A selective nanocatalyst for an efficient Ugi reaction: Magnetically recoverable Cu(acac)₂/NH₂-T/SiO₂@Fe₃O₄ nanoparticles

MONIREH GHAVAMI, MARYAM KOOHI and MOHAMMAD ZAMAN KASSAEI*

Department of Chemistry, Tarbiat Modares University, P.O. Box 14155-4838, Tehran, Iran

e-mail: kassaeem@modares.ac.ir

MS received 13 April 2013; revised 13 August 2013; accepted 13 August 2013

Abstract. A novel, magnetically recoverable nanocatalyst is fabricated through simple immobilization of copper(II) acetylacetonate on the surface of amine-terminated silica-coated Fe₃O₄ nanoparticles: Cu(acac)₂/NH₂-T/SiO₂@Fe₃O₄NPs. Unambiguous bonding of Cu to the terminal amine is indicated by X-ray photoelectron spectroscopy (XPS). Further characterizations are carried out by different techniques. Selectivity of this catalyst is demonstrated through one-pot synthesis of fourteen α -aminoacyl amides using Ugi four-component reaction of cyclohexyl isocyanide, acetic acid, amines and various aldehydes. Interestingly, all aromatic aldehydes react with short reaction times and high yields, but heteroaromatic aldehydes do not yield any product. Catalyst efficiency remains unaltered through three consecutive experiments.

Keywords. Nano; Fe₃O₄; copper(II) acetylacetonate; Ugi reaction; nanocatalyst.

1. Introduction

Transition-metal-catalysed reactions have contributed greatly to the straightforward and facile construction of carbon-carbon or carbon-heteroatom bonds.¹ Significant progress in this area has been achieved with a variety of homogeneous copper catalysts.² Copper complexes are extensively used as efficient catalysts in multicomponent reactions.³ Nevertheless, homogeneous catalysis suffers from the problematic separation of catalyst from the product for reuse.⁴ This problem is of particular environmental and economic concerns in large-scale syntheses. Heterogeneity of the existing homogeneous copper catalysts could be an attractive solution to this problem.^{5,6} In fact, the last decade has witnessed a growing interest in the heterogenization of homogeneous metal complexes using several types of supports and many immobilization strategies.^{7–10} Initially, the complexes are just ion-exchanged or adsorbed on the porous supports and could be susceptible to leaching.^{11,12} More recently, various grafting and tethering procedures have been developed for covalent attachment of transition-metal complexes to organic polymers, silica, zeolites as well as other micro- and mesoporous inorganic materials.^{7–10}

Copper(II) acetylacetonate has already been immobilized in a polymer,¹³ hexagonal mesoporous silica

(HMS),⁵ and activated carbon.^{14,15} These materials have acted as recoverable and reusable heterogeneous catalysts for the aziridination of olefins. In the first case, the copper(II) complex is microencapsulated in polystyrene, and in the second, a hexagonal mesoporous silica (HMS) is chosen to anchor copper(II) acetylacetonate. In the latter, it is anchored onto an amine-functionalized activated carbon.¹⁴ All three heterogeneous catalysts present similar catalytic parameters as those obtained in homogeneous-phase reaction using [Cu(acac)₂]. Under similar experimental conditions, no significant metal complex leaching is observed after the catalytic reactions.^{13,15} However, in the case where activated carbon is used as support, inherent diffusion limitations are observed due to the porous structure of the support. Thus, a decrease in the initial activity (TOF) and an increase in the reaction time are observed.¹⁵ Furthermore, the spectroscopic characterization of new carbon-based heterogeneous catalysts proved to be difficult and impossible, respectively, due to the highly absorbing carbon matrix, which limits the gathering of information about the copper(II) complex forms on the surface of the amine-functionalized activated carbon.

Magnetite Fe₃O₄ nanoparticles (Fe₃O₄NPs) have recently emerged as promising supports for immobilization because Fe₃O₄-supported catalysts can be separated from the reaction medium by an external magnet.^{16–23} This circumvents time-consuming and laborious separation steps, and allows for practical continuous catalysis. In particular, Fe₃O₄NPs coated with a thin-layer of silica

*For correspondence

Scheme 1. Stepwise synthesis of our magnetic nanocatalyst ($\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$): (a) aqueous ammonia (25%), rt; (b) tetraethyl orthosilicate, EtOH, aqueous ammonia (10%), rt, 10 h then 40°C, 12 h; (c) (3-aminopropyl)triethoxysilane, toluene, 105°C, 24 h; (d) $\text{Cu}(\text{acac})_2$, toluene, 105°C, 5 h.

