Ring Opening of Epoxides by Nucleophiles in Nitromethane without Any Catalyst at Room Temperature

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***Abstract*—**In this Letter, we describe a mild and efficient method for the nucleophilic ring-opening of epoxides with amines and alcohols in the presence of nitromethane as a polar solvent without using any catalyst. The reactions are highly regioselective and afford the products in excellent yields within a short period of time at room temperature.

***Keywords*—**Epoxide, Ring opening, Nitromethane, Regioselective

I. Introduction

EPOXIDES are versatile intermediates in organic synthesis [1], [2]. They are important functional groups of natural products [3] and medicinal [4] polymer [5], and supramolecular [6] compounds. Epoxide ring-opening reactions are useful instruments in organic chemistry [5], [6] for most natural epoxides, catalytic addition of water to yield 1, 2-diols is the main route of metabolism in vivo. This reaction is catalyzed by a family of enzymes called epoxide hydrolases [7]. In nature, epoxide ring opening is catalysed by the phenolic proton of a tyrosine moiety [8], but in the research laboratory, the cleavage usually occurs in non-aqueous media in presence of a Lewis acid catalyst like Li+ [9], MgCl2 [10], Zn(ClO4)2-Al2O3 [11], BiCl3 [12], CeCl3.7H2O-NaI [13], TaCl5 [14]etc. They can be easily cleaved with different nucleophils and can be formed regio and stereoselective products [2], [15], [16], Recently, various methods have been reported using metal triflates [17], [18] and some heterogeneous catalysts [19], [20].

But there are some limitations such as poor yields, regioselectivity, use of air, moisture sensitive catalysts, requirement of stoichiometric amounts of catalyst and problems in the recovery of the catalysts. In most of the epoxide ring-opening reactions under acidic conditions, the formation of a mixture of regioisomers and polymerization are observed.

There are a few reports where use of a catalyst has not been necessary [21], [22] For example, The epoxide ring in 5, 6-dihydro-5, 6-epoxy-1, 10-phenanthroline (L) opens up in its reaction with 4- methylaniline and 4-methoxyaniline in water at room temperature without any Lewis acid catalyst [23]. Recently, azizi et al. reported a different way for aminolysis of aliphatic epoxides with aliphatic amines in water without any addition of catalyst [23]. But Most of the organic substances are insoluble in water and many reagents are decomposed or deactivated by water. Thus many reactions are accomplished in organic solvents [24]. On the other hand, many compounds are prepared by aminolysis of epoxides with amines under basic or acidic catalysts in organic solvents [25].

It is commonly recognized that the epoxide ring–opening reaction under basic or Neutral conditions proceeds via SN_2 mechanism, but under acidic conditions, a borderline SN_2 mechanism has been evoked to justify the electronic pull on the oxygen by an Acid [1], [2]. Furthermore, ring opening of epoxide is an important method of forming alcohols [26].

Consequently the introduction of new methods for the nucleophilic ring-opening of epoxides that work under appropriate conditions is important in organic chemistry.

In general, the efficiency of a synthetic process can be enhanced by increasing concentration of the reactants and using a suitable catalyst, thus, to accomplish our goal, we relied on the reaction without any catalyst in the polar solvent. In this work, we explain our results on ring opening of epoxide aided by nitromethane with amines and alcohols.

II. Experimental

A. Materials and methods

All the chemicals were purchased from Merck or Fluka chemical companies and used without purification. The 1H NMR (400MHZ) or (500MHZ) and the 13C NMR (125 MHz) were recorded on a Bruker Avance 300 MHz instrument. Chemical shifts are reported in ppm downfield from TMS as the internal standard. IR spectra were recorded on a Bruker model tensor 27 spectrometer and only major peaks are reported. The progress of the reactions was monitored by TLC.

B. General procedure for ring opening of epoxide with amines, alcohols and water in nitromethane gures

A mixture of styrene oxide (1 mmol), nucleophil (3mmol) and nitromethane (37 mmol) was stirred at ambient temperature for the time mentioned in table 1. The progress of the reaction was followed by TLC using (n-hexane-EtOAc 70:30). The reaction mixture was quenched with water and extracted with dichloromethaneme, then dried by anhydrous Na2SO4 and filtered and concentrated. For more purification, the residue was purified by column chromatography (n-hexane-Ethyl acetate). Structure confirmed by comparison of IR and 1H NMR and 13C NMR with those of authentic material

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http://dx.doi.org/10.15242/IICBE.C0915048

III. Results And Discussion

In this study, we have demonstrated a catalyst-free method for the synthesis of amino alcohols and □–hydroxy ether and diol with the reaction of epoxide and nucleophils in nitromethane. Under the optimized reaction conditions the generality of this reaction has been investigated with aromatic and aliphatic amines to open the styrene oxide (fig.1).

