© 2018 IJSRST | Volume 4 | Issue 2 | Print ISSN: 2395-6011 | Online ISSN: 2395-602X
Themed Section: Science and Technology

Copper (0) an Efficient Catalyst for the Synthesis of Biologically Active 1, 2-Amino Alcohols

Santosh S. Devkate*[1], Arvind S. Burungale[2], Ashok S. Pise[2], Ramesh B. Gawade[2], Mohan B. Kale[2] , Sunil D. Jadhav[3]

*[1]Department of Chemistry, S. M. Joshi college Hadapsar, Pune, Maharashtra, India
[2]Department of Chemistry, S. M. Joshi College Hadapsar, Pune, Maharashtra, India
[3]Department of Chemistry, M. P.A.C.S. College Panvel, Raigad, Maharashtra, India

ABSTRACT

The regioselective epoxide ring opening with nucleophiles like amines gives well known 1, 2-difunctionalized amino alcohols. These are present in many natural and synthetic products. The ring opening of epoxide is achieved by cleavage with amine in presence of copper (0) as a catalyst. We have observed that lithium napthalenide reduction of copper (I) produces a highly reactive form of copper (0) that acts as a catalyst for ring opening of epoxides with an amine.

Keywords : Copper (0), Napthalenide, Epoxide, Eugenol, Amino Alcohol, Biological Activity, Spectroscopy.

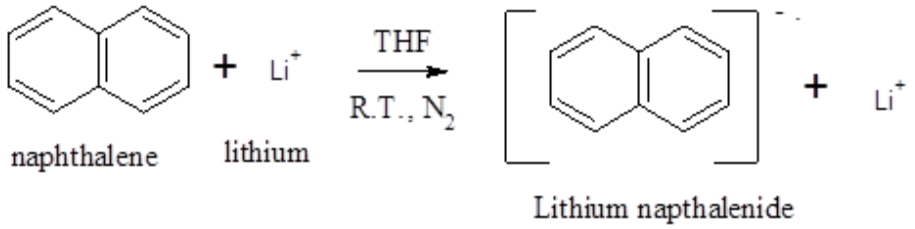
I. INTRODUCTION

1, 2- amino alcohols are the important intermediates in the preparation of many biologically active compounds. The preparation of these compounds are obtained by different routes but the most important route is by ring opening of epoxide with an amine. 1, 2- amino alcohols are the versatile intermediates for many organic compounds[1-4]. 1, 2- amino alcohol constitutes a range of beta blockers used to treat cardiovascular diseases like hypertension[5-10]. For example use of drug like Propranolol. The 1, 2- amino alcohols are present in a number of biologically active molecules. It falls into three main classes these are as natural amino alcohols, synthetic amino alcohols and chiral catalysts[11-13]. These amino alcohols acts as chiral ligands in many asymmetric reactions[14-20]. The synthesis of 1, 2- amino alcohols can be derived from aminolysis of epoxides and it can also be synthesized from aminohydroxylation of alkenes[21-23]. There are several methods of synthesis of amino alcohols from epoxides by using amines with different catalysts[24-27]. Generally 1,2- amino alcohols are prepared by heating epoxides with excess amines at different temperatures[28], but these copper (0) catalysed ring opening of epoxides gives products regioselectively. Epoxides are the versatile intermediates in the organic synthesis, there are several methods of synthesis of epoxides. Epoxides are important in organic synthesis due to their strained three membered ring[29].

II. EXPERIMENTAL

Typical procedure for the preparation of lithium napthalenide:

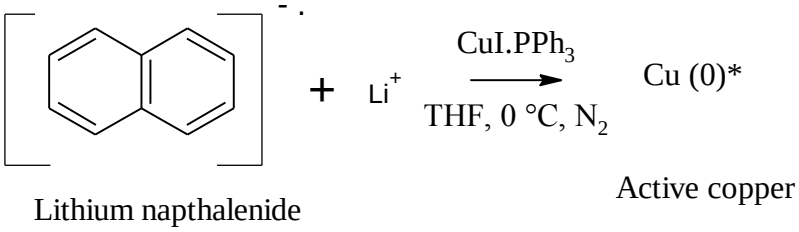
In a 50 ml two necked round bottom flask added naphthalene (10 mmol) and lithium metal (10 mmol) to which added 10 ml dry THF and continued stirring for about 4 hrs under atmoshphere of nitrogen gas at room temperature, the green coloured homogeneous solution has been formed which is stable under anhydrous conditions for several days.



