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Aerobic Cu and amine free Sonogashira and Stille couplings of aryl bromides/chlorides with a magnetically recoverable Fe_3O_4@SiO_2 immobilized Pd(II)-thioether containing NHC

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ABSTRACT

Two value added C—C cross coupling reactions; Sonogashira and Stille couplings were achieved at milder conditions in the catalytic presence of a magnetically recoverable heterogeneous catalyst Fe_3O_4@SiO_2@NHC^SPh-Pd(II). The catalyst was earlier reported for Suzuki-Miyaura reaction, and as an extension of its catalytic efficiency, the Stille and Sonogashira cross coupling reactions under aerobic condition has been explored in present report. The Sonogashira coupling of aryl bromides and terminal alkynes produced an excellent yield (~96% at 0.25 mol% Pd) of the desired coupling product under copper and amines free conditions. Moreover, an excellent Stille coupling of readily available and more latent aryl chlorides and trialkylstannane was obtained (yields up to 95% at 0.25 mol% Pd) in absence of toxic fluorides additives. The broad substrate scope of the catalyst for both the coupling reactions and the magnetically recoverable feature of catalyst make this reaction highly desirable for industrial applications of present heterogeneous catalysis.

The C—C bond forming reactions catalyzed by palladium based catalysts [1] are currently rank amongst most versatile and straight forward protocols in laboratory as well as industrial organic synthesis of pharmaceuticals, agrochemicals, natural products, therapeutic agents and many other value added organic materials [2]. The Pd and Cu (as co-catalyst) catalyzed Sonogashira coupling of terminal alkynes and aryl/vinyl halide/triflate is of utmost importance among the Pd catalyzed coupling reactions [3]. The Sonogashira cross coupling has shown outstanding applications in the synthesis of biaryl derivatives of acetylene which are key intermediates in the multistep synthesis of several naturally occurring compounds, pharmaceutical, organic-LEDs, sensing of carbohydrates, new carbon allotropes and carbon rich materials [4]. However, the certain limitations of Sonogashira coupling which are quiet predominant are the use of amine and co-catalyst copper salt. In presence of co-catalyst copper salt, the copper acetylide undergo Glaser-Hay homo coupling under aerobic conditions [5]. Moreover, the use of amines for deprotonation in such cross coupling reactions is not environmental benign. Therefore, the development of new catalytic system is required, which can avoid the use of copper and amine in coupling reactions. For biaryl formation, the Stille coupling is an important Pd catalyzed cross coupling reaction which coupled the organostannanes and organic halides/triflate in the presence of metal fluorides activators [6,7]. However, the toxicity of organostannane compounds which are used in stoichiometric amount is still a prime drawback of the reaction, but some reports indicate the isolation of toxic tin residue from the desired product [8].

A broad spectrum of Pd based homogeneous catalysts containing sterically hindered phosphanes [9], PEPPSI based Pd catalyst [10], palladacycles [9b,11] and NHC-Pd catalyst [12] have been envisioned for Pd activated cross coupling reactions. The catalytic systems reported for Sonogashira reaction required high Pd loading (generally 1.0 mol% or more), and high working temperature [13,14]. Furthermore, the recovery and reusability of the catalyst is also a major issue associated with homogeneous catalytic systems. The removal of the catalyst from the reaction is highly essential to avoid the metal contaminations especially in the pharmaceutical and drugs molecules [15]. Therefore, given the current scenario of catalysis, the main focus is to develop a catalyst which can fulfill both the criteria of (i) good activity as homogeneous catalyst (ii) and good recoverability to avoid the wastage of non-renewable precious metals. Solid supported metal catalysts offer a combination of both the properties, and also make them

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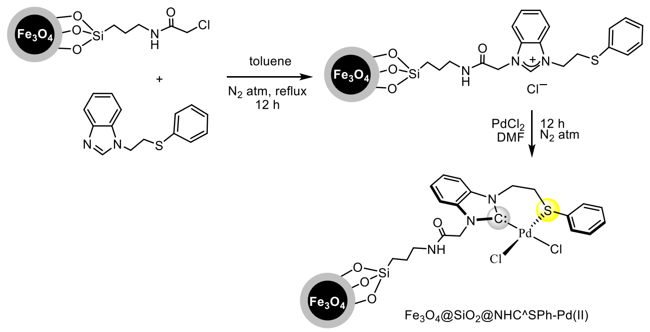
economically viable and applicable to a broad range of essential catalytic conversions [16]. In this context, the NHCs have gained wide applications in organometallic chemistry and serve as better alternative of toxic, expensive, difficult to handle and sterically hindered phosphines [13c,17]. Owing to the availability of two electrons stronger σ-donor and very weak π-accepting coordination behavior of NHC ligands, their NHC-metal complexes have gained a unique balance of stability versus reactivity, which is highly desired in catalysis [13c,17,18]. The NHC ligands are strongly coordinated to the metal center and thereby contribute the much needed stability of the catalytic system and also prevent leaching of metal during the catalytic process. Apart of that, NHC ligands also favor the metal center more electron-rich and provide affluence in the important oxidative addition process of reaction. In contrast to phosphines, the organochalcogen containing complexes are robustly works in air/moisture and aqueous system with greater efficiency [19]. Therefore, having a mindset of a unique combinations of NHC and thioether donors, both had mixed and a heterogeneous catalyst Fe_3O_4@SiO_2@NHC^SPh-Pd(II) was crafted [19e]. The catalyst is fully explored for the Sonogashira and Stille cross coupling reactions. The catalyst have shown an excellent activity, and emerged as an efficient recoverable Pd catalyst for Sonogashira coupling under aerobic condition, and Stille cross coupling reactions of highly desirable, readily available and inexpensive chloroarenes.

