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Regioselective ring-opening reactions of 1,2-epoxides with thiols and arylselenols directly promoted by [Bmim]BF_4

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ABSTRACT

Regioselective ring-opening reactions of 1,2-epoxides with ArSH and ArSeH promoted by ionic liquid [Bmim]BF_4 were investigated. A variety of β-hydroxy selenides and β-hydroxy sulfides were obtained in excellent yields (81–99%) with good regioselectivities using a mild, simple and environmentally benign procedure.

β-Hydroxy sulfides and β-hydroxy selenides are important intermediates in medicinal chemistry and organic synthesis,[1] especially for the synthesis of natural products such as leukotrienes,[1c] pancratistatin,[2] and schweinfurthin B.[3] The effective method for synthesis of β-hydroxy sulfides and β-hydroxy selenides is through ring-opening reactions of epoxides with thiols and arylselenols. While there are a few examples utilizing water or solvent-free conditions,[4] most examples involve toxic solvent and Lewis acid catalysts, such as $InCl_3$,[5] $ZnCl_2$,[6] $AlPW_{12}O_{40}$,[7] gallium complexes,[8] lanthanide complexes,[9] and titanium complexes.[10] Compared with the synthesis of β-hydroxy sulfides, less attention has been paid to the synthesis of β-hydroxy selenides by the ring-opening reaction of epoxides with ArSeH.[11] Therefore, it is of significant interest to find a mild, simple and environmentally benign method for the synthesis of both β-hydroxy sulfides and β-hydroxy selenides.

From both environmental and economical point of view, the concept of recyclable reaction media has gained more and more attentions. In recent years, room temperature ionic liquids (RTILs), which can be easily recovered and reused compared to organic solvents, have been used in organic synthesis. Their attractive properties, such as negligible vapor pressure, high polarity, nonflammable, and easy handling, have made them excellent reaction media and environmentally benign solvents.[12] Moreover, some ionic liquids even show enhancement in reaction rates and selectivity.[12a,13] Recently, our research was focused on the ring-opening reaction of epoxides with nucleophiles to obtain β-hydroxy selenides and β-hydroxyacetylene.[11b,c,14] Herein, we report the regioselective ring-opening reaction of 1,2-epoxides with thiols and arylselenols promoted by [Bmim]BF_4 in the absence of metal salts and organic solvents.

The reaction of cyclohexene oxide with *p*-methylthiophenol was initially investigated in different reaction media. The results are shown in Table 1. It was found that *trans*-2-phenylthio-1-cyclohexanol was obtained in only 6% yield without a catalyst in toluene at 50 °C after 6 h (entry 1). In the presence of RTILs, such as [Bmim]Br and [Bmim]Cl, products were obtained in 40–46% yields (entries 2–4), indicating that these ionic liquids are moderately effective for the ring-opening reaction. Inspired by these interesting results, we utilized [Bmim]BF_4 as catalyst and were pleased to find that the yield was enhanced to 70% under the same reaction conditions (entry 5). When the reaction was carried out at 60 °C for 6 h, the yield was further enhanced to 81% (entry 6). We then turned our attentions to examine the substrate scope under this optimized condition.

Table 1
Reaction of cyclohexene oxide with *p*-methylthiophenol[a]

Entry	Ionic liquid or solvent	Temperature (°C)	Yield[b] (%)
1	Toluene	50	6
2	[Bmim]Br	50	43
3	[Bmim]Cl	50	46
4	[Bmim]BF_4	50	70
5	[Bmim]BF_4	60	81

[a] Reaction conditions: cyclohexene oxide (1.0 mmol), *p*-methylthiophenol (1.1 mmol), RILTs or toluene (1.0 ml), 6 h.
[b] Isolated yields.

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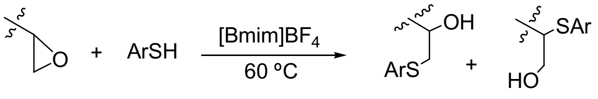
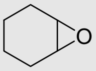
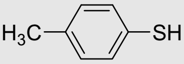
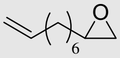
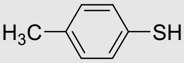
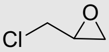
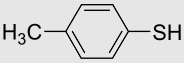
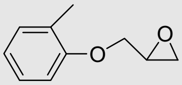
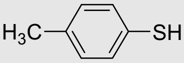
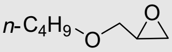
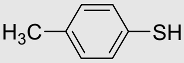
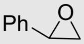
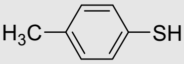
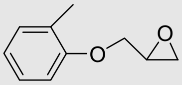
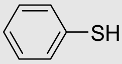
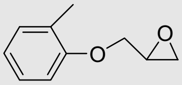
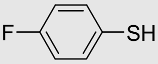
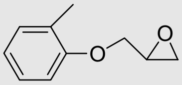
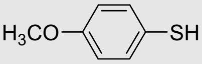
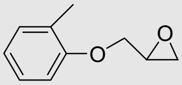
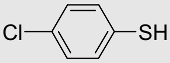
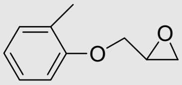
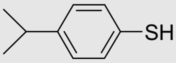
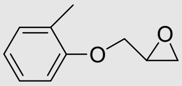
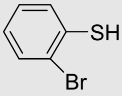
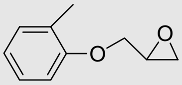
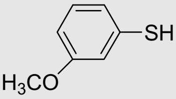
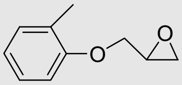
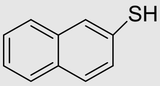
Table 2
Reaction of epoxides reacting with ArSH promoted by [Bmim]BF_4[a]