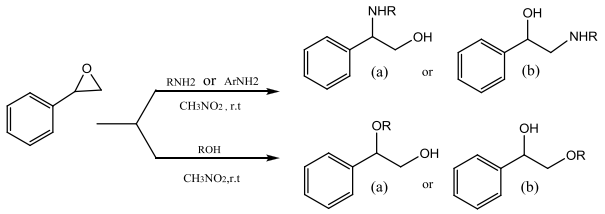


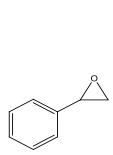
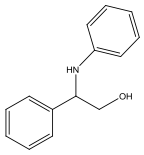
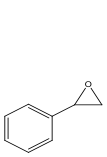
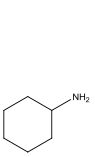
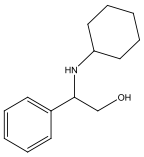
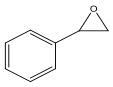
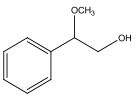
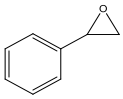
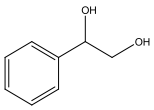
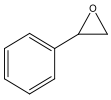
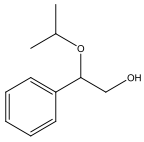
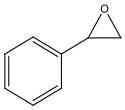
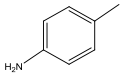
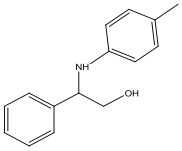
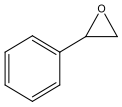
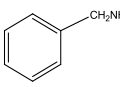
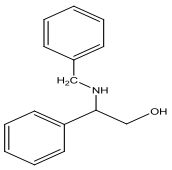
Fig.1 Epoxide ring opening with alcohol and amine in nitromethane at room temperature.

This method is simple and useful and gives good yields of products without use of any catalyst. Catalyst-free reactions are completely in compliance with the philosophy of green chemistry because of reducing the hazardous materials and by reducing the number of steps needed for the purification of the products.

Initially, the reactions were carried out in refluxing without solvent, but the reaction did not improve considerably. Therefore Polar solvent (nitromethane) was chosen for this purpose. Nitromethane is the highly polar liquid commonly applied as a solvent in a variety of industrial applications. We examined the reaction of styrene oxide in nitromethane with aniline at room temperature. Treating styrene epoxide (1mmol) with aniline (3mmol) in the presence of nitromethane under catalyst-free at room temperature (7h) provided amino alcohol in 84% yield (Entry1). We applied similar reaction conditions to the ring opening of styrene oxide with cyclohexyle amine (Entry 2) and benzyle amine (Entry 7).

In all cases, the cleavage of epoxides took place with high regioselectivity and aryl epoxide underwent a regioselective ring opening at the benzylic position (species (a) in fig.1). Furthermore, styrene oxide reacted easily with various alcohols such as Methanol, in the presence of nitromethane and yielded the corresponding □-hydroxy ethers in good yields as shown in Table 1. Ring opening of epoxide with water in the presence of nitromethane was also examined, the result are reported in Table 1(Entry 4). The basis of the dramatic effect of nitromethane in this ring opening reaction could be attributed to its partial acidic nature. The regioselectivity was further examined by ^{1}H and ^{13}C NMR spectroscopy.

TABLE I
Ring Opening Of Epoxide With Nucleophiles In Nitromethane At Room Temperature.

Entry	Substrate	Nucleophile	Product [a]	Time (h)	Yield (%) [b]
1		C6H5NH2		7	84
2				6	85
3		CH3OH		3	95
4		H2O		3	95
5				3.5	90
6				5.5	89
7				7.5	82

a) All the products were characterized by the usual spectroscopic technique
b) Isolated yields

IV. Conclusion

The regioselectivity for ring opening of epoxide has been investigated using experimental ^{13}C NMR and ^{1}H NMR studies. This methodology should constitute a powerful tool in applied chemistry. In summary, we have shown a mild and efficient method for the ring opening of epoxides without any catalyst in polar solvent.

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