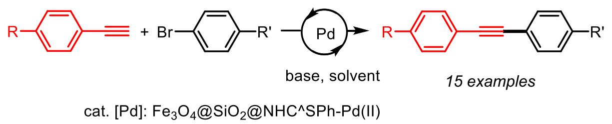
The solid supported Pd catalyst; Fe_3O_4@SiO_2@NHC^SPh-Pd(II) was synthesized by reported method (Scheme 1) [19e]. The quantity of the palladium bonded to the surface of Fe_3O_4@SiO_2 nanoparticles was determined by ICP-AES analysis of Fe_3O_4@SiO_2 supported Pd(II)-thioether-NHC complex. The concentration of Pd was estimated to be 0.167 mmol of Pd/g.

Activity of Fe_3O_4@SiO_2@NHC^SPh-Pd(II) in catalysis for Sonogashira Cross Coupling

To elucidate the catalytic potential of Fe_3O_4@SiO_2@NHC^SPh-Pd (II) for various cross coupling reactions, the Sonogashira cross-coupling reaction of the acetylene and aryl bromide in DMF solvent under open air conditions was investigated, and good to excellent transformation of respective coupling products was recorded (Scheme 2).



Scheme 1. Synthesis of Fe_3O_4@SiO_2 supported Pd(II)-thioether-NHC catalyst.

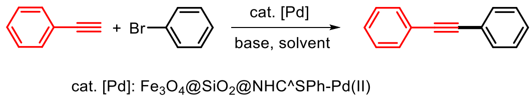


Scheme 2. Copper and amine free Sonogashira cross coupling catalyzed with Fe_3O_4@SiO_2 supported Pd(II)-thioether-NHC heterogeneous catalyst.

To find the optimum conditions for the significant transformations, the optimization of various reaction parameters was initiated and summarized in Table 1. It was begin with the solvent optimization, and a range of polar and non-polar solvents were screened, the first trial was carried out in neat water at 90 °C, but no product formation observed (Table 1, entry 1). The reaction was again repeated in water along with the addition of a phase transfer catalyst tetra-*n*-butylammonium bromide (TBAB) to enhance the catalyst activity in water, reaction initiated but only the trace of coupling product was obtained (Table 1, entry 2). Various other solvents including the DMSO, toluene, 1,4-dioxane and acetonitrile were also investigated but all together failed to improve the yield of product (Table 1, entries 3–8). However, an excellent yield of the product (96%) was exclusively obtained in DMF solvent, hence, DMF was found to be ideal solvent for the present reaction.

Traditionally, the Sonogashira reactions essentially desire the presence of copper as a co-catalyst and a significant amount of amines. In the present method, Sonogashira coupling performed well in the absenteeism of both copper and amines. However, it is observed that base is essentially required for the reaction, as reaction does not work in the absence of base (Table 1, entry 9). Various strong and weak bases such as potassium carbonate, cesium carbonate, sodium acetate, sodium hydroxide and potassium hydroxide were investigated (Table 1, entries 3 and 10–13). It was observed that reaction is selectively works in presence of K_2CO_3 (up to 96% yield), while other base failed to mimic the reactions The amount of catalyst was also examined and it was found that 15 mg of the catalyst (contains 0.25 mol% of Pd, determined by ICP-AES analysis) significantly bring the optimum transformations (Table 1, entry 3). Reducing the catalyst amount, drastically reduces the product yield (Table 1, entries 14–17). During the opti-

Table 1
Reaction parameters optimizations for Sonogashira cross coupling catalyzed with Fe_3O_4@SiO_2 supported Pd(II)-thioether-NHC catalyst.[a]



