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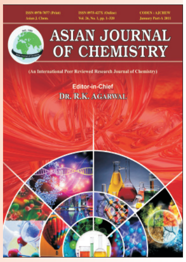

MINI REVIEW

Evolution of Epoxides to Synthesize β-amino Alcohols

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The present short review about a great deal of researches have been dedicated to the development of the reaction (catalyzing the ring opening of epoxide with amines for the corresponding amino-alcohols) in recent years.

Keywords: Epoxide, β-Amino alcohols, Metal-catalyzed, Green progression.

INTRODUCTION

β-Amino alcohols are one of the most powerful molecules in organic synthesis and medicinal chemistry. There are many routes to prepare β-amino alcohols, but the most straightforward synthetic procedures for the preparation of β-amino alcohols involve heating an epoxide in a protic solvent with excess amine which is available in many cases[1]. The preparation of the β-amino alcohols presents numerous challenges and limitations, including issues of non-nucleophilic, bulky amines typically react poorly, requirement of using excess amine, extended reaction times and elevated temperatures which have spurred the development of many powerful catalytic methods of processes to address these issues. Indeed, numerous catalysts for β-amino alcohols have been reported in recent years, including small organomolecule catalysts and metal complexes, with special emphasis on selectivity, substrate scope, mild conditions and current limitations.

Epoxides are valuable carbon electrophiles capable of reacting with various nucleophiles which make them prone to react with a large number of organic compounds. Their structures prone to undergo ring opening reactions which contributes to their synthetic value.

Metal-catalyzed processes to synthesize β-amino alcohols: A variety of metal-catalyzed processes have been reported for the direct catalyzed epoxides to synthesize asymmetric β-amino alcohols. Metal based catalyst has been the backbone of the conventional strategies for the activation of the electrophilic species toward nucleophilic attack.

Lewis acids: According to Lewis[2] an acid is an electron pair acceptor. This definition is more general than that given by Bronsted, according to which an acid is a molecule that is able to give protons.

Indeed, a proton is a particular case of an electron pair acceptor[3]. So we can assume the mechanism of the direct procedure for epoxides to synthesize asymmetric β-amino alcohols is similar. A mechanism for cobaltous chloride-catalyzed reaction was reported in 2004 by Sundararajan *et al.*[4] (Fig. 1). They discovered that anilines act as superior ring opening reagents even when the reactions were performed with $CoCl_2.6H_2O$ or under aerobic conditions thereby ruling out the possibility of the mediation by free radicals and speculate that an ionic process occurs, which explains the regioselectivity of the reaction. The Lewis acid coordinates with the oxirane oxygen to promote nucleophilic attack of the anilines leading to two regioisomers A and/or B. Attack of the nucleophile is governed by the nature of the oxirane and the stability of the incipient carbonium ion. In case of metal coordinated styrene oxide, the positive charge on oxygen appears to be localized on the more highly substituted benzylic carbon. Thus the nucleophile attacks the benzylic carbon of the styrene oxide leading to amino alcohol B. The mechanism of A amino alcohol is reported by Chakraborti in 2003[5].

At begin, a remarkable improvement was recently accomplished when metal salts, particularly lithium perchlorate, were recommended as promotors which has been responsible for so many accidents. Augé and Leroy find that lithium trifluoromethanesulfonate turned out to be an excellent substitute for

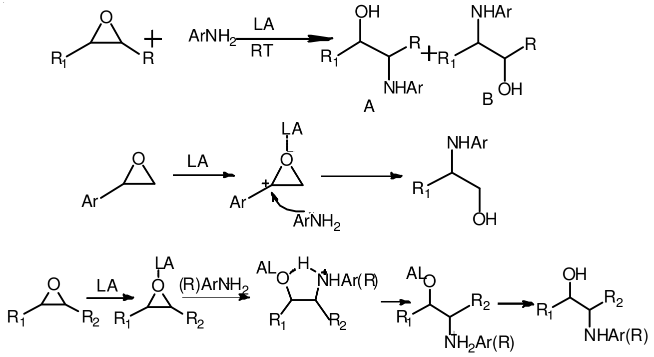


Fig. 1. Mechanism of the ionic intermediate in ring-open reaction mediated by Lewis acid

the unsafe lithium perchlorate. They reported the use of 50 % anhydrous lithium trifluoromethanesulfonate for 4 h with very good yields[6]. Unfortunately the regioselective of product is low, although the loading catalyst and the yield are high.

Chini *et al.*[7] reported the use of lanthanide(III) trifluoromethanesulfonates (triflates), such as Yb(OTf)$_3$, Nd(OTf)$_3$ and Gd(OTf)$_3$, as catalysts in a extraordinarily efficient way the aminolysis of 1,2-epoxides, affording the corresponding β-amino alcohols, at room temperature and in a non-protic solvent (CH_2Cl_2 or toluene), in very good yields. The reactions are completely anti-stereoselective and highly regioselective.

