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# Recyclable, highly efficient and low cost nano-MgO for amide synthesis under SFRC: A convenient and greener 'NOSE' approach

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# ARTICLE INFO

## ABSTRACT

native for the large scale synthesis.

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# 1. Introduction

Recently, in the domain of catalysis, nano magnesium oxide (MgO) has gained a respectable status as catalyst [1,2]. MgO has a basic property which is exploited in the high-yield synthesis of important molecules [3]. Its adsorptive properties [4] can be used in toxic waste remediation [5]. It has a high activity against bacteria, spores and viruses because of its large surface area [6].

The widespread importance of amide moiety as one of the most versatile functionalities in chemistry and biology has been acknowledged [7]. Several catalysts and reagents [8–10] have been reported to effect the amidation reaction. The drawbacks inherited with these reagents and catalysts are their instability, sensitivity to moisture, harsh reaction condition, prolonged reaction time, modest yield, toxic/corrosive by-products and costly waste streams. More recently, hydroxyapatite-supported silver NPs have been used for the synthesis of amides via selective hydration of nitriles in water [10]. Kobayashi et al. reported gold or gold/iron NPs catalyzed amide synthesis [11]. Mizuno and coworkers synthesized amides by hydration of nitriles promoted by amorphous MgO using reduced amounts of water [12]. Mizuno et al. also reported the synthesis of amides by MgO promoted liquid-phase aerobic oxidation

of methylarenes using ammonia surrogates [13]. In the recent work [14], amide synthesis was achieved by water-soluble Gold/DNA catalvst. However, main difficulties associated with these cited works were very high reaction temperature, longer reaction time and application of expensive catalysts. Therefore, the synthesis of amide eliminating these drawbacks is still a demanding and challenging work for the chemists. Our group recently reported the synthesis of N-methylamide catalyzed by water tolerant zirconyl chloride under MWI [15]. Reddy et al. have reported an acknowledgeable work on nano-MgO catalyzed N-formylation of aryl/alkyl amines using formic acid under MWI [16]. As a part of our ongoing research program for the development of the 'NOSE' (Nanoparticles-catalyzed Organic Synthesis Enhancement) [17] chemistry in our laboratory, we herein report recyclable nano-MgO for the synthesis of amides 3 in good to excellent yields under SFRC by reacting carboxylic acids 1 with amines 2 (Scheme 1).

# 2. Experimental

## 2.1. General procedure for the synthesis of amides

A clean synthesis of amide derivatives has successfully been accomplished utilizing reusable nano-MgO

under 'SFRC' (solvent free reaction condition). The 'green-ness' of this protocol makes it a benign alter-

In an oven dried round bottomed flask (50 mL) nano-MgO (5.0 mol%) were added and then alky/aryl amines (5.0 mmol) and aromatic/aliphatic acid (5.0 mmol) was added. After that it was allowed to stir on a pre heated oil bath at 70 °C under aerobic condition till the required time (the progress of the reaction was judged by TLC). After the completion, the reaction mixture was brought to room temperature and ethyl acetate ( $3 \times 10 \text{ mL}$ ) was added to





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Scheme 1. General representative scheme for the synthesis of amides.



Fig. 1. EDX analysis of pure nano-MgO.

it and then centrifuged at 3500 rpm to recover the nano catalyst. Having done this, the reaction mixture was washed with water and brine, dried over anhydrous  $Na_2SO_4$ , concentrated in a rotary evaporator and finally the crude product was charged to column chromatography (ethylacetate:hexane (3:7) as an eluent) for purification and wherever necessary the products were recrystallized from hot ethanol.

# 3. Results and discussion

# 3.1. Characterization of the catalyst

To characterize nano-MgO (procured from Sigma-Aldrich), at first EDX analyses (Fig. 1) were performed to determine the elemental constituents of it. It showed that weight% of Mg and O is 57.29 and 42.71 and atomic% is 50.12 and 50.88 respectively. Thus, the EDX suggests the presence of only Mg and O in the nano-MgO sample.

For the identification of functional groups, bonding information, study of strength and fraction of hydrogen bonding, the FT-IR spectrum (Fig. 2) was recorded. It is revealed from Fig. 2 that there are two types of OH bonding exist in these spectra. First, is the



Fig. 2. FTIR spectrum of nano-MgO.

