

An Environmentally Friendly Oxidation System for the Selective Oxygenation of Aldimines to Oxaziridines with Anhydrous TBHP and Alumina-Supported MoO₃ as a Recyclable Heterogeneous Catalyst

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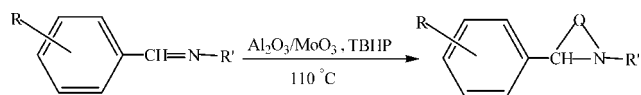
A highly efficient and selective protocol for the oxygenation of various aldimines to oxaziridines, which proceeds in excellent yields with enhanced selectivity by using alumina-supported MoO₃ as a recyclable heterogeneous catalyst and anhydrous TBHP as the ultimate oxidant, is described.

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Introduction

The replacement of conventional oxidation methods, which involve the use of metal oxidants that generate enormous amounts of undesirable waste products, with atom efficient catalytic processes that use green and inexpensive oxidants such as O₂, H₂O₂, TBHP, etc., has gained considerable attention in recent years. In particular, heterogeneous catalysts are preferred because of their inherent advantages, which include its ease of use, its ease of separation from the product, its decreased corrosiveness and its high atom economy, stability and reusability.^[1] In this context, supported metal catalysts such as metal-containing zeolites and alumina-supported metal oxides are extensively used in the development of industrial oxidation processes. However, the major drawbacks of these catalysts are their low activity, their tendency to leach metal catalysts from the support during the reaction and their requirement for high temperatures and pressures. Furthermore, the presence of water in the system not only facilitates the leaching of the metal catalyst from the support, but it also makes the oxidation reactions less efficient and selective as a result of the formation of byproducts. These limitations led us to become interested in the development of environmentally benign oxidation methodologies that use anhydrous oxidants. Recently, TBHP in decane was used as an anhydrous oxidant for the epoxidation of olefins by using immobilized Mo^{VI} complexes on functionalized silica as the heterogeneous catalyst.^[2] Oxygenation of imines is an important synthetic

transformation as oxaziridines are synthetically important building blocks that find wide application in asymmetric synthesis,^[3–5] in the preparation of biologically active compounds^[6,7] and extensively used as nitrogen^[8,9] and oxygen^[10,11] transfer reagents in various synthetically important reactions. A variety of oxidizing agents such as *m*-CPBA,^[12–16] Ac₂O/H₂O₂,^[17] urea/H₂O₂,^[18] H₂O₂/nitrile,^[19,20] *tert*-amyl hydroperoxide^[21] and molecular oxygen^[22,23] in the presence of transition metals were used to accomplish this transformation. However, most of these methods are associated with drawbacks such as harsh reaction conditions, the use of aldehydes as a sacrificial agent, the formation of side products, poor yields and difficult work up procedures, which leaves room to develop an efficient and simple process for the oxygenation of imines to oxaziridines. Herein, we wish to reveal, for the first time, a highly efficient oxidation system for the oxygenation of aldimines to the corresponding 2-alkyl-3-aryl oxaziridines in excellent yields by employing alumina-supported MoO₃ as a heterogeneous recyclable catalyst and anhydrous TBHP in toluene^[24] as the oxidant without using additional organic solvent under mild reaction conditions (Scheme 1).



Scheme 1.

Results and Discussion

A 16 wt-% MoO₃/Al₂O₃ catalyst was prepared on a γ -Al₂O₃ support (Condea, Germany) [BET surface area: 280 m²g⁻¹, total pore volume: 0.7 mLg⁻¹, total acidity: 0.31 mmolg⁻¹ (strong)] by an incipient wet impregnation

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method with the use of ammonium heptamolybdate $[(\text{NH}_4)_6\text{Mo}_7\text{O}_{24} \cdot 4\text{H}_2\text{O}]$ salt. The catalyst was dried at 110 °C (overnight) and finally calcined at 550 °C for six hours.^[25]

Physicochemical Characterization of the Catalyst: The Mo content was estimated by ICP-AES and measured as 16%. XRD pattern did not show any characteristic peak for MoO_3 , which indicates that MoO_3 is finely dispersed over the Al_2O_3 surface. This was in agreement with low-temperature oxygen chemisorption (LTOC) studies, which indicated the crystallite size of MoO_3 to be 16.1 Å with an equivalent molybdenum surface area of $38.6 \text{ m}^2 \text{ g}^{-1}$, surface coverage (θ) 9.1%. Temperature programmed reduction (TPR) studies of the catalyst showed two characteristic peaks first at 500 °C for Mo^{VI} to Mo^{IV} and second at 900 °C for Mo^{IV} to Mo^0 .^[26]

