Green Chemistry

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Cite this: DOI: 10.1039/c3gc36761d

# Iron-catalyzed cross-coupling reaction: recyclable heterogeneous iron catalyst for selective olefination of aryl iodides in poly(ethylene glycol) medium†

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Received 7th November 2012,
Accepted 10th February 2013

DOI: 10.1039/c3gc36761d

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An environmentally friendly iron-based catalyst supported on acac-functionalized silica was successfully prepared and evaluated as a heterogeneous catalyst for Mizoroki–Heck reaction of aryl iodides and olefins. Our catalytic system showed good activities that were comparable to that of palladium catalysts. The catalyst was simply recovered from the reaction mixture and recycled five times. Furthermore, the reaction was carried out in poly(ethylene glycol) as a green solvent. Interestingly, using this catalyst, aryl iodides were selectively olefinated in the presence of aryl bromides.

## Introduction

The palladium-catalyzed Mizoroki–Heck cross-coupling reaction represents one of the most valuable methods for carbon–carbon bond formation in organic synthesis.[1] Thus, a number of efficient catalytic systems have been developed for this cross-coupling reaction. The catalyst in the standard Heck reaction is a Pd(0) species stabilized by two phosphine ligands. However, phosphine ligands have some drawbacks; they are expensive, toxic, unrecoverable, and sensitive to oxygen and water.[2] On the other hand, due to the high cost of palladium, researchers are also interested in the Heck reactions catalysed by inexpensive transition metals such as Ni,[3,4] Co,[5,6] Cu[7] and Mn.[4]

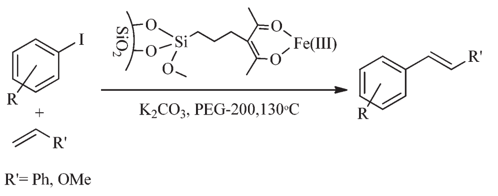
Nevertheless, the stress of modern efficiency criteria has prompted the search for alternative catalysts that address the economic and ecological disadvantages associated with the use of palladium, cobalt and nickel catalysts.

In contrast to the above mentioned metals, iron is one of the most abundant metals on earth, and one of the most inexpensive and environmentally friendly ones. Iron catalysts have recently been introduced to address these economic and ecological challenges. Many biological systems rely on the rich chemistry of iron-containing enzymes. It is also a vital metal for life, and thus constitutes an attractive metal for a vast array of chemical synthetic transformations as no severe toxicity and side effects exist. Also, iron(III) catalysts are air and moisture stable and easy to store for long periods under normal laboratory conditions.

In the field of C–C bond formation *via* Grignard derivatives,[8–12] Suzuki–Miyaura[13,14] and Sonogashira reactions[15–19] a variety of works were accomplished and the iron-catalyzed cross-coupling method is able to compete with the palladium-catalysed one. However, to the best of our knowledge, only one work on iron catalyzed Heck cross-coupling reaction has been reported[20] and heterogeneous iron catalysts have never been used in Heck reaction.

The recent report by Vogel and co-workers[20] on iron-catalyzed Heck reaction urges us to present our own studies on this topic. They demonstrated a novel iron-catalysed arylation of styrenes using a rather large amount of $FeCl_2$ (20 mol%) along with picolinic acid as ligand (80 mol%) and $^{t}$BuOK as base (4 mol%) in DMSO under mild conditions at 60 °C. The presence of strong base resulted in the polymerization of acrylate esters.

Here, we report a simple, cost-effective, environmentally benign, recyclable, and efficient covalently silica supported iron(III)-acac catalytic system for the Heck reaction of aromatic iodides and olefins (styrene and acrylates) under ligand-less conditions (Scheme 1). In this work, only a catalytic amount of iron in poly(ethylene glycol) is used as a green solvent.



