

Recoverable and Recyclable Catalysts for Multi-Step Reaction Networks

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ABSTRACT

Amine functionalized superparamagnetic cobalt spinel ferrite nanoparticles have been synthesized and evaluated in one-pot, acid/base catalyzed cascade reactions. When combined with traditional, nonmagnetic catalysts, use of these nanoparticles facilitated the straightforward recovery of multiple, different catalysts from one-pot, multi-step reactions. Sulfonic acid functionalized Amberlyst polymer resins catalyzed the deacetalization of benzaldehyde dimethylacetal to benzaldehyde. The amine functionalized nanoparticles then catalyzed the Knoevenagel reaction of benzaldehyde with malononitrile. Post-reaction, the acidic resin and basic nanoparticle catalysts were separated magnetically and recovered in pure form. Kinetics of initial and recycle reactions indicate no catalyst deactivation. This research illustrates the first example of recovering pure catalysts from one-pot, multi-step reactions, made possible by utilizing the superparamagnetic character of the CoFe_2O_4 nanoparticles.

Keywords: magnetic nanoparticle, heterogeneous catalysis, one-pot, cascade, recyclable

1 INTRODUCTION

Living cells synthesize the complex organic molecules required for survival through intricate multi-step reaction networks catalyzed by highly specific enzymes [1]. Much research has been completed to mimic these cascade reactions in a laboratory setting, but most chemical syntheses still involve step-wise single reactions followed by product purifications. The reason is because multiple homogeneous catalysts in a single reaction vessel can deactivate one another. Natural systems do not experience this problem because a plethora of enzymes can co-exist within a single cell without deactivating one another. This serves as a stark comparison to the one catalyst per reaction per vessel paradigm of modern synthetic chemistry.

Nature's ability to house multiple opposing enzymes within a cell can be mimicked in a laboratory setting by immobilizing the catalysts on heterogeneous supports. The low probability of solid-solid interactions maintains the integrity of the opposing functional catalysts, thus allowing the homogeneously self-quenching catalysts to remain active in the presence of the opposing catalyst. This is the case for

the one-pot acid/base reactions, as studied by Avnir and Blum [2].

Natural systems are able to catalyze multiple reaction networks within a cell using the same catalysts. The ability to catalyze multiple reaction networks in a laboratory setting has not been studied. A method to imitate this ability within a chemical synthesis paradigm is to effectively separate the individual catalysts from a one-pot reaction in pure form. These recovered catalysts could then be reused in different one-pot reaction networks [3].

Here, we demonstrate an attempt to mimic the natural ability of utilizing catalysts in a multiple reaction networks. This ability is made possible though the use of superparamagnetic nanoparticle catalysts that can be selectively recovered from other catalysts by utilizing their magnetic character. The other catalysts are recovered gravimetrically and though the use of membranes.

2 EXPERIMENTAL

2.1 Nanoparticle Synthesis

Superparamagnetic cobalt spinel ferrite (CoFe_2O_4) nanoparticles (MNP) were synthesized using reported procedures [4]. Two liters of DI H_2O were purged of dissolved oxygen by bubbling nitrogen overnight. Into 500 mL nitrogen purged DI H_2O , was dissolved 0.9 g CoCl_2 and 1.9 FeCl_2 . The solution was transferred into a 3 L round bottom flask. A solution of 12.98 g sodium dodecyl sulfate surfactant in 500 mL purged DI H_2O was added to the flask, stirred for 30 minutes, and then warmed to 65 °C. A solution of 300 mL 40% aqueous methylamine in 700 mL purged DI H_2O was heated to the same temperature, added to the flask, and stirred overnight. The cobalt spinel ferrite superparamagnetic nanoparticles (MNP) were recovered by centrifugation. Surfactant was removed by suspending the MNP in 100 mL ethanol via sonication, and the MNP were collected magnetically. The washing process was repeated three times. The MNP were dried at 60 °C under vacuum overnight, yielding approximately 1.7 g CoFe_2O_4 nanoparticles. The MNP were stored in a nitrogen drybox.

2.2 Nanoparticle Base Functionalization

The nanoparticles were functionalized similar to reported procedures [5]. The MNP nanoparticles (1.1 g)

were sonicated for 30 min in an equal volume ethanol/water mixture (150 mL). Ammonium hydroxide (15 mL, 29% v/v aqueous solution) was added, and the mixture was stirred vigorously overnight at 60 °C. The MNP were washed with copious amounts of DI H₂O, ethanol, and hexanes and separated by magnetic decantation. The resulting MNP were redispersed by sonication (30 min) in an equal volume mixture of ethanol and water (150 ml). N-[3-(trimethoxysilyl)propyl]ethylenediamine (1g) was then added, and the solution was heated at 60 °C with vigorous stirring overnight under an argon atmosphere. The final product was washed with copious amounts of DI H₂O, ethanol, and hexanes by magnetic decantation and dried under vacuum overnight at room temperature, yielding 1.1 g amino-functionalized magnetic nanoparticles (MNP-NH₂).