O–H stretching and bending bonded with Mg and secondly, O–H stretching and bending attached at the surface of the samples. The O–H stretching bonded with Mg appeared as a sharp peak at  $3703 \text{ cm}^{-1}$ , bending bond at  $1443 \text{ cm}^{-1}$ . For the second, O–H stretching appeared as a broad band at  $3430 \text{ cm}^{-1}$  while the bending at  $1630 \text{ cm}^{-1}$ . These bands had been previously characterized by several researchers [18,19].

The result from X-ray diffractogram (Fig. 3) presented the peaks corresponding to  $(2 \ 1 \ 1)$ ,  $(2 \ 2 \ 0)$ ,  $(3 \ 1 \ 1)$ ,  $(4 \ 1 \ 1)$  and  $(3 \ 3 \ 1)$  planes that gave a clear indication of the existence of cubic primitive MgO with a lattice constant *a*, of 0.4839 nm and the peaks can be assigned to the pure phase of MgO (JCPDS PDF # 76-1363).

The crystalline sizes were determined by using Scherrer equation by considering the two intense peaks (2 2 0) and (3 1 1) from XRD pattern. The crystalline sizes were found to lie between 17.4 and 16.4 nm calculated from the X-ray line broadening by applying full width half maximum (FWHM) of characteristic peaks (2 2 0) and (3 1 1) to the Scherrer equation. The theoretical particle size was also calculated from the surface area assuming particles to be spherical in shape and the average particle diameter calculated was 18.12 nm ( $S_{\text{BET}}$  = 92.458 m<sup>2</sup> g<sup>-1</sup> and  $\rho$  = 3.58 g cm<sup>-3</sup>). The total pore volume of MgO nanopowder is found to be 0.4313 mLg<sup>-1</sup>.

The surface morphology of nano-MgO was studied using scanning electron microscope (Fig. 4(A) and (B)). It is evident from Fig. 4(A) and (B) that the MgO NPs has an irregular shape and poor microstructure resulting from agglomeration of MgO particles.

Particle size and external morphology of nano-MgO particles were observed on a transmission electron microscope (Fig. 5). Fig. 5(A) shows isolated particles with an average diameter of  $45 \pm 2$  nm as well as a network of connected particles. The particles with an average diameter of  $15 \pm 2$  nm and  $6 \pm 2$  nm can be evident



Fig. 3. XRD pattern of MgO nanoparticles.



Fig. 4. SEM micrographs of (A) MgO nanopowder at lower resolution and (B) MgO nanopowder at higher resolution.



Fig. 5. TEM images of nano-MgO at (A) 0.5 µm, (B) 50 nm and (C) 20 nm.

from Fig. 5(B) and (C). It can also be seen that some agglomeration was present and this was attributed to the large surface area of nano-MgO.

The TGA curve measures the compositional changes associated with the calcinations processes and is shown in Fig. 6. The two step pattern of weight loss has been indicated in Fig. 6 in the temperature range of around 110 °C and 345 °C.

# 3.2. Optimization of the reaction condition

To optimize the reaction condition (Table 1), a model reaction (Scheme 2) between benzoic acid 1a (1 mmol, 122 mg) and aniline



2a (1 mmol, 0.09 mL) was considered. The reaction progress was monitored initially at room temperature and then by heating on preheated oil bath up to 120°C. Under this condition the reaction did not proceed and the starting materials remained intact (Table 1, entry 1). Then we increased the temperature up to 150 °C maintaining the same reaction condition but it also failed to yield the product (Table 1, entry 2). Observing these negative results, the importance of catalyst was realized. With this notion in mind, we started the reaction with 10 mol% of nano-MgO at 120 °C that provided 32% yield (Table 1, entry 3). Next, we carried out the same reaction at 70 °C expecting a better outcome with shorter rate. To our delight, a yield of 70% was obtained (Table 1. entry 4). For further improvement in the yield of amide and to understand the role of nano-MgO, the model reaction was performed at low catalyst loading. Significant increase in product formation was observed using 5 mol% of nano-MgO which gave 96% yield in 10 min (Table 1, entry 6). Increasing the catalyst loading to more than 5 mol% might have reduced the surface area due to the aggregation of the particles which in turn decreased the yield of the desired products. The results of catalyst loading (Table 1, entries 4-8) indicate that catalytic activity of nano-MgO increases from 1 to 3 mol%, attains the maximum activity at 5 mol% and after that