The protocol developed for the oxygenation of various aldimines consists of the addition of anhydrous TBHP in toluene to the stirred reaction mixture of the substrate and the 16 wt-% $\text{MoO}_3/\text{Al}_2\text{O}_3$ catalyst (5 mol-%) at 110 °C without the addition of further organic solvent as the reaction media under a nitrogen atmosphere. We first selected *N*-benzylidene-*tert*-butylamine as a model substrate and studied its oxygenation with TBHP using alumina supported MoO_3 as the catalyst to optimize the reaction conditions. The results of these optimization experiments are presented in Table 1. The effect of various additional solvents such as acetonitrile, dichloroethane and methanol on the oxygenation of *N*-benzylidene-*tert*-butylamine under refluxing conditions is shown in Table 1, Entries 1–4. Surprisingly the reaction was found to be very slow in the presence of additional solvent and required a longer reaction time for completion. In the absence of additional solvent at 110 °C, the reaction was complete within 2.5 h and gave maximum yield of the corresponding oxaziridine. In a controlled blank experiment under similar reaction conditions, the oxygenation of *N*-benzylidene-*tert*-butylamine did not proceed in the absence of catalyst. We also performed the oxygenation of *N*-benzylidene-*tert*-butylamine using pure thermally treated alumina support as the catalyst under otherwise similar reaction conditions. The reaction did not proceed, which indicates that molybdenum oxide is the main promoter for this reaction. Further, the oxygenation of *N*-benzylidene-*tert*-butylamine was found to be highly dependant upon the reaction temperature. At room temperature, the reaction was very slow (Table 1, Entry 5), whereas 110 °C was found to be the optimum temperature for this reaction in terms of reaction time and yield of the product.

To generalize the developed protocol, we studied the oxygenation of various substituted aldimines and these results are depicted in Table 2. All the aldimines except benzylidene-aniline were selectively converted into the corresponding oxaziridines without any evidence for the formation of nitrones or other side products. The oxidation of benzylidene-aniline under these reaction conditions yielded benzaldehyde as the sole product (Table 2, Compound **1k**). Among the various aldimines studied, those having elec-

Table 1. Oxidation of *N*-benzylidene-*tert*-butylamine (**1a**) with anhydrous TBHP by using $\text{MoO}_3/\text{Al}_2\text{O}_3$ as the catalyst under various conditions.

Entry	Additional solvent	Oxidant	Temp. [°C]	Reaction time [h]	Yield [%] ^[a]
1	acetonitrile	anhyd. TBHP	80	5.5	50
2	1,2-dichloroethane	anhyd. TBHP	80	7.0	30
3	methanol	anhyd. TBHP	67	10	55
4	–	anhyd. TBHP	110	2.5	96
5	–	anhyd. TBHP	room	6.0	trace
6	–	anhyd. TBHP	80	4.5	45
7	acetonitrile	70% aq. TBHP	80	5.5	60

[a] Isolated yields.

tron-donating groups on the phenyl ring attached to the C-atom of the aldimine were found to be the most reactive and required shorter reaction times under the described reaction conditions (Table 2, Compounds **1d–f**). Aldimines having electron-withdrawing groups on the phenyl ring were generally found to be less reactive (Table 2, Compounds **1g,h**) than aldimines derived from benzaldehyde and the corresponding amine (Table 2, Compounds **1a–c**, **1i**). However, furfurylidene-*tert*-butylamine was found to be the least reactive and afforded a poor yield of the corresponding oxaziridine under these reaction conditions (Table 2, Compound **1j**).

To compare the efficiency of this method, we performed the oxygenation of *N*-benzylidene-*tert*-butylamine using commercially available aq. TBHP (70%) in combination with 5 mol-% alumina-supported MoO_3 as a catalyst in refluxing acetonitrile. The oxygenation reaction was slow and proceeded with lower selectivity and afforded an intricate mixture of products (Table 1, Entry 7). In addition, we did observe the leaching of the metal while using aq. TBHP as the oxidant. This is probably due to the presence of water, which facilitates the leaching of metal catalysts from the support.

