

## A green synthesis of di-indolyloxindols catalyzed by CuO/g-C<sub>3</sub>N<sub>4</sub> nanocomposite under mild conditions

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### ABSTRACT

In this study, novel CuO/g-C<sub>3</sub>N<sub>4</sub> nanocomposite was simply synthesized by impregnation of g-C<sub>3</sub>N<sub>4</sub> with CuO nanoparticles. Then, the heterogeneous catalyst was characterized by various techniques including Fourier transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD), thermogravimetric analysis (TGA) and transmission electron microscopy (TEM). Moreover, the Friedel–Crafts 3-indolylation reaction of isatin with indole derivatives in water as a green solvent was investigated using catalytic amount of CuO/g-C<sub>3</sub>N<sub>4</sub> nanocomposite. The results showed that di-indolyloxindole derivatives are synthesized in good to excellent yields at mild conditions. Finally, this method has some advantages including the use of water as a green solvent, short reaction time, room temperature, easy work up and excellent yields.

**Keywords:** CuO/g-C<sub>3</sub>N<sub>4</sub> nanocomposite, Di-indolyloxindols; Indole, Isatin.

### 1. Introduction

Recently, Cu and Cu<sub>x</sub>O nanoparticles attracted great attention for catalyzing N-arylation reaction in the synthesis of N-heterocycles because of economic and industrial points [1-3]. Copper (I) nanoparticles catalyzed the synthesis of quinazolinones using 2-halobenzamide and benzylamine [4]. CuO nanoparticle is also applied as a novel catalyst in several N, O and S-arylation reactions [5-9]. From green chemistry view points, water as a green solvent offers many advantages in the synthesis of organic compounds because it is cheap, non-toxic and non-flammable readily available, but a major challenge in handling the nanoparticles in water is the tendency of the nanoparticles to aggregate quickly into micrometer-sized particles due to van der Waal forces [10-15]. Composite materials which are made by the decoration of the nanoparticles onto the surface of some platforms like graphene nanosheets, which made a strong interface between the filler and matrix, significantly reduced the nanoparticle agglomeration and the composites with larger surface area show superior properties, compared with bare nanomaterials.

Graphitic carbon nitride (g-C<sub>3</sub>N<sub>4</sub>) as an organic polymer and metal-free organic semiconductor consisting mainly of carbon and nitrogen has attracted widespread attention due to its special characteristics in heterogeneous (photo) catalysis and can be a good candidate for the preparation of composite materials [16,17]. g-C<sub>3</sub>N<sub>4</sub> is easily-synthesized by polymerization of cheap materials like thiourea, urea, cyanamide, melamine, and dicyandiamide [18-24]. The g-C<sub>3</sub>N<sub>4</sub> possesses advantages such as high stability, large surface areas, non-toxicity, easy functionalization, high thermal stability, particular physical features, easy recycling, and good bio-compatibility [25,26]. The immobilization of metal and metal oxide nanoparticles onto g-C<sub>3</sub>N<sub>4</sub> promotes the charge separation at the interface of the metal and metal oxide nanoparticles heterojunction and improves the catalytic performance and also restricts the aggregation of nanoparticles leading to an enhancement of selectivity and catalytic activity [27,28].

Di-indolyloxindoles as heterocyclic compounds which have antibacterial, anti-inflammatory and laxative effects are synthesized by the reaction of isatin or its derivatives with barbituric acid, pyrazolones, aromatic in triflic acid, and other routes. Di-indolyloxindoles are also isolated from plants [29,30]. Several methods have been reported for the synthesis of oxindole derivatives.

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A variety of catalysts such as  $\text{KAl}(\text{SO}_4)_2$ ,  $\text{FeCl}_3$ ,  $\text{I}_2$ , ceric ammonium nitrate,  $\text{N,N,N,N}$ -tetramethylguanidinium trifluoroacetate,  $\text{TfOH}$ ,  $\text{Bi}(\text{OTf})_3$ , and silica sulfuric acid, montmorillonite-K10 clay, KSF, Amberlyst-15, phosphotungstic acid, ionic liquids, boron trifluoride supported on nano- $\text{SiO}_2$  and prolinium triflate (ProTf) [31-47] have been used to achieve these compounds, and some drawbacks were observed in these protocols. Therefore, the introduction of new efficient methods in this field is still important. Now, in continuation of our previous study on the synthesis of biologically important compounds using simple, efficient and non-toxic catalysts [48-51] herein, we report the synthesis of di-indolyloxindole derivatives by the coupling of isatin and indole derivatives in the presence of  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocomposite as an inexpensive and efficient catalyst in an aqueous solvent.

## 2. Experimental

### 2.1. Materials

All chemicals were purchased from Merck Company and used without purification. IR spectra were recorded using Bruker Vector-22 FT-IR spectrometer (AVATR-370) in a KBr pellet, scanning from 4000 to  $400\text{ cm}^{-1}$  at room temperature. The Philips CM10 instrument was used for TEM images. The Bruker D<sub>8</sub>-advance X-ray diffractometer with Cu  $K_\alpha$  radiation ( $k = 1.5406\text{ \AA}$ ) was employed for XRD measurements. TGA patterns were recorded using a Perkin-Elmer Diamond TG/DTA thermal analyzer by heating the samples in an Argon flow at a rate of  $100\text{ mL min}^{-1}$  with a heating rate of  $10^\circ\text{C min}^{-1}$ .  $^1\text{H}$  and  $^{13}\text{C}$ NMR spectra were carried out using Bruker DPX-250 Advance instrument at 250 MHz and 62.9 MHz in  $\text{DMSO-d}_6$  using TMS as an internal standard.

### 2.2. Synthesis of $g\text{-C}_3\text{N}_4$ nanosheets

The  $g\text{-C}_3\text{N}_4$  powder was synthesized according to the literature [52]. Briefly, melamine (10 g) was added to an alumina crucible with a cover and heated to  $550^\circ\text{C}$  in a muffle furnace at a rate of  $2^\circ\text{C min}^{-1}$  under air conditions. The crucible was kept at this temperature for 4 h. The resulting yellow polymer was finely ground into powder for further use. Finally, 0.05 g of  $g\text{-C}_3\text{N}_4$  was ultrasonicated in 50 mL of water for 24 h and centrifuged to remove the unexfoliated  $g\text{-C}_3\text{N}_4$ .

