

Short communication

Phosphomolybdic acid- Al_2O_3 : A mild, efficient, heterogeneous and reusable catalyst for regioselective opening of oxiranes with amines to β -amino alcohols

S. Ramesh Kumar*, P. Leelavathi

Department of Chemistry, College for Women, Koti, Osmania University, Hyderabad 500 095, India

Received 20 September 2006; received in revised form 20 October 2006; accepted 21 October 2006

Available online 27 October 2006

Abstract

Epoxides undergo smoothly ring-opening reaction with various amines catalyzed by solid acid containing phosphomolybdic acid-neutral alumina under mild reaction conditions. All the reactions were carried out at room temperature to afford the corresponding β -amino alcohols in excellent yields and with high regioselectivity. The catalyst was recovered and reused for further reactions with very good efficiency.
© 2006 Elsevier B.V. All rights reserved.

Keywords: Epoxides; Amines; Solid acid; PMA (phosphomolybdic acid); Alumina; 2-Amino alcohols

1. Introduction

2-Amino alcohols are versatile intermediates for the synthesis of various biologically active natural products, unnatural amino acids, β -blockers, insecticidal agents, chiral auxiliaries and oxazolines [1]. One of the most straightforward synthetic approaches for the preparation of β -amino alcohols involves the heating of an epoxide with an excess of amines at elevated temperature [2]. Since some functional groups are sensitive to high temperature, a variety of activators such as metal halides [3], metal perchlorates [4], metal triflates [5], ionic liquids and hexafluoro-2-propanol [6], metal complexes [7] have been developed for this conversion. However, many of these methods involve the use of expensive and stoichiometric amounts of reagents, suffer from poor regioselectivity and also require extended reaction times. Therefore, the development of a new and efficient protocol for this transformation under mild and more convenient conditions is still needed. Phosphomolybdic acid (PMA) belongs to the class of heteropoly acids (HPA). The catalyst using HPAs and related polyoxometalate compounds is the field of growing interest. HPAs are commercially cheap and again the attention of researchers as environmentally benign

protocols for various organic transformations. It has been shown that in organic media, the molar catalytic activity of HPAs is often 100–1000 times higher than that of H_2SO_4 . Therefore, this makes it, possible to carry out catalytic processes at low concentration. Supported HPAs are more active than typical solid acids. The acidic or neutral solid substances like silica gel, alumina, ion exchange resin and active carbon are suitable supports. The more conveniently being used as neutral solid support in many organic transformations is neutral alumina [8].

2. Results and discussions

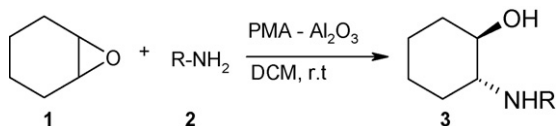
As part of our ongoing program towards the development of new synthetic methodologies, we report herein our results on regioselective ring opening of various oxiranes with a variety of amines using the catalyst phosphomolybdic acid doped on neutral alumina [9] under mild reaction conditions (Scheme 1).

To optimize the reaction conditions, equimolar amounts of styrene oxide (2 mmol) and aniline (2 mmol) were treated in presence of phosphomolybdic acid-alumina catalyst at room temperature to obtain the corresponding β -amino alcohol in 93% yield (entry **a**). The reaction was carried out in methylene dichloride solvent and completed within 0.5 h. The epoxide opening took place in a regioselective manner with the attack of the nucleophile at the benzylic position. After completion of reaction, the catalyst was filtered, washed with solvent and used for next reac-

* Corresponding author. Tel.: +91 40 27221412; fax: +90 40 23818059.
E-mail address: rameshteja_2001@yahoo.co.in (S. Ramesh Kumar).



Scheme 1. .



Scheme 2. .

tion. In a similar manner, *p*-anisidine and styrene oxide reaction was completed with in 1.0 h, giving the corresponding 2-amino alcohol in 91% yield (entry **b**). The same styrene oxide and benzyl amine gave the major product as benzylic opening and minor amount (5%) of terminal opening (entry **c**). Whereas, in the case of butyl amine and styrene oxide, only one product of least hindered of terminal opening took place to afford the corresponding β -amino alcohols in very good yields (entry **d**). The structures of the products were confirmed by their ^1H NMR spectrum.

However, in the case of cyclohexene oxide and with various amines like aromatic, substituted aromatic, benzylic and aliphatic amines reacted smoothly and the ring opening took place in $\text{S}_{\text{N}}2$ fashion to afford the corresponding β -amino alcohols (entries **e–h**) in very good yields. The stereochemistry of the ring opening products was found to be *trans* from the coupling constants of the ring protons in ^1H NMR spectrum (Scheme 2).

