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CRITICAL REVIEW
G. Chatel *et al.*
Heterogeneous catalytic oxidation for lignin valorization into valuable chemicals: what results? What limitations? What trends?

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Pd/Cu-free Heck and Sonogashira cross-coupling reaction by Co nanoparticles immobilized on magnetic chitosan as reusable catalyst

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The chitosan (CS) is a porous self-standing nanofibrillar microspheres which can be used as a metal carrier. Amino-groups on CS enable to modulation of cobalt coordination using safe organic ligand (methyl salicylate). This catalyst efficiently promote Heck cross-coupling of a large library of functional substrates under mild and sustainable conditions (polyethylene glycol as solvent at 80 °C in short time (1 h)). The cobalt complex was also used as a heterogonous efficient, inexpensive and green catalyst for Sonogashira cross-coupling reactions. The reactions of various aryl halides and phenylacetylene provided the corresponding products with moderate to good yields. More importantly, this phosphine, copper and palladium-free catalyst is stable under the reaction conditions and can be reused easily by an external magnet for at least five successive runs without discernible decrease in its catalytic activity.

Introduction

The carbon–carbon bond forming reaction is one of the most important reaction in organic synthesis and in the pharmaceutical, agrochemical, and fine chemical industries.[1-3] So, improvement of efficient methodologies for generating carbon–carbon bonds received considerable attention.[4-8] However, performance of convenient, safe, green and inexpensive approaches have proved to be a serious challenging problem.

Over the past decade there has been an increased focus on cross coupling reactions using novel transition-metal catalysts.[9] The high cost and toxicity of palladium complexes[10] has stimulated the search for alternative affordable transition metal catalysts, including nickel,[11] copper,[12] iron[13] and cobalt[14-16] to the more sustainable metal-free cross-coupling catalysis.[17] Unfortunately, these approach in homogeneous catalysis and appalling harsh reaction conditions appears to be promising; so, using novel catalyst which can overcome to these limitations is required.

Indeed, a large library of inorganic and organic supports have been already applied including charcoal, inorganic silica, alumina and synthetic polystyrene. For instance, carbon nanotubes exhibits unique features;[18-22] but, it have been found as a serious health hazard material through assessment on its toxicity and environmental health risks.[23] As well as mesoporous silicas represent some advantages while their porous system is instable in aqueous and basic conditions, necessary for cross coupling catalysis.[24-25] In this regards uses of environment-friendly polymer supports are very promising due to low cost and less toxicity.[26] Chitosan, a byproduct of the fishing industry, is a linear polysaccharide which known as important family of bioresources with enormous potential functionalization properties due to the presence of free amino and alcoholic groups.[27]

Currently, magnetic nanoparticles (MNPs) supports provides a very useful separation approach with an external magnet. Meanwhile, various metal complex immobilized on MNPs have been developed the more stable, efficient and user-friendly catalysts in a number of C–C coupling reactions.[28] To date there are only a few examples of metal-chitosan anchored to MNPs with the catalytic behaviour in the organic transformations.[29]

Considering to economical and environmental factors, encourage to our previous work on cobalt-catalyzed C–C-coupling reactions[30-32] and on successfully prepared of an environmentally friendly and heterogeneous palladium-based catalyst supported on chitosan and their good performance in cross-coupling reaction,[33] we designed and prepared cobalt tagged on MNPs-chitosan functionalized with methyl salicylate (Co-MS@MNPs/CS) as a new highly stable catalyst and investigated its application in Heck and Sonogashira reactions.

The Sonogashira reaction is one of the most valid metal-catalyzed carbon–carbon cross-coupling reactions of aryl halides with terminal acetylene.[34-42]

The original catalytic system for Sonogashira couplings contain the use of palladium catalyst and a co-catalyst of copper (I) salt.[34] Many different synthetic methods based on copper free palladium catalysts have been reported for this reaction.[42] But

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the use of effective palladium-free systems is much more interesting in view of modern organic synthesis, due to the high cost and toxicity of palladium. Recent attention has been concerned with employing copper-only catalytic systems in Sonogashira coupling reactions. To overcome some disadvantages of this more economical catalytic systems, such as unrecoverable or complicated recovery and instability of the copper(I) salt, using other types of metal complexes immobilizing on solid supports such as cobalt would be logical and interesting. In continuation of our recent studies on the development of green catalytic systems for Sonogashira cross-coupling reactions.[44-46] Herein, we report the new palladium and copper free catalytic system using cobalt complex. To the best of our knowledge, Sonogashira reactions employing heterogonous cobalt complexes were not reported previously.

