

Catalysis Science & Technology

Accepted Manuscript



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the [Information for Authors](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the [Ethical guidelines](#) still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.



Journal Name

ARTICLE

Amine modified mesoporous Al₂O₃@MCM-41: An efficient, synergetic and recyclable catalyst for the formylation of amines using carbon dioxide and DMAB under solvent free and mild reaction condition

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Deepak B. Nale,^a Dharitri Rath,^b K. M. Parida,^b Aravind Gajengi^a and Bhalchandra M. Bhanage^{a,*}

This work reports amine modified meso Al₂O₃@MCM-41 particularly the ordered mesoporous silica as the catalysts for the formylation of amines with carbon dioxide (CO₂) and dimethylamine-borane (DMAB) as a green reducing source. This new developed catalytic system represents a heterogeneous and environmentally benign protocol. Besides this, catalyst could be reused for five consecutive cycles without any significant loss in its catalytic activity towards the synthesis of formamides. The catalysts amine modified meso Al₂O₃@MCM-41 were well characterized by high and low angle XRD, temperature programmed desorption (TPD), BET-surface area, TGA/DTA and FT-IR analysis techniques. Effect of various reaction parameters such as temperature, CO₂ pressure, time and the ratio of substrate to DMAB for the synthesis of formamides has been investigated. The developed protocol can be applicable for the synthesis of most important key intermediates like Formoterol, Orlistat, Leucovarin and Iguratimod in the biological active compounds.

Introduction

In the last few decades, the application of carbon dioxide (CO₂, a green house gas) in the synthesis of high-value-added chemicals or fine chemicals is one of the immense importance to the synthetic as well as an environmental chemistry.¹ In view of the fact that, CO₂ is an abundant, non-toxic, inexpensive, non-flammable and therefore as a renewable C1 feedstock source in the regarding of "atom economy", "green chemistry" and "sustainable development". However, due to the inherent thermodynamic and kinetic stability of CO₂ (inertness), it is challenging to activate CO₂ and achieve its transformation especially under mild conditions.² In this respect, chemically reduction of CO₂ into organic compounds is really challenging.

In order to reduce the emission of atmospheric CO₂ to protect an environment from the global warming and utilize the carbon source, it is feasible to load amines on porous materials forming new and efficient catalysts have been explored. The catalytic reduction (by transfer hydrogenation) of CO₂ to high value-added chemical fuels,³ such as gasoline, alcohols and

also related higher long hydrocarbons, is one of the attractive approaches. In which hydrogen gas is the cleanest and most atom economical reductant, but due to harsh reaction conditions (high reaction pressure and high temperature) avoids broad application of the reducing agent. In this context, the use of boranes⁴ or hydrosilanes⁵ as reducing agents facilitated the catalytic reduction of CO₂ to the synthesis of formamides under much milder reaction conditions. For that another view is the synthesis of carbonyl containing chemicals such as oxazolidinones, carbonates, formamides, derivatives of various carbonyl compounds like, lactones, carbamates, quinazoline-2,4(1*H*,3*H*)-diones, etc.⁶ through a catalytic reaction, among all, the formation of formamides has attracted much more attention because it plays an important role in the industry.

In the literature study, the reduction of CO₂ is mainly achieved by using silanes and molecular hydrogen. But, still there is a need to develop highly desirable transition metal-free and transfer hydrogenation protocol which could minimize the number of waste streams and unit operations. Transfer hydrogenation is a more practical and consistent method as a production of hydrogen can be easily controlled in the reaction medium. Generally, NaBH₄, LiAlH₄, MgH₂, and NH₃BH₃ have been widely used as hydrogen sources.⁷ Among these, eco-friendly dimethylamine-borane (DMAB) is easily accessible, non-toxic, non-flammable, highly stable, inexpensive, water-soluble and also has a high volume to mass hydrogen density (3.5 wt%).⁸ Thus, DMAB used as a green hydrogen source for the synthesis of formamides.

^a Department of Chemistry, Institute of Chemical Technology, Matunga, Mumbai-400 019, India.

^b Department of Chemistry, Centre for Nano Science and Nano Technology, Institute of Technical Education & Research, Siksha 'O' Anusandhan University, Khandagiri, Bhubaneswar-751 030, India. Email: kulamaniparida@soauniversity.ac.in

* Corresponding author: E-mail: bm.bhanage@ictmumbai.edu.in; Tel: +91 22 33612601; Fax: +91 22 33611020;

Electronic Supplementary Information (ESI) available: [Materials and methods, ¹H, ¹³C NMR of the products]. See DOI: 10.1039/x0xx00000x

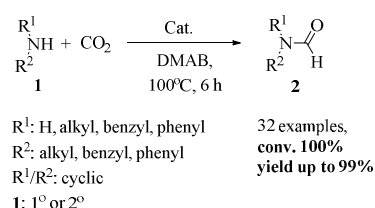
Formamide is one of the most versatile chemical and important building blocks with widespread applications in the industry as solvents, raw materials, intermediates in various synthetic processes, especially as a precursor to isocyanides and formamidines.⁹ The formamide moiety have a functional group that serves a fundamental role in protein biosynthesis and post-translational regulation steps and has a high biological activity in various pharmaceuticals drugs such as Leucovorin, Formoterol, Orlistat and Igratimod, etc.¹⁰

Traditionally, formamides are commonly produced *via* the formylation of amines. Instead of toxic CO source, we used CO₂ for the N-formylation reaction and hence CO₂ is an attractive and green alternative for the production of formamides.¹¹ However, most of the reported catalytic routes have some drawbacks such as requiring metal catalysts, toxic organic solvents, inert gas atmosphere, complicated reaction system, severe reaction conditions (*i.e.* high temperature and pressure) and difficulty in catalyst separation among others. Apart from this, narrow substrate scope, tedious work up procedures and problem in catalysts recovery which hinder the commercial feasibility of these processes. Therefore, the development of a highly efficient, simple, recyclable, green catalytic system remains a challenge. Therefore, we look for a heterogeneous and recyclable catalyst which could efficiently catalyze the formylation reaction under milder reaction conditions without the aid of phosphine ligands is focus of the present work.

Recently, researchers have interest in MCM-41 grafted with different amines which was reported to catalyze many organic syntheses.¹² Siliceous mesoporous materials in neat form are lacking active sites on their surface. Hence their applications are restricted and their surface functionalization is required essential according to their application. In order to utilize the unique properties of the mesoporous materials for specific applications like catalysis, sorption, sensing, ion exchange etc., introduction of reactive organic functional groups is performed. The incorporation of organic components as part of the silicate walls or trapped within the channels to form inorganic-organic hybrid materials remains the main issue. The advantages of these materials arise from the fact that the inorganic components can provide mechanical, thermal or structural stability, while the organic features can readily be modified for various specific applications.