### 2.3. Synthesis of CuO nanoparticles

To synthesize the CuO nanocrystals, polyvinylpyrrolidone (PVP, 1.5 g) was dissolved in 100 mL of distilled water, followed by the addition of 0.17 g of  $\text{CuCl}_2$  [53,54]. Then, the NaOH solution (6.0 M, 20 mL) and ammonia solution (25%, 3.9 mL) were added drop

wise into the above mixture with continuous stirring and the solution was further stirred for 0.5 h. Finally, ascorbic acid solution (0.3 M, 20 mL) was added drop wise to the mixture stirred for 3 h at  $55^\circ\text{C}$ . The mixture was centrifuged and the precipitate was collected, washed with distilled water and ethanol and dried in a vacuum oven at  $80^\circ\text{C}$  for 8 h.

### 2.4. Fabrication of $\text{CuO}@g\text{-C}_3\text{N}_4$ octahedra nanocomposite

In a typical procedure,  $g\text{-C}_3\text{N}_4$  (1 g) was dispersed in 50 mL of water for 24 h. Then, CuO (0.1 g) was added to the mixture and stirred for 48 h. After evaporation of the water, a powder sample of  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocomposite was obtained and dried at  $80^\circ\text{C}$  for 12 h.

### 2.5. General procedure for the synthesis of di-indolyloxindoles

Typically, heterogeneous  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocatalyst (75 mg) was dispersed for 30 min in water (3 mL) followed by addition of indole (2.0 mmol) and isatin (1.0 mmol). The mixture was stirred for the appropriate time and the progress of the reaction was monitored by thin layer chromatography. After the reaction was completed, the product was extracted with ethyl acetate and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The crude product was recrystallized in hot ethanol. The  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocatalyst was separated by centrifuging, washed with EtOH, dried and reused for the next run.

#### Selected spectral data [38,55,56]

##### 5-Bromo-1-ethyl-3,3-bis(1-methyl-1H-indol-3-yl)indolin-2-one (Table 4, entry 8):

White solid. m.p.=  $324\text{-}326^\circ\text{C}$ . IR (KBr):  $\bar{\nu}$ = 3425, 3345, 3103, 3045, 1694, 1608, 1461, 1095,  $724\text{ cm}^{-1}$ .  $^1\text{H}$ NMR (250 MHz,  $\text{DMSO-d}_6$ ):  $\delta$ = 1.25 (t, 3H,  $\text{CH}_3\text{-CH}_2$ ), 3.35 (q, 2H,  $\text{CH}_2\text{-CH}_3$ ), 3.7 (CH<sub>3</sub>), 6.82-6.90 (m, 4H), 7.05-7.18 (m, 4H), 7.33-7.39 (m, 2H), 7.48-7.52 (m, H) ppm.  $^{13}\text{C}$ NMR (62.9 MHz, DMSO):  $\delta$ = 12.8 (CH<sub>3</sub>), 32.8 (CH<sub>2</sub>), 52.6 (C), 110.5 (C-H), 111.6 (C-H), 112.9 (C-H), 114.3 (C), 119.2 (C-H), 121.3 (C-H), 121.8 (C-H), 126.1 (C-H), 128.6 (C-H), 129.1 (C-H), 131.4 (C), 136.8 (C), 137.9 (C-H), 141.5 (C), 176.5 (C=O) ppm.

##### 3,3-bis(1-methyl-1H-indol-3-yl)indolin-2-one (Table 4, entry 2):

White solid. m.p.= $335\text{-}337^\circ\text{C}$ . IR (KBr):  $\bar{\nu}$ = 3344, 3043, 1699, 1607, 1466, 1105,  $737\text{ cm}^{-1}$ .  $^1\text{H}$ NMR (250 MHz,  $\text{DMSO-d}_6$ ):  $\delta$ = 3.68(s, 6H, 2CH<sub>3</sub>), 6.8-7.08 (m, 6H), 7.20-7.34 (m, 6H), 10.60 (s, H, NH Isatin) ppm.  $^{13}\text{C}$ NMR (62.9 MHz,  $\text{DMSO-d}_6$ ):  $\delta$ = 37.56 (2CH<sub>3</sub>), 57.61 (C), 114.85 (C), 114.99 (C-H), 118.67 (C-H),

123.60 (C-H), 126.15 (C-H), 126.30 (C-H), 126.80 (C), 130.12 (C-H), 131.25 (C-H), 133.14 (C-H), 133.69(C), 139.72 (C), 142.55 (C-H), 146.49(C), 183.78 (C=O) ppm.

### 3,3-di (1H-indol-3-yl) indolin-2-one (Table 4, entry 1):

White solid. m.p.=312-313°C. IR (KBr):  $\bar{\nu}$ = 3362, 3125, 3034, 1702, 1618, 1489, 1096, 731  $\text{cm}^{-1}$ .  $^1\text{H}$ NMR (250 MHz, DMSO- $d_6$ ):  $\delta$ = 6.76-7.05 (m, 7H), 7.21 (m, 3H), 7.30-7.34(m, 2H), 10.58 (s, H, NH Isatin), 10.96 (s, 2H, 2NH, Indol) ppm.  $^{13}\text{C}$ NMR (62.9 MHz, DMSO- $d_6$ ):  $\delta$ = 57.81 (C), 114.87 (C), 116.86 (C-H), 119.53 (C-H), 123.49 (C-H), 125.98 (C-H), 126.22 (C-H), 126.75 (C-H), 129.47 (C-H), 130.12 (C), 130.91 (C-H), 133.10 (C), 139.82(C), 142.15, 146.46(C), 184.06 (C=O) ppm.

## 3. Results and Discussion

CuO nanoparticle was synthesized by the reaction of  $\text{CuCl}_2$  with PVP in deionized water. The g- $\text{C}_3\text{N}_4$  was synthesized by the heating of melamine (Scheme 1).

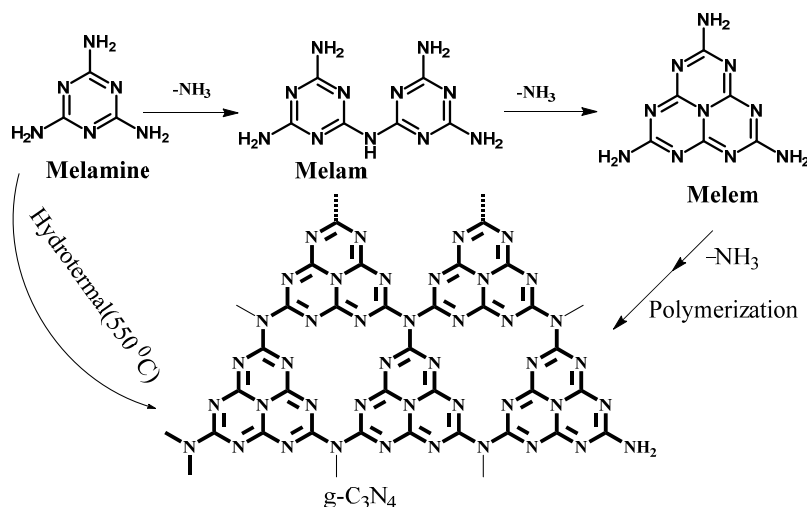
g- $\text{C}_3\text{N}_4$  was dispersed in water, followed by addition of CuO nanoparticle then, the mixture was stirred for 48 h at room temperature. The solution was heated to remove

water and the obtained powder was dried at 80°C for 12 h (Scheme 2).