In a similar manner, glycidyl aryl ether oxirane with aromatic, aliphatic and alicyclic amines reacted efficiently to afford the corresponding β -amino alcohols in very good yields with high regioselectivity (entries **i–l**). In these cases, the epoxide opening took place in regioselective manner preferentially by terminal attack of the nucleophile. In these reactions also, the product was obtained as a single isomer and the structure of which was confirmed by their ^1H NMR spectrum.

In general all the reactions were completed with in 0.5–2.5 h and the obtained yields also in very good to excellent (84–93%). The catalyst phosphomolybdic acid-alumina was conveniently separated from the reaction mixture by simple filtration. The recovered catalyst showed almost equal efficiency (with little variation) in consecutive three cycles for the same conversion without loss of activity. All the reactions were carried out at room temperature in methylenedichloride as the solvent. The catalyst system can easily be prepared from readily available PMA and neutral alumina. Thus, the process is environmentally benign.

3. Conclusion

In conclusion, we have demonstrated a novel and highly efficient methodology for the regioselective ring opening of various epoxides with a variety of amines using phosphomolybdic acid-alumina catalyst system. The notable features of this procedure are mild reaction conditions, excellent regioselectivity, cleaner reactions, improved yields, enhanced reaction rates, reusabil-

ity of the catalyst and simplicity in operation, which makes it a useful and attractive process for the synthesis of β -amino alcohols.

4. Experimental section

4.1. General methods

IR spectra were recorded on a Perkin-Elmer FT-IR 240-c spectrophotometer. ^1H NMR spectra were recorded on Gemini-200 spectrometer in CDCl_3 using TMS as internal standard. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70 eV. The spectroscopic data of products was compared with the data reported in the literature.

4.2. General procedure

To a mixture of epoxide (2 mmol) and amine (2 mmol) in dichloromethane (10 ml) was added phosphomolybdic acid-alumina (200 mg) and the resulting mixture was stirred at room temperature for a specified period (Table 1). The progress of the reaction was monitored by TLC. After complete conversion of the starting material, as indicated by TLC, the reaction mixture was filtered and the catalyst washed with methylenedichloride (2×10 ml). The filtrate was directly adsorbed on silica gel (60–120 mesh) and eluted with ethyl acetate and *n*-hexane (3:7) mixture to afford the corresponding pure 2-amino alcohol in excellent yields.

4.3. Spectral data for selected compounds

4.3.1. 2-(Phenylamino)-2-phenylethanol (**a**)

IR (KBr): ν 3341, 3267, 3047, 3051, 2972, 2847, 1605, 1543, 1511, 1438, 1361, 1310, 1232, 1128, 1045, 1005, 986, 878, 746 cm^{-1} . ^1H NMR (CDCl_3): δ 3.78 (dd, 1H, $J=5.0, 10.5$ Hz), 3.90 (dd, 1H, $J=4.0, 10.5$ Hz), 4.55 (dd, 1H, $J=6.5, 10.8$ Hz), 6.40 (d, 2H, $J=7.5$ Hz), 6.80 (t, 1H, $J=7.8$ Hz), 6.95 (d, 2H, $J=8.0$ Hz), 7.35–7.45 (m, 5H). EIMS: m/z (%): 213 (M^+ 25), 195 (18), 185 (10), 107 (100), 91 (35), 77 (28), 57 (40).

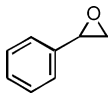

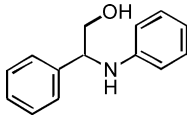
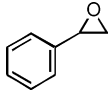
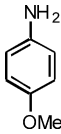
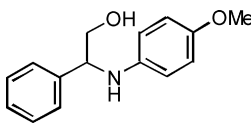
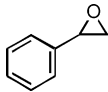
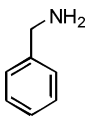
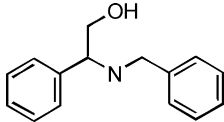
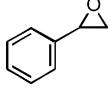
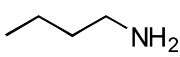
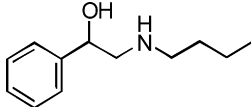
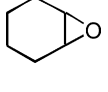

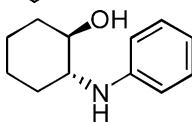
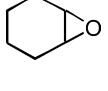
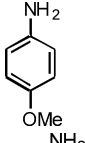
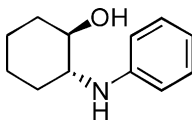
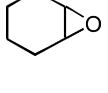
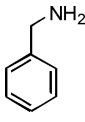
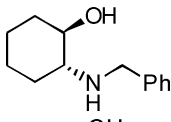
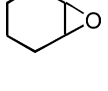
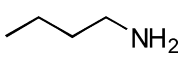
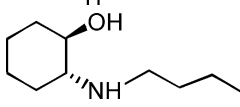
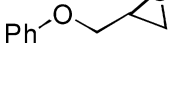