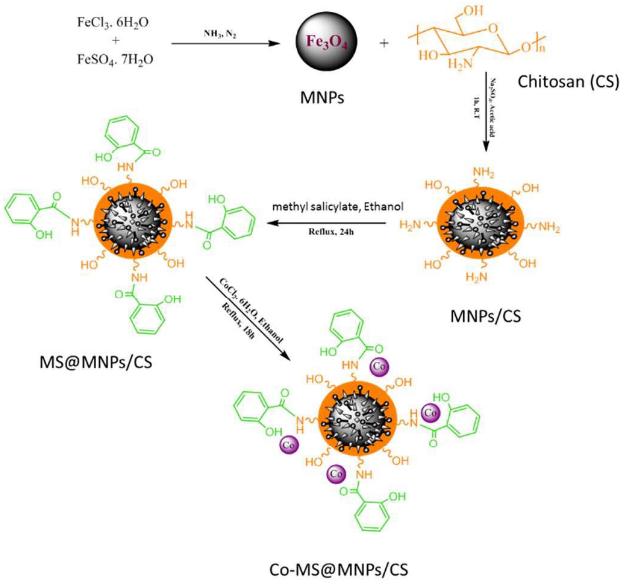
Cobalt-catalyzed couplings are of interest in organic synthesis, because cobalt is readily available, non-toxic, low-cost, stable and exhibits powerful catalytic activities.[47-49]

For the Heck reactions, in spite of rarity of using cobalt catalyst in this reaction, a few reports which refer to the application of cobalt catalysts in this coupling reaction are available.[50-53] For example, in 2009, Qi *et al*. reported Heck reaction using cobalt nanoparticles during long reaction time at extremely high temperature (150 °C).[50] Application of uniform Co−B amorphous alloy nanoparticles as catalyst in C–C coupling reaction was also described by Zhu and his co-workers in 2012 (at 120 °C using DMF/water as solvent and during 12–24 h).[51] These reported cobalt catalysts have various advantages such as good mechanical and excellent chemical stabilities and better economic and ecological properties compared to palladium catalysts. In contrast, they exhibited lower activity in Mizoroki–Heck reaction in an expanded range of aryl halides, in spite of spending high temperature and long reaction time. Therefore, to overcome these problems, more convenient approaches using a cobalt catalyst are required.

In the present Letter, we wish to report a new green and inexpensive strategy for Mizoroki–Heck and Sonogashira coupling reaction. Therefore, the cobalt was supported on magnetic chitosan applying methyl salicylate as a green and safe ligand for the first time. Using our catalytic system, the reaction conditions can be improved and it accelerated the Heck reaction without using palladium and phosphine. Moreover, it is an effective catalyst for palladium and copper (I) free Sonogashira cross-coupling reactions.

Results and discussion

A novel synthetic method was used for the preparation of a Co-MS@MNPs/CS complex in the form of a recyclable solid catalyst (Scheme 1). The NH_2 functional group in CS was reacted with methyl salicylate, yielding salicylic-functionalized chitosan via an amide bond formation. Then, the resulting salicylic acid-functionalized chitosan was treated with cobalt salt to form the complex as shown in Scheme 1. These processes were monitored by FT-IR, thermogravimetric analysis (TGA) and elemental analysis.



Scheme 1. Synthesis of the catalyst

The synthesis of CS-supported Pd(II) has been reported in the literature, as well as CS-imine derivatives used in C–C coupling reactions.[54-55] Studies on the structure of CS supported ligand-free Pd(II) have been also reported[56] However, as we know, only a few reports refer to the application of such complexes in coupling reactions,[57] Opportunely, this is the first report of application of magnetic CS-supported Co catalyst in Heck and Sonogashira coupling reactions without any co-catalyst and additives.

Our catalytic system in comparison with previous unrecyclable palladium-free catalysts,[58-60] not only is low cost, but also are readily prepared in few steps from available starting materials and can remove easily from the reaction media due to its ferromagnetic nature. This is very important because the remaining metal-based catalyst in the product can be unsafe; especially in the cases that the end product is directly related to human life such as in pharmaceutical synthesis. Furthermore, the nan size characteristic catalysts provides a large accessible surface area for better interaction with reactants in the media with applying small amount of the catalysts in short times.

In the FT-IR spectrum of chitosan (Fig. 1(a)), the characteristic absorption bands appeared at 1641 cm^{-1} ascribe to N-H bending vibration. The presence of a strong band at 565 cm^{-1} was related to the Fe-O band in MNPs and MNPs/CS. The 1383 cm^{-1} band is related to the C-O stretching of primary alcoholic group of chitosan in MNPs/CS and the peak around 3422 cm^{-1} ascribe to O-H and N-H groups vibrations. (Fig.1 (b) and (c)). In comparison of the spectrum of chitosan composite with those of MNPs/CS, the 1641 cm^{-1} peak of N-H bending vibration shifted to 1615 cm^{-1}. In final catalyst, the absorption bands which appear in the spectrum at 1657 cm^{-1} and 754 cm^{-1} correspond to C=O group and aromatic C-H angular out- of-plan deformation, respectively. (Fig.1 (d)).[61]

