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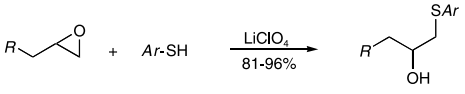
Graphical Abstract



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Solvent-Free Thiolysis of Epoxides under Lithium Perchlorate Catalysis

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Summary. Solvent-free ring opening of 1,2-epoxides with thiols using catalytic amounts of lithium perchlorate affords high yields of β-hydroxy sulfides. Nucleophilic attack of the thiols occurs regioselectively at the sterically less hindered side of the epoxides.

Keywords. Thiols; Epoxides; Catalytic; Lithium perchlorate; Solvent-free.

Introduction

Ring opening of epoxides with thiols is an important class of organic transformations and has found many uses in pharmaceutical [1] and natural product chemistry [2], particularly for the synthesis of leukotrienes [3]. The classical approach for the synthesis of β-hydroxy derivatives of sulfides involves thermal or *Lewis* acid mediated nucleophilic opening of epoxides with thiols [4] (Scheme 1). In many of these cases, the ring opening of epoxides is carried out in a halogenated solvent and normally requires long time treatment under reflux temperatures or environmentally unfriendly conditions.

Prompted by stringent environmental protection laws in recent years, there has been increasing emphasis on the use and design of eco-friendly reagents, solid state procedures, and solvent-free reactions [5]. In recent years, lithium perchlorate has been widely used for various organic transformations [6]. We decided to extend our previous experiences on the use of lithium perchlorate in synthetic organic chemistry [7]. In the present article, an efficient methodology for solvent-free ring opening of epoxides with thiols in the presence of catalytic amounts of lithium perchlorate at room temperature is described (Scheme 2). To the best of our knowledge, the present procedure is one of the most efficient and reliable methods for the synthesis of the title compounds.

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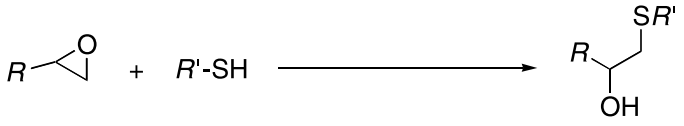
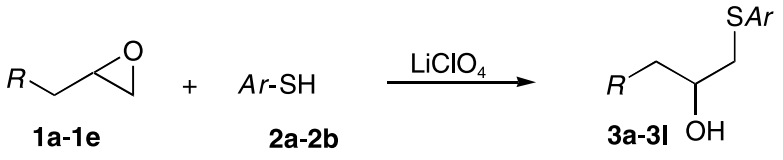


Scheme 1



Scheme 2

Results and Discussions

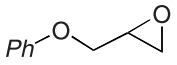
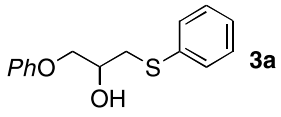
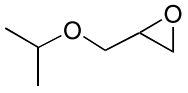
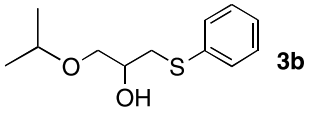
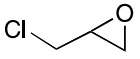
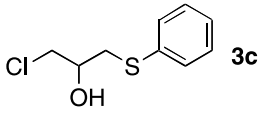
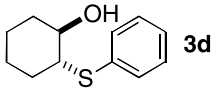
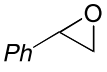
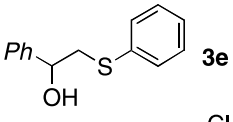
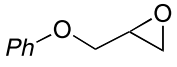
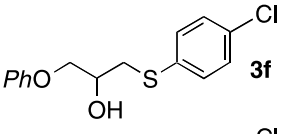
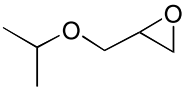
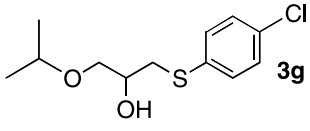
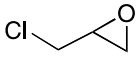
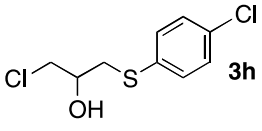
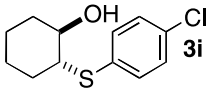
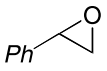
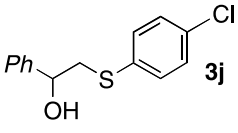
We first examined the reaction between 1,2-epoxy-3-phenoxypropane (**1a**) with an equimolar amount of thiophenol (**2a**) in the presence of 20 mol% anhydrous lithium perchlorate under solvent-free conditions. TLC showed complete disappearance of the starting epoxide within a few minutes. The ^{1}H NMR spectrum showed the presence of the β-hydroxy sulfide **3a** as the sole compound in the reaction mixture illustrating that the nucleophilic attack of the thiol occurs regioselectively on the less hindered side of the epoxide. Extraction of the reaction mixture gave 96% of the desired product (Table 1, entry 1). A control experiment confirmed the promoting effect of the catalyst. Thus, when a mixture of thiophenol (**2a**) and epoxide **1a** was stirred at room temperature for 24 h in the absence of lithium perchlorate, no formation of product was detected and the starting materials were recovered. Under the same conditions other epoxides (**1b**–**1e**) reacted in a similar manner with thiophenol **2a** producing 84–96% of **3b**–**3e** (entries 2–5). The generality of the method was demonstrated by subjecting epoxides **1a**–**1e** to react with *p*-chlorothiophenol (**2b**) (entries 6–10). Consequently, products **3f**–**3j** were obtained in 81–96% yields within a few minutes.