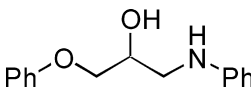
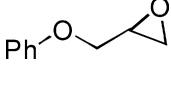
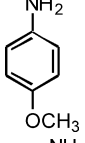
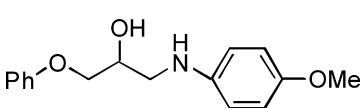
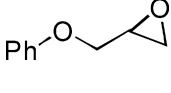
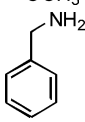
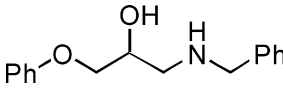
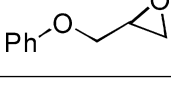
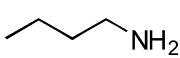
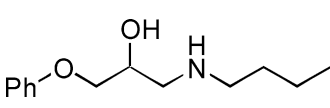
4.3.2. *trans*-2-(Phenylamino) cyclohexanol (**e**)

IR (KBr): ν 3358, 3269, 3047, 2938, 2856, 1605, 1571, 1508, 1450, 1318, 1241, 1126, 1065, 1012, 985, 863, 742 cm^{-1} . ^1H NMR (CDCl_3): δ 1.05–1.40 (m, 4H), 1.48 (brs, 1H, OH), 2.15–2.25 (m, 2H), 2.80–2.90 (m, 2H), 3.20 (ddd, 1H, $J=3.5, 10.0, 10.0$ Hz), 3.40 (ddd, 1H, $J=4.0, 10.0, 10.0$ Hz), 3.80 (brs, 1H), 6.80–7.10 (m, 5H). EIMS: m/z (%): 191 (M^+ 20), 174 (15), 114 (45), 92 (22), 82 (10), 77 (100), 63 (10), 51 (20), 43 (25).

4.3.3. *trans*-2-(OMe-phenylamino) cyclohexanol (**f**)

IR (KBr): ν 3361, 3274, 3052, 2943, 2851, 1608, 1569, 1506, 1452, 1315, 1243, 1205, 1122, 1062, 1015, 987, 857, 743 cm^{-1} . ^1H NMR (CDCl_3): δ 1.08–1.30 (m, 1H), 1.38–1.48 (m, 3H), 1.75–1.83 (m, 2H), 2.20–2.30 (m, 2H), 3.20 (ddd, 1H, $J=3.5, 10.0, 10.0$ Hz), 3.40 (ddd, 1H, $J=4.0, 10.0, 10.0$ Hz), 3.80 (brs, 1H), 3.90 (s, 3H), 6.85 (d, 2H, $J=7.0$ Hz), 7.30 (d,

Table 1
PMA-Al₂O₃ catalyzed opening of oxiranes with amines

Entry	Epoxide (1)	Amine (2)	Product (3a–3l)	Reaction time (h)	Yield (%)
a				0.5	93
b				1.0	91
c				1.5	89
d				2.0	87
e				1.0	90
f				1.5	88
g				2.0	86
h				2.5	84
i				1.5	91
j				1.5	90
k				2.0	88
l				2.5	86

2H, $J=7.0$ Hz). EIMS: m/z (%): 221 (M^+ 20), 206 (12), 190 (100), 174 (10), 114 (55), 86 (28), 76 (61), 51 (22), 43 (18).

References

- [1] (a) P.W. Erhardt, C.W. Woo, W.G. Anderson, Gorczyński, J. Med. Chem. 25 (1982) 1408;
(b) A.V. Narsaiah, Synth. Commun. 2006 (1897);

- (c) D.J. Ager, I. Prakash, D.R. Schaad, Chem. Rev. 96 (1996) 835;
(d) E.J. Corey, F. Zhang, Angew. Chem. Int. Ed. Engl. 38 (1999) 1931;
(e) D.S. Bose, A.V. Narsaiah, Bioorg. Med. Chem. (2005) 627;
(f) P. O'Brien, Angew. Chem. Int. Ed. Engl. 38 (1999) 326.
[2] (a) R.M. Hanson, Chem. Rev. 91 (1991) 437;
(b) S.C. Bergmeier, Tetrahedron 56 (2000) 2561;
(c) J.A. Deyrup, C.L. Moyer, J. Org. Chem. 34 (1969) 175;
(d) R. Gupta, S. Paul, A.K. Gupta, P.L. Kachroo, Dandia, Ind. J. Chem. (1997) 281;