2.3 Acid Catalyst Preparation

Amberlyst 15, a sulfonic acid functionalized polymer resin) was purchased from Aldrich. The catalyst was washed with copious THF and DCM prior to use to remove any free sulfonic acid and dried under vacuum at 50 °C.

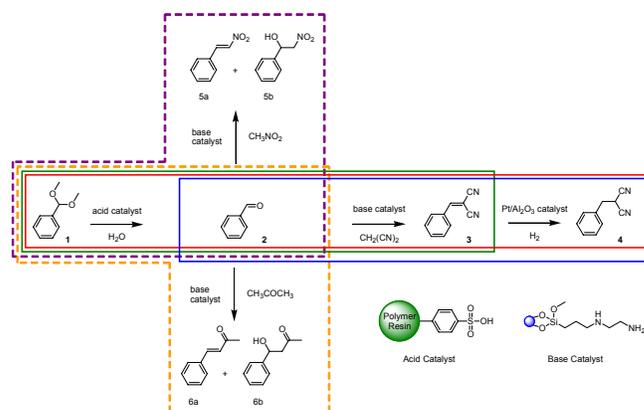
2.4.1 One-Pot Deacetalization-Knoevenagel Reaction

The one-pot deacetalization-Knoevenagel reaction (Scheme 1, green box) was performed by combining basic magnetic nanoparticles (8 mg), cation exchange resin (50 mg), toluene (4 ml), benzaldehyde dimethylacetal (15.2 mg, 0.1 mmol), malononitrile (13.8 mg, 0.2 mmol), and m-xylene (10.6 mg, 0.1 mmol) into a 10 mL glass vessel. The mixture was stirred at room temperature under an argon atmosphere. Reaction conversion was monitored by GC with reference to m-xylene.

Upon completion, the nanoparticles were magnetically separated from the resin catalyst, dried under vacuum overnight at room temperature, and reused with a new solid catalyst, Pt/Al₂O₃, in a second one-pot reaction. The separated resin catalyst was stored for further use. Elemental analysis was used to determine the purity of the recovered catalysts. The acid resin catalyst was tested for iron, which acted as a chemical identifier of MNP-NH₂. The basic nanoparticles were tested for sulfur, which acted as a chemical identifier of the acidic polymer resin.

2.4.2 One-Pot Knoevenagel-Hydrogenation Reaction

The Knoevenagel-hydrogenation reaction (Scheme 1, blue box) was performed by combining basic magnetic nanoparticles recovered from the first one-pot reaction, benzaldehyde (10.6 mg, 0.1 mmol), malononitrile (13.8 mg, 0.2 mmol), and m-xylene (10.6 mg, 0.1 mmol), and toluene (4 ml) in a 10 mL glass vessel and stirred at room temperature for 1 h under an argon atmosphere. Upon



Scheme 1 - One-pot reaction networks catalyzed by combinations of solid catalysts.

quantitative conversion, the platinum catalyst (0.5% Pt on Al₂O₃, 100 mg) was added, and the mixture was transferred to a stainless steel Parr autoclave. The autoclave was flushed repeatedly with hydrogen, then pressurized with hydrogen to 1000 psi, and stirred at 500 rpm at room temperature for 24 h. The MNP-NH₂ were magnetically separated from the platinum catalyst and reused in a third one-pot reaction. A parallel, one-pot experiment was performed with all reagents and catalysts were added to the autoclave at time zero.

2.4.3 One-Pot Deacetalization-Knoevenagel-hydrogenation Reaction

A one-pot deacetalization-Knoevenagel-hydrogenation reaction (Scheme 1, red box) was performed by combining MNP-NH₂ (50 mg), cation exchange resin (300 mg), toluene (40 ml), benzaldehyde dimethylacetal (91 mg, 0.6 mmol), malononitrile (79 mg, 1.2 mmol), and m-xylene (64 mg, 0.6 mmol) in a stainless steel Parr autoclave. Platinum catalyst (0.5% Pt on Al₂O₃, 600 mg) was ground into fine powder, enclosed in a molecularporous membrane, and placed inside the autoclave. The mixture was stirred at room temperature for 1 h. The autoclave was purged with hydrogen, pressurized to 1000 psi, and stirred at 500 rpm at room temperature for 48 h. The membrane-enclosed, platinum catalyst was separated from the reaction mixture. The MNP-NH₂ were separated from the resin catalyst by magnetic decantation. A parallel experiment was performed with the platinum catalyst was not isolated inside a molecularporous membrane.