Sekar and Singh[8] reported the use of 5 mol % Cu(OTf)$_2$ for 30 h and 5 mol % Sn(OTf)$_2$ for 20 h, at room temperature with very good yields. The reactions are completely anti-stereoselective and highly regioselective. The worthy feature of the reaction is that highly deactivated amines such as *p*-nitroaniline also opened the epoxides in a reasonable yield[8]. We can find the isolated yield in the epoxide opening reaction with aromatic amines catalyzed by Cu(OTf)$_2$ and Sn(OTf)$_2$ is comparable, the reaction was faster with the latter catalyst with same loading catalyst. The drawback of this reaction is that only aromatic amines opened the epoxides.

Mancilla and co-workers[9] used 10 mol % Sn(OTf)$_2$ in anhydrous acetonitrile and heated to 80 °C for 24 h. This is the first report of the use of Sn(OTf)$_2$ to catalyze the opening of an epoxide by aliphatic amines. It is a pity that Sn(OTf)$_2$ catalyzes opening of styrene oxide with aliphatic amines in moderate to high yields but with a lower degree of regioselectivity.

Cepanec *et al*[10]. found that calcium trifluoromethanesulfonate efficiently catalyzes aminolysis of wide variety of epoxides in the presence of 10-50 mol % Ca(OTf)$_2$ as homogeneous catalyst at room temperature. The substrates have expanded from the simple aliphatic amines, benzyl amine, di benzyl amine, aniline and its derivates to Primary and secondary aliphatic amines. Also, the reaction appears to be limited to anilines with electron accepting substituents, sterically hindered anilines and the catalyst loading.

Williams and Lawton[11,12] Al(OTf)$_3$ is an extremely effective catalyst for ring opening reactions of epoxides using a range of alcohols and in 2006 they found that a range of epoxides was ring-opened using various alkyl- and aryl amines under the action of Al(OTf)$_3$ as a catalyst. This catalyst was found to be highly active, producing the desired amino alcohol products in high yields with low catalyst loadings. Additionally, it was shown that the aluminium triflate catalyst is recyclable by simple extraction into water and may be recycled several times[11,12]. In this report, the reaction times were very long and the condition of recycle is tough. In 2009, Williams and Cullen described the use of Al(OTf)$_3$ as a good catalyst for the ring opening of epoxides, forming β-amino alcohols bearing the piperazine motif[13] (Fig. 2). Two different strategies direct catalyzed epoxide to synthesize asymmetric β-amino alcohol were examined. The reaction is also noteworthy, as these motifs are frequently synthesized.

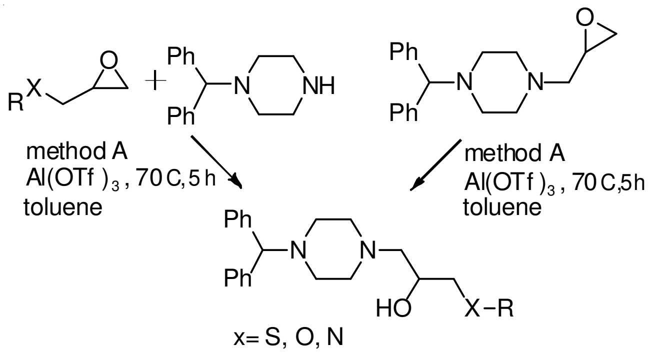


Fig. 2. Approaches for obtaining β-amino alcohol

Placzek and co-workers[14] found a simple and efficient method for the synthesis of β-amino alcohols by ring opening of epoxides in the presence of a catalytic amount of Sc(OTf)$_3$ at room temperature under solvent-free conditions[14]. The reaction works well with both aromatic and aliphatic amines. High regioselectivity and overcoming main disadvantages of most existing methods can be considered as notable advantages of this method. Nowadays Sc(OTf)$_3$ is one of the most versatile and reactive catalysts.

Procopio and co-workers[15] developed Lewis acid-catalyzed methods, they found Er(OTf)$_3$ can work under neutral conditions and catalyst for several acid-catalyzed reactions. The Er(OTf)$_3$ needed to prolong reaction time with the aromatic amines, but it showed more active with aliphatic amines. The two key points of the report were efficient and reusable. The Er(OTf)$_3$ was found to be better than other recently reported catalysts in terms of conversion and yield. The report also provided a method to recycle the catalyst which was used in aqueous conditions.

The application of lanthanide derivatives in catalysis have grown rapidly due to their high lewis acid properties and their non-toxicity. In 2004, Carre'e and co-workers[16] did a typical experiment, addition of the aromatic amine to 10 % SmI$_2$(THF)$_2$ suspended in methylene chloride was followed by addition of the epoxide and the had good yield (70 %) after one night at room temperature. Reddy and co-workers[17] had attempted for the first time cleavage of epoxides with aromatic amines to generate β-amino alcohols using cerium chloride as an efficient catalyst. They used $CeCl_3.7H_2O$-NaI (0.3eq) in dichloromethane at room temperature to give 75 % yield. In summary, lanthanide derivatives is a novel at ten years ago, we need find new way to modern synthetic methodology.