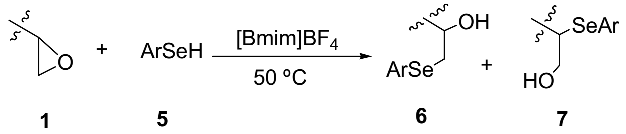
1 2 3 4

Entry	Epoxide	ArSeH	Product	Time (h)	Yield[b] (%)
1	 **1a**	 **2a**	**3aa**	6	81
2	 **1b**	 **2a**	**3ba**:**4ba** = 4:1[c]	5	83[c]
3	 **1c**	 **2a**	**3ca**	3	85
4	 **1d**	 **2a**	**3da**	3	93
5	 **1e**	 **2a**	**3ea**	5	83
6	 **1f**	 **2a**	**3fa**:**4fa** = 1:9[c]	3	91[d]
7	 **1d**	 **2b**	**3db**	3	96
8	 **1d**	 **2c**	**3dc**	3	99
9	 **1d**	 **2d**	**3dd**	5	87
10	 **1d**	 **2e**	**3de**	3	99
11	 **1d**	 **2f**	**3df**	3	91
12	 **1d**	 **2g**	**3dg**	3	99
13	 **1d**	 **2h**	**3dh**	3	95
14	 **1d**	 **2i**	**3di**	3	99

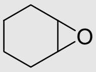
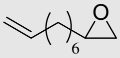
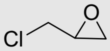
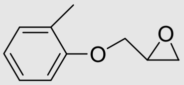
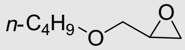
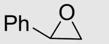
[a] Epoxides (1.0 mmol), thiols (1.1 mmol), [Bmim]BF_4 (1.0 ml).
[b] Isolated yields.
[c] Determined by ^1H NMR and the ratio of two isomers yields.
[d] Total yield of two isomers.

As listed in Table 2, all the reactions went well and gave corresponding products in high yields (81–99%) when promoted by [Bmim]BF_4 at 60 °C for 3–6 h. Thiolysis of epoxides was sensitive to the structures of both 1,2-epoxides and substituted thiophenols. For *p*-methylthiophenol, the sterically hindered epoxide **1a** was found to be less reactive than other epoxides **1b**, **1c**, **1d**, **1e**, and

Table 3
Reaction of epoxides with ArSeH promoted by [Bmim]BF$_4$[a]



5a: Ar = Ph-
5b: Ar = 1-naphthyl-

Entry	Epoxide	ArSeH	Product	Time (h)	Yield[b] (%)
1	 **1a**	**5a**	**6aa**	2	94
2		**5b**	**6ab**	2	94
3	 **1b**	**5a**	**6ba**:**7ba** = 82:18[c]	2	93[d]
4		**5b**	**6bb**:**7bb** = 78:22[c]	2	92[d]
5	 **1c**	**5a**	**6ca**	1	96
6		**5b**	**6cb**	1	95
7	 **1d**	**5a**	**6da**	1	98
8		**5b**	**6db**	1	98
9	 **1e**	**5a**	**6ea**	2	92
10		**5b**	**6eb**	2	91
11	 **1f**	**5a**	**6fa**:**7fa** = 1:4,[c]	1	95[d]
12		**5b**	**6fb**:**7fb** = 2:7[c]	1	93[d]

[a] Epoxides (1.0 mmol), arylselenols (1.1 mmol), [Bmim]BF$_4$ (1.0 ml).
[b] Isolated yields.
[c] Determined by ^{1}H NMR and the ratio of two isomers yields.
[d] Total yield of two isomers.