2.4.4 One-Pot Deacetalization-Nitroaldol & Deacetalization-Aldol Reactions

The one-pot (a) deacetalization-nitroaldol (Scheme 1, purple dashed box) and (b) deacetalization-aldol (Scheme 1, orange dashed box) reactions were carried out using the magnetic base catalyst recovered from the second one-pot

reaction and the acid resin catalyst separated from the first one-pot reaction. The recovered catalysts, benzaldehyde dimethylacetal (15.2 mg, 0.1 mmol), and m-xylene (10.6 mg, 0.1 mmol) as internal standard in (a) nitromethane (4 ml) or (b) acetone (4 mL) were placed into a 10 mL glass vessel. The mixture was heated at (a) 100 °C and (b) 50 °C under an argon atmosphere with constant stirring for 20 h.

3 RESULTS AND DISCUSSION

3.1 Nanoparticle Synthesis

Transmission electron microscopy (TEM) illustrated the synthesized CoFe_2O_4 magnetic nanoparticles exhibited diameters of ca. 5 nm and aggregated into spherical clusters ca. 30 nm in diameter (Figure 1).

3.2 Nanoparticle Base Functionalization

No observable difference was noted from TEM upon functionalization of the CoFe_2O_4 magnetic nanoparticles with basic amine sites (Figure 1). X-ray diffraction (XRD) patterns of the functionalized nanoparticles were consistent with literature patterns of the non-functionalized particles (Figure 2) [2]. This indicated the surface functionalization step did not affect the crystal structure of the nanoparticles. Thermogravimetric analysis (TGA) indicated 0.3 mmol/g of the diamine was immobilized onto the nanoparticles. Nitrogen physisorption analysis reported a surface area of 200 m^2/g for the MNP-NH_2 with no mesoporosity.

3.3 Acid Catalyst Preparation

Scanning electron microscopy of the Amberlyst resin indicated a mean diameter of 600 μm . The resin appeared nearly perfectly spherical with minor surface cracks.

3.4.1 One-Pot Deacetalization-Knoevenagel Reaction

Complete conversion of 1 to 2 and 2 to 3 (see Scheme 1 for chemical references 1 - 6) was reported via GC in less than 30 minutes (Figure 3). Control experiments confirmed the tandem action of both solid acid and base catalysts was required to achieve conversion of 1 to 3. With a solid acid catalyst only, 100% conversion of 1 to 2 was observed, but 0% from 2 to 3. In the four cases of (a) solid base catalyst only, (b) solid acid and homogeneous base, (c) solid base and homogeneous acid, and (d) homogeneous acid and base, no conversion of 1 to 2 or 2 to 3 was observed.

The superparamagnetic character of the nanoparticles proved highly advantageous for the one-pot reactions by allowing the nanoparticles to have no magnetic moment in the absence of a magnetic field, thus preventing clustering. The particles were dispersed into the reaction media via

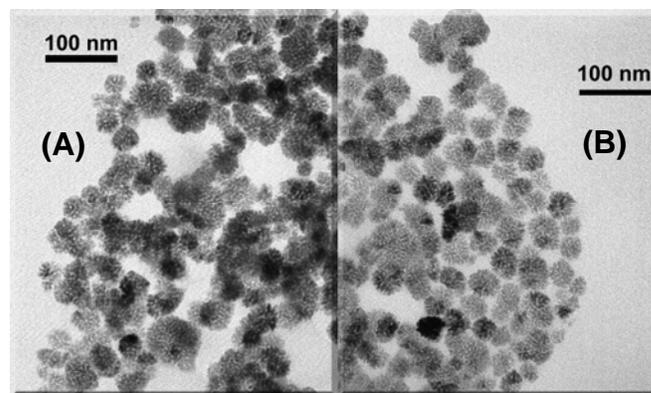


Figure 1 - Cobalt spinel ferrite superparamagnetic nanoparticles before (a) and after (b) functionalization with basic amine sites. (Image adapted from reference [3])

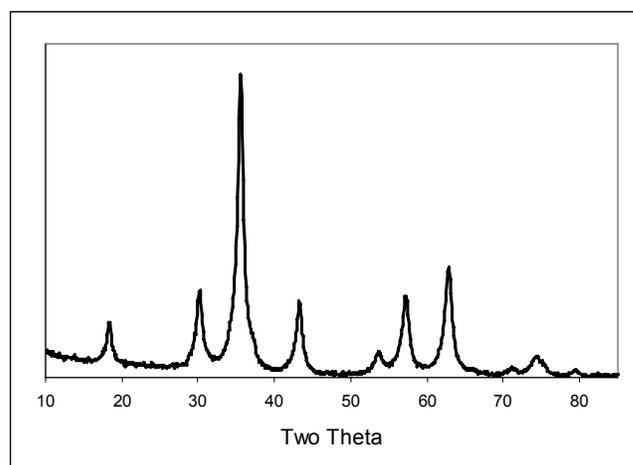


Figure 2 – X-ray powder diffraction pattern for the amine functionalized nanoparticles.

