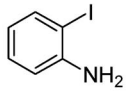
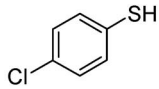
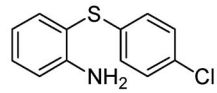
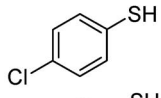
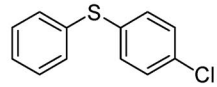
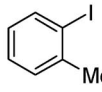
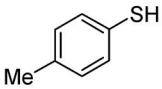
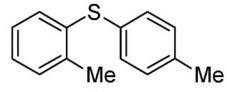
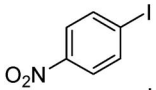
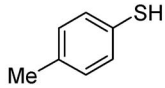
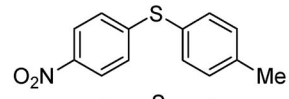
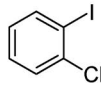
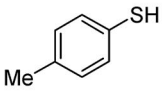
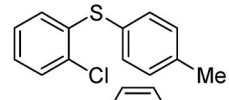
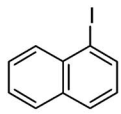
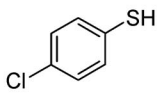
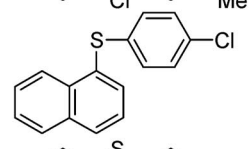
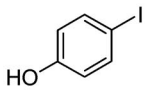
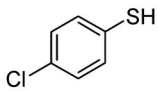
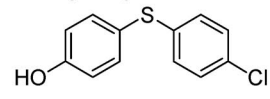
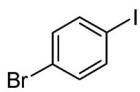
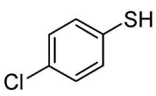
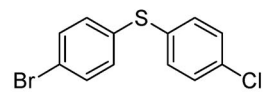


Scheme 6

The experimental procedure is very simple and convenient. A mixture of an aryl iodide and thiophenol/alkanethiol in dimethylformamide (DMF) was treated under microwave irradiation with K_2CO_3 and Cu nanoparticles (4–6 nm). Usual work-up provided the product. In the absence of a base, the progress of the reaction was only marginal. Although any conventional base such as Na_2CO_3, K_2CO_3, K_3PO_4, and NaOH may be used, K_2CO_3 was chosen, giving better results in terms of yields.

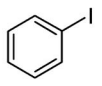
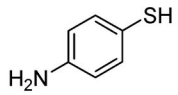
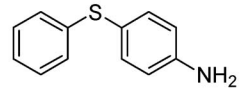
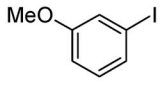
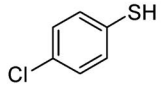
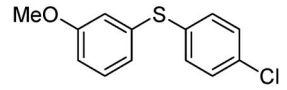
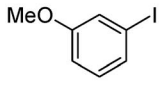
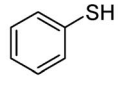
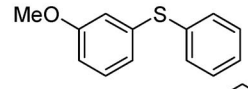
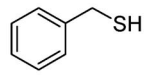
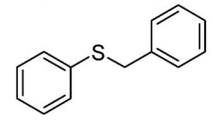
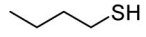
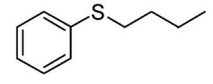
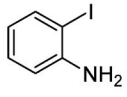
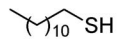
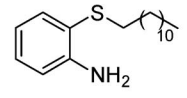
Several diversely substituted aryl iodides underwent reactions with a variety of substituted thiophenols, benzyl mercaptan, butane, and dodecane thiols by this procedure to produce the corresponding diaryl/aryl-alkyl sulfides. The results were summarized in Table 5. Both electron-donating and -withdrawing groups substituted aryl iodides participated in this reaction with similar efficiency. The substitution at the ortho position (entries 4, 6, 8, 17, Table 5) did not affect the reaction. The coupling also proceeded well with substituted thiophenols and alkane thiols. This reaction is also very chemoselective. Aryl iodides coupled with thiols without affecting bromo and chloro groups present in the aryl ring (entries 8, 11, Table 5). However, in coupling of *p*-nitroiodobenzene (entry 7, Table 5) a small amount (5 %) of product with nitro group reduced to amino, was obtained.

Table 5 Cross-coupling reaction of aryl iodide with thiols catalyzed by Cu nanoparticles.