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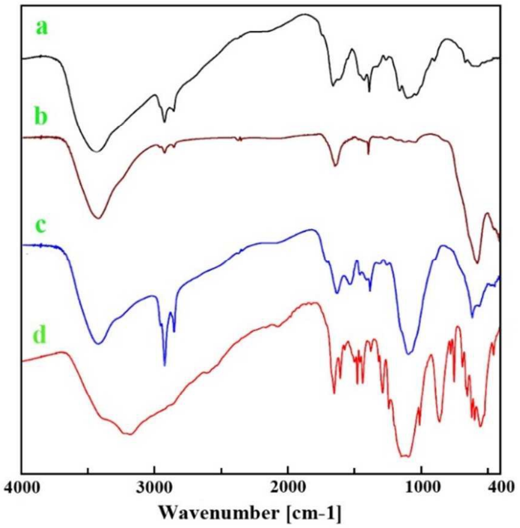

Figure 1. FT-IR spectra: (a)MNPs; (b)MNPs/CS (c) MS@MNPs/CS; (d)Co-MS@MNPs/CS

The amount of organic moieties in the magnetic chitosan-functionalized methyl salicylate cobalt complex Co-MS@MNPs/CS was determined by TGA and elemental analysis. The total amount of organic moieties on MS@MNPs/CS was about 2.3 mmolg^{-1}. The weight loss of MNPs/CS between 30–800 ºC as a function of temperature was determined using TGA, which is an irreversible process because of thermal decomposition. The TGA plots of MNPs/CS and Co-MS@MNPs/CS (Figure 2) depict a two-step thermal decomposition. The first step of weight loss in the cases corresponds to the removal of physically adsorbed water, whereas, the main weight loss in the second step is due to the removal of organic moieties on the surface. The TGA results are summarized in Table 1. The observed total weight losses for MNPs, MNPs/CS and MS@MNPs/CS are 0 %, 61 % and 70 %, respectively. A good agreement was observed between elemental analysis and TGA data (Table 1).

After preparation and characterization of MNPs/CS-MS, the cobalt were immobilized onto this ligand. As shown in Scheme 1, the cobalt immobilized on magnetic chitosan-functionalized with methyl salicylate (Co-MS@MNPs/CS) was prepared by addition of cobalt chloride in ethanol at 80ºC in the presence of MNPs/CS-MS.

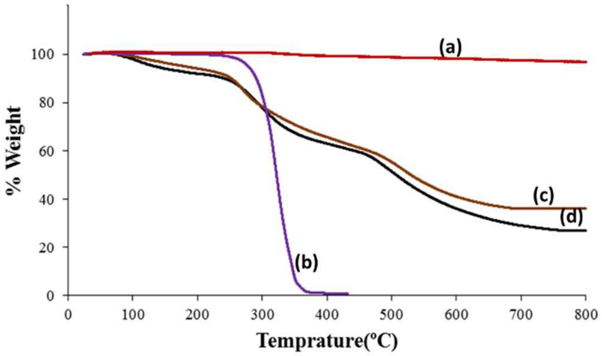

Figure 2. TGA thermogram: (a)MNPs; (b)Cs (c)MNPs/CS (d) MS@MNPs/CS

Table 1. Thermogravimetric analysis (TGA) and elemental analysis (EA) results

Sample	Organic [Wt. %]	Organic [mmolg^{-1} MNPs]	EA (wt%)			Total
			C	H	N	
MNPs	0	0	-	-	-	0
MNPs/CS	61^{a}	3.84^{a}	2.629	0.473	0.438	3.54
MS@MNPs/CS	70^{b}	2.45^{b}	1.996	0.227	0.166	2.39

^{a}Chitosan; ^{b}Chitosan+ methyl salicylate

The XRD spectrum (Fig. 3) provided more evidence for the presence of cobalt and iron in the catalyst. As presented in Fig. 3, 8 characteristic diffraction peaks 2θ = 30.1°, 35.5°, 43.1°, 47.2°, 53.5°, 57.0°, 62.6° and 75.1° can be clearly considered for Fe_3O_4 nanoparticles, which are related to the cubic phase of Fe_3O_4. According to Fig. 3, characteristic diffraction peaks 2θ= 33.1°, 38.0°, 58.6° and 62.1° confirms the crystalline nature of the cobalt species, which are related to the cubic phase of cobalt nanoparticles.

