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ARTICLE

Oxidative Amidation of Benzaldehydes and Benzylamines with *N*-Substituted Formamides over Co/Al Hydrotalcite-derived Catalyst

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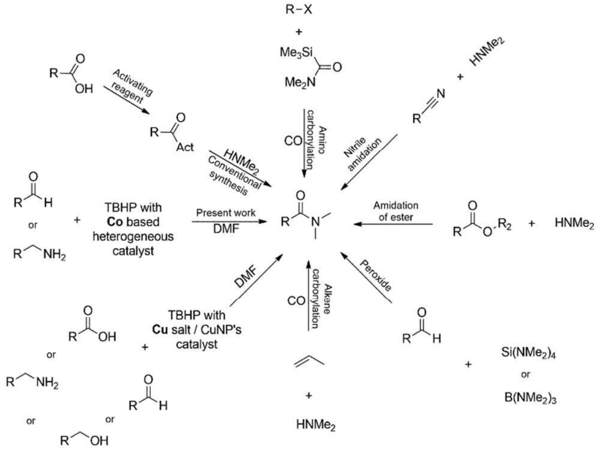
Abstract: Present work describes a highly efficient synthetic strategy for amides via oxidative coupling of benzaldehydes or benzylamines with *N*-substituted formamides using heterogeneous Co/Al hydrotalcite-derived catalyst in the presence of TBHP. A series of Co/Al hydrotalcite-derived catalysts (Cat-2, Cat-3, and Cat-4 with Co^{2+}/Al^{3+} molar ratio in the synthesis mixture as 1/1, 2/1 and 3/1) have been prepared by a simple co-precipitation method and characterized using powder XRD, XPS, FEG-SEM, EDS, FT-IR, DTG-TGA and N_2 physical adsorption techniques. Among the as-prepared catalysts, Cat-3 exhibited excellent catalytic activity towards the direct amidation of benzaldehydes as well as benzylamines bearing various substituents into the corresponding amides at 100 °C using TBHP as an oxidant. The mechanistic investigation of the amidation reaction revealed that the reaction follows a radical pathway. Furthermore, the catalyst is easily separable and recyclable without considerable loss in catalytic activity.

Introduction

Amides are important structural moiety with ubiquitous applications in biomolecules, polymers, agrochemicals and pharmaceuticals.[1–5] The great importance and wide applicability of amides demand the development of highly efficient strategies for their synthesis.[6–8] In the context, the most frequently used synthetic route for amide involves activation of carboxylic acids followed by their subsequent coupling with amines.[9–12] However, for this method stoichiometric amount of activating reagent is required to transform the hydroxyl group of carboxylic acid into a good leaving group. Recently, M.A. Ali et al. have shown the amidation of a range of carboxylic acids with amines by using reusable Nb_2O_5 as a solid Lewis acid catalyst.[13] Other efficient catalytic approaches for amide synthesis involve amino carbonylation of aryl halides, carbonylation reaction of alkenes or alkynes, rearrangement of oximes, amidation of nitriles, C-H oxidative amidation and amidation of carboxylic acid esters[14–18] (Scheme 1). Recently, Kim et al.[19] and Xie et al.[20] have demonstrated the use of azides towards the amidation of aldimines and phenylacetaldehydes, respectively. Nguyen and Hull have shown amidation of sterically hindered alcohols as well as aldehydes.[21] In recent years, the synthesis of amides are carried out via oxidative amidation of aldehydes, in this regard Li et al.[22] and Wu et al.[23] have reported the amidation of aldehydes using $AgIO_3$ and TBHP as oxidants over copper and zinc metal oxide catalysts respectively. Despite the considerable progress made on this reaction, these coupling reactions portray some limitations such as: the use of activating reagent in stoichiometric amount, harsh reaction conditions and production of large quantities of hazardous chemical wastes.[24] Therefore, these approaches needs to be reviewed in order to achieve environmentally benign synthesis of amides. N,N-dimethylformamide (DMF) has been extensively used as a polar solvent and a multipurpose reagent in various organic reactions. DMF molecule contains two functional groups:



Scheme 1. General synthetic strategies for amide bond formation.

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aldehyde and amine, offering its applicability to be used as an precursor for -CONMe$_2$, -CHO, -NMe$_2$, -CO, O and -Me groups in various organic synthesis.[25,26] Amidation reactions involving DMF as the precursor for -NMe$_2$ group provide considerable scope and has attracted attention of several researchers. In this regard, Z. Wang and co-workers [27,28] have developed amidation of benzyl amine and benzyl alcohol with DMF using iodine and TBHP in the presence of HCl and NaOH, respectively. Reddy et al.[29], Zhang et al.[30] and previously our research group[31] have reported oxidative amidation of carboxylic acids with DMF using TBHP as an oxidant over Cu-based catalysts. Appreciable yields of amides were achieved over these catalytic systems however, these methods involves tedious work-up procedures also the catalyst separation and recycling were the major challenge. Recently, Y. Li et al. have reported amidation of aldehydes with DMF using cobalt supported on metal organic frameworks in the presence of TBHP as an oxidant.[32] Taking an account of easy separation and recyclability of heterogeneous catalysts, it is highly desirable to develop recyclable catalytic system for such transformations.

