Solid lithium perchlorate as a powerful catalyst for the synthesis of β-aminoalcohols under solvent-free conditions

Najmodin Azizi and Mohammad R. Saidi

Abstract: Lithium perchlorate catalyzed the ring opening of epoxides with amines to provide the corresponding β-aminoalcohols in excellent yields with high regioselectivity. The reaction proceeds rapidly under mild and neutral conditions and worked well with primary, secondary, aliphatic, aromatic, and hindered amines in short times at room temperature, in the absence of solvent.

Key words: epoxide, lithium perchlorate, β-aminoalcohols, solvent-free.

Résumé : Le perchlorate de lithium catalyse l'ouverture de cycle des époxydes avec des amines qui conduit aux β-aminoalcools correspondants avec d'excellents rendements et une régiosélectivité élevée. La réaction se produit rapidement dans des conditions douces et neutres et elle se produit rapidement avec les amines primaires, secondaires, aliphatiques, aromatiques et empêchées, à la température ambiante et en l'absence de solvant.

Mots clés : époxyde, perchlorate de lithium, β-aminoalcools, sans solvant.

[Traduit par la Rédaction]

Introduction

β-Aminoalcohols are versatile intermediates in the synthesis of a vast variety of biologically active natural and synthetic products (1), unnatural amino acids (2), and chiral auxiliaries for asymmetric synthesis (3). The classical synthesis of β-aminoalcohols consists of heating an epoxide with an excess of amine at elevated temperatures (4). High temperatures may not be appropriate for certain functional groups. Also, a variety of air-sensitive or expensive catalysts had been reported in the literature to perform epoxide opening at room temperature. Many of these catalysts are either corrosive, or in some cases, they are being applied to aromatic amines with poor regioselectivity and with undesirable side reactions such as rearrangement and polymerization (5–7). However, there are still some limitations with the reported methods in the literature. For example, deactivated amines failed to open up the epoxides or require high temperatures. Furthermore, they require a high catalyst-to-substrate ratio, have a long reaction time, and they need volatile organic solvents that eventually results in the generation of a large amount of toxic waste. To overcome these limitations, the development of a better catalyst for the activation of epoxides, rendering them more susceptible to nucleophilic attack under a mild, efficient, and general method, is of great interest.

Received 26 July 2004. Published on the NRC Research Press Web site at http://canjchem.nrc.ca on 18 May 2005.

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In recent years, to minimize the harmful organic solvents used in chemical processes, much attention has been devoted to the use of alternative media. Besides the use of supercritical fluid water and ionic liquids, the possibility of performing chemical reactions in the absence of solvent has been receiving more attention (8).

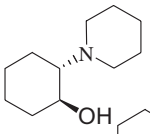
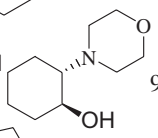
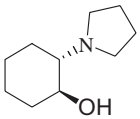
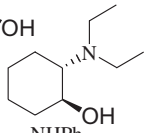
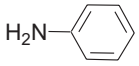
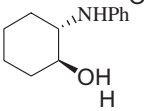
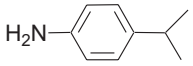
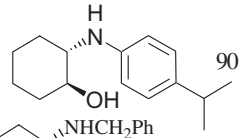
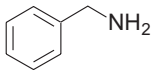
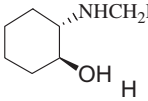
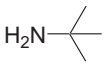
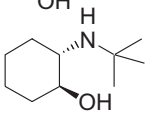
Results and discussion

Because of our interest for developing solvent-free and environmentally benign synthetic methods (9), herein, we report a more simple, general, and new catalytic route for the synthesis of β-aminoalcohols via opening of epoxides with amines under solvent-free conditions in the presence of a catalytic amount of $LiClO_4$. At first, we examined the reaction of cyclohexene oxide with aniline and 0.2 equiv. of solid $LiClO_4$ at room temperature. Complete conversion took place within 120 min, leading to quantitative yield of *trans*-2-phenyl amino cyclohexanol. This success encouraged us to exploit the generality and scope of this reaction for the opening of other epoxides with various aromatic and aliphatic amines under catalytic amounts of $LiClO_4$. The reaction proceeded well with aromatic, aliphatic, hindered, and unhindered amines. The role of $LiClO_4$ in catalyzing the opening of epoxide rings with amines maybe realized through the coordination of Li^+ with the epoxide oxygen and renders the epoxide more susceptible to nucleophilic attack by the amine, which after protonation forms the aminoalcohol (Table 1).

