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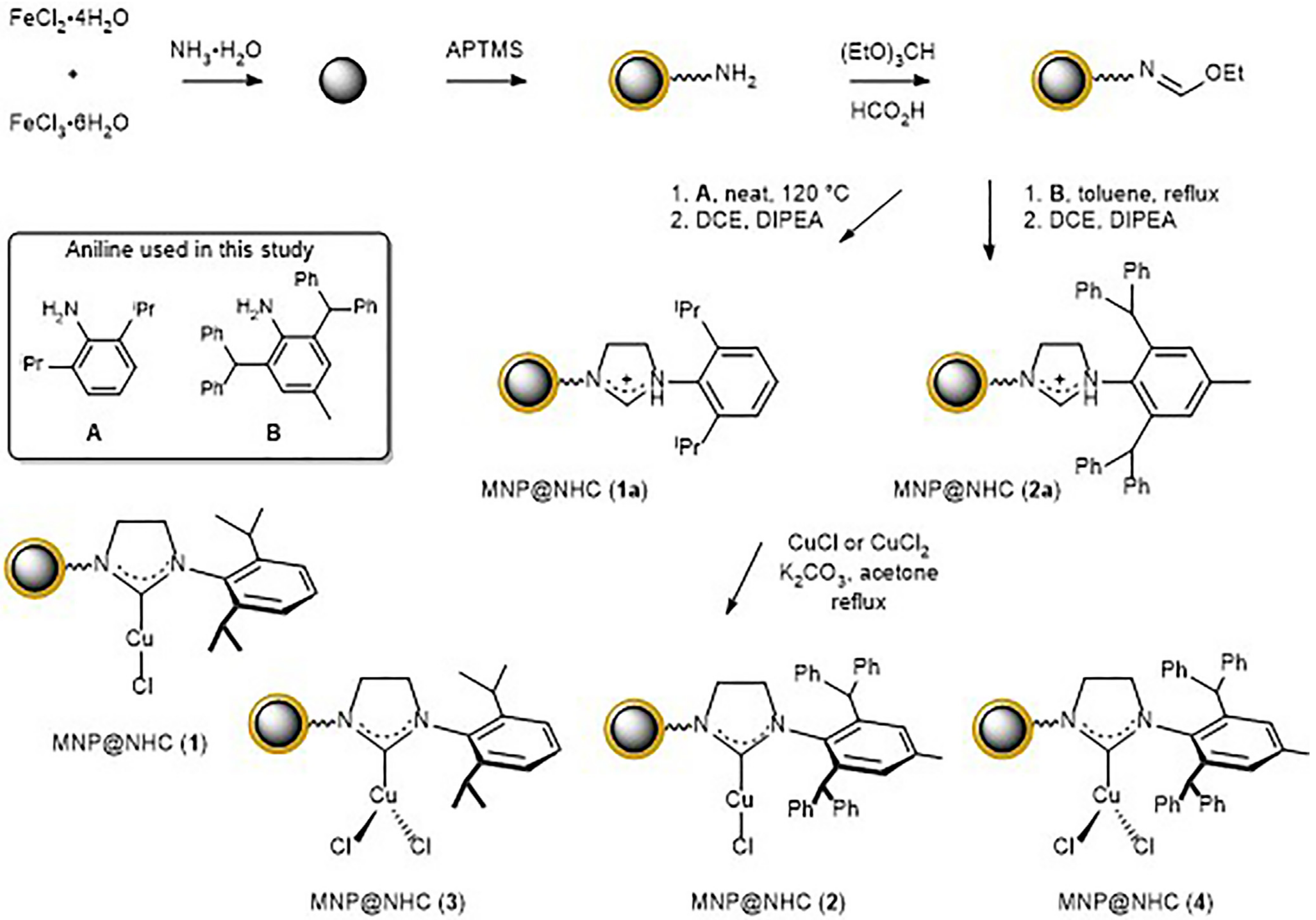
Subsequently, the obtained MNP-supported NHC ligands were used to prepare the corresponding copper(I) and copper(II) com-



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

plexes (Scheme 1). The synthesis of copper(I) complexes was accomplished by a procedure developed by Cazin et al. [61] However, the corresponding copper(I) complexes MNP@NHC (**1**) and MNP@NHC (**2**) appeared to be air- and moisture-sensitive. Bearing in mind further applications from the green chemistry point of view, we turned our attention to copper(II) complexes which we expected to be resistant to the aerobic conditions. Indeed, application of the above-mentioned protocol furnished cleanly the corresponding copper(II) complexes MNP@NHC (**3**) and MNP@NHC (**4**) which appeared to be stable after one week of storage in an open flask. It should be stressed that the synthesis of NHC-copper(II) complexes has met with limited success so far (*vide infra*).