Entry No.	Pd catalyst (in mg)	Base used	Temp. (°C)	Solvent (2.0 mL)	Yield (%)
1	15	K_2CO_3	90	Water	Nd
2[b]	15	K_2CO_3	90	Water[b]	Trace
3	15	K_2CO_3	90	DMF	96
4	15	K_2CO_3	90	Toluene	Nd
5	15	K_2CO_3	90	1,4-Dioxane	Nd
6	15	K_2CO_3	90	THF	Nd
7	15	K_2CO_3	90	DMSO	Nd
8	15	K_2CO_3	90	Acetonitrile	Nd
9	15	No base	90	DMF	Nd
10	15	Cs_2CO_3	90	DMF	Nd
11	15	NaOAc	90	DMF	Nd
12	15	NaOH	90	DMF	Nd
13	15	KOH	90	DMF	Nd
14	12	K_2CO_3	90	DMF	85
15	10	K_2CO_3	90	DMF	70
16	8	K_2CO_3	90	DMF	Trace
17	5	K_2CO_3	90	DMF	Nd
18	15	K_2CO_3	60	DMF	Nd
19	15	K_2CO_3	70	DMF	49
20	15	K_2CO_3	80	DMF	80
21	15	K_2CO_3	100	DMF	96

[a] Conditions: bromobenzene (0.157 g, 1.0 mmol), phenyl acetylene (0.122 g, 1.2 mmol), 15 mg Pd catalyst contains 0.25 mol% Pd, time (12 h), isolated yield after column chromatography, solvent (2.0 mL), base (1.4 mmol).

[b] TBAB (0.161 g, 0.5 mmol) used; Nd (not detected).

mization of reaction temperature, the reaction was screened from room temperature but no product was obtained up to 60 °C, however, a trace of the product was observed at 70 °C. Moving towards the higher temperature, significantly increased the yield of product (Table 1, entries 18–21) and a maximum 90% yield was obtained at 90 °C. Among all screened conditions, 1.0 mmol of aryl bromide, 1.2 mmol of phenylacetylene, 1.4 mmol of K_2CO_3, 0.25 mol% (15 mg) of catalyst in 2 mL of DMF at 90 °C under aerobic conditions furnished the optimum yields of cross-coupled product in 12 h. The product yield was significantly affected by the duration of reaction. The time profile of a representative Sonogashira coupling reaction of bromobenzene with phenyl acetylene was studied and shown in Fig. 1. The formation of the desire cross-coupled product was detected just after 1 h of the reaction. The % conversion of the substrate consistently increases with time and the highest yield was achieved in 12 h. Further stirring the reaction mixture does not produce any significant changes in the yield of the product.

With the optimized conditions in hand, the present coupling reaction was further generalized for a vast substrate scope of both the reactants; the aryl bromide and terminal alkynes (Table 2). A high level of reactivity in the Sonogashira coupling of bromobenzene and electron accepting group (R = CN, CHO, $COCH_3$, NO_2, CF_3) substituted aryl bromides such as 4-bromobenzonitrile, 1-bromo-4-nitrobenzene, 1-acetyl-4-bromobenzene, 4-bromobenzaldehyde and 1-bromo-4-(trifluoromethyl)benzene with phenyl acetylene was observed (Table 2, entries **1b**-**1f**). A series of linear π-conjugated systems having a strong electron accepting group at an end (electron pull system) were successfully synthesized. Outstanding results in the coupling of electron donating group ($-OCH_3$) substituted aryl bromide with phenyl acetylene was also observed and one end electron push linear π-conjugated system was synthesized in good yield (Table 2, entry **1g**). The reaction scope for terminal alkyne derivatives was investigated in and several substituted aryl acetylene substrates including the ones with the electron donating groups as well as the electron withdrawing groups were used and good yields of desire cross coupling products was obtained (Table 2, entries **1h**-**1m**). Here, it is worth mentioning that by using the combinations of substituted aryl bromides and aryl acetylene, some pull-pull (Table 2, compound **1j** and **1k**) and push–pull (Table 2, compounds **1i**, **1l** and **1m**) systems were successfully prepared in good yields. Moreover, reaction also works well for heteroaryl bromides, as the coupling of 3-(phenylethynyl) quinoline and 3-(phenylethynyl)pyridine with phenylacetylene resulted 69% and 75% yield of the desired products (**1m** and **1n**). A typical Sonogashira cross coupling reaction require an inert atmosphere under strict air and moisture free dry conditions [3,20], while present Sonogashira reaction is performed in a reaction tube in an open air conditions.

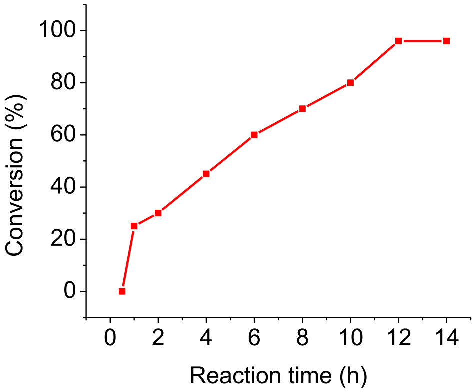
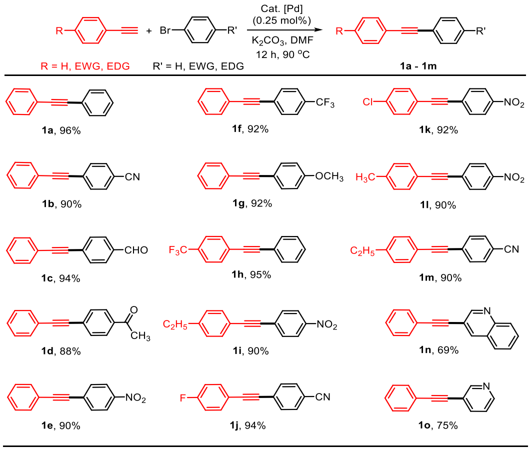


Fig. 1. Time profile of the Sonogashira coupling of bromobenzene and phenyl acetylene catalyzed with Pd(II)-thioether-NHC catalyst.