We used anhydrous TBHP in toluene as the oxidant in these experiments; as a result of the absence of water in the system, leaching of the catalyst from the support was not expected. We carried out a catalyst-leaching experiment and studied the oxygenation of *N*-benzylidene-*tert*-butylamine under similar reaction conditions. After completion of the reaction to 50% conversion, we filtered off the catalyst from the reaction mixture and continued the reaction as such at the same reaction temperature. The reaction did not proceed any further, which confirms that there is no catalyst leaching during the reaction. Further, it was ascertained by inductively coupled plasma atomic emission spectroscopy (ICP-AES) that the Mo content of the recovered $\text{MoO}_3/\text{Al}_2\text{O}_3$ catalyst was the same as that of fresh $\text{MoO}_3/\text{Al}_2\text{O}_3$ and there was no dissolved molybdate in the filtrate. To check the recyclability and reusability of alumina-supported MoO_3 with anhydrous TBHP, we carried out the oxygenation of *N*-benzylidene-*tert*-butylamine under similar reaction conditions. After completion of the reaction, the catalyst could be separated by filtration and reused as such for subsequent oxygenation of *N*-benzylidene-*tert*-butylamine

Table 2. MoO₃/Al₂O₃ catalyzed oxidation of aldimines with anhydrous TBHP in toluene.^[a]

Compound	Aldimine (1)	Product (2)	Time [h]	Yield [%] ^[b]
a			2.5	96
b			2.0	98
c			2.0	96
d			1.5	98
e			0.50	96
f			1.50	97
g			3.0	96
h			3.5	94
i			1.5	97
j			4.5	80
k			1.25	98

[a] Reaction conditions: substrate (10 mmol), TBHP in toluene (20 mmol), 16 wt-% MoO₃/Al₂O₃ (5 mol%) at 110 °C under a nitrogen atmosphere without adding further solvent. [b] Isolated yields.

(for three runs) after adding fresh substrate and oxidant (anhydrous TBHP in toluene) under similar reaction conditions. In these experiments, reaction times and yields of the oxaziridine remained almost the same as those reported in Table 3.

Table 3. Results of the reusability study of alumina-supported MoO₃.

Entry	Substrate	Run	Yield ^[a]
1	1a	1	96
2	1a	2	94
3	1a	3	94

[a] Isolated yield.

The use of anhydrous TBHP as a clean and more selective oxidant, the recyclability/reusability of the catalyst with consistent reactivity and no leaching of the Mo species from

the catalyst during the reaction established the merits of this developed protocol over previously known methods.

The exact mechanism of the reaction is not clear at this stage. The reaction probably involves the Mo-catalyzed oxygen transfer from TBHP to substrate promoted by the support.

Conclusions

In summary, we have developed a new and highly efficient methodology for the selective oxygenation of various aldimines to the corresponding oxaziridines in excellent yields using catalytic amounts of 16 wt% MoO₃/Al₂O₃ as a catalyst and anhydrous TBHP as the oxidant. The key advantages of this developed protocol are: (1) the use of anhydrous TBHP as the oxidant provides a nearly water-free atmosphere, which makes the reactions more selective

towards the oxaziridines rather than ring-opening products, (2) the supported $\text{MoO}_3/\text{Al}_2\text{O}_3$ catalyst can be recycled and reused without loss of activity and (3) no leaching of the Mo species from the catalyst during the reaction is observed. Easy work up, high yields of the products, recyclability of catalyst and mild reaction conditions make this method an improved, clean and environmentally acceptable synthetic tool for the oxygenation of imines to oxaziridines.

Experimental Section

General Experimental Procedure: A 33% anhydrous TBHP solution in toluene (20 mmol) was added dropwise to a stirred mixture of aldimine (10 mmol) and 16 wt-% $\text{MoO}_3/\text{Al}_2\text{O}_3$ (5 mol%) at 110 °C under a nitrogen atmosphere without the addition of further solvent. The progress of the reaction was monitored by TLC (SiO_2). After completion, the reaction mixture was cooled to room temperature and diluted with ethyl acetate. The catalyst was separated by filtration through a Buchner funnel and reused as such for subsequent experiments. The filtrate obtained was washed with water (6×). The organic layer was dried with anhydrous Na_2SO_4 , and the solvent was removed under reduced pressure. The crude product was purified by passage through a short column of silica gel (ethyl acetate/hexane, 4:6). The yields and reaction times of the oxaziridines are presented in Table 2.

Supporting Information (see footnote on the first page of this article): Preparation of the catalyst and product characterization data.

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