have beneficial properties such as invariant catalytic activity and stability.²⁴

On the other hand, Ugi four-component reaction (U-4CR) is arguably one of the most important isocyanide-based multicomponent reactions, IMCRs.^{25–27} It is a valuable method for generating α -aminoacyl amide derivatives in a very straightforward manner by condensing an aldehyde, amine, carboxylic acid, and isocyanide in one-pot reaction.²⁵ Lewis acids are not required for majority of the reported IMCRs, but they have been applied as catalyst for U-4CR.^{28–37} Yet, conventional U-4CR gives good yields, but shows no selectivity, taking 24–72 h to complete at room temperature.²⁶ Due to the great diversity of products which can be obtained by the post-modifications of the U-4CR with other reactions, selectivity and the time of this reaction remain as important parameters in

combinational strategy.²⁷ Thus, we present herein the possibility of a new U-4CR design, using a novel catalyst, for decreasing reaction time and increasing selectivity. In this context, we are reporting a facile route for synthesis of our magnetic nanocatalyst, $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ (scheme 1); followed by examination of its feasibility as a heterogeneous catalyst in U-4CR (scheme 2).

Catalytic activity of the heterogeneous copper complex is compared with the parent-free complex $[\text{Cu}(\text{acac})_2]$. In this context, the former heterogeneous catalyst showed similar catalytic efficiency, turnover numbers (TON) and turnover frequency (TOF), compared to the free $[\text{Cu}(\text{acac})_2]$ in the homogeneous phase, under similar experimental conditions.

2. Experimental

2.1 Chemicals and instruments

Reagents and solvents used in this study are obtained from Fluka or Merck and used without any further purification. Nanostructures are characterized using a Holland Philips Xpert X-ray powder diffraction (XRD) diffractometer ($\text{Cu K}\alpha$, radiation, $\lambda = 1.54 \text{ \AA}$), at a scanning speed of $2^\circ/\text{min}$ from 10° to 80° (2θ). Particle size and morphology are investigated by PHILIPS (EM208S, The Netherlands) transmission electron

Scheme 2. One-pot catalytic synthesis of α -aminoacyl amides (**I**) through Ugi reaction via $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$.

microscopy (TEM) at 100 kV of acceleration voltage and scanning electron microscopy (SEM) of a Holland Philips XL30 microscope with an accelerating voltage of 25 kV. Fourier transform infrared (FTIR) measurements are performed using KBr disc on a Thermo IR-100 spectrometer (Nicolet). ^1H - and ^{13}C -spectra are measured at 500.1 and 125.7 MHz, respectively, on a Bruker DRX 500-Avance NMR instrument with CDCl_3 or $\text{DMSO}-d_6$ as the solvent. Melting points are measured on an Electrothermal 9100 apparatus. X-ray photoelectron spectroscopy (XPS) experiment is carried out on a TWIN ANODE XR3E2 X-RAY source system with Al $K\alpha$ radiation ($h\nu = 1486.6\text{ eV}$). Thermogravimetric analysis (TGA) curves are recorded using a PL-TGA device, manufactured by Polymer Laboratories. Magnetic properties of Fe_3O_4 NPs and $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs are measured as a function of the applied magnetic field H using a LDJ 9600 vibrating sample magnetometer (VSM) (AGFM-Meghnatis Daghigh Kavir Co.) with a maximum applied magnetic field of 10 kOe. Hysteresis of the magnetization is obtained by varying H between +10000 and -10000 Oe at 300 K.

2.2 Synthesis of Fe_3O_4 NPs

In the formation of Fe_3O_4 NPs, 2 g FeCl_3 and 1.2 g of $\text{FeCl}_2\cdot 4\text{H}_2\text{O}$, with molar ratio of ($\text{Fe}^{3+} : \text{Fe}^{2+} = 2 : 1$) are dissolved in aqueous hydrochloride acid (2 M, 25 ml), then sonicated until the salts dissolve completely. Aqueous ammonia (25%, 20 ml) is added slowly over 20 min to the solution with vigorous stirring under argon atmosphere at room temperature followed by stirring for about 30 min with mechanical stirrer. The Fe_3O_4 NPs are separated by external magnet and washed thrice with deionized water and ethanol. The final product could either be obtained after drying under vacuum, or stored as a suspension in ethanol in refrigerator, for future use.

2.3 Synthesis of silica-coated Fe_3O_4 nanoparticles ($\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs)

$\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs is produced by hydrolysis of tetraethylorthosilicate (TEOS) on the surfaces of the Fe_3O_4 NPs. The precipitate Fe_3O_4 is ultrasonically redispersed in a solution containing 35 ml ethanol and 6 ml water. The pH value is adjusted to 9 with an ammonia solution, then 1.5 ml 3-aminopropyltriethoxysilane (APTES) is added under vigorous stirring for 10 h. To further hydrolyse, the ferro-fluid is heated at 50°C for

12 h. Consequently, the iron oxide nanoparticles with a thin-layer of silica ($\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs) are separated by an external magnet and washed thrice with ethanol and dried under vacuum.