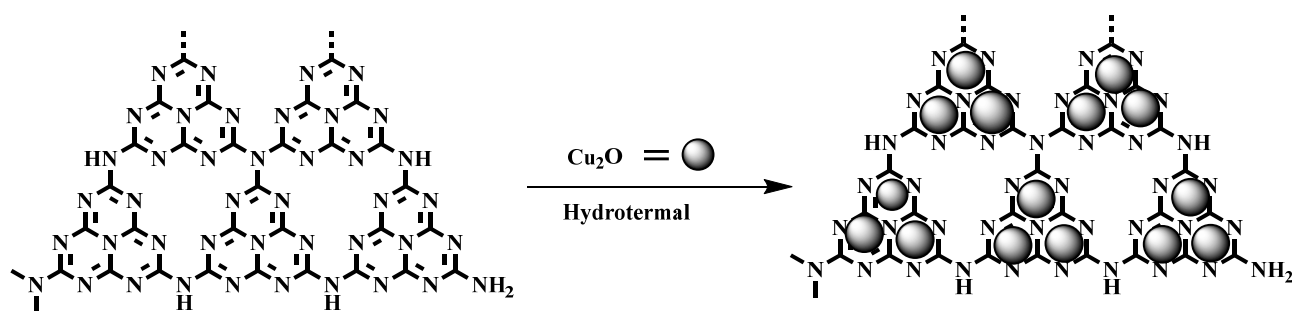
### 3.1. Characterizations of catalyst

The  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocatalyst was characterized by different techniques. To calculate the content of CuO nanoparticles in g- $\text{C}_3\text{N}_4$  nanosheets, the TGA image of g- $\text{C}_3\text{N}_4$ , and  $\text{CuO}@g\text{-C}_3\text{N}_4$  nano composites was performed under air atmosphere from room temperature to 800°C (Fig. 1).

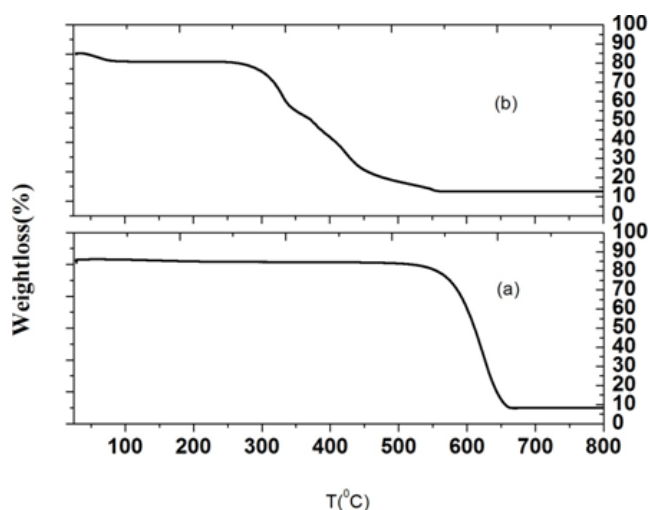
In airflow, pure g- $\text{C}_3\text{N}_4$  is stable below 550°C, but with the temperature higher than 550°C, the decomposition or sublimation of g- $\text{C}_3\text{N}_4$  was occurring. This decomposition is completed at about 650°C (Fig. 1a). The stability of the  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocomposites was obviously decreased due to the oxidation and decomposition of g- $\text{C}_3\text{N}_4$  in the  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocomposites. The decomposition temperature decreased to 550°C, which indicated that there was a tight contact between CuO nanoparticles and g- $\text{C}_3\text{N}_4$  (Fig. 1b). It can be calculated from the mass loss of  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocomposites that the mass fraction of CuO and g- $\text{C}_3\text{N}_4$  in the  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocomposites are 5 and 95%, respectively.



Scheme 1. Schematic representation for the synthesis of  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocomposites [57,58].



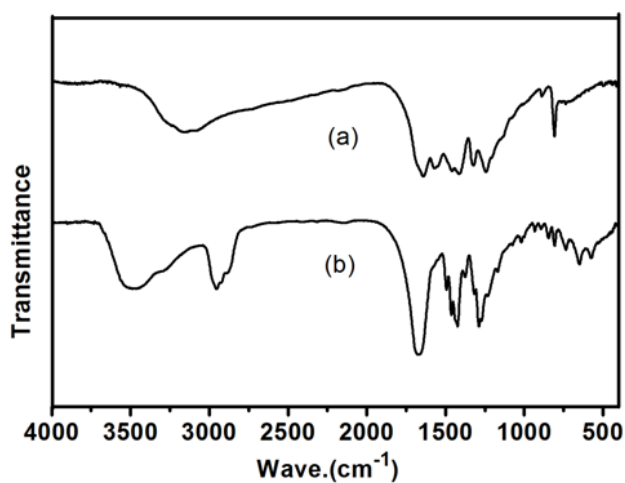
Scheme 2. Schematic representation for the synthesis of  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocomposites.



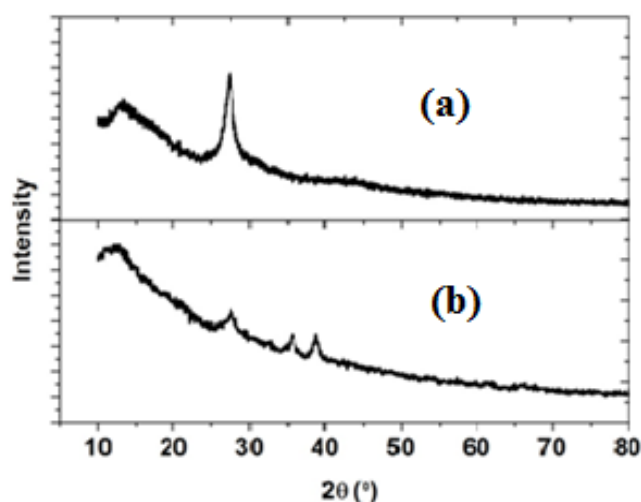
**Fig. 1.** Thermogravimetric weight loss pattern of (a)  $g\text{-C}_3\text{N}_4$  and (b)  $\text{CuO}@g\text{-C}_3\text{N}_4$  with temperature raised from  $10^\circ\text{C}/\text{min}$ .