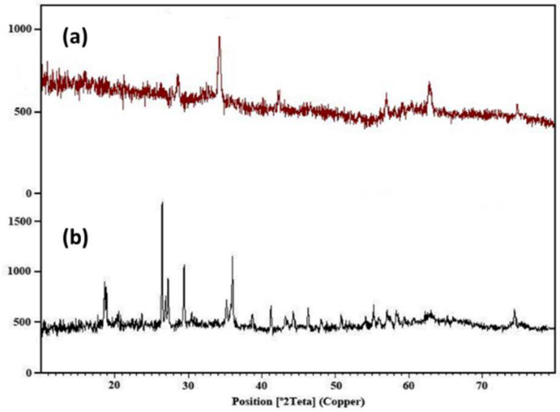

Figure 3. XRD pattern: (a)MNPs/CS and (b)Co-MS@MNPs/CS

The morphology of the surfaces of Co-MS@MNPs/CS were studied by field emission scanning electron microscopy (FE-SEM) (Figure 4). The energy dispersive X-ray (EDX) results, obtained from SEM analysis for the Co-MS@MNPs/CS clearly show the presence of cobalt nanoparticles in catalyst.

Further characterization of catalyst was performed by transmission electron microscopy (TEM). The TEM images showed well-defined spherical Co particles dispersed in MNPs/CS (Figure 5). The size distribution of Co nanoparticles was about 13.5 nm, indicating that cobalt nanoparticles did not aggregate upon immobilization on MNPs/CS. All these observations indicate that the magnetic chitosan functionalized with methyl salicylate polymer is a good host and ligand for cobalt nanoparticles.

The cobalt content of the catalyst, measured by ICP, showed a value 2.17 mmolg^{-1}.

The magnetization curves of catalyst was shown in Figure 6, the magnetization value for Fe_3O_4 is equal to 69.4 emu/g and for catalyst is equal to 21.1 emu/g. This investigation proved the paramagnetic behaviour of catalyst which is found significantly lower than the bulk magnetite due to the coating of magnetic nanoparticles with chitosan.

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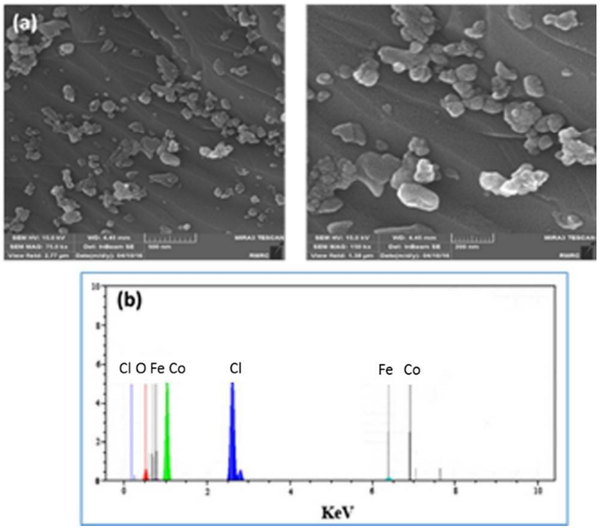

Figure 4. (a) FE-SEM images and (b) SEM-EDX spectra of catalyst

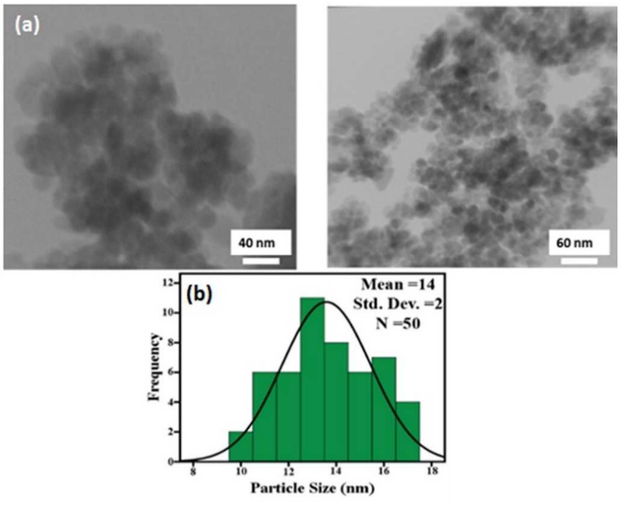

Figure 5. (a) TEM images and (b) particle size distribution for catalyst

To test the catalytic activity of the Co-MS@MNPs/CS, it was applied in the Mizoroki-Heck and Sonogashira reaction.

Initially, the Heck cross-coupling of iodobenzene with methyl acrylate in the presence of catalyst was chosen as a model for the optimization of reaction parameters such as the base and solvent types, temperature and catalyst loading. The results are summarized in Table 2. The model reaction was first performed in the presence of different bases such as K_2CO_3, Li_2CO_3, KOH, $NaHSO_4$ and K_3PO_4; amongst them K_3PO_4 was found to be the most effective base. Then, the same reaction was carried out in different solvents. Among the solvents examined, PEG was proved to be the best reaction medium. The effects of the amount of catalyst were also explored; the best result was obtained using 5 mg of catalyst. Therefore, it was concluded that the optimum reaction conditions involved iodobenzene (1 mmol), methyl acrylate (1.1 mmol), K_3PO_4 (4 mmol) and Co-MS@MNPs/CS (5 mg) in PEG (3 mL) at 80 ºC (Table 2, entry 13).