In conclusion, efficient ring opening of epoxides with thiols using a catalytic amount of lithium perchlorate and no solvent was observed in less than 5 minutes. In comparison with other methods existing in literature, the present procedure is environmentally friendly and affords high yields of the desired products. In addition, high regioselectivity of the ring opening, rapid completion of the reaction, and the use of catalytic amounts of *Lewis* acid are among other advantages of this protocol.

Experimental

All reported yields are isolated yields. IR spectra were recorded on a FT-IR Bruker Vector 22 infrared spectrophotometer using KBr disks. NMR spectra were recorded on FT-NMR Bruker AC 500 MHz or Bruker AC 80 MHz as $CDCl_3$ solutions with *TMS* as internal reference. GC-MS spectra were obtained on a Fisons 8000 Trio instrument at an ionization potential of 70 eV. Elemental analyses were found to agree favourably with calculated values.

Table 1. Solvent-free thiolysis of 1,2-epoxides using $LiClO_4$

Entry	Epoxide	Thiol	Product	Yield/%[a]	Reference
1		C_6H_5SH	 **3a**	96	[4k]
2		C_6H_5SH	 **3b**	95	–
3		C_6H_5SH	 **3c**	94	[4l]
4		C_6H_5SH	 **3d**	84	[4k]
5		C_6H_5SH	 **3e**	96	[4m]
6		4-ClC_6H_4SH	 **3f**	93	[4j]
7		4-ClC_6H_4SH	 **3g**	92	–
8		4-ClC_6H_4SH	 **3h**	81	[4o]
9		4-ClC_6H_4SH	 **3i**	96	[4n]
10		4-ClC_6H_4SH	 **3j**	92	–

[a] Isolated yields

General Procedure

A mixture of 5.0 mmol epoxide, 5.0 mmol thiophenol, and 1.0 mmol anhydrous $LiClO_4$ was stirred at room temperature for appropriate length of time (TLC, <5 min). The mixture was extracted 3 times with 10 cm^3 portions of ether. The combined etheral phases were washed with H_2O and filtered through a short Na_2SO_4 column. The solvent was removed under reduced pressure and the product was fractionated using column chromatography over silica gel or purified with bulb-to-bulb distillation,

if necessary. The NMR, IR, and GC-MS spectra of the products were obtained and compared perfectly to those existing in literature.

1-Isopropoxy-3-(phenylsulfanyl)propan-2-ol (**3b**, $C_{12}H_{18}O_2S$)
Mp 44°C; ^{1}H NMR ($CDCl_3$, 80 MHz): $\delta = 1.13$ (d, $J = 6.5$ Hz, 6H), 2.55–2.70 (m, 1H), 2.93–3.20 (m, 2H), 3.50–3.95 (m, 4H), 7.10–7.45 (m, 5H) ppm; ^{13}C NMR ($CDCl_3$, 20 MHz): $\delta = 22.0$, 38.1, 69.5, 71.3, 73.0, 127.5, 128.0, 129.3, 137.5 ppm; IR (KBr disk): $\bar{\nu} = 3431$, 1588, 1086, 738 cm^{-1}; MS: $m/z = 226$ (M^+).

1-(4-Chlorophenylsulfanyl)-3-isopropoxypropan-2-ol (**3g**, $C_{12}H_{17}ClO_2S$)
^{1}H NMR ($CDCl_3$, 80 MHz): $\delta = 1.18$ (d, $J = 6.5$ Hz, 6H), 3.02–3.20 (m, 2H), 3.45–3.65 (m, 4H), 3.86–3.92 (m, 1H), 7.26–7.45 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 20 MHz): $\delta = 21.7$, 37.3, 69.0, 70.1, 72.0, 128.8, 130.4, 132.0, 134.4 ppm; IR (neat): $\bar{\nu} = 3443$, 1575, 1093, 747 cm^{-1}; MS: $m/z = 260$ (M^+).

2-(4-Chlorophenylsulfanyl)-1-phenyl-ethanol (**3j**, $C_{14}H_{13}ClOS$)
^{1}H NMR ($CDCl_3$, 80 MHz): $\delta = 2.57$ (br s, 1H), 3.84 (d, $J = 6.5$ Hz, 2H), 4.20 (d, $J = 6.5$ Hz, 1H), 6.95–7.30 (m, 9H) ppm; ^{13}C NMR ($CDCl_3$, 20 MHz): $\delta = 55.9$, 65.0, 127.6, 127.9, 128.5, 128.8, 129.7, 132.2, 133.6, 138.6 ppm; IR (neat): $\bar{\nu} = 3421$, 1573, 1094 cm^{-1}; MS: $m/z = 264$ (M^+).

Acknowledgements

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