The stability of higher oxidation states, namely NHC-copper(II) is usually enhanced by the presence of a chelating arm attached to the NHC core in the case of five-membered rings [62–68] or by applying six-membered congeners [69]. In addition, a synthetic approach to NHC-copper(II) halide complexes has failed, leading to haloimidinium salts [69,70]. To the best of our knowledge, Cazin's method allowed to obtain the first stable NHC-copper(II) chloride complexes. The expansion of the scope of this method is in progress, with promising results.

2.2. Catalytic activity

With NHC-copper complexes in hand, their catalytic activity and reusability was examined. At the outset of our studies, the reaction between benzyl bromide, propargyl alcohol (1.5 equiv) and sodium azide (2.5 equiv) was selected (Table 1). The activity of the NHC-copper complexes was directly compared to the activity of CuCl and $CuCl_2$ (Table 1), in order to gauge the beneficial effect of NHC ligands.

In the case of complexes **1** and **2**, THF was used as the solvent and DIPEA as the base, analogously to the previously studied reactions under inert conditions [71]. After 24 h at 40 °C, the product was obtained in high 80% and 77% yields (for complex **1** and **2**, respectively, Table 1, entries 2 and 4). It should be mentioned that copper(I) chloride was not active in the reaction. This observation clearly confirms that NHC-copper complexes **1** and **2** are active catalysts, and their activity is not caused by CuCl simply adsorbed on the solid phase. In the case of complexes **3** and **4**, MeOH was chosen as the solvent due to the good reactivity of copper(II) catalysts in polar solvents [72,73]. At first, the reactions catalyzed by **3** and **4** were carried out at room temperature with the addition of sodium ascorbate. After 3 h of stirring, only 30% of conversion was observed, and after 24 h the yields reached only 39% and 32% for catalyst **3** and **4**, respectively (Table 1, entry 7 and 10). For this reason, the reactions temperature was increased to the boiling point of MeOH, and after 3 h the completion of the reactions was observed. The model reactions catalyzed by **3** and **4** were conducted with the addition of a reducing agent (sodium ascorbate). In both cases, moderate to high yields were obtained (56% and 96%, respectively). According to the research by Zhu [73], copper (II) species can catalyze CuAAC reactions without using a reducing agent. Therefore, the catalytic activity of **3** and **4** was examined in sodium ascorbate-free conditions. The product was obtained in high yields (86% for catalyst **3**, and 80% for catalyst **4**), confirming the observation made by Zhu's group.

Additionally, the influence of catalyst loading (benzyl bromide to catalyst ratio) on the efficiency of the model reaction was examined, and the results are presented in Fig. 1. 0.2 mmol of benzyl bromide to 5 mg of catalyst was found to be the optimal ratio for completion of the reaction in high yield (e.g. 96% for catalyst **4**). This ratio was used in further activity studies. The difference in the activity of catalysts immobilized on MNPs (Fig. 1) can be caused by various effects. Application of a high amount of the catalysts (see column A, Fig. 1) can cause their agglomeration and the decrease in their activity during the reaction. In contrast, a lower

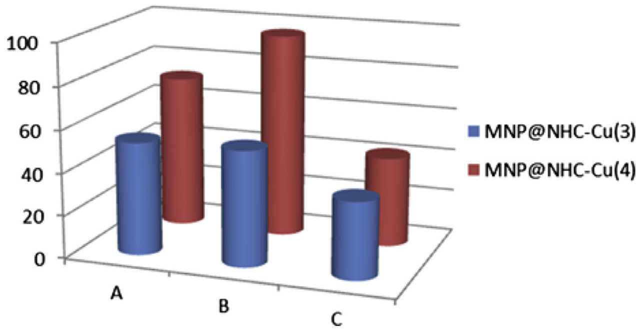
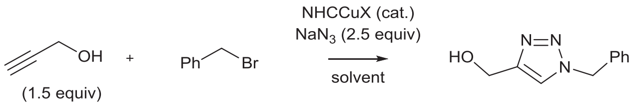


Fig. 1. Catalytic activity of MNP@NHC-Cu(**3**) and MNP@NHC-Cu(**4**) towards propargyl alcohol and benzyl azide generated *in situ* in click reaction, with different benzyl bromide to catalyst (mmol/mg) ratios with the addition of sodium ascorbate: (A) 0.2/10; (B) 0.2/5 and (C) 0.2/2.5.