It is well known that zinc perchlorate [$Zn(ClO_4)_2$] belongs to the class of Lewis acids. The catalyst using zinc perchlorate supported on neutral alumina and a related solid acid catalyzed reaction was the field of growing interest. The acidic or neutral solid substances like silica gel, alumina, ion exchange resin and active carbon are suitable supports and the more commonly being used one is neutral alumina for various organic transformations[18]. In their report, they have described a mild and efficient method for ring-opening of epoxides with amines in the presence of heterogeneous catalyst zinc perchlorate-neutral alumina to generate β-amino alcohols in excellent yields, high regioselectivity, operational simplicity, short reaction times (from 1 h to 3 h) and reduction of by-products. We can also find the preparation of $Zn(ClO_4)_2$-Al_2O_3 is difficult, which need high temperature to calcine and store under argon for future use.

The article reported the reaction $ZrCl_4$ works well with aromatic and aliphatic amines in short times at room temperature in the absence of solvent by Chakraborti and Kondaskar[5] The report showed aromatic amines exhibit excellent regioselectivity for preferential nucleophilic attack at the sterically less hindered position during the reaction with unsymmetrical epoxides. However, in case of aliphatic amines, selective formation of the benzylic amine was observed during the reactions styrene oxide. The high contained of zirconium in the earth's crust would make zirconium compounds less costly. According to the increasing environmental concerns, the low cost and low mammalian toxicity of zirconium make it available.

Ligand-based catalysts: Numerous catalysts have been developed that are based on the structure of BINOL. In 1998, Wu *et al.*[19] reported the use of a catalyst generated from BINOL ligand and Yb triflate (1.2 mmol: 1 mmol), for the asymmetric ring-opening of *meso*-epoxides with anilines. They found the better enantioselectivities were achieved when a tertiary amine was used as the additive rather than primary and secondary amines, so they used Ph_2NBn in toluene. The reaction of cyclohexene oxide with an aniline having an electron-withdrawing group in the para-position, higher ee values than electron-donating group (Fig. 3).

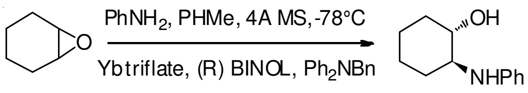


Fig 3. BINOL ligand and Yb triflate for obtaining b-amino alcohol

In 2004, Carrée *et al.*[16] reported that *bis*-binaphthoxy iodosamarium (prepared from samarium triiodide and bispotassium (R)-binaphthoxide) catalyzes the reaction of cyclohexene oxide and cyclohexadiene monoxide with *o*-anisidine, affording the corresponding β-amino alcohols in good yields and with respectively, 52 and 68 % enantiomeric excess at room temperature and 0 °C (Fig. 4).

Carrée *et al.*[20] later reported lanthanide iodo binaphtholates are efficient enantioselective catalysts for the ring opening of meso-epoxides by various aromatic amines. Compared with before report, we can find the change of the order of addition of substrates and new additive (4A MS) could contain more enantiomeric excess. They also examined the influence of temperature on selectivity for aminolysis of cyclohexene oxide and found the enantiomeric excess increased first when the temperature was decreased to reach a maximum value of 91 % at -40 °C.

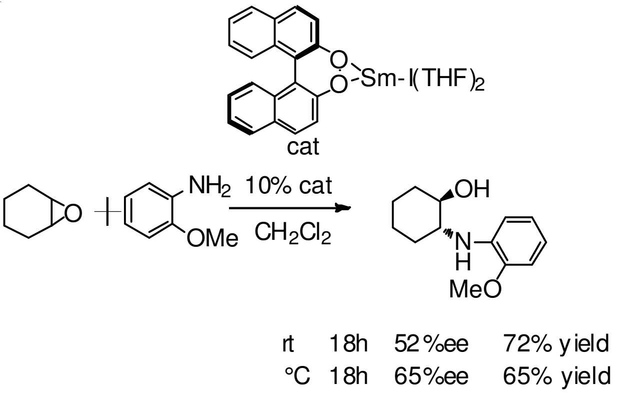


Fig. 4. BINOL ligand and Sm for obtaining β-amino alcohol

Martin *et al.*[21] used samarium iodo binaphtholate in same condition as Carrée mentioned in 2005 to catalyse *meso*-epoxides including a heterocycle. New β-amino alcohols have been isolated with enantiomeric excesses up to 70 %. In 2010, Martin *et al.*[22] expand the variety of heterocycles, aggregated structures for samarium iodo binaphtholate and a bimetallic active species for the aminolysis of epoxides. Under the report by Carrée and Martin, in 2011 Martin *et al.*[23] synthesized a new family of chiral lanthanide complexes derived from (R)-binaphthol (Fig. 5). There catalysts can be synthesized by commercially available substrates, which is better than before, came though many procedures. β-Amino alcohols including heterocycles have been isolated with enantiomeric excesses up to 84 %.

