Zn/$CeCl_3.7H_2O$-TBPB: A New and 'Green' Promoter System for Rapid and Regioselective Thiolyzation of 1,2-Epoxides with Aryl Disulfides

Ahmad R. Khosropour,* Mohammad M. Khodaei,* and Kazem Ghozati
Department of Chemistry, Faculty of Science, Razi University, Kermanshah 67149, Iran

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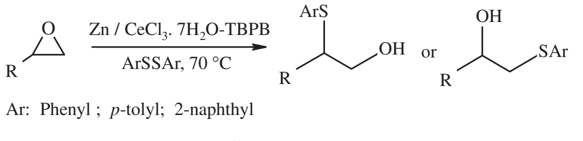
A new, efficient, clean, and regioselective 'one-pot' procedure for thiolyzation of epoxides with aryl disulfides catalyzed by cerium(III) chloride heptahydrate immobilized on tetrabutyl phosphonium bromide as an ionic liquid is reported.

The vicinal thioalcohols are a common structural component in a vast group of natural products or synthetic molecules with biological and pharmaceutical activities.[1] One of the most straightforward routes to synthesis of these compounds involves the ring opening of epoxides with thiols.[2] This reaction is generally carried out with large excess of the thiols with unpleasant odor at elevated temperatures. The high temperature reaction conditions are not only detrimentally to certain functional groups, but also to the control of regioselectivity. Subsequently, due to the harsh reaction conditions and long reaction times some catalytic methods have recently been developed.[3–7] However, in spite of their potential utility, many of these methods involve expensive or stoichiometric amounts of reagents, strongly acidic conditions, use of toxic solvents, poor selectivity, unsatisfactory yields that entail undesirable side reactions such as polymerization or rearrangement and generation of a large amount of toxic waste that leads this classic reaction to serious disadvantages. In fact acid-catalyzed ring opening of epoxides with thiols is requiring the careful control of the acidity to prevent side reactions. Since β-hydroxy sulfides have become increasingly useful and important especially in pharmaceuticals, thus development of simple, efficient, and environmentally friendly approach for their synthesis is highly desirable.

Recently, ionic liquids have emerged as an alternative reaction media for the immobilization of transition metal catalysts, Lewis acids and enzymes.[8,9] They are being used as green solvents with unique properties such as good solvating ability, high thermal stability, negligible vapor pressure, and ease of recyclability. In continuation of our research on the ring opening reaction of epoxides,[10] recently we investigated the applicability of Lewis acids immoblized on ionic liquid in aminolysis of epoxides with anilines.[11] We report herein, for the first time, one-pot region- and chemoselective ring opening reaction of 1,2-epoxides with aryl disulfides by zinc powder in the presence of catalytic amount of $CeCl_3$. $7H_2O$ immoblized on tetrabutylphosphonium bromide (TBPB) as an ionic liquid (Scheme 1).

Cerium(III) chloride heptahydrate was chosen because it has emerged as potentially useful Lewis acid imparting high regio- and chemoselectivity in various chemical transformations, with the additional advantages, that it is cheap, water-tolerant and nontoxic.[12]



Scheme 1.

In order to investigate the influence of the catalyst in different media, the thiolysis of styrene oxide with $(PhS)_2$ was carried out in CH_3CN, diisopropyl ether, CH_2Cl_2, TBAB (tetrabutylammonium bromide), TBAF (tetrabutylammonium fluoride), TBAI (tetrabutylammonium iodide), and under solvent-free conditions. The results are summarized in Table 1.

Table 1. Thiolysis of styrene oxide with $(PhS)_2$ in the presence of zinc powder and different catalytic conditions