Herein, we have made an effort to construct an amide linkage via catalytic oxidative amidation of benzaldehydes and benzylamines with DMF (through aldehydic C-H bond functionalization) using simple Co/Al hydrotalcite-derived heterogeneous catalyst. Hydrotalcites (HT) facilitate the design of high surface area materials possessing exposed active sites due to the incorporation of metals in brucite like layers, which enhances the catalytic and adsorption properties.[33,34] The control experimentations of amidation reaction suggest that the reaction proceeds via formation of a radical intermediate of TBHP which on further reaction with benzaldehydes or benzylamines and DMF produces the corresponding amides. Furthermore, the Co/Al hydrotalcite-derived mixed metal oxide catalyst was easily isolated from the reaction mixture by simple filtration and recycled for four times without considerable loss in catalytic activity towards amidation reaction.

Results and discussion

Catalytic activity

X-ray diffraction (XRD) patterns of the metal oxides Cat-1 (Co^{2+}/Fe^{3+} molar ratio 1:1), Cat-2, and Cat-5 (Co$_3$O$_4$) show sharp diffraction peaks (**Fig. 1 a-c**), which can be attributed to the high crystallinity of the materials. As shown in (**Fig. 2 a**) the un-calcined Cat-3 sample exhibited X-ray diffraction peaks at the 2θ value of 11°, 22°, 35°, 60° and 61° which are indexed to (003), (006), (009), (110) and (113) crystal planes. These XRD peaks are characteristic of hydrotalcite materials (JCPDS 51-0045) and reveal high dispersion of metal cations in the brucite like layers.[35] After calcination of Cat-3 sample in air, the diffraction peaks corresponding to the hydrotalcite phase disappeared and new diffraction peaks were appeared (**Fig. 2 b**) at 2θ value of 19°, 31°, 36°, 39°, 45°, 55°, 59° and 65° corresponding to the oxide spinel phase (JCPDS 38-0814). Thus, XRD results indicate transformation of hydrotalcite phase into the mixed metal oxide phase on calcination in air. XRD of Cat-2, Cat-3 and Cat-4 in oxide phase are shown in Fig. S1 (ESI).

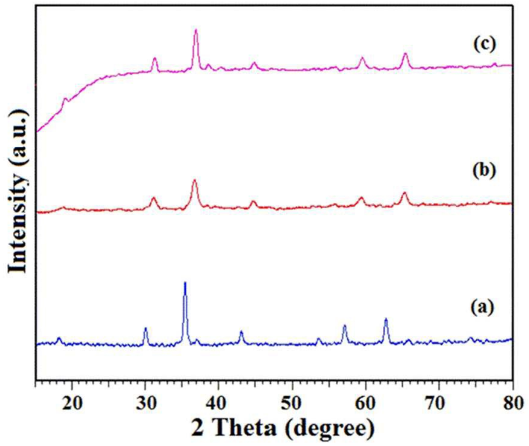

Fig. 1. XRD patterns of (a) Cat-1, (b) Cat-2 and (c) Cat-5.

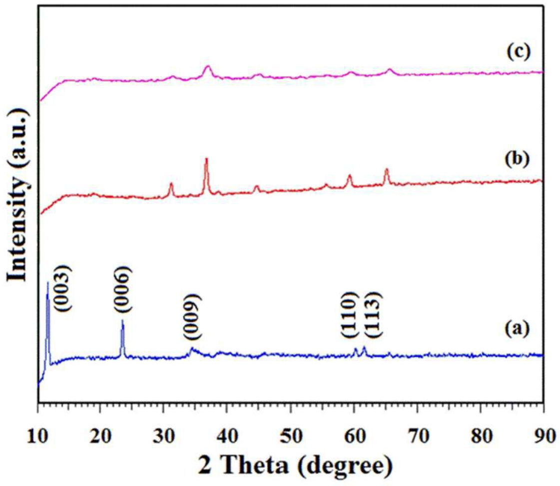

Fig. 2. XRD patterns of Cat-3 (a) hydrotalcite phase, (b) oxide phase and (c) recycled catalyst.

XPS analysis was conducted to find out the chemical states of the metals present in the catalyst. The XPS survey scan (**Fig. 3a**) of Cat-3 suggests the presence of Co, Al and O elements in the catalyst. Two strong peaks at 782 eV and 797 eV (**Fig. 3b**) corresponding to Co 2p$^{3/2}$ and Co 2p$^{1/2}$ suggest the presence of cobalt in Co^{2+} oxidation state. Hydrotalcite material exhibits weight loss generally in three prominent steps (1) dehydration (2) layer dehydroxylation and (3) anion decomposition.[36–38] TGA analysis of un-calcined Cat-3 (Fig. S2 ESI) exhibited first weight loss in the range of 200-250 °C which can be attributed to the layer dehydroxylation. The next weight loss occurred in the range of 300-350 °C due to the decomposition of interlayer carbonate and nitrate anions leading to collapse of the layered structure.[39] Weight loss corresponding to dehydration step

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was not observed in TGA analysis of un-calcined Cat-3 sample as the material was dried in hot air oven at 100 °C for 12 h prior to the TGA analysis.