Moreover, mesoporous materials with high textural properties such as high surface area, wide pore volume and narrow pore diameter have been seen as an excellent support for many catalytic applications.¹³ Mesoporous materials, basically mesoporous silica (MCM-41) and mesoporous alumina have been treated as an efficient catalyst and catalyst support for many catalyzed reactions due to high textural property, mesoporosity, high thermal stability, strong covalent character etc.¹⁴ Again, MCM-41 and mesoporous alumina with high textural properties stabilized the metal and metal ions. That means the metal and metal ions are bonded or anchored properly in the mesoporous supports like MCM-41 and mesoporous alumina which increases the catalytic activity of the materials.

The industrial interest of alumina is highlighted by its intensive use as catalyst or as catalytic support materials for the petroleum refinement and as automobile emission controller.¹⁵ The use of alumina can be ascribed to both high thermal stability and moderate Lewis acidity as well as to the fact that it is a rather inexpensive material. γ -Al₂O₃ is commonly used as support for nanocrystals of MoS₂ doped with Co or Ni for hydrodesulfurization (HDS) processes.¹⁶ Recently, high surface area nanostructured alumina has allowed increasing the catalytic behaviour of HDS catalysts.¹⁷ Therefore, it is important to develop strategies to design simple, reproducible and easy to scale-up procedures leading to high surface area, high pore volume and high pore size alumina by simple methods to be implemented in industrial processes.¹⁸ Since, the improvement of these materials (recovery and recyclability) as compared with homogeneous systems can lead to environmentally benign chemical methods. Therefore, amine modified meso Al₂O₃@MCM-41 have wide potential in designing the high performance and environmentally benign catalysts. Based on our research interest in mesoporous materials,^{6b,c} here we have reported modified mesoporous silica *i.e.* amine modified meso Al₂O₃@MCM-41 catalyst, as a solid base catalyst for formylation reaction. We envisaged that the existence of amino as a functional group of catalyst MCM-41 have a immense potential to accelerate the rate of reaction in the forward direction by transforming amine into corresponding bioactive formamide derivatives. In this present study, we have prepared mesoporous nano composites (amine modified meso Al₂O₃@MCM-41) consisting of mesoporous silica and alumina followed by amine functionalization. The inorganic-organic hybrid materials were well characterized and demonstrated as a well-organized, efficient, stable, recyclable and commercially feasible catalyst for the synthesis of formamides from CO₂ and amines by using DMAB as a hydrogen source under solvent free and mild reaction conditions (Scheme 1).



Scheme 1 Synthesis of formamide derivatives from amines, CO₂ and DMAB.

Experimental section

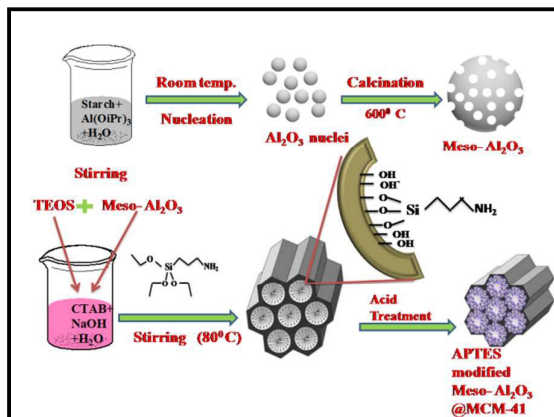
Preparation and characterization of amine modified meso Al₂O₃@MCM-41 catalyst

Synthesis of mesoporous Al₂O₃

Mesoporous Al₂O₃ (MA) was prepared using starch as template. 20.2 g of starch was dissolved in 100 mL of deionized water. Then 10.2 g of aluminium isopropoxide was added and stirred vigorously for 30 min at room temperature. The pH of the solution was maintained at 6 and then the solution was

kept as it is for 5 h. After complete hydrolysis of aluminium isopropoxide a high texture mesoporous Al_2O_3 . The mixture was dried at 100 °C in order to remove the volatile impurities. The resultant solid was calcined at 600 °C for 6 h for complete removal of the template.

General procedure for preparation of amine modified meso Al_2O_3 @MCM-41 catalysts



Scheme 2 Schematic representation for synthesis of APTES modified meso- Al_2O_3 @MCM-41.

The material was synthesized by *in situ* method. 2.4 g of Cetyltrimethylammonium bromide (CTAB) was dissolved in 200 mL of deionized water. 7 mL of 2 M NaOH solution was added and the solution was stirred at 80 °C for 30 min. The pH was balanced at 12.4. To the above solution 0.95 g of meso Al_2O_3 was added followed by 10 mL of tetra ethyl ortho silicate (TEOS) (Si/Al = 10). Different amounts of APTES (0.25 mL to 1.56 mL) were added to get different wt% of APTES modified meso Al_2O_3 @MCM-41. A white precipitate was obtained after stirring for 2 h at 80 °C.

The above products were filtered hot, washed with water and ethanol. The as synthesized material was treated with ethanol and conc. HCl (100:1) at 80 °C for 6 h to remove the surfactant. The sample was filtered, washed with ethanol and dried at 60 °C. The synthesized materials were denoted as x wt% Amine modified meso Al_2O_3 @MCM-41 (x = 3.2, 6.4, 12.8, 16.0 and 20.0 wt% respectively) (Scheme 2).

The amine modified meso Al_2O_3 @MCM-41 catalyst was well characterized by low angle XRD, temperature programmed desorption (TPD), BET-surface area, FT-IR and TGA/DTA analysis techniques.

The high angle ($2\theta = 10\text{--}70^\circ$) XRD peaks are due to mesoporous crystalline Al_2O_3 . The sharp peaks are assigned to the 220, 311, 222, 400, 511 and 440 reflection planes of γ - Al_2O_3 (JCPDS, 10-0425).¹⁹ The different wt% of APTES loading influenced the material crystallinity. The 6.4 wt% APTES loaded Al_2O_3 /MCM-41 shows the sharp peaks and then after the intensity of the peaks decreased gradually. This may be due to the multi layer of amine deposition on the surface of Al_2O_3 /MCM-41. As a result, the long range ordering and crystallinity of the materials are affected.

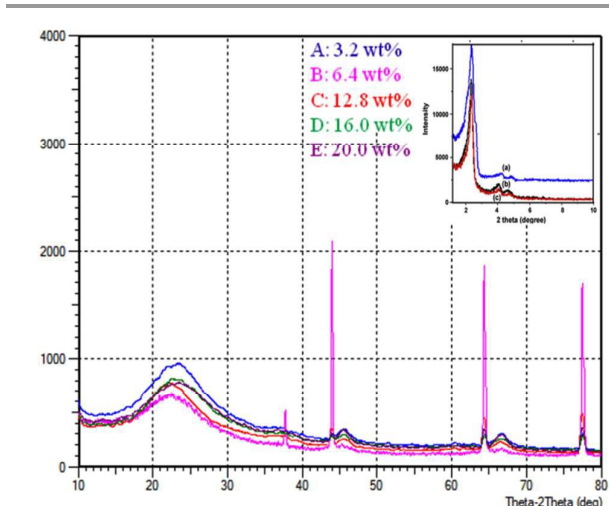


Figure 1 XRD of APTES meso Al_2O_3 @MCM-41 (Low angle XRD inserted above).

