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Citric Acid Coated Magnetite Nanoparticles: An Efficient and Reusable Green Catalyst for Rapid Acetylation of Alcohols and Phenols

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The acetylation of various alcohols and phenols was performed successfully using acetic anhydride in the presence of Citric acid coated magnetite nanoparticles as catalyst under solvent-free condition and at 45 °C. The catalyst showed high thermal stability and was recovered and reused at least 5 times without any considerable loss of activity. The present process is environmentally benign and economical.

Keywords: Magnetic nanoparticles, Citric acid, Acetylation, Green catalyst

INTRODUCTION

Citric acid is a natural, weak organic acid that is found in many fruits and vegetables, especially citrus. Citric acid is a by-product of the citric acid cycle [1], which is also produced by many living organisms, including mold. Citric acid consists of one hydroxyl and three carboxyl (R-COOH) groups. Recent studies show that Citric acid plays a role analogous to those of the powerful catalysts used in various organic transformations [2]. In 2011, Radhakrishnan, proposed that citric acid could be used as a green catalyst for rapid one pot synthesis of quinoxaline derivatives [3]. Organocatalysis has emerged during the last decade as one of the major issues in the development of catalytic chemical technology [4].

Acylation of alcohols and phenols is a frequently utilized transformation in synthetic chemistry [5]. Acid anhydrides have been the most commonly used reagents in the presence of an acid or base catalyst [6]. Typically, acylation of alcohols and phenols is performed under homogeneous catalysis with acetic acid or acetyl chloride or acetyl anhydride, in the presence of a convenient basic catalyst such as triethylamine or pyridine [7]. In addition,

zinc chloride [8], carbon tetrabromide in ethyl acetate [9], cerium(III) triflate [10], *p*-toluenesulfonic acid [11], 4-(dimethyl amino)pyridine, 4-pyrrolidinopyridine [12], iodine [13], magnesium bromide [14] sulfamic acid [15], have been also applied for the acetylation of alcohols and phenols. However, there are several factors in some of these methods which limit their applications. In many of these methods, toxicity of reagents, harsh reaction conditions, harmful organic solvents, and tedious work-up procedures are the main obstacles. Also long reaction times and by-product formation are other drawbacks of these protocols. One of the most promising solutions to these problems seems to be immobilization of catalysts or using eco-friendly solvent-free conditions. When an immobilized catalyst is used, the insoluble catalyst can be separated easily and the catalyst can be recovered and recycled. Furthermore, the reported examples have demonstrated that heterogeneous catalysts give generally higher selectivity and typically require easier work-up procedures. Also, solvent-free synthetic methods are valuable for environmental and economical reasons. The use of Lewis and Bronsted acid catalysts has high priority from laboratories to chemical manufacturing plants. Proton is the most versatile catalyst for extraordinary range of organic reactions and biological and synthetic transformations [16].

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Due to their high surface area, nanoparticles have received increasing attention as an alternative catalytic support [17]. Although tedious recycling of nano catalysts *via* filtration and inevitable loss of solid nano catalysts during the separation process have strongly limited their applications. Furthermore, nanometer-sized catalysts are often easily dispersible in solution by forming stable suspensions and therefore, expensive ultra-centrifugation is often the only way to separate them from the products [18]. Fabrication of core-shell magnetic nanocatalysts having a magnetic core and an inorganic shell is one of the solutions to overcome this difficulty. Such core-shell materials combine the unique magnetic properties of the core with the functionalization possibilities of inorganic surface [19]. It was reported that formation of a passive coating of magnetic nanoparticles could prevent their aggregation in solutions and thus improve their chemical stability [20]. Owing to its good stability, high surface area and easy synthesis, magnetic Fe_3O_4 nanoparticles have been recently used as heterogeneous catalytic supports [21]. Following high importance of acetylation and strong demand for a highly efficient and environmentally benign method in their reaction, the present work illustrates the immobilization of citric acid on magnetic nanoparticle (Fe_3O_4 @Citric acid) [22], as a magnetic and recoverable catalyst for the use as solid acid catalyst in acetylation of alcohols and phenols (Fig. 1).