Entry	Aryl iodide	Thiol	Time (min)	Aryl sulfide	Yield (%)
1			5		98
2			5		94
3			5		93
4			6		97
5			5		95
6			6		91
7			5		87
8			6		91
9			5		95
10			7		72
11			6		81

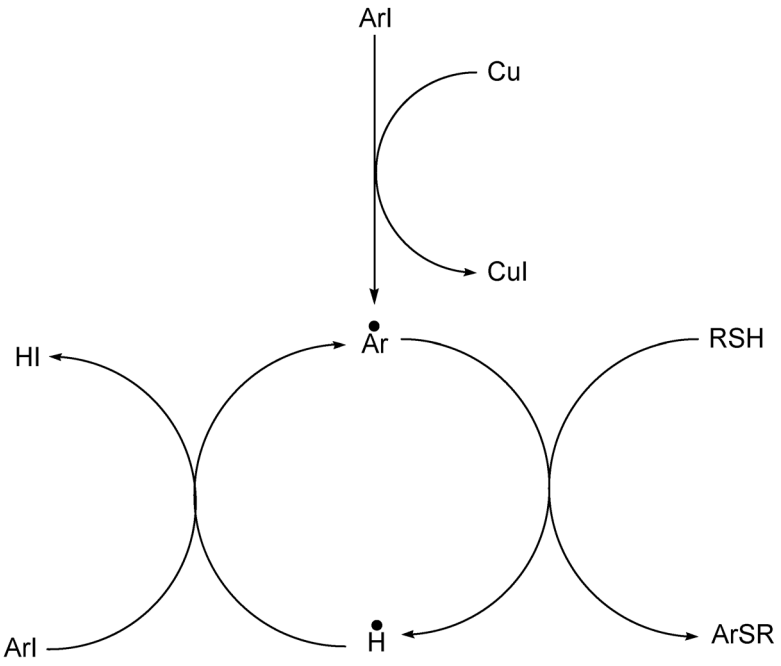
(*continues on next page*)

Table 5 (*Continued*).

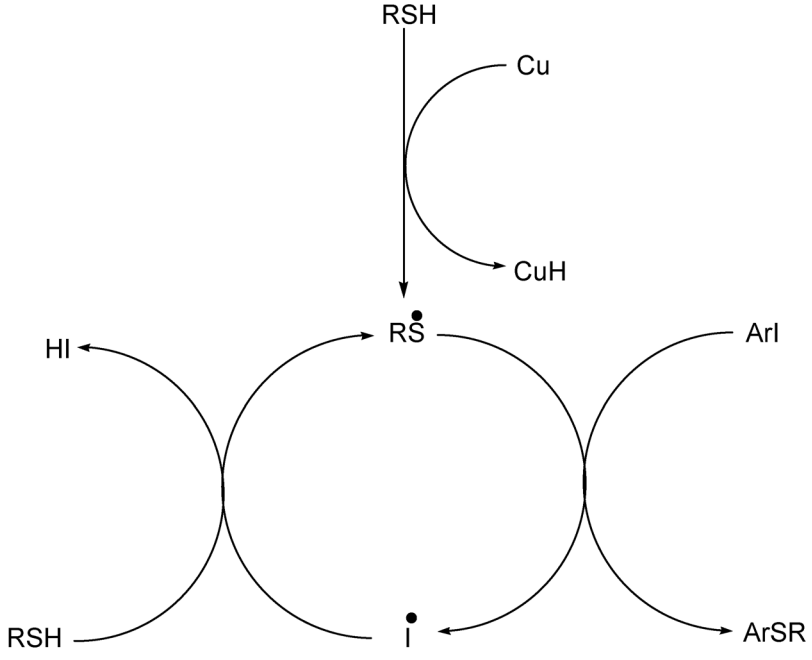
Entry	Aryl iodide	Thiol	Time (min)	Aryl sulfide	Yield (%)
12			7		88
13			5		86
14			5		93
15			6		82
16			10		63
17			6		61

In general, the reactions were very clean and high yielding. However, in several reactions (entries 6, 8, 13–16, Table 5) a small amount (2–5 %) of diaryl/dialkyl disulfides were isolated, which were easily separated during purification by column chromatography. In the absence of Cu nanoparticles, coupling reaction was not initiated at all. It was found that 20 mol % of Cu nanoparticles provided the best results in terms of reaction time and yield. When the reaction was carried out at 120 °C by conventional heating, it required 12–15 h to be completed, whereas under microwave irradiation the reactions were complete within 5–7 min. DMF was found to be the solvent of choice, furnishing best results among other solvents such as toluene and THF. The reaction medium is mild enough to tolerate a variety of functional groups such as OMe, OH, Cl, Br, NH_2, etc.