A) 3.2 wt% APTES meso Al_2O_3 @MCM-41, B) 6.4 wt% APTES meso Al_2O_3 @MCM-41, C) 12.8 wt% APTES meso Al_2O_3 @MCM-41, D) 16 wt% APTES meso Al_2O_3 @MCM-41, E) 20 wt% APTES meso Al_2O_3 @MCM-41.

The low angle XRD patterns for MCM-41, Al_2O_3 @MCM-41 composite and 16 wt% of APTES modified composites are shown in figure 1. All the samples showed a typical mesoporous structure with three sharp peaks corresponding (100), (110) and (200) planes which indicate the long range ordering in the materials. After the modification with APTES, the intensity of the peak is slightly reduced and peak position is slightly shifted towards right but this material still remained intact and shows the mesoporosity like MCM-41.

N_2 adsorption-desorption study

The N_2 adsorption-desorption isotherm and pore size distribution of MCM-41, meso Al_2O_3 , Al_2O_3 @MCM-41 and 16 wt% APTES Al_2O_3 @MCM-41 are shown in the figure S1(a-c) and figure S2 respectively (See ESI). The textural properties such as BET surface area, pore diameter and pore volume derived from the N_2 adsorption-desorption measurements are included in Table S1 (See ESI). N_2 sorption resulted typical type IV isotherm which is defined by Brunauer *et al.*²⁰ it indicated that all the samples are mesoporous in nature. A steeper N_2 adsorption step in the mid-relative pressure range of 0.1 to 0.8 is indicative of relatively intra particle mesoporosity, which is shown in the figure S1 (See ESI). All the materials showed a monomodal peak in the pore size distribution curves (See ESI, Figure S2). The pore size of the parent meso Al_2O_3 is 7.8 nm. After APTES modification the pore size decreased up to 2-3 nm.

According to table S1 (See ESI), the BET surface area of parent MCM-41 and meso Al_2O_3 is 878 m^2/g and 213 m^2/g , respectively. The composite of the above two materials *i.e.* meso Al_2O_3 @MCM-41 showed an enhanced BET surface area of 1045 m^2/g . The increase in specific surface area value is due to substitution of Si by Al in the framework as well as formation of nanocomposites. After modification with APTES, the surface area of parent meso Al_2O_3 @MCM-41 decreases

further. This is due to the bonding of the organic amine with the Si-OH and Al-OH groups in the framework which results in surface coverage of the parent material. The pore volume data of the amine modified meso Al_2O_3 @MCM-41 also showed the same trend as that of the surface area values. From all the above surface analysis data, it is confirmed that the Al_2O_3 is modified into the framework of MCM-41 and APTES is modified onto the framework of meso Al_2O_3 @MCM-41 composite.

FTIR Analysis

The FT-IR analysis results for meso Al_2O_3 , meso Al_2O_3 @MCM-41 composite, 3.2, 6.4, 12.8 and 16 wt% of APTES modified meso Al_2O_3 @MCM-41 are shown in figure S3 (See ESI). FT-IR spectroscopy analysis data confirms the presence of different functional groups present in the synthesized materials. The broad peaks present around 3500 cm^{-1} in all the samples are due to adsorbed water by the molecules. Presence of H-O-H bending vibrations is confirmed by the peak at 1630 cm^{-1} in all the materials. The amine modified samples showed the -NH_2 bending vibrations at 1532 cm^{-1} . This peak is absent in the parent materials *i.e.* meso- Al_2O_3 and meso Al_2O_3 @MCM-41 indicating the successful incorporation of amines in the materials. In addition to that, peak at 750 cm^{-1} indicates the N-H bending vibrations in amine modified materials. The 960 cm^{-1} peak is for Al-O-Si stretching vibrations which indicate the successful modification of the parent MCM-41 frame work by Al_2O_3 .

CO_2 -TPD Analysis

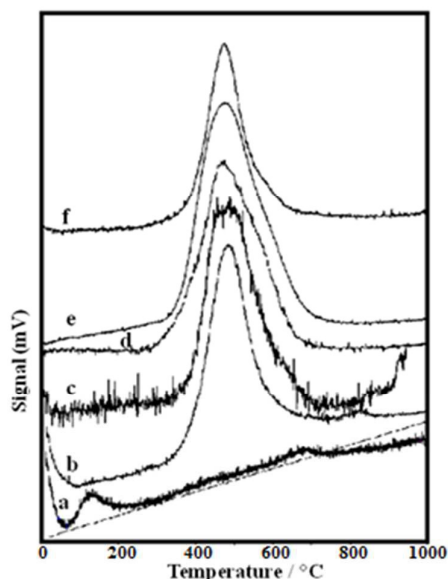


Figure 2 CO_2 -TPD of APTES modified meso Al_2O_3 @MCM-41 at different wt% of (a) 0 (b) 3.2 (c) 6.4 (d) 12.8 (e) 16.0 (f) 20.0

The CO_2 TPD of all the amine modified meso Al_2O_3 @MCM-41 are recorded and shown in figure 2. It is the property to measure the basic sites present in the sample. All the samples

showed sharp peaks ranging from $400\text{ }^\circ\text{C}$ to $800\text{ }^\circ\text{C}$. The peaks are due to both the physically and chemically adsorbed CO_2 . This indicates that the APTES modified materials contain strong basic sites required for the organic condensation reactions. The 16 wt% APTES modified meso Al_2O_3 @MCM-41 showed the highest CO_2 adsorption ($1564\text{ }\mu\text{mole/g}$) hence expected to have highest basic sites.

Thermo-gravimetric Analysis

The thermal gravimetric analysis (TGA) of Al_2O_3 @MCM-41 and APTES modified meso Al_2O_3 @MCM-41 samples are shown in figure S4 (See ESI). All the samples showed weight loss in three stages. First peak is below $120\text{ }^\circ\text{C}$, second is in the range $300\text{--}400\text{ }^\circ\text{C}$ and the third is a broad peak around $500\text{ }^\circ\text{C}$. The highest weight loss is at $120\text{ }^\circ\text{C}$ is for removal of physically adsorbed water molecules. Compared to parent Al_2O_3 @MCM-41, amine modified samples showed a higher rate of weight loss indicating the functionalization of APTES with Al_2O_3 @MCM-41. The weight loss around $300\text{--}400\text{ }^\circ\text{C}$ is due to break down of APTES-O-Al (in case of substituted Si-O bond by Al-O bond) or APTES-O-Si linkage. The highest temperature peak (around $500\text{ }^\circ\text{C}$) is due to removal of surfactant from the materials.

