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Cyclopropanation of diazoesters with styrene derivatives catalyzed by magnetically recoverable copper-plated iron nanoparticles

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ABSTRACT

Simple bare copper-plated iron nanoparticles catalyzed the cyclopropanation of diazoesters with styrene derivatives. The reaction proceeded smoothly and provided the desired products in moderate to good yields, with selectivity for the *trans* isomer in neat conditions. The reaction scope was explored and di or tri-substituted cyclopropanes were synthesized. The catalysts could be magnetically separated and re-usable up to five times. It was also characterized by TEM, XPS, and ICP-MS. A gram-scale reaction was performed with a yield of 72%.

1. Introduction

Cyclopropanes can be found in a wide variety of biologically active natural products[1] and pharmaceuticals,[2] and constitute useful synthetic building blocks.[3] Several methods exist to access cyclopropanes, including the Simmons–Smith,[4] the Corey–Chaykovsky,[5] and the Kulinkovich reactions,[6] as well as others.[7] Recently, pathways involving diazoesters have attracted attention because these molecules allow the generation of active carbenoid intermediates in mild condition, in the presence of transition metal catalysts, opening routes towards not only cyclopropanes but also other functionalities.[8] Copper, ruthenium, and rhodium homogeneous catalysts were recognized as among the most efficient catalysts for cyclopropanation.[8,9] Especially, rhodium and ruthenium catalysts are powerful enough to provide complex cyclopropanes. However, these metals are precious, expensive, and in limited amount in natural resources. As a consequence, efforts have been made to immobilize these catalysts onto polymer matrices or metal oxides to enable easy recycling.[10] The use of copper catalysts is a desirable alternative because the metal is a cheaper, more abundant material and they provide good reactivity for the reaction. Conversely, fewer successful examples of heterogenized copper catalysts are reported.

Copper-based heterogeneous catalysts have also been reported for this reaction using supports, such as a polymer,[11] aluminum oxide,[12] silica gel,[13] zeolite,[14] or clay.[15] In 2003, Liu et al. reported that CuO over monolayer-TiO_2–Al_2O_3 catalyzed the cyclopropanation of ethyl diazoacetate with styrene in yields up to 94%.[12] In 2008, Lim et al. achieved asymmetric cyclopropanation using chiral aza(bisoxazoline)-copper (I) catalyst on siliceous mesocellular form (MCF) to provide the desired products in about 80% yield and 92% ee up to eight cycles without significant loss of catalytic activity.[13] In 2011, Shi et al. reported metal-organic-frameworks (MOFs) based on copper (I) sulfate and 4,4′-bipyridine catalyzing the cyclopropanation of styrene.[16] The catalysts showed high *trans* diastereoselectivity and were reusable up to three times, despite a low styrene conversion of 30%.

Nanoparticles (NPs) have been recognized as one of the most powerful heterogeneous catalysts in organic reactions, both because of their high surface/volume ratio and their unique electronic properties, resulting in high catalytic activity and tunability.[17] Iron-based magnetic NPs have attracted much attention[18] because they are cheap, non-toxic, robust, earth-abundant, and easily recyclable by the use of an external magnet after reaction. Recently, we demonstrated that simple, bare ferrite NPs catalyzed the A^3 coupling, the cross-dehydrogenative coupling reaction, and the Huisgen's 'click' condensation.[19] Zero-valent iron NPs (ZVINs) also enable interesting applications for organic transformations. For example, we demonstrated that iron(0) and iron/iron oxide core shell NPs catalyzed alkene hydrogenation both in batch and flow

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reactors.[20] Iron/iron oxide core shell NPs could also be used as reducer and support for other metals to access novel reactivity. Following this idea, palladium-plated iron NPs were used for Suzuki coupling.[21] We have subsequently demonstrated that copper-plated iron NPs (Cu@FeNPs) were effective catalysts for the azide-alkyne 'click' reaction in water.[22]

We describe herein that Cu@FeNPs are effective catalysts for the cyclopropanation of diazoesters and styrene derivatives. This simple, yet powerful, catalyst provided the desired products in moderate to very good yields with selectivity for the *trans* isomer. Various substrates were examined and the catalysts could be reused up to five times without significant loss of catalytic activity. The nature of the catalysts was investigated by transition electron microscopy (TEM), X-ray photoelectron spectroscopy (XPS), and inductive coupled plasma-mass spectroscopy (ICP-MS). Reaction mechanism was also explored.

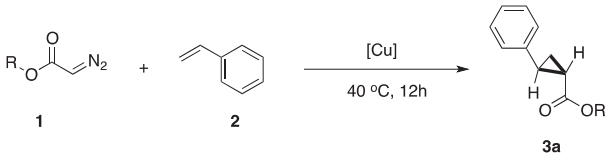
2. Results and discussion

2.1. Synthesis of copper-plated iron nanoparticles (Cu@FeNPs)

Cu@FeNPs were prepared by galvanic reduction of $CuSO_4$ onto iron/iron oxide core/shell NPs, following a method we reported previously.[22] The nanoparticles were characterized by TEM, XPS, and ICP-MS. TEM micrographs revealed the morphology of the Cu@FeNP catalysts. Fig. 1a features iron/iron oxide core/shell structures, arranged in chain-like structures,[23] prior to the copper deposition. Following the Cu plating, Fig. 1b reveals that the particles are covered with well distributed, small copper containing nanoclusters (Fig. 1b). EDX pattern recorded on the Cu-plated Fe NPs using the electron beam tightly focused on the edge of the structure (See Supplementary data, Fig. 1b) confirms the presence of Cu on the structures, as revealed by the presence of the Cu Kα peak (the Ni peaks are due to spurious X-rays from the Ni-grid). The oxidation state of Cu in Cu@FeNPs was determined by XPS (Fig. 1c). The high resolution scan for Cu 2p in fresh Cu@FeNPs revealed Cu $2p^{3/2}$ and Cu $2p^{1/2}$ binding energy peaks at 934.1 and 953.9 eV for Cu(II), and 932.2 and 952.0 eV for Cu(I), respectively. Cu(I) species are expected to result from the reduction of Cu(II) by iron. Cu(0) may also have formed, but was not measured by XPS, possibly because of air oxidation prior to measurement. The amount of Cu in Cu@FeNPs was determined to be 2.1 mmol g^{-1} by means of ICP-MS analysis.