Scheme 2. Model reaction.

| Table 1            |                  |
|--------------------|------------------|
| Catalyst screening | and optimization |

| Entry           | Catalyst                       | Solvent            | Temp. (°C) | Time (h) | Yield (%) <sup>b</sup> | TON  |
|-----------------|--------------------------------|--------------------|------------|----------|------------------------|------|
| 1               | None                           | SFRC               | 120        | 9        | NR <sup>c</sup>        | 0    |
| 2               | None                           | SFRC               | 150        | 9        | NR <sup>c</sup>        | 0    |
| 3 <sup>d</sup>  | Nano-MgO <sup>i</sup>          | SFRC               | 120        | 2        | 32                     | 12.8 |
| 4 <sup>d</sup>  | Nano-MgO <sup>i</sup>          | SFRC               | 70         | 1        | 70                     | 28   |
| 5 <sup>e</sup>  | Nano-MgO <sup>i</sup>          | SFRC               | 70         | 50 min   | 74                     | 29.6 |
| 6 <sup>f</sup>  | Nano-MgO <sup>i</sup>          | SFRC               | 70         | 10 min   | 96                     | 38.4 |
| 7 <sup>g</sup>  | Nano-MgO <sup>i</sup>          | SFRC               | 70         | 1.5      | 64                     | 25.6 |
| 8 <sup>h</sup>  | Nano-MgO <sup>i</sup>          | SFRC               | 70         | 3        | 30                     | 12   |
| 9 <sup>f</sup>  | Et <sub>3</sub> N              | SFRC               | 70         | 7        | 5                      | 2    |
| 10 <sup>f</sup> | Imidazole                      | SFRC               | 70         | 7        | 12                     | 4.8  |
| 11 <sup>f</sup> | Pyridine                       | SFRC               | 70         | 7        | 5                      | 2    |
| 12 <sup>f</sup> | PPh <sub>3</sub>               | SFRC               | 70         | 7        | Trace                  | 0    |
| 13              | K <sub>2</sub> CO <sub>3</sub> | SFRC               | 70         | 7        | Trace                  | 0    |
| 14              | Nano-MgO <sup>i</sup>          | CH <sub>3</sub> CN | 70         | 3        | 35                     | 14   |
| 15              | Nano-MgO <sup>i</sup>          | H <sub>2</sub> O   | 70         | 5        | 30                     | 12   |
| 16              | Nano-MgO <sup>i</sup>          | CH <sub>3</sub> OH | 70         | 5        | >27                    | 10.8 |
| 17              | Nano-MgO <sup>i</sup>          | THF                | 70         | 4        | 40                     | 16   |
| 18              | Nano-MgO <sup>i</sup>          | Toluene            | 70         | 6        | 44                     | 17.6 |
| 19              | Nano-MgO <sup>i</sup>          | DMSO               | 70         | 2        | 20                     | 8    |
| 20              | Nano-MgO <sup>i</sup>          | Xylene             | 70         | 5        | 60                     | 24   |
| 21              | Nano-MgO <sup>i</sup>          | DMF                | 70         | 8        | 64                     | 25.6 |
| 22 <sup>f</sup> | Bulk-MgO                       | SFRC               | 70         | 8        | 23                     | 9.2  |

<sup>a</sup> Reaction condition: **2a** (0.2 mL, 3 mmol), **1a** (366 mg, 3 mmol), SFRC or solvent (5 mL).

<sup>c</sup> No reaction.

<sup>d</sup> 10 mol% catalyst was used.

e 7 mol% catalyst was used.

<sup>f</sup> 5 mol% catalyst was used.

<sup>g</sup> 3 mol% catalyst was used.

h 1 mol% catalyst was used.

