ONE-POT SYNTHESIS OF BENZIMIDAZOLE SCHIFF'S BASES BY USING HETEROGENEOUS REUSABLE COPPER NANOPARTICLES

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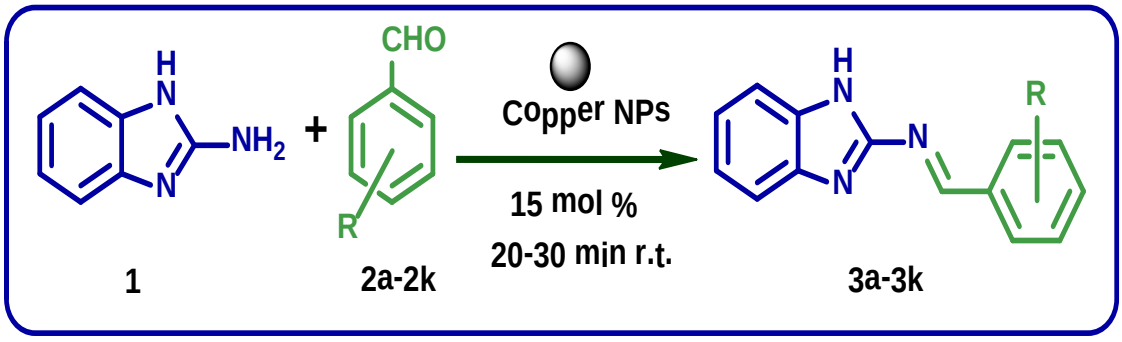
Abstract: In the present article reported an efficient catalytic application of copper nanoparticle (Cu NPs) in a synthesis of benzimidazole Schiff's bases *via* the reaction of aromatic aldehydes with 2-aminobenzimidazole under solvent free condition. Interestingly, further, we were investigated an excellent recyclability and reusability of nanoparticle up to four times without any additional treatment. The present methodology offers several advantages in terms of green synthesis organic derivatives. The copper nanoparticle of a crystalline size around 40 nm was synthesized *via* chemical reduction method and characterized by various standard spectroscopic techniques to determine the size, shape, and composition.

Keywords: Copper nanoparticles; Heterogeneous nanocatalyst; 2-aminobenzimidazole; Schiff Bases

GRAPHICAL ABSTRACT



1. Introduction

Benzimidazoles and 2-aminobenzimidazoles are privileged organic compounds due to their interesting biological properties. Compounds containing a benzimidazole moiety attached to a heterocyclic system are important chemical classes as a result of their significant biological activities against several viruses such as HIV, RNA, herpes (HSV-1), influenza, human cytomegalovirus (HCMV) and Epstein-Barr [1-5]. Moreover, benzimidazole derivatives have been studied as anticancer and anti-proliferative chemicals [6-8]. Schiff bases derived from aromatic amines and aromatic aldehydes are also a very important class of organic compounds because of their applications in many fields including biological, inorganic and analytical chemistry [9-11].Today, one of the

major goals of synthetic organic chemistry lies in the research, discovery, and exploitation of environmentally friendly methods. Recently, several techniques for the efficient use of solvent-free reactions and multi-component reactions have been developed individually but when these two wings of green chemistry can be combined, an excellent green chemistry protocol is expected. Multi-component condensation reactions are a compelling method for the synthesis of organic compounds, since the products are formed in a single step and diversity can be achieved by simply varying each component.

The hybrid molecules composed of the combination of part of a heterocyclic ring, like benzimidazole and part of the Schiff's base may exert potential biological activities [12]. Several synthetic methods have been reported for the synthesis of Schiff's bases [13-15]. However, most of them have limitations including long reaction times, need for a special catalyst, low yields, and extensive recrystallization. Therefore, the more convenient and practical synthetic methods for preparation of these compounds still remains an active research area. Recently, use of several nanoparticles as a catalyst like metal NPs, metal oxide NPs, and nanocomposites in organic synthesis has attracted considerable attention. They have many advantages such as their handling, low cost, and being environmentally safe [16]. Therefore, all over the world the solid state chemists are trying to make eco-friendly, creative and innovative work by using metal/metal oxide nanoparticles. Keeping this in mind we have initially prepared nanoparticles through the alternative technique by taking a different concentration of surfactant, and then used newly synthesized nanoparticles as a nanocatalyst in organic reaction transformations.