2.4 Functionalization of the $\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs with APTES ($\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs)

$\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs is ultrasonically dispersed in a solution containing 20 ml toluene. 3-aminopropyltriethoxysilane (APTES) (1 ml) is added drop-wise into the bottle under magnetic stirring. After hydrolysing for 24 h at room temperature, the particles are collected by an external magnet and washed with toluene several times with the help of an external magnet, then dried under vacuum. Thus, silica-coated Fe_3O_4 NPs, functionalized by $-\text{NH}_2$ groups are obtained: $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs.

2.5 Synthesis of $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs

Synthesized $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs (1.0 g) is added to 50 ml of a solution of $[\text{Cu}(\text{acac})_2]$ (4 mmol) in toluene, the mixture is refluxed for 5 h. A progressive disappearance of solution colour is observed. The resulting material ($\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs) is extensively washed with toluene and then dried at 50°C for 13 h.

2.6 General procedure for Ugi four-component reaction (U-4CR)

Butylamine (1 mmol) is added to a solution of aldehyde (1 mmol) and $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs (0.85 mol%) in methanol (5 ml), and the reaction mixture is stirred at room temperature for 1 h. Then, acetic acid (1 mmol) is added and stirring is continued for 15 min. Cyclohexyl isocyanide (1 mmol) is added and stirring is continued for 4 h until the reaction is completed (indication by thin layer chromatography (TLC)). The catalyst is recovered after placing a magnet on the reactor wall and decanting the reaction mixture which contains the product in either insoluble or soluble form. Filtration and/or column chromatography of the reaction mixture on silica (ethyl acetate/hexane) affords the pure product. The recovered catalyst is washed twice with methanol and dried at 50°C, then reused in the next run. Loss of the catalyst, in the process of separation, appears minimal and is negligible.

3. Results and discussion

In this section, complete characterization of our nanocatalyst ($\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$) is followed by its synthetic application. In the following subsections, morphology and particle size of constituting $\text{Fe}_3\text{O}_4\text{NPs}$ are characterized by SEM and TEM. Surface area of the catalyst is estimated by Brunauer-Emmet-Teller (BET). Evidence for the effective irreversible attachment of $[\text{Cu}(\text{acac})_2]$ on the surface of $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ is indicated by colour change and confirmed by XRD, XPS, Inductively coupled plasma (ICP), FTIR, and TGA analyses. Magnetic properties of $\text{Fe}_3\text{O}_4\text{NPs}$ and $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ are determined by VSM. Subsequently, the applicability, selectivity, efficiency, and reusability of the catalyst are discussed in light of one-pot synthesis of α -aminoacyl amides (**I**) using Ugi four-component reaction (U-4CR) of cyclohexyl isocyanide, acetic acid, various amines and aldehydes.

3.1 Morphology, particle size and surface area (via SEM, TEM and BET)

The Fe_3O_4 magnetic nanoparticles ($\text{Fe}_3\text{O}_4\text{NPs}$) come into view with an approximate spherical shape in

SEM and TEM (figure 1). In accord with TEM, which provides rather more accurate information on the particle size than SEM, average diameter of the core is around 9.8 nm (figure 1b and c). Using BET method, surface area (S_{BET}) and the total pore volume (V_p) appear fairly ideal for active $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$, with $29 \text{ m}^2 \text{ g}^{-1}$ and $0.12 \text{ cm}^3 \text{ g}^{-1}$, respectively. Owing to the remarkable increase in particle size during functionalization of Fe_3O_4 NPs, specific surface area is greatly reduced from $\text{Fe}_3\text{O}_4\text{NPs}$ ($221.5 \text{ m}^2 \text{ g}^{-1}$) to $\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ ($58.1 \text{ m}^2 \text{ g}^{-1}$), $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ ($42 \text{ m}^2 \text{ g}^{-1}$), and $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ ($29 \text{ m}^2 \text{ g}^{-1}$). These results confirm $\text{Fe}_3\text{O}_4\text{NPs}$ functionalizations.

3.2 Structural analysis of the catalyst and its components (via XRD)

The XRD patterns are compared and contrasted for $\text{Fe}_3\text{O}_4\text{NPs}$, $\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$, $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$, and $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ (figure 2). The position and relative intensities of all peaks coincide with standard XRD pattern of Fe_3O_4 (JCPDS card No. 19-0629), indicating retention of the crystalline structure during functionalization of $\text{Fe}_3\text{O}_4\text{NPs}$. Average $\text{Fe}_3\text{O}_4\text{NPs}$ core diameter is calculated to be 10 nm from

Figure 1. (a) SEM, (b) TEM images, and (c) Particle size histogram of our Fe_3O_4 NPs.