Table 1
The CuAAC reaction conditions (catalysts were used in 0.2/5 mmol/mg benzyl bromide to catalyst ratio)



Entry	Cat.	Solvent	Temp.	Sodium ascorbate	Base[a]	Time [h]	Isolated yield [%]
1	**CuCl**[b]	THF	40 °C	–	DIPEA	24	0
2	**1**	THF	40 °C	–	DIPEA	24	80
3	**1**	MeOH	Reflux	–	DIPEA	3	49
4	**2**	THF	40 °C	–	DIPEA	24	77
5	**2**	MeOH	Reflux	–	DIPEA	3	62
6	**$CuCl_2$**[b]	MeOH	Reflux	+	–	3	20
7	**3**	MeOH	rt	+	–	24	39
8	**3**	MeOH	Reflux	+	–	3	56
9	**3**	MeOH	Reflux	–	–	3	86
10	**4**	MeOH	rt	+	–	24	32
11	**4**	MeOH	Reflux	+	–	3	96
12	**4**	MeOH	Reflux	–	–	3	80

The model reaction of copper-catalyzed alkyne-azide cycloaddition (CuAAC). Cu(I) catalysts were used without the addition of a reductive agent, but in the presence of a base. In reactions catalyzed by Cu(II) complexes, sodium ascorbate was added (0.04 mmol). All four catalysts were used in 0.2/5 mmol/mg benzyl bromide to catalyst ratio. Approx. mol% of the catalysts was 5%, 5%, 3%, and 2% for 1, 2 3 and 4 respectively (calculations based on SEM/EDX measurements, for methodology see Supporting Information).

[a] 2 equiv of base was used.

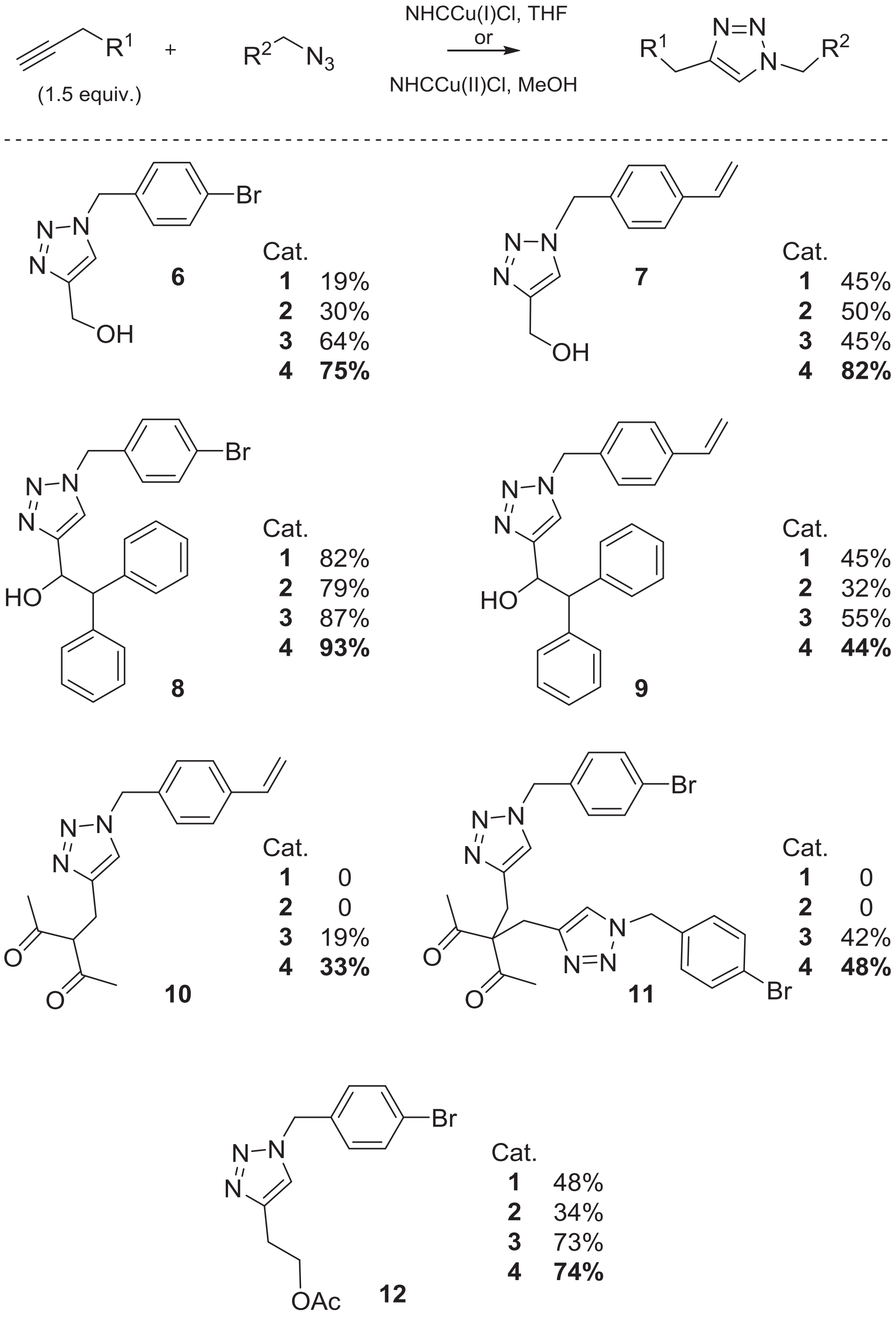
[b] 1 mol% of catalyst was used.

substrate-to-catalyst ratio improves the yields (Fig. 1, column B). It should be noted that the amount of the catalyst needs to be carefully calculated because, as shown in Fig. 1 (column C), the reduction of the ratio to 0.2/2.5 mmol·mg^{-1} again decreases the yield.