In continuation with our previous research work on facile synthesis, spectroscopic characterization, catalytical and biological investigation of some metal and metal oxide nanoparticles [17-20], in the present work, we have reported facile and efficient catalytical role of Cu NPs in a one-pot synthesis of benzimidazole Schiff's bases *via* the reaction of aromatic aldehydes with 2-aminobenzimidazole under solvent free condition. Furthermore, we found out an efficient and reusability of Cu NPs up towards solvent free synthesis of benzimidazole Schiff's bases and its derivatives. Interestingly, catalyst exhibited an excellent recyclability and reusability (up to 4 times) without any additional treatment.

2. Experimental

2.1. Materials and method

All the chemicals were used of analytical reagent grade (AR) and without purification. Used copper nanoparticles as a catalyst were characterized by microscopic and spectroscopic techniques, and published elsewhere. All the prepared compounds were well known and identified by comparing with melting points, FT-IR spectra, mass analysis and ^{1}H NMR spectra of some selected compounds with those of the authentic samples. Infrared spectroscopy was recorded at a 2 cm^{-1} resolution from 4000 to 400 cm^{-1} on a Bruker IFS 66v Fourier transform spectrometer using KBr pellets. ^{1}H NMR spectra of organic compounds were carried out on NMR Spectrometer model Avance-II (Bruker) is the acquisition in the SAIF Chandigarh, India. The instrument is equipped with a cryomagnet of field strength 9.4 T. Its ^{1}H frequency is 400 MHz.

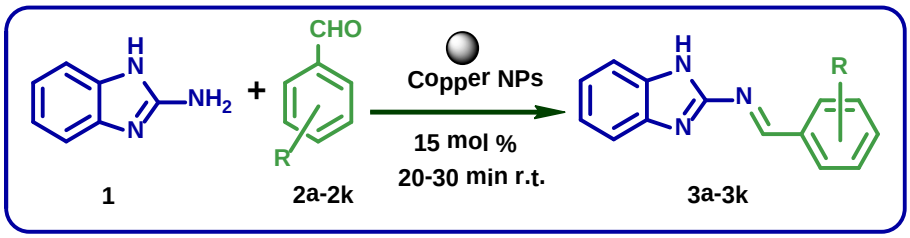
2.2 Synthesis of Cu NPs

A chemical reduction method was used to synthesis of a copper nanoparticle; usually, it involves the reduction of metal salts in a solvent using a reducing agent. In the present investigation, Schiff base derivatives were synthesized by using copper nanoparticles, however copper nanoparticles was synthesized, characterized by FTIR, UV, TG/DTG, XRD, EDS, SEM, TEM, and published elsewhere [21].

2.3 Synthesis of Benzimidazole Schiff's bases by Cu NPs in solvent free condition:

To a solution of 2-aminobenzimidazole (1 mmol) added a corresponding aromatic aldehyde (1 mmol) and copper nanoparticles (15 mol %), and then reaction mixture stirred at room temperature for the desired time (Scheme 1). The progress of the reaction was checked by TLC. After the completion of the reaction, 15 ml of ethyl acetate was added to the reaction mixture and the catalyst was separated by filtration and evaporated under reduced pressure to leave solid, which was recrystallized from ethanol. Nanoparticles were recovered by centrifuging the aqueous layer and reutilized

four times for the same reaction. The obtained products were characterized by various spectroscopy techniques and then compared with authentic samples in the literature.



Scheme 1: Synthesis of Benzimidazole Schiff's bases catalyzed by Cu NPs (15 mol %) under

Spectral data

Selected data for typical compounds are given below.

1. ***N*-benzylidene-1*H*-benzo[d]imidazol-2-amine** (Table 2; 3a)**:** Green solid; FTIR (KBr), cm^{-1}: 3686, 2609, 2916, 2221, 1592, 1524, 1208, 1150, 950; ^{1}H-NMR (400 MHz, DMSO-d_6) δ, ppm: 11.87 (s, 1H, NH), 7.28-7.08 (m, 9H, H*Arom.*) and 5.54 (s, 1H, CH).