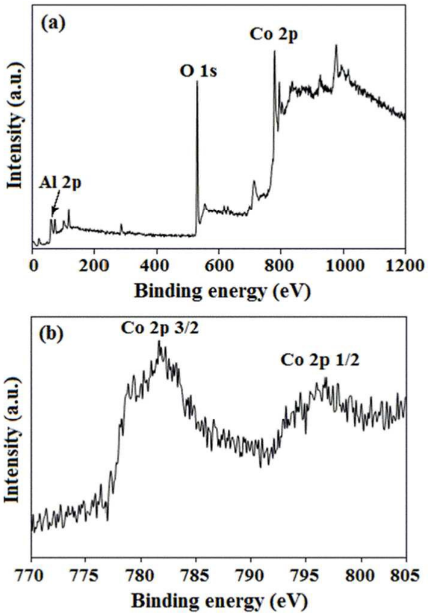

Fig. 3. XPS of Cat-3 (a) Survey scan and (b) Co 2p high resolution scan.

FT-IR spectrums of Cat-3 sample in oxide form (Calcined) as well as in hydrotalcite form (Un-calcined) are illustrated in Fig. S3 (ESI). The IR spectra of un-calcined Cat-3 show peaks, which typically represent the hydrotalcite structure with intercalated carbonate anions.[40,41] The broad band at 3440 cm^{-1}, can be attributed to the O-H stretching vibrations of adsorbed water molecules and -OH groups from brucite layers. The sharp peak at 1361 cm^{-1} is characteristic of O-C-O linkage of intercalated CO_3^{2-} anions, while the absorption bands below 1000 cm^{-1} were resulted from metal-oxygen-metal stretching modes.[42,43]

In the IR spectra of calcined Cat-3, the absorptions corresponding to H_2O molecules and -OH groups of brucite layer and intercalated carbonate anions at 3440 cm^{-1} and 1361 cm^{-1} respectively disappeared due to dehydration and decomposition during calcination at 600 °C. Absorptions at 661 cm^{-1}, 554 cm^{-1} and 531 cm^{-1} correspond to metal-oxygen (Co-O and/or Al-O) stretching modes. TGA-DTG and FT-IR results confirm the transformation of hydrotalcite phase into mixed oxide phase, which is in agreement with the XRD results.

Surface morphology and chemical compositions of Cat-3 sample were determined by FEG-SEM and elemental analysis as shown in Fig. S4 (ESI). Elemental mappings (**Fig. 4**) shows uniform distribution of Co, Al and O in the as-prepared catalyst. FEG-SEM images of recycled Cat-3 sample (**Fig. 5b**) reveals slight agglomeration of the catalyst particles as compared to the fresh Cat-3 sample (**Fig. 5a**).

Surface area analysis of Cat-3 samples in hydrotalcite form exhibited the surface area 38 m^2/g and after calcination at 600 °C for 6h the surface area was increased to 67 m^2/g. During calcination, the intercalated water and carbonates were removed leading to the development of porous structure in the catalyst.[44–46] The N_2 adsorption/desorption isotherms (Fig. S5 ESI) of Cat-3 sample in hydrotalcite and oxide forms exhibited type IV isotherm as per the IUPAC classification which represents typical mesoporous materials such as hydrotalcites.[47,48]

The as-synthesized cobalt based catalysts were screened for the amidation of benzaldehyde and various reaction parameters were optimized using benzaldehyde and DMF as the model substrates. In a preliminary screening, Cat-1 was used for the reaction and N,N-dimethylbenzamide (3) was obtained in 66 % yield (Table 1, entry 2) whereas 74 % yield of the product (3) was obtained when Cat-2 was employed under similar reaction conditions which indicates alumina is a better support material for the catalyst. With this observation, a series of Co/Al hydrotalcite-derived catalysts with different molar ratios of Co^{2+} and Al^{3+} (1:1, 2:1 and 3:1) in synthesis mixture were synthesized and tested for the amidation of benzaldehyde, significant increase in the yield of (3) was observed from 74 % to 86 % with Cat-3 (Table 1, entry 4).

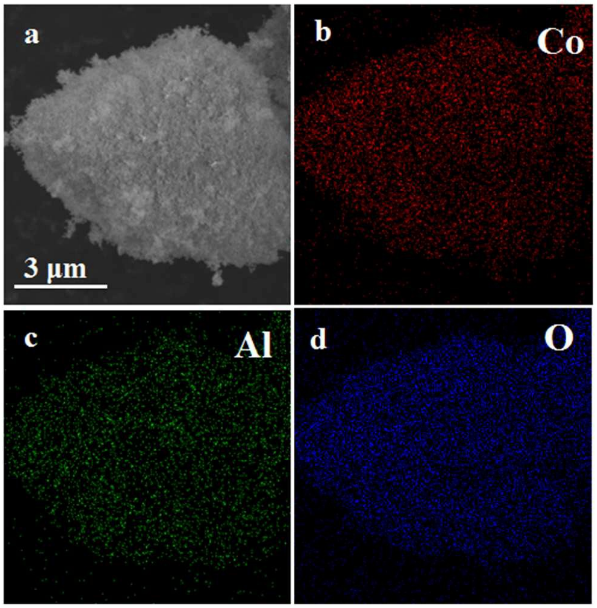

Fig. 4. FEG-SEM image of (a) Cat-3 sample and the corresponding (b) Co, (c) Al and (d) O elemental maps.

