Pergamon

Tetrahedron Letters 41 (2000) 2895–2898

TETRAHEDRON LETTERS

Fluoro alcohol as reaction medium: one-pot synthesis of β-hydroxy sulfoxides from epoxides

Venkitasamy Kesavan, Danièle Bonnet-Delpon and Jean-Pierre Bégué *

Laboratoire BIOCIS associé au CNRS, Centre d'Etudes Pharmaceutiques, Rue J. B. Clément, 92296 Châtenay-Malabry, France

Received 26 December 1999; accepted 16 February 2000

Abstract

β-Hydroxy sulfoxides were obtained in one-pot synthesis by the ring opening of oxiranes with thiols in hexafluoroisopropanol (HFIP) without any catalyst, followed by in situ oxidation under neutral conditions. The reaction is *anti*-selective. β-Hydroxy sulfoxides were transformed by pyrolysis in the corresponding allylic alcohols.

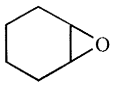
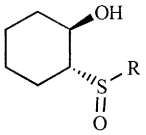
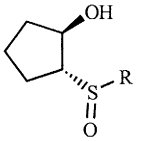
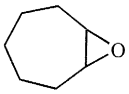
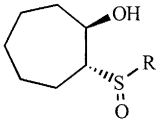
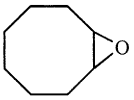
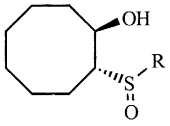
The ring opening process of oxiranes with various nucleophiles (e.g. amines, thiols, Me_3SiCN etc.) is an important synthetic transformation for an easy access to a large number of functionalised intermediates.[1] β-Hydroxy sulfoxides and β-hydroxy sulfides are important intermediates in organic synthesis.[2] Trost developed an efficient route for alkene synthesis involving elimination of sulfinyl group[3] from β-hydroxy sulfoxides which are commonly synthesised by oxidation of β-hydroxy sulfides. β-Hydroxy sulfides are of great interest in the field of natural products, particularly in the synthesis of leukotrienes.[4] They are generally obtained by oxirane ring opening with thiolates.[5] Epoxide ring opening with thiols can be promoted by acids, Lewis acids or metal salts.[6] Similar results were obtained when the reaction was performed in presence of alumina doped with thiol.[7] In the absence of any acidic or basic promotors, ring opening with thiols provide only very low yields of β-hydroxy thioether even after several hours at high temperature.[6c] So there is a need for the development of new methodology for ring opening with thiols under neutral conditions.

In our search for new environmentally friendly methodology we have already showed the specific role of fluoroalkyl alcohols used as solvents in different reactions: oxidation of olefins, sulfides and thiols.[8] Very recently we have reported ring opening of epoxides with aromatic amines using hexafluoroisopropanol (HFIP) as the reaction medium.[9] We envisaged to take advantage of the facilitated oxirane ring opening in fluoroalkyl alcohols and of the selective oxidation of sulfides to sulfoxides in the same solvent,[8b] to prepare β-hydroxy sulfoxides from epoxides in one-pot. We investigated the ring opening of epoxides with thiol and our successful results are reported in this communication (Table 1).

* Corresponding author. Fax: 33 1 46 83 57 38; e-mail: Jean-Pierre.Begue@cep.u-psud.fr (J.-P. Bégué)

0040-4039/00/$ - see front matter
PII: S0040-4039(00)00305-1

Table 1
Ring opening of cyclic epoxides with thiols in HFIP

Entry	Substrate	Thiol	Product[a]
1.	 **1**	**a** Ph-SH **b** MeO-C_6H_4SH **c** $C_6H_5CH_2SH$	 **2a-c**
2.	 **3**	**a** **b** **c**	 **4a-c**
3.	 **5**	**a** **b** **c**	 **6a-c**
4.	 **7**	**a** **b** **c**	 **8a-c**

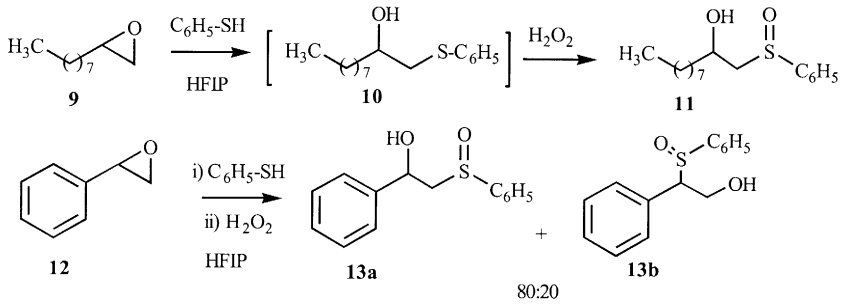
[a] The intermediates β-hydroxy sulfides were not isolated