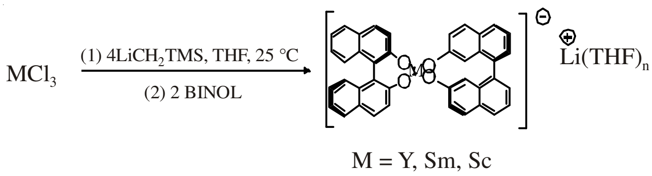


Fig. 5. The synthesized structure of BINOL ligand and M

In 2007, Arai *et al.*[24] discovered and expanded new Lewis acid system based on a complex formed, a novel tetradentate BINOL derivative. The system was shown to be extremely effective in promoting the reaction to excellent yields (up to 84 %) and excellent enantioselectivity (up to 95 % ee). it was most convenient to conduct the reactions with 10 mol % catalyst loading at 0.16 M, at higher overall concentration the reaction still proceeded efficiently with as little as 0.25 mol % catalyst to give the desired products with no significant reduction in yields or enantioselectivities (Fig. 6).

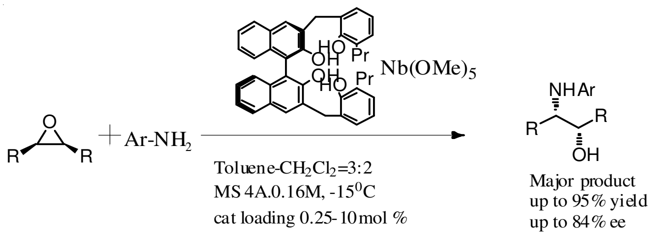


Fig. 6. BINOL derivative ligand for obtaining β-amino alcohols

In 2004, Bartoli and co-workers reported carbamates as the nucleophile catalyzed by (salen) Co^{III} complex provides a practical and straightforward method for the synthesis of both aliphatic and aromatic N-Boc-or N-Cbz-protected 1,2-amino alcohols in almost enantiomerically pure form (ee 99 %)[25]. In 2005, The optimal procedure was achieved by 2-ethyloxirane (2.1 equiv) and urethane (1 equiv) at room temperature with the commercially available complex (salen)Co^{III} (1.5 mol % relative to racemic epoxides) and *p*-nitrobenzoic acid (3 mol %) in undistilled *tert*-butyl methylether (TBME) (Fig. 7)[26].

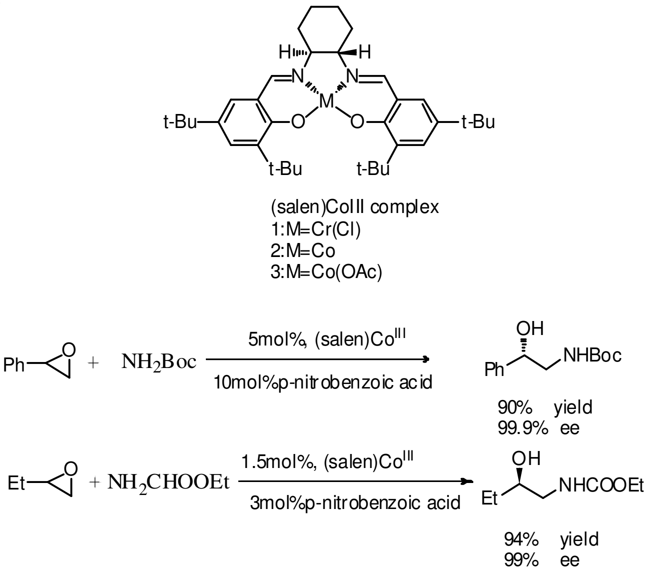


Fig. 7. (salen)Co^{III} complex ligand for obtaining β-amino alcohols

Indium and its salts have emerged as promising catalysts for enantioselective ring opening, which has been reported with various aniline derivatives. Chirality has been achieved with a new proline-based complex[27,28]. Using the new proline-based indium *tris* (triflate) complex was achieved in high yields (up to 99 %) with excellent enantioselectivities (up to 99 % ee) under mild conditions. Rodri´guez and Navarro reported the use of indium tribromide for the direct opening reaction of aromatic amine with epoxide[29]. The report focused on the reaction was completely regioselective because the only products isolated were those coming from the attack of the amine to the less substituent carbon of the epoxide. The selectivity of indium tribromide was rather low, using for aromatic amine not aliphatic amine (Fig. 8).

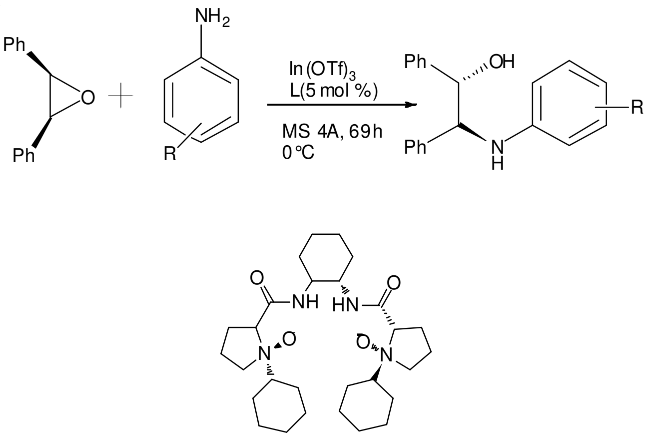


Fig. 8. New proline-based indium *tris*(triflate) complex catalyst various epoxides for obtaining β-amino alcohols