To provide a mechanistic rationale of this nano Cu-catalyzed coupling of aryl iodides and thiols, a tentative pathway was proposed based on some experimental findings. In a metallic Cu-catalyzed coupling reaction of thiophenols with aryl halides, Yamamoto [19e] postulated an intermediate of diaryl disulfide which then led to diaryl sulfide. To check the involvement of this intermediate in our reaction, a coupling reaction of aryl iodide with diphenyl disulfide was carried out under identical reaction conditions. However, no reaction occurred, and the starting materials remained unaffected. Thus, the possiblity of this pathway was ruled out. It may be recalled that the progressive decrease in size of metal particles having a diameter in the nano range is accompanied by an increase in Fermi potential. Thus, a stepwise lowering in the radox potential value takes place, and this makes it easier for a nanoparticle to transfer electron to other species. Hence, the possibility of a single electron-transfer process is considered. It was observed that when the reaction was carried out in the presence of 2,2,6,6-tetramethylpiperidine *N*-oxide (TEMPO), a radical quencher, under idential reaction conditions, the reaction was substantially (>60 %) arrested. Thus, a radical pathway may be a possibility. Two possible routes were considered (Scheme 7, a and b). In route a, Cu initiates the redical chain process by transferring its one electron to ArI to form an Ar radical which then combines with RSH to provide the product ArSR and H radical which propagates the process (Scheme 2, route a). However, we did not isolate any biaryl compound, Ar–Ar or ArH in any amount from this reaction, which is usually expected from this



Scheme 7a



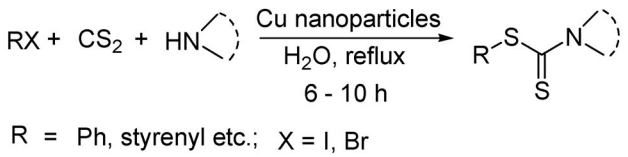
Scheme 7b

type of free radical reaction. Our attempts to trap this Ar radical by electron-deficient unit also failed. This led us to explore the possibility of an alternative route b where nano Cu transfers its electron to the thiol to produce the RS radical which then in interaction with ArI forms the product, ArSR, releasing iodo radical. The iodo radical then propagates the process, forming fresh RS radical. If the reaction takes this course, CuH should be produced in the intial electron-transfer reaction of Cu nanoparticle. The evidence of the formation of CuH is now substantiated by an observation of reduction of the nitro group in the reaction of *p*-nitro iodobenzene with *p*-methyl thiophenol (entry 7, Table 5), as mentioned earlier. The formation of CuH in this process is also confirmed by a reaction of thiophenol with *m*-nitro toluene in the place of iodobenzene under identical reaction conditions producing *m*-toluidine and diphenyl disulfide. This route also gains support by isolation of 2–5 % of disulfides, ArS–SAr in several reactions (entries 6, 8, 13–16). The HI produced during the reaction was neutralized by K_2CO_3. The mechanism in route b is also supported by the fact that the RS radical is logically to favor formation of RSAr through S–C bond rather than RSSR by S–S bond because of the greater stability of S–C bond compared to S–S, as indicated by the larger value of relative free energy for S–C bond scission (approx. 108 kcal/mol) in diphenyl sulfide compared to S–S bond scission (47 kcal/mol) in diphenyl disulfide. In view of this evidence, route b is suggested as the possible pathway.

In conclusion, the present procedure using Cu nanoparticles provides a very efficient and convenient methodology for the coupling of aryl iodides and thiophenols. To the best of our knowledge, this is the first report of aryl-sulfur bond formation using nano Cu [21]. The significant improvements offered by this procedure are operational simplicity, no involvement of ligand, general applicability to both aromatic and aliphatic thiols, fast reaction (5–7 min), and comparatively high isolated yields of products. Moreover, this work demonstrates the potential of Cu nanoparticles in carbon-heteroatom bond formation, which is less explored compared to C–C bond formation involving nano metals.