**Scheme 1** Iron catalysed Heck reaction.

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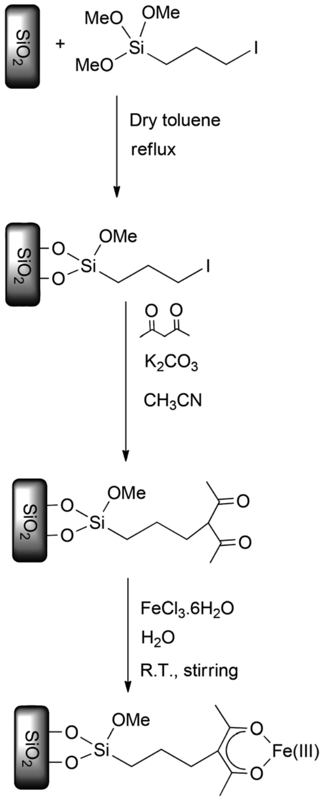
† Electronic supplementary information (ESI) available. See DOI: 10.1039/c3gc36761d



**Scheme 2** Preparation of silica supported iron catalyst.

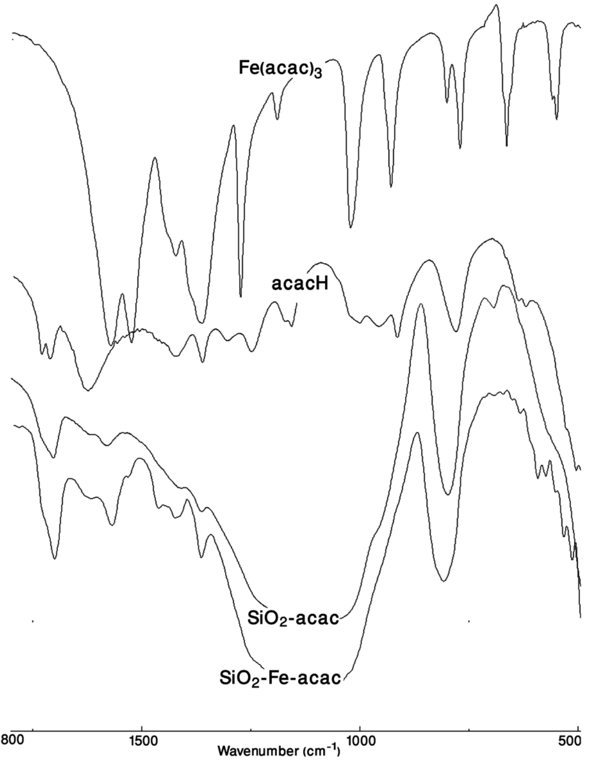


**Fig. 1** FT-IR spectrum of catalyst compared with $Fe(acac)_3$.

## Results and discussion

The synthesis of the silica-acac was performed in three steps using grafting-methodology (Scheme 2). First, the reaction of 3-chloropropyl trimethoxysilane and NaI was carried out in acetone. In the second step, 3-iodopropyl trimethoxysilane reacts with silica gel in dry toluene. Then, modified silica treated with acacH and $K_2CO_3$ as base activator in order to obtain the silica-acac support.

Iron catalyst formed when silica-acac was mixed with a $FeCl_3 \cdot 6H_2O$ aqueous solution and extensively washed until no more iron leaching was observed. The resulting dark orange solid was assigned as silica-$Fe^{III}$(acac).

The presence of the organic phase in the silica-acac was confirmed by FT-IR spectroscopy, XPS and CHN elemental analysis. In the FT-IR spectrum shown in Fig. 1, bands at 1569, 1523, 1422, 1362 and 661 $cm^{-1}$ correspond to the diketone ligand coordinated to iron. Other bands at 1273, 1188, 1021, 928, and 801 $cm^{-1}$ covered with strong and broad bands of silica support. The inorganic silica component can also be identified by the presence of the typical silica overtone bands of 1864 $cm^{-1}$.

The presence of the organic phase in the silica-acac support was also confirmed by elemental analysis. The total amount of carbon was 77 mmol $g^{-1}$. The metal immobilization was confirmed by the EDX and XPS analyses (see ESI†).

In the XRD spectrum of the catalyst (see ESI†), a broad maximum is observed instead of typical $Fe(acac)_3$ peaks. This confirms the presence of highly dispersed iron deposited on the silica matrix.