Scheme 1. preparation of lithium napthalenide.

Typical procedure for the preparation of copper (0) catalyst:

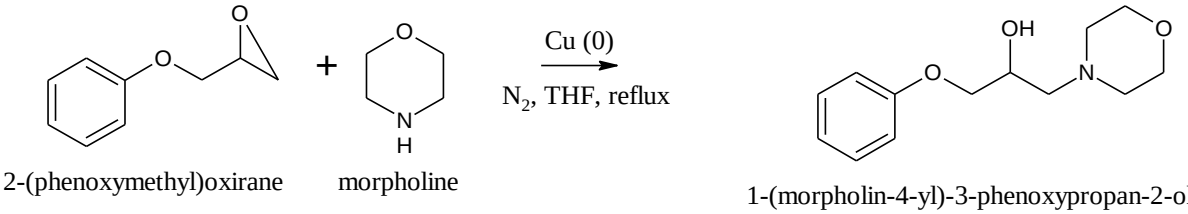
In a 50 ml two necked round bottom flask added solution of CuI.PPh3 complex (10 mmol) to which added lithium napthalenide solution (10 mmol) by syringe under magnetic stirring and continued stirring for about 30 min. at 0^0c temperature in the atmoshphere of nitrogen gas. The very reactive form of reduced copper is formed from copper (I) to copper (0).



Scheme 2. Preparation of copper (0) catalyst.

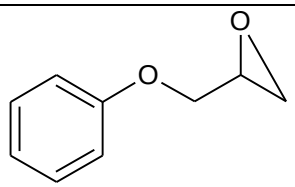
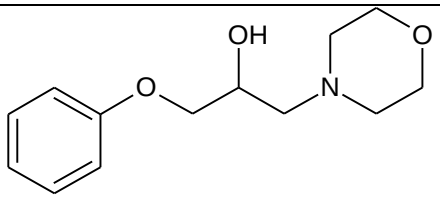
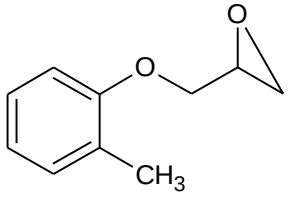
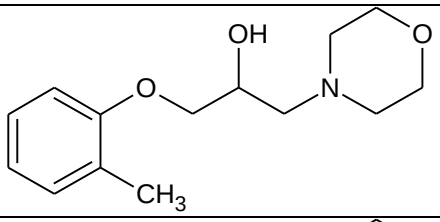
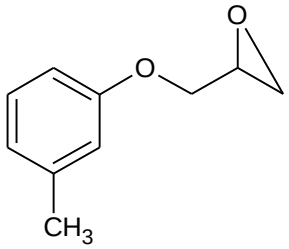
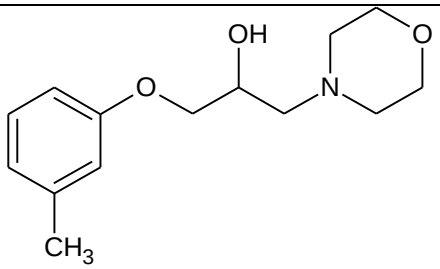
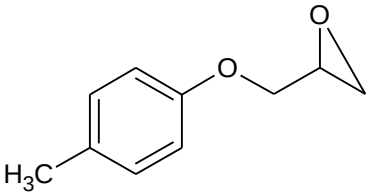
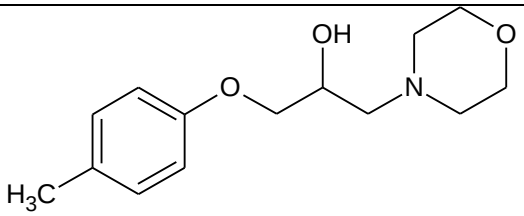
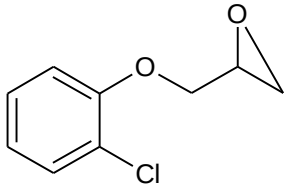
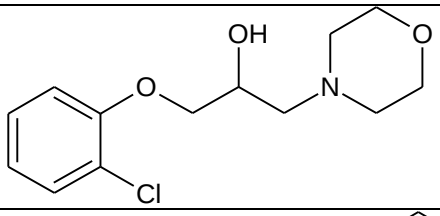
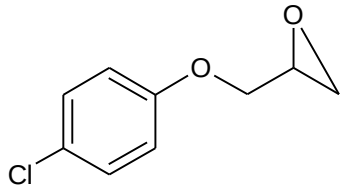
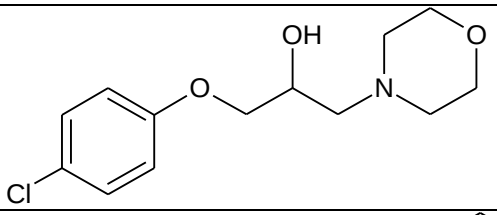
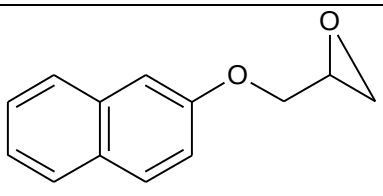
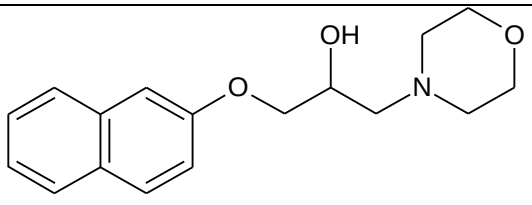
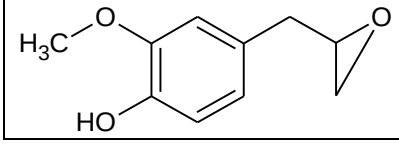
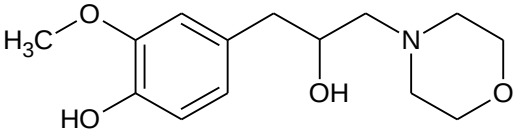
Typical procedure for preparation of 1,2- amino alcohol from epoxide with an amine:

