

Oxidation of secondary and tertiary amines by a solid base catalyst

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Abstract

A novel recyclable protocol is developed for the oxidation of secondary and tertiary amines to nitrones and amine *N*-oxides, respectively, by Mg–Al–O⁺Bu hydrotalcite (HT–O⁺Bu) catalyst, and benzonitrile as an additive in methanol using 30% hydrogen peroxide at a faster rate in quantitative yields for the first time.

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1. Introduction

Nitrones, which are prepared by oxidation of secondary amines, are highly valuable synthetic intermediates [1] and aliphatic *tert*-amine *N*-oxides prepared from tertiary amines are essential and major components in biomedical area as well as for hair conditioners, shampoos, laundry detergent powders, etc. [2,3]. Various oxidising reagents, hydrogen peroxide [4], peracids [5], and dioxiranes [6] are used for the oxidation of secondary and tertiary amines. The use of these reagents in these reactions encounters disposal of huge amounts of organic waste originated from the reagents and formation of undesirable side products in the reactions, which affects the environment. Later several homogeneous catalytic systems involving metal complexes have been evolved for the oxidation of secondary and tertiary amines include Na₂WO₄–H₂O₂ [7], UHP–M (M: Mo, W) [8], MTO–H₂O₂ [9]. It has been shown by Payne et al. that the use of benzonitrile which gives peroxy-carboximidic acid [10] by the interaction of H₂O₂ with a soluble base, thus formed peroxy-carboximidic acid reacts with double bond of an olefin to give epoxide [10]. The peroxy-carboximidic acid

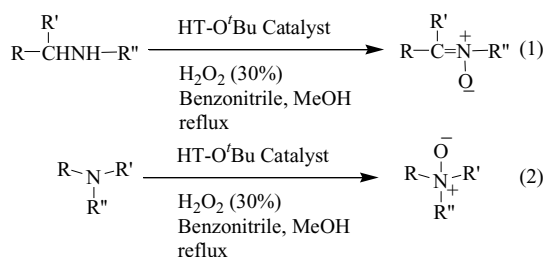
is too reactive to be isolated but its existence was proved by vibrational spectroscopy [11].

The heterogeneous metal catalysts are better candidates as these solid catalysts are tunable, recyclable, and easily separable from the liquid mixtures.

We believe that the hydrotalcites (HT) could be a material of choice for these oxidation reactions in view of their specific basic properties as underlined and their potential usefulness as catalysts [12,13]. The structure of HT consists of brucite [Mg(OH)₂] type octahedral layers in which a part of the M^{II} cations are isomorphously substituted by M^{III} cations. The excess positive charge of the octahedral layers resulting from this substitution is compensated by interstitial layers built of anions, such as carbonates, nitrates, chlorides, cyanides and crystal water. These materials are represented by the general formula [M^{II}_(1-x)M^{III}_x · (OH)₂]^{x+}[(A^{y-})_{x/y} · nH₂O]^{x-}, where M^{II} is a divalent cation and M^{III} is a trivalent cation; Aⁿ⁻ is the interlayer anion, such as OH⁻, Cl⁻, CO₃²⁻, NO₃⁻, SO₄²⁻ and the value of *x* is in the range of 0.1–0.33. The basicity and activity can be easily tuned up by changing the ratio M^{II}/M^{III} elements and or by incorporating different anions, such as OH⁻ or F⁻ in the interlayers of brucite [14,15]. We have recently reported oxidation of secondary and tertiary amines by tungstate-exchanged Mg–Al layered double hydroxides [16,17]. We have also designed and developed HT–O⁺Bu by incorporating O⁺Bu anion in the HT composed Mg^{II} and Al^{III} to enhance the basicity of the

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Scheme 1. The *N*-oxidation of secondary (Eq. (1)) and tertiary amines (Eq. (2)) by HT-O^tBu (cat. A).

HT and found it as an excellent solid base material, displaying manifold activity for Wadsworth–Emmons reactions and in some C–C bond forming reactions [18].

Like in Paynes system, with HTs, the best additives are benzonitrile and dicyanobenzene [19] and the same effect can be obtained by adding an amide [20]. This reaction enables the epoxidation of a large spectrum of substrates [21] and also to the oxidation of thioethers to sulfones using calcined HTs including MgLa mixed oxide [22], but leads to the consumption of the nitrile or amide, additive. Herein we wish to report HT-O^tBu, a recyclable and bio-compatible heterogeneous catalyst for the oxidation of secondary and tertiary amines to nitrones, amine *N*-oxides (Scheme 1) respectively using benzonitrile as an additive.