Figure 2. XRD patterns of (a) Fe₃O₄NPs, (b) SiO₂@Fe₃O₄NPs, (c) NH₂-T/SiO₂@Fe₃O₄NPs and (d) Cu(acac)₂/NH₂-T/SiO₂@Fe₃O₄NPs.

the XRD results by Scherrer's equation, $D = k\lambda/\beta\cos\theta$, where k is a constant (generally considered as 0.94), λ is the wavelength of Cu K α (1.54 Å), β is the corrected diffraction line full-width at half-maximum (FWHM), and θ is Bragg's angle,³⁸ which is in good accordance with its TEM. A weak broad band at $2\theta = 18$ – 27° could be assigned to the amorphous silane shell formed around the magnetic cores (figure 2b and c).³⁹ The XRD pattern of Cu(acac)₂/NH₂-T/SiO₂@Fe₃O₄NPs indicates an effective anchorage of Cu(acac)₂ onto the surface of NH₂-T/SiO₂@Fe₃O₄NPs, with lines at $2\theta = 11.70$, 15.55 , 17.12 , 24.73 and 27.27 (figure 2d).⁴⁰

3.3 Structural characterization of the catalyst (via XPS and ICP)

The XPS binding energy of C 1s, O 1s, Si 2p, N 1s and Cu 2p, along with the corresponding atomic % data,

confirm the structure of our catalyst, Cu(acac)₂/NH₂-T/SiO₂@Fe₃O₄NPs (table 1, figure 3).

For carbon spectra, the main change is the appearance of a new shoulder around 288.0 eV in Cu(acac)₂/NH₂-T/SiO₂@Fe₃O₄NPs (figure 3, C 1s, S₄), which could be attributed to the C=N, C–N, and C=O groups, indicating the anchoring of Cu(acac)₂ in NH₂-T/SiO₂@Fe₃O₄NPs.

Oxygen anions in the lattice of Fe₃O₄NPs give the O 1s peak at 528 eV (figure 3, O 1s, S₁).⁴¹ Oxygen anions in SiO₂@Fe₃O₄NPs and NH₂-T/SiO₂@Fe₃O₄NPs samples give a shoulder at 528 eV (figure 3, O 1s, S₂ and S₃), while the region near 530 eV (figure 3, O 1s, S₂, S₃, and S₄) could be attributed to either C–O and/or C=O and Si–O surface species.⁴² As XPS can only measure the elements on the most outer surface, there is no signal at 528 eV in (Cu(acac)₂/NH₂-T/SiO₂@Fe₃O₄NPs) (figure 3, O 1s, S₄). This is in agreement with the BET results.

The Si 2p spectra consist of major peaks centred at approximately 103 eV (Si–O) (figure 3, Si 2p S₂). Both NH₂-T/SiO₂@Fe₃O₄NPs and Cu(acac)₂/NH₂-T/SiO₂@Fe₃O₄NPs give similar spectra. XPS results of the two samples show a new weak shoulder around 101.1 eV,⁴³ which could be attributed to the C–Si–O₃, indicating the grafting of the APTES to SiO₂@Fe₃O₄NPs (figure 3, Si 2p S₃ and S₄).

Specifically, deconvolution of C 1s into five components indicates C–Si (A), hydrocarbon or hydrocarbon groups (B), C=N (C), C–N (D), and C=O (E) at 283.22, 284.71, 285.61, 286.38, and 288.32 eV, respectively (figure 4).⁴⁴ The latter binding energy establishes unambiguous formation of C=N bond and hence the anchorage of Cu(acac)₂ onto the surface of NH₂-T/SiO₂@Fe₃O₄NPs. Similarly N 1s peak is deconvoluted into peaks with maxima at 398.31 and 399.45 eV, corresponding to C–N and C=N, respectively (not shown here). The C=N binding energies extracted from

Table 1. Structural characterization by XPS data; Cu amounts (wt.%) obtained by ICP and XPS analyses.

Atoms and C-bonds	BE (eV)	Atomic (%)	Bond (%)	%Cu _{XPS}	%Cu _{ICP}	Cu _{XPS} / Cu _{ICP}
C	285.18	49.8	-	-	-	-
O	533.44	36.5	-	-	-	-
Si	101.11	9.8	-	-	-	-
N	398.2	1.5	-	-	-	-
Cu 2p _{3/2}	932.47	1.2	-	10.2	5.4	1.9
Cu 2p _{1/2}	952.92	1.2	-	-	-	-
C–Si	283.22	-	19.3	-	-	-
C–C, C–H	284.71	-	43.5	-	-	-
C=N	285.61	-	9.9	-	-	-
C–N	286.38	-	18.4	-	-	-
C=O	288.32	-	8.9	-	-	-

Figure 3. XPS spectra of Fe_3O_4 NPs (S_1), $\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs (S_2), $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs (S_3), and $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs (S_4) in the regions of C 1s, O 1s, Si 2p, N 1s, and Cu 2p.