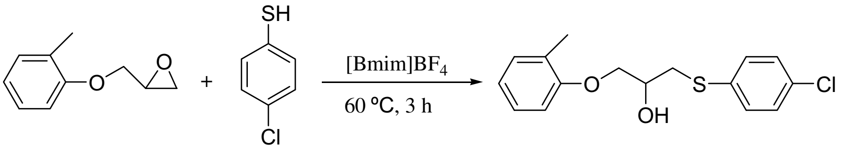
1f (entries 1–6). For the reactions of epoxide **1d**, an electron-withdrawing substituent on the thiophenol (e.g., a chloro or fluoro group) was found to increase the reactivity, while electron-donating substituents such as methoxy and isopropyl groups were found to lower the reactivity (entries 8–13). When the sterically hindered naphthylthiol replaced thiophenol, the yield increased slightly (entry 14 vs entry 7). In term of regioselectivity, the reactions were sensitive to the structure of epoxides. In general, for most 1,2-epoxides except **1b** and **1f**, reactions were completely regioselective as typically observed with the attack of nucleophiles on the less substituted carbon.

Due to the importance of β-hydroxy selenides, the ring-opening reactions of epoxides with phenylselenol and naphthylselenol directly promoted by [Bmim]BF$_4$ were also examined. The results are summarized in Table 3. All the reactions gave products in excellent yields (91–98%) in 1–2 h at 50 °C, which indicated that ArSeH was more reactive than ArSH. Except the reactions of epoxides **1b** and **1f** with ArSeH, all the reactions gave products with exclusive regioselectivity. When the sterically hindered naphthylselenol replaced thiophenol, the yields were similar. However, the regioselectivities decreased slightly in some cases.

One of the attractive properties of ionic liquids is that they can be recycled. Therefore, the recovery potential of [Bim]BF$_4$ in the reaction of **1d** and 4-chlorophenylthiol was investigated. As shown in Table 4, we are pleased to find that the reaction only showed very slight decrease in yields in a few cycles. For example, in the fourth run, the yield was still 96%.

While the ring-opening reaction of epoxides with TMSCl and ArHN$_2$ directly promoted by ionic liquids have been reported,[13b,13c] the catalytic mechanism is not clear yet. To study the possible mechanism about this type of transformation, n-Bu$_4$Cl (100 mol %) was used as a promoter to the reaction of cyclohexene

Table 4
Reuse of [Bmim]BF$_4$ for the reaction of epoxide **1d** with p-chlorophenylthiol[a]



Cycle	1	2	3	4
Yield[b] (%)	99	99	97	96

[a] Reaction conditions: **1d** (2.0 mmol), p-chlorothiophenol (2.2 mmol), [Bmim]BF$_4$ (2.0 ml), 60 °C, 3 h. After reaction, the ionic liquid was concentrated in vacuo (5 torr for 1 h at 110 °C), and further amounts of reactants were added and next turn began.
[b] Isolated yields.

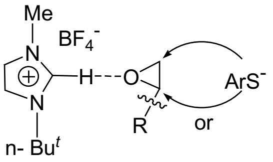


Figure 1. Proposed key intermediate for the ring-opening reaction promoted by [Bmim]BF_4.

oxide with *p*-methylthiophenol and *trans*-2-phenylthio-1-cyclohexanol was obtained in 21% yield at 50 °C after 6 h. When [Bmim]Br or [Bmim]Cl was used as the promoter, products were obtained in 43% and 46% yields, respectively, under the similar reaction conditions (Table 1, entries 2 and 3). This implied that 1-*n*-butyl-3-methylimidazolium moiety may play a key role to this transformation. To learn mechanism of this reaction, the change of proton chemical shift at C2 of the imidazolium cation was investigated using ^{1}H NMR. It was found that the C2 proton singlet of the imidazolium cation was shifted downfield from 8.961 ppm to 8.984 ppm in the presence of styrene oxide. The proposed key intermediate of this reaction is shown in Figure 1. Due to the acidity of C2 proton of the imidazolium cation,[15] the hydrogen bond interaction of imidazolium cation with the epoxide oxygen may make it easy to cleave C–O bond of epoxides[16] and then nucleophile ArS^- may attack the carbon to afford the desired product.[11c]

In summary, we have demonstrated that the ring-opening reaction of 1,2-epoxides with thiols and arylselenols in ionic liquid [Bmim]BF_4 gave good yields and regioselectivities and the proposed mechanism was also discussed. The present procedure opens a novel entry to the synthesis of β-hydroxy selenides and β-hydroxy sulfides using a recyclable ionic liquid, which acts as both promoter and reaction medium. The additional advantage is that this reaction is carried out under economical, environmentally benign and simple conditions.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.08.109.