Differential Thermal Analysis

The differential thermal analysis curves for amine modified meso Al_2O_3 @MCM-41 is shown in figure S4 (See ESI). The DTA curves are complementing the TGA curves very well. They showed three endothermic peaks correspond to the three peaks in TGA pattern. The first peak (around $100\text{ }^\circ\text{C}$) is due to removal of water. The second and third peaks (at $300\text{--}400\text{ }^\circ\text{C}$ and $500\text{ }^\circ\text{C}$) correspond to the removal of amine and surfactant respectively.

General experimental procedure for synthesis of formamides from amine, CO_2 and DMAB

The experiments were carried out in a 100 mL high-pressure reactor, in a typical reaction procedure; the catalyst (15 wt% with respect to starting substrate) was introduced into a reactor containing amine (1 mmol), DMAB (2 mmol), CO_2 pressure (2 MPa) at room temperature and then reactor pressurized to 2.0 MPa of CO_2 pressure and heated to a specified temperature. After the completion of reaction, the autoclave was cooled to room temperature and then the excess CO_2 was released slowly. The resultant reaction mixture filtered off by simple filtration. The filtrate was then collected in sample vial and the product was extracted for further analysis which confirmed by GC, GC-MS, ^1H and ^{13}C NMR spectroscopic techniques and also matched with those of reported authentic data.

Results and discussion

Catalytic activity of amine modified meso Al_2O_3 @MCM-41 catalysts

We have developed an efficient methodology for the synthesis of formamides (**2a–2ff**) derivatives from various amines

(1a–1ff) with CO₂ as a C1 source and DMAB as the green reductant by using amine modified meso Al₂O₃@MCM-41 under solvent free and mild reaction condition (Table 3, entries 1-32). We have prepared six types of thermally stable and covalently linked amines loaded on the meso Al₂O₃@MCM-41 catalysts by varying the amine loading such as 0, 3.2, 6.4, 12.8, 16.0 and 20.0 wt%, respectively (Table 1, entries 1-7). Initially, the reaction was carried out in the absence of catalyst and it was found that the desired product was not afforded indicating that the amine modified meso Al₂O₃@MCM-41 was only responsible for the formation of desired product (Table 1, entry 1). On the other hand, we noticed that 16 wt% amine modified meso Al₂O₃@MCM-41 catalyst is the best among all, to furnish the desired product up to 99 % as an isolated yield of **2a** (Table 1, entry 6).

Further, we have carefully performed the reactions in presence of meso Al₂O₃ and amine (APTES) without support as catalysts to the formylation of amines with CO₂ and DMAB, it was found that the formation of the desired product in lower yield (Table 1, entries 8 and 9).

Table 1 Catalyst screening for the formylation of *N*-benzylmethylamine.^a

Entry	Wt% of amine loaded on Al ₂ O ₃ @MCM-41 catalyst	Yield (%) ^b
1	-	n.d.
2	0 (meso Al ₂ O ₃ @MCM-41)	10
3	3.2	62
4	6.4	70
5	12.8	89
6	16.0	99
7	20.0	99
8	meso-Al ₂ O ₃	12
9	APTES without support	25

^a Reaction conditions: *N*-benzylmethylamine (1 mmol), catalyst (15 wt% with respect to starting substrate), CO₂ pressure (2 MPa), DMAB (2 mmol), temperature (100 °C), time (6 h). ^b Based on GC-GC/MS analysis. The yield is quantified by using the external standard method using *N*-benzyl-*N*-methylformamide as a reference compound. n.d. = not detected. APTES = (3-Aminopropyl)triethoxysilane.

In order to optimize the reaction parameters, the preliminary studies were carried out by using amine modified meso Al₂O₃@MCM-41 (16 wt%) as a choice of catalyst for the synthesis of formamides from amines and CO₂ as a best model reaction. Various reaction parameters such as catalyst screening, catalyst loading, temperature, pressure, time and DMAB ratio were studied.

Effect of Catalyst Loading

Next, the experiments were carried out by using different catalytic concentrations of amine modified meso Al₂O₃@MCM-41 (16 wt%) for the title reaction and the distinctive results was shown in Table 2 (Entries 1–3). It was examined that the **2a** yield was an excellent and almost constant at 20 wt% and 15 wt% for this catalyst (Table 2, entries 1-2) On the other hand, by decreasing the concentration of catalyst, decrease in yield of the desired product was obtained (Table 2, entry 3).

Thus, using amine modified meso Al₂O₃@MCM-41 (16 wt%) as the choice of catalyst, we studied the effects of other reaction parameters such as temperature, time, pressure and DMAB ratio, to estimate the scope and limitation of the present catalyst system.

Table 2 Effect of reaction parameters for the formylation of *N*-benzylmethylamine.^a

Entry	1:DMAB (mmol)	Cat. (wt%)	CO ₂ (MPa)	Temp. (°C)	Time (h)	Yield of 2a (%) ^b
<i>Catalyst loading</i>						
1	1:2	20	2	100	6	99
2	1:2	15	2	100	6	99
3	1:2	10	2	100	6	90
<i>Effect of Temperature</i>						
4	1:2	15	2	120	6	99
5	1:2	15	2	80	6	79
6	1:2	15	2	60	6	51
<i>Effect of Time</i>						
7	1:2	15	2	100	10	99
8	1:2	15	2	100	8	99
9	1:2	15	2	100	4	81
<i>Effect of CO₂ pressure</i>						
10	1:2	15	4	100	6	99
11	1:2	15	3	100	6	99
12	1:2	15	1	100	6	76
<i>Effect of DMA-borane</i>						
13	1:4	15	2	100	6	99
14	1:0	15	2	100	6	n.d.

^a Reaction conditions: *N*-benzylmethylamine (mmol), catalyst (wt% with respect to starting substrate), CO₂ pressure (MPa), DMAB (mmol), temperature (°C), time (h). ^b Based on GC-GC/MS analysis. The yield is quantified by using the external standard method using *N*-benzyl-*N*-methylformamide as a reference compound. n.d. = not detected.

Effect of temperature

We have also performed the reactions to observe the effect of temperature ranging from 60 °C to 120 °C was screened on the yield of **2a** (Table 2, entries 4-6). The experimental studies revealed that 100 °C was the optimum temperature required to reach the highest yield of **2a**.