The acidity of Citric acid loaded on Fe_3O_4 was confirmed by the back-titration method. Thus, triplicate ~100 mg samples were added to 10 ml of 0.1 N NaOH solution. To ensure that all of the Citric acid has been reacted with NaOH, an excess amount of NaOH was used. The mixture was sonicated for 10 min. To each vessel, was added two drops of phenolphthalein pH-indicator. Back-titration was accomplished by titrating the unreacted base in solution with standardized 0.1 N HCl solutions to the first permanent cloudy pink colour. This was subtracted from the initial value of the base to find the amount of base actually reacted with the Citric acid and hence the quantity of supported Citric acid on the MNPs. The acidity value was obtained as 1 mmol g^{-1} by adding 9 ml HCl.

Total number of moles of NaOH added to the sample: 1

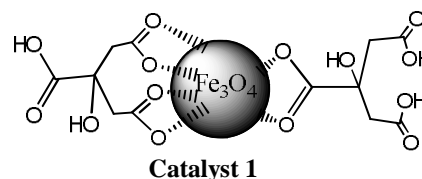
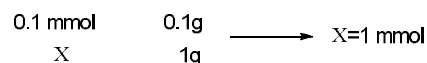


Fig. 1. The proposed structure for Citric acid coated Fe_3O_4 nanoparticles (Fe_3O_4 @Citric acid).

mmol, total volume of HCl added to each vessel: 9 ml, number of moles of consumed HCl: 0.9 mmol, average number of moles of excess NaOH left after the reaction was completed: 0.1 mmol.

Thus:



EXPERIMENTAL

Catalyst Preparation

The magnetic (Fe_3O_4) nanoparticle was synthesized by a chemical co-precipitation technique of ferrous and ferric ions in alkali solution [22]. 5 mmol $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (1.25 g) and 2.5 mmol $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (1.99 g) were dissolved in deionized water (20 ml) separately, followed by the two iron salt solutions being mixed under vigorous stirring (800 rpm). Then NH_4OH solution (0.6 M, 200 ml) was added to the above mixture at room temperature until the pH was raised between 11 and 12. The resulting black dispersion was continuously stirred for 1 h at room temperature and then heated to reflux for 1 h to yield a brown dispersion. The mixture was washed three times with Et_2O , air-dried to obtain Fe_3O_4 .

After magnetite synthesis, 5 g of Citric acid in 10 ml water was added and the temperature was raised to 90 °C under continuous stirring for 90 min. The mixture was washed three times with Et_2O , air-dried to obtain Fe_3O_4 @Citric acid.

General Procedure for the Acylation of Alcohols and Phenols

General procedure for the acetylation of alcohols and

phenols: To a solution of substrate (1 mmol) and acetic anhydride (1.2 mmol) was added supported Citric acid catalyst 1 (10 mg) and the mixture was stirred at 45 °C. After completion of the reaction (TLC), CH₂Cl₂ was added to the mixture to remove the catalyst by an external magnet. Water (10 ml) was added and the phases were separated. The organic phase was washed with saturated NaHCO₃ solution, brine, dried (Na₂SO₄) and concentrated to give the pure product. The catalyst was washed with methanol and dried to reuse. The catalyst could be recycled 5 times without a measurable loss of activity. The desired pure

products were characterized by comparison of their physical data with those of known compounds.

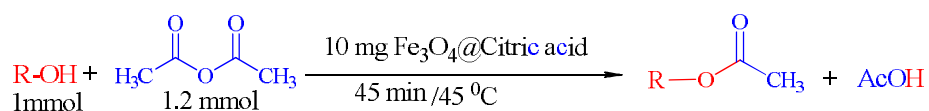
RESULTS AND DISCUSSION

In an initial study, benzyl alcohol was used as a model substrate to optimize the conditions for the acylation of alcohols and phenols. Acylation of this substrate in solvent-free conditions at 45 °C, in the absence of a catalyst, was tested and formation of a small amount of the desired product showed that the presence of a catalyst was necessary for this reaction (Table 1, entry 1). Accordingly,