2. ***N*-(4-nitrobenzylidene)-1*H*-benzo[d]imidazol-2-amine** (Table 2; 3b)**:** Brown solid; FTIR (KBr), cm^{-1}: 3167, 3080, 1614, 1591, 1514, 1425, 1342, 1228, 1109, 833, 763, 680, 441; ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 11.89 (s, 1H, NH), 9.58 (s, 1H, CH), 7.37-7.16 (m, 4H, H*Arom*) and 6.60-6.20 (m, 4H, H*Arom*).

3. ***N*-(2-chlorobenzylidene)-1*H*-benzo[d]imidazol-2-amine** (Table 2; 3g)**:** Green solid; FTIR (KBr), cm^{-1}: 3053, 2986, 1604, 1520, 1427, 1273, 1053, 756, 684, 451; ^{1}H-NMR (400 MHz, DMSO-d_6) δ, ppm: 12.86 (s, 1H, NH), 9.78 (s, 1H, CH), 8.28 (d, J=7.7 Hz, 1H,H*Arom.*), 7.65-7.48 (m, 5H, H*Arom.*) and 7.21 (q, 2H, H*Arom.*).

4. ***N*-(4-chlorobenzylidene)-1*H*-benzo[d]imidazol-2-amine** (Table 2; 3d)**:** Green solid; FTIR (KBr), cm^{-1}: 3375, 3065, 2993, 1612, 1570, 1500, 1429, 1311,1234, 1089, 821, 738, 505; ^{1}H-NMR (400 MHz, DMSO-d_6) δ, ppm: 12.86 (s, 1H, NH), 9.46 (s, 1H, CH) and 8.08-7.18 (m, 8H,H *Arom.*)

5. ***N*-(4-bromobenzylidene)-1*H*-benzo[d]imidazol-2-amine** (Table 2; 3f)**:** Green solid; FTIR (KBr), cm^{-1}: 3422, 3063, 2991, 1610, 1489, 1429, 1070, 819,738; ^{1}H-NMR (400 MHz, DMSO-d_6) δ, ppm: 12.75 (s, 1H, NH), 9.44 (s, 1H, CH) and 7.99-7.18 (m, 8H,H*Arom.*).

6. ***N*-(3-nitrobenzylidene)-1*H*-benzo[d]imidazol-2-amine** (Table 2; 3c)**:** Green solid; FTIR (KBr), cm^{-1}: 3346, 3088, 1608, 1529, 1431, 1350, 1278,1085, 742, 665; ^{1}H-NMR (400 MHz, DMSO-d_6) δ, ppm: 12.86 (s, 1H, NH), 9.61 (s, 1H, CH) and 8.88-7.21 (m, 8H,H*Arom.*).

3. Result and Discussion

At present, there are various numbers of methods available in the literature for the synthesis of copper nanoparticles like conventional polyol process, spray-pyrolysis, precipitation, chemical/electrochemical and plasma deposition [22-26]. Among them, chemical reduction method is more appropriate for the production of Cu NPs with controlled morphology. A chemical reduction method usually involves the reduction of metal salts in some type of solvent and a separate reducing agent. The metal particles were synthesized in an ambient atmosphere that determined to be phase-pure copper without any impurity phase. The synthesized Cu NPs were characterized by various spectroscopic techniques in order to validate its formation and their size in nano scale. Also, SEM and TEM images of copper nanoparticle were exposed a spherical shape, however, average size estimated from TEM images around 40 nm, and also calculated crystallite size around 40 nm by using XRD data through Debye-Scherrer formula. Synthesis, spectroscopic and morphological

characterization of copper nanoparticle was reported previously [21].