References and notes

1. (a) Conte, V.; Furia, D. F.; Licini, G.; Modena, G.; Sbampto, G.; Valle, G. *Tetrahedron: Asymmetry* **1991**, *2*, 257–276; (b) Luly, J. R.; Yi, N.; Soderquist, J.; Stein, H.; Cohen, J.; Perun, T. J.; Plattner, J. J. *J. Med. Chem.* **1987**, *30*, 1609–1616; (c) Corey, E. J.; Clark, D. A.; Goto, G.; Marfat, A.; Mioskowski, C.; Samuelsson, B.; Hammarstrom, S. *J. Am. Chem. Soc.* **1980**, *102*, 1436–1439; (d) Wirth, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 3740–3749; (e) Tiecco, M.; Testaferri, L.; Santi, C.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3131–3133.
2. Rigby, J. H.; Maharoof, U. S. M.; Mateo, M. E. *J. Am. Chem. Soc.* **2000**, *122*, 6624–6628.
3. Treadwell, E. M.; Neighbors, J. D.; Wiemer, D. F. *Org. Lett.* **2002**, *4*, 3639–3642.
4. (a) Fringuelli, F.; Pizzo, F.; Vittoriani, C.; Vaccaro, L. *Eur. J. Org. Chem.* **2006**, *2006*, 1231–1236; (b) Fringuelli, F.; Pizzo, F.; Tortoioli, S.; Vaccaro, L. *J. Org. Chem.* **2004**, *69*, 8780–8785; (c) Reddy, M. S.; Srinivas, B.; Sridhar, R.; Narender, M.; Rao, K. R. *J. Mol. Catal. A: Chem.* **2006**, *255*, 180–183.
5. (a) Fringuelli, F.; Pizzo, F.; Tortoioli, S.; Vaccaro, L. *Org. Lett.* **2005**, *7*, 4411–4414; (b) Fringuelli, F.; Pizzo, F.; Tortoioli, S.; Vaccaro, L. *Adv. Synth. Catal.* **2002**, *344*, 379–384.
6. (a) Amantini, D.; Fringuelli, F.; Pizzo, F.; Tortoioli, S.; Vaccaro, L. *Synlett* **2003**, 2292–2296; (b) Fringuelli, F.; Pizzo, F.; Tortoioli, S.; Vaccaro, L. *J. Org. Chem.* **2003**, *68*, 8248–8251.
7. Firouzabadi, H.; Iranpoor, N.; Jafari, A. A.; Makarem, S. *J. Mol. Catal. A: Chem.* **2006**, *250*, 237–242.
8. Iida, T.; Yamamoto, N.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1997**, *119*, 4783–4784.
9. Vougioukes, A. E.; Kagan, H. B. *Tetrahedron Lett.* **1987**, *28*, 6065–6068.
10. Wu, J.; Hou, X.; Dai, L.; Xia, L.; Tang, M. *Tetrahedron: Asymmetry* **1998**, *9*, 3431–3436.
11. (a) Sridhar, R.; Srinivas, B.; Surendra, K.; Krishnaveni, N. S.; Rao, K. R. *Tetrahedron Lett.* **2005**, *46*, 8837–8839; (b) Yang, M.; Zhu, C.; Yuan, F.; Huang, Y.; Pan, Y. *Org. Lett.* **2005**, *7*, 1927–1930; (c) Yang, M.; Yuan, C.; Pan, Y.; Zhu, C. *Chin. J. Chem.* **2006**, *24*, 669–673.
12. (a) Welton, T. *Chem. Rev.* **1999**, *99*, 2071–2084; (b) Dupont, J.; Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667–3692; (c) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772–3789.
13. (a) Sheldon, R. *Chem. Commun.* **2001**, 2399–2407; (b) Xu, L.; Li, L.; Xia, C.; Zhao, P. *Tetrahedron Lett.* **2004**, *45*, 2435–2438; (c) Yadav, J. S.; Reddy, B. V. S.; Basak, A. K.; Narsaiah, A. V. *Tetrahedron Lett.* **2003**, *44*, 1047–1050; (d) Lv, X.; Wang, Z.; Bao, W. *Tetrahedron* **2006**, *62*, 4756–4761.
14. Zhu, C.; Yang, M.; Sun, J.; Pan, Y. *Synlett* **2004**, 465–468.
15. (a) Chu, Y.; Deng, H.; Cheng, J. *J. Org. Chem.* **2007**, *72*, 7790–7793; (b) Kim, Y.-J.; Streitwieser, A. *J. Am. Chem. Soc.* **2002**, *124*, 5757–5761; (c) Amyes, T. L.; Diver, S. T.; Richard, J. P.; Rivas, F. M.; Toth, K. *J. Am. Chem. Soc.* **2004**, *126*, 4366–4374.
16. Welton, T. In *Ionic Liquids in Synthesis*; Wasserscheid, P., Welton, T., Eds.; Wiley-VCH: Weinheim, 2002; pp 100–101.