2. Experimental

2.1. Preparation of HT-NO₃ (Mg/Al, 3/1)

The preparation of HT-NO₃ (Mg/Al, 3/1) was based on a literature procedure [12].

2.2. HT-O^tBu: (cat. A)

HT-NO₃ (Mg/Al, 3/1) was calcined at 723 K in a flow of air for 6 h (temperature raised 25 K min⁻¹) and cooled to room temperature in a flow of dry nitrogen to obtain calcined HT. The calcined HT (1.214 g) was added to a solution of KO^tBu (0.1 M) prepared by dissolving KO^tBu (1.12 g, 10 mmol) in freshly dried THF (100 ml). The solution was stirred for 24 h in a nitrogen atmosphere and then filtered under nitrogen. A white solid, HT-O^tBu (cat. A, 1.432 g), which was obtained, was washed with excess of THF (300 ml admixed with 0.1% of decarbonated water). This protocol restores the partial layered structure of the HT. ^tBuO⁻ was present to an extent of 7.4% as indicated by elemental analysis and rechecked with GC analysis of the desorbed anion [18].

2.3. Mg-Al-OH HT (cat. B)

The Mg-Al-OH HT (Mg/Al, 3:1) was synthesised was prepared as described [14]. Mg-Al-NO₃ (Mg/Al, 3/1)

synthesised as above was first calcined at 450 °C in flow of air at the rate of 10 °C per minute to reach 450 °C and maintained for 8 h. The solid was then rehydrated at room temperature under flow of nitrogen gas (6 l/h) saturated with water vapour for about 6 h and used for the reactions.

2.4. Mg-Al-F HT (cat. C)

The Mg-Al-F HT (Mg/Al, 3:1) was synthesised as detailed in our earlier report [15]. The Mg-Al NO₃ HT synthesised as above was calcined at 450 °C for 8 h in flow of air (ramping at a rate of 10 °C min⁻¹) then cooled to room temperature under a flow of nitrogen. Then the sample of calcined HT (1.0 g) was treated with a solution of (0.1 M, 0.581 g) in 100 ml of deionised and decarbonated water under stirring at room temperature for 24 h to obtain solid of Mg-Al-F HT which was filtered under nitrogen atmosphere and washed with 400 ml of deionised water and vacuum dried at 80 °C.

2.5. General procedure for the oxidation of amines using H₂O₂

To the stirred solution of amine (2 mmol), cat. A (50 mg) and benzonitrile (2 mmol) in methanol (10 ml), was added aqueous solution of 30% (w/w) hydrogen peroxide (6 mmol, 0.66 ml) in two to three portions at room temperature. The temperature is raised to 65–75 °C and continued the reaction. After completion of the reaction (followed by TLC), the catalyst was filtered off and washed with ethyl acetate (2 ml × 10 ml). To the filtrate a small amount of MnO₂ was added to decompose the unreacted H₂O₂. The treated reaction mixture was filtered to remove solid MnO₂, and the product is extracted with ethyl acetate, dried over Na₂SO₄ and evaporated in vacuo to afford the product. Analytical pure compound was obtained after column chromatography (silica gel, hexane/ethyl acetate). The products were characterised by ¹H NMR, mass and IR spectroscopy.

3. Results and discussion

All the catalysts were prepared in our laboratory as detailed in the experimental section following our earlier procedures. HT-O^tBu (Mg/Al, 3:1) (cat. A) was prepared from calcined HT-NO₃. HT-OH (Mg/Al, 3:1) (cat. B) was prepared by calcination of HT-NO₃ followed by rehydration [14]. HT-F (Mg/Al, 3:1, cat. C) was prepared as detailed in our earlier report [15].

All the catalysts listed in Table 1 (cat. A–C) are well characterized [14,15,18]. The HT catalysts (cat. A–C) and their homogeneous analogues were evaluated in the oxidation of secondary (dibutylamine) and tertiary amines (*N*-methyl morpholine) using three molar equivalents of H₂O₂ per mole of the substrate in methanol in an effort to identify the best catalyst (Table 1). The order of the activity of HT catalysts is cat. A > cat. C > cat. B. Essentially, there was no

Table 1

The catalytic *N*-oxidation of *N*-methylmorpholine and dibutylamine using various solid base catalysts and their homogeneous analogues^a