Table 2

Substrate scope of aryl bromides and terminal alkynes used for Sonogashira cross coupling catalyzed with Fe_3O_4@SiO_2@NHC^SPh-Pd(II) catalyst.[a]



[a] Optimized Conditions: aryl or heteroaryl bromide (1.0 mmol), acetylene derivative (1.2 mmol), Cat. [Pd]: Fe_3O_4@SiO_2@NHC^SPh-Pd(II) (0.015 g, 0.25 mol% Pd), temp (90 °C), time (12 h), isolated yields are given, DMF (2.0 mL), K_2CO_3 (0.200 g, 1.4 mmol), EWG (electron withdrawing groups) and EDG (electron donating groups).

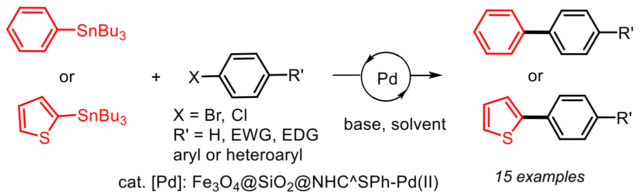
A comparison of the catalytic activity of Fe_3O_4@SiO_2@NHC^SPh-Pd(II) with previously reported Pd catalyst for copper and amine free Sonogashira coupling reaction has been made. A recyclable heterogeneous Pd catalyst supported on zeolite was reported for copper free Sonogashira coupling of aryl bromides but the catalyst needed 1 mol% of Pd along with 10 mmol of Et_3N under inert atmosphere to achieve maximum conversions [21]. $PdCl_2(PPh_3)_2$ complex with tetra-*n*-butylammonium fluoride (TBAF) as activator [22] reported as efficient homogeneous catalyst for copper, amine and solvent free Sonogashira coupling of ArI, Br and Cl under dry reaction conditions, however, reaction demands a high catalyst loading (3.0 mol% Pd) [23].

A nonsymmetrical PCN pincer Pd complex was also reported to catalyze Sonogashira coupling under copper free condition but it was only applicable for aryl iodide substrates and needs amine base and larger catalyst loading (2 mol%) [24]. The palladacycle (40 °C, 0.5 mol% Pd, Et_3N) [25] and $Pd(NH_3)_2Cl_2$ complex with 2,2′-dipyridylamine ligand (rt, 0.1 mol%, aryl iodide substrate) [26] are also found a bit less efficient to present recyclable Pd-catalyst under copper free, amine free and inert atmosphere free Sonogashira coupling. Elhage et al. reported [27] TiO_2 (Pd@TiO_2), CND (Pd@CND) or Nb_2O_5 (Pd@Nb_2O_5) supported Pd NPs as efficient air/moisture tolerant catalysts for the copper/amine free Sonogashira coupling reaction of aryl iodides. Their catalytic studies demonstrated that direct visible excitation of the Pd NP is required and the catalyst can be reused a couple of times but lost activity due to a reductive photochemical reaction. Furthermore, the catalyst activated the Sonogashira coupling of aryl iodides substrates only. The chalcogen containing palladacycles were also reported as air, moisture insensitive and efficient catalyst for copper/amine free Sonogashira coupling under aerobic conditions [28]. These chalcogen containing palladacycles were comparable with the present catalyst in terms of air/moisture insensitivity, Pd catalyst loading, copper or amine free condition, temperature, recyclability but the nature of the catalysis is of cocktail type between homogeneous and heterogeneous [28]. The present catalyst is undoubtedly an efficient recyclable heterogeneous Pd(II) catalyst with having additional filtration-free, magnetically retrievable features for the catalysis of copper and amine free Sonogashira coupling reaction under aerobic conditions and also this is for the first time when the organochalcogen functionalized NHC-Pd(II) complex is studied in the catalysis of Sonogashira coupling reaction.

Activity of Fe_3O_4@SiO_2@NHC^SPh-Pd(II) catalyst for Stille cross coupling reaction

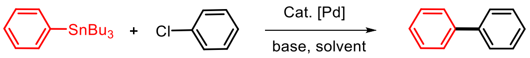
Encouraged by the outstanding catalytic potential of the Fe_3O_4@SiO_2 supported Pd(II)-thioether-NHC catalyst for Suzuki-Miyaura coupling [19e], copper/amine free Sonogashira coupling, the catalyst was also investigated for Stille cross coupling reaction. The Pd-catalyst work efficiently and it also activates the readily available and more latent aryl chlorides to produce the desire coupling product under aerobic reaction conditions (Scheme 3).

