Alumina-supported Molybdenum (VI) Oxide: An Efficient and Recyclable Heterogeneous Catalyst for Regioselective Ring Opening of Epoxides with Thiols, Acetic Anhydride, and Alcohols under Solvent-free Conditions

Sweety Singhal, Suman L. Jain, and Bir Sain*
Chemical and Biotechnology Division, Indian Institute of Petroleum, Dehradun-248005, India

(Received March 24, 2008; CL-080315)

An efficient and simple protocol for regioselective ring opening of epoxides with thiols, acetic anhydride, and alcohols using 16 wt % MoO_3 supported on alumina as a recyclable catalyst is described.

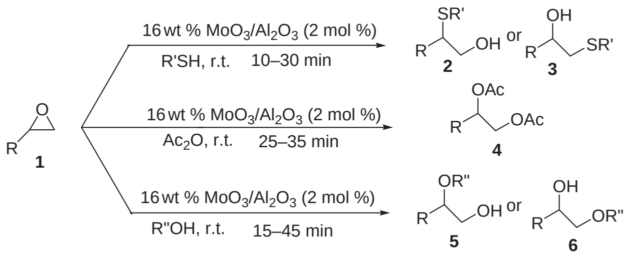
Epoxides are highly versatile synthetic intermediates in organic synthesis as they undergo ring-opening reactions with various nucleophiles to afford 1,2-difunctionalized compounds.

β-Hydroxysulphides, 1,2-diacetates, and β-alkoxyalcohols are valuable synthones and being extensively used as key intermediates in the synthesis of various biologically active natural and synthetic products.[1] The easiest and straightforward approach for their synthesis involves the ring opening of epoxides with appropriate nucleophile under acidic or basic conditions. Since alcohols, thiols, and acetic anhydride are comparatively poor nucleophiles than amines, therefore require strong acidic or basic conditions, high temperature, and large excess of nucleophile. These limitations led to the development of mild catalytic methodologies involving the use of metal salts/complexes,[2] metal triflates,[3] microwave irradiation,[4] ionic liquids,[5] and solvent-free protocols. However, most of the existing methods suffer from one or more drawbacks such as the use of expensive reagents, toxic/volatile organic solvents, homogeneous nature of the catalyst, low regioselectivity, extended reaction times, and poor yields. Recent developments have focused considerable attention towards the use of heterogeneous catalysts due to their ease of handling, facile recovery from the reaction mixture, higher stability and recyclability. Further, solventless synthetic methods are valuable not only for green chemistry reasons but also for simplicity in procedure and provide high yield of the desired product.[6]

In this context, heterogeneous catalysts such as mesoporous aluminosilicates,[7] HBF_4–SiO_2,[8] ammonium 12-molybdophosphate,[9] and aluminododecatungstoposphate ($AlPW_{12}O_{40}$)[10] have been utilized for the regioselective ring opening of epoxides by using thiols, alcohols, and acetic anhydride as nucleophiles. However, the drawbacks associated with most of these methods are tedious preparation of catalysts and longer reaction times.

In the present letter we wish to report that MoO_3 supported on alumina, an easily accessible, stable catalyst can efficiently be applied as a recyclable heterogeneous catalyst for the regioselective ring opening of epoxides with thiols, acetic anhydride and alcohols to afford corresponding β-hydroxysulphides, 1,2-diacetates, and β-alkoxyalcohols in a very good to excellent yields under solvent-free conditions (Scheme 1).

16 wt % MoO_3/Al_2O_3 catalyst was prepared on γ-Al_2O_3 support by the incipient wet impregnation method using ammonium heptamolybdate [$(NH_4)_6Mo_7O_{24}\cdot 4H_2O$] salt following the literature procedure.[11] The prepared catalyst was dried at 110 °C (overnight) and finally calcined at 550 °C for 6 h. Physicochemical characterization data of the prepared catalyst are given in another literature report.[12]



R = alkyl, aryl, cycloalkyl
R' = aryl, benzyl
R" = alkyl, benzyl

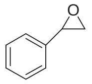
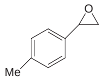
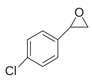
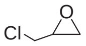
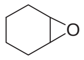
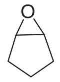
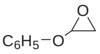
Scheme 1.