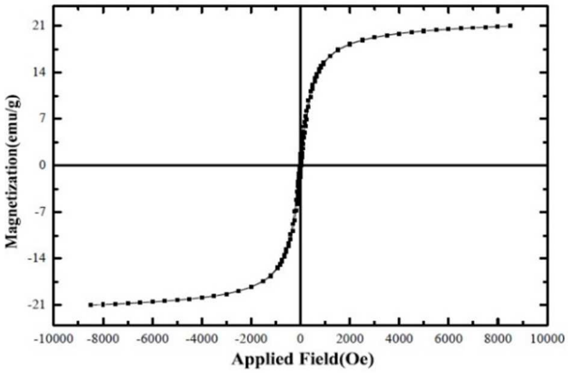

Figure 6. Room temperature magnetization curves of catalyst

Table 2. Optimization of reaction conditions on Heck reaction of iodobenzene with methyl acrylate in the presence of catalyst[a]

Entry	Cat (mg/mol%Co)	Base	Solvent	Temp. (ºC)	Yield[b] (%)
1	10/2.2	K_2CO_3	DMF	100	81
2	10/2.2	K_2CO_3	DMSO	100	89
3	10/2.2	K_2CO_3	NMP	100	67
4	10/2.2	K_2CO_3	PEG	100	82
5	10/2.2	Li_2CO_3	PEG	100	81
6	10/2.2	$NaHCO_3$	PEG	100	85
7	10/2.2	KOH	PEG	100	79
8	10/2.2	K_3PO_4	PEG	100	91
9	10/2.2	-	PEG	100	-
10	10/2.2	K_3PO_4	PEG	80	89
11	10/2.2	K_3PO_4	PEG	50	43
12	10/2.2	K_3PO_4	PEG	r.t.	-
13	**5/1.1**	**K_3PO_4**	**PEG**	**80**	**88**
14	2/0.5	K_3PO_4	PEG	80	77
15	-	K3PO4	PEG	80	-

[a] The reaction was carried out with iodobenzene (1.0 mmol), methyl acrylate (1.1 mmol), base (4 eq.) solvent (3.0 mL) for 1 h.
[b] GC yield

Encouraged by our initial studies, we then examined the generality and versatility of this supported cobalt-catalyzed Mizoroki–Heck cross-coupling of aryl halides with olefins. As can be seen in Table 3, under the optimized conditions, a diversity of aryl iodides, bromides and chloride containing electron-donating and electron-withdrawing substituents reacted efficiently with methyl acrylate and styrene under air atmosphere at relatively mild conditions of 80 ºC to afford the desired cross-coupling products in high yields (Table 4, entries 1–14). The experimental results showed that the electronic properties of the substituents on the aromatic rings of the starting materials had no significant effect on the reaction, however, aryl iodides were found to be more reactive than aryl bromides.[32] Among aryl halides, aryl chlorides are ideal substrates for coupling reactions due to they are inexpensive and widely available comparison to their bromide or iodide counterparts. The first step in catalytic coupling reactions (oxidative addition) disfavour in aryl chlorides substrates because of high strength of C-Cl bond. The most reported methods required high loadings palladium catalyst and harsh conditions; anyway they show little or no activity with aryl

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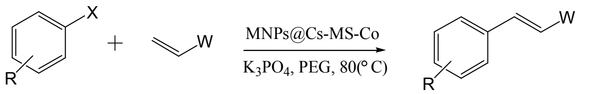
chloride substrates. In order to further explore the efficiency and applicability of this method, the cross-coupling of aryl chlorides with olefins was also checked under the same conditions. Aryl chlorides proceeded smoothly in the presence of the same catalyst amount as used for aryl iodides and bromides. It is important to note that reported cobalt catalytic system, used in Heck reaction, was totally inactive for aryl chlorides.[31,32,51] Herein, we report good results in Heck coupling of less reactive aryl chloride derivatives with olefins in presented cobalt catalyst for the first time.

It is noteworthy that, based on NMR spectra, in all Heck olefination reactions, the trans-product was obtained with 100% selectivity.