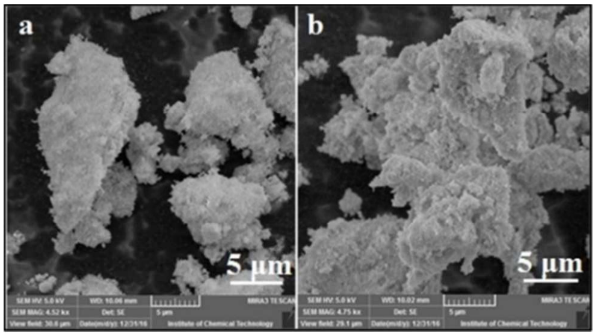

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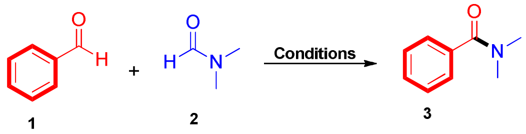
Fig. 5. FEG-SEM images of Cat-3 (a) fresh and (b) recycled catalyst.

However, no considerable increase in the yield of (3) could be noted on further increasing the Co^{2+}/Al^{3+} molar ratios to 3:1 (Table 1, entry 5). The use of Co_3O_4 as a catalyst produced the desired product (3) in low yield under the similar reaction conditions (Table 1, entry 6). The un-calcined sample Cat-3 gave only 12 % of the desired product (3) (Table 1, entry 7) indicating that mixed metal oxide phase catalyses the amidation reaction effectively. The reaction produced trace amount of product (2 %) in a blank run (without a catalyst) under the investigated conditions (Table 1, entry 1) indicating that the catalyst is essential to catalyse the amidation reaction. Using Cat-3 sample, a range of solvents, including water, acetonitrile, toluene and DMF were examined for the reaction (Table 1, entries 8-10), highest yield of (**3**) was observed in DMF among the investigated solvents. Employing water and acetonitrile as the solvents, no product formation was observed. However, when toluene was used as a solvent for amidation of benzaldehyde, a small amount of bibenzyl (14 %) was formed as a side product along with the desired product (**3**) and this could be due to the formation of toluene radical in the presence of TBHP and subsequent coupling of the two toluene radicals to afford bibenzyl as the side product which was quantified and confirmed by GC-MS analysis (ESI). Different oxidants were also screened for the amidation of benzaldehyde with DMF. No formation of desired product **(3)** was observed without an oxidant (Table 1, entry 16) suggesting that oxidant is necessary for the reaction to proceed. It is worth noting that no product (**3**) formation was seen when other oxidants, such as H_2O_2 and O_2 were used for the reaction (Table 1, entries 11, 12). Increasing the quantity of TBHP led to the reduced yield of amide (**3**) due to the side reactions such as oxidation of a small amount of benzaldehyde into benzoic acid (Table 1, entry 15) and formation of t-butyl benzoate. Reaction temperature and time were also optimized (Table 1, entries 17-20) and maximum yield of the desired product *N,N*-dimehtylbenzamide was obtained at 100 °C in 24 h. With these optimized reaction parameters, a broad spectrum of aldehydes bearing various substituents were explored for the oxidative amidation with DMF. As shown in Table 2, various aromatic aldehydes substituted with electron-donating groups at *ortho*, *meta* and *para* positions produced the corresponding amides in good to excellent yields. Interestingly, aldehydes with fluoride, chloride

Table 1. Optimization of the reaction parameters for amidation of benzaldehyde with DMF [a].



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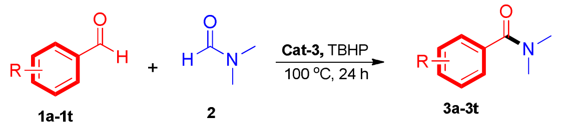
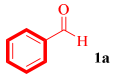
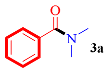
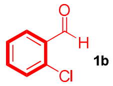
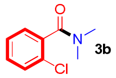
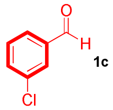
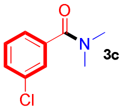
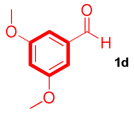
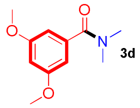
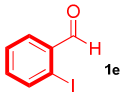
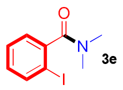
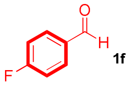
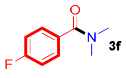
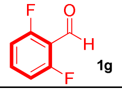
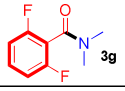
#	Cat.	Catalyst composition	Molar ratios of metal cations in synthesis mixture	Oxidant	Solvent	T (°C)	Yield (%)[f]
1	-	-	-	TBHP	DMF	100	02
2	Cat-1	Co-Fe	1:1	TBHP	DMF	100	66
3	Cat-2	Co-Al	1:1	TBHP	DMF	100	74
4	Cat-3	Co-Al	2:1	TBHP	DMF	100	86
5	Cat-4	Co-Al	3:1	TBHP	DMF	100	88
6	Cat-5	Co_3O_4	-	TBHP	DMF	100	56
7	Cat-3	Co-Al Un-calcined	2:1	TBHP	DMF	100	12
8[b]	Cat-3	Co-Al	2:1	TBHP	Acetonitrile	100	-
9[b]	Cat-3	Co-Al	2:1	TBHP	Toluene	100	48
10[b]	Cat-3	Co-Al	2:1	TBHP	Water	100	-
11	Cat-3	Co-Al	2:1	H_2O_2	DMF	100	-
12	Cat-3	Co-Al	2:1	O_2	DMF	100	-
13[c]	Cat-3	Co-Al	2:1	TBHP	DMF	100	82
14[d]	Cat-3	Co-Al	2:1	TBHP	DMF	100	85
15[e]	Cat-3	Co-Al	2:1	TBHP	DMF	100	80
16	Cat-3	Co-Al	2:1	-	DMF	100	-
17	Cat-3	Co-Al	2:1	TBHP	DMF	RT	10
18	Cat-3	Co-Al	2:1	TBHP	DMF	80	69
19	Cat-3	Co-Al	2:1	TBHP	DMF	90	77
20	Cat-3	Co-Al	2:1	TBHP	DMF	110	87

