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Alumina supported MoO_3: an efficient and recyclable catalyst for selective oxidation of tertiary nitrogen compounds to N-oxides using anhydrous TBHP as oxidant under mild reaction conditions

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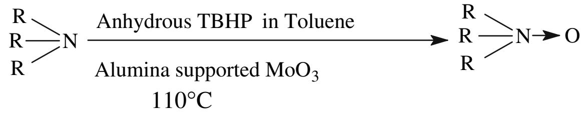
Alumina-supported MoO_3 was found to be an efficient heterogeneous and recyclable catalyst for the oxidation of tertiary nitrogen compounds to N-oxides in excellent yields using anhydrous *t*-BuOOH as oxidant under mild reaction conditions.

KEY WORDS: oxidation; heterogeneous catalysis; MoO3; TBHP; tertiaryamines.

1. Introduction

Development of environmentally clean synthetic methodologies is an ultimate goal of the present day research. The most promising approach towards the "Green chemistry" is to replace the conventional methods employing toxic/or hazardous stoichiometric reagents by atom efficient catalytic processes using transition metals as catalysts [1]. The oxidation of tertiary nitrogen compounds is an important synthetic transformation as N-oxides are extensively used as oxidants, offer functional group manipulation/structural modification possibilities which are not accessible by other methods [2–8]. Although a variety of effective oxidants have been reported in the literature to accomplish this transformation [9–13], most of them suffer from drawbacks such as use of stoichiometric amounts of corrosive acids or toxic metallic compounds that generate copious amounts of undesirable wastes. Catalytic processes using molecular oxygen/hydrogen peroxide/tert-butylhydroperoxide as green oxidants and MTO [14–16], TS-1[17], Mn-porphyrin [18], flavin [19, 20], tungstate exchanged Mg/Al-double hydroxide [21], selenium [22], Ru [23], Co-Schiff bases [24], $VO(acac)_2$ [25,26] as catalysts have also been reported in the literature. Owing to the drawbacks such as difficult separation and regeneration of expensive homogeneous catalysts, the oxidation of tertiary nitrogen compounds to N-oxides using heterogeneous catalysts gaining considerable interest in the recent years. The use of heterogeneous catalysts offer several inherent advantages such as ease of recovery/recycling, safe handling, high atom economy, enhanced stability and long lifetime of the catalyst [27,28]. Although Mo-based systems have been extensively used in various synthetically important oxidation reactions using TBHP as oxidant, to the best of our knowledge there is no literature report on oxidation of tertiary nitrogen compounds. Herein we reveal an efficient heterogeneous oxidative methodology for the oxidation of tertiary nitrogen compounds to N-oxides with the use of anhydrous TBHP in toluene as oxidant and alumina-supported MoO_3 as a recyclable catalyst (Sch. 1).



Scheme 1.

2. Experimental

2.1. Material

All the tertiary amines were commercially available. Catalyst 16 wt% MoO_3 on alumina was obtained as a gift sample from the catalyst preparation lab of this Institute. The anhydrous TBHP was prepared in our laboratory following the literature procedure [29]. The strength of the solution was analyzed by sodium thiosulphate/KI method and was found to be 33%.

2.2. General experimental procedure

The mixture of substrate (10 mmol), anhydrous 33% TBHP in toluene (20 mmol) and catalyst (5 mol%) was stirred at 110 °C for the appropriate time as shown in Table 2. The progress of the reaction was monitored by TLC (SiO_2). After completion of the reaction, catalyst was separated by filtration and the filtrate was concen-

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Table 1
Results of optimization experiments[a]

Entry	Substrate	Solvent	Oxidant	Temperature(°C)	Yield (%)[b]
1	4-picoline	Acetonitrile	Anhyd. TBHP	80	60
2	4-picoline	1,2-Dicholoroethane	Anhyd. TBHP	80	45
3	4-picoline	Dichloromethane	Anhyd. TBHP	35	30
4	4-picoline	–	Anhyd. TBHP	Room	40
5	4-picoline	–	Anhyd. TBHP	50	65
6	4-picoline	–	Anhyd. TBHP	110	92
7	4-picoline	–	70 % TBHP	80	50

[a] Catalyst: 16 wt% MoO_3 supported on Alumina; Reaction time: 3.5 h.
[b] Isolated yields.

trated under reduced pressure. The residue thus obtained was purified by passing through a short silica gel column using ethyl acetate/hexane (4:6) as eluent. Evaporation of the solvent under reduced pressure yielded pure corresponding N-oxides, which were characterized by comparing their physical and spectral data with the literature values.

3. Results and discussion

At first, we selected 4-picoline as the model substrate and studied its oxidation using alumina-supported MoO_3 as catalyst and anhydrous TBHP in toluene as oxidant, to optimize the reaction conditions. Results of these optimization experiments are presented in Table 1. The effect of various additional solvents such as acetonitrile, dichloroethane, dichloromethane into the reaction mixture of 4-picoline, anhydrous TBHP in toluene and catalyst is presented in Table 1, entries 1–4. The neat condition, without adding further solvent at 110 °C was found to be more efficient for this oxidation (Table 1, entry 6). The effect of reaction temperature was also studied by carrying out the oxidation of 4-picoline under similar reaction conditions. At room temperature the reaction was found to be very slow and it could be conducted more efficiently at 110 °C as shown in Table 1, entries 4–6.