<sup>i</sup> Particles size (17.4–16.4 nm).

it starts decreasing. Increasing the catalyst loading to more than 5 mol% might have reduced the surface area due to the aggregation of the particles which in turn decreased the yield of the desired products. It is important to note that when the model reaction was performed at different mol% (other than 5 mol%) of nano-MgO by keeping the scavenging time constant (10 min), poor yields (5–19%) were obtained. As nano-MgO is basic in nature, therefore, we compared the catalytic activity of nano-MgO with several base catalysts (Table 1). It is evident from the Table 1 that nano-MgO showed the best performance amongst all as some of the catalysts decomposed at 70 °C (Table 1, entry 9). In some cases, catalyst isolation was noticeably tedious (Table 1, entries 10 and 11) and a few of them provided trace yield (Table 1, entry 12). We have also checked the effect of solvent on the yield and the rate of the amide formation. However, application of solvent could not dramatically enhance both the rate and yield of amide at 70 °C using 5 mol% of nano-MgO (Table 1, entries 14-21). When bulk MgO was introduced in the model reaction for comparing its activity with the nano-MgO, it was observed that bulk MgO could catalyze the reaction by giving poor yield and longer reaction time (Table 1, entry 22). The crucial breakthrough was observed under SFRC (Table 1, entry 6). The turn over number (TON) was also calculated for each catalyst and the graph is shown in Fig. 7. From the graph it is seen that the TON was the highest under SFRC at 70 °C. These outcomes provoked us to continue the reaction under SFRC using our 'NOSE' approach.

#### 3.3. Basicity measurement of nano-MgO

The basicity of nano-MgO was determined using Hammett indicator and benzoic acid titration method [20,21]. The following Hammett indicators with their base strength (H\_) were used for the basicity determination: Bromothymol Blue (H\_=7.2), phenolphthalein (H\_=9.8), 2,4-dinitroaniline (H\_=15.0) and 4-nitroaniline (H\_=18.4). With all these indicators except for 4-nitroaniline a change in color was observed. Thus, the strength of basicity of nano-MgO used in this study is in the range  $9.8 < H_{-} < 15.0$ . The basic strength and total basicity of various loading of nano-MgO is presented in Table 2. Nano-MgO has the stronger base strength and a higher amount of basicity at 5 mol% loading (Table 2, entry 3) than the mentioned ones (Table 2, entries 1–2 and 4–5).

As suggested by the results in Table 2, strong base sites are difficult to generate with low loading of nano-MgO (Table 2, entries 1 and 2). When the loading of nano-MgO was increased to 7 mol% and 10 mol%, the base strength also got decreased which might be attributed to the aggregation of particles reducing the active sites and surface area. Hence, nano-MgO attained the maximum basicity at 5 mol% loading for synthesizing amide in excellent yield (96%).

With this encouraging catalysis by nano-MgO in the amidation reaction, we then extended our 'NOSE' approach to other nanocatalysts considering the same model reaction (Scheme 2) to investigate the efficiency of the different nanocatalysts in the amide synthesis. The results summarized in Table 3 evident that at 5 mol% catalyst loading, only nano-MgO showed the best catalytic performance at 70 °C (Table 3, entry 7). But, the other mentioned nanocatalysts



Fig. 7. TON of various catalysts from Table 1.

<sup>&</sup>lt;sup>b</sup> Isolated yields.

# 122 Table 2

| $-$ Dank invariant viewer of an inverse interviewer of an optimal of matching of matching $v_{i}$ | Basicity and | vield of amide using | , different amount o | of loading of nano-MgO |
|---|--------------|----------------------|----------------------|------------------------|
|---|--------------|----------------------|----------------------|------------------------|

| Entry | Catalyst loading (mol%) | Basicity (mmol/g) |                 |                  | Total basicity (mmol/g) | Yield (%) <sup>a</sup> |
|-------|-------------------------|-------------------|-----------------|------------------|-------------------------|------------------------|
|       |                         | 7.2 < H_ < 9.8    | 9.8 < H_ < 15.0 | 15.0 < H_ < 18.4 |                         |                        |
| 1     | 1                       | 0.83              | 2.5             | 3.3              | 6.6                     | 30                     |
| 2     | 3                       | 1.6               | 3.8             | 5.2              | 10.6                    | 64                     |
| 3     | 5                       | 2.2               | 5.3             | 7.1              | 14.6                    | 96                     |
| 4     | 7                       | 1.9               | 4.1             | 5.7              | 11.7                    | 74                     |
| 5     | 10                      | 1.7               | 3.3             | 4.7              | 9.7                     | 70                     |

<sup>a</sup> Isolated yield.