Initially, we studied the reaction of styrene oxide with benzenethiol in the presence of catalytic amount of 16 wt % MoO_3/Al_2O_3 (2 mol %) at room temperature under solvent-free reaction condition. The reaction was completed within 10 min and yielded **2a** regioselectively in a nearly quantitative yield being formed by the cleavage at benzylic position (Table 1, Entry 1). The reaction did not occur neither in the absence of the MoO_3/Al_2O_3 nor with the use of thermally treated pure Al_2O_3 as catalyst. Whereas the reaction was found to be slow with the use of thermally treated pure MoO_3 (Aldrich) as a catalyst and led to the product in a very poor yield even after prolonged reaction time. We assume that the higher catalytic activity of 16 wt % MoO_3/Al_2O_3 is probably due to the increased Lewis acidity of the Mo oxide dispersed on alumina support.

To generalize the reaction, we carried out the thiolysis of various alkyl, aryl, and cycloalkyl epoxides with a variety of thiols under similar reaction conditions.[13] In all cases, the reaction was found to be regioselective in nature and afforded very good to excellent yields of the corresponding β-hydroxysulfide. These results are presented in Table 1. We observed that aryl epoxides underwent cleavage at the benzylic position (Table 1, Entries 1, 2, 8–11, 15, and 16), probably due to the formation of stabilized benzylic cation as reactive intermediate, while alkyl epoxides such as epichlorohydrin **3a** and **3b** underwent ring opening with the preferential attack at terminal position. Nevertheless, Posner and Rogers reported the Woelm 200 neutral chromatographic alumina catalyzed nucleophilic ring opening of epoxides under mild reaction conditions.[14] However, the use of excess alumina (7.5 g for 1 mmol of epoxide) as well as nucleophile (>4 mmol/mmol of epoxide), comparatively lower product yields and need to use large amount of solvent (diethyl ether) for the reaction as well as work-up makes its utility limited.

To extend the scope of the protocol developed we also stud-

Table 1. 16 wt % MoO_3/Al_2O_3 catalyzed ring opening of epoxides with various nucleophiles[a,b]

Entry	Epoxide **1**	Nucleophile	Product	Time /min	Yield[c] /%
1		PhSH	**2a**	10	97
2		$PhCH_2SH$	**2b**	15	89
3		Ac_2O	**4a**	25	96
4		MeOH	**5a**	15	96
5		$PhCH_2OH$	**5b**	45	80
6		*i*-PrOH	**5c**	30	90
7		*t*-BuOH	**5d**	40	91
8		PhSH	**2c**	15	94
9		$PhCH_2SH$	**2d**	25	88
10		*p*-$CH_3C_6H_4SH$	**2e**	15	92
11		*p*-ClC_6H_4SH	**2f**	15	89
12		Ac_2O	**4b**	30	95
13		MeOH	**5e**	15	94
14		*i*-PrOH	**5f**	35	91
15		PhSH	**2g**	15	96
16		*p*-BrC_6H_4SH	**2h**	20	90
17		Ac_2O	**4c**	30	97
18		MeOH	**5g**	20	97
19		*i*-PrOH	**5h**	30	93
20		PhSH	**3a**	20	90
21		$PhCH_2SH$	**3b**	30	85
22		*p*-ClC_6H_4SH	**3c**	20	89
23		Ac_2O	**4d**	35	89
24		MeOH	**6a**	40	90
25		*i*-PrOH	**6b**	45	89
26		PhSH	**3d**	15	97
27		*p*-ClC_6H_4SH	**3e**	20	88
28		Ac_2O	**4e**	30	94
29		*i*-PrOH	**6c**	30	91
30		PhSH	**3f**	15	96
31		$C_6H_5CH_2SH$	**3g**	20	88
32		Ac_2O	**4f**	30	94
33		MeOH	**6d**	15	93
34		*i*-PrOH	**6e**	15	90
35		PhSH	**3h**	25	90
36		$C_6H_5CH_2SH$	**3i**	30	87
37		Ac_2O	**4g**	15	90
38		MeOH	**6f**	20	90

[a]Reaction condition: Epoxide **1** (2 mmol), nucleophile **2** (2.2 mmol), 16 wt % MoO_3/Al_2O_3 (2 mol %) at room temperature. [b]For alcoholysis 4 mmol of alcohol was used. [c]Isolated yields.

ied the ring opening of epoxides with acetic anhydride under similar reaction conditions. In all cases, the conversion was completed in 25–35 min and yielded exclusively 1,2-diacetates in high yields (Table 1, Entries 3, 12, 17, 23, 28, 32, and 37). Similarly, the procedure worked well for alcoholysis of epoxides with a variety of benzylic, primary, secondary, and tertiary alcohols under the same experimental conditions. All the reactions were found to be selective and afforded corresponding β-alkoxy-alcohols in very good to excellent yields. These results are presented in Table 1 (Entries 4–7, 13, 14, 18, 19, 24, 25, 29, 33, 34, and 38). In contrast to most of the reported methods, which are effective only with primary alcohols, the present methodology worked equally well with secondary and tertiary alcohols and afforded high yields of the products **5c**, **5d**, **5f**, **5h**, **6b**, **6c**, and **6e** being formed via regioselective ring opening of epoxides.[7]

Next we checked the recycling of the catalyst using the reaction of styrene oxide and benzenethiol as a representative example. At the end of the reaction, the catalyst could easily be recovered from the reaction mixture by simple filtration and reused as such for subsequent four runs without loss in catalytic activity.

