

# Alumina supported MoO<sub>3</sub> as a highly efficient and recyclable heterogeneous catalyst for the chemoselective acetylation of alcohols, phenols amines and thiols with acetic anhydride under solvent free conditions

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## Abstract

A variety of alcohols, phenols, amines and thiols were selectively and efficiently converted into corresponding acetates by treatment with acetic anhydride in presence of catalytic amount of alumina supported MoO<sub>3</sub> under solvent free conditions at room temperature.

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*Keywords:* Acetylation; Alcohols; Amines; Thiols; Phenols; Heterogeneous catalysis

## 1. Introduction

Functional group manipulations through protection and deprotection strategies are of enormous importance in organic synthesis and extensively used in the preparation of multifunctional target molecules. Among the various protecting methodologies known, acetylation of alcohols, phenols, amines and thiols with acetic anhydride is an important and most preferable approach due to the ease of formation, stability under mild acidic, basic conditions and ease of deprotection of acetates [1,2]. Apart from the use of stoichiometric amounts of bases such as pyridine, triethylamine, DMAP [3] and tributylphosphine [4], which are toxic, flammable and having unpleasant odours, numerous improved protocols which uses metal triflates [5–15], perchlorates [16], zirconia [17], Nafion [18], zeolites [19], iodine [20], La(NO<sub>3</sub>)<sub>3</sub>·6H<sub>2</sub>O [21] as catalysts are reported in the literature to accomplish acetylation of these functional groups with acetic anhydride. However most of these methods are associated with the one or more drawbacks such as stringent reaction conditions, use of expensive, moisture sensitive catalysts such as metal triflates and perchlorates, intolerance of other functional groups, tedious preparation of catalysts (Nafion), harsh reaction conditions, utilization of halogenated volatile organic solvents

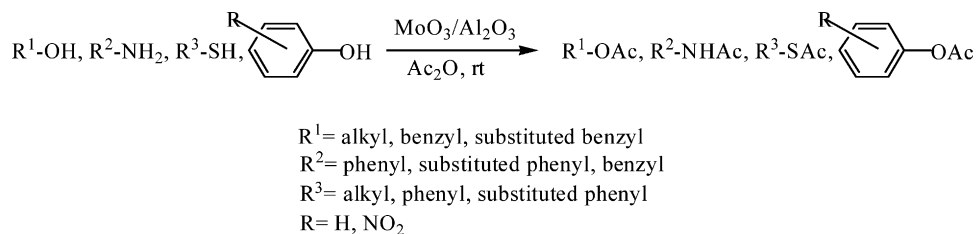
and poor yields of the desired products. Owing to the growing environmental considerations, development of green processes using heterogeneous catalysts under solvent free conditions has aroused great interest in the recent years. Nevertheless, heterogeneous catalysts are more advantageous over homogeneous acid catalysts as they can be easily recovered from reaction mixture by simple filtration and can be reused several times, making the process more economically and environmentally viable.

In continuation to our ongoing research, we reveal herein a new, mild and efficient protocol for acetylation of alcohols, phenols, amines and thiols to esters, phenyl esters, amides and thioesters with acetic anhydride using alumina supported MoO<sub>3</sub> as a recyclable heterogeneous catalyst at room temperature under solvent free conditions (Scheme 1).

## 2. Results and discussions

Protocol developed for acetylation of a variety of benzylic, primary, secondary and hindered tertiary alcohols (5 mmol) consist of the addition of acetic anhydride (10 mmol) in presence of catalytic amount of alumina supported MoO<sub>3</sub> (5 mol%) at room temperature under solvent free conditions. The results of these experiments are summarized in Table 1. All the alcohols were selectively converted to the corresponding acetates in quantitative yields without any evidence for the formation of side products. Among the various hydroxy compounds studied benzylic alcohols were found to be most reactive, giving

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Scheme 1.

Table 1  
Alumina supported MoO<sub>3</sub> catalyzed acetylation of alcohols with acetic anhydride<sup>a</sup>

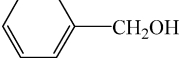
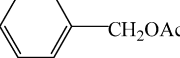
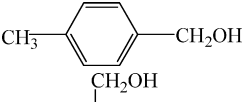
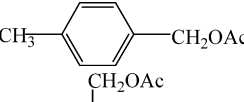
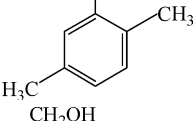
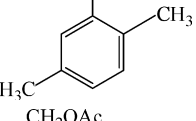
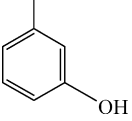
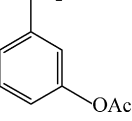
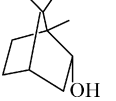
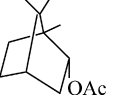
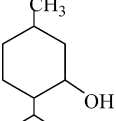
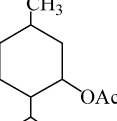
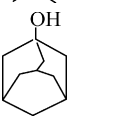
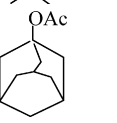
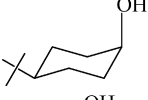
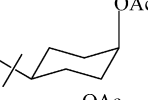
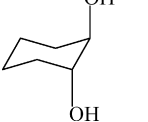
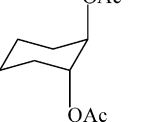
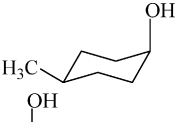
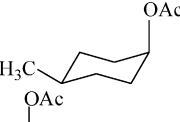
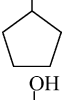
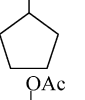
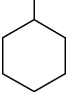
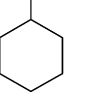
Entry	Substrate	Product	Time (min)	Yield (%) <sup>b</sup>
1	CH <sub>3</sub> -(CH <sub>2</sub> ) <sub>7</sub> -OH	CH <sub>3</sub> -(CH <sub>2</sub> ) <sub>7</sub> -OAc	15	98
2			20	99
3			20	98
4			25	98
5			25	99
6			90	94
7			45	93
8			120	95
9			35	96
10			40	95
11			35	94
12			30	93
13			30	95