3.1 Synthesis of benzimidazole Schiff's bases using Cu NPs as a catalyst

We have made attempts to synthesize new organic derivatives by using nano catalyst. In the present article, we tried to develop an alternative method for the synthesis of benzimidazole Schiff's bases under solvent free condition using Cu NPs catalyst. Initially, we sought a mild and convenient method for the synthesis of benzimidazole Schiff bases at room temperature. In our initial study, for optimization of reaction conditions, the reaction of 2-amino benzamide and benzaldehyde was used as a model reaction to optimize the reaction conditions. First, the reaction was conducted in various solvents using Cu NPs as a catalyst under refluxing conditions and also under solvent-free conditions. As it can be seen from Table 1; the best results under solvent free conditions

.**Table 1:** Synthesis of benzimidazole Schiff's bases in various solvents and under solvent free conditions using Cu NPs as a catalyst *via* stirring conditions

Entry	Solvent	Time(min)	Yield(%)[a]
1	Ethanol	60	62
2	Methanol	60	58
3	CH_3CNs	60	57
4	$CHCl_3$	60	53
5	Toluene	60	45
6[b]	Solvent-free Condition	60	**88,80,77,65**

[a]Isolated yield, [b]catalyzed recycled four times

The catalytic activity graph with the amount of catalyst is shown in Figure 1. The reaction was carried out with various amounts of Cu NPs as a catalyst (5 mol % to 25 mol %) for the synthesis of benzimidazole Schiff's bases. The yield of product increases remarkably from 54 % to 88 % by increase the concentration of catalyst amount from 5 mol % to 25 mol %. When the catalyst amount was increased from 5 mol % to 15 mol % no further increase in the yield of product was observed. Therefore, the amount of 15 mol % of Cu NPs was selected for all subsequences reaction. Under the optimized reaction conditions, a series of benzimidazole Schiff's bases derivatives (*3a–3k*) were synthesized. The results are summarized in Table 2.

Table 2: Synthesis of Schiff's bases derived from reaction of 2-aminobenzimidazole with aromatic aldehydes in the presence of 15 mol % of copper NPs

Entry	Aldehyde	Product	Stirring time (h)	Yield(%)[a]	mp(°C)	mp(°C) (Lit)[13-15]
1	Ph	3a	1	88	149-152	152-154
2	4-$NO_2C_6H_4$	3b	1.5	90	264-266	266-268
3	3-$NO_2C_6H_4$	3c	1.5	94	198-194	191-193
4	4-ClC_6H_4	3d	1	92	230-231	231-233
5	2-OHC_6H_4	3e	1.5	90	225-226	226-228
6	4-BrC_6H_4	3f	1.5	90	245-246	264-265
7	2-ClC_6H_4	3g	1	93	212-213	212-214
8	4-$OCH_3C_6H_4$	3h	2	91	222-223	222-224
9	2-ClC_6H_4	3i	2	90	205-207	205-208
10	4-$CH_3C_6H_4$	3j	2	80	212-213	218-219
11	3-$CHOC_6H_4$	3k	2	70	257-261	261-262