The reaction conditions were optimized using the representative substrate combination for Stille coupling reaction (Table 3). The reaction of tributylphenylstannane and chlorobenzene was initially performed in water and TBAB, a considerable yield was observed (Table 3, entry 1). The ionic species formed with the phase transfer catalyst (TBAB) during the course of coupling reaction are soluble in both organic as well as aqueous phases, and continuously transfer between both the phases facilitating coupling reaction [29]. Therefore, TBAB plays important role to accelerate the cross coupling reaction by facilitating the solvation of the base (inorganic species) in organic solvent as well as the solvation of organic substrates in water during catalysis. In order to further improve the yield, the reaction was investigated with various solvent trials (Table 3, entry 2–6). The yield was improved satisfactorily when DMF-Water solvent mixture was used (Table 3, entry 2). The best result in terms of product yield was obtained when dry DMF was used for the reaction (Table 3, entry 3). It was observed that the base is an essential requisite for the successful completion and best output of the reaction. Hence, different bases including K_2CO_3, Cs_2CO_3, CH_3COONa, NaOH, and KOH were investigated for the reaction (Table 2, entry 7–10), of these, the sodium acetate and potassium carbonate was found to be efficient for the present coupling reaction and gave 90% and 95% yield of the desired products respectively. In all the optimization reactions, 15 mg of catalyst was used, it works well for all reactions. Decreasing the amount of catalyst from 15 mg, drastically reduced the product yield (Table 3, entry 11–15). In all the optimization reactions the working temperature was 90 °C. A diminished yield of the cross coupled product was observed on lowering the reaction temperature. Hence, after all the optimizations, aryl bromide (1.0 mmol), tributylphenylstannane (1.0 mmol), K_2CO_3 (1.5 mmol), catalyst (0.015 g) in 2 mL of DMF at 90 °C under aerobic conditions resulted the maximum yields of the desired product in 6 h.



Scheme 3. Stille cross coupling catalyzed with Fe_3O_4@SiO_2 supported Pd(II)-thioether-NHC heterogeneous catalyst.

Table 3
Reaction parameters optimizations for Stille cross coupling catalyzed with Fe_3O_4@SiO_2 supported Pd(II)-thioether-NHC catalyst.[a]



Entry No.	Pd Cat. (in mg)	Base used	Temp. (°C)	Solvent	Yield (%)
1	15	K_2CO_3	90	Water, TBAB	58
2	15	K_2CO_3	90	DMF-Water	75
3	15	K_2CO_3	90	DMF	95
4	15	K_2CO_3	90	Toluene	Nd
5	15	K_2CO_3	90	1,4-Dioxane	Nd
6	15	K_2CO_3	90	THF	Nd
7	15	Cs_2CO_3	90	DMF	Nd
8	15	NaOAc	90	DMF	90
9	15	NaOH	90	DMF	Nd
10	15	KOH	90	DMF	Nd
11	15	K_2CO_3	90	DMF	95
12	14	K_2CO_3	90	DMF	89
13	12	K_2CO_3	90	DMF	60
14	10	K_2CO_3	90	DMF	50
15	8	K_2CO_3	90	DMF	Nd

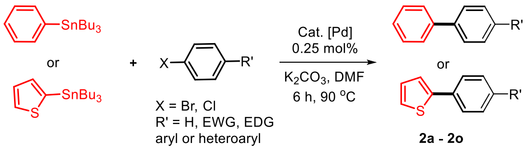
[a] Reaction conditions: Chlorobenzene (0.157 g, 1.0 mmol), tributylphenylstannane (0.367 g, 1.0 mmol), Cat. [Pd]: Fe_3O_4@SiO_2@NHC^SPh-Pd(II) (0.015 g, 0.25 mol % Pd), time (6 h), isolated yield after column chromatography, solvent (2.0 mL), Nd (not detected).

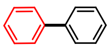
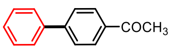
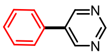
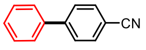
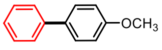
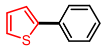
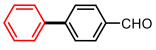
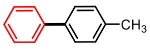
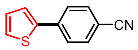
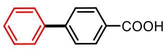
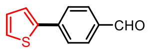
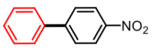
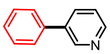
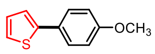
After having the best possible combinations of reaction parameters, the general scope of Stille coupling for a variety of aryl bromides/chlorides and organostannes compounds in presence of Fe_3O_4@SiO_2 supported Pd(II)-thioether-NHC catalyst at 90 °C under aerobic conditions was investigated. It was noted, that the traditional Stille cross coupling reaction require fluoride reagents, those are toxic but essential to activate the organotin compounds for transmetallation. The present reaction was performed in complete absence of toxic fluoride additive.

