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Dimercaptoethane oxirane ring opening reaction: β,β′-dihydroxy dithioether synthesis

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Abstract—The action of dimercaptoethane on alkyl oxiranes in the presence of benzyltrimethylammonium hydroxide (Triton B) allows, via regiospecific opening reaction, the preparation of the corresponding β,β′-dihydroxy dithioethers in excellent yields. © 2001 Elsevier Science Ltd. All rights reserved.

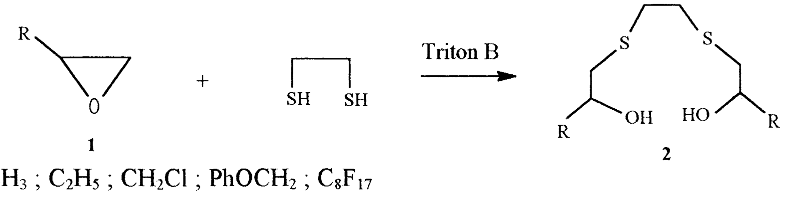
The ring opening of oxiranes[1] with various nucleophiles is an important synthetic transformation in organic chemistry. The preparation of β-hydroxy thioethers is generally realized by the action of thiolates[2] or thiols in the presence of acids or metal salts.[3] Ring opening reaction by thiols was also carried out in the presence of alumina[4] or polyethylene glycol.[5] This reaction has been recently performed in hexafluoroisopropanol without a catalyst.[6] Herein, we report the ring opening reaction of two mole equivalents of epoxides with dimercaptoethane using benzyltrimethylammonium hydroxide (Triton B) as catalyst[7] (Scheme 1).

As shown in Table 1, this reaction allows the preparation of β,β′-dihydroxy dithioethers in excellent yields. For the starting oxiranes **1a**–**e**, the epoxide ring was regiospecifically opened by nucleophilic attack on the terminal carbon atoms affording a secondary diol. This regiospecificity was not observed in the case of styrene oxide **1f**, which gave a mixture of three isomeric derivatives.[8] Compounds **2a**–**f** should be obtained as a mixture of diastereomers, but the two stereogenic centers within the molecule are far from each other so they could not be discerned by NMR technique. The ^{1}H NMR spectrum shows a sharp singlet for the two methylene groups of the dimercaptoethane moiety.

This is not the case for the cyclohexanic compound **2g**, for which two singlets of the same intensity were observed for these methylene groups. The existence of two diastereomers for the cyclohexanic compound may be explained if we assume that the cyclohexene oxide **1g** gave exclusively *trans* products,[9,10] which were formed as an equimolar mixture of *meso* and *threo*[11] (Scheme 2).

By adding D-camphosulfonic acid,[12] splitting of one of the two singlets was not observed, but the more deshielded one broadens so it may be attributed to the *threo* isomer.

The β,β′-dihydroxy dithioethers obtained were characterized by spectroscopic and HRMS methods.[13] These new compounds may be useful intermediates for the synthesis of lipophilic thiacrown ethers.[14]



Scheme 1.

Keywords: epoxides; dimercaptoethane; thioethers.

