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NHC-copper complexes immobilized on magnetic nanoparticles: Synthesis and catalytic activity in the CuAAC reactions

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ABSTRACT

A series of N-heterocyclic carbene copper(I) and rare copper(II) complexes (NHCCuCl or NHCCuCl_2) were covalently immobilized directly on the surface of magnetic nanoparticles (MNPs) for the first time. The physicochemical properties were investigated by a broad range of techniques, including SEM and TEM microscopy, and TG analysis. The supported complexes exhibited excellent activity in the Huisgen cycloaddition with *in situ* generated azides. Unexpectedly, a direct comparison of NHCCuCl and NHCCuCl_2 complexes anchored to the magnetic nanoparticles confirmed the higher activity of the latter for the formation of 1,2,3-triazoles, also under ascorbate-free conditions.

1. Introduction

Since the first isolation and characterization of an N-heterocyclic carbene (NHC) in 1991 by Arduengo [1] N-heterocyclic carbene ligands revolutionized the field of modern catalysis. Many challenging C—C and C-heteroatom bond-forming processes involving these ligands have been developed so far [2–4], including enantioselective ones [5]. Although tremendous advances in the field of the homogenous N-heterocyclic carbene metal complex catalysis have been made, the development of green, sustainable, and economical processes constitutes a major challenge in modern organic and organometallic chemistry, and is of special importance for the transfer of academic achievements to industrial applications. For these reasons, homogenous metal catalysis acceptable on laboratory scale creates many difficulties in commercial processes, associated with the environmental pollution, waste issues, atom efficiency, and catalyst recovery. Bearing in mind these complications, heterogenization of homogenous catalysts on solid support seems to be a natural choice which has proved useful in many processes to date, allowing for the straightforward recovery of the catalyst. Among many solid supports available, polymers, carbon, silica or metal oxides are the most commonly used ones for the anchoring of metal complexes. However, conventional separation techniques such as centrifugation and filtration have to be used in order to allow the separation and further reuse of the active catalyst, which can be tedious in some cases. In this respect, the application of magnetic nanoparticles (MNPs) offers a better platform for recovering the metal complexes by using an external magnetic field, which dramatically reduces the cost of the process [6–11]. Moreover, MNPs are usually non-toxic, recyclable, and allow the covalent binding of metal complexes on the quasi-homogenous nanoparticles surface, which is beneficial for the catalytic activity. Among N-heterocyclic carbene metal complexes, palladium [12–24] has garnered a lot of interest lately. Besides nickel [25], iridium [26], platinum [27], ruthenium [12,28,29], and gold [30–33] complexes supported on MNPs have been marginally reported. To the best our knowledge, NHC-copper complexes have never been supported on magnetic nanoparticles so far. There are only some simple examples of other solid supports such as silica, cellulose, or nanotubes [34–44]. The excellent reactivity of NHC-copper complexes in many challenging transformations under homogenous conditions [45,46], e.g. hydroboration of alkenes and alkynes, hydrothiolation, hydroaminaton or hydroalkoxylation, C—H bond arylation, and, last but not least, 1,2,3-triazole formation are of high importance from the point of view of organic chemistry and further industrial applications. For example, the widely used 1,2,3-triazoles possess a range of biological activity such as antifungal [47], antibacterial [48] or antiviral [49] activities, and constitute a powerful linkage between disjoint chemical/biological components such as polymers, proteins or peptides [50–53]. Despite all these advantages, copper-catalyzed reactions suffer from several drawbacks which limit their use in medicinal chemistry as well as

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material science and engineering [54]. The contamination of organic compounds with toxic copper residues usually results in changes of cellular metabolism when used in biological systems [55]. In contrast, NHC-copper complexes have recently found applications in medicinal chemistry due to their low cytotoxicity [56–59]. For these reasons, the search for new efficient methods for the immobilization of NHC-copper complexes is highly desirable. From the angle of industrial applications, we anticipated that the immobilization of stable NHC-copper complexes should deliver a practical approach towards highly active, easily recoverable and reusable copper catalysts.

Herein, we present for the first time a simple and efficient method of immobilizing NHC-copper(I) and NHC-copper(II) complexes directly on the surface of MNPs, and their successful application in the Huisgen cycloaddition as reusable catalysts for 1,2,3-triazole formation under aerobic conditions.