#### Table 3

Optimization of model reaction (Scheme 2) with nanocatalysts.<sup>a</sup>

| Entry | Nanocatalysts (size)                                | Temp. (°C) | Time (min) | Yield (%) <sup>b</sup> |
|-------|---|------------|------------|------------------------|
| 1     | $\alpha$ -Fe <sub>2</sub> O <sub>3</sub> (19 nm)    | 70         | 180        | 44                     |
| 2     | $\gamma$ -Fe <sub>2</sub> O <sub>3</sub> (8 nm)     | 70         | 100        | 35                     |
| 3     | Fe <sub>2</sub> O <sub>3</sub> (12 nm)              | 70         | 90         | 40                     |
| 4     | Fe <sub>3</sub> O <sub>4</sub> (<50 nm)             | 70         | 60         | 55                     |
| 5     | FeO(OH) (20–40 nm)                                  | 70         | 80         | 36                     |
| 6     | TiO <sub>2</sub> (<80 nm)                           | 70         | 300        | Trace                  |
| 7     | MgO (17.4–16.4 nm)                                  | 70         | 10         | 96                     |
| 8     | Basic Al <sub>2</sub> O <sub>3</sub> (37.4–39.7 nm) | 70         | 60         | 15                     |

<sup>a</sup> 5 mol% of catalyst was used.

<sup>b</sup> Isolated yield.

provided comparatively poorer yield at 70  $^\circ\text{C}$  with longer reaction time.

#### 3.4. Synthesis of amide derivatives catalyzed by nano-MgO

Prompted by this convenient experimental reaction condition, we next approached to assess the generality of various aromatic, heterocyclic and aliphatic amines with carboxylic acids under the standardized condition and the outcomes are summarized in Table 4. It can be seen from Table 4 that nano-MgO exhibits outstanding activity in the amide synthesis for both electron rich and electron poor anilines and benzoic acids (Table 4, entries 1-15). However, anilines substituted with electron withdrawing groups gave slightly lower yields (Table 4, entries 4, 5 and 8-10) than those substituted with electron donating moieties (Table 4, entries 11-15). Benzoic acid having electron donating groups produced higher yield (Table 4, entry 3) than those with electron pulling motifs (Table 4, entries 2, 6 and 7). Benzylamine also reacted with several aromatic acids providing good to excellent yields (Table 4, entries 16-18). Aliphatic amines under the present reaction condition when treated with benzoic acid gave excellent yields (Table 4, entries 19 and 20). 2,6-Dimethyl-4-nitro-phenylamine having both electron pulling and pushing groups on the benzene ring also provided high yield (Table 4, entry 21). Benzylamine underwent reaction readily with phenylacetic acid producing good yield (Table 4, entry 22). We also studied the reaction of acetic acid with aniline substituted with both electron donating and electron withdrawing groups and we obtained acetamide derivatives in good to excellent yields (Table 4, entries 23-33). It is interesting to note that when o-phenylenediamine was treated with acetic acid, instead of amide bond formation, cyclization occurred affording 2-methylbenzimidazole in excellent yield (Table 4, entry 34). Aliphatic amines also reacted with acetic acid to furnish the products in excellent vields (Table 4, entries 35 and 36). The reaction of propanoic acid and butanoic acid with aryl amines also afforded the expected products in elevated yields (Table 4, entries 37 and 38). The reaction of methylamine with propanoic acid, and aniline with cyclohexanoic acid also proceeded efficiently giving the corresponding products in good yields (Table 4, entries 39 and 40). The attempts of producing amides using cyanoacetic acid and trifluoroacetic acid failed under the current methodology. It might be due to the fast decarboxylation under the reaction condition and rapidly formed carboxylate salts of aniline decomposed kinetically before condensation with amines. However, dicarboxylic acids (such as adipic and malonic acid) and the long chain monocarboxylic acids (such as lauric and behenic acid) remained unreactive with aniline even after stirring at 80–100 °C for more than 24 h. The tolerability of different electron withdrawing and electron donating groups in the amines established the compatibility of those moieties toward the reaction condition.