In a 50 ml two necked round bottom flask added epoxide (10 mmol) to which added amine (morpholine) (10 mmol), added 10 ml dry THF under stirring, then added solution of copper (0) catalyst (10 mol %) by syringe under nitrogen atmoshphere, after completion of reaction product isolated by extraction with ethyl acetate (03x10 ml), combined product layers dried over sodium sulphate.



Scheme 3. Preparation of 1, 2- amino alcohol from epoxide and amine in presence of copper (0) catalyst.

Table 1: Reaction scheme: Preparation of desired products from epoxide with an amine.

Reactant	Product	Time (hrs)	Yield (%)
		0.75	80
		2.5	66
		2.0	69
		1.25	72
		3.0	67
		2.5	77
		1.75	82
		2.0	86

III. RESULTS AND DISCUSSION

The chemicals for the reactions were purchased from Merck and used after purification. These chemicals were purified by using distillation technique. The solvents used for the reactions were dried by different techniques like Na-Benzophenone method for THF drying. All the starting compound epoxides were synthesized by alkylation of phenol and substituted phenol derivatives with epichlorohydrin. Eugenol oxide obtained from epoxidation process using metachloro perbenzoic acid and methylene dichloride as a solvent. The lithium napthalenide were prepared by using inert atmoshphere of nitrogen gas. The copper (0) used in this method were prepared by Rieke method[30]. It has been observed that only mono substituted product obtained in the presence of secondary amine and both mono and disubstituted products were obtained in the presence of primary amine. The possibility of disubstituted products were completely eliminated with secondary amine. The reactivity of copper (0) were determined by reacting it with heterocyclic amine to form corresponding 1, 2-amino alcohols. The reaction progress were monitored by using thin layer chromatography and products were purified by coloumn chromatography and analysed by I. R. and ^{1}H NMR spectroscopic methods.