In the initial attempts to improve this iron-catalyzed Heck cross-coupling reaction, iodobenzene was chosen as a test substrate to optimize the reaction conditions. A DMF solution of iodobenzene was allowed to react with methyl acrylate (MA) (1.1 equivalents) at 130 °C in the presence of a catalytic amount of iron catalyst (10 mg catalyst, $6 \times 10^{-4}$ mmol Fe) and 1.5 equivalents of $NaHCO_3$. After warming at 130 °C for 3 h, the reaction afforded the cross-coupling product with complete conversion of the iodobenzene.

To get information on the optimal catalyst conditions, we carried out intensive investigations to define the best solvent for this transformation. Seven different solvents were tested for 3 h using 10 mg catalyst. Table 1 shows the data collected for the synthesis of methyl cinnamate as a model reaction. Among the different solvents screened, in some solvents such as toluene, dioxane and ethanol, only low conversions were observed (Table 1, entries 1, 4 and 6). DMF was shown to be the best solvent for this transformation.

Our initial goal was to use a green media for the Heck reaction. Fortunately, the reaction takes place in excellent conversion in poly(ethylene glycol) (PEG) as solvent. Thus we choose PEG instead of DMF as the solvent.

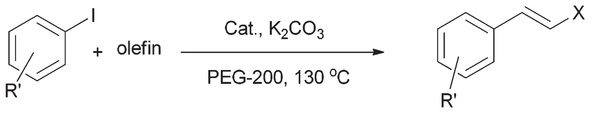
The nature of the base is also crucial to the Heck reaction. When $NEt_3$, $NEt_4(OH)$ or NaOAc were used as base (1.5 equivalents) instead of $NaHCO_3$, the formation of lower amount of the desired product was detected on GC, but $K_2CO_3$ afforded a higher yield than $NaHCO_3$ (Table 1, entries 8 and 9). The

**Table 1** Optimization of reaction conditions

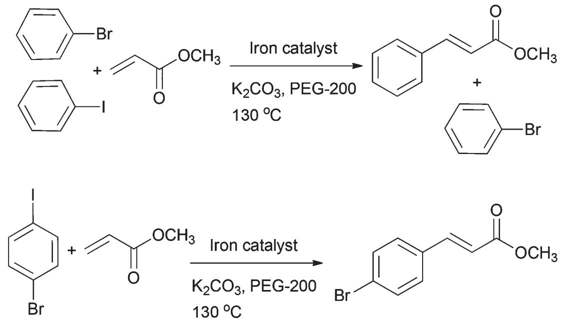
| Entry | Solvent | Base (equiv.) | Catalyst (mg) | Conversion[a,b] (%) |
|---|---|---|---|---|
| 1 | Dioxane | $NaHCO_3$ (1.5) | 10 | 1.2 |
| 2 | DMAc | $NaHCO_3$ (1.5) | 10 | 33.3 |
| 3 | DMF | $NaHCO_3$ (1.5) | 10 | 99.5 |
| 4 | EtOH | $NaHCO_3$ (1.5) | 10 | 4.0 |
| 5 | NMP | $NaHCO_3$ (1.5) | 10 | 54.0 |
| 6 | Toluene | $NaHCO_3$ (1.5) | 10 | 5.0 |
| 7 | PEG | $NaHCO_3$ (1.5) | 10 | 92.4 |
| 8 | PEG | $K_2CO_3$ (1.5) | 10 | 95.0 |
| 9 | PEG | $K_2CO_3$ (2) | 10 | 99.0 |
| 10 | PEG | NaOAc (1.5) | 10 | 92.4 |
| 11 | PEG | $Et_3NOH$ (1.5) | 10 | 68 |
| 12 | PEG | $Et_3N$ (1.5) | 10 | 79.3 |
| 13 | PEG | $K_2CO_3$ (2) | 5 | 58.0 |
| 15 | PEG | $K_2CO_3$ (2) | 15 | 99.0 |
| 16 | PEG | $K_2CO_3$ (2) | 25 | 99.5 |

[a] GC conversion. [b] Reaction conditions: iodobenzene (0.25 mmol, 30 μL), MA (1.2 equiv.), base, solvent (1.5 mL), 130 °C, 1.5 h.