Cu nanoparticle-catalyzed synthesis of aryl dithiocarbamate

Organic dithiocarbamates are of much importance as versatile synthetic intermediates, and linkers in solid-phase organic synthesis [22]. Moreover, their occurrence in a variety of biologically active compounds, their pivotal roles in agriculture, and their medicinal and biological properties, prompted interest in the development of convenient synthetic procedures for these compounds. The conventional methods involve reactions of amines with thiophosgene and its derivatives, which are not desirable for environmental concerns [23]. We report here a one-pot, three-component condensation of an amine, carbon disulfide, and an aryl iodide or styrenyl bromide catalyzed by Cu nanoparticles in water under ligand- and base-free conditions leading to the synthesis of aryl or styrenyl dithiocarbamates (Scheme 8).

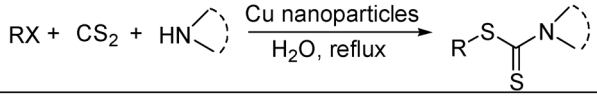


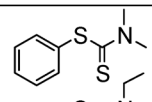
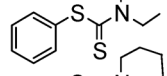
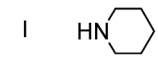
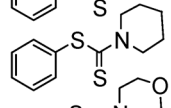
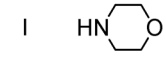
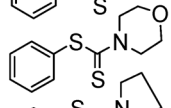
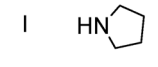
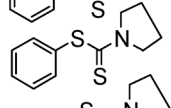
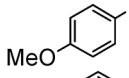
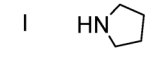
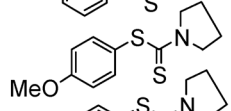
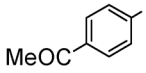
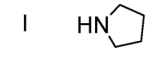
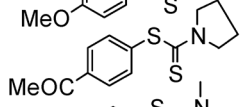
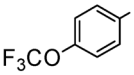
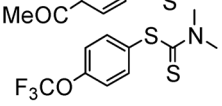
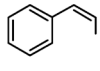
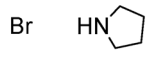
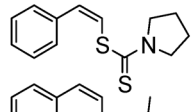
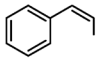
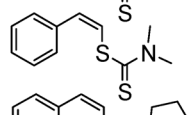
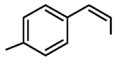
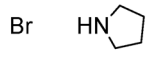
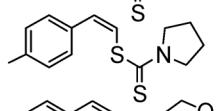
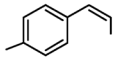
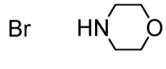
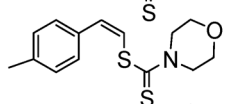
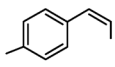
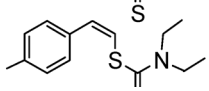
Scheme 8

The experimental procedure is very simple. A mixture of aryl iodide or styrenyl bromide, carbon disulfide, amine was heated under reflux in water in the presence of Cu nanoparticles for a required period of time (TLC). Standard work-up provided the product. The aqueous part containing Cu nanoparticles, left after work-up was recycled up to four times without appreciable loss of efficiency for a representative reaction of 2-(4-methylphenyl)vinyl bromide and pyrrolidine.

Several substituted aryl iodides and styrenyl bromides underwent coupling with dithiocarbamate anion, generated in situ by the reaction of carbon disulfide and amine to provide the corresponding dithiocarbamate derivatives. The results are summarized in Table 6. A variety of substituents in the aromatic ring, such as Cl, OCH_3, OCF_3, and $COCH_3$ are compatible in this reaction. The open-chain as well as cyclic amines participated uniformly. Significantly, the reactions of vinyl bromides are highly stereoselective. The (*Z*)-vinyl bromides (Table 6, entries 9–16) provided the corresponding (*Z*)-vinyl dithiocarbamates (no *E*-isomer was detected/isolated), while the (*E*)-bromides (Table 6, entries 17–21) furnished the (*E*)-dithiocarbamates predominantly with a trace amount (1–3 %) of (*Z*)-isomers. The (*E*)- and (*Z*)-isomers were characterized by their ^1H and ^{13}C NMR spectroscopy.

Table 6 Cu nanoparticle-catalyzed coupling of aryl- and vinyl halides with dithiocarbamate anion.



Entry	R	X	Amine	Time /h	Product	Yield (%)[a]
1		I	$HNMe_2$	8		94
2		I	$HNEt_2$	8		91
3		I		8		92
4		I		8.2		88
5		I		8		87
6		I		9		75
7		I		8.5		80
8		I	$HNMe_2$	8		85
9		Br		6		92
10		Br	$HNMe_2$	6		95
11		Br		7		91
12		Br		9		87
13		Br	$HNEt_2$	8		88

(*continues on next page*)

Table 6 (*Continued*).