In the plausible mechanism, it has been hypothesized that nano-MgO activates the aryl/alkyl carboxylic acid on its surface



Scheme 3. Tentative mechanism for the synthesis of amides.

| Table 4                                   |
|---|
| Nano-MgO catalyzed synthesis of amides 3. |

| Entry             | R <sub>1</sub>                                   | R <sub>2</sub>   | Time (min) | Yield (%) <sup>a,b</sup> | Melting point (°C) |
|-------------------|--|--|------------|--------------------------|--------------------|
| 1                 | C <sub>6</sub> H <sub>5</sub>                    | C <sub>6</sub> H <sub>5</sub>  | 10         | 96                       | 162.5-163.5        |
| 2                 | $4-ClC_6H_4$                                     | $C_6H_5$   | 18         | 92                       | 200.3-201.3        |
| 3                 | 2-OHC <sub>6</sub> H <sub>4</sub>                | C <sub>6</sub> H <sub>5</sub>  | 15         | 94                       | 137.2-138.3        |
| 4                 | C <sub>6</sub> H <sub>5</sub>                    | 3-ClC <sub>6</sub> H <sub>4</sub>  | 15         | 90                       | 172.2-173.4        |
| 5                 | C <sub>6</sub> H <sub>5</sub>                    | 4-ClC <sub>6</sub> H <sub>4</sub>  | 17         | 90                       | 177.0-178.7        |
| 6                 | $3-NO_2C_6H_4$                                   | $C_6H_5$   | 20         | 92                       | 93.1-94.6          |
| 7                 | $4-NO_2C_6H_4$                                   | $C_6H_5$   | 22         | 92                       | 98.0-100.4         |
| 8                 | C <sub>6</sub> H <sub>5</sub>                    | $2-NO_2C_6H_4$   | 20         | 90                       | 95.4-96.8          |
| 9                 | C <sub>6</sub> H <sub>5</sub>                    | $3-NO_2C_6H_4$   | 19         | 90                       | 156.2-157.2        |
| 10                | C <sub>6</sub> H <sub>5</sub>                    | $4-NO_2C_6H_4$   | 25         | 90                       | 196.8-198.5        |
| 11                | C <sub>6</sub> H <sub>5</sub>                    | $2-OCH_3C_6H_4$  | 10         | 96                       | 58.1-59.8          |
| 12                | C <sub>6</sub> H <sub>5</sub>                    | 3-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>                                     | 10         | 96                       | 104.1-105.3        |
| 13                | C <sub>6</sub> H <sub>5</sub>                    | $4-OCH_3C_6H_4$  | 10         | 96                       | 155.3-156.3        |
| 14                | C <sub>6</sub> H <sub>5</sub>                    | $2-CH_3C_6H_4$   | 10         | 95                       | 144.5-145.5        |
| 15                | C <sub>6</sub> H <sub>5</sub>                    | $4-CH_3C_6H_4$   | 10         | 95                       | 156.5-157.2        |
| 16                | C <sub>6</sub> H <sub>5</sub>                    | C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>  | 12         | 98                       | 106.6-107.5        |
| 17                | 4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> | C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>  | 16         | 91                       | с                  |
|                   | $\sim$   |  |            |                          |                    |
| 18                |  | $C_6H_5CH_2$   | 27         | 88                       | d                  |
| 19                | C <sub>6</sub> H <sub>5</sub>                    | CH <sub>3</sub>  | 10         | 98                       | 76.1-78.1          |
| 20                | C <sub>6</sub> H <sub>5</sub>                    | C <sub>6</sub> H <sub>11</sub>   | 30         | 92                       | 144.7-145.2        |
| 21                | C <sub>6</sub> H <sub>5</sub>                    | 2,6-(CH <sub>3</sub> ) <sub>2</sub> -4-NO <sub>2</sub> C <sub>6</sub> H <sub>2</sub> | 22         | 90                       | 195.1-197.1        |
| 22                | C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>    | $C_6H_5CH_2$   | 33         | 90                       | 118.1-119.5        |
| 23                | CH <sub>3</sub>                                  | C <sub>6</sub> H <sub>5</sub>  | 10         | 98                       | 111.0-112.8        |
| 24                | CH <sub>3</sub>                                  | 2-ClC <sub>6</sub> H <sub>4</sub>  | 20         | 96                       | 88.7-89.1          |
| 25                | CH <sub>3</sub>                                  | 3-ClC <sub>6</sub> H <sub>4</sub>  | 17         | 92                       | 179.3-180.9        |
| 26                | CH <sub>3</sub>                                  | $2-NO_2C_6H_4$   | 20         | 90                       | 93.3-94.2          |
| 27                | CH <sub>3</sub>                                  | $3-NO_2C_6H_4$   | 30         | 90                       | 156.6-158.0        |
| 28                | CH <sub>3</sub>                                  | $4-NO_2C_6H_4$   | 33         | 88                       | 208.4-209.8        |
| 29                | CH <sub>3</sub>                                  | $4-OCH_3C_6H_4$  | 15         | 97                       | 137.7-138.4        |
| 30                | CH <sub>3</sub>                                  | $4-CH_3C_6H_4$   | 15         | 97                       | 154.0-155.0        |
| 31                | CH <sub>3</sub>                                  | $4-OHC_6H_4$   | 10         | 93                       | 170.5-171.8        |
| 32                | CH <sub>3</sub>                                  | 4-COOHC <sub>6</sub> H <sub>4</sub>  | 35         | 91                       | 259.3-261.9        |
| 33                | CH <sub>3</sub>                                  | $C_6H_5CH_2$   | 25         | 95                       | 60.5-62.0          |
| 34 <sup>e,f</sup> | CH <sub>3</sub>                                  | $2-NH_2C_6H_4$   | 30         | 94                       | 175.6-177.1        |
| 35                | CH <sub>3</sub>                                  | CH₃  | 60         | 98                       | 26.1-27.5          |
| 36                | CH <sub>3</sub>                                  | C <sub>6</sub> H <sub>11</sub>   | 80         | 96                       | 101.0-103.3        |
| 37                | CH <sub>3</sub> CH <sub>2</sub>                  | C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>  | 90         | 89                       | 128.3-129.1        |
| 38                | CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub>  | C <sub>6</sub> H <sub>5</sub>  | 120        | 90                       | 93.6-94.8          |
| 39                | CH <sub>3</sub> CH <sub>2</sub>                  | CH <sub>3</sub>  | 85         | 92                       | d                  |
| 40                | C <sub>6</sub> H <sub>11</sub>                   | C <sub>6</sub> H <sub>5</sub>  | 30         | 90                       | 148.2-149.5        |