[a] Reaction conditions: **1** (1 mmol), oxidant (5 mmol), catalyst (20 wt%), DMF (5 mL), 24 h. [b] Reaction conditions: **1** (1 mmol), DMF (2 mmol), TBHP (5 mmol), catalyst (20 wt%), solvent (5 mL), 24 h. [c] TBHP (3 mmol), [d] TBHP (4 mmol), [e] TBHP (6 mmol], [f] Yield was determined by GC-MS analysis.

and iodide groups, which are usually reactive and form dehalogenated products in the presence of copper catalyst, were found to be compatible with the Co/Al mixed metal oxide catalyst and all gave good yields of the desired product (Table 2, entries 2, 3, 5, 6, 7 and 8). In comparison to the benzaldehyde, the presence of substituents at *meta* and *para* positions did not change the yield significantly however, when the substituent was at the *ortho* position, the yield was dropped considerably and this could be due to the steric hindrance (Table 2, entries 2, 5, 7, 8, 11, 13, 14 and 17). The presence of nitro group in aldehydes resulted in diminished yields of the corresponding amides under similar reaction conditions (Table 2, entries 14, 15 and 16).

Table 2. Oxidative amidation of various aldehydes with DMF [a].



#	Substrate	Product	Yield (%)[b]
1	 1a	 3a	86
2	 1b	 3b	64
3	 1c	 3c	72
4	 1d	 3d	67
5	 1e	 3e	67
6	 1f	 3f	88
7	 1g	 3g	62

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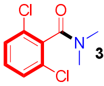
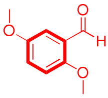
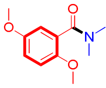
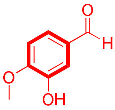
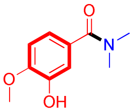
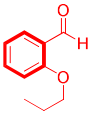
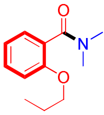
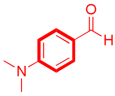
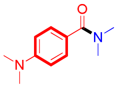
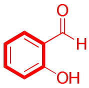
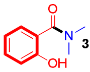
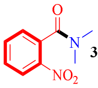
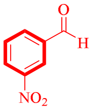
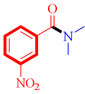
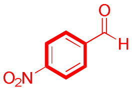
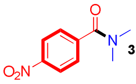
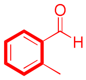
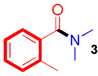
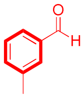
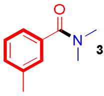
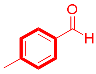
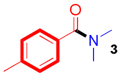
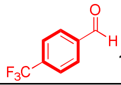
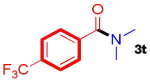
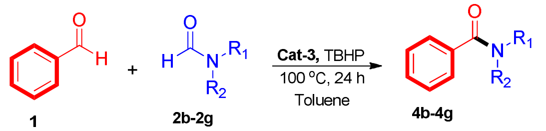
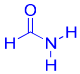
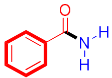
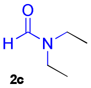
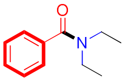
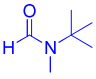
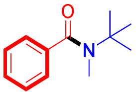
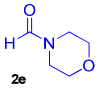
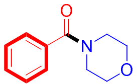
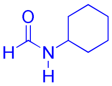
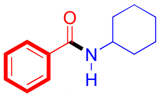
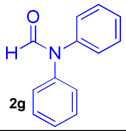
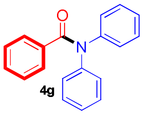
8	 **1h**	 **3h**	57
9	 **1i**	 **3i**	72
10	 **1j**	 **3j**	64
11	 **1k**	 **3k**	68
12	 **1l**	 **3l**	74
13	 **1m**	 **3m**	62
14	 **1n**	 **3n**	50[c]
15	 **1o**	 **3o**	57[c]
16	 **1p**	 **3p**	53[c]
17	 **1q**	 **3q**	76
18	 **1r**	 **3r**	85
19	 **1s**	 **3s**	92
20	 **1t**	 **3t**	70

[a] Reaction conditions: **1a-1t** (1 mmol), TBHP (5 mmol), Cat-3 (20 wt.%), DMF (5 mL), 100 °C, 24 h. [b] Yield was determined by GC-MS analysis. [c] Isolated yields.