Moreover, after the completion of reaction, the Bu_3SnX salt was easily removed by passing it through silica (with 2–5% triethylamine in the eluent) or immediately purifying by standard column chromatography. Coupling of electron withdrawing substituent at *para* position of aryl chlorides e.g. 4-chloro- benzaldehyde, 4-chlorobenzonitrile, 4-chloronitrobenzene, 4-chloroaceophenone and 4-chlorobenzoic acid gave good yield of cross coupling products (Table 4, entries **2b**-**2f**). The present coupling reaction does not work with the aryl chlorides containing an electron donating group. The Stille coupling of activated bromoarenes with tributylphenylstannane was completed in optimum time of 6 h. The deactivated para substituted aryl bromides were also found to provide the high yield of biaryl cross coupled products (Table 4, entries **2g** and **2h**). Both 4-bromoanisole and 4-bromotoluene with tributylphenylstannane gave unambiguously results in the form of 90% and 93% yield of cross coupled product, respectively. The *N*-heterocyclic aromatic halides for Stille coupling reactions were also tested in present catalytic investigations (Table 4, entries **2i**-**2k**). The catalyst worked efficiently in case of heteroaryl bromide substrates as the yield up to 92% was obtained with 5-bromopyrimidine (Table 4, entry **2k**). Some Stille coupling reactions by using a thiophene containing organotin compound; 2-(tributylstannyl)thiophene with aryl bromides/chloride were also explored to test the catalytic efficiency of present Pd catalyst (Table 4, entries **2m**-**2o**) and a decent yields of respective cross coupled product was obtained.

In contrast to previous reports on Stille cross couplings, comparisons have been made between the previous catalysts and the current recyclable palladium catalyst. Su et al., reported $Pd_2(dba)_3$, and proazaphosphatrane (supporting ligand), as an efficient system for homogeneous catalysis of Stille cross couplings of aryl chloride. But higher Pd-catalyst loading (1.5 mol%), use of toxic fluoride additive (CsF), longer reaction time (24–48 h) and requirement of argon atmospheres increase the overall cost of the

Table 4
Substrate scope of Stille cross coupling reaction catalyzed with $Fe_3O_4@SiO_2$ supported Pd(II)-thioether-NHC catalyst.[a]



 **2a**, 96%, (95%)^b	 **2f**, 90%, (82%)^b	 **2k**, 92%
 **2b**, 90%, (88%)^b	 **2g**, 90%	 **2l**, 96%, (85%)^b
 **2c**, 90%, (85%)^b	 **2h**, 93%	 **2m**, 92% (75%)^b
 **2d**, 90%	 **2i**, 86%	 **2n**, 90% (72%)^b
 **2e**, 92%, (70%)^b	 **2j**, 90%	 **2o**, 92% (68%)^b

[b] Yield isolated ArCl substrates, solvent (2.0 mL), EWG (electron withdrawing group) and EDG (electron donating group).

[a] Reaction conditions: ArBr/Cl (1.0 mmol), tributylphenylstannane (0.367 g, 1.0 mmol), Pd catalyst (0.015 g, 0.0025 mmol, 0.5 mol% Pd), K_2CO_3 (0.200 g, 1.4 mmol), temp (90 °C), time (6 h), isolated yield after column chromatography.

synthesis [30]. Pd nanoparticles were also reported as efficient recyclable catalyst for Stille coupling reaction of aryl bromide and chloride but requirement of higher Pd loading (2.5 mol%) for good conversions is again a major drawback of the reaction [31]. A heterogeneous approach has been developed for chloro derivatives with 0.05 mol% palladium, however, use of CsF additive was an essential requisite of the reaction [32]. A organosilica anchored Pd(II) complex was found to work as a recyclable and efficient catalyst for the Stille coupling reaction but reaction is sensitive and only works in argon atmosphere [33], moreover, good conversion demands a CsF additive, more reaction time and a relatively higher temperature than the present method. Pd catalyst based on Pd NPs supported on magnetite (magnetically retrievable) has also been employed for Stille coupling [34], it was established as a phosphine-free heterogeneous Pd catalyst, it worked efficiently, stable and recyclable but it was found to be selective only for aryl bromides [34]. Pd nanoparticles supported on mesoporous graphitic carbon nitride were also found highly effective and can be reused further for Stille coupling of aryl bromide/iodides under mild conditions but at high catalyst loading (3.28 mol%) [35]. In 2017, Ghasimi et al. reported a Pd- free Stille coupling reaction catalyzed by conjugated microporous polymer based photo-catalyst under visible light irradiation at room temperature, however, the scope of reaction was limited up to aryl iodide, while only one product of each aryl bromide/chloride has been explored [36]. Thus, the present thioether-NHC Pd(II) complex immobilized on $SiO_2@Fe_3O_4$ NPs may be labeled as highly efficient, reusable catalyst as the yields up to 96% (ArBr) and 82% (ArCl) without any fluoride additive. The catalytic process is also simple, much more effective in terms of reaction time, does not demand fluorides salts, catalyst recyclability and gives biaryls in good amount for a range of aryl and heteroaryl substrates. It should be noted that the Pd(II) complex of organochalcogen ligands and any chalcogenated NHC have not been applied yet for the catalysis of Stille cross coupling reaction and therefore, this is the first example of the organochalcogen functionalized NHC-Pd(II) complex studied for the catalysis of Stille cross coupling reaction so far.