Fig. 2 Shows the FT-IR spectrum of  $g\text{-C}_3\text{N}_4$  and  $\text{CuO}@g\text{-C}_3\text{N}_4$ . The broad peak ranging from  $3150$  to  $3400\text{ cm}^{-1}$  is assigned to the N-H bond. The peak at  $1645\text{ cm}^{-1}$  was related to heterocyclic C=N stretching, vibration bond, while the peaks at  $1238$ ,  $1317$ ,  $1405$  and  $1543\text{ cm}^{-1}$  were considered as C-N stretching of tri-s-triazine. Besides, the sharp peak centered at  $806\text{ cm}^{-1}$  is corresponding to the out-of plane bending vibration of triazine cycle (Fig. 2a) [59-61]. The FT-IR spectrum of  $\text{CuO}@g\text{-C}_3\text{N}_4$  shows the vibration bands at  $525$ ,  $580$  and  $675\text{ cm}^{-1}$  which are assigned to the CuO nanoparticles (Fig. 2b) [62-64].

The XRD patterns of  $g\text{-C}_3\text{N}_4$  and  $\text{CuO}@g\text{-C}_3\text{N}_4$  were shown in Fig. 3. The peaks at  $13.1^\circ$  and  $27.4^\circ$  could be assigned to the hexagonal phase of  $g\text{-C}_3\text{N}_4$  (JCPDS 087-1526). Furthermore, the (100) weak diffraction peak at  $13.1^\circ$  was related to the in-plane repeated units in the  $g\text{-C}_3\text{N}_4$ .



**Fig. 2.** FT-IR spectra of (a)  $g\text{-C}_3\text{N}_4$  and (b)  $\text{CuO}@g\text{-C}_3\text{N}_4$ .



**Fig. 3.** XRD image of (a)  $g\text{-C}_3\text{N}_4$  and (b)  $\text{CuO}@g\text{-C}_3\text{N}_4$ .

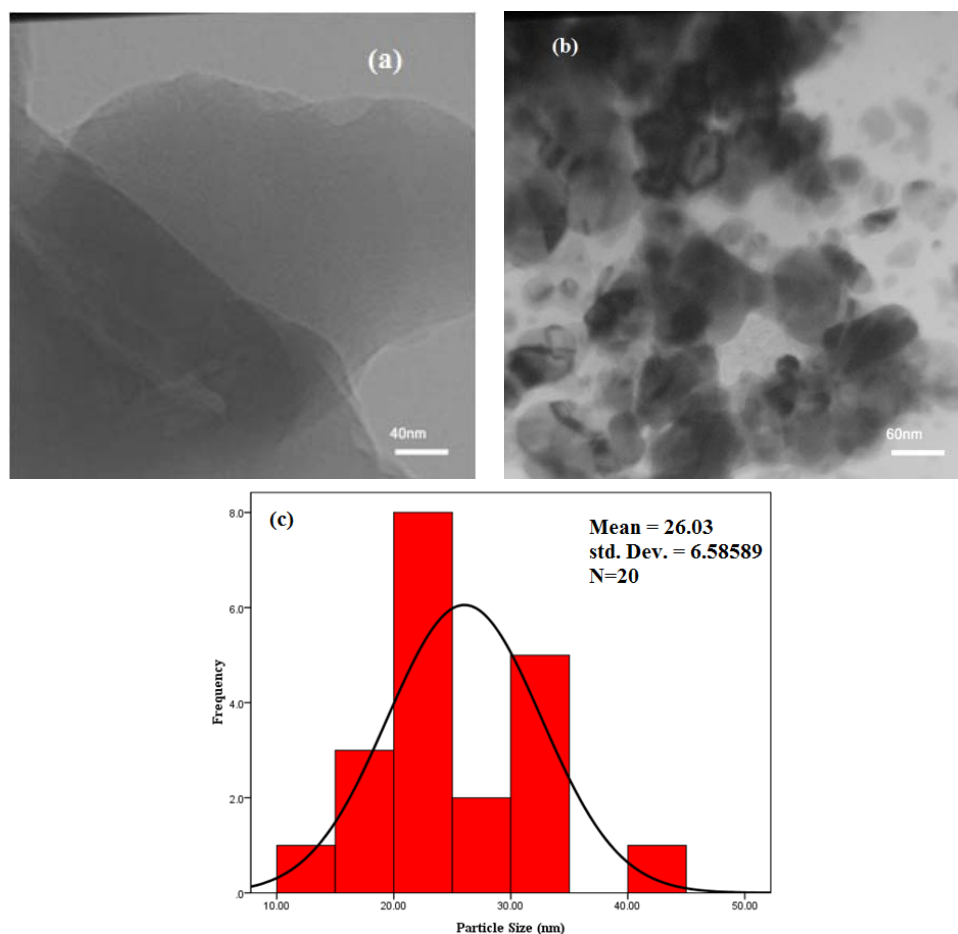
The strong peak at  $27.4^\circ$  is corresponding to the characteristic (002) interlayer stacking peak of  $g\text{-C}_3\text{N}_4$  [58,59]. In the composite sample pattern, no obvious diffraction peaks of the other phases or impurities can be detected. After loading CuO nanoparticles, the intensity of the peak centered at  $27.4^\circ$  decreased milder as a result of the dilution effect. Furthermore, new typical peaks which are located at  $35.3^\circ$ ,  $39.4^\circ$ , and  $74.1^\circ$  and indexed as (111), (200), (220) appeared in the XRD pattern of  $\text{CuO}@g\text{-C}_3\text{N}_4$  [66]. Using the Debye-Scheerer equation, the average particle size of CuO nanoparticles was  $22\text{ nm}$ .

Fig. 4 shows the TEM image of Pure  $g\text{-C}_3\text{N}_4$  and  $\text{CuO}@g\text{-C}_3\text{N}_4$ . As shown in the fig. 4a, the agglomeration of the lamellar structure was observed. The TEM image of  $\text{CuO}@g\text{-C}_3\text{N}_4$  exhibited that CuO nanoparticles were homogeneously dispersed on the surface of the  $g\text{-C}_3\text{N}_4$  with an average particle size of about  $26\text{ nm}$ , which is consistent with the results of XRD. The hydrodynamic diameter distribution of CuO nanoparticles is also determined by dynamic light scattering (DLS) (Fig. 4c). 20 numbers of CuO nanoparticles were selected and the mean values of these nanoparticles was obtained by DLS with standard deviation of  $6.58$ . Consequently, the size distribution of CuO is centered at a value of  $26,03\text{ nm}$ .