Nanoscale metal: Nanoscale metal oxides[30] have been efficiently used in the destruction of hazardous chemicals and catalysts for organic transformations. These high reactivities depend on large surface areas or unusually reactive morphologies to a certain extent. In 2012, Chen and co-workers reported nano-TiO$_2$ is an effective heterogeneous catalyst for the ring opening of epoxides with aromatic amines to afford amino alcohols in good to excellent yields at room temperature under solvent-free conditions. It was found that the catalyst is recyclable and the activity of the catalyst was not weakened markedly even after several reaction cycles. As reported, different regioisomer leaded to different substituted unsymmetric epoxide.

In 2007, Sreedhar *et al.*[31] found regioselective ring opening of epoxides with amines was using monodispersed silica nanoparticles in water under ambient conditions in shorter reaction times.

In 2010, Robinson and co-workers[32] reported a new nanoporous aluminosilicate materials as highly selective heterogeneous catalysts for the formation of β-amino alcohols from aromatic amines and epoxides. They also found the narrower pore size distribution and larger surface areas, the more activity of catalyst.

Catalysts contained mineral salt: Kotsuki and co-workers reported the use of high-pressure and silica gel catalyst a variety of epoxides with amines for β-amino alcohols[33]. Although the method proved a considerable utility under fairy mild condition, the diastereomeric products were found and the rate of reaction is slow.

Robinson *et al.*[34] demonstrated that mesoporous aluminosilicates efficiently catalyze the formation of β-amino alcohols from aromatic amines and epoxides in short reaction times and in high yields under mild reaction condition. The shortcoming of the reaction is high quantity of catalyst (120 mg/mmol).

Miscellaneous catalysts: Lu and co-workers[35] reported the use of $(C_4H_{12}N_2)_2Cl{\cdot}H_2O$ (1 mol %) catalyst various epoxides with aromatic, aliphatic and heterocyclic amines for β-amino alcohols at room temperature under solvent-free conditions (Fig. 9). The authors noted that the reaction of aromatic amine with aliphatic epoxides without catalyst was examined and only one product was observed. Only product B in the reaction mixture with an ideal yield of more than 84 % within 5-10 min. The reaction of aromatic amine with styrene oxide provided a yield of more than 90 % with a regioselectivity of product A by using $(C_4H_{12}N_2)_2Cl{\cdot}H_2O$. Unfortunately, the procedure of $(C_4H_{12}N_2)_2Cl{\cdot}H_2O$ is complex, although this catalyst can be reused several times without losing of its activity.

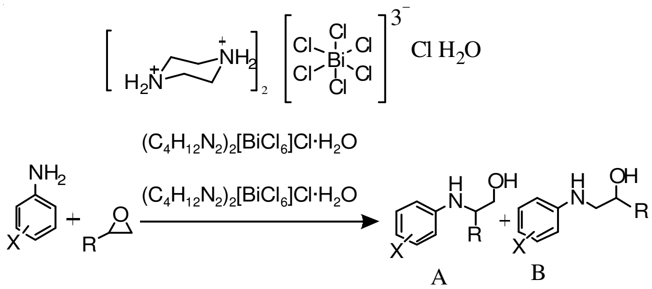


Fig. 9. $(C_4H_{12}N_2)_2Cl{\cdot}H_2O$ (1 mol %) catalyst various epoxides for obtaining β-amino alcohol

Kotsuki and co-workers reported the use of high-pressure and silica gel catalyst a variety of epoxides with amines for β-amino alcohols[33]. Although the method proved a considerable utility under fairy mild condition, the diastereomeric products were found and the rate of reaction is slow.

Albanese and co-workers have studied on the ring opening of a number of epoxides with trifluoroacetamide was catalyzed under solid-liquid phase transfer catalysis (SL-PTC) conditions by catalytic solid K_2CO_3. The reaction is totally regioselective affording β-amido alcohols deriving from the attack of the nucleophile to the less substituted carbon atom of the oxirane ring (Fig. 10)[36].

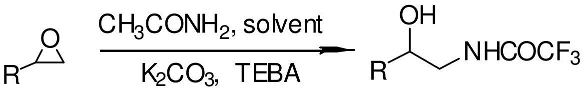


Fig. 10. (SL-PTC) and K_2CO_3 catalyst various epoxides for obtaining β-amino alcohol

Khodaei *et al.*[37] reported a facile and efficient synthesis of β-amino alcohols by ring opening of epoxides with anilines in good to excellent yields in the presence of catalytic amounts of Bi(III) salts(1-3 mol %) *via* the use of molten tetrabutylammonium bromide (TBAB) as an ionic liquid. In addition, the observed chemoselectivity can be considered as a noteworthy advantage of this method and the reaction achieved good yield under mild condition with low catalyst loading is worth mentioning.