2.3. The activity of catalysts 1–4 in reactions of various alkynes and azides

Since the activity of the catalyst depends not only on its structure, but also on the reactivity of the starting material, thus, the activity of the four new catalysts was investigated and compared using a variety of alkynes and benzyl azides. It was observed that complexes **1** and **2** show low activity in this type of reactions. Even the addition of sodium ascorbate, for oxidation prevention of the catalyst, did not raise the yields. The results are presented in Scheme 2. It was also proven that magnetic NHC-Cu complexes made from $CuCl_2$ (catalysts **3** and **4**) show higher activity than the catalysts made from CuCl (**1** and **2**) (Scheme 2).

In almost all studied reactions, catalyst **4** showed the best activity, as well as high stability. It should be noted that 1,2,3-triazole



Scheme 2. Comparison of the activity of four different catalysts in the CuAAC reaction of various alkynes and azides. Reaction conditions: reactions were performed using 4-bromo benzyl azide or 4-vinyl benzyl azide as starting materials, see general procedure in experimental section. Catalysts **1**, **2**, **3** and **4** were used in 0.2/5 mmol/mg benzyl azide derivative to catalyst ratio, 0.04 mmol of sodium ascorbate was added·THF was used as a solvent in reactions catalyzed by **1** and **2**, MeOH for those catalyzed by **3** and **4**. Maximum Turnover Numbers were obtained in the synthesis of **8** and the maximum value was obtained for catalyst 3 – TON = 38, TOF = 12.5/h (for the rest of the results see Table S1 in Supplementary Information).

formation is generally catalyzed by copper(I) salts and corresponding complexes. On the other hand, the more stable copper(II) has been also applied in the presence of a reductant, usually sodium ascorbate [54,74,75]. Only recently copper(II)-catalyzed reactions under reductant-free conditions have been reported [72,73,76,77]. Mechanistic investigations and DFT calculations have proved that the active copper(I) species is formed as a result of copper(II)-assisted oxidation of solvents such as MeOH, EtOH or *i*-PrOH [73,78,79] or homocoupling of alkynes [80,81]. Beyond many useful copper(I) and copper(II) complexes, NHC-copper(I) complexes have been recently applied exhibiting a remarkable activity in CuAAC reactions [78,79,82–86]. Unfortunately, NHC-copper(II) have never been applied in this reaction before. To our delight, we present the first example of an NHCCu(II)-catalyzed Huisgen reaction. As mentioned above, NHC-copper(II) complexes showed higher activity in the CuAAC reaction. However, the exact nature of this behavior could not be explained without a detailed mechanistic study, due to the complicated mechanistic scenario of the CuAAC reaction. Recent theoretical and experimental studies have proved that dimeric or higher order copper species are involved [81,87–90].

2.4. The recycling

The magnetic solid phase allows quick and easy separation of the immobilized catalysts. Due to the highest activity of complexes **3** and **4**, only the recycling of these two catalysts was investigated. After completion of the model reactions, the catalysts were separated from the reaction mixtures, and then washed once with water and three times with MeOH. After purification, the solvent was evaporated and the catalyst was reused. Fig. 2 presents the model reaction yields after each reuse in a relation to the catalyst amount. Also, recycling without using a reducing agent was performed (Fig. 2).