### 3.2. Catalytic activity studies

#### 3.2.1. Synthesis of di-indolyloxindole

To evaluate the catalytic ability of  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocomposite, the synthesis of di-indolyloxindole from indole and isatin with the nanocomposite as a catalyst was investigated at room temperature (model reaction). The reaction was carried out using  $75\text{ mg}$  of  $\text{CuO}@g\text{-C}_3\text{N}_4$  in water under ambient temperature (Scheme 3).



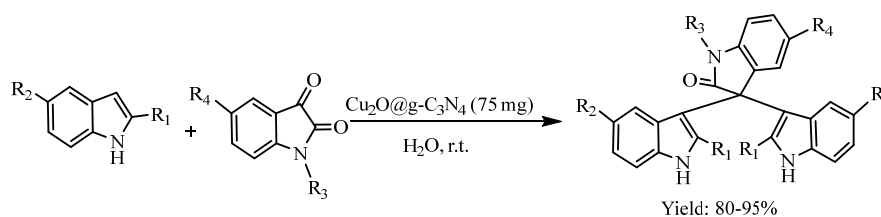
**Fig. 4.** TEM image of (a)  $g\text{-C}_3\text{N}_4$ , (b)  $\text{CuO}@g\text{-C}_3\text{N}_4$  and (c) DLS image of  $\text{CuO}$ .

The results showed that the amount of catalyst loading was very important in the progress of the reaction. The reaction required 2 h to give 31 % of the oxindole product in the presence of 20 mg of catalyst (Table 1, entry 1). Moreover, the increase of catalyst loading to 60 mg improves the yield to 82 % (Table 1, entry 3). The  $\text{CuO}@g\text{-C}_3\text{N}_4$  catalyst with 75 mg loading was very effective as it afforded the product in the quantitative yield (95 %, Table 1, entry 4) within 1 hour. Further increase in the amount of catalyst loading did not significantly improve the yield (Table 1, entries 5,6).

A control experiment with  $g\text{-C}_3\text{N}_4$  under similar condition was conducted and the desired product was

traced (Table 1, entry 7). Considering this, it was concluded that there is a synergistic effect between the  $\text{CuO}$  and the  $g\text{-C}_3\text{N}_4$ , which is responsible for the high catalytic activity of the  $\text{CuO}@g\text{-C}_3\text{N}_4$  catalyst. The effect of reaction time was determined (10-70 min) on the synthesis of di-indolyloxindoles (Table 2).

As shown in Table 2, the yields were increased by increasing the time up to 60 min and further increasing at the time did not affect the yields. The model reaction was also conducted in the presence of  $\text{CuO}$  nanoparticles and despite the better yield in the first run, the yields were clearly decreased in the reusing step of catalyst (not listed).



**Scheme 3.** The synthesis of di-indolyloxindole derivatives in the presence of catalytic amount of  $\text{CuO}@g\text{-C}_3\text{N}_4$  nanocomposite in water.

**Table 1.** The effect of different amounts of CuO@g-C<sub>3</sub>N<sub>4</sub> on the synthesis of di-indolyloxindole.<sup>a</sup>

Entry	CuO@g-C <sub>3</sub> N <sub>4</sub> (mg)	Yield (%)
1	20	31
2	40	59
3	60	82
4	75	95
5	80	97
6	85	98
c7	75	trace

<sup>a</sup>Reaction conditions: Isatin (1.0 mole), indole (2 mmol).

This may happen due to the aggregation of catalyst in the water solvent [65]. To investigate the effect of solvents, the model reaction was carried out in various solvents with the range of polarity (nonpolar to polar solvents) with CuO@g-C<sub>3</sub>N<sub>4</sub> (75 mg) as a catalyst at room temperature. The reaction proceeded in polar solvents and the best yield was observed in water media (Table 3, entries 6–10), while the yields decreased in nonpolar solvents (Table 3, entries 1–5).

Although CuO nanoparticle can promote the reaction better than CuO@g-C<sub>3</sub>N<sub>4</sub>, a series of problems always occurs in the presence of metal and metal oxide nanoparticles. One of these problems is aggregation, which is solved by g-C<sub>3</sub>N<sub>4</sub>. As mentioned earlier, the g-C<sub>3</sub>N<sub>4</sub> as “active support” restricts the aggregation of metal and metal oxide nanoparticles, leading to enhancing the selectivity and activity.

**Table 2.** The effect of time on the synthesis of di-indolyloxindole in the presence of CuO@g-C<sub>3</sub>N<sub>4</sub>.<sup>a</sup>

Entry	Time (min)	Yield (%)
1	10	20
2	20	41
3	30	59
4	40	73
5	50	85
6	60	95
7	65	97
8	70	98

<sup>a</sup>Reaction conditions: Isatin (1.0 mmol), indole (2 mmol), catalyst (75 mg).

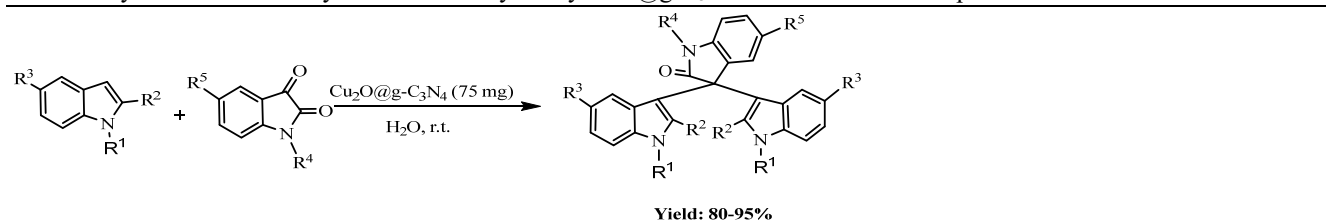
**Table 3.** The effect of different solvents on the reaction of indole and isatin catalyzed by CuO@g-C<sub>3</sub>N<sub>4</sub>.<sup>a</sup>

Entry	Solvent	Yield (%)
1	THF	13
2	DMF	22
3	CHCl <sub>3</sub>	29
4	CH <sub>2</sub> Cl <sub>2</sub>	31
5	C <sub>2</sub> H <sub>4</sub> Cl <sub>2</sub>	35
6	DMSO	55
7	CH <sub>3</sub> CN	60
8	MeOH	65
9	EtOH	66
10	Water	95

<sup>a</sup>Reaction conditions: Isatin (1.0 mmol), indole (2 mmol), CuO@g-C<sub>3</sub>N<sub>4</sub> (75 mg), solvent (3 mL) at room temperature during 1 h.