Table 3. Scope of Mizoroki–Heck cross coupling reaction[a]



Entry	X	R	Olefin	Yield[b] (%)
1	I	H	MA	88
2	I	4-OMe	MA	92
3	I	3-Me	MA	90
4	Br	H	MA	81
5	Br	4-OMe	MA	87
6	Br	4-NO_2	MA	79
7	Br	2-Me	MA	73
8	Br	2-Cl	MA	67
9	Br	4-CHO	MA	41
10	Br	2-NO_2	MA	53
11	Cl	H	MA	71
12	Cl	4-CN	MA	65
13	Cl	3-NO_2	MA	45
14	I	H	Styrene	75
15	I	4-OMe	Styrene	79
16	I	3-Me	Styrene	71
17	I	H	Styrene	69
18	Br	4-OMe	Styrene	71
19	Br	4-NO_2	Styrene	63
20	Br	2-Me	Styrene	49
21	Br	2-Cl	Styrene	35
22	Br	4-CHO	Styrene	15
23	Br	2-NO_2	Styrene	22
24	Cl	H	Styrene	57
25	Cl	4-CN	Styrene	41
26	Cl	3-NO_2	Styrene	30

[a] The reaction was carried out with aryl halide (1.0 mmol), alkene (1.1 mmol), K_3PO_4 (4.0 equiv.) in 3.0 mL PEG, 5 mg of catalyst (1.1 mol % of Co) at 80 ºC for 1 h.

[b] Isolated yield

Encouraged by the obtained results in the Heck cross-coupling, we then investigated the potential of our Co-MS@MNPs/CS catalyst in the Sonogashira reaction. In order to obtain the optimum experimental conditions, the reaction of phenyl acetylene with iodobenzene was considered as a model reaction in the presence of our catalyst.

The effects of the reaction conditions such as the type of base and solvent, temperature and catalyst amount was tested and a summary of the optimization experiments is provided in Table 4. As can be seen, the best result was obtained using iodobenzene (1 mmol), phenyl acetylene (1.1 mmol), KOH (1.5 mmol) and 10 mg of Co-MS@MNPs/CS (1.1 mol% Co) in DMSO at 140 ºC (Table 4, entry 14).

Table 4. Optimization of reaction conditions on Sonogashira reaction of iodobenzene with phenyl acetylene in the presence of catalyst[a]

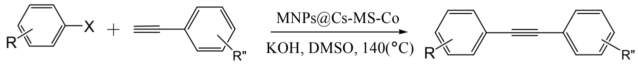
Entry	Solvent	base	Cat (mg)	Temp. (ºC)	Yield[b](%)
1	DMSO	$NaHCO_3$	10	140	51
2	DMSO	Li_2CO_3	10	140	56
3	DMSO	K_3PO_4	10	140	68
4	DMSO	KOH	10	140	72
5	DMSO	-	10	140	-
6	EtOH	KOH	10	140	-
7	PEG	KOH	10	140	11
8	DMF	KOH	10	140	69
9	DMSO	KOH	10	120	39
10	DMSO	KOH	10	100	16
11	DMSO	KOH	10	80	-
12	DMSO	KOH	-	140	-
13	DMSO	KOH	5	140	31
14	**DMSO**	**KOH**	**10**	**140**	**72**
15	DMSO	KOH	20	140	74

[a] The reaction was carried out with iodobenzene (1.0 mmol), phenyl acetylene (1.1 mmol), base (4 eq.) solvent (3.0 mL) for 10 h.

[b] GC yield

Using the optimized reaction conditions, a variety of structurally divergent aryl iodides, bromides and chlorides was used in the reaction with phenyl acetylene to generate the desired coupling products in (Table 5).

Table 5. Sonogashira cross-coupling of various aryl halides in the presence of catalyst[a]



Entry	R	R"	X	Time(h)	Yield[b] (%)
1	H	H	I	10	72
2	4-OMe	H	I	10	69
3	4-NO_2	H	I	10	80
4	4-$COCH_3$	H	I	10	78
5	H	H	Br	12	56
6	4-OMe	H	Br	12	45
7	4-$COCH_3$	H	Br	12	58
8	4-NO_2	H	Br	12	61
9	4-Cl	H	Br	12	53
10	4-COH	H	Br	12	52
11	2-NO_2	H	Br	12	55
12	H	H	Cl	24	-
13	4-NO_2	H	Cl	24	-
14	4-NH_2	H	Cl	24	-
15	4-$COCH_3$	4-Me	Br	12	57
16	4-OMe	4-Me	Br	12	43
17	4-COCH3	2-NO_2	Br	12	66
18	4-OMe	2-NO2	Br	12	61

[a] The reaction was carried out with aryl halide (1.0 mmol), phenyl acetylene (1.1 mmol), KOH (4.0 equiv.) in 3.0 mL DMSO , 10 mg of catalyst (2.2 mol % of Co) at 140 ºC .

[b] Isolated yield

The corresponding alkyne products were obtained in moderate to good yields. The electronic and steric effects on the yields was examined in this reaction system. This catalyst was compatible with a wide range of functional groups such as nitro, methoxy and carbonyl on the aryl halides. Aryl halides substituted with electron-withdrawing groups in comparison with electron-donating substituents gave better conversions. As can be seen in Table 5, aryl iodides were converted to the

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corresponding Sonogashira products in good yields. The reactivity of aryl bromides was lower than that of aryl iodides and they required longer times giving lower yields. Aryl chlorides were inactive in this reaction system.[45]

The Co-MS@MNPs/CS display high activities which may be related to good dispersion and small size of cobalt nanoparticles and good synergistic effects of cobalt nanoparticles with ligand which grafted on MNPs-Cs.