Urea and thiourea derivatives can activate oxygen containing functional groups, as has been proved in the seminal work of Curran[38,39] and subsequent studies by Jacobson[40] and Schreiner[41].

Rampalli and co-workers[42] reported a type reducing agent diisopropoxyaluminum trifluoroacetate which can be used with ainiline and benzylamine gaving ome regioisomer at room temperature in good yield. The main shortcoming of the reaction is high catalyst loading.

Green progression for synthesis: One design to change a reaction into a green process consists of having a two phase liquid system in which the catalysts remains dissolved in one of the solvents, while the products can be extracted by another immiscible liquid. After reaction, we can use the catalyst-phase for another reaction .The assumption offer new opportunities to replace conventional organic solvents in synthesis and industrial processes. We took efforts to conduct green catalysis in mixtures of organic solvent/water or even in pure aqueous media. In these cases, besides the solubility of organic reagents and products, the crucial issue is the stability of the catalyst in water. The best way, it is using free-solvent, which need to concern the nature of substrates.

Reaction in supercritical CO_2: Supercritical carbon dioxide is an environmentally friendly solvent that has attracted much attention as an alternative to the use of less tolerable organic solvents. For catalytic reactions in supercritical CO_2, the temperature and pressure play an important role by varying the viscosity, solubility, polarity and other parameters that influence the ability of CO_2 to act as a solvent[43]. Numerous advantages include that CO_2 is environment benign, low cost and easily separated from products.

Shi and Chen[44] reported that the ring-opening reactions with aromatic amine can be carried out in the presence of a Lewis acid $Yb(OTf)_3$ (5 %) in the equipment of supercritical carbon dioxide (Fig. 11). The epoxides are reactive and polar epoxide itself can modify the physical property of supercritical CO_2 to dissolve Lewis acid $Yb(OTf)_3$ very well. Thus, the ring-opening reactions of epoxides with nucleophiles take place more easily in a homogeneous phase and supercritical CO_2 is rapidly emerging as an ideal medium for carrying out a diverse range of synthetic reactions. Unfortunately, there are mono-substituent product and disubstituted in well yield under the high pressure and further investigations to develop the reaction epoxides with other nucleophiles in supercritical CO_2 or modified supercritical CO_2 are now in progress.

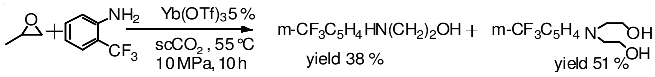


Fig. 11. Ring-opening reactions in the presence of a Lewis acid $Yb(OTf)_3$ (5 %) in the equipment of supercritical carbon dioxide

Reaction in water as solvent: Thirupathi and co-workers reported solid acid catalysts based on zirconia materials for the first time as catalysts for regioselective organic synthesis under environmentally benign and mild conditions in 2010[45]. They tested various solid acids catalysts for the synthesis β-amino alcohols and found a novel TiO_2-ZrO_2 mixed oxide catalyst led to two distinct products by the formation of an N-C bond (β-amino alcohols) (Fig. 12). From the investigation, we are observed the amines with electron-donating groups afforded the corresponding products in good yield and rapid reaction, by contrast to the amines with electron-withdrawing groups. The regioselectivity in the case of cyclohexene oxide is high, though the scope of the substrates is rather low.

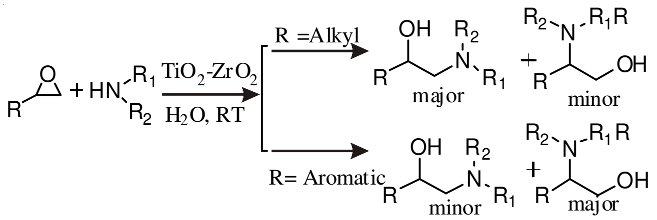


Fig. 12. Ring-opening reactions in the presence of TiO_2-ZrO_2

Azizi and Saidi have reported the opening of epoxides (except styrene oxide) by aliphatic and aromatic amines in water without any catalyst with high yield (84-97 %) and excellent selectivity (Fig. 13)[46]. They also test the chemoselecitivity by commingling cyclohexene oxide, aniline and piperidine. The result of mixture indicated that piperidine reacted with cyclohexene oxide first. After 2 years, they reported the cyclohexene oxide with aniline was catalyzed by heteropoly acids[47] (0.35 mol % $H_3PW_{12}O_{40}$ and 0.55 mol % $H_3PMo_{12}O_{40}$) at room temperature and the desired product was obtained in high yield (94-93 %) in 2 h in water. Unfortunately, the report indicated low solubility of epoxides and amine in water may affect the process.