Effect of Pressure and time

The effect on reaction time was studied and it was observed that increasing the time from 4 h to 10 h, increase in yield of the desired product was obtained (Table 2, entries 7-9). As the time increases, the yield of **2a** was remains the same with increasing the time from 6 to 10 h, indicating that the completion of the reaction in 6 h (Table 2, entries 2, 7, 8). Therefore, 6 h is optimum reaction time.

Next, the study of CO₂ pressure on the yield of **2a** was examined at 100 °C in 6 h shown in Table 2 (Entries 10-12). The yield of **2a** increased significantly with increasing the CO₂ pressure from 1 to 2 MPa, but above increasing the pressure from 2 to 4 MPa, the yield was not so changed. Hence, the optimum reaction pressure was achieved at 2 MPa.

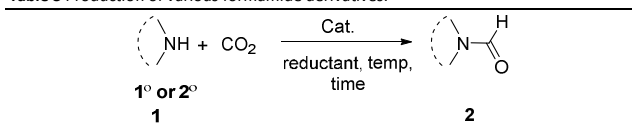
Effect of Substrate to DMAB ratio

Besides this, we have also studied the effect of mole ratio of amine to DMAB and it was shown that, without DMAB the reaction did not offer the desired product (Table 2, entry 14). Subsequently, it was found that 1 mmol of amine and 2 mmol of DMAB was furnished the higher yield of the desired product while further increasing the concentration to 4 mmol, the yield remained constant at 6 h. Hence, the best optimized reaction conditions for the desired product **2a** are: *N*-benzylmethylamine (1.0 mmol), catalyst amine modified meso Al₂O₃@MCM-41 (15 wt% with respect to starting substrate), CO₂ pressure (2 MPa), DMAB (2.0 mmol) at 100 °C for 6 h under solvent free condition.

Further, to examine the utility and generality of this approach, we investigated the scope of the reactive 1° or 2° aliphatic as well as aromatic amine substrates (**1a–1ff**) were formylated to the corresponding formamides (**2a–2ff**) in moderate to excellent yields under the optimized reaction conditions and the results are shown in Table 3 (Entries 1-32). Interestingly, for every 1° or 2° aliphatic as well as aromatic amines, solely formylated product was obtained without any other by-product.

N-benzylmethylamine (**1a**) reacted with CO₂ providing 99% as an excellent yield of **2a** under the optimized reaction conditions (Table 3, entry 1). Dibenzylamine showed good reactivity, providing **2b** in a yield of 95% (Table 3, entry 2), and interestingly, the sterically hindered *tert*-butyl group on nitrogen atom of the *N*-benzyl-2-methylpropan-2-amine was also easily converted into **2c** with 86% yield (Table 3, entry 3). Moreover, the developed catalyst could efficiently catalyze the formylation of *N*-methylaniline, affording **2d** in a good yield of 97% (Table 3, entry 4). It was observed that our system was failed to give **2e** due to electron withdrawing nitro group ortho to the amino group (Table 3, entry 5). Some of the protocols^{11a,b} failed to convert from **1f** to **2f** product. But our system likely proved to be a highly efficient for the synthesis of diphenyl formamide in good yield of 45% (Table 3, entry 6). The substrate of both the indole and indoline undergoes the same product *i.e.* **2g** with an excellent yield of the *N*-formylation (Table 3, entries 7, 8). Whereas it was observed that 1,2,3,4-tetrahydroquinoline also provided desired product a good yield of **2h** (Table 3, entry 9).

Table 3 Production of various formamide derivatives.^a



Entry	Substrate	Product	Yield (%) ^b
1			99
2			95
3			86
4			97
5			n.d.
6			45
7			84
8			98
9			69
10			99
11			98
12			95
13			97
14			88
15			82
16			84
17			74

18	98
19	90
20	87
21	89
22	91
23	65
24	89
25	80
26	91
27	75
28	83
29	85
30	51
31	69
32	81

and excellent yields of the cyclic formamides **2j–p** were achieved (Table 3, entries 10-16). In case of the substrate **1p**, the formylation occurred only at unhindered amine provided with 84% yield of **2p**. The experiments were also successful for the N-formylation of secondary amines with longer dialkyl chains seemed to be more favourable (**1q–w**), and providing good to an excellent yield (65%-98%) of the corresponding desired products (Table 3, entries 17-23).

Furthermore, we were also applying this developed system to check the effectiveness of catalyst for the primary aliphatic amines such as cyclohexyl amine and *tert*-butylamine and provided the formamides **2x**, **2y** with 89%, 80% yields respectively (Table 3, entries 24-25). Subsequently, we also evaluated different from the above primary amines, the formylation of aniline and its sterically hindered derivatives (**1z–1ff**) which only afforded to the mono formylated products of the corresponding products **2z–2ff** with good to excellent yield of 51%-91% than others^{11c,h} (Table 3, entries 26-32).

Therefore, the synthetic utility of this developed methodology and the above results robustly demonstrated that the formylation of 1° or 2° aliphatic as well as aromatic amines from CO₂ with DMAB under solvent free and mild reaction conditions.

However, the recent studies reported that a reaction forwarded through the hydroboration of carbon dioxide by a Lewis base promotes intramolecular hydride delivery. It was found that the amino group of the catalyst played synergistic role in catalyzing the formylation reactions.^{21,4h}

Recyclability study

In order to craft the developed methodology, one of the most important works for the heterogeneous catalysis is reusability or consecutive recyclability. Hence the reusability of the amine modified meso Al₂O₃@MCM-41 (16 wt%) catalyst was also studied for the synthesis of formamide derivatives from amines and CO₂ under the optimized reaction conditions (Figure 3).

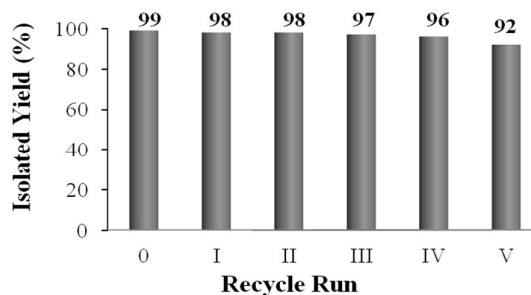


Figure 3 Recyclability study of 16.0 wt% amine modified meso Al₂O₃@MCM-41 catalyst.

^a Reaction conditions: Substrate (1 mmol), Cat. 16 wt% amine modified meso Al₂O₃@MCM-41 (15 wt%), CO₂ pressure (2 MPa), DMAB (2 mmol), temp. (100 °C), time (6 h).

^a Reaction conditions: Substrate (1 mmol), catalyst (15 wt%), DMAB (2 mmol), temperature (100 °C), time (6 h). ^b Based on GC/GC-MS analysis. The yield is quantified by using the external standard method using *N*-benzyl-*N*-methylformamide. ^c Isolated yield after column chromatography purification. n.d. = not detected.