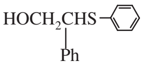
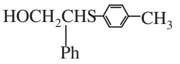
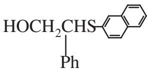
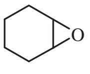
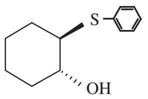
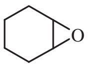
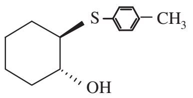
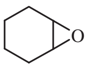
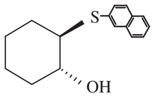
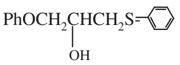
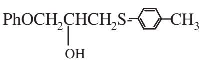
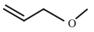
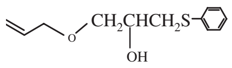
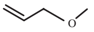
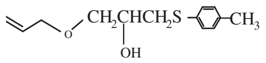
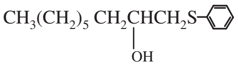
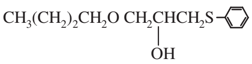
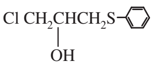
Entry	Catalytic conditions	Reaction time / min	Yield / %
1	none	120	0
2	$CeCl_3$. $7H_2O/CH_3CN$[a]	120	6
3	$CeCl_3$. $7H_2O$/Diisopropyl ether[a]	120	4
4	$CeCl_3$. $7H_2O/CH_2Cl_2$[a]	120	trace
3	$CeCl_3$. $7H_2O$[b]	120	0
4	$CeCl_3$. $7H_2O$/TBAB[c]	120	53
5	$CeCl_3$. $7H_2O$/TBAF[c]	120	64
6	$CeCl_3$. $7H_2O$/TBAI[c]	120	48
7	$CeCl_3$. $7H_2O$/TBPB[c]	20	92

[a] In the presence of 0.2 mmol of $CeCl_3$. $7H_2O$ and 5 mL of the solvent. [b] Solvent free conditions. [c] In the presence of 0.2 mmol of $CeCl_3$. $7H_2O$ and 0.5 mmol of the ionic liquid.

Initially we studied the reactivity of symmetrical aliphatic and aromatic disulfides using styrene oxide as a model substrate. The reaction took place at 70 °C with addition of 1 mmol of styrene oxide, 1 mmol of the disulfide and 1 mmol of zinc powder in the molten mixture of 0.2 mmol $CeCl_3$. $7H_2O$ and 0.5 mmol of TBPB. Under these conditions, the epoxide was reacted only with aryl disulfides and aliphatic disulfides remain intake. Consequently, we focused our attention only on aryl disulfides with various epoxides. All the experimental results are summarized in Table 2.

In the method described here, a variety of epoxides with different functional groups such as PhO-, RO-, $ClCH_2$- and allyl ether were converted to the products with high efficiency and chemoselectivity. It is important to note that in the case of terminal epoxides (Table 2, Entries 7–13), the products obtained by the attack on the terminal carbon. This regioselectivity is probably due to the steric hinderance of nucleophile that attacks on the less-hindered carbon of the epoxides. However, in the case of reaction with styrene oxide we observed a reverse regioselectivity in which the attack on the benzylic carbon was preferred. The product obtained using cyclohexene oxide was shown to posses a *trans*-configuration by ^1H NMR spectroscopy. These high reactivity and selectivity are similar to those observed in

Table 2. Thiolysis of 1,2-epoxides with aryl disulfides in the presence of Zn/$CeCl_3$. $7H_2O$-TBPB at 70 °C

Entry	R or Epoxide	Product [a]	Yield /%[b]/ Time /min
1	Ph		92/20(89)[c]
2	Ph		90/20
3	Ph		87/20
4			80/45
5			80/55
6			78/50
7	$PhOCH_2$		90/30(87)[c]
8	$PhOCH_2$		89/35
9			85/50
10			80/55
11	$CH_3(CH_2)_4CH_2$		85/30
12	$CH_3(CH_2)_3OCH_2$		86/45
13	$ClCH_2$		82/60

[a]All products were identified by comparison of their physical and spectral data with those of authentic samples. [b]Isolated yields. [c]The yield achieved from the recycled promoter.

the case of strong Lewis acids with thiophenols.[3–7]

These results indicated that this reaction not only needs the presence of the catalyst for proceeding, but also it is performed only in the presence of the ionic liquids and among them TBPB showed more effective in this transformation.

Another advantage of this method for this transformation is recyclability of this promoter system. Since Zn–$CeCl_3.7H_2O$/TBPB was weakly soluble in Et_2O, this was separated by washing with Et_2O and dried at 80 °C under reduced pressure and reused in three runs without any loss of activity (Table 1, Entries 1, 2).

In conclusion, a new, powerful, regioselective chemoselective and environmentally friendly method is described for thiolysis of 1,2-epoxides with odorless aryl disulfides instead of the thiols in good to high yields. In addition, short reaction times, relatively mild reaction conditions and high yields with straightforward work-up, reusability, stability and non-toxicity of the catalyst and ionic liquid make the present method efficient, convenient and 'green,' which could be a very efficient alternative to the classic methodology.