The reusability of Pd catalyst; $Fe_3O_4@SiO_2@NHC^{\wedge}SPh\text{-}Pd(II)$ was studied for both the Sonogashira and Stille coupling reactions by using the representative reactions of bromobenzene with phenylacetylene and tributylphenylstannane, respectively (see details in experimental section). After completion of reaction, the catalyst was magnetically retrieved (as shown in Figure 2) and the cross coupling product was decanted out by mixing with organic solvent thereof.

In each recycling run, new batch of bromobenzene, phenylacetylene (Sonogashira coupling), tributylphenylstannane (Stille coupling), K_2CO_3 and DMF were added to the reaction tube and the reaction mixture was subjected to continuous stir under optimized reaction conditions. The present Pd catalyst exhibited appreciable recyclability up to three cycles with very less decrease in efficiency but after third run a larger decrease (~10% decrease in yield) in efficiency was observed. The results of all recycling experiments is depicted in Figure 3, which shows the yields observed in five cycles for both the coupling reactions catalyzed by the solid supported Pd catalyst. The approximate 10% decrease in yield of cross coupled product after 2–3 run may be due to the leaching of discrete Pd from the silica coated Fe_3O_4 NPs. The Pd content in the $Fe_3O_4@SiO_2$ supported Pd catalyst was determined by ICP-AES analysis of the sample, before and after three catalytic cycles.

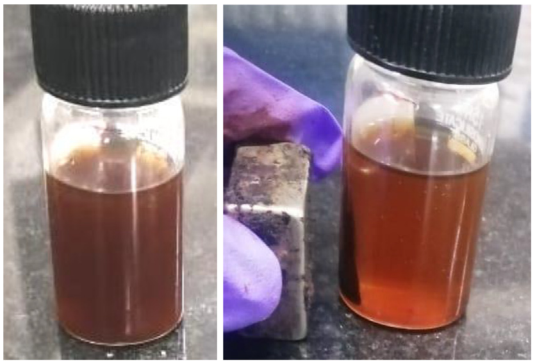


Fig. 2. Magnetic removal of the catalyst after catalytic run (a) after catalyzing reaction (b) separation of the catalyst using an external magnet.

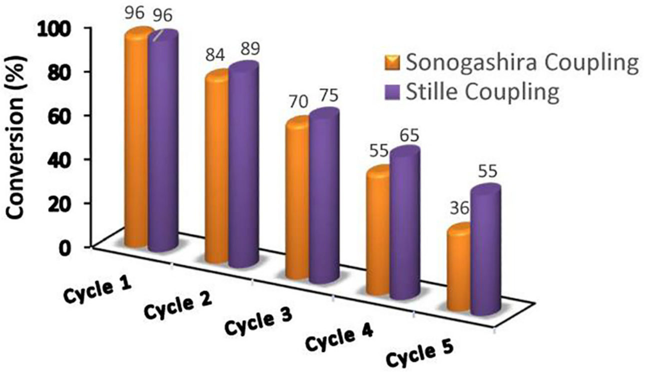


Fig. 3. Recycling of the Pd catalyst for Sonogashira and Stille coupling reactions under optimized reaction parameters.

For fresh sample of the catalyst, the wt% of Pd was measured to 1.78% and after three cycles it was reduced to 1.42% due to the leaching of Pd from the surface of Fe_3O_4@SiO_2 supported Pd catalyst. The leached Pd content is probably the amide/amine coordinated Pd which decomposed in the first and second run of the catalysis. It is possible that some amide/amine groups might left intact during the immobilization of thioether functionalized benzimidazole moiety on to the surface of Fe_3O_4@SiO_2–NH_2 or Fe_3O_4@SiO_2-amide-NH_2 NPs. The disruption of the silica coating due to the mechanical stirring stress may also be another possible reason for the observed decrease in the catalyst efficiency during its reuse.