To show the generality of the heterogeneous catalyst in organic reactions, CuO@g-C<sub>3</sub>N<sub>4</sub> was used as an efficient and novel heterogeneous nanocomposite for the synthesis of a series of di-indolyloxindoles derivatives using isatins and indoles derivatives and the results are summarized in Table 4. Either substrate containing electron-releasing or electron-withdrawing groups employed 75 mg of CuO@g-C<sub>3</sub>N<sub>4</sub> as the catalyst (Table 4, entries 1–18). As can be seen in Table 4, the reaction promoted well and gave the excellent yields (92-95 %), when indoles with bearing electron-releasing substituents on the carbon neighboring the nitrogen were employed (Table 4, entries 2, 5 and 8). In contrast, indoles with electron-withdrawing groups on the phenyl ring decreased the yields (80 %) in 75 min (Table 4, entry 3). Furthermore, N-benzyl isatin with electron-releasing groups gave lower yields (80-86 %) in 75 min (Table 4, entries 13-15). Finally, the best yields were achieved with isatins bearing electron-withdrawing groups on the R<sup>4</sup> position and indoles bearing electron-releasing substituents in the R<sup>1</sup> position (Table 4, entry 8).

A small amount of starting materials left untreated and no side product is formed. Also, the high activity of the CuO@g-C<sub>3</sub>N<sub>4</sub> may be due to the uniform distribution of CuO nanoparticles, which are stabilized by  $\pi$ -conjugated graphitic carbon nitrides and readily accessible surface exposed CuO nanoparticles which obviously favor the C–C bond forming reactions.

**Table 4.** Synthesis of di-indolyloxindoles catalyzed by SiO<sub>2</sub>@g-C<sub>3</sub>N<sub>4</sub> in water at room temperature.<sup>a</sup>

Entry	Indole			Isatin		Time (min)	Yield (%) <sup>b</sup>
	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	R <sup>5</sup>		
1	H	H	H	H	H	60	95
2	Me	H	H	H	H	55	95
3	H	H	Br	H	H	75	80
4	H	H	H	H	Cl	55	94
5	H	Me	H	H	Cl	45	93
6	H	H	Br	H	Cl	75	88
7	Me	H	H	H	Br	60	87
8	Me	H	H	CH <sub>2</sub> CH <sub>3</sub>	Br	45	95
9	H	H	Br	H	Br	75	83
10	H	H	H	H	NO <sub>2</sub>	70	95
11	H	Me	H	H	NO <sub>2</sub>	65	95
12	H	H	Br	H	NO <sub>2</sub>	75	94
13	H	H	H	PhCH <sub>2</sub>	H	75	80
14	H	Me	H	PhCH <sub>2</sub>	H	75	86
15	H	H	Br	PhCH <sub>2</sub>	H	75	80
16	H	H	H	Me	H	75	89
17	H	Me	H	Me	H	75	90
18	H	H	Br	Me	H	75	81

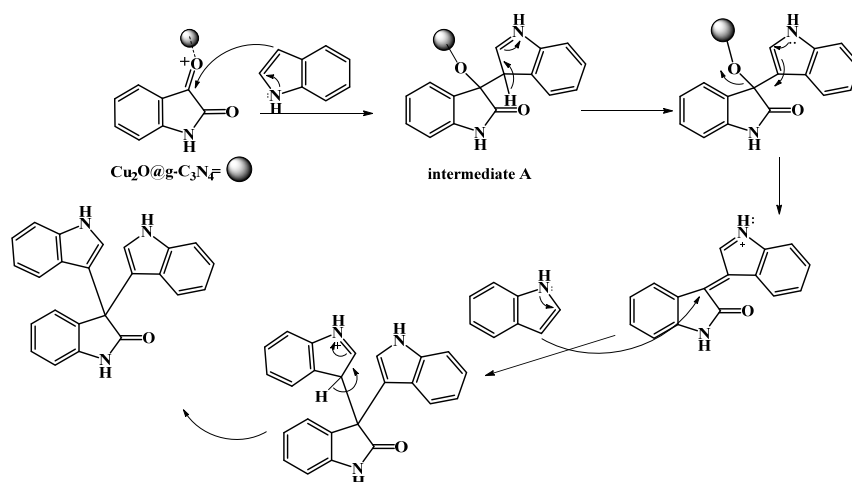
<sup>a</sup>Reaction conditions: Isatin derivatives (1.0 mmol), indole derivatives (2 mmol), catalyst (75 mg) and water (3 mL).

The aqueous filtered phase was analyzed by atomic absorption to investigate leaching of CuO from the solid CuO@g-C<sub>3</sub>N<sub>4</sub> catalyst and no leaching of Cu metal was detected in it. Therefore, the mesoporous graphitic carbon nitride containing CuO could serve as an efficient heterogeneous catalyst for the synthesis of oxindole derivatives. The reaction can be rationalized by assuming the following mechanism (Scheme 4). As shown in Scheme 3, CuO@g-C<sub>3</sub>N<sub>4</sub> activates the carbonyl groups of isatin followed by the nucleophilic addition of indole to isatin to form the intermediate (A). This intermediate undergoes a further nucleophilic attack with the second indole molecule to afford di-indolyloxindole derivatives.

The efficiency of our method was also compared with some other published works in the literature

[31,35,40,66-72]. As the results shown in Table 5, CuO@g-C<sub>3</sub>N<sub>4</sub> showed sufficient efficiency compared to the other catalysts (Table 5, entry 11).

From an industrial perspective, long-term stability, recovery, and reusability are the main objects of using heterogeneous catalysts. For this purpose, under optimized conditions the model reaction was performed as previously described, followed by separating, washing and drying the catalyst and reusing in another four successive catalytic cycles under identical reaction conditions. The results showed excellent yields with a negligible decrease in a catalytic activity (The yields were 95, 94, 91, 88 and 88 %, respectively). So, the performance of CuO@g-C<sub>3</sub>N<sub>4</sub> nanocomposite was consistent and validates its recyclability.



**Scheme 4.** A proposed mechanism for the synthesis of di-indolyloxindole catalyzed by CuO@g-C<sub>3</sub>N<sub>4</sub>.

#### 4. Conclusions

In conclusion, a green and rapid hydrothermal method was introduced for the synthesis of CuO@g-C<sub>3</sub>N<sub>4</sub> nanocomposites. Then, CuO@g-C<sub>3</sub>N<sub>4</sub> nanocomposites was characterized by various techniques. The prepared CuO@g-C<sub>3</sub>N<sub>4</sub> nanocomposites was applied for the synthesis of biologically active di-indolyloxindole derivatives in good to excellent yields (95 %). In addition, the reusability of nanocomposite was investigated and the results showed that the catalyst has good reusability after 5 cycles. This protocol provides a straightforward approach for deposition of CuO nanoparticles onto the g-C<sub>3</sub>N<sub>4</sub> nanosheets and can be readily extended to the preparation of other classes of metal hybrids based on g-C<sub>3</sub>N<sub>4</sub> nanosheets for technological and industrial applications.