According to previous studies;[62-63] dendritic and highly branched polymers are spherical three-dimensional macromolecules. Due to their structure and multiple internal and external functional groups, these can selectively act as suitable hosts for a wide range of ions and molecules and the immobilization of nanoparticle-based catalytic systems on these solid supports makes the catalyst recyclable and reusable, and minimizes the leaching of the particles. To investigate the effect of ligand (MS), the efficiency and reusability of Co@MNPs/CS in Heck cross-coupling reaction was investigated and compared with our catalyst Co-MS@MNPs/CS. The results which given in Table 7 confirmed the good and effective role of ligand (MS) in our catalyst. Nevertheless, reusability of Co@MNPs/CS in the Mizoroki–Heck reaction was also studied and it was reused three times without significant loss of activity, the results was given in Table 6

Leaching of metal ions is a serious problem for supported metal catalysts, and prevents catalyst separation and recycling. To explore the leaching of the catalyst, two similar control experiments were performed. To this end, the reaction between iodobenzene and methyl acrylate was carried out simultaneously in two different vessels under the exactly same conditions. In each case, the reaction progress was monitored using GC, after 30 min the catalyst were separated from one of these vessels using magnetic bar, while the other was remained unchanged. Thereafter, both of the reactions were continued under the same conditions. After another 30 min, both the reactions was stopped and their completion was again examined using GC. The results showed that the reactions in the absence of the catalyst were not proceeded any more, while the reaction in other vessel was improved. In fact, the leaching phenomenon does not present here. This result suggested that this novel catalyst was heterogeneous in nature perhaps because of the specific nature of designed catalyst.

Moreover, the catalyst recycling is an important property from economic, environmental and industrial points of view. Therefore, the catalyst reusability was checked in the Mizoroki–Heck reaction of iodobenzene (1.0 mmol) and methyl acrylate (1.1 mmol). At the end of each reaction, the catalyst was separated, using an external magnetic field, washed with ethanol and acetone and reused. As reported in figure 2, the catalyst was reused five times without significant loss of activity. The yield for the fifth run is 84 % for the heterogeneous catalyst. The TEM images of recovered catalyst was also investigated. As shown in Fig. 8. TEM micrographs indicate that the nano-sized particles have been well distributed in the recovered catalyst; although some aggregations are observed. Therefore, it can be realized that the nano-sized particles in catalyst was preserved after use in the reaction media. Additionally, ICP of catalyst was carried out after five reuses and the results showed that only a very small amount (less than 1%) of cobalt metal was removed from the catalyst.

Table 6. Recyclability in the Mizoroki–Heck reaction

Run	Yield[a,b]	Yield[a,c]
1	88	53
2	88	50
3	86	46
4	85	-
5	83	-

[a] Isolated yield
[b] catalyst (Co-MS@MNPs/CS)
[c] Co@MNPs/CS

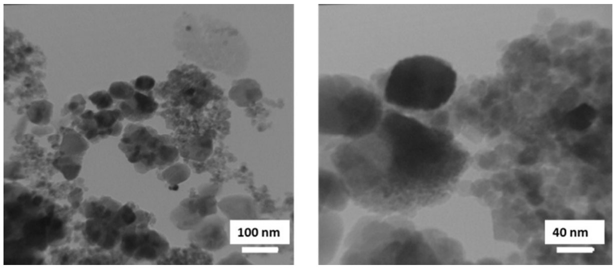

Figure 8. TEM of recovered catalyst.

Nevertheless it should be noted that, to the best of our knowledge, this phosphine and palladium-free catalyst is one the rare demonstration of the combination of cobalt and organic ligands supported onto magnetic chitosan to generate a high efficient and recyclable catalyst which can be used more than five time without any considerable loss of its catalytic activity. In addition, this is efficient catalytic system which result the Mizoroki–Heck cross-coupling reactions in significantly faster reaction times, lower temperatures and greener media (moderate temperature and safe metal and green media) in comparison with current methods.[51-53, 32-33]

The present catalytic method was compared with some procedures published for the Mizoroki–Heck reaction of iodobenzene and methyl acrylate in the literature, and the results are shown in Table 7. Evidently, the reaction conditions are mild, but the most important benefits of this study are contributed to the advantages of heterogeneous catalysis such as easy separation, efficient recycling, minimization of metal contamination and low cost.

