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Eco-friendly and highly efficient multigram synthesis of 3-chloro-1,2-propanediol using sonochemistry

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Abstract: A new short, simple, green and inexpensive industrially practical process for the preparation of 3-chloro-1,2-propanediol was developed by using ultrasound irradiation avoiding the use of solvents, of acidic or basic conditions. The only reagent used is water and no waste is generated. Optimal conditions and yield (82%) were obtained by using 2.2 molar equivalents of water at 90 W for 1 hr.

Keywords: Epoxide; 3-chloro-1,2-propanediol; eco-friendly; scalable; sonochemistry.

Introduction

Epoxides (cyclic ethers) are a class of compounds, which are widely used in chemistry and have diverse applications [1]. Epichlorohydrin (1,2-epoxy-3-chloropropane) is used for the preparation of resins, dyes, paper, rubber, textiles, cosmetics, and shampoos [2]. Moreover, epichlorohydrin is an important reagent for the production of various pharmaceuticals [3]. The industrial preparation of epichlorohydrin comprises three steps: chlorination of propylene to afford allyl chloride, addition of hypochlorous acid to allyl chloride to afford a mixture of glycerol dichlorohydrin isomers, and dehydrochlorination of glycerol dichlorohydrin isomers with sodium hydroxide to afford epichlorohydrin [4]. The reactions of epoxides are generally based on the ring opening using diverse conditions, catalysts, reagents and nucleophiles [5-9]. For example, 1,2-diols are prepared by the ring opening of epoxides with water as the nucleophile, and the reaction is catalyzed by basic or Lewis acids [10]. Qu and co-workers developed an important method for the ring opening of several epoxides and aziridines with hot water [11].

3-Chloro-1,2-propanediol is an important building block in organic synthesis [12], with a wild range of applications on drug discovery being one of its stereoisomers used in the synthesis of linezolid, a 1,3-oxazolidinone drug utilized against antibiotic-resistant Gram-positive bacteria [13]. This building block was also used in the asymmetric synthesis of (R)- and (S)-moprolol an important β-adrenergic block [14] and it utilized as a chiral starting material in the synthesis of L-carnitine, an important drug that acts in the transport of long-chain fatty acids into mitochondria where β-oxidation takes place [15]. Synthesis of ethyl (R)-(-)-4-cyano-3-hydroxy-butyrate, intermediate of atorvastatin, from (S)-3-chloro-1,2-propanediol [16] is another application of this compound. In recent years, environment-friendly and cost effective chemical processes have been and continue to be developed both academically and industrially [17,18]. In this context, the development of simple and efficient synthetic methods that reduce the use of reagents and preferably employ no solvent has attracted much interest.

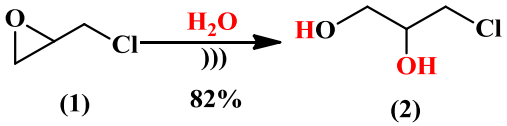

Figure 1. Conversion epichlorohydrin to 3-chloro-1,2-propanediol using ultrasonic irradiation.

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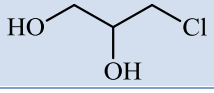
Considering that this paper reports an eco-friendly, scalable and highly efficient method for the conversion epichlorohydrin to 3-chloro-1,2-propanediol using ultrasonic irradiation (Figure 1). This procedure involving the addition of only water avoiding the use of solvents and avoiding acidic or basic conditions to afford 3-chloro-1,2-propanediol in nearly yield (82%) without any further purification, so no waste is generated.

Results and Discussion

In our previous work, we report the optimization of reaction of opening of the 1,2-epoxy-3-chloropropane ring by using thermal reaction at 80 ℃ with vigorous magnetic stirring [19]. In this work we developed a new procedure by using ultrasound irradiation. Optimal conditions and yield were obtained by using 2.2 molar equivalents of water at 90 W for 1 hr. The major advantage of using ultrasonic procedure, over the thermal procedure, is the greatly reduced reaction times: 1 hour compared to 24 hours. It's important to mention that excess water (82.8 mL) and epichlorohydrin not reacted (18 %) were removed by distillation under reduced pressure (0.5 mm Hg) at 80 ℃ and 3-chloro-1,2-propanediol (346.5 g, 82 %) was obtained as a colorless oil, bp. 104-105 ℃/3.0 mm Hg lit [14]. and 82-85 ℃/0.5 mm Hg. Under these conditions the starting material was recovered, however the recovered epichlorohydrin is not used again in the reaction.

Table 1. Comparison of ultrasonic and thermal methods to obtain the desired product **(2)**

Compound, 2	US (90W)		Thermal (80°C)	
	Yield (%)	Time (hr)	Yield (%)	Time (hrs)
	82[a]	1	99	24

[a]The yield is without recovery of the starting material

Conclusion

In conclusion, a new short, simple, green and inexpensive industrially practical process for the preparation of 3-chloro-1,2-propanediol was developed by using sonochemistry avoiding the use of solvents, of acidic or basic conditions. The only reagent used is water and no waste is generated. Moreover, the use of ultrasonic irradiation has found to be an excellent energy source for formation from **2**.

Experimental Section

A Multiwave Eco-sonics QR750 ultrasonic generator (20 kHz, 750 W) equipped with a converter/transducer, and titanium oscillator (horn, diameter = 4 mm) was used for the ultrasonic irradiation. ^{1}H NMR spectra were determined in DMSO using a Bruker AC 400 spectrometer at operating at 400 MHz, using TMS as an internal standard. Splitting patterns are as follows: s, singlet; d, duplet; m, multiplet; sl, broad signal. The ^{13}C NMR spectrum was obtained using the same apparatus described above at 100 MHz. Epichlorohydrin was purchased from Sigma-Aldrich and was utilized as the chromatographic standard in TLC analysis. The progress of the reactions was monitored by TLC on 2.0 cm x 4.0 cm aluminum sheets pre-coated with silica gel 60 (HF-254, Merck) to a thickness of 0.25 mm, eluent: hexane-ethyl acetate (1:1). The chromatograms were visualized using a solution 10% of phosphomolybdic acid in ethanol. Distillation using a vacuum pump (E2M8, EDWARDS, Brazil).

A two-phase mixture of epichlorohydrin (354.9 g, 3.83 mol) and water (151.9 g, 8.43 mol) in a flask 1L was stirred at room temperature, ultrasonic irradiation was applied (frequency = 20 kHz, amplitude = 90% of the maximum power output) without a pulse for 1 hr; Initially was added water (82.8 g, 4.60 mol) to the flask containing epichlorydrin (354.9 g, 3.83 mol) for 30 min. After cooling the reaction mixture was added more water (69.0 g, 3.83 mol) for 30 min. The progress of the reaction was monitored by TLC (hexane-ethyl acetate 1:1).

3-Chloro-1,2-propanediol, colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.12 (1H, d, CHOH, exchangeable with D_2O); 4.73 (1H, t, CH_2OH, exchangeable with D_2O); 3.67-3.62 (2H, m, CH_2Cl); 3.53-3.50 (1H, m, CHOH); 3.39-3.35 (2H, m, CH_2OH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 71.1 (CHOH), 62.5 (CH_2OH), 47.1 (CH_2Cl).

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