C 1s and N 1s (285.61, and 399.45 eV, respectively) belong to the same range as those reported for organic molecules, e.g. pyridine (285.5 and 400.6 eV), polyacrylonitrile (286.4 and 399.57 eV) and hexamethylenetetramine (286.9 and 398.8 eV).^{45,46} In the XPS spectrum of $\text{Cu}(\text{acac})_2$, a doublet structure appears at 932.47 and 952.92 eV, which correspond to $\text{Cu } 2p_{3/2}$ and $\text{Cu } 2p_{1/2}$ (figure 3e). These peaks are associated with the exis-

tence of unpaired electrons in $\text{Cu}(\text{acac})_2$, and are consistent with literature values of 932.6 and 952.2 eV, respectively.^{47,48} The ICP and XPS copper content of our catalyst are 5.4% and 10.2%, respectively (table 2). The ratio of $\text{Cu}_{\text{XPS}}/\text{Cu}_{\text{ICP}}$, with its value of 1.9, indicates that the $\text{Cu}(\text{acac})_2$ is approximately homogeneously distributed on the surface of $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs.⁴⁹

Figure 4. Deconvoluted spectrum of C 1s.

3.4 Structural analysis of the catalyst and its components (via FTIR)

Comparing FTIR spectra of Fe_3O_4 NPs, $\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs, $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs and $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs appears instructive (figure 5). The two bands at 600.08 and 437.55 cm^{-1} are attributed to the stretching vibrations of Fe–O in Fe_3O_4 nanoparticles (composed of FeO and Fe_2O_3). Owing to the size reduction in the nano structure, these vibrations are red-shifted compared to those observed in the bulk Fe_3O_4 samples (570 and 375 cm^{-1} , respectively).^{50,51} FTIR spectra

Table 2. Optimization of the amount of catalyst in Ugi reaction of benzaldehyde, aniline, acetic acid and cyclohexyl isocyanide (scheme 2).^a

Entry	Catalyst (mol%)	Yield (%)	TON ^b	TOF ^c
1	-	10	12	3
2	$\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs (0.25)	54	63	16
3	$\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs (0.45)	82	96	24
4	$\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs (0.85)	98	115	29
5	$\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs (1)	98	115	29
6	$\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs (1.2)	98	115	29
7	$\text{Cu}(\text{acac})_2$ (0.85)	96	112	28

^aReaction conditions: aldehyde (1 mmol), amine (1 mmol), $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs (0.85 mol%), methanol (5 ml), RT, 1 h, then acetic acid (1 mmol), 15 min, then cyclohexyl isocyanide (1 mmol), 4 h

^bTON (turnover number): mols of product obtained per mol of the catalyst

^cTOF (turnover frequency) for 4 h of reaction

of $\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs, $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs and $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs show Fe-O vibrations in the same vicinity. It was reported that Fe_3O_4 nanoparticles can take up extensive hydroxyl groups on their surface upon contact with aqueous phase through adsorption of OH^- on Fe and H^+ on O.⁵² This is confirmed by the broad O-H stretching band at 3399 cm^{-1} . The Si-O-Si asymmetric stretching vibration at 1082 cm^{-1} and symmetric stretching vibration at 796 cm^{-1} appear in all the samples, but Fe_3O_4 NPs, which indicates that silica is successfully coated on the surface of Fe_3O_4 nanocrystals upon hydrolysis of TEOS. Introduction of APTES to the surface of Fe_3O_4 NPs is confirmed by the band at 1082 cm^{-1} , which is assigned to the Si-O stretching vibration. The broad band at 3404 cm^{-1} corresponds to N-H stretching vibration.⁵³ Presence of anchored propyl group

is confirmed by C-H stretchings at 2928 cm^{-1} . Spectrum of $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs exhibits well-defined bands at about 1593 and 1418 cm^{-1} due to $\nu(\text{C}=\text{O}$ and/or $\text{C}=\text{N})$ and $\nu(\text{C}=\text{C})$, respectively (figure 1d). This is a strong evidence for anchoring of $[\text{Cu}(\text{acac})_2]$ on the surface of $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs through the Schiff condensation of $-\text{NH}_2$ and $-\text{CO}$ groups.

3.5 Structural analysis of the catalyst and its components (via TGA)

Thermogravimetric analysis curves of the $\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs, $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs and $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs show the mass loss of organic materials as they decompose upon heating (figure 6). Initial weight loss from the $\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs up to 126°C is due to the removal of physically adsorbed

Figure 5. Comparative FTIR spectra for (a) Fe_3O_4 NPs, (b) $\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs, (c) $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs, (d) $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs and (e) recovered catalyst after usage.