**Table 2** Scope of iodides in iron-catalyzed coupling reaction with olefins



| Entry | R′ | Olefin | Time (h) | Yield |
|---|---|---|---|---|
| 1 | H | MA | 1.5 | 85 |
| Run 2 | | | 1.5 | 85 |
| Run 3 | | | 1.5 | 85 |
| Run 4 | | | 2 | 84 |
| Run 5 | | | 2 | 80 |
| Run 6 | | | 3 | 77 |
| 2 | 4-$NO_2$ | MA | 1 | 80 |
| 3 | 3-$NO_2$ | MA | 1.2 | 83 |
| 4 | 4-$OCH_3$ | MA | 2.5 | 77 |
| 5 | 4-$CH_3$ | MA | 2.5 | 79 |
| 6 | 3-$CH_3$ | MA | 2.5 | 80 |
| 7 | 4-Br | MA | 2 | 80 |
| 8 | 4-Cl | MA | 2 | 82 |
| 9 | 4-CN | MA | 1.5 | 85 |
| 10 | H | Styrene | 7 | 80 |
| 11 | 4-$NO_2$ | Styrene | 5 | 82 |
| 12 | 3-$NO_2$ | Styrene | 5 | 79 |
| 13 | 4-$OCH_3$ | Styrene | 6 | 69 |
| 14 | 4-$CH_3$ | Styrene | 5 | 76 |
| 15 | 3-$CH_3$ | Styrene | 5 | 78 |
| 16 | 4-Br | Styrene | 5 | 70 |
| 17 | 4-Cl | Styrene | 5 | 77 |
| 18 | 4-CN | Styrene | 5 | 81 |
| 19 | H | MMA | 6 | 79 |
| 20 | 4-$NO_2$ | MMA | 6 | 82 |
| 21 | 4-CN | MMA | 6 | 80 |
| 22 | 4-$CH_3$ | MMA | 6 | 72 |



**Scheme 3** Study of selectivity between iodo and bromoarenes.

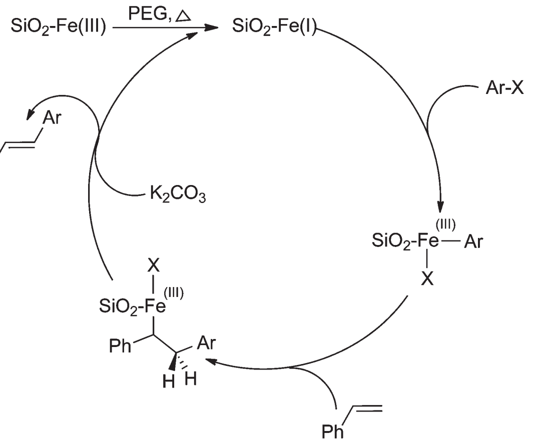
optimal amount of $K_2CO_3$ was 2 equivalents with respect to aryl halide (entry 9). Another experiment was set up to determine the optimal amount of catalyst. A control experiment in the absence of iron catalyst confirmed the crucial role which iron catalyst played in the described reaction as the reaction did not occur. A 25 mg catalyst ($1.5 \times 10^{-3}$ mmol Fe) resulted in the complete conversion in 1.5 hours at 130 °C (Table 1, entry 16).

We next examined the scope and limitations of this iron-catalyzed cross-coupling reaction with various types of aryliodo derivatives[21] and olefins (Table 2). All reactions were carried out using 25 mg catalyst in PEG-200 at 130 °C in the presence of 2 equivalents of $K_2CO_3$.

In order to investigate the effect of substituent groups on iodobenzene, various substituted iodobenzenes were examined. The cross-coupling reaction of iodoaryl derivative was amenable to both electron-rich and electron-poor iodoaryl derivatives and the reaction gave the corresponding coupling compounds in good to excellent yields. As Vogel *et al.* reported,[20] 4-iodonitrobenzene is destroyed in the presence of $FeCl_2$ in the Heck reaction. It is noteworthy that the cross-coupling reaction works successfully with 4-iodonitrobenzene under our reaction conditions (Table 2, entries 2, 3, 11 and 12). Methyl methacrylate and styrene had longer reaction times under our reaction conditions (Table 2, entries 10–22).

It should also be noted that aryl iodides can be selectively olefinated in the presence of aryl bromides. Interestingly, the Heck reaction, in many cases, shows selectivity for aryl bromides and aryl iodides in the presence of aryl chlorides. However, to date, no selectivity has been reported between aryl bromides and aryl iodides.