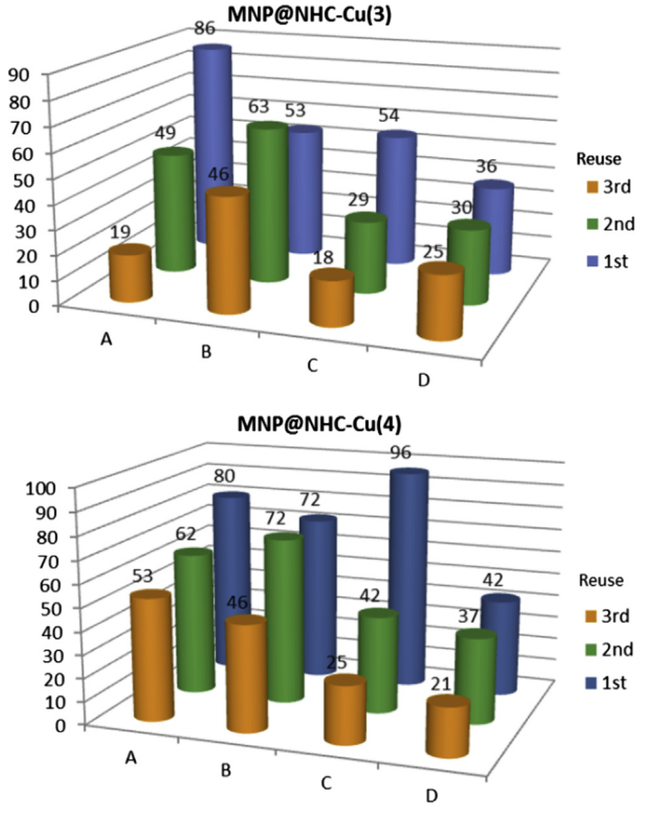


Fig. 2. Catalytic activity of MNP@NHC (3) (up) and MNP@NHC (4) (bottom) towards propargyl alcohol and benzyl azide generated *in situ* click reaction, with different benzyl bromide to catalyst (mmol/mg) ratios: (A) 0.2/10 without sodium ascorbate; (B), (C) and (D) - 0.2/10, 0.2/5 and 0.2/2.5, respectively, with the addition of sodium ascorbate.

It appears that catalysts **3** and **4** have a good activity in methanol both with and without the addition of sodium ascorbate. The activity of catalysts **3** and **4** decreased after each reuse, indicating their deactivation during the catalytic processes. Furthermore, the activity of the reused catalyst with regard to the amount of the catalyst was studied (Fig. 2, columns B, C, and D). It appeared that the best yields for catalyst **3** (after the second run – 63%, after the third run – 46%) and for catalyst **4** (72% and 46%) were obtained when 20 mg (0.2/10) of the catalyst was used (Fig. 2, column B). It was probably caused by the presence of the catalytic centres which did not participate in the reaction during the first run. Therefore, they were not deactivated and could be active in the next run. The high yields in the first run were observed even in the absence of sodium ascorbate (Fig. 2, column A, 86% and 80% for catalysts **3** and **4**, respectively). In the second and the third run, the activity of catalysts **3** and **4** was higher when sodium ascorbate was present (Fig. 2, column B).

These results show that the catalyst is deactivated during the reaction cycle. The mechanism of the deactivation needs to be further investigated in order to develop more active catalysts.

3. Characterization

3.1. Copper content measurements

The copper mass content was investigated by SEM/EDX (Fig. 3). The results show that catalyst **4** contains more copper than catalyst **3** (9 and 6 %mass, respectively). This can be assigned to stronger complexing properties of NHC precursor **2a**. The copper content in catalysts **1** and **2** was also investigated. Surprisingly, catalysts **1** and **2** presented higher copper ion mass content (17% for both catalysts) than catalysts **3** and **4**. This fact does not correspond with the lower activity of complexes **1** and **2**. Furthermore, the copper content after each reuse was measured and the results are presented in Fig. 3. The graph clearly shows that copper content in catalysts **3** and **4** decreases after each reuse. The differences are slight but they significantly influence the activity of the catalysts. After the first run yields drop down by half (Fig. 2, column C). This decrease of the activity cannot be explained only by the leakage of copper (the drop of the yield is not directly proportional to the copper content decrease). Deactivation of the catalyst poisoned by reaction by-products is an alternative explanation. Further experiments were performed without the use of any additional reducing agent (i.e. sodium ascorbate). Results show a similar decrease of the activity of the tested catalysts in the second and the third reuse.

The Cu leakage was investigated by AAS spectroscopy. Generally, after the separation of the catalyst, the reaction mixture was washed by water. The aqueous layer was then analyzed by Atomic Absorption Spectroscopy.

The leakage of copper from catalysts **1** (65.34 μg/ml) and **2** (256.45 μg/ml) is much higher than from **3** (7.94 μg/ml) and **4** (2.22 μg/ml), indicating lower stability of copper(I) complexes in comparison to their copper(II) analogues.

In some cases, the activity of an immobilized catalyst can be influenced by the engagement of a catalytically active free metal, which can be present in the reaction mixture due to leakage [91]. In such cases, the yield is proportional to the metal ion content in the reaction mixture after the completion of the process. In our research no such tendency for copper ion leakage is observed. Furthermore, the yields are not directly influenced by the free metal ion content (high leakages of copper ions from catalysts **1** and **2** do not cause high yields).