Experimental

General procedure for the catalyst preparation

The magnetic nanoparticles (MNPs) were prepared according to the literature.[64] based on precipitation of magnetite nanoparticles from the mixture of iron (III) chloride and iron(II) sulfate by ammonia (25% solution in water). Subsequent, in a round-bottom flask equipped with mechanical stirrer and condenser a mixture of magnetic nanoparticles and sodium sulfate (20%, W⍰V) was added to a solution of chitosan (1%, W⍰V) in acetic acid (2%, W⍰V) on stirring.

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Table 7. Comparison of catalytic activities of our catalyst with literature examples for Heck reaction between iodobenzene and methyl acrylate

Entry	Catalyst^{ref}	Reaction conditions	Time (h)	Yield (%)
1	Nano Co^{50}	Co (2 mol%) in NMP at 130 ºC	14	78
2	Co/Al$_2$O$_3$^{53}	Co (10 mol%) in NMP at 150 ºC	24	56
3	Nano Co^{52}	Co (2 mol%) in NMP at 140 ºC	16	85
4	Co-B^{51}	Co (5 mol %) in water/DMF (5/5) at 130 ºC	12	98
5	Co–NHC@MWCNTs^{32}	Co (3.5 mol %) in PEG at 80 ºC	5	85
6	Co-IL@MWCNTs^{33}	Co (5 mol %) in toluene at 100 ºC	3	87
7	Co@MNPs/CS	Co (1.1 mol %) in PEG at 80 ºC	1	53
7	Present catalyst	Co (1.1 mol %) in PEG at 80 ºC	1	88

It was continued for 1h to obtain the aqueous suspension of MNPs/CS. After this time, the magnetic nanoparticles were separated from the reaction mixture by an external permanent magnet, washed with ethanol and methanol several times and dried under vacuum at 70 ºC. For the preparation of supported methyl salicylate ligands, a solution of ethanol suspension of MNPs/CS (1.5 g/10 mL) was added to methyl salicylate (6.5 mmol) and the mixture was stirred at 60 ºC for 24h. The final Co-MS@MNPs/CS was obtained as a brown solid by addition of $CoCl_2.6H_2O$ (4.2 mmol) solved in 10 mL ethanol to dispersed mixture of MNPs/CS-MS (1.01 g) in ethanol (5 mL) and stirred at 60 ºC for 18 h. The resulting complex was collected by an external permanent magnet and washed with ethanol (3 × 10 mL) to remove the unreacted materials and finally dried under air (89 % yield based on the amount Co in the catalyst determined by ICP).

General procedure for the Heck reaction

In a round-bottom flask equipped with a mechanical stirring, a mixture of K_3PO_4 (4 eq), olefin (1.1 mmol) and aryl halide (1 mmol) in solvent (3 mL) were added 5 mg of catalyst (1.1 mol% of Co) and equipped with a condenser for refluxing. The above mixture was heated at 80 ºC in an oil bath. The reaction's progress was monitored by TLC (hexane/EtOAc, 80:20) and gas chromatography (GC). After completion of the reaction the mixture was diluted with dichloromethane and water. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography. The products were characterized by comparing their physical pmroperties m.p., IR, ^{1}H, ^{13}C NMR spectra with those found in the literature.[65-69]

General procedure for Sonogashira reaction

In a round- bottomed flask equipped with a mechanical stirring, phenyl acetylene (1.2 mmol), aryl halide (1.0 mmol), catalyst (10mg) and KOH (2eq) in DMSO (3 mL) were stirred under air atmosphere at 140 ºC. The progress of the reaction was monitored using TLC and GC. After completion of the reaction the mixture was diluted with dichloromethane and water. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The product was isolated by column chromatography to afford the corresponding products in yield of 55-80%. The products were characterized by comparing their physical properties m.p., IR, ^{1}H, ^{13}C NMR spectra with those found in the literature.

Conclusions

To summarize, this work highlights the multifaceted advantages of CS as a sustainable material for textural engineering of macroporous supports, while chemical modification of its amino groups with safe and green organic compounds such as methyl salicylate allows the tuning of the metal-support interaction. Mild and sustainable reaction conditions (palladium and copper-free, polyethylene glycol as solvent, 80 °C) enables Heck cross coupling catalysis to be performed in good yields with low metal contamination, easy and good recyclability. This straightforward and sustainable chemistry affords useful and eco-efficient catalysts bearing many useful properties: their green and easy conditions to produce catalyst (without using toxic agents and solvent) and good efficiency in Heck and Sonogashira coupling reaction. In generally, this work presents the first example of the application of functionalization of magnetic chitosan with methyl salicylate to prepare the stable heterogonous cobalt complex. The requirement energy and time for the Heck reaction extremely minimized in this method compared to previously report cobalt-catalyzed Heck cross-coupling reactions as an inevitable trend in development of green chemistry. Moreover, it is the first report of applying cobalt catalyst in Sonogashira reaction.

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