Procopio and co-workers[15] reported $Er(OTf)_3$ can work under neutral conditions in water. The method made it envi-

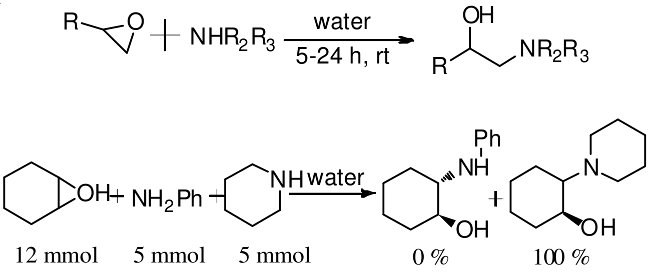


Fig 13, Ring-opening reactions in the presence of water

ronmentally friendly and potentially useful for industrial applications.

Reaction in solvent-free condition: Abdul and Masum[48] reported an efficient method for the method for the preparation of biologically important imidazolyl alcohols *via* ring-opening of epoxides with N-silylated imidazole catalyzed by LiBr under solvent-free conditions (Fig. 14). The reaction under mild heating at 60 °C gave only product in high isolated yield. At room temperature the reaction was slow and required 40 h to complete. We can find the different products with different substituted unsymmetric epoxide.

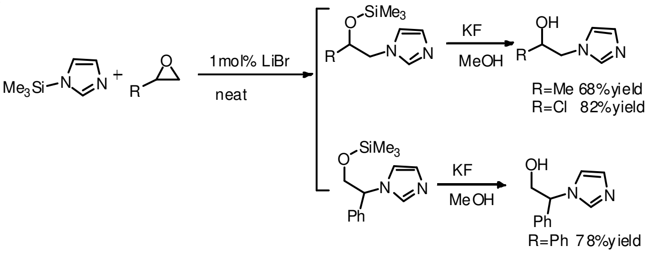


Fig.14. Ring-opening reactions in solvent-free condition

Lu and co-workers[35] reported the use of $(C_4H_{12}N_2)_2Cl\cdot H_2O$ (1 mol %) catalyst various amines for β-amino alcohols at room temperature under solvent-free conditions.

Fringuelli and co-workers[49] had concerned about the reaction of epoxides with the bihaptic amine 2-picolylamine by using 5 mol % of $Al(OTf)_3$ in water or in solvent-free conditions under mild conditions (Fig. 15). The reaction protocol is simple and does not require dry glassware and reagents. The final amino alcohol from cyclohexene oxide with 2-picolylamine at 70 °C by using $Al(OTf)_3$ under SFC was isolated in 99 % (purity in 95 % yield). They also accomplished the synthesis of two new lonic liquid from the final amino.

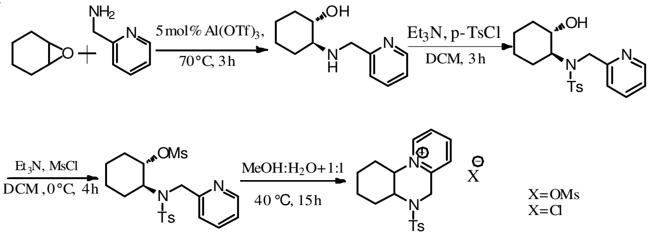


Fig. 15. Synthesis of ionic liquids from cyclohexene and oxide ring-opening reactions in $Al(OTf)_3$

Torregrosa and co-workers[50] reported the reaction of different epoxides with commercially available imidazole at 60 °C under solvent-free conditions leads to the formation of the corresponding product in a regioselective manner (Fig. 16). When the reaction is applied to a chiral epoxide, the expected chiral alcohol is isolated with the same enantiomeric excess. For example, performing the reaction with (R)-styrene oxide produced the corresponding product in 62 % yield and the same enantiomeric excess as the starting epoxide (98 % ee).

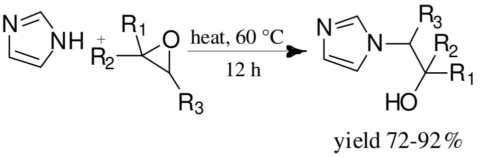
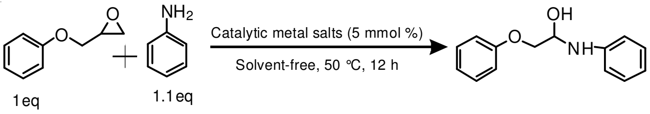


Fig. 16. Ring opening of epoxides with imidazole under solvent-free condition

A few reports are available on transtion metal salts-catalytic approach for the reaction under solvent-free condition. Zhao and co-workers[51] developed efficient ring-opening reaction with a wide rang of transation metal salts under solvent-free conditions with good to excellent yield (Fig. 17).