<sup>a</sup> Yields refer to the isolated pure products.

<sup>b</sup> Products were characterized by IR and NMR (<sup>1</sup>H and <sup>13</sup>C) spectroscopy, MS and also by comparing their melting points with the authentic ones.

<sup>c</sup> Colorless oil.

<sup>d</sup> Liquid compound.

<sup>e</sup> 2 equiv. of acetic acid was used.

<sup>f</sup> 2-Methylbenzimidazole was formed.

throughout the formation of amides (Scheme 3). A mechanism akin to this has been reported previously [16].

# 3.5. Recycling experiment of nano-MgO

The recyclability of a catalyst is a key point in the framework of green chemistry. The recycling experiment for nano-MgO was carried out by considering the model reaction under the standardized condition (Scheme 2).

After the reaction, ethyl acetate was poured into the reaction mixture and then ultra centrifuged (3500 rpm) to pellet out the nano-MgO. The separated particles were washed with hot ethanol ( $5 \times 10 \text{ mL}$ ) to remove all the organic impurities. Finally, it was decanted and dried in an oven at  $100 \,^{\circ}$ C for 7 h. Then the catalyst was reused in the next run in the reaction as shown in Scheme 4.



Scheme 4. Measurement of green metrics.

It is demonstrated in the Table 5 that nano-MgO maintained its catalytic activity up to the 5th cycle and after that yield of *N*-phenylbenzamide went down markedly.

In the present work, we also conducted a comparative study on FTIR spectra of fresh and reused nano-MgO (after 5th run). It is found that there are shifts in the values of stretching frequencies as depicted in Fig. 8(A) which may be the reason for lower yield of *N*-phenylbenzamide (Scheme 4) after 5th run. Moreover, there is an appearance of a new peak at 1121 cm<sup>-1</sup> which might be due to the presence of impurity after 5th run. The scanning electron micrograph of recycled nano-MgO after 5th run (Fig. 8(B)) was also recorded. The recovered nano-MgO after 5th cycle showed a clear picture of highly agglomerated particles whose omnipresence in the reaction system might play a key role in reducing the yield of the product and in increasing time.