a Isolated Yields

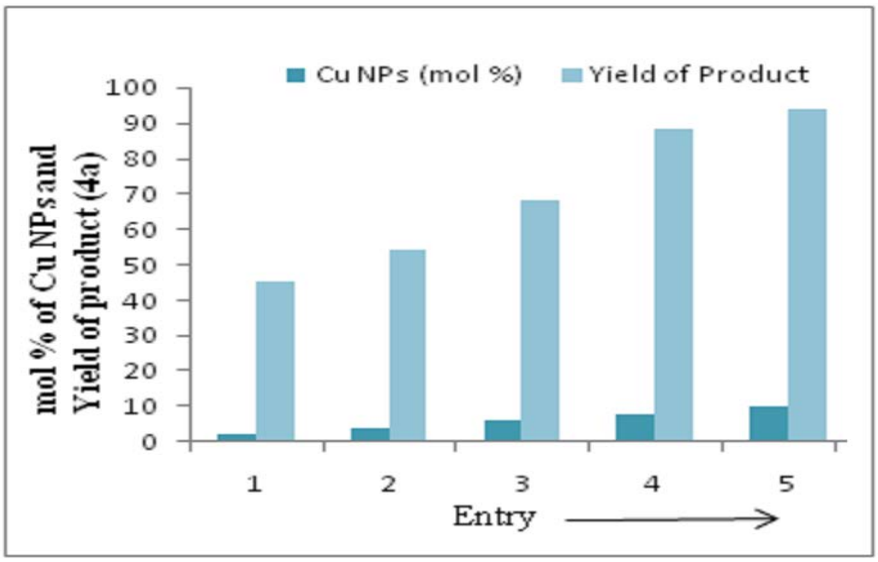
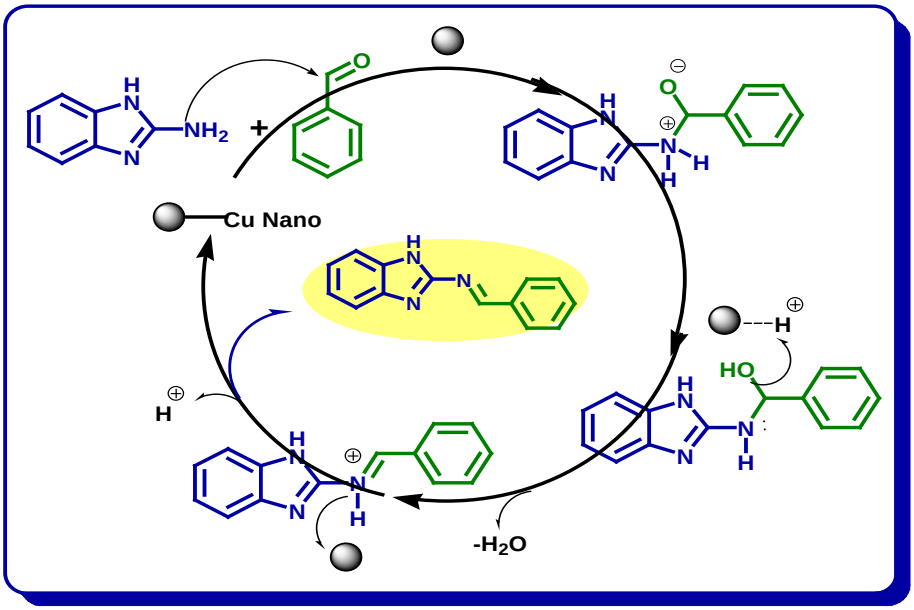


Figure 1: Effect of amount of Cu NPs catalyst used for the synthesis of benzimidazole Schiff's bases

3.2 Reusability of the catalyst

The reusability of the catalyst is one of the most important benefits and makes it useful for commercial applications. We have examined the recovery and reuse of the catalyst. The catalysts were recovered by a simple work-up using the centrifugation method and reused during four consecutive runs without any apparent loss of activity for the same reaction. It noteworthy that the yield of the product in the second, third, and fourth uses was almost the same as that in the first run as has been shown in Table 1.

In order to determine the catalytic behavior of Cu NPs as catalyst for the synthesis of benzimidazole Schiff's bases, a plausible reaction mechanism for the reaction of different aromatic aldehydes and 2-aminobenzimidazoleby using Cu NPs as NPs shown in Scheme 2. We propose that Cu NPs facilitate the proton and co-ordinate for removal of a water molecule to form the final base. [18]. Finally, the Schiff's base product was obtained and Cu NPs nanoparticles released for further reactions.



Scheme 2: The plausible reaction mechanism for benzimidazole Schiff bases by Cu NPs

4. Conclusions

In conclusion, we have demonstrated straightforward and green method for efficient synthesis of benzimidazole Schiff's bases *via* condensation of aromatic aldehydes with 2-aminobenzimidazole under solvent free condition using Cu NPs as a heterogeneous nano catalyst. The yield of product increases remarkably from 54 % to 88 % by increase the concentration of catalyst amount from 5 mol %

to 25 mol %. Nanocatalyst able to exhibited an excellent recyclability and reusability up to four times without any additional treatment. The present methodology offers several advantages including trouble-free procedure, spectacular yields, and short reaction time.

Acknowledgement
The authors gratefully acknowledge to IIT Mumbai, SAIF Cochin, STIC Chandigarh and SYNZEL Gandhinagar (Gujarat) for their valuable spectral analyses.

Disclosure statement
No potential conflict of interest is reported by the authors.

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