Similarly, cyclic aliphatic amine containing oxygen on its ring (**1j**) and other cyclic aliphatic amines (**1k–p**) were also tested

After the completion of reaction, the product was separated through simple filtration technique. The catalyst was washed with distilled water and ethyl acetate, dried under vacuum and then reused for successive runs. The catalyst was found to be

effective up to five consecutive runs without any significant loss in its catalytic activity and stability of the prepared catalyst.

Conclusions

In conclusion, we have developed an efficient, green, economical, phosphine-free and heterogeneous catalytic methodology for the synthesis of formamides from amines and CO₂ using amine modified meso Al₂O₃@MCM-41 as a catalyst under solvent free and mild reaction conditions. After completion of the reaction the catalyst was easily recovered and again reused for five successive times without considerable loss in its catalytic activity. This protocol was highly efficient with respect to the various types of amines (1°/2° aliphatic as well as aromatic). The present catalytic reaction seems to be one of the ideal synthetic reactions.

Acknowledgements

The authors D. B. Nale thankful to the university grant commission, India for providing financial support under UGC-SAP-SRF program, Institute of Chemical Technology (ICT), Mumbai, India.

Notes and references

- (a) G. A. Olah, A. Goeppert, G. K. S. Prakash, *Beyond Oil and Gas: The Methanol Economy*, Wiley-VCH, Weinheim, Germany, 2006; (b) J. Louie, *Curr. Org. Chem.*, 2005, **9**, 605–623; (c) M. Mori, *Eur. J. Org. Chem.*, 2007, 4981–4993; (d) T. Sakakura, J. C. Choi, H. Yasuda, *Chem. Rev.*, 2007, **107**, 2365–2387; (e) M. Aresta, A. Dibenedetto, *Dalton Trans.*, 2007, 2975–2992; (f) A. Correa, R. Martin, *Angew. Chem. Int. Ed.*, 2009, **48**, 6201–6204; *Angew. Chem.*, 2009, **121**, 6317–6320; (g) S. N. Riduan, Y. Zhang, *Dalton Trans.*, 2010, **39**, 3347–3357; (h) A. Behr, G. Henze, *Green Chem.*, 2011, **13**, 25–39; (i) K. Huang, C. L. Sun, Z. J. Shi, *Chem. Soc. Rev.*, 2011, **40**, 2435–2452; (j) X. B. Lu, D. J. Darensbourg, *Chem. Soc. Rev.*, 2012, **41**, 1462–1484; (k) W. Z. Zhang, X. B. Lu, *Chin. J. Catal.*, 2012, **33**, 745–756; (l) L. Zhang, Z. M. Hou, *Chem. Sci.*, 2013, **4**, 3395–3403; (m) W. F. Xiong, C. R. Qi, H. T. He, O. Y. Lu, M. Zhang, H. F. Jiang, *Angew. Chem. Int. Ed.*, 2015, **54**, 3084–3087; *Angew. Chem.*, 2015, **127**, 3127–3130.
- (a) L. Yang, H. Wang, *ChemSusChem*, 2014, **7**, 962–998; (b) D. W. Stephan, G. Erker, *Chem. Sci.*, 2014, **5**, 2625–2641; (c) L. J. Hounjet, C. B. Caputo, D. W. Stephan, *Angew. Chem. Int. Ed.*, 2012, **51**, 4714–4717; *Angew. Chem.*, 2012, **124**, 4792–4795; (d) C. M. Mömmling, E. Otten, G. Kehr, R. Fröhlich, S. Grimme, D. W. Stephan, G. Erker, *Angew. Chem. Int. Ed.*, 2009, **48**, 6643–6646; *Angew. Chem.*, 2009, **121**, 6770–6773; (e) C. B. Caputo, K. Zhu, V. N. Vukotic, S. J. Loeb, D. W. Stephan, *Angew. Chem. Int. Ed.*, 2013, **52**, 960–963; *Angew. Chem.*, 2013, **125**, 994–997; (f) A. H. Liu, B. Yu, L. N. He, *Greenhouse Gases: Sci. Technol.*, 2015, **5**, 17–26.
- (a) A. Behr and V. A. Brehme, *J. Mol. Catal. A: Chem.*, 2002, **187**, 69–80; (b) F. L. Liao, Y. Q. Huang, J. W. Ge, W. R. Zheng, K. Tedsree, P. Collier, X. L. Hong and S. C. Tsang, *Angew. Chem., Int. Ed.*, 2011, **50**, 2162–2165; (c) I. Kasatkin, P. Kurr, B. Kniep, A. Trunschke and R. Schlögl, *Angew. Chem., Int. Ed.*, 2007, **46**, 7324–7327; (d) F. C. Meunier, *Angew. Chem., Int. Ed.*, 2011, **50**, 4053–4054; (e) G. A. Olah, *Angew. Chem., Int. Ed.*, 2005, **44**, 2636–2639; (f) S. Schimpf, A. Rittermeier, X. N. Zhang, Z. A. Li, M. Spasova, M. W. E. van den Berg, M. Farle, Y. M. Wang, R. A. Fischer and M. Muhler, *ChemCatChem*, 2010, **2**, 214–222; (g) D. Sperling, *Energy*, 2007, **28**, 178–179; (h) X. W. Zhou, J. Qu, F. Xu, J. P. Hu, J. S. Foord, Z. Y. Zeng, X. L. Hong and S. C. E. Tsang, *Chem. Commun.*, 2013, **49**, 1747–1749.
- (a) S. Chakraborty, J. Zhang, J. A. Krause, H. Guan, *J. Am. Chem. Soc.*, 2010, **132**, 8872–8873; (b) S. Bontemps, L. Vendier, S. Sabo-Etienne, *Angew. Chem. Int. Ed.*, 2012, **51**, 1671–1674; *Angew. Chem.*, 2012, **124**, 1703–1706; (c) M. A. Courtemanche, M. A. Legare, L. Maron, F. G. Fontaine, *J. Am. Chem. Soc.*, 2013, **135**, 9326–9329; (d) C. D. N. Gomes, E. Blondiaux, P. Thuery, T. Cantat, *Chem. Eur. J.*, 2014, **20**, 7098–7106; (e) T. Wang, D. W. Stephan, *Chem. Eur. J.*, 2014, **20**, 3036–3039; (f) S. Bontemps and S. Sabo-Etienne, *Angew. Chem., Int. Ed.*, 2013, **52**, 10253–10255. (g) S. Bontemps, L. Vendier and S. Sabo-Etienne, *J. Am. Chem. Soc.*, 2014, **136**, 4419–4425. (h) R. Shintani and K. Nozaki, *Organometallics*, 2013, **32**, 2459–2462.
- (a) F. J. Fernandez-Alvarez, A. M. Aitani, L. A. Oro, *Catal. Sci. Technol.*, 2014, **4**, 611–624; (b) D. B. Nale and B. M. Bhanage, *Green Chem.*, 2015, **17**, 2480–2486; (c) D. B. Nale and B. M. Bhanage, *Synlett*, 2015, **26**, 2835–2842.
- (a) B. M. Bhanage, S. Fujita, Y. Ikushima and M. Arai, *Appl. Catal., A*, 2001, **219**, 259–266; (b) D. B. Nale, S. Rana, K. M. Parida and B. M. Bhanage, *Catal. Sci. Technol.*, 2014, **4**, 1608–1614; (c) D. B. Nale, S. Rana, K. M. Parida and B. M. Bhanage, *Appl. Catal. A*, 2014, **469**, 340–349; (d) D. B. Nale, S. D. Saigaonkar and B. M. Bhanage, *J. CO₂ Util.*, 2014, **8**, 67–73; (e) R. A. Watile, K. M. Deshmukh, K. P. Dhake and B. M. Bhanage, *Catal. Sci. Technol.*, 2012, **2**, 1051–1055; (f) M. Honda, A. Suzuki, B. Noorjahan, K. Fujimoto, K. Suzuki and K. Tomishige, *Chem. Commun.*, 2009, 4596–4598; (g) F. Shi, Y. Q. Deng, T. L. SiMa, J. J. Peng, Y. L. Gu and B. T. Qiao, *Angew. Chem., Int. Ed.*, 2003, **42**, 3257–3260; (h) M. Shi and K. M. Nicholas, *J. Am. Chem. Soc.*, 1997, **119**, 5057–5058; (i) R. Srivastava, M. D. Manju, D. Srinivas and P. Ratnasamy, *Catal. Lett.*, 2004, **97**, 41–47; (j) J. S. Tian, J. Q. Wang, J. Y. Chen, J. G. Fan, F. Cai and L. N. He, *Appl. Catal., A*, 2006, **301**, 215–221; (k) M. Yoshida, N. Hara and S. Okuyama, *Chem. Commun.*, 2000, 151–152; (l) K. Yamaguchi, Y. Wang, N. Mizuno, *Chem. Lett.*, 2012, **41**, 633–635; (m) K. Yamaguchi, H. Kobayashi, Y. Wang, T. Oishi, Y. Ogasawara and N. Mizuno, *Catal. Sci. Technol.*, 2013, **3**, 318–327; (n) T. Kimura, H. Sunaba, K. Kamata and N. Mizuno, *Inorg. Chem.*, 2012, **51**, 13001–13008.
- (a) H. Goksu, H. Can, K. Sendil, M. S. Gultekin and O. Metin, *Appl. Catal. A*, 2014, **488**, 176–182; (b) H. Goksu, S. F. Ho, O. Metin, K. Korkmaz, A. M. Garcia, M. S. Gultekin and S. Sun, *ACS Catal.*, 2014, **4**, 1777–1782; (c) U. B. Demirci and P. Miele, *Phys. Chem. Chem. Phys.*, 2014, **16**, 6872–6885; (d) H. Goksu, *New J. Chem.*, 2015, **39**, 8498–8504; (e) Z. Li, F. Zhai, Q. Wan, Z. Liu, J. Shan, P. Li, A. A. Volinsky and X. Qu, *RSC Adv.*, 2014, **4**, 18989–18997; (f) H. Liu, X. Wang, Y. Liu, Z. Dong, G. Cao, S. Li and M. Yan, *J. Mater. Chem. A*, 2013, **1**, 12527–12535.
- (a) T. D. Nixon, M. K. Whittlesey and J. M. J. Williams, *Tetrahedron Lett.*, 2011, **52**, 6652–6654; (b) F. Sen and G. Gokagac, *J. Phys. Chem. C*, 2007, **111**, 1467–1473; (c) H. Goksu, Y. Yildiz, B. Çelik, M. Yazici, B. Kilbas and F. Sen, *Catal. Sci. Technol.* 2015, DOI: 10.1039/c5cy01462j.
- (a) J. Pouessel, O. Jacquet and T. Cantat, *ChemCatChem*, 2013, **5**, 3552–3556; (b) K. Weissmermel, H. J. Arpe, *Industrial Organic Chemistry*, 3rd ed., Translated by C. R. Lindley, Wiley-VCH, Weinheim, 1997.
- (a) M. Kozak, *Microbiol. Rev.*, 1983, **47**, 1–45; (b) J. R. Wisniewski, A. Zougman, M. Mann, *Nucleic Acids Res.*, 2008,