In this work, the competing reactions of bromobenzene and iodobenzene with methyl acrylate were studied to evaluate the selectivity of our catalyst in the Heck reaction. Another substrate which contains both iodo and bromo substituents, 1-bromo-4-iodobenzene, was also tested in this reaction. In the first reaction shown in Scheme 3, iodobenzene was the only reagent participating in reaction and bromobenzene was fully recovered after the purification. On the other hand, in the second reaction, 1-bromo-4-iodobenzene was converted to methyl-4-bromocinnamate as the only product. The reusability of the catalyst was tested using iodobenzene and MA as the substrates. After each run, the catalyst was recovered by decantation, followed by washing with acetone (3 mL × 3). After drying, the catalyst was reused directly for the next run. The results for the five repeated runs are also presented in Table 2. The activity of the catalyst remained unchanged after it was reused five times, indicating that the catalyst was not only very active, but also very stable.



**Scheme 4** Possible mechanism for vinylation of aryl iodides in the presence of iron catalyst.

The mechanism of the vinylation of iodobenzenes with supported iron(III) catalyst in PEG solvent with $Na_2CO_3$ is proposed, which is shown in Scheme 4. At the first step, we believe that the reaction started with the oxidation of alcoholic groups of PEG by iron complex to form reduced iron(I) species, followed by an oxidative addition of aryl iodide. Thereafter, the reaction continues to go according to the accepted mechanism of the Heck reaction.

## Experimental

### Synthesis of silica-acac support

(3-Chloropropyl) trimethoxysilane (5 mmol) was added to a solution of anhydrous sodium iodide (5 mmol) in dry acetone (50 mL), and the mixture was heated under reflux for 12 h. The solvent was removed under reduced pressure and the flask charged with 50 mL dry toluene. Silica-gel (60–120 mesh) (5 g) was dried at 300 °C for 5 h and added to the above toluene flask. The solution was refluxed for 48 h. The solvent was decanted and the silica was washed thoroughly with toluene, before transferring to a Soxhlet thimble and extracted with dichloromethane for 5 h. The silica was then dried in a vacuum for 8 h. 3-Iodopropyl functionalized silica was added to a suspension of $K_2CO_3$ (5 mmol) and acetyl acetone (5 mmol) in acetonitrile. The mixture was refluxed for 24 h to give the crude Si-acac support. The white powder transferred to a Soxhlet thimble and extracted with dichloromethane for 5 h.

### Iron complexation to silica-acac

A solution of iron(III) chloride hexahydrate ($FeCl_3 \cdot 6H_2O$) (5 mmol) in 30 mL of distilled water was prepared. The silica-acac powder was added to this solution under stirring for 30 min at room temperature. After the complexation with iron (III) salt, the solid phase was filtered and extensively washed with water, ethyl alcohol and acetone at room temperature, until no Fe(III) has been detected using the potassium thiocyanate solution. The solid was dried at 80 °C for 5 h. The iron content of the catalyst was $6 \times 10^{-2}$ mmol $g^{-1}$ based on atomic absorption spectroscopy.

### General experimental procedure for the cross coupling reactions

A 5 mL vial equipped with a stirrer bar was charged with the requisite aryl halide (0.25 mmol), $K_2CO_3$ (0.5 mmol), methyl acrylate (0.3 mmol), 0.01 g of $SiO_2$-Fe(acac) catalyst and 1.5 mL PEG-200. The reaction mixture was heated at 130 °C. The progress of the reaction was monitored by GC (small sample of reaction mixture was extracted by hexane). After completion of the reaction, the reaction mixture was extracted with hexane. The combined organic layers were dried with anhydrous $Na_2SO_4$. The solvent was evaporated under vacuum to give the crude product, which was purified by column chromatography (hexane : EtOAc, 75 : 25) to yield the expected product.

## Conclusions

We have demonstrated that silica supported iron(III) complex is an efficient and recyclable catalyst for the coupling of aryl iodides and olefins in the presence of PEG as solvent. The iron catalyst is highly active and easily recyclable by a simple filtration. This reaction provides a novel environmentally friendly and economical route for the Heck reaction.

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