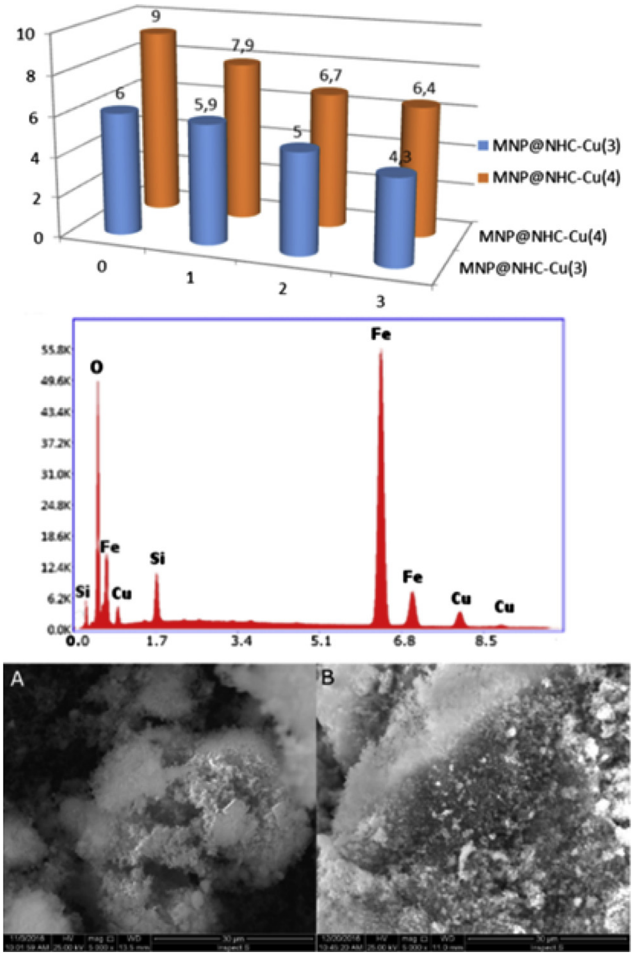


Fig. 3. The Cu %mass content in catalysts **3** and **4** before and after each reuse (SEM/EDX investigations, signals were collected from the surface of the probe), an example of the EDX spectrum of catalyst **3** (middle) and SEM pictures (bottom) of catalyst **4** before (A) and after the first use (B).

3.2. IR spectra

The ATR-IR spectra of all synthesized catalysts before reactions as well as after reuse were collected and presented in Fig. 4 and in the Supporting Information. In the IR spectrum of 2a one can find characteristic peaks which represent C—H aromatic stretch (3040 cm^{-1}), C—H aliphatic stretch (2934 cm^{-1}), and vibrations of C—H present in the imidazoline ring (1697 cm^{-1}) which intensity decreased after complexation with copper(II) (catalyst **4**). This tendency appears also in the IR spectrum of catalyst **3** (Supporting Information). In the case of catalysts **1**, **2**, **3**, and **4**, after each reuse, no significant changes in the IR spectra were observed (Supporting Information).

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3.3. TGA analyses

Thermogravimetric studies were carried out in order to investigate the thermal properties of the obtained magnetic hybrids. Fig. 5 shows TG (5A) and DTG (5B) curves of MNP@NH$_2$, two imidazolinium salts: **1a** and **2a**; four catalysts: **1** and **2** obtained from copper(I) and **3** and **4** obtained from copper(II). The TG curve refers to the temperature-dependent mass change in percent, whereas the DTG curve refers to the rate of mass change. The TG curve of the starting material (MNP@NH$_2$) shows the total weight loss equal to 10%. The increase of the total weight loss to around 21% is observed for particles **1a** and **2a** containing imidazolinium salts. This weight loss is related to the decomposition of the aminosiloxane shell, as well as organic imidazolinium groups which are present on the MNP surface. After the formation of copper(I) and copper(II) complexes, the total weight loss in all four samples is higher (25% for **1** and **3**, 31% and 24% for **2** and **4**, respectively). TG and DTG curves of the presented nanohybrids (Fig. 5A and B) show three stages of weight loss at temperature ranges of 150–240 °C, 250–370 °C, and 640–830 °C.

The first two are most likely related to the decomposition of the imidazolinium part, whereas the third one, with the maximum at 755 °C, is attributed to the degradation of the siloxane shell. In

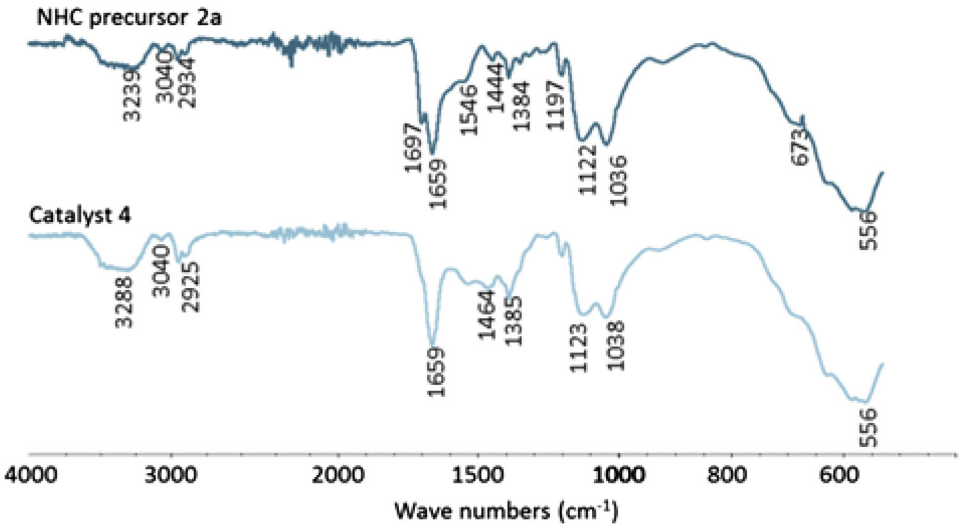

Fig. 4. ATR-IR spectra of the catalyst **4** and the NHC precursor **2a**.