Various *N*-substituted formamides were also explored for the oxidative amidation of benzaldehyde. As summarized in Table 3, various *N*-substituted formamides were found to be active and produced the corresponding products in good to excellent yields. Unfortunately, formamide and *N,N*-diphenylformamide were found to be non-reactive for amidation reaction under similar reaction conditions (Table 3, entries 1 and 5).

Table 3. Oxidative amidation of benzaldehyde using various N-substituted formamides [a].

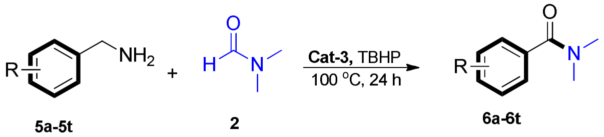


#	Substrate	Product	Yield (%)[b]
1	 **2b**	 **4b**	-
2	 **2c**	 **4c**	67
3	 **2d**	 **4d**	53
4	 **2e**	 **4e**	90
5	 **2f**	 **4f**	82
6	 **2g**	 **4g**	-

[a] Reaction conditions: Benzaldehyde (1 mmol), **2b-2f** (1 mmol), TBHP (5 mmol), Cat-3 (20 wt%), Toluene (5 mL), 100 °C, 24 h. [b] Yield was determined by GC-MS analysis.

It is interesting to note that the various substituted bezylamines afforded the corresponding amides in good to moderate yields under standard reaction conditions using Cat-3. Benzylamine **A**, (Scheme 3) under oxidative conditions forms intermediate phenylmethaneimine **B** which on hydrolysis produces benzaldehyde **C** and on subsequent oxidative coupling of benzaldehyde with DMF leads to the formation of desired product *N,N*-dimethylbenzamide. As summarized in Table 4, oxidative amidation of various substituted benzylamines afforded lower yields of desired products as compared to the oxidative amidation of aldehydes due to the formation of *N*-formylated side product (Scheme 2d).

Table 4. Oxidative amidation of various benzylamines with DMF [a].



#	Substrate	Product	Yield (%)[b]

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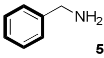
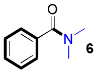
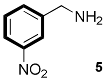
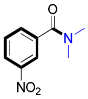
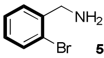
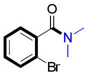
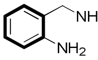
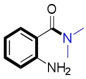
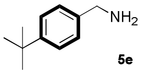
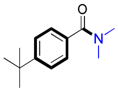
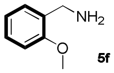
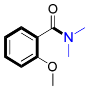
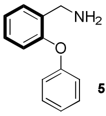
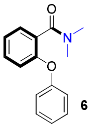
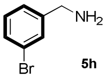
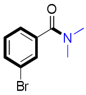
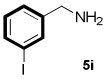
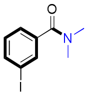
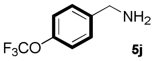
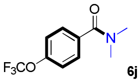
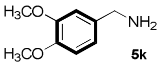
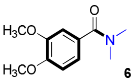
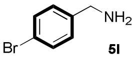
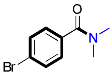
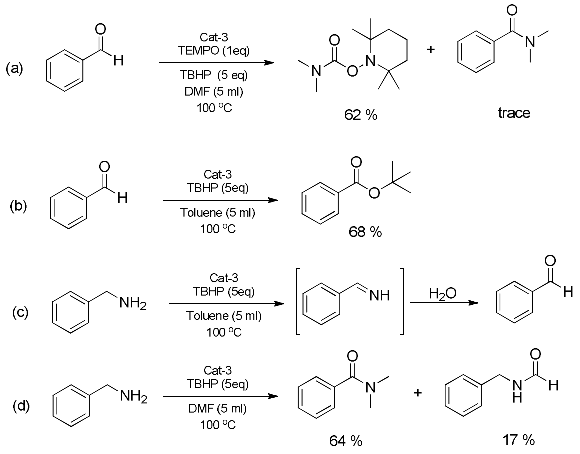
1	 5a	 6a	64
2	 5b	 6b	47[c]
3	 5c	 6c	53
4	 5d	 6d	46
5	 5e	 6e	59
6	 5f	 6f	55
7	 5g	 6g	53
8	 5h	 6h	65
9	 5i	 6i	61
10	 5j	 6j	60
11	 5k	 6k	59
12	 5l	 6l	66

[a] Reaction conditions: **5a-5l** (1 mmol), TBHP (5 mmol), Cat-3 (20 wt.%), DMF (5 mL), 100 °C, 24 h. [b] Yield was determined by GC-MS analysis. [c] Isolated yields.