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References and Notes

1 F. Viola, G. Balliano, P. Milla, L. Cattel, F. Rocco, and M. Ceruti, *Bioorg. Med. Chem.*, **8**, 223 (2000).

2 M. E. Peach, "The Chemistry of the Thiol Group," John Wiley, New York (1974), Part 3, p 771.

3 a) D. Amantini, F. Fringuelli, F. Pizzo, S. Tortoioli, and L. Vaccaro, *Synlett*, **2003**, 2292. b) B. Movassagh, S. Sobhani, F. Kheirdoush, and Z. Fadaei, *Synth. Commun.*, **33**, 3103 (2003). c) J. Downsland, F. Mckerlie, and D. J. Procter, *Tetrahedron Lett.*, **41**, 4923 (2000).

4 F. Fringuelli, F. Pizzo, S. Tortoioli, and L. Vaccaro, *J. Org. Chem.*, **68**, 8248 (2003).

5 R. Fan and X.-L. Hou, *J. Org. Chem.*, **68**, 726 (2003).

6 S. Chanrasekar, C. R. Reddy, B. N. Babu, and G. Chandrashekar, *Tetrahedron Lett.*, **43**, 3801 (2002).

7 a) F. Fringuelli, F. Pizzo, S. Tortoioli, and L. Vaccaro, *Adv. Synth. Catal.*, **344**, 379 (2002). b) M. Romdhani Younes, M. M. Chaabouni, and A. Baklouti, *Tetrahedron Lett.*, **42**, 3167 (2001).

8 a) J. S. Yadav, B. V. S. Reddy, A. K. Basak, and A. Venkat Narsaiah, *Tetrahedron Lett.*, **44**, 1047 (2003).

9 a) R. Sheldon, *Chem. Commun.*, **2001**, 2399. b) P. Wasserscheid and W. Keim, *Angew. Chem., Int. Ed.*, **39**, 3772 (2000).

10 a) A. R. Khosropour, M. M. Khodaei, and K. Ghozati, *Chem. Lett.*, **34**, 303 (2004). b) I. Mohammadpoor-Baltork and A. R. Khosropour, *Synth. Commun.*, **22**, 3411 (2001).

11 M. M. Khodaei, A. R. Khosropour, and K. Ghozati, *Tetrahedron Lett.*, **45**, 3525 (2004).

12 a) G. Bartoli, E. Marcantoni, and L. Sambri, *Synlett*, **2003**, 2101. b) J. S. Yadav, B. V. S. Reddy, C. V. Rao, P. K. Chand, and A. R. Prasad, *Synlett*, **2002**, 137. c) J. S. Yadav, B. V. S. Reddy, M. S. Reddy, and G. Sabitha, *Synlett*, **2001**, 1134.

13 Typical procedure for preparation of *trans*-2-phenylthiocyclohexanol (Table 2, Entry 4): To a molten mixture of $(PhS)_2$ (1 mmol), $CeCl_3$. $7H_2O$ (0.2 mmol), and TBPB (0.5 mmol), cyclohexene oxide (1 mmol) and zinc powder (1 mmol) were added. The reaction mixture was stirred at 70 °C for 45 min (monitored by TLC). After completion of the reaction, the mixture was washed with Et_2O (3×10 mL) and the organic layer was evaporated. The residue was chromatographied on silica gel (petroleum ether–EtOAc) to afford the pure product (80%). IR (KBr) ν_{max} 3620, 3200, 1580, 1435, 690. ^1H NMR (200 MHz, $CDCl_3$): δ 1.22–1.42 (m, 4H), 1.62–1.83 (m, 2H), 2.10–2.39 (m, 2H), 2.85 (ddd, 1H, $J = 11.6$, 9.8, 4.5 Hz), 3.15 (br, 1H, OH), 3.42 (ddd, 1H, $J = 9.8$, 9.8, 4.5 Hz), 7.25–7.42 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.7, 26.6, 33.1, 34.2, 56.9, 72.4, 128.2, 129.3, 133.0, 134.2. Anal. Calcd. for $C_{12}H_{16}OS$ (208.317): C, 69.19; H, 7.74; S, 15.39%. Found: C, 69.21; H, 7.76; S, 15.43%.

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