In a controlled blank experiment without adding catalyst reaction did not proceed under similar reaction conditions (Table 2, entry 1). To compare the efficiency of this method we studied the oxidation of 4-picoline using aq. About 70% TBHP as oxidant without adding organic solvent under otherwise similar reaction conditions. The oxidation was found to be very slow and gave poor yield of the 4-picoline N-oxide as shown in Table 1, entry 7. To generalize the reaction, oxidation of various tertiary nitrogen compounds was conducted using substrate (10 mmol) and anhydrous TBHP in toluene (20 mmol) in the presence of catalytic amount of alumina-supported MoO_3 (5 mol%) at 110 °C under nitrogen atmosphere, these results are presented in Table 2. In general, aliphatic tertiary amines were found to be most reactive while substituted anilines were found to be more reactive than pyridines. Among the various pyridines those substituted with electron donating groups were found to be more reactive and required shorter reaction time for their oxidation (Table 2, entry 3, 4, 7).

To check the reusability and recyclability of the catalyst we have carried out the oxidation of 4-picoline under similar reaction conditions. After completion of the reaction the catalyst could be separated by filtration and re-used as such for subsequent experiments (for three runs) after adding fresh substrate and oxidant (anhydrous TBHP in toluene) under similar reaction conditions. The catalyst was found to be equally active and provided high yields of 4-picoline-N-oxide, indicating the reusability of the catalyst without loss of activity. Furthermore to check the leaching, the catalyst was heated in toluene containing anhydrous TBHP at 110 °C for 3.5 h. The catalyst was separated by filtration and filtrate was used for the oxidation of 4-picoline under similar reaction condition without adding catalyst and oxidant. No oxidation was observed, indicating that catalyst was not leached out during the reaction. Therefore recycling of the catalyst without loss of activity, no leaching and higher yields of N-oxides established the superiority of the developed protocol for the selective oxidation of tertiary nitrogen compounds to N-oxides.

4. Conclusion

In summary, we have described a new and efficient system for the oxidation of tertiary nitrogen compounds to N-oxides using alumina supported MoO_3 as heterogeneous recyclable catalyst and anhydrous TBHP as oxidant.

Acknowledgment

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Table 2
Alumina-supported molybdenum catalyzed oxidation of tertiary nitrogen compounds using anhydrous TBHP as oxidant[a]

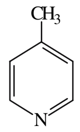
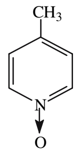
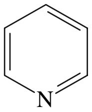
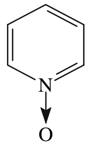
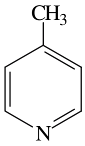
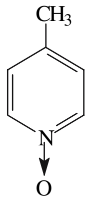
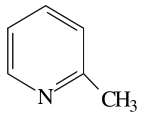
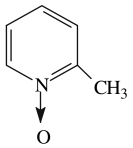
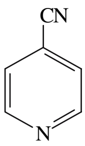
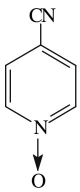
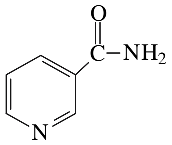
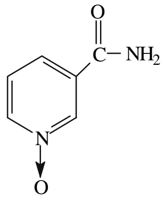
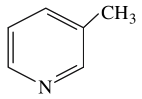
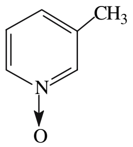
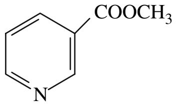
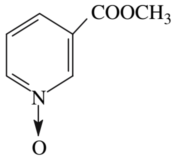
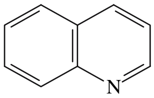
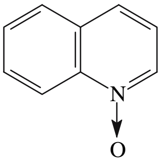
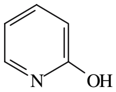
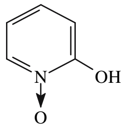
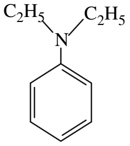
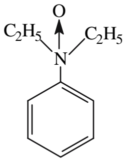
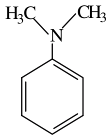
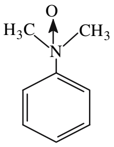
Entry	Substrate	Product	Time (h)	Yield (%)[b]
1[c]			8.0	—
2			4.5	90
3			3.5	92
4			3.5	89
5			5.5	75
6			6.75	70
7			3.75	90
8			5.5	75

Table 2
(*Continued*)

Entry	Substrate	Product	Time (h)	Yield (%)[b]
9			7.25	55
10			4.25	70
11			1.25	92
12			1.0	95
13	Et_3N	$Et_3N \rightarrow O$	1.0	95

[a] Reaction conditions:Substrate (10 mmol), anhyd.TBHP (20 mmol), MoO_3/Al_2O_3 (5 mol%), Temperature 110°C.
[b] *Isolated yields.*
[c] Experiment carried out in the absence of the catalyst.

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