2. Results and discussion

2.1. The preparation of immobilized NHC-copper complexes

The preparation of the respective copper complexes was accomplished by the synthetic route presented in Scheme 1. First, NHC ligands were anchored to magnetic nanoparticles consisting of iron oxides. Magnetic nanoparticles were prepared according to a procedure published by Massart and subsequently covered by a silane shell [60]. The synthesis of NHC salts was accomplished following a general procedure, recently developed by us, through a formamidinium intermediate [16]. The presented sequence contains well-known reactions which were adjusted to the synthesis on the magnetic solid phase. After each step, the modified nanoparticles were separated from the reaction mixture and then washed several times with an appropriate solvent (for details, see Supporting Information). The penultimate step of the synthesis required the usage of an aniline derivative. The reaction with 1,6-isopropylaniline (liquid) was carried out at 120 °C neat, whereas the reaction with 2,6-bis(diphenylmethyl)-4-methylaniline (solid) was performed in its saturated solution in toluene at reflux.

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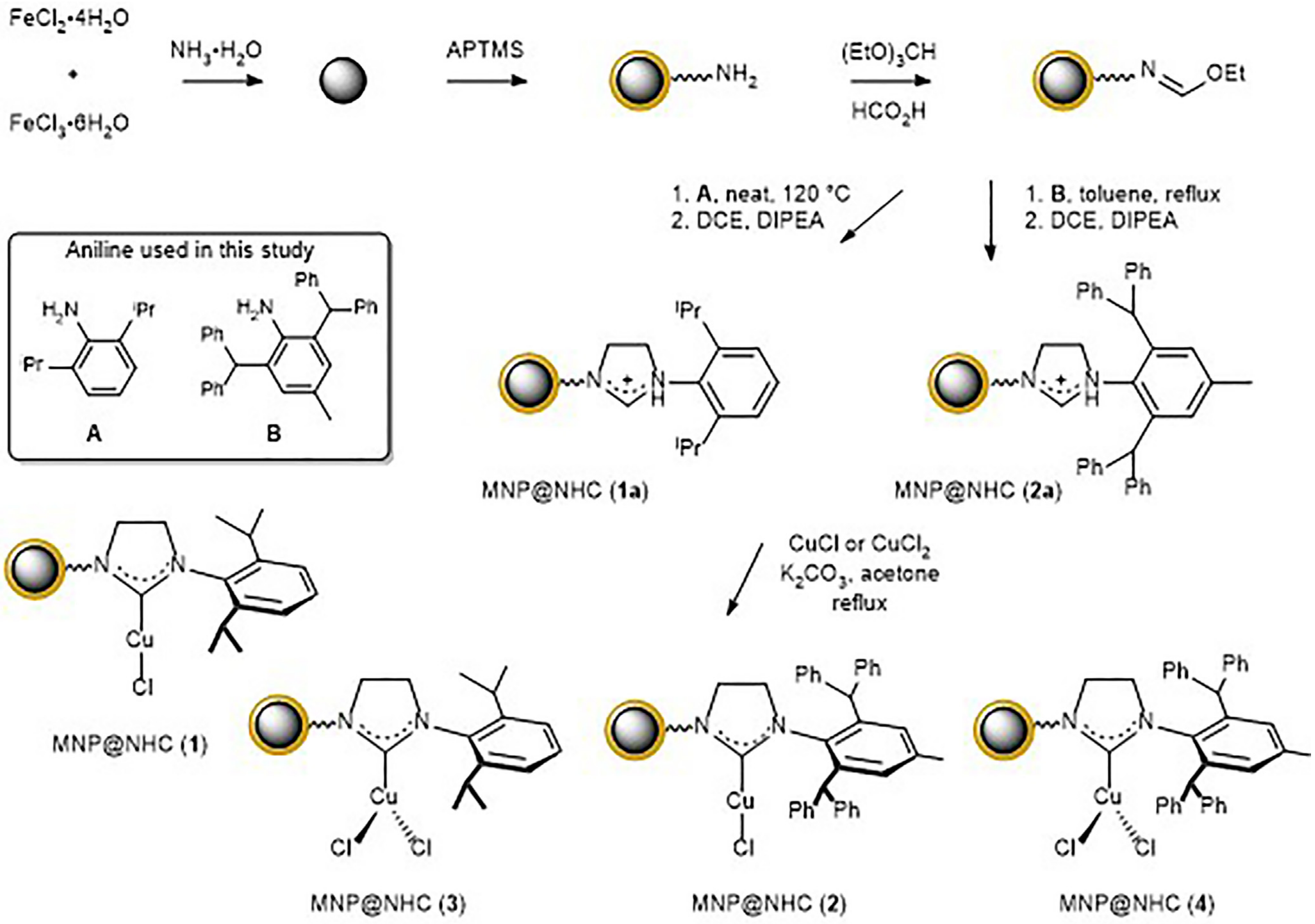
Subsequently, the obtained MNP-supported NHC ligands were used to prepare the corresponding copper(I) and copper(II) com-



Scheme 1. Direct synthesis of NHC precursors on magnetic nanoparticles; APTMS – (3-Aminopropyl)-trimethoxysilane; DIPEA – Diisopropylethylamine.