In the next step, we have examined various amines using styrene oxide as the unsymmetrical epoxide to investigate the regioselectivity outcome of the reaction. In all cases, the ring openings take place in highly regioselective fashion, affording the β-aminoalcohols in high yields. It should also be

 doi: 10.1139/V05-062

Table 1. β-Aminoalcohols prepared from cyclohexene oxide.

Entry	Epoxide	Amine	Product	Yield (%)[a]	Time (min)
1				93	80
2				92	40
3				94	40
4				86	80
5				95	120
6				90	120
7				90	120
8				80	120

[a]Isolated yields.

mentioned that without using solid $LiClO_4$, no reaction was observed among various amines and styrene oxide. On each occasion, the regioselectivity and the ratio of the two regioisomers were determined by ^1H NMR and by comparison with the reported value in the literature (6, 7).

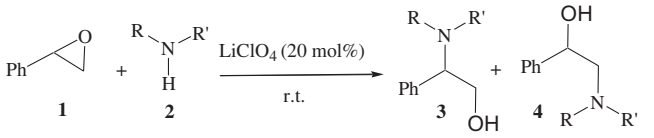
In conclusion, we have shown that $LiClO_4$ is a new, highly efficient catalyst for the opening of epoxides with amines leading to the synthesis of β-aminoalcohols. In fact, this reaction proceeds smoothly in solvent-free conditions, which is an important feature for the development of green chemistry.

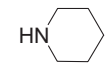
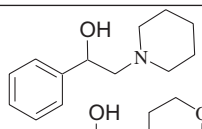
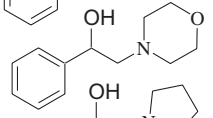
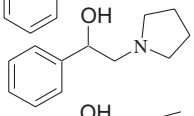
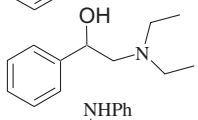
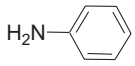
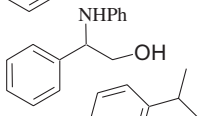
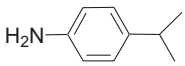
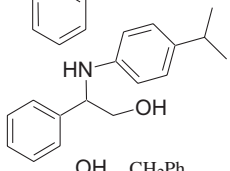
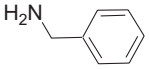
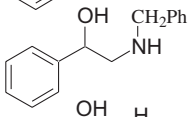
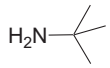
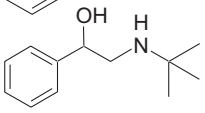
Experimental

General procedure for the preparation of β-aminoalcohols

To a mixture of epoxide (5 mmol) and amine (6 mmol) in the test tube, anhydr. $LiClO_4$ was added (0.1 g), and the mixture was stirred at room temperature for 30–180 min. When the reaction was completed, as indicated by TLC or GC, the reaction mixture was diluted with diethyl ether or ethyl acetate (15 mL) and washed with water; the organic phase was separated, dried with Na_2SO_4, and solvent was removed using a rotary evaporator. In all cases, almost pure compound was obtained. Further purification was carried out by short column chromatography on silica gel (ethyl acetate – petroleum ether). All compounds were characterized on the basis of their spectroscopic data (IR, NMR, and GC) and by comparison with those reported in the literature (Table 2).

Table 2. β-Aminoalcohols produced from styrene oxide.



Entry	Amine	Major Product	Yield[a] (%)	Ratio **3:4**	Time (min)
1			95	83:17	30
2			96	76:24	30
3			97	84:16	30
4			92	98:2	60
5			96	10:90	80
6			93	8:92	80
7			92	86:16	90
8			82	81:19	90

[a]Isolated yields.

Acknowledgments

We are grateful to the Research Council of Sharif University of Technology for financial support. We also thank Volkswagen-Stiftung, Federal Republic of Germany for financial support towards the purchase of chemicals.

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