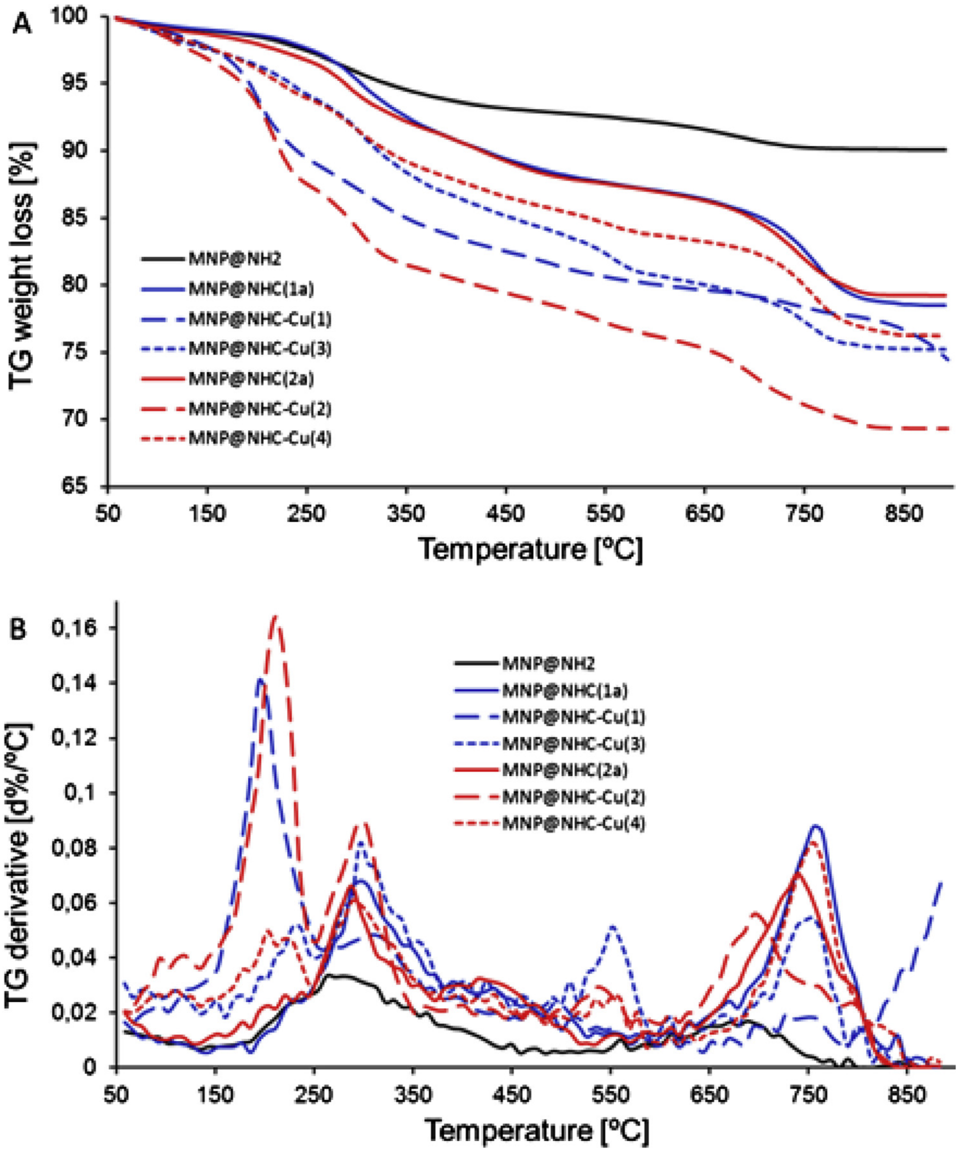

Fig. 5. TG (A) and DTG (B) curves of: aminosiloxane-coated nanoparticles (MNP@NH_2), imidazolinium salts: **1a** and **2a**, and their complexes with Cu (**1**–**4**).

the DTG curves it can be observed that the catalysts containing copper(I) ions are less stable in comparison to those obtained from copper(II) salt (faster decomposition of **1** and **2**). The first step of degradation starts faster in the case of catalysts **1** and **2**, the maxima of the degradation rate are observed at 202 °C and 210 °C, respectively.