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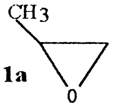
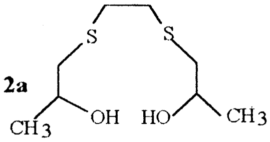
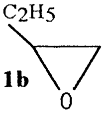
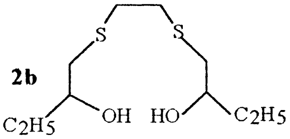
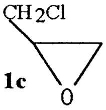
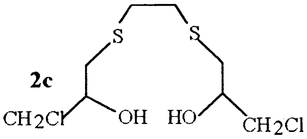
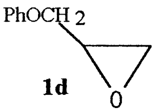
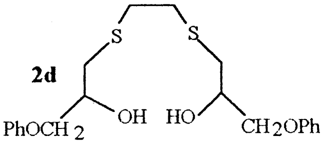
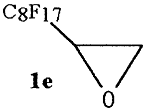
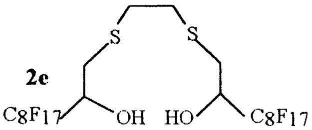
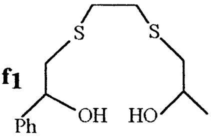
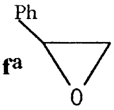
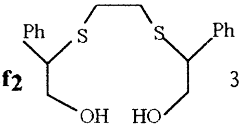
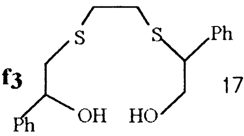
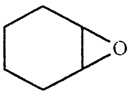
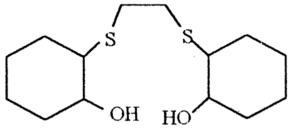
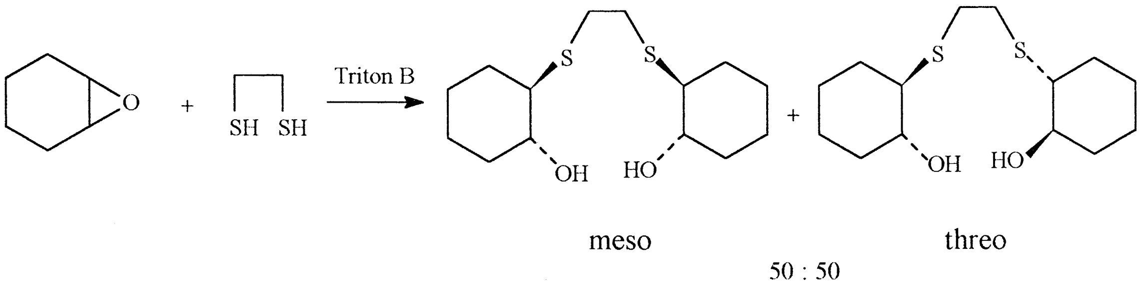
Table 1. Ring opening of epoxides with dimercaptoethane

Epoxide	β,β'-dihydroxy dithioethers	Time (h)	bP (°C)/Torr or mP (°C)	Yield (%)
1a 	**2a** 	0.5	140/0.025	94
1b 	**2b** 	0.5	150/0.015	96
1c 	**2c** 	0.5	oil	95
1d 	**2d** 	0.5	79	96
1e 	**2e** 	0.5	124	98
	2f$_1$  52%			
1f[a] 	**2f$_2$**  31%	0.5	oil [b]	96
	2f$_3$  17%			
1g 	**2g** 	2	70	98

[a] The ratio of the three isomers was determined by GC and ^{1}H NMR. [b] The mixture of isomeric products was purified by column chromatography (silica gel, hexane–diethyl ether, 1:1).



Scheme 2.