in neat condition (Table 1, entries 1–4). The reaction proceeded smoothly and gave the desired product **3a** in 74% NMR yield, with a *trans*/*cis* ratio of 1.7 (Table 1, entry 3). In absence of catalyst, or with FeNP catalysts (Table 1, entries 1 and 2), yields dropped below 10%, which indicates that Cu is essential for catalysis, through the generation of active Cu carbenoids. Copper ferrite ($CuFe_2O_4$) NPs are known to be one of the most powerful magnetically recoverable catalysts in organic reactions, however in this case, they demonstrated poor activity (Table 1, entry 4).[24]

Table 1
Optimization of the reaction conditions[a]



1 2 3a

Entries	Catalyst (mol %)	R	Styrene (equiv)	Yield[b] (%)	*trans*/*cis*[b]
1	None	Bn	10	9	N.D.
2	FeNPs (5 mg)	Bn	10	<5	N.D.
3	Cu@FeNPs (10.5)	Bn	10	74	1.7
4	$CuFe_2O_4$ (10)	Bn	10	Trace	N.D.
5	Cu@FeNPs (5.3)	Bn	10	70	1.7
6	Cu@FeNPs (15.8)	Bn	10	83	1.6
7	Cu@FeNPs (21.0)	Bn	10	77	1.6
8	Cu@FeNPs (15.8)	Bn	5	67	1.6
9	Cu@FeNPs (15.8)	Bn	3	52	1.8
10	Cu@FeNPs (15.8)	Bn	1.5	40	1.7
11	Cu@FeNPs (10.5)	Et	10	45	1.6
12	Cu@FeNPs (10.5)	PMP[c]	10	83	1.3
13	Cu@FeNPs (10.5)	BHT[d]	10	15	>20

[a] Conditions: **1** (0.10 mmol) and given quantities of copper catalysts and styrene.
[b] Determined by the ^{1}H NMR analysis of the crude mixture using internal standard.
[c] PMP: *p*-methoxyphenyl.
[d] BHT: 2,6-di-*tert*-butyl-2,4-methylophenyl.

Next, we determined the minimum amount of catalyst necessary for the reaction (Table 1, entries 3, 5, 6, and 7). 15.8 mol % catalyst loading was sufficient to afford a very good yield of 83%. The amount of styrene was reduced successfully to 1.5 equiv, despite the dimerization of diazoesters affecting the yield (Table 1, entries 6, 7, 9, and 10). To widen the scope of the reaction, three additional diazoesters were examined (Table 1, entries 11, 12, and

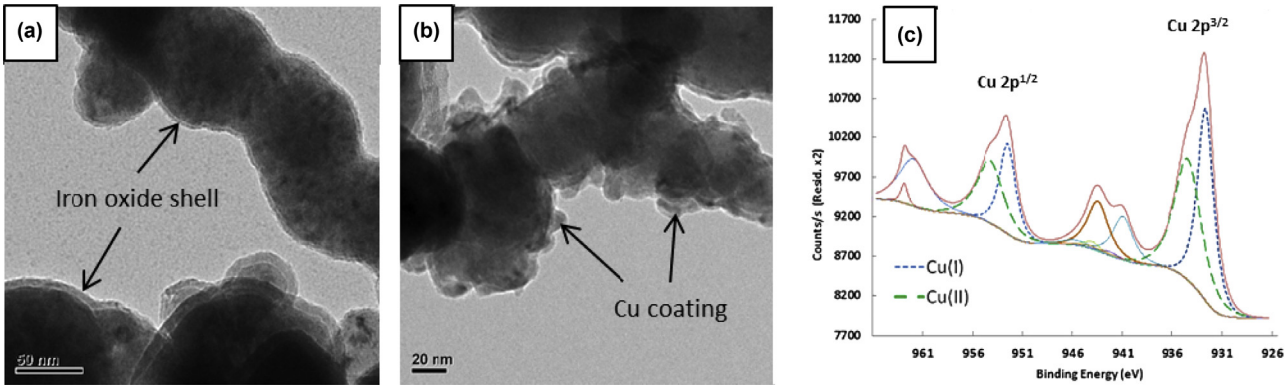


Fig. 1. TEM images of (a) iron/iron oxide core/shell NPs (before copper deposition) and (b) fresh Cu@FeNPs, and (c) XPS spectrum of fresh Cu@FeNPs.

2.2. The catalytic activity for cyclopropanation

First, we examined the catalytic activity of Cu@FeNPs by choosing benzyl diazoacetate **1** and styrene **2** as model substrates

13). Ethyl diazoacetate provided the desired product in poor yield. *p*-Methoxyphenyl diazoesters gave the product in good yield with slightly lower diasteroselectivity compared to benzyl diazoacetate (Table 1, entries 11 and 12). 2,6-Di-*tert*-butyl-2,4-methylphenyl