Table 1. Optimization of the Reaction Conditions Using the Model System^a





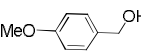
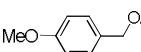




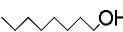
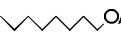
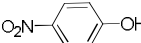
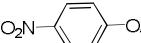
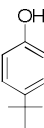
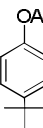
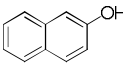
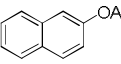






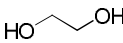
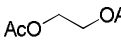


Entry	Catalyst	Solvent	Temp. (°C)	Time (min)	Yield (%) ^b
1	No catalyst	Free	45	45	10
2	No catalyst	DMSO	r.t.	120	13
3	Fe ₃ O ₄	Free	r.t.	45	5
4	Fe ₃ O ₄	Free	45	45	10
5	Fe ₃ O ₄ @Citric acid	Free	r.t.	45	70
6	Fe ₃ O ₄ @Citric acid	CH ₂ Cl ₂	r.t.	45	0
7	Fe ₃ O ₄ @Citric acid	CH ₂ Cl ₂	45	45	5
8	Fe₃O₄@Citric acid	Free	45	45	95
9	Fe ₃ O ₄ @Citric acid	CH ₃ CN	r.t.	45	0
10	Fe ₃ O ₄ @Citric acid	CH ₃ CN	45	45	0
11	Fe ₃ O ₄ @Citric acid	n-Hexane	45	45	0
12	Fe ₃ O ₄ @Citric acid	DMSO	45	45	10
13	Citric acid	Free	45	45	98
14	Citric acid	CH ₂ Cl ₂	45	45	10

^aReaction conditions: Catalyst (1 mol%), benzyl alcohol (1 mmol), acetic anhydride (1.2 mmol), solvent free and 45 °C. ^bIsolated yield.



Scheme 1. Acetylation of alcohols and phenols in the presence of Fe₃O₄@Citric acid as the catalyst.

Table 2. Acetylation of Alcohols and Phenols Catalyzed by Citric Acid Coated Magnetite Nanoparticles

Entry	Substrate	Product	Time (min)	Yield (%) ^a
1			45	95
2			30	80
3			25	90
4			30	95
5			30	80
6			25	100
7			5	100
8			5	80
9			20	100
10			35	85
11			20	95
12			45	85
13			20	80
14			45	10

^aIsolated yield.

Table 3. Reusability of the Catalyst in the Acetylation of Benzyl Alcohol with Acetic Anhydride^a

Run	Yield (%) ^b
1	95
2	95
3	95
4	93
5	90

^aReaction conditions: benzyl alcohol (1 mmol), catalyst (10 mg), acetic anhydride (1.2 mmol.), solvent free, 45 min at 45 °C.

^bIsolated yield

the optimum conditions for this reaction are as follows: 1 mol% of catalyst, solvent free, 45 °C (Table 1, entry 8).

Increasing the amount of catalyst reduced the reaction time but did not increase the yield of benzyl alcohol. To show the generality and scope of this procedure, the reaction was examined with various alcohols such as primary, secondary, and tertiary alcohols and phenols (Scheme 1). The results are shown in Table 2. Various alcohol and phenols were acetylated in moderate to good yields. All the products are known compounds. Primary and secondary alcohols were acetylated easily with acetic anhydride in the presence of the supported Citric acid catalyst at 45 °C (Table 2, entry 1 and 12), whereas tertiary alcohols required longer reaction times for completion of the reaction (Table 2, entry 14).

Reusability of the catalyst was tested by studying the acetylation of benzyl alcohol with acetic anhydride as a model reaction under the optimized reaction conditions. The recovered catalyst was reused for 5 subsequent runs without significant loss in catalytic activity (Table 3).

CONCLUSIONS

In conclusion, this protocol presents an improved and efficient methodology compared to others based on acid

catalysis. The simplicity of the procedure and easy work-up are advantages of the present protocol.

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