Experiment number	Catalyst	Time (h)	Yield ^b	Time (h)	Yield ^c
1	HT-O ^t Bu (cat. A)	0.5	98, 92 ^d	5	88, 82 ^d
2	HT-OH (cat. B)	5	10	–	–
3	HT-F (cat. C)	5	30	–	–
4	HT-calcined	5	30	5	Nr ^e
5	KO ^t Bu	1.10	95	5	50
6	NaOH	0.75	98	–	–
7	KF	1.5	95	–	–
8	None	24	25	24	Nr ^e

^a Reaction conditions as exemplified in experimental section.^b Isolated yields of *N*-methyl morpholine *N*-oxide.^c Isolated yields of *N*-butylidene butyl amine *N*-oxide.^d Yield after fifth recycle.^e No reaction.

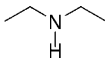
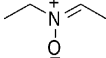
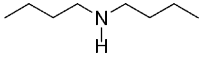
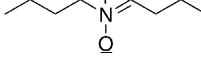
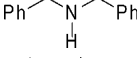
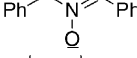
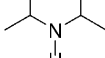
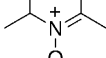
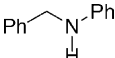
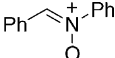






reaction for secondary amines with calcined HT, the precursor of cat. **A** (Table 1, entry 4) and no reaction occurred without catalyst in the oxidation of dibutyl amine (Table 1, entry 8). Aqueous H₂O₂ (30%) is found to be the best oxidant among the oxidants, *tert*-butyl hydroperoxide (TBHP) and molecular oxygen. The oxidant TBHP gave very inferior results, whereas the reaction conducted with molecular oxygen did not proceed under these reaction conditions.

Several secondary and tertiary amines having different kinds of R groups attached to the secondary and

tertiary nitrogen atom were subjected for the oxidation using HT-O^tBu. The results are summarised in Tables 2 and 3. The tertiary amine *N*-oxides thus obtained are the useful additives for the surfactants [23], for example, *N,N'*-dimethyldecylamine *N*-oxide (Table 3, entry 6) sold under trade name *Barlox 10S* [2]. Acyclic and cyclic secondary amines were converted into the corresponding nitrones in good to excellent yields (75–95%) without formation of hydroxylamines in contrast to earlier report [9b]. Similarly, the oxidation of *tert*-amines composed

Table 2

Oxidation of secondary amines catalysed by HT-O^tBu (cat. **A**)^a

Entry	Sec-amine (a)	Nitron (b)	Time (h)	Yield (%) ^b
1			5	85
2			5	88 (82) ^c
3			5	75
4			5	95
5			5	92
6			5	92
7			5	90
8			3	72

^a Reaction conditions are as exemplified in Section 2.^b Isolated yield.^c Yield after fifth recycle.

Table 3
Oxidation of tertiary amines catalysed by HT-O^tBu (cat. A)^a

Entry	Tertiary amine (a)	Amine oxide (b)	Time (min)	Yield ^b
1			30	98 (92) ^c
2			45	96
3			45	94
4			45	96
5			45	97
6			30	97
7			30	95
8			45	95
9			45	79

^a Reaction conditions are as exemplified in Section 2.

^b Isolated yield.

^c Yield after fifth recycle.

of benzylic moiety provided *N*-oxide selectively without over oxidation of benzylic group. The use of benzonitrile which gives peroxyoxycarboximide [10] by the interaction of H₂O₂ however, prompted the *N*-oxidation of amines. Furthermore the cat. A is reused¹ for several cycles (see Table 3, entry 1) and (Table 2, entry 2) without significant loss of its activity and selectivity. In this system, the resultant benzamide could be further employed for the *N*-oxidation: benzamide was formed as a co-product from benzonitrile, which was recovered quantitatively by column chromatography. By using dehydrating reagent, such as P₂O₅, benzamide could be easily regenerated to benzonitrile [24]. No reaction occurred when the reaction is conducted with the filtrate obtained after the removal of the solid catalyst after the reaction, which indicates the active ingredient was not leached out of the solid catalyst.

4. Conclusions

In conclusion, the present study represents the synthesis of amine *N*-oxides and nitrones, wherein the heterogenised HT-O^tBu is used in catalytic amounts and benzonitrile as an additive for several cycles without significant loss of its activity and selectivity. Further more the present protocol dispenses the use of transition metals and their supported catalysts thus avoiding the contamination of toxic metals in their products and conforms the 'greener technology'.

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¹ The protocol for reusability experiments was adopted as detailed in our earlier report using cat A [18].

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