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ORIGINAL PAPER

$CuFe_2O_4$ Nanoparticles: A Magnetically Recoverable Catalyst for Selective Deacetylation of Carbohydrate Derivatives

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Abstract An efficient protocol for the rapid room temperature deacetylation of carbohydrate derivatives using $CuFe_2O_4$ nanoparticles as an inexpensive and reusable catalyst is presented. After separation of the catalyst with an external magnet, the reaction products are easily obtained in good purity and excellent yields.

Keywords Mixed metal oxide spinel · Selective deacetylation · Carbohydrates derivatives

1 Introduction

Synthetic studies in sugar chemistry frequently require the introduction of *O*-protective groups and their subsequent removal. The acetyl group is a very useful protecting group and it has been employed widely in carbohydrate chemistry [1]. Partially acetylated monosaccharides are very important and versatile in many ways. Selective deprotection, generally performed by homogeneous catalysts, is often a key step in synthesis of sugar derivatives. Zemplén deacylation is one of the commonly used deblocking reactions in carbohydrate chemistry. Using this transesterification reaction, OH-functions can be regenerated in methanol with sodium methoxide [2]. A large number of reagents are reported to perform the selective deacetylation of carbohydrates. The selective transamidation with benzylamine [3], hydrazine [4], piperidine [5] and recently the use of lanthanide triflates [6] produce the removal of the acetyl group at the anomeric position. Several homogeneous catalysis systems have been reported allowing the O-deacetylation in the presence of other esters, e.g. guanidine [7], Sm/I_2 [8], DBU [9], HCl/MeOH [10], $HBF_4.Et_2O$ [11], *p*-TsOH [12], etc. However, these methods suffer a number of problems, such as expensive and toxic reagents, tedious separation, filtration or neutralization of the catalyst and hardly purification process.

Although the scope of homogeneous catalysis has been well demonstrated, [13] heterogeneous systems are preferred from both environmental and economical points of view. Some of the advantages of heterogeneous catalysts are efficient recycling and an easily handling; which results in overall lower costs. Magnetic particles have emerged as a useful group of heterogeneous catalysts due to their numerous applications in synthesis and catalysis [14–17]. Magnetic separation is an attractive alternative to filtration or centrifugation as it prevents loss of catalyst and enhances reusability, making the catalyst to have beneficial cost and to be promissory for industrial applications.

We present herein a method for the rapid acetate cleavage using a magnetic metal oxide [18–20] as environmentally friendly solid catalysts [21]. We have investigated the possible use of Cu–Fe spinel catalyst ($CuFe_2O_4$) for the deacetylation reaction. To the best of our knowledge it is the first report to use a magnetically recoverable catalytic agent in the deprotection reaction.

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2 Experimental Section

2.1 Catalyst Preparation

$CuFe_2O_4$ nanoparticles were prepared by a co-precipitation method at reduced temperatures [22]. A known amount of $Cu(NO_3)_2{\cdot}3H_2O$ and 2 equiv. of $Fe(NO_3)_3{\cdot}9H_2O$ were dissolved in distilled water, then added into 4 M NaOH solution followed by heating at 90 °C for 2 h, then filtered, washed with water and dried at 80 °C overnight. The solid product was ground and heated in a furnace at 700 °C.

2.2 Catalyst Characterization

The samples were fully characterized by X-Ray Diffraction (XRD) and Fourier Transform Infrared Spectroscopy (FTIR). XRD patterns were performed on a Philips PW 1732/10 equipment by using Cu K_α radiation ($k = 1.5404$ Å).

The FTIR spectra were measured using a Magna 550 Nicolet instrument equipped with CsI optics using the KBr pellets technique.

2.3 Deacetylation Procedure

All sugar derivatives were prepared and carefully purified by known methods and fully characterized by ^1H and ^{13}C NMR. A typical procedure in the deprotection reactions was used. The substrate was dissolved in dried MeOH (1 mL) and then $CuFe_2O_4$ (10 mol%) was added. The mixture was stirred at room temperature, agitation was provided by means of a shaker, and completion of the reaction was monitored by thin layer chromatography (TLC) after which a magnet was used to separate the catalyst from the reaction mixture. The pure product was isolated by column chromatography and confirmed with ^1H and ^{13}C NMR. NMR spectra were recorded with a Varian Mercury Plus (200 MHz) in D_2O, DMSO-d6 or $CDCl_3$. TLC chromatography was performed on DC-Aulofolien/Kieselgel 60 F245 (Merck) and column chromatography, through silica gel Merck 60 (230–400 mesh).

After the reaction is complete, the catalyst is separated, washed with methanol and CH_2Cl_2, dried under vacuum and reused for the deacetylation reaction, the procedure described above was followed.