Heterogeneous nature of catalysis

The heterogeneous nature of this Fe_3O_4@SiO_2 supported Pd catalyst has been established in earlier report for the catalysis of Suzuki-Miyaura coupling reaction in which the Pd leaching was analyzed through ICP-AES measurement and hot-filtration test. Present study also includes a hot filtration test for the typical Sonogashira coupling of 4-bromobenzaldehyde with phenylacetylene for to ascertain the heterogeneous or homogeneous nature of catalysis. After the initial 3 h of Sonogashira coupling, the yield of the cross coupled product was measured (~40%, NMR yield) and Pd-nanoparticles were magnetically separated from the reaction. The reaction mixture was then split in two equal halves; one half was transferred in another reaction tube and let the reaction run without catalyst, while the isolated Pd-catalyst NPs were added into another half reaction mixture. Both reactions tube were allowed to stir under optimized reaction conditions for another 12 h and product yield was measured through ^{1}H NMR. Reaction without any added catalyst shows ~48% NMR yield, while reaction with added catalyst shows ~94% yield of the desire coupling product. These results supports the heterogeneous nature of the catalysis, here, the strong binding interaction of the Pd(II)–NHC-thioether on the surface of Fe_3O_4@SiO_2 NPs prevent the leaching of discrete palladium into the solution. It also has been supported through the poor conversion of 48% observed in 12 h of the reaction, whereas the 40% transformation was observed in initial 3 h of reaction before magnetically isolation of the catalyst.

Conclusion

In conclusion, the magnetically recoverable Fe_3O_4@SiO_2 supported Pd(II)-thioether-NHC heterogeneous catalyst is efficiently work for Sonogashira and Stille cross coupling reactions under aerobic conditions. The catalyst found to be highly efficient and recyclable for Sonogashira coupling reactions and it coupled a wide varieties of aryl bromides with terminal alkynes in copper and amine free conditions. The present catalyst is an ideal example of highly desirable, efficient and recyclable heterogeneous Pd-catalysts, which efficiently works for Stille cross coupling under aerobic conditions, and smoothly coupled aryl chlorides and aryl bromides. The catalyst can be easily separated and reused up to three catalytic cycles without much loss in its catalytic efficiency.

Experimental

Procedure for Sonogashira coupling reaction

A mixture of terminal alkyne (1.5 mmol), K_2CO_3 (1.4 mmol, 0.200 g), aryl bromides (1.0 mmol) and catalyst (0.015 g) in DMF (2.0 mL) was stirred at 90 °C. Reaction was monitored on TLC until the optimum conversion of the cross coupled product was obtained. After the completion of the reaction, the crude product was extracted in diethyl ether. The solvent was removed by rotary evaporator and the desired cross coupled product was obtained after column chromatographic purifications on silica gel.

General procedure for Stille cross coupling reaction

A mixture of organostannes (1.0 mmol) and aryl/heteroaryl chloride/bromide (1.0 mmol), K_2CO_3 (0.200 g, 1.4 mmol) and catalyst (15 mg) in DMF (2.0 mL) was stirred at 90 °C in reaction tube. The reaction was continuously monitored on TLC until the maximum conversion of the desired product obtained. On completion, the product was extracted in diethyl ether (20×2 mL). The solvent was removed with a rotary evaporator, and then subjected to chromatographic separation to get the purified cross coupling products.

Procedure for recyclability of the catalyst

In a reaction tube, bromobenzene (1.0 mmol), phenyl acetylene/organostannes (1.0 mmol), Pd catalyst (15 mg), K_2CO_3 (1.4 mmol), were mixed in DMF (2 mL). The mixture was then stirred at optimized temperature on oil bath. After 3 h, the mixture was cooled to room temperature and 50 µL from the reaction mixture was pipette out to analyze the conversion% by proton NMR. The solution was decanted and the catalyst was washed and dried with suitable solvent (diethyl ether or ethyl acetate) by putting an external magnet on outer wall of the reaction tube. Thereafter, a new lot of substrate and base was added without new catalyst loading and the reaction mixture was again allowed to run again for maximum standardized reaction time under similar reaction conditions. The procedure was keep on repeating for further catalytic cycles.

Hot-filtration test

In order to ascertain the nature of catalysis, homogeneous or heterogeneous, a typical Sonogashira coupling of 4-bromobenzaldehyde and phenylacetylene in presence of Fe_3O_4@SiO_2 immobilized Pd catalyst was investigated in detail under the optimized reaction conditions. 4-bromobenzaldehyde (0.185 g, 1.0 mmol), phenylacetylene (0.122 g, 1.2 mmol), K_2CO_3 (0.207 g, 1.5 mmol), catalyst (15 mg, 0.25 mol%) and DMF (2.0 mL) were taken in a reaction tube and stirred at 90 °C. After 1 h, the catalyst was removed magnetically by using an external magnet and the reaction mixture was decanted off and also filtered with G4-crucible. The liquid filtrate was then divided in two halves; one half was transferred into another reaction tube and further run the reaction without addition of catalyst, while the isolated Pd-catalyst NPs were added into the remaining half. Both reaction tubes were allowed to stir under optimized similar reaction conditions for next 12 h and yield of expected product was analyzed through ^{1}H NMR.

Conflict of Interest

No conflict of interest exists.

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Research Ethics

We further confirm that any aspect of the work covered in this manuscript does not involved any human patients or studies.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2021.152844.

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