The TEM image of reused nano-MgO after 5th run (Fig. 9(A)) manifested the rupture in the network of connected particles which might have taken part in the marginal loss of its activity. The network structure of nano-MgO may have tailored its high catalytic activity. The XRD pattern of fresh nano-MgO was also compared with reused one (after 5th run) and is shown in Fig. 9(B). It showed some important changes. Thus, it is evident (Fig. 9(B)) that the

# Table 5

Reusability of nano-MgO on the yield of N-phenylbenzamide.

| No. of cycles <sup>a</sup>           | Fresh    | 1st run  | 2nd run  | 3rd run  | 4th run  | 5th run  | 6th run  | 7th run  |
|--------------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|
| Yield (%) <sup>b</sup><br>Time (min) | 96<br>10 | 96<br>10 | 96<br>10 | 96<br>10 | 96<br>10 | 96<br>10 | 88<br>30 | 80<br>60 |
| TON                                  | 38.4     | 38.4     | 38.4     | 38.4     | 38.4     | 38.4     | 35.2     | 32       |

<sup>a</sup> Reaction condition: 5 mmol aniline, 5 mmol benzoic acid, 0.25 mmol (5 mol%) nano basic MgO, 70 °C.

<sup>b</sup> Yields refer to the isolated pure *N*-phenylbenzamide.



Fig. 8. (A) Comparison of FTIR spectrum of fresh nano-MgO with recycled one after 5th run, (B) SEM micrograph of reused nano-MgO after 5th run.



Fig. 9. (A) TEM image of reused nano-MgO after 5th run, (B) comparison of XRD pattern of fresh nano-MgO with the reused one after 5th run.

sintensity of the highest peak (2 2 0) in fresh nano-MgO is decreased completely in the recycled one. Apart from this, the intensities of the peaks (3 1 1), (4 1 1) and (3 3 1) also diminished in the reused nano-MgO. It may be due to either the leaching of  $Mg^{2+}$  from MgO or blockage of the active pores which in turn perhaps reduced the yield of *N*-phenylbenzamide after 5th run (Scheme 4). Moreover, there is an appearance of a new peak at about 62° which might be referred to the impurity stuck into the catalyst during the consecutive cycles.

# 3.6. Leaching study of nano-MgO

To verify the amount of  $Mg^{2+}$  lost from nano-MgO during its recycling (after 5th cycle) which caused decrease in the yield of amidation product, the leaching study was performed on a UV visible spectrophotometer (Fig. 10). The reused nano-MgO experienced 34.7%  $Mg^{2+}$  leaching from its surface which might have reduced its catalytic activity after 5th run (Scheme 4).

| Table | 6 |
|-------|---|
|-------|---|

| Catalysts/reagents | E-factor <sup>a</sup> | Mass intensity | Atom economy (%) | Yield (%) <sup>b</sup> |
|--------------------|-----------------------|----------------|------------------|------------------------|
| IBA <sup>c</sup>   | 251.7                 | 397.3          | 92.13            | 50 [22]                |
| CDI <sup>d</sup>   | 31.8                  | 32.9           | 53.9             | 92 [23]                |
| DCC                | 22.6                  | 67             | 48.5             | 82 [24]                |
| SOCl <sub>2</sub>  | 17                    | 25             | 85.3             | 72 [25]                |
| Sulfated tungstate | 9.3                   | 26.3           | 92.13            | 81 [26]                |
| Nano-MgO           | 1.07                  | 1.09           | 92.13            | 98 (our work)          |

<sup>a</sup> E-factor shown does not account for the waste produced in the synthesis of reagents/catalysts.

<sup>b</sup> Yield refers to the isolated pure *N*-benzylbenzamide.

<sup>c</sup> ortho-N,N-diisopropylbenzylaminoboronic acid catalyst.

<sup>d</sup> N,N-carbonyldiimidazole.



Fig. 10. UV-vis spectra of fresh and reused nano-MgO.

# 3.7. Measurement of "green-ness" by using green metrics

The "green-ness" of the present methodology was evaluated by making use of different parameters of green chemistry (Table 6), that shows the superiority of nano-MgO over other catalysts.

The waste produced during the course of the reaction is the least in our protocol compared to the other methodologies [22–26]. Moreover, the issues like solvent reusability and catalyst recyclability are omitted by *E*-factor which absolutely raises the accuracy.

#### 4. Conclusions

In conclusion, we have developed a practical and greener 'NOSE' protocol for the clean synthesis of both aliphatic and aromatic amides utilizing nano-MgO as an efficient, reusable and cheap catalyst under SFRC. Simple experimental condition, varied substrate compatibility, high yields of the products, chemo selectivity, and non-hygroscopic nature of catalyst make our protocol a more potent benign alternative over conventional ones for amide synthesis.

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# Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.apcata. 2013.02.016.

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