- 36, 570–577; (c) T. Inaba, K. Tanaka, R. Takeno, H. Nagaki, C. Yoshida, S. Takano, *Chem. Pharm. Bull.*, 2000, **48**, 131–139.
- 11 (a) O. Jacquet, C. D. N. Gomes, M. Ephritikhine, T. Cantat, *J. Am. Chem. Soc.*, 2012, **134**, 2934–2937; (b) C. D. N. Gomes, O. Jacquet, C. Villiers, P. Thuery, M. Ephritikhine, T. Cantat, *Angew. Chem., Int. Ed.*, 2012, **51**, 187–190; (c) X. J. Cui, Y. Zhang, Y. Q. Deng, F. Shi, *Chem. Commun.*, 2014, **50**, 189–191; (d) J. L. Liu, C. K. Guo, Z. F. Zhang, T. Jiang, H. Z. Liu, J. L. Song, H. L. Fan, B. X. Han, *Chem. Commun.* 2010, **46**, 5770–5772; (e) P. Munshi, D. J. Heldebrant, E. P. McKoon, P. A. Kelly, C. C. Tai, P. G. Jessop, *Tetrahedron Lett.*, 2003, **44**, 2725–2727; (f) S. Kumar, S. L. Jain, *RSC Adv.*, 2014, **4**, 64277–64279; (g) K. Motokura, N. Takahashi, D. Kashiwame, S. Yamaguchi, A. Miyaji, T. Baba, *Catal. Sci. Technol.*, 2013, **3**, 2392–2396; (h) T. V. Q. Nguyen, W. J. Yoo and S. Kobayashi, *Angew. Chem.*, 2015, **127**, 9341–9344.
- 12 (a) K. M. Parida, D. Rath, *J. Mol. Catal. A: Chem.*, 2009, **310**, 93–100; (b) J. N. Appaturi, F. Adam, *Appl. Catal. B*, 2013, **136–137**, 150–159; (c) S. Huh, J. W. Wiench, J. C. Yoo, M. Pruski, V. S. Y. Lin, *Chem. Mater.* 2003, **15**, 4247–4256; (d) S. Udayakumar, M. K. Lee, H. L. Shim, D. W. Park, *Appl. Catal. A*, 2009, **365**, 88–95; (e) M. R. Mello, D. Phanon, G. Q. Silveira, P. L. Llewellyn, C. M. Ronconi, *Microporous Mesoporous Mater.*, 2011, **143**, 174–179; (f) M. Caplow, *J. Am. Chem. Soc.*, 1968, **24**, 6795–6803; (g) P. V. Dankwerts, *Chem. Eng. Sci.*, 1979, **34**, 443–446.
- 13 (a) Q. Liu, A. Wang, X. Wang, P. Gao, X. Wang and T. Zhang, *Microporous Mesoporous Mater.*, 2008, **111**, 323–333; (b) I. A. Lemus, Y. V. Gomez and L. A. Contreras, *Int. J. Electrochem. Sci.*, 2011, **6**, 4176–4187; (c) K. M. Parida, A. C. Pradhan, J. Das and N. Sahu, *Mater. Chem. Phys.*, 2009, **113**, 244–248.
- 14 (a) N. Bejenaru, C. Lancelot, P. Blanchard, C. Lamonier, L. Rouleau, E. Payen, F. Dumeignil and S. Royer, *Chem. Mater.*, 2009, **21**, 522–533; (b) K. M. Kolonia, D. E. Petrakis and A. K. Ladavos, *Phys. Chem. Chem. Phys.*, 2003, **5**, 217–222; (c) A. Sayari, D. Shee, N. Al-Yassir and Y. Yang, *Top. Catal.*, 2010, **53**, 154–167; (d) T. A. Konovalova, Y. Gao, R. Schad and L. D. Kispert, *J. Phys. Chem. B*, 2001, **105**, 7459–7464.
- 15 (a) C. M. Alvarez, N. Zilkova, J. P. Pariente, J. Cejka, *Catal. Rev.*, 2008, **50**, 222–286; (b) H. Liu, G. Lu, Y. Guo, Y. Wang, Y. Guo, *Catal. Commun.* 2009, **10**, 1324–1329.
- 16 R. Prins, V. H. de Beer, G. A. Somorjai, *Catal. Rev. Sci. Eng.*, 1989, **31**, 1–41.
- 17 N. Bejenaru, C. Lancelot, P. Blanchard, C. Lamonier, L. Rouleau, E. Payen, R. S. Dumeignil, *Chem. Mater.*, 2009, **21**, 522–533.
- 18 (a) A. Sayari, Y. Belmabkhout, *J. Am. Chem. Soc.*, 2010, **132**, 6312–6314; (b) S. Builes, L. F. Vega, *J. Phys. Chem. C*, 2012, **116**, 3017–3024.
- 19 Q. Wu, F. Zhang, J. Yang, Q. Li, B. Tu, D. Zhao, *Microporous Mesoporous Mater.*, 2011, **143**, 406–412.
- 20 S. Brunauer, L. S. Deming, E. Deming and E. Teller, *J. Am. Chem. Soc.*, 1940, **62**, 1723–1732.
- 21 (a) E. J. Corey and J. O. Link, *Tetrahedron Lett.*, 1989, **30**, 6275–6278; (b) E. J. Corey and R. K. Bakshi, *Tetrahedron Lett.*, 1990, **31**, 611–614; (c) M. A. Courtemanche, M. A. Legare, L. Maron and F. G. Fontaine, *J. Am. Chem. Soc.*, 2014, **136**, 10708–10717; (d) Z. Z. Yang, L. N. He, J. Gao, A. H. Liu, B. Yu, *Energy Environ. Sci.*, 2012, **5**, 6602–6639; (e) W. C. Chen, J. S. Shen, T. Jurca, C. J. Peng, Y. H. Lin, Y. P. Wang, W. C. Shih, G. P. A. Yap and T. G. Ong, *Angew. Chem. Int. Ed.*, 2015, **54**, 15207–15212.