3 Results and Discussion

Characterization of the catalyst confirm the structure proposed and no impurities were detected. $CuFe_2O_4$ crystallized after calcining at 700 °C and no water, amorphous copper or iron hydroxides were detected in the catalyst by XRD as shown in Fig. 1.

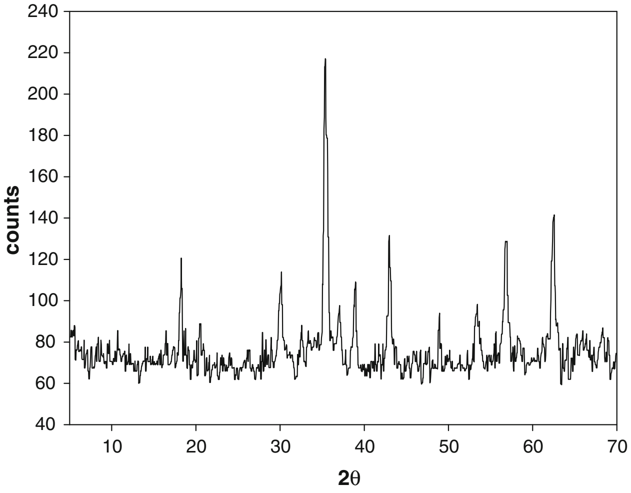


Fig. 1 The X-ray diffraction patterns of the $CuFe_2O_4$ catalyst treated at 700 °C

XRD patterns of dried precipitate are mainly composed of $CuFe_2O_4$ (tetragonal, JCPDS card N° 34-0425) and show peaks characteristic of the tetragonal $CuFe_2O_4$, with a good crystallinity, and CuO segregated. The copper ferrite calcined at 700 °C present a particle size of ≈14 nm, calculated from the broadening of the peak at $2\theta = 35.4$ using the Scherrer equation. Assuming that all the particles to be spherical, a value of 40 m^2/g for the specific surface area, was calculated from the relation proposed by George et al. [23].

The most distinctive feature of the FTIR spectra is that two significant bands centered in ~600 and ~400 cm^{-1} appear at low energy. These intense absorptions are undoubtedly assigned to $CuFe_2O_4$ (Fig. 2).

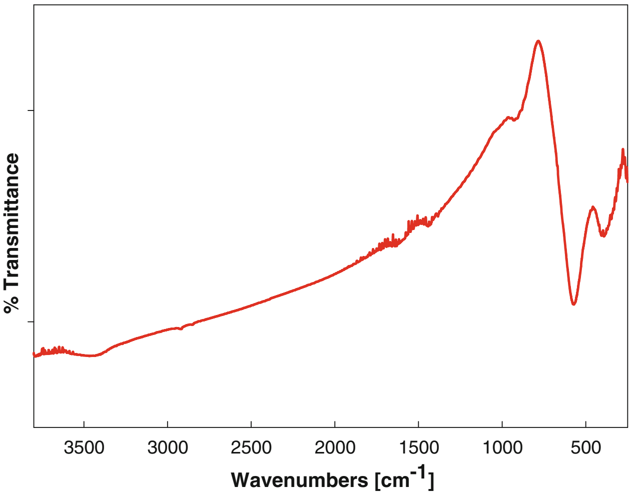
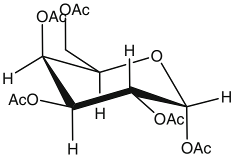
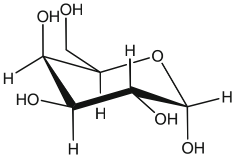
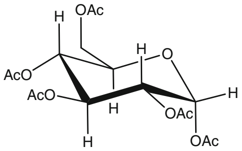
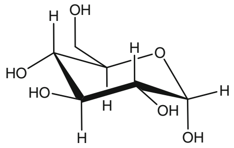
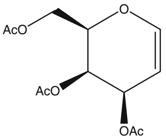
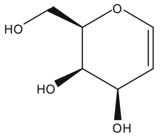
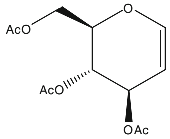
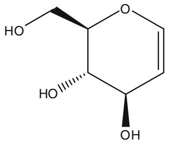
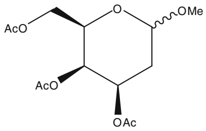
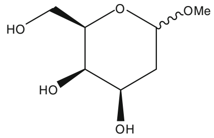
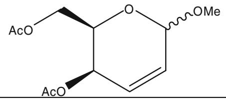
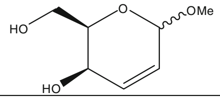


Fig. 2 FTIR spectra of the $CuFe_2O_4$ catalyst treated at 700 °C

Fig. 3 $CuFe_2O_4$ catalyst during reaction, under stirring and removal by external magnet