Figure 6. TGA curve of (a) $\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs, (b) $\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs and (c) $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs.

Figure 7. Magnetization curves for (a) $\text{Fe}_3\text{O}_4\text{NPs}$ and (b) $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ at room temperature.

solvent and surface hydroxyl groups. Weight loss of about 1.67% between 192° and 310°C may be associated with the thermal crystal phase transformation from Fe_3O_4 to $\gamma\text{-Fe}_2\text{O}_3$ (figure 6a and b).⁴⁹ High rate of weight loss in the temperature ranging from 250–600°C for $\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ may be attributed to the condensation of silanol groups in $\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$.⁵⁵ Weight loss of APTES-modified $\text{Fe}_3\text{O}_4\text{NPs}$ is about 3.06% at 379–568°C, which is contributed to the thermal decomposition of the 3-aminopropyl groups (figure 6b). For $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$,

there is a well-defined mass weight loss of 21.3% between 135° and 282°C related to the breakdown of the $\text{Cu}(\text{acac})_2$ moieties. On the basis of these results, the well grafting of APTES and $\text{Cu}(\text{acac})_2$ groups on the $\text{Fe}_3\text{O}_4\text{NPs}$ is verified.

3.6 Magnetic properties of $\text{Fe}_3\text{O}_4\text{NPs}$ and $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ (via VSM)

Super-paramagnetic behaviour is attributed to both $\text{Fe}_3\text{O}_4\text{NPs}$ precursor and $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ for exhibiting VSM magnetization values of 60.0 and 23.0 emu/g, respectively⁵⁶ (figure 7). Evidently, lower magnetization of the latter is due to the extensive silica coatings of the magnetic core and its functionalizations. Yet, decrease in magnetization does not prevent $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ from being readily separated by conventional magnets.

3.7 Evaluation of catalyst activity through U-4CR

In order to evaluate the catalytic activity of our $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$, it is applied to U-4CR²⁵ for generating α -aminoacyl amide derivatives by condensing an aldehyde, amine, carboxylic acid and isocyanide.

Table 3. Ugi one-pot catalytic synthesis of α -aminoacyl amides (**I**, scheme 2) via $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$.^a

Entry	R^1	R^2	Time (h)	Catalyst	Yield (% I)
1	Phenyl	<i>n</i> -Butyl	4	✓	89
2	2-Methylphenyl	<i>n</i> -Butyl	4	✓	95
3	4-Methylphenyl	<i>n</i> -Butyl	4	✓	94
4	2-Chlorophenyl	<i>n</i> -Butyl	4	✓	87
5	4-Bromophenyl	<i>n</i> -Butyl	4	✓	92
6	4-Hydroxyphenyl	<i>n</i> -Butyl	4	✓	85
7	4-Trifluoromethylphenyl	<i>n</i> -Butyl	4	✓	93
8	Phenyl	Phenyl	4	✓	98
9	2-Methylphenyl	Phenyl	4	✓	96
10	Ethyl	Phenyl	4	✓	76
11	Pyridine-2-yl	<i>n</i> -Butyl	24	✓	—
12	Pyridine-3-yl	<i>n</i> -Butyl	24	✓	—
13	Pyridine-4-yl	<i>n</i> -Butyl	24	✓	—
14	Pyrrole-2-yl	<i>n</i> -Butyl	24	✓	—
15	Phenyl	<i>n</i> -Butyl	24	—	54
16	Phenyl	Phenyl	24	—	68
17	2-Methylphenyl	Phenyl	24	—	75

^aReaction conditions: aldehyde (1 mmol), amine (1 mmol), $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4\text{NPs}$ (0.85 mol%), methanol (5 ml), RT, 1 h, then acetic acid (1 mmol), 15 min, then cyclohexyl isocyanide (1 mmol), 4 h

Scheme 3. A provisional mechanism for the role of $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs in U-4CR.

In order to optimize amount of catalyst, Ugi reaction is carried out using benzaldehyde, aniline, acetic acid and cyclohexyl isocyanide, in MeOH at room temperature. In the absence of the catalyst, about 10% of product is obtained after 4 h (table 2, entry 1). The yield of product is increased with increase of the amount of nanocatalyst from 0.25 to 0.85 mol% (table 2, entries 2–4). However, greater amounts than 0.85 mol% have no significant effect on the yield (table 2, entries 5 and 6). So, the optimum amount of catalyst is 0.85 mol%/mmol of benzaldehyde which resulted in 98% yield of the product after 4 h.