Acknowledgements

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6. Kesavan, V.; Bennet-delpar, D.; Bégué, J. P. *Tetrahedron Lett.* **2000**, *41*, 2895–2898.
7. Dimercaptoethane (27 mmol) was added dropwise over 30 minutes to a stirred solution of epoxide **1** (50 mmol) and Triton B (1.5 mmol) at room temperature. The consumption of the epoxide was monitored by TLC (silica gel 60 F_{254}, hexane–diethylether, 1:1). The obtained mixture was purified by distillation (**2a** and **2b**), column chromatography (**2f**, **2c**) and by recrystallization from carbon tetrachloride (**2d**, **2e** and **2g**).
8. Compound **2f**. HRMS: mol. mass calcd 335.113950 (for $C_{18}H_{23}O_2S_2$), found 335.113860 $(M+H)^+$.
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10. Epoxides are normally subsect to *anti* ring opening. Rickborn, B. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; pp. 733–734.
11. Examination of the ^{13}C NMR spectra of **2g** showed doubling of a number of the peaks. ^1H NMR spectra of **2g** exhibited good integrals but it showed two signals for OH and CH_2S. The isomers ratio is determined from CH_2S signals intensity.
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13. Spectral data: compound **2a**: ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.25$ (d, $J=6.3$ Hz, 6H), 2.51 (m, 2H), 2.73 (m, 2H), 2.78 (s, 4H), 2.95 (br, 2H), 3.87 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=21.98$ ($2CH_3$), 32.43 ($2CH_2S$), 41.42 ($2CH_2$), 65.95 (2CH). HRMS: mol. mass calcd 233.064595 (for $C_8H_{18}NaO_2S_2$), found 233.064180 $(M+Na)^+$. Compound **2b**: ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.97$ (t, J 7.5 Hz, 6H), 1.54 (m, 4H), 2.52 (m, 2H), 2.75 (m, 2H), 2.78 (s, 4H), 2.95 (br, 2H), 3.61 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=9.82$ ($2CH_3$), 28.87 ($2CH_2$), 32.24 ($2CH_2S$), 39.46 ($2CH_2$), 71.02 (2CH). HRMS: mol. mass calcd 239.113950 (for $C_{10}H_{23}O_2S_2$), found 239.113090 $(M+H)^+$. Compound **2c**: ^1H NMR (300 MHz, CD_3COCD_3): $\delta=2.78$ (m, 4H), 2.84 (S, 4H), 3.69 (m, 4H), 3.98 (br, 2H), 4.48 (m, 2H). ^{13}C NMR (75 MHz, CD_3COCD_3): δ 33.21 ($2CH_2S$), 36.21 ($2CH_2$), 48.68 ($2CH_2Cl$), 71.56 (2CH). HRMS: mol. mass calcd 300.98665 (for $C_8H_{16}NaO_2S_2Cl_2$), found 300.98704 $(M+Na)^+$. Compound **2d**: ^1H NMR (300 MHz, CD_3COCD_3): $\delta=2.78$ (m, 4H), 2.84 (S, 4H), 4.03 (m, 2H), 4.11 (m, 2H), 4.13 (m, 4H), 6.88–7.27 (m, 10H). ^{13}C NMR (75 MHz, CD_3COCD_3): $\delta=33.14$ ($2CH_2S$), 35.83 ($2CH_2$), 69.95 ($2CH_2O$), 70.95 (2CH), 114.94, 121.13, 120.78, 159.27 (2Ph); mol. mass calcd 417.11702 (for $C_{20}H_{26}NaO_4S_2$), found 417.11728 $(M+Na)^+$. Compound **2e**: ^1H NMR (300 MHz, CD_3COCD_3): $\delta=2.88$–2.99 (m, 8H), 4.40 (m, 2H), 5.67 (br, 2H). ^{19}F NMR (282 MHz, C_6F_6): $\delta=85.54$ (6F, $2CF_3$), 47.81 (2F, $2CF_{A\alpha}$), 45.36 (4F, $2CF_{2\delta}$), 44.70 (12F, $2CF_{2\delta}$, $2CF_{2\varepsilon}$, $CF_{2\zeta}$), 43.89 (4F, $2CF_{2\beta}$), 40.43 (4F, $2CF_{2\omega}$), 40.28 (2F, $2CF_{B\alpha}$) mol. mass calcd 1040.96335 (for $C_{24}H_{12}NaO_2S_2$), found 1040.96340 $(M+Na)^+$. Compound **2g**: ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.26$–1.40 (m, 8H), 1.74 (m, 4H), 2.09 (m, 4H), 2.41 (m, 2H), 2.80 and 2.83 (two singlets, 4H), 3.18 and 3.37 (two peaks, 2H), 3.31 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=24.22$, 26.08, 30.77 and 31.16 (two peaks), 32.92 and 33.01 (two peaks), 33.87, 53.38 and 53.47 (two peaks), 72.46 and 72.83 (two peaks). HRMS: mol. mass calcd 313.127195 (for $C_{14}H_{26}NaO_2S_2$), found 313.127210 $(M+Na)^+$.
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