In the thermograms of samples **3** and **4**, the rate of mass change is different. In these cases, maxima in DTG curves are harder to distinguish. The first two degradation stages merge into one broad peak (150–390 °C). The differences in the thermograms of nanohybrids indicate diverse chemical structure of the coating surrounding the MNPs. Additionally, TG analysis of complex **4** after first reuse was performed. No significant changes in weight loss were noticed (Figs. S5–S8 in Supporting Information).

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4. Experimental section

4.1. Materials and methods

All reagents were purchased from Aldrich Chemical Company and used as received. MeOH and THF were purchased from Avantor Performance Materials Poland S.A. 3-Propargyl-penta-2,4-dione [71], 3,3-bis-propargyl-penta-2,4-dione [92], 4-vinylbenzyl azide and 4-bromobenzyl azide were synthesized according to a literature procedure.

The formation of magnetic nanoparticles, particle size and morphology were confirmed by transmission electron microscopy (TEM) (Tecnai G2 X-TWIN). Samples for TEM were prepared on holey carbon copper grids. Energy-dispersive X-ray spectroscopy (EDX – detector OctanePro) analyses were collected from samples imaged by SEM (Inspect S50). Surface modifications were confirmed by FT-IR (Nicolet 6700). Thermogravimetric analysis (TGA) was performed on a Mettler Toledo Star TGA/DSC unit. Differential scanning calorimetry (DSC) was performed on a Mettler Toledo Star DSC system. Argon was used as a purge gas (10 mL·min^{-1}). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance II spectrometer (400 MHz and 100 MHz respectively). Melting points were measured by Mettler Toledo MP 70 Melting point System. Elemental Analyses were performed on VarioMicroCube (Elementar) and HRMS spectra on Accurate Mass Q-TOF LC/MS 6530 Spectrometer.

4.2. Preparation of catalysts

Preparation of MNP@NHC copper complexes. Nanoparticles (100 mg) with NHC-modified shell were dispersed in 40 mL of acetone (30 min in ultrasonic bath) and then K_2CO_3 (50 mg) was added. After 30 min of stirring, 100 mg of CuCl (or $CuCl_2$) was added. The mixture was stirred for 24 h at rt. Next, nanoparticles were magnetically separated and washed once with water and twice with MeOH, and then dried overnight at 50 °C. Formation of the product was confirmed by FT-IR spectroscopy. The copper mass content was investigated by EDX detector conjugated with SEM microscope.

4.3. CuAAC reactions

The general procedure for CuAAC reactions. The catalyst was sonically dispersed in 4 mL of solvent. Then starting materials, alkyne (1.5 mmol), benzyl bromide (1 mmol) and sodium azide (2.5 mmol) were added. In the synthesis of products **6**–**12**, previously obtained (due to known procedure [71]) appropriate azide (1 mmol), in place of alkyl halide and sodium azide, was used. In synthesis of **6**–**12** with **3** and **4** as catalyst, sodium ascorbate was added (0.04 mmol). Mixtures were stirred for the indicated time at given temperatures. After completion of the reaction, the catalyst was separated by external magnetic field, washed several times with THF or MeOH and dried at 50 °C. The isolated solution was evaporated, then DCM was added and the solution was washed once with water. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated. The crude product was purified by column chromatography (eluent–hexane, hexane:AcOEt 8:2 and 7:3). The best results for copper(II) complexes were accomplished when MeOH was used as a solvent and mixture was stirred for 3 h at reflux. For Cu(I) complexes, the best yields were obtained in THF at 50 °C.

5. Conclusions

In conclusion, we developed an efficient synthesis of four magnetically retrievable N-heterocyclic carbene copper complexes differing in the oxidation state and in the NHC ligand structure. Their synthesis does not require chromatography and the product could be easily separated after each step of the synthesis using an external magnetic field. The first examples of stable NHC copper(II) chloride complexes are reported. The obtained copper complexes anchored to the surface of magnetic nanoparticles were characterized by common techniques, including SEM and TEM microscopy, TG analysis, and IR spectroscopy. Furthermore, the catalytic activity of the prepared complexes was evaluated in copper-catalyzed azide-alkyne cycloaddition (CuAAC) reactions with *in situ* generated azide under reductant-free and aerobic conditions. The NHC-copper(II) complexes were applied for the first time in this reaction. Unexpectedly, copper(II) complexes exhibited better activity in comparison to copper(I) compounds in the series of 1,2,3-triazole formation reactions. Further investigations proved that the corresponding NHC-copper complexes anchored to magnetic nanoparticles could be easily separated by external magnetic field and reused in CuAAC reactions. In addition, the copper content was measured by Atomic Absorption Spectroscopy after each cycle in the reaction mixture after separation of the magnetic nanoparticles. Low levels of toxic copper residues in the case of copper(II) complexes were detected, enabling further applications for the synthesis of biologically relevant molecules, which are a work in progress.

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