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#### References

- [1] S.G. Babu, K. Ramasamy, *Ind. Eng. Chem. Res.* 50 (2011) 9594–9600.
- [2] F. Monnier, M. Taillefer, *Angew. Chem. Int. Ed.* 48 (2009) 6954–6971.
- [3] G. Evano, N. Blanchard, M. Toumi, *Chem. Rev.* 108 (2008) 3054–3131.
- [4] W. Xu, Y. Jin, H. Liu, Y. Jiang, H. Fu, *Org. Lett.* 13 (2011) 1274–1277.
- [5] H. Wang, X. Cao, L. Xiangxiang, S. Fuhong, G-J. Deng, *Org. Lett.* 15 (2013) 4900–4903.
- [6] B-Q. Hu, L-X. Wang, J-F. Xiang, L. Yang, Y-L. Tang, *Chin. Chem. Lett.* 26 (2015) 369–372.

**Table 5.** The comparison of the efficiency of CuO@g-C<sub>3</sub>N<sub>4</sub> with different catalysts.<sup>a</sup>

Entry	Catalyst	Solvent/Temp.(°C)	Time (min)	Yield (%)	Ref.
1	Cellulose sulfuric acid (5 mol %)	Solvent-free/ r.t.	120	88	[66]
2	Tungstic acid (10 mol %)	EtOH/ r.t.	360	92	[67]
3	Fe <sub>3</sub> O <sub>4</sub> -SO <sub>3</sub> H (0.1 g)	CH <sub>3</sub> CN/ 60°C	60	93	[68]
4	I <sub>2</sub> (10 mol %)	CH <sub>2</sub> Cl <sub>2</sub> / r.t.	840	82	[69]
5	LiClO <sub>4</sub> (10 mol %)	EtOH/ 60°C	240	93	[70]
6	Nano-NiO (0.004 gr)	H <sub>2</sub> O/ 70°C	30	98	[71]
7	SiO <sub>2</sub> -OSO <sub>3</sub> H (0.2 g)	CH <sub>2</sub> Cl <sub>2</sub> / r.t.	120	94	[40]
8	Bi (OTf) <sub>3</sub>	CH <sub>3</sub> CN/ r.t.	180	92	[35]
9	Ceric ammonium nitrate	EtOH/ U.S.	180	95	[31]
10	PEG/OSO <sub>3</sub> H	CH <sub>3</sub> CN/ r.t.	150	93	[72]
11	CuO@g-C <sub>3</sub> N <sub>4</sub>	H <sub>2</sub> O/ r.t.	50	95	This work

<sup>a</sup>Reaction conditions: Indole(2.0 mmol), isatin (1 mmol).