To gain some understanding of the reaction mechanism, when 1 equivalent of radical inhibitor, *TEMPO* (2,2,6,6-tetramethylpiperidine-N-oxyl) was introduced to the reaction mixture of benzaldehyde, TBHP, Cat-3 and DMF (Scheme 2a), the *TEMPO* adduct was formed predominantly (62 %) instead of the desired product suggesting that the amidation reaction follows radical mechanism. Mixture of benzaldehyde, TBHP and Cat-3 produced *t*-butyl benzoate (Scheme 2b) suggesting that the reaction involves formation of acyl radical and *t*-butoxyl radical and their subsequent couplings afforded the product ester.



Scheme 2. Control experiments for mechanistic investigation.

On the basis of controlled experiments and previous related reports [49], a tentative mechanism for oxidative amidation of benzaldehydes or benzylamines with *N*-substituted formamides using heterogeneous Co/Al hydrotalcite-derived catalyst in the presence of TBHP has been proposed and shown in Scheme 3. Initially, *t*-butoxyl and *t*-butylperoxyl radicals are generated with the assistance of Co/Al hydrotalcite-derived catalyst (step I). Then, these radicals abstract hydrogen from the aldehyde **C** and *N*-substituted formamide **E** to form acyl radical **D** and aminyl radical **G** respectively (Step II). Finally cross coupling of radicals **D** and **G** leads to the formation of corresponding amide **H**.

Catalyst recyclability

The stability and recyclability of Cat-3 was studied towards amidation of benzaldehyde with DMF. After the reaction, catalyst was isolated from the reaction mixture by simple filtration and washed several times with DMF and then dried under vacuum for 10 h at 100 °C and used for the next catalytic run. As shown in **Fig. 6** the catalyst was recycled for 4 times without considerable loss in the catalytic activity for oxidative amidation of benzaldehyde with DMF under optimised conditions. The X-ray diffraction pattern of the Cat-3 recycled for four times was recorded (**Fig. 2c**). In comparison to the fresh catalyst, all the characteristic diffraction peaks and crystallinity of the catalyst were retained in the recycled catalyst. The heterogeneity of the catalyst was examined by the leaching test. The reaction was stopped after 10 h, then the solid catalyst was isolated by filtration and then the reaction was continued with filtrate for next 10 h, it was noted that reaction did not proceed further. ICP-AES analysis of the reaction mass after the isolation of the catalyst shows the absence of metals in the filtrate indicating high stability of the catalyst.

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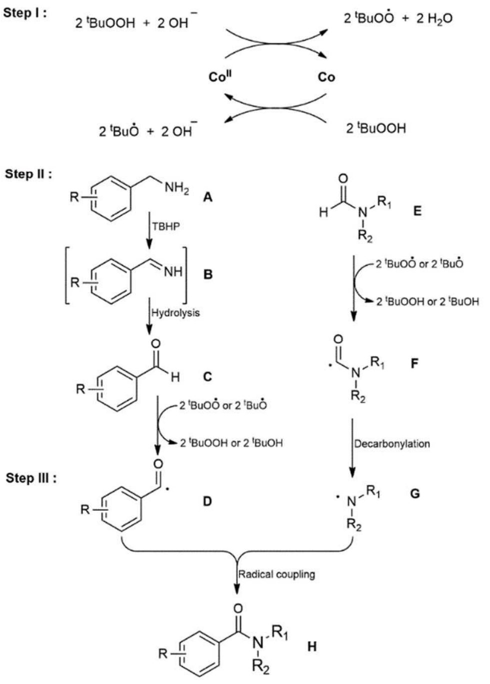

Scheme 3. Proposed reaction mechanism for oxidative

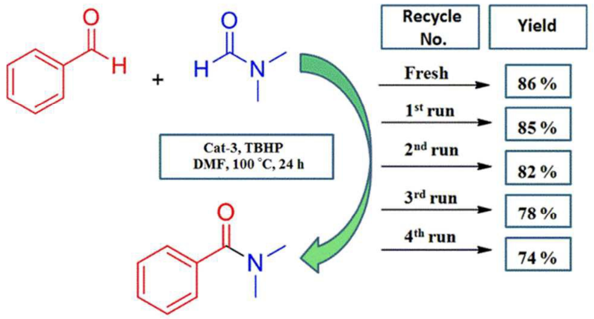

Fig. 6. Recyclability study of Cat-3 for amidation of benzaldehyde with DMF.

Conclusions

In summary, a highly efficient catalytic approach for amide bond formation via aldehydic C-H bond functionalization has been demonstrated. Oxidative amidation of benzaldehydes as well as benzylamines with *N*-substituted formamides over heterogeneous Co/Al hydrotalcite-derived catalyst produced the desired products in excellent yields. The catalyst is highly active towards amidation of benzaldehydes and benzylamines bearing various substituents with excellent functional group tolerability. The Co/Al hydrotalcite-derived catalyst is easily separable and recyclable without considerable loss in catalytic activity towards amidation. Mechanistic study suggested that the reaction proceeds through formation of radical intermediates followed by their subsequent coupling to afford the product. The present work provides an environmentally benign synthetic strategy for amides using recyclable heterogeneous catalytic system.