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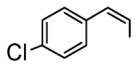
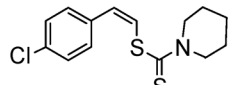
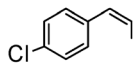
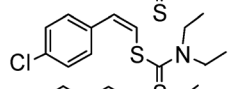
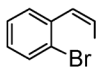
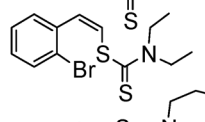
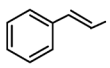
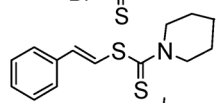
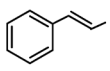
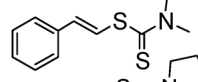
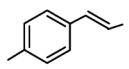
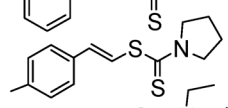
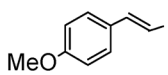
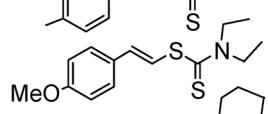
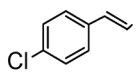
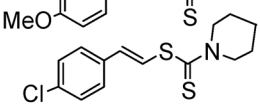
14		Br	HN	8.2		89
15		Br	$HNEt_2$	8		92
16		Br	$HNEt_2$	10		76
17		Br	HN	8.2		86[b]
18		Br	$HNMe_2$	8		89[b]
19		Br	HN	8.5		84[b]
20		Br	$HNEt_2$	8.4		92[b]
21		Br	HN	8		86

[a] Isolated yields of pure products (^1H and ^{13}C)

[b] The substrates in entries 17-20 gave a trace amount (1-3%) of the corresponding *Z*-isomers as determined by ^1H NMR.

We believe that the reaction proceeds in a catalytic cycle where the aryl/styrenyl halide undergoes oxidative addition to Cu to form ArCuI which combines with dithiocarbamate anion, generated in situ by the reaction of amine and carbon disulfide, to give an intermediate, which leads to product by subsequent reductive elimination. The liberated Cu(0) initiates further reaction and propagates the cycle. We believe that Cu nanoparticles facilitate oxidative coupling with aryl iodide because of their inherent character to transfer electrons more easily than metallic Cu.

Presumably, use of water also makes this reaction more facile because of its amphoteric nature and thus not requiring any base.

The reactions were very clean and high yielding, and no side products were isolated. A comparison of results of reactions by Cu nanoparticles with those by metallic Cu distinctly demonstrates the superior efficiency of Cu nanoparticles compared to metallic Cu. Our procedure also offers significant improvements to that catalyzed by CuI [24] with regard to catalyst loading (3.0 vs. 15 mol %), reaction medium (H_2O vs. DMF), and reaction time (6–10 h vs. 22 h). The present procedure provides a one-pot operation and avoids the use of sodio-salt of dithiocarbamic acid used in CuI one. The preparation and purification of the sodio-salt is very tedious and is also commercially very expensive. In addition, our reaction did not require a ligand or a base, whereas the CuI-catalyzed one [24] did not proceed without ligand. The stereoselectivities achieved for vinyl dithiocarbamates by this Cu nanoparticle-catalyzed reaction is also better than those in the CuI-catalyzed one. In fact, highly diastereoselective synthesis of vinyl dithiocarbamates was not addressed earlier.

To conclude, the present procedure using Cu nanoparticles provides a very efficient and convenient methodology for the synthesis of aryl- and styrenyl dithiocarbamates by a one-pot three-component

condensation of aryl/styrenyl halide, carbon disulfide, and amine in water [25]. The advantages offered by this procedure are operational simplicity, general applicability to acyclic and cyclic amines, ligand- and base-free reaction, high yields of products, excellent diastereoselectivity for styrenyl dithiocarbamates, and green protocol providing recyclability of catalyst up to four times without loss of efficiency, and use of water as reaction medium.

SUMMARY

We demonstrated here a few useful reactions involving C–C and C–S bond formation by the catalysis of Pd and Cu nanoparticles. The efficiency observed in all of these reactions is better than those reported by the corresponding metal salts. This shows the potential of metal nanoparticles in catalysis and leaves great promise for more useful applications in organic synthesis.

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