The $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@\text{Fe}_3\text{O}_4$ NPs acts as a heterogeneous catalyst in Ugi reaction, with TON and TOF similar to the ones obtained with homogeneous phase reaction performed with $[\text{Cu}(\text{acac})_2]$, under comparable experimental conditions (table 2, entries 4 and 7).

Products of various aromatic as well as aliphatic aldehydes and amines are isolated by filtration or column chromatography, in good to excellent yields (table 3). Purity and structural analysis of the products are mainly established by NMR, IR and mass spectroscopy (supporting information). Reaction time decreases to the unprecedented 4 h, which is a noticeable improvement from the previously reported 24–72 h.²⁶ Another advantage of our new catalyst is its

selectivity between aromatic and heteroaromatic aldehydes. While aromatic (and aliphatic) aldehydes render pure products in good to high yields, within 4 h (entry 1–10, table 3); heteroaromatic aldehydes do not produce any product, even with an extended reaction time of 24 h (entry 11–14, table 3). In the absence of catalyst,

Figure 8. Efficiency of catalyst in Ugi reaction of benzaldehyde, aniline, acetic acid and cyclohexyl isocyanide (scheme 2) after each run.

similar reactions result in low yields with long reaction times (entry 15–17, table 3).

The role of our catalyst may be explained in light of its ability to provide a suitable surface for performing U-4CR (scheme 3). Sequentially, $\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@ \text{Fe}_3\text{O}_4\text{NPs}$ facilitates the formation of imine, by increasing the electrophilicity of the carbonyl group of the aldehyde. The reaction proceeds *via* activation of resulting imine, by the nanocatalyst and its further reaction with acetic acid and cyclohexyl isocyanide to form an intermediate, which in turn rearranges to the α -aminoacyl amide. On the other hand, heteroaromatic aldehydes seem to poison the catalyst giving no product at all. This adds to the value of the nanocatalyst for making it highly selective.

Preservation of structural integrity of the catalyst is suggested by the minimal changes in its efficiency after three runs (figure 8) and confirmed by the comparison of its FTIR spectra before and after its implementation (figure 5d vs. e).

4. Conclusion

We have successfully prepared a new magnetically recoverable nanocatalyst ($\text{Cu}(\text{acac})_2/\text{NH}_2\text{-T}/\text{SiO}_2@ \text{Fe}_3\text{O}_4\text{NPs}$), which is applied to one-pot synthesis of α -aminoacyl amides, through Ugi four-component reaction (U-4CRs). This investigation clearly shows that our catalytic system drastically decreases reaction time, increases yield, and more importantly exhibits a high selectivity for aromatic aldehydes, to the extent that it forms no product from the heteroaromatic ones.

Supporting information

Data of NMR and IR spectra are given as supporting information and can be seen at www.ias.ac.in/chemsci website.