- (e) D.M. Hodgson, A.R. Gibbs, G.P. Lee, *Tetrahedron* 52 (1996) 14361.
- [3] (a) T. Ollevier, G. Lavie-Compin, *Tetrahedron Lett.* 43 (2002) 7891;
(b) J. Iqbal, A. Pandey, *Tetrahedron Lett.* 31 (1990) 575;
(c) L.D. Pachon, J.J.M. Gamez, Van Bassel, Reedijk, *Tetrahedron Lett.* 44 (2003) 6025;
(d) A.K. Chakraborti, A. Kondaskar, *Tetrahedron Lett.* 44 (2003) 8315;
(e) J.S. Yadav, B.V.S. Reddy, K. Harikishan, Ch. Madhan, A.V. Narsaiah, *Synthesis* (2005) 2897;
(f) A.K. Chakraborti, S. Rudrawar, A. Kondaskar, *Eur. J. Org. Chem.* (2004) 3597.
- [4] (a) M. Chini, P. Crotti, F. Macchia, *J. Org. Chem.* 56 (1991) 5939;
(b) N. Azizi, M.R. Saidi, *Can. J. Chem.* (2005).
- [5] (a) J. Auge, F. Leroy, *Tetrahedron Lett.* 37 (1996) 7715;
(b) G. Sekhar, V.K. Singh, *J. Org. Chem.* 64 (1999) 287;
(c) N. Meguro, N. Asao, Y. Yamamoto, *Perkins Trans. 1* (1994) 2597;
(d) I. Cepanec, M. Latvic, H. Mikuldas, A. Bartolincic, V. Vinkovic, *Tetrahedron* 59 (2003) 2435;
(e) M. Fujiwara, M. Imada, A. Baba, H. Matsuda, *Tetrahedron Lett.* 30 (1989) 739;
(f) J.S. Yadav, A.R.R. Reddy, A.V. Narsaiah, B.V.S. Reddy, *J. Mol. Catal. A* 261 (2006) 207;
(g) T. Ollevier, G. Lavie-Compin, *Tetrahedron Lett.* 45 (2004) 49.
- [6] (a) R.H. Fan, X.L. Hou, *J. Org. Chem.* 68 (2003) 726;
(b) J.S. Yadav, B.V.S. Reddy, A.K. Basak, A.V. Narsaiah, *Tetrahedron Lett.* 44 (2003) 1047;
- (c) U. Das, B. Crousse, V. Kesavan, D. Bonnet-Delpon, J.P. Begue, *J. Org. Chem.* 65 (2000) 6749.
- [7] (a) P.Q. Zhao, L.W. Xu, C.G. Xia, *Synlett* (2004) 846;
(b) A. Kamal, P. Ramu, M.A. Azhar, G.B.R. Khanna, *Tetrahedron Lett.* 46 (2005) 2675;
(c) S. Rampalli, S.S. Chaudhari, G. Akamanchi, *Synthesis* (2000) 78;
(d) J. Cossy, V. Bellosta, C. Hamoir, J.R. Desmurs, *Tetrahedron Lett.* 43 (2002) 7083;
(e) M. Caron, K.B. Sharpless, *J. Org. Chem.* 50 (1985) 1557;
(f) W.H. Leung, E.K.F. Chow, M.C. Wu, P.W.Y. Kum, L.L. Yeung, *Tetrahedron Lett.* 36 (1995) 107.
- [8] (a) R.S. Varma, R. Dahiya, R.K. Saini, *Tetrahedron Lett.* 38 (1997) 7029;
(b) G.P. Kalena, A. Jain, A. Benerji, *Molecules* (1997) 100;
(c) Ch. Ramesh, J. Banerjee, R. Pal, B. Das, *Adv. Synth. Catal.* 345 (2003) 557;
(d) D.S. Bose, B.J. Lakshmi, A.V. Narsaiah, *Synthesis* (2000) 67;
(e) D.S. Bose, A.V. Narsaiah, *Tetrahedron Lett.* 39 (1998) 6533;
(f) N. Mizuno, M. Misono, *Chem. Rev.* (1998) 199;
(g) T. Okuhara, N. Mizuno, M. Misono, *Adv. Catal.* 41 (1996) 113.
- [9] Catalyst preparation: a mixture of phosphomolybdic acid (1 g) and neutral alumina (10 g) were taken in methylenedichloride (50 ml) and stirred well. The solvent was removed under reduced pressure, the obtained powdered catalyst mixture was used for reactions.