To check the leaching of metal during the reaction, the catalyst was separated by filtration and the filtrate so obtained was analyzed by inductively coupled plasma atomic emission spectroscopy (ICP-AES). There was no solved molybdate detected, establishing that the reaction is completely heterogeneous in nature.

The merits of the protocol developed reflected by the fact that MoO_3 supported on alumina is an easy accessible, inexpensive, and versatile catalyst which can efficiently be applied for the regioseelctive ring opening of epoxides with various nucleophiles in high yields under solvent-free condition and could be recycled without loss in activity.

We kindly acknowledge the Director, IIP for his kind permission to publish these results and SS, SJ are thankful to CSIR for their research fellowships.

References and Notes

1 J. R. Luly, N. Yi, J. Soderquist, H. Stein, J. Cohen, T. J. Perun, J. J. Plattner, *J. Med Chem.* **1987**, *30*, 1609; E. J. Corey, D. A. Clark, G. Goto, A. Marfat, C. Moiskowski, B. Samuelsson, S. Hammarstrom, *J. Am. Chem. Soc.* **1980**, *102*, 1436; P. G. Williams, W. Y. Yoshida, R. E. Moore, V. J. Paul, *J. Nat. Prod.* **2002**, *65*, 29.

2 Shivani, A. K. Chakraborti, *J. Mol. Catal. A: Chem.* **2007**, *263*, 137; W. Su, J. Chen, H. Wu, C. Jin, *J. Org. Chem.* **2007**, *72*, 4524; N. Iranpoor, H. Adibi, *Bull. Chem. Soc. Jpn.* **2000**, *73*, 675.

3 N. Iranpoor, M. Shekarriz, F. Shiriny, *Synth. Commun.* **1998**, *28*, 347.

4 V. Pironti, S. Colonna, *Green Chem.* **2005**, *7*, 43.

5 J. Chen, H. Wu, C. Jin, X. Zhang, Y. Xie, W. Su, *Green Chem.* **2006**, *8*, 330; B. C. Ranu, T. Mandal, S. Banerjee, S. S. Dey, *Aust. J. Chem.* **2007**, *60*, 278.

6 K. Tanaka, F. Toda, *Chem. Rev.* **2000**, *100*, 1025; A. Loupy, A. Petit, J. Hamelin, F. Texier-Boullet, P. Jacquault, D. Mathe, *Synthesis* **1998**, 1213.

7 M. W. C. Robinson, R. Buckle, I. Mabbett, G. M. Grant, A. E. Graham, *Tetrahedron Lett.* **2007**, *48*, 4723.

8 B. P. Bandgar, A. V. Patil, O. S. Chavan, V. T. Kamble, *Catal. Commun.* **2007**, *8*, 1065.

9 B. Das, V. S. Reddy, F. Tehseen, *Tetrahedron Lett.* **2006**, *47*, 6865.

10 H. Firouzabadi, N. Iranpoor, A. A. Jafari, S. Makarem, *J. Mol. Catal. A: Chem.* **2006**, *250*, 237.

11 B. M. Reddy, E. P. Reddy, S. T. Srinivas, *J. Catal.* **1992**, *136*, 50.

12 S. Singhal, S. L. Jain, V. V. D. N. Prasad, B. Sain, *Eur. J. Org. Chem.* **2007**, 2051.

13 General experimental procedure: Into a stirred mixture of an epoxide (2 mmol) and 16 wt % MoO_3/Al_2O_3 (2 mol %) contained in a 25-mL round-bottomed flask was added nucleophile (2.2 mmol, in case of alcoholysis 4 mmol of alcohol was used). The reaction was further continued at room temperature with stirring for the time period as mentioned in the Table 1. After completion of the reaction, reaction mixture was dissolved in Et_2O (5 mL) and catalyst was recovered by filtration. The organic layer was washed with water (3 × 10 mL), dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography to yield pure 1,2-difunctionalized products. The recovered catalyst was washed with Et_2O, dried under vacuum and reused for further experiments.

14 G. H. Posner, D. Z. Rogers, *J. Am. Chem. Soc.* **1977**, *99*, 8208; G. H. Posner, *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 487.