- [7] D.K. Sreenivas, N. Ramkumar, R. Nagarajan, *Org. Biomol. Chem.* 10 (2012) 3417-3423.
- [8] A. Kumar, D. Saxena, M.K. Gupta, *Green Chem.* 15 (2013) 2699-2703.
- [9] N. Khatun, S.K. Santra, A. Banerjee, B.K. Patel, *Eur. J. Org. Chem.* 6 (2015) 1309-1313
- [10] (a) S.K. Rout, S. Guin, J. Nath, B.K. Patel, *Green Chem.* 14 (2012) 2491-2498. (b) M. Baghbanzadeh, P. Salehi, M. Dabiri, G. Kozehgary, *Synthesis* (2006) 344-348.
- [11] S.K. Friedlander, *Smoke, Dust, and Haze: Fundamentals of aerosol dynamics*, New York, Oxford University Press (2000)
- [12] C.H. Nam, R. Pfeffer, R.N. Dave, S. Sundaresan, *AIChE. J.* 50 (2004) 1776-1785.
- [13] Q. Yu, R.N. Dave, C. Zhu, J.A. Quevedo, R. Pfeffer, *AIChE. J.* 51 (2005) 1971-1979.
- [14] J.A. Kurkela, D.P. Brown, J. Raula, E.I. Kauppinen, *Powder Technol.* 180 (2008) 164-171.
- [15] W. Yao, G. Suangsheng, W. Fei, W. Jun, *Powder Technol.* 124 (2002) 152-159.
- [16] Y. Wang, X. Wang, M. Antonietti, *Angew. Chem. Int. Ed.* 51 (2012) 68-89.
- [17] S. Cao, J. Low, J. Yu, M. Jaroniec, *Adv. Mater.* 27 (2015) 2150-2176.
- [18] K. Takanabe, K. Kamata, X. Wang, M. Antonietti, J. Kubota, K. Domen, *Phys. Chem. Chem. Phys.* 12 (2010) 13020-13025.
- [19] F. Dong, L.W. Wu, Y.J. Sun, M. Fu, Z.B. Wu, S.C. Lee, *J. Mater. Chem.* 21 (2011) 15171-15174.
- [20] J.H. Liu, Y.W. Zhang, L.H. Lu, G. Wu, W. Chen, *Chem. Commun.* 48 (2012) 8826-8828.
- [21] Y.W. Zhang, J.H. Liu, G. Wu, W. Chen, *Nanoscale* 4 (2012) 5300-5303.
- [22] J.D. Hong, X.Y. Xia, Y.S. Wang, R. Xu, *J. Mater. Chem.* 22 (2012) 15006-15012.
- [23] Y.J. Wang, Z.X. Wang, S. Muhammad, J. He, *CrystEngComm* 14 (2012) 5065-5070.
- [24] J.S. Zhang, M.W. Zhang, R.Q. Sun, X.C. Wang, *Angew. Chem. Int. Ed.* 51 (2012) 10145-10149.
- [25] L.C. Chen, X.T. Zeng, P. Si, Y.M. Chen, Y.W. Chi, D.H. Kim, G. Chen, *Anal. Chem.* 86 (2014) 4188-4195.
- [26] A. Thomas, A. Fischer, F. Goettmann, M. Antonietti, J.-O. Müller, R. Schlögl, J.M. Carlsson, *J. Mater. Chem.* 18 (2008) 4893-4908.
- [27] X. Wang, K. Maeda, A. Thomas, K. Takanabe, *Nat. Mater.* 8 (2009) 76-80.
- [28] B. Long, J. Lin, X. Wang, *J. Mater. Chem. A* 2 (2014) 2942-2951.
- [29] J. Bergman, N. Eklund, *Tetrahedron* 36 (1980) 1445-1450.
- [30] J. Azizian, A.A. Mohammadi, A.R. Karimi, M.R. Mohammadzadeh, *J. Chem. Res.* 6 (2004) 424-426.
- [31] S.Y. Wang, S.J. Ji, *Tetrahedron* 62 (2006) 1527-1535.
- [32] P. Paira, A. Hazra, S. Kumar, R. Paira, K.B. Sahu, S. Naskar, P. Saha, S. Mondal, A. Maity, S. Banerjee, N.B. Mondal, *Bioorg. Med. Chem. Lett.* 19 (2009) 4786-4789.
- [33] K. Rad-Moghadam, M. Sharifi-Kiasaraie, H. Taheri-Amlashi, *Tetrahedron* 66 (2010) 2316-2321.
- [34] A. Kamal, Y.V.V. Srikanth, M.N.A. Khan, T.B. Shaik, M. Ashraf, *Bioorg. Med. Chem. Lett.* 20 (2010) 5229-5231.
- [35] J.S. Yadav, B.V.S. Reddy, K.U. Gayathri, S. Meraj, A.R. Prasad, *Synthesis* (2006) 4121-4123.
- [36] D.A. Klumpp, K.Y. Yeung, G.K.S. Prakash, G.A. Olah, *J. Org. Chem.* 63 (1998) 4481-4484.
- [37] J. Azizian, A.A. Mohammadi, N. Karimi, M.R. Mohammadzadeh, A.R. Karimi, *Catal. Commun.* 7 (2006) 752-755.
- [38] K. Alimohammadi, Y. Sarrafi, M. Tajbakhsh, *Monatsh. Chem.* 139 (2008) 1037-1039.
- [39] M. Chakrabarty, S. Sarkar, Y. Harigaya, *J. Chem. Res.* (2005) 540-542.
- [40] M. Nikpasand, M. Mamaghani, Kh. Tabatabaeian, H.A. Samimi, *Synth. Commun.* 40 (2010) 3552-3560.
- [41] M. Haghghi, K. Nikoofar, *J. Saudi Chem. Soc.* 20 (2016) 101-106.
- [42] N. Karimi, H. Oskooi, M.M. Heravi, M. Saeedi, M. Zakeri, N. Tavakoli, *Chin. J. Chem.* 29 (2011) 321-323.
- [43] Y. Sarrafi, K. Alimohammadi, M. Sadatshahabi, N. Norozipoor, *Monatsh. Chem.* 143 (2012) 1519-1522.
- [44] M. Shiri, *J. Iran. Chem. Soc.* 10 (2013) 1019-1023.
- [45] A. Saffar-Teluri, *Res. Chem. Intermed.* 40 (2014) 1061-1067.
- [46] I. Sharma, A. Saxena, C.K. Ojha, C.K.P. Paradasani, R.T. Paradasani, T. Mukherjee, *Chem. Sci.* 114 (2002) 523-531.
- [47] F.X. Felpin, O. Ibarguren, L. Nassar-Hardy, E. Fouquet, *J. Org. Chem.* 74 (2009) 1349-1352.
- [48] M.A. Nasser, A. Allahresani, A.A. Esmaili, *Lett. Org. Chem.* 11 (2014) 91-96.
- [49] M.A. Nasser, A. Allahresani, H. Raissi, *Iran J. Catal.* 4 (2014) 33-40.
- [50] M.A. Nasser, A. Allahresani, H. Raissi, *RSC Adv.* 4 (2014) 26087-26093.
- [51] A. Allahresani, M.A. Nasser, *RSC Adv.* 4 (2014) 60702-60710.
- [52] L.S. Yin, Y.P. Yuan, S.W. Cao, Z.Y. Zhang, C. Xu, *RSC Adv.* 4 (2014) 6127-6132.
- [53] L. Liu, Y. Qi, J. Hu, Y. Liang, W. Cui, *Appl. Surf. Sci.* 351 (2015) 1146-1154.
- [54] X. Liu, B. Geng, Q. Du, J. Ma, X. Liu, *Mater. Sci. Eng. A* 448 (2007) 7-14.
- [55] B. Das, K. Damodar, N. Chowdhury, *J. Mol. Catal. A: Chem.* 269 (2007) 81-84.
- [56] M. Vijender, P. Kishore, P. Narender, B. Satyanarayana, *J. Mol. Catal. A: Chem.* 266 (2007) 290-293.
- [57] Q. Su, J. Sun, J. Wang, Z. Yang, W. Cheng, S. Zhang, *Catal. Sci. Technol.* 4 (2014) 1556-1562.
- [58] J. Xu, H.-T. Wu, X. Wang, B. Xue, Y.-X. Li, Y. Cao, *Phys. Chem. Chem. Phys.* 15 (2013) 4510-4517.
- [59] J.H. Sun, J.S. Zhang, M.W. Zhang, M. Antonietti, X.Z. Fu, X.C. Wang, *Nat. Commun.* 3 (2012) 1139-1145.
- [60] Y.J. Cui, J.S. Zhang, G.G. Zhang, J.H. Huang, P. Liu, M. Antonietti, X.C. Wang, *J. Mater. Chem.* 21 (2011) 13032-13039.

- [61] F.T. Li, Y.B. Xue, B. Li, Y.J. Hao, X.J. Wang, R.H. Liu, J. Zhao, *Ind. Eng. Chem. Res.* 53 (2014) 19540-19549.
- [62] W. Lu, B. Liu, Q. Qiu, F. Wang, Z. Luo, P. Zhang, S. Wei, *J. Alloy Compd.* 479 (2009) 480-483
- [63] R. Sankar, P. Manikandan, V. Malarvizhi, T. Fathima, K.S. Shivashangari, V. Ravikumar, *Spectrochim. Acta. A* 121 (2014) 746-750.
- [64] R. Sankar, R. Maheswari, S. Karthik, K.S. Shivashangari, V. Ravikumar, *Mater. Sci. Eng. C* 44 (2014) 234-239.
- [65] J. Zhang, J. Buffle, *J. Colloid Interface Sci.* 174 (1995) 500-509.
- [66] H. Alinezhad, A. H. Haghghi, F. Salehian, *Chin. Chem. Lett.* 21 (2010) 183-186.
- [67] G.M. Patel, P.T. Deota, *Heterocycl. Commun.* 19 (2013) 421-424.
- [68] A.R. Karimi, Z. Dalirnasab, G.H. Yousefi, A. Akbarizadeh, *Res. Chem Intermed.* 41 (2015) 10007-10016
- [69] B.V. Subba Reddy, N. Rajeswari, M. Sarangapani, Y. Prashanthi, R.J. Ganji, A. Addlagatta, *Bioorg. Med. Chem. Lett.* 22 (2012) 2460-2463.
- [70] K. Rad-Moghadam, S. Gholizadeh, *Iran J. Catal.* 4 (2014) 41-47.
- [71] M.A. Nasser, F. Ahrari, B. Zakerinasab, *RSC Adv.* 5 (2015) 26517-26520.
- [72] M.A. Nasser, B. Zakerinasab, *Iran J. Catal.* 5 (2013) 109-116.