IV. CONCLUSION

We have used copper (0) as a simple and efficient catalyst for the regioselective ring opening of epoxides by heterocyclic amines. The yields obtained by this method are higher and this method is found to be effective and convenient for the synthesis of desired biologically active 1, 2- amino alcohols as described.

V. REFERENCES

[1]. Liebscher, J. et. Al. synthetic applications of chiral pool derived heterocycles. J. Heterocyclic Chem. 2000, 37, 509-518.

[2]. Corey, E. J; Zhang, F; Org. Lett, 1999, 1, 1287-1290.

[3]. V. T. Kamble; N. S. Joshi; Green Chemistry Letters and Reviews, 2010, 3-4, 275-281.

[4]. Connolly, M. E; et. Al. Prog. Cardiovasc Dis. 1976, 19, 203-234.

[5]. Michael J. P; Indolizidine and Quinolizidine alkaloids. Nat. Prod. Rep, 2001, 18, 520- 542.

[6]. Anil K. Kinage, Pravin P. Upare, Anaandkumar B. Shivarkar, Sunil P. Gupte, Green and Sustainable Chemistry, 2011, 1, 7684.

[7]. Shivani, B; Pujala, A. K; Chakraborti, J. Org Chem., 2007, 72, 3713-3722.

[8]. N. Azizi; M. R. Saidi, Org. Lett. 2005, 7, 3649-3651.

[9]. J. R. Lizza, G. Moura-Letts, Synthesis, 2017, 49, 1231-1242.

[10]. S. Azoulay, K. Manabe, S. Kobayashi, Org. Lett., 2005, 7, 4593-4595.

[11]. Bergmeier, S. C; Tetrahedron, 2000, 56, 2561-2576.

[12]. A. Heydari, M. Mehrdad, A. Maleki, N. Ahmadi; Synthesis, 2004, 1557-1558.

[13]. M. Kumar, R. I. Kureshy, S. Saravanan, S. Verma, A. Jakhar, N. H. Khan, S. H. R. Abdi, H. C. Bajaj, Org Lett. 2014, 16, 2798-2801.

[14]. Ager, D.J; Prakash, I; Schaad D. R; Chem. Rev. 1996, 96, 835-875.

[15]. A, k. Chakraborti, S. Rudrawar, A. Kondaskar, Org. Biomol. Chem. 2004, 2, 1277-1280.

[16]. H. Y. Kim, A. Talukdar, M. Cushman; Org. Lett. 2006, 8, 1085-1087.

[17]. A. B. Shivarkar, S. P. Gupte, R. V. Chaudhari, Synlett, 2006, 1374-1378.

[18]. C. Wang, H. Yamamoto, J. Am. Chem. Soc., 2014, 136, 6888-6891.

[19]. Mark Ruschgen Klaas; Siegfried Warwel, Org. Lett., 1999, 1, 1025-1026.

[20]. Ahmed Kamal, R. Ramu, Mohd. Ameruddin Azhar, G. B. Ramesh Khanna, Tetrahedron Letters, 2005, 46, 2675-2677.

[21]. Li, G; Chang, H. T; Sharpless, B. K; Angew; Chem. Int. Ed. 1996, 35, 451-454.
[22]. Huirong Yao, David E. Richardson, J. Am. Chem. Soc. 2000, 122, 3220-3221.
[23]. Murphy A, Pace A, Stack T. D. P., Org. Lett., 2004, 6, 3139.
[24]. Lindstrom, U. M; Franckowiak, R; Pinault, N; Somfai, P; Tetrahedron Lett. 1997, 38, 2027-2030.
[25]. Liu Y, Murata K, Inaba M., J. Chem. Soc. Chem. Commun. , 2004, 582.
[26]. Kan J. T.W; Toy P. H; Tetrahedron Lett. , 2004, 45, 6357.
[27]. Shi Y; Acc. Chem. Res., 2004, 37, 488.
[28]. Deyrup, J. A; Moyer, C. L; J. Org. Chem. 1969, 34, 175-179.
[29]. Behrevs, C. H; Ko, S. Y; Sharpless, K. B; Walker, F. J; J. Org. Chem. 1985, 50, 5687.
[30]. Rieke R. D; Rhyne L. D; J. Org. Chem., 1984,49, 3445.