Experimental Section

Catalyst preparation

A series of hydrotalcite-derived catalysts such as Co/Fe (molar ratios of Co^{2+}/Fe^{3+} was 1:1 in the synthesis mixture) and Co/Al (with molar ratios of Co^{2+}/Al^{3+} varying from 1:1, 2:1 and 3:1 in the synthesis mixture) were prepared by a simple co-precipitation method as described in earlier reports with some modifications. [50]

In a typical synthesis of Cat-3, aqueous solutions of $Co(NO_3)_2.6H_2O$ (10 g, 0.034 mol) and $Al(NO_3)_3.9H_2O$ (6.4 g, 0.017 mol) were prepared separately by dissolving respective metal salts in a beaker containing 50 mL of distilled water. The resulting solutions were mixed together and labelled as ***Solution A***. Aqueous solutions of 2M NaOH (8 g, 0.2 mol) and 3M Na_2CO_3 (10.6 g, 0.1 mol) 100 mL each were prepared separately and the resulting solutions were mixed together and labelled as ***Solution B***. ***Solution A*** and ***Solution B*** were drop wise added to a 500 mL glass beaker containing 50 mL of distilled water over a period of 30 min under continuous stirring and pH of the reaction mixture was maintained in the range of 9-10. The resulting slurry was agitated at room temperature for 4 h followed by ageing for 4 h at 70 °C and resulting mixture was cooled at room temperature. The precipitate was filtered and washed thoroughly with distilled water until the filtrate became neutral to the pH paper. The obtained solid was dried in hot air oven at 100 °C for 12 h and then grinded to the fine powders and finally hydrotalcite precursors were calcined in air atmosphere at 600 °C for 6 h to get mixed metal oxides. The remaining catalysts were prepared in a similar way using respective metal precursors and there proportions.

Procedure for the oxidative amidation of various aldehydes using DMF

A mixture of aldehyde (1 mmol), TBHP (5 mmol), catalyst (20 wt %) and DMF (5 mL) was placed in a 50 mL round bottom flask. The reaction was carried out at 100 °C for 24 h under atmospheric pressure. After the reaction, the mixture was allowed to cool at room temperature and catalyst was isolated by simple filtration and then 100 mL of water was added to the filtrate. The organic compounds were extracted with ethyl acetate (2 x 50 mL). The organic layers were combined and dried over Na_2SO_4. Solvent was removed under reduced pressure to give the crude product. The purified product was obtained by column chromatography using silica gel (100-200 mesh) and mixture of petroleum ether and ethyl acetate (1:1 to 2:1) as the eluent. All products were confirmed by GC-MS and ^1H and ^{13}C NMR spectrums were recorded for selected compounds (ESI).

Procedure for the oxidative amidation of benzaldehyde using various *N*-substituted formamides

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A mixture of benzaldehyde (1 mmol), *N*- substituted formamide (1 mmol), TBHP (5 mmol), catalyst (20 wt %) and toluene (5 mL) was placed in a 50 mL round bottom flask. The reaction mixture was stirred for 24 h at 100 °C under atmospheric pressure. Same procedures were followed for catalyst separation, reaction work-up and product purification as described earlier under amidation of various aldehydes with DMF.

Procedure for the oxidative amidation of various benzylamines using DMF

A mixture of benzylamine (1 mmol), TBHP (5 mmol), catalyst (20 wt %) and DMF (5 mL) was placed in a 50 mL round bottom flask. The reaction was carried out at 100 °C for 24 h under atmospheric pressure. Same procedures were followed for catalyst separation, reaction work-up and product purification as described earlier under amidation of various aldehydes with DMF.

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Oxidative Amidation of Benzaldehydes and Benzylamines with *N*-Substituted Formamides over Co/Al Hydrotalcite-derived Catalyst

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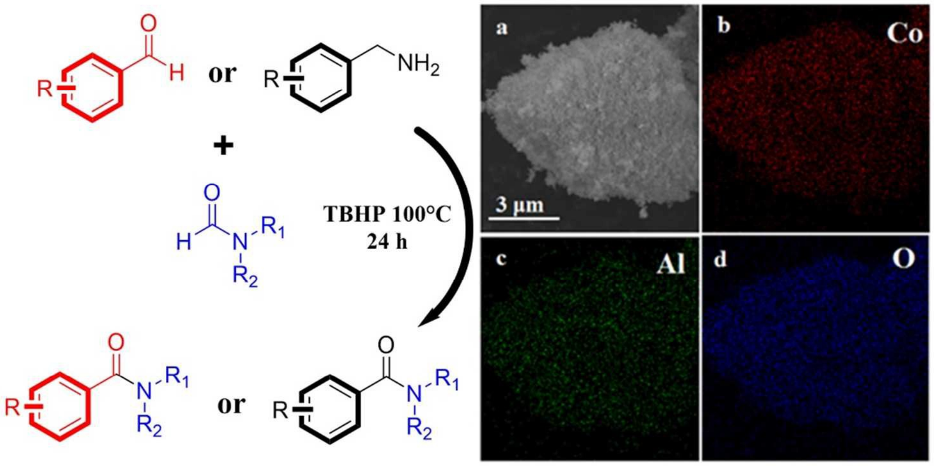

A highly efficient synthetic strategy for amide bond formation by oxidative amidation of various derivatives of benzaldehydes or benzylamines with *N*-substituted formamide using cobalt based heterogeneous recyclable catalytic system has been reported.