Table 1 (Continued)

Entry	Substrate	Product	Time (min)	Yield (%) <sup>b</sup>
14			60	96
15	HO-CH <sub>2</sub> -CH=CH-CH <sub>2</sub> -OH HO-CH <sub>2</sub> -CH=CH-CH <sub>2</sub> -OH	AcO-CH <sub>2</sub> -CH=CH-CH <sub>2</sub> -OAc AcO-CH <sub>2</sub> -CH=CH-CH <sub>2</sub> -OAc	45	90
16	$\text{CH}\equiv\text{C}-\text{CH}(\text{OH})(\text{CH}_2)_4\text{CH}_3$	$\text{CH}\equiv\text{C}-\text{CH}(\text{OAc})(\text{CH}_2)_4\text{CH}_3$	60	85

<sup>a</sup> Reaction conditions: substrate (5 mmol), alumina supported MoO<sub>3</sub> (5 mol%), acetic anhydride (10 mmol) at room temperature under solvent free conditions.

<sup>b</sup> Isolated yields.

corresponding acetylated products within a very short reaction times and the reactivity order for other hydroxy compounds was found to be primary > secondary > tertiary. Non-activated secondary alcohols such as borneol, menthol and hindered tertiary alcohols such as adamantanol could also be converted selectively to corresponding acetylated products in good yields under similar reaction conditions (Table 1, entries 6–8). In a controlled blank experiment, acetylation of 1-octanol with acetic anhydride under similar reaction conditions did not proceed in the absence of catalyst. Alcohols containing other functional groups such but-2-ene-1,4-diol and 1-octyne-3-ol (Table 1, entries 15, 16) were selectively converted to the corresponding acetates and multiple bonds remained intact under these reaction conditions. To explore the potential of this catalytic system, we studied the acetylation of a variety of phenols, amines and thiols under solvent free conditions. Results of these experiments are presented in Table 2. In general acetylation of phenols proceeded relatively slowly as compared to amines. Among the various amines studied, acetylation of primary aromatic amines and anilines was found to be faster than secondary amines and required lesser reaction times.

To check the recyclability and reusability of the catalyst we studied the acetylation of 1-octanol with acetic anhydride under similar reaction conditions. After completion of the reaction the catalyst could be separated by simple filtration and reused as such for subsequent experiments (three times). The yield of the product and reaction time were remained same, indicating the recyclability and reusability of the catalyst without loss of activity.

### 3. Experimental

All the substrates are commercially available and used as obtained. The catalyst used was 16 wt% MoO<sub>3</sub> supported on alumina and obtained as a gift sample from catalyst preparation lab of the Institute. Acetic anhydride was distilled before use.

#### 3.1. General experimental procedure for acetylation of alcohols, amines, thiols and phenols

To a stirred mixture of substrate (5 mmol) and acetic anhydride (10 mmol) was added alumina supported MoO<sub>3</sub> (5 mol%)

Table 2

Alumina supported MoO<sub>3</sub> catalyzed acetylation of amines, thiols, phenols with acetic anhydride<sup>a</sup>

Entry	Substrate	Product	Time (min)	Yield (%) <sup>b</sup>
1			20	99
2			25	96
3			25	97
4			35	95
5			35	98
6			45	95
7	CH <sub>3</sub> -(CH <sub>2</sub> ) <sub>11</sub> -SH	CH <sub>3</sub> -(CH <sub>2</sub> ) <sub>11</sub> -SAc	40	85
8			60	94
9			90	90

<sup>a</sup> Reaction conditions: substrate (5 mmol), alumina supported MoO<sub>3</sub> (5 mol%), acetic anhydride (10 mmol) at room temperature under solvent free conditions.

<sup>b</sup> Isolated yields.

at the room temperature and the reaction was continued under solvent free conditions. The progress of the reaction was monitored by TLC (SiO<sub>2</sub>). At the end of the reaction the catalyst was separated by filtration through a Buckner funnel and reused as such for next experiment. Excess acetic anhydride from the filtrate was removed under reduced pressure. Residue thus obtained was dissolved in ethyl acetate, washed with brine (3 × 5 mL). The combined organic layer was then dried over anhydrous sodium sulphate. Evaporation of the solvent under vacuum yielded pure acetates. The reaction times and yields of the products are presented in Table 1.

#### 4. Conclusion

In summary, we have developed an efficient catalytic procedure for the chemoselective acetylation for protecting various nucleophilic substrates like alcohols, phenols, amines and thiols using alumina supported MoO<sub>3</sub> as recyclable heterogeneous catalyst at room temperature under solvent free mild reaction conditions. The catalyst was found to be recyclable and reusable without further purification several times with out loss of activity. Easy preparation/heterogeneous nature of catalyst, solvent free mild reaction conditions, higher yields, compatibility to various functional groups and versatility towards various substrates make this method a facile tool for acetylation of various functional groups.

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