Table 1 Deacetylation of peracetylated sugar derivatives[a]

Entry	Substrate	Product	Yield
1			95%
2			97%
3			92%
4			94%
5[b]			98%
6[b]			90%

[a] All the reactions were performed in dried MeOH (1 mL) using 10 mol% of $CuFe_2O_4$ and 0.1 mmol of acetylated sugar at room temperature for 1.5 h

[b] An α/β mixture of the *OMe*-glycosides **5** and **6** were used without separation

Separation and recovery of the catalyst is an important aspect for the synthesis of fine chemicals; which is generally performed by filtration or centrifugation with reduced efficiency. In our catalytic system it can be recovered simply using external magnets, the catalyst was deposited on the magnetic bar within 40–50 s with high efficiency and up to 95% recovery of catalyst (Fig. 3).

In order to test $CuFe_2O_4$ catalyst we carried out the fully deacetylation of some carbohydrate derivatives. Deacetylation of peracetylated *O*-glycopyranosides, endo-glycals and 2,3-unsaturated *O*-glycosides was performed in less than 2 h with excellent yields at room temperature and the results are summarized in Table 1. NMR spectra and melting points of the products were in total accordance with the literature.

From the NMR spectra of crude product it is evident that the *O*-deacylation is quantitative in all compounds examined. The mechanistic course of the deacylation process involves an overall transesterification which suggest that it proceeds via a nucleophilic displacement of an acyl group by a methoxy anion generated by the spinel catalyst in contact with methanol.

As it is shown in Fig. 4, the catalyst could be reused three times with a slight activity loss for the complete deacetylation of 1,2,3,4,6-penta-O-acetyl-α-D-glucopyranose.

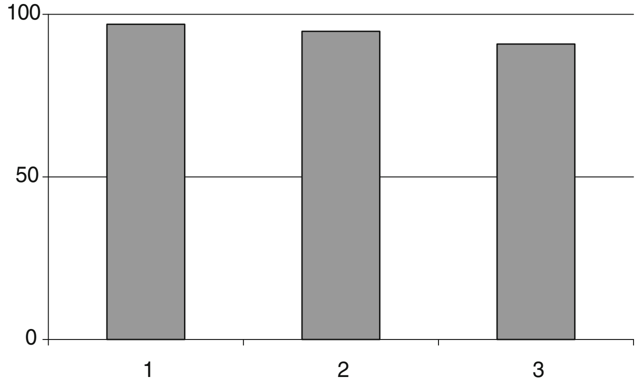


Fig. 4 Activity lost as a function of the number of reused times of the $CuFe_2O_4$ catalyst

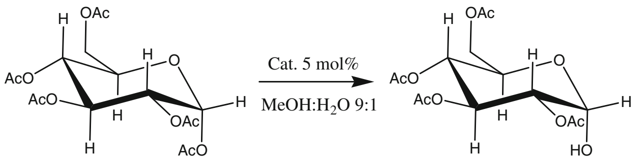


Fig. 5 The reaction scheme of the selective deacetylation of pentaacyl-(alpha)-glucose at the anomeric conditions with $CuFe_2O_4$ as catalyst

The acylated carbohydrates studied present a variety of *O*-acyl groups whose reactivity depends on their position and configuration. In general, it is observed that the anomeric position was the first to be deacetylated due to the hemiacetal structure [24]. Based on this assumption we studied the selective anomeric deacetylation by the use of 1,2,3,4,6-penta-O-acetyl-α-D-glucopyranose as model compound (Fig. 5).

Different solvent conditions were examined to improve the selectivity. On monitoring all attempted reactions by qualitatively thin-layer chromatography it was found that, in MeOH/H_2O (9:1), the reaction proceeds moderately at room temperature. Best results were obtained with 5 mol% of the $CuFe_2O_4$ catalyst in 1 mL of solvent mixture after 2.5 h. After chromatographic separation on silica gel, the 1-OH compound was obtained in 45% yield.

4 Conclusions

Although there exist several methods to remove acetate groups, there are still demands for environmentally friendly procedures promoted by fully recoverable heterogeneous catalysts. Cu–Fe spinel ($CuFe_2O_4$) was proven to be an excellent catalyst for the deacetylation reaction due to its low cost, magnetic separation and no toxicity.

A facile, room-temperature, rapid, under neutral conditions, virtually quantitative method for catalyzed removal of acetate groups at all positions in a variety of sugar derivatives is presented. Furthermore, by changing the reaction conditions, solvent and catalyst amount, these reactions lead to selective anomeric deacetylation in moderate yields.

The obtained results are very useful since carbohydrate derivatives are products of interest as key intermediates for the synthesis of a number of biologically active compounds.

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