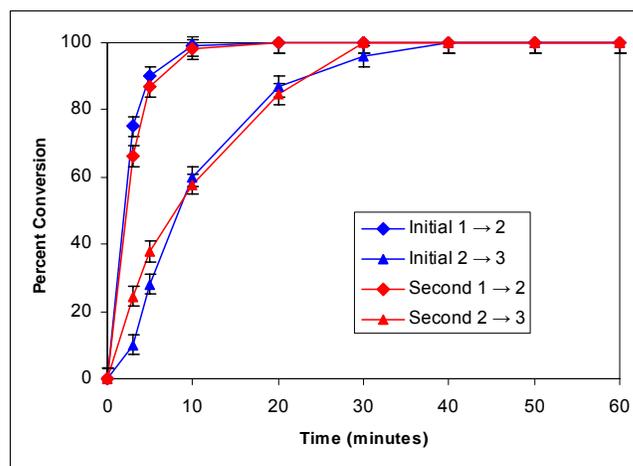


Figure 3 - One-pot sequential reactions with acid and base catalysts. Squares and triangles display conversion data for the reactions of 1 to 2 and 2 to 3, respectively.

sonication, thereby maximizing the available surface area for catalysis. The MNP-NH₂ were easily recovered from the reaction media in the presence of an external magnetic field, here provided by a small NdFeB magnet.

Elemental analysis of the used acid and base catalysts indicated both could be recovered in essentially pure form. The basic nanoparticles tested 0.07 % and 0.05 % sulfur before and after reaction, respectively. The acidic polymer resin tested 0.01 % and 0.03 % iron before and after reaction, respectively. These values indicated essentially no acidic polymer resin was present in the recovered MNP-NH₂ and no MNP-NH₂ were present in the recovered acidic polymer resin.

3.4.2 One-Pot Knoevenagel-Hydrogenation Reaction

Complete conversion of 2 to 3 and 3 to 4 was observed for the base and platinum catalyzed Knoevenagel-hydrogenation reaction. Kinetic data for the conversion of 2 to 3 using the recycled nanoparticle catalyst appears in Figure 3. Complete conversion of 2 to 4 was also observed when the reaction was pressurized to 1000 psig at time zero. This reaction demonstrated the MNP-NH₂ could be recycled without loss of activity.

3.4.3 One-Pot Deacetalization-Knoevenagel-hydrogenation Reaction

The conversion of 1 to 2 and 2 to 3 reached 100 % while conversion of 3 to 4 reached 78 % after the 48 hour reaction period when the Pt on Al₂O₃ was enclosed in a membrane. Conversion of 3 to 4 in the parallel reaction with Pt on Al₂O₃ not enclosed in a membrane reached 100 % after the prescribed period. However, in this case, the Pt on Al₂O₃ could not be separated from the acidic polymer resin catalyst. The increased conversion was attributed to the absence of mass transfer limitations across the membrane.

3.4.4 One-Pot Deacetalization-Nitroaldol & Deacetalization-Aldol Reactions

Conversion of one-pot deacetalization-nitroaldol reaction reached 100 % for 1 to 2 and 2 to 5a and 5b. This reaction sequence utilized the nanoparticles from the first two reaction sequences (1→2→3 and 2→3→4) along with the recycled acidic polymer resin from the first reaction (1→2→3). Kinetic data for the conversion of 1 to 2 using the recycled polymer resin appears in Figure 3. This sequence illustrated how manipulating the reactants yielded different products but utilizing the same catalysts. Similar results were achieved in the one-pot deacetalization-aldol reaction, which reached conversions of 100 % for 1 to 2 and 82 % for 2 to 5a and 5b.

These reactions demonstrated the original MNP-NH₂ and acidic polymer resin could be continuously recycled in different reaction sequences while maintaining activity. This capacity to separate and reuse different combinations of catalysts (acidic polymer resin, MNP-NH₂, and Pt on Al₂O₃) with different reactants demonstrated the utility of stepwise control of the reaction sequence for this system.

4 CONCLUSIONS

We have shown how excellent control over a reaction sequence can be achieved by utilizing versatile catalysts, immobilization of the active catalyst site, and specific reaction conditions. The combination of magnetically and gravimetrically recoverable catalysts allowed for the first demonstration of opposing catalysts in sequential, one-pot, reactions where the individual catalysts could be recovered in pure form. The reaction pathway could be easily steered by choice of reactants and catalysts. The versatility of this approach is illustrated by the ability to utilize recycled catalysts with other catalysts in other unrelated reactions. In this manner, a collection of recoverable catalysts could be created to run desired multistep, one-pot reaction sequences from a variety of reactants. The reaction sequence could be greatly extended through the use of membrane encapsulation and other means of catalyst separation.

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