Entry	MXn Catalyst	Yield (%)
1	$NiCl_2$	89
2	$CuCl_2\cdot 2H_2O$	80
3	$Mn(OAc)_2\cdot 4H_2O$	84
4	$FeCl_3\cdot 6H_2O$	88
5	$CrCl_3\cdot 6H_2O$	90
6	$AuCl_3\cdot 4H_2O$	80
7	$Cu(OAc)_2\cdot 4H_2O$	86
8	CuI	72
9	$FeSO_4\cdot 7H_2O$	70
10	$Ni(OAc)_2\cdot 2H_2O$	88

Fig. 17. Activity of different transition metal salts under solvent-free condition

In 2006, Ishida and co-workers[52] reported a novel polymeric rare earth complexes, $RE_2(BPDS)_3$ (RE = rare earth metal, BPDS = biphenyl-4,4'-disulfonate), such as $Sc_2(BPDS)_3$ and $Yb_2(BPDS)_3$ in which the metal ions are homogeneously dispersed, were synthesized by the self-organization of the metal ion and the corresponding aryldisulfonate and successfully used as a reusable Lewis acid catalyst for the ring-opening reaction of epoxides with amines to give the desired β-amino alcohols in excellent yields under solvent-free heterogeneous conditions[52]. The catalysts can be quantitatively recovered and reused more than five times without decreasing their activities.

Reaction in ionic liquids: Ionic liquids, normally were nitrogenated or phosphonated organic cations having inorganic counter anions, plays important role in green chemistry, as it is hoped that they constitute an alternative to volatile organic solvents as reaction medium[53,54].

In 2007, Kantam and co-workers[55] found under the optimized reaction conditions, styrene oxide underwent reaction with aniline, in the presence of 3 mol % $Cu(acac)_2$ immobilized in 1 mL of ionic liquid at room temperature, to give the corresponding amino alcohols in good yields (92 %, after fourth cycle 88 %) with high regioselectivities. The report determined Cu(acac)$_2$ is to be a more effective catalyst in ionic liquids than other solvents.

Reaction on solid: The development of a highly efficient and a nonhazardous catalyst, which is easy to handle, is highly imperative for the development of catalysts. Some of these problems can be overcome by employing heterogeneous catalysts, which have several intrinsic advantages like the ease of product separation, recyclability of the catalyst and the minimization of waste production[31,56].

In 2008, Maheswara *et al.*[57] reported a simple and efficient method for the synthesis of β-amino alcohols by regioselective ring-opening of epoxides with amines in the presence of heterogeneous recyclable catalyst zinc perchlorate-neutral alumina at room temperature in excellent yields (Fig. 18)[57]. Although they reported that pentyl amine and hexyl amine did not give any satisfactory yields less than 20 % in the reaction of aliphatic epoxide of propylene oxide, the reaction have several advantages such as operational simplicity, short reaction times, reduction of by-products, high yields and excellent regioselectivity. In 2008, Zhang and co-workers[58] reported the recyclable catalyst B$_2$O$_3$/Al$_2$O$_3$ promoted highly regioselective ring opening of epoxides with aromatic amines in good to excellent yields at room temperature.

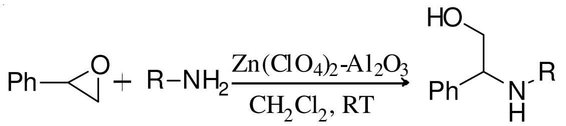


Fig. 18. Ring opening of epoxides with catalyst zinc perchlorate-neutral alumina

In 2012, Tajbakhsh *et al.*[59] reported silica-bonded S-sulfonic acid (SBSSA) was used as a recyclable and reusable catalyst for the synthesis of β-amino alcohols in high yield under solvent-free conditions at room temperature.

Reaction of other solvent as "green" solvent: In 2004 Begue *et al.*[60] introduced the use of TFE and HFIP to catalyze the ring opening of epoxide with aromatic amines at reflux and led to high yields of the corresponding amino-alcohols. The reaction was performed with more nucleophilic amines such as diethylamine, *n*-butylamine, or piperidine, no reaction occurred even after 4 days at reflux.

Khaksar and co-workers[61] found a facile and efficient synthesis using 2,2,2-trifluoroethanol (TFE) as a metal-free and reusable medium (Fig. 19). They carried out the reaction between 2,3-epoxy-propylphenyl ether and aniline in TFE which can not happen in other solvents, the corresponding amino alcohol derivative was obtained in high yield (86 %) at ambient temperature.

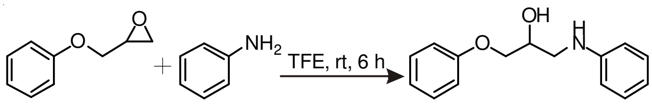


Fig. 19. Ring opening of epoxides with 2,3- epoxy-propylphenyl ether and aniline in TFE

Conclusion

Since β-amino alcohols have become increasingly useful and important in drugs and pharmaceuticals, the development of simple, efficient and environmentally friendly processes for their synthesis, are well appreciated.The rearrangement of epoxides to allyl alcohols under basic conditions as well as polymerization in strongly acidic conditions gets many by-products, which resulting in a low yield of the desired products. Moreover, the main disadvantage of above mentioned methods is that the catalysts cannot be recovered or reused because it will be destroyed in the procedure.

A great deal of research has been dedicated to the development of the reaction in recent years. The most practical of the described catalysts is Lewis acid. Despite the growing number of reported catalysts, however, very few increase the reactivity of parent system dramatically, although the yield and regioselectivity have been increased through use of alternate catalysts. Some of the most notable achievements are development of green progression for synthesis.

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