Graphical Abstract

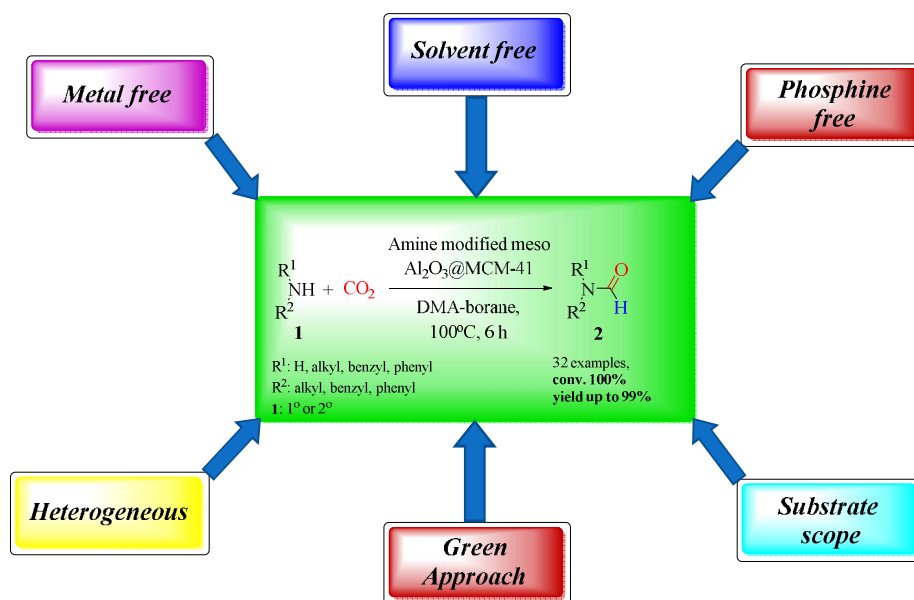
Amine modified mesoporous Al₂O₃@MCM-41: An efficient, synergetic and recyclable catalyst for the formylation of amines using carbon dioxide and DMAB under solvent free and mild reaction condition

Deepak B. Nale,^a Dharitri Rath,^b K. M. Parida,^b Aravind Gajengi^a and Bhalchandra M. Bhanage^{a,*}

^a Department of Chemistry, Institute of Chemical Technology, N. Parekh Marg, Matunga, Mumbai 400 019, India.

^b Department of Chemistry, Centre for Nano Science and Nano Technology, Institute of Technical Education and Research, Siksha 'O' Anusandhan University, Khandagiri, Bhubaneswar- 751 030, Odisha, India.

* Corresponding author Tel.: +91- 22 3361 1111/2222; Fax: +91- 22 3361 1020.
E-mail address: Prof. B. M. Bhanage: bm.bhanage@ictmumbai.edu.in and
Dr. K. M. Parida: paridakulamani@yahoo.com



A novel covalently linked amine modified meso Al₂O₃@MCM-41 catalysts were investigated as a highly efficient, heterogeneous, environmental-friendly and sustainable mesoporous catalytic system for the synthesis of formamides from 1°/2° aliphatic as well as aromatic amines, CO₂ and DMAB as a green reductant under solvent free and mild reaction conditions.