References

- Beller M and Bolm C 2004 In *Transition metals for organic synthesis*, 2nd ed. (Weinheim: Wiley-VCH)
- Lam P Y S, Vincent G, Bonne D and Clark C G 2003 *Tetrahedron Lett.* **44** 4927
- Beveridge R E, Fernando D and Gerstenberger B S 2010 *Tetrahedron Lett.* **51** 5005
- Garrett C E and Prasad K 2004 *Adv. Synth. Catal.* **346** 889
- Silva A R, Wilson K, Whitwood A, Clark J and Freire C 2006 *Eur. J. Inorg. Chem.* 1275
- Panda N, Jena A K and Mohapatra S 2012 *Appl. Catal. A: Gen.* **433–434** 258
- Karthikeyan P, Muskawar P N, Aswar S A, Bhagat P R and Sythana S K 2012 *J. Mol. Catal. A: Chem.* **358** 112
- Fan Q-H, Li Y-M and Chan A S C 2002 *Chem. Rev.* **102** 3385
- Esmailpour M, Sardarian A R and Javidi J 2012 *Appl. Catal. A: Gen.* **28** 359
- Leadbeater N E and Marco M 2002 *Chem. Rev.* **102** 3217
- Rafelt J S and Clark J H 2000 *Catal. Today* **57** 33
- Arends I W C E and Sheldon R A 2001 *Appl. Catal. A: Gen.* **212** 175
- Kantam M L, Kavita B, Neeraja V, Haritha Y, Chaudhuri M K and Dehury S K 2003 *Tetrahedron Lett.* **44** 9029
- Silva A R, Martins M, Freitas M M A, Figueiredo J L, Freire C and de Castro B 2004 *Eur. J. Inorg. Chem.* 2027
- Silva A R, Figueiredo J L, Freire C and de Castro B 2005 *Catal. Today* **102** 154
- Cano R, Yus M and Ramón D J 2011 *Tetrahedron* **67** 8079
- Khoobia M, Ma'mania L, Rezazadehb F, Zareieb Z, Foroumadi A, Ramazanib A and Shafiee A 2012 *J. Mol. Catal. A: Chem.* **356** 74
- Kong A, Wang P, Zhang H, Yanga F, Huang S and Shan Y 2012 *Appl. Catal. A: Gen.* **417–418** 183
- Claesson E M, Mehendale N C, Gebbink R J M K, Koten G V and Philipse A P 2007 *J. Magn. Magn. Mater.* **311** 41
- Masteri-Farahani M and Kashef Z 2012 *J. Magn. Magn. Mater.* **324** 1431
- Bagheri M, Masteri-Farahani M and Ghorbani M 2013 *J. Magn. Magn. Mater.* **327** 58
- Masteri-Farahani M and Tayyebi N 2011 *J. Mol. Catal. A: Chem.* **348** 83
- Masteri-Farahani M, Movassagh J, Taghavi F, Eghbali P and Salimi F 2012 *Chem. Eng. J.* **184** 342
- Deng Y, Qi D, Deng C, Zhang X and Zhao D 2008 *J. Am. Chem. Soc.* **130** 28
- Dömling A and Ugi I 2000 *Angew. Chem. Int. Ed.* **39** 3169
- Krasavin M, Parchinsky V, Shumsky A, Konstantinov I and Vantskul A 2010 *Tetrahedron Lett.* **51** 1367
- Dömling A 2006 *Chem. Rev.* **106** 17
- Kunz H and Pfrengle W 1988 *J. Am. Chem. Soc.* **110** 651
- Kunz H and Pfrengle W 1988 *Tetrahedron* **44** 5487
- Kunz H, Pfrengle W and Sager W 1989 *Tetrahedron Lett.* **30** 4109
- Kunz H, Pfrengle W, Rück K and Sager W 1991 *Synthesis* **11** 1039
- Goebel M and Ugi I 1991 *Synthesis* 1095
- Lehnhoff S, Goebel M, Karl R M, Klösel R and Ugi I 1995 *Angew. Chem. Int. Ed.* **34** 1104
- Oertel K, Zech G and Kunz H 2000 *Angew. Chem. Int. Ed.* **39** 1431
- Ross G F, Herdtweck E and Ugi I 2002 *Tetrahedron* **58** 6127
- Godet T, Bonvin Y, Vincent G, Merle D, Thozet A and Ciufolini M A 2004 *Org. Lett.* **6** 3281
- Dai W-M and Li H 2007 *Tetrahedron* **63** 12866
- Cullity B D and Stock S R 2001 In *Elements of X-ray diffraction*, 3rd ed. (Englewood Cliffs: Prentice-Hall)
- Jiang Y, Jiang J, Gao Q, Ruan M, Yu H and Qi L 2008 *Nanotechnology* **19** 75714
- Nasibulin A G, Kauppinen E I, Brown D P and Jokiniemi J K 2001 *J. Phys. Chem.* **B105** 11067

41. Liu B and Zeng H C 2008 *Chem. Mater.* **20** 2711
42. Chen X and Burda C 2004 *J. Phys. Chem.* **B108** 15446
43. Iwanowskia R J, Fronca K, Paszkowicza W and Heinonenb M 1999 *J. Alloys Compd.* **286** 143
44. Bhattacharyya S, Hong J and Turban G 1998 *J. Appl. Phys.* **83** 3917
45. Marton D, Boyd K J, Al-Bayati A H, Todorov S S and Rabalais J W 1994 *Phys. Rev. Lett.* **73** 118
46. Tabbal M, Mérel P, Moisa S, Chaker M, Ricard A and Moisan M 1996 *Appl. Phys. Lett.* **69** 1698
47. Valente A, Botelho do Rego A M, Reis M J, Silva I F, Ramos A M and Vital J 2001 *Appl. Catal. A: Gen.* **207** 221
48. de Groot F 2005 *Coord. Chem. Rev.* **249** 31
49. Castilla C M, Cadenas A P, Hódar F M, Marín F C and Fierro J L 2003 *Carbon* **41** 1157
50. Rao Z M, Wu T H and Peng S Y 1995 *Acta Phys. Chim. Sin.* **11** 395
51. Waldron R D 1955 *Phys. Rev.* **99** 1727
52. Shinkai M, Honda H and Kobayashi T 1991 *Biocatalysis* **5** 61
53. Xu Z, Liu Q and Finch J A 1997 *Appl. Surf. Sci.* **120** 269
54. Cornell R M and Schwertmann U 1996 *The iron oxides* (New York: VCH)
55. Feng G, Hu D, Yang L, Cui Y, Cui X and Li H 2010 *Sep. Purif. Technol.* **74** 253
56. Laska U, Frost C G, Price G J and Plucinski P K 2009 *J. Catal.* **268** 318