Initially, cyclohexene oxide and thiophenol were chosen as substrates for the study in trifluoroethanol (pKa 12.8). Cyclohexene oxide (1 mmol) was stirred with thiophenol (1.1 mmol) in trifluoroethanol (1 ml) at room temperature for a period of 72 h under argon. No product was observed under these conditions. However when the reaction was carried out at reflux of trifluoroethanol, 18% of β-hydroxy thioether after 72 h was obtained. Taking into account the possible influence of the acidity of the fluoro alcohol, hexafluoroisopropanol (HFIP) with a pKa of 9.3 was then chosen as the solvent. Cyclohexene oxide (1 mmol) was stirred with thiophenol (1.1 mmol) in HFIP (1 ml) at reflux temperature under argon until the complete disappearance of starting materials (28 h). When the similar experiment was carried out in isopropanol at reflux temperature there was only little formation of the product even after 36 h. This clearly shows that the ring opening with thiol is accelerated in HFIP. As we have previously demonstrated that HFIP was a solvent of choice for the selective oxidation of sulfides to sulfoxides we added directly 1.1 equivalent of H_2O_2[8b] in the reaction medium at 0°C. The product *trans* β-hydroxy sulfoxide was isolated in 84% yield as a 65:35 mixture of two diastereoisomers. The *trans* configuration was deduced from the J_{H-H} coupling constants (C*H*-SO-Ph 2.74 ppm, ddd, *J*=11.6, 10.4, 3.9 Hz) and 2.68 (ddd, *J*=12.4, 10.5, 3.9 Hz) in ^{1}H NMR spectrum and no *syn*-adduct was observed.[10] The ring opening reaction was completely *anti*-stereoselective whereas Lewis acid catalysed ring opening was less selective due to the cationic character of the reaction. However, there was only a moderate diastereoselectivity in the formation of the sulfoxide.

Under the similar conditions cyclopentene oxide **3**, cycloheptene oxide **5** and cyclooctene oxide **7** were subjected to ring opening with aromatic and benzylic thiols, followed by oxidation with H_2O_2 to afford β-hydroxy sulfoxides **4a–c**, **6a–c** and **8a–c**, respectively, in very good yields (75–87%).

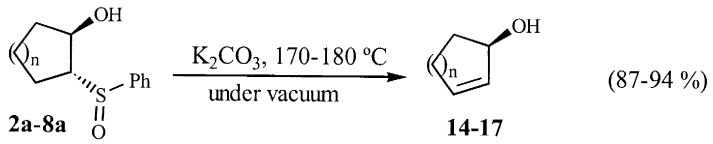
The reaction is also facile with aliphatic and styrene oxides. In the case of terminal epoxide **9**, the

reaction with thiophenol was completely regioselective as usually observed with the attack of nucleophile on the less substituted carbon to yield terminal sulfide **10**. The thioether **10**, was selectively oxidised in situ to sulfoxide **11**.[8b] The exception was styrene oxide **13** which led to the mixture of the two regioisomers (80:20) with contra-Markovnikov type adduct **13a** as the major product (Scheme 1). In reactions performed with the same substrates but with an electrophilic catalysis the regioselectivity is already described to be highly dependent on the metal and experimental conditions.[6] The presence of a phenyl group and the polarisation of C–O bond in presence of Lewis acids could make competitive the attack on both carbons and even reverse the regioselectivity. In our case the attack on the less substituted carbon still remains the major one.



Scheme 1.

Having in hand a good access to β-hydroxy sulfoxides **2a**–**8a**, we could easily prepare allylic alcohols according to the literature.[3] 2-Phenylsulfinyl cycloalkanols were subjected to pyrolysis and afforded the corresponding allylic alcohols in excellent yields (Scheme 2). 2-Cyclohexen-1-ol **14** was obtained in 77% overall yield starting from epoxide **1** so we could obtain allylic alcohols from epoxides in two steps in good yields. This is a good alternative to the formation of allylic alcohols from epoxides under basic conditions, a reaction always in competition with ring opening depending on the basicity/nucleophilicity.



Scheme 2.

We have described a one-pot preparation of β-hydroxy sulfoxides by ring opening of epoxides with thiols in hexafluoroisopropanol followed by selective oxidation. No catalyst was used and the only effluent is water. We assume that the hydrogen bonding ability of HFIP allows an activation of the ring opening without the possible disadvantages of acidic/metal catalysis. The ring opening is completely stereoselective. Allylic alcohols were obtained from epoxides in good yields.

Acknowledgements

We thank CEFIPRA for financial support and for a position of research associateship (V.K.). We are grateful to the Central Glass Co. for a generous gift of chemicals (Dr. Komata).

References

1. (a) Lidy, W.; Sundermeyer, W. *Tetrahedron Lett.* **1973**, *14*, 1449–1452. (b) Mullis, J. C.; Weber, W. P. *J. Org. Chem.* **1983**, *47*, 2873–2876. (c) Blandy, C.; Choukroun, T. L.; Gervais, D. *Tetrahedron Lett.* **1983**, *47*, 2873–2876. (d) Guddenheim, T. L. *J. Am. Chem. Soc.* **1982**, *104*, 5849–5851. (e) Gassman, P. G.; Gremban, R. S. *Tetrahedron Lett.* **1984**, *25*, 3259–3262. (f) Babu, M. H.; Frei, B. *Helv. Chim. Acta* **1986**, *69*, 415–422. (g) Sinou, D.; Emziane, M. *Tetrahedron Lett.* **1986**, *27*, 4423–4426.
2. (a) Conte, V.; Di Furia, F.; Licini, G.; Modena, G.; Sbampto, G.; Valle, G. *Tetrahedron Asymmetry* **1991**, *2*, 257–268. (b) Solladie, G.; Almario, A.; Dominguez, C. *Pure. Appl. Chem.* **1994**, *66*, 2159–2175 (c) Gabbi, C.; Ghelfi, F.; Grandi, R. *Synth. Commun.* **1997**, *27*, 2857–2863 and references cited therein.
3. (a) Trost, B. M. In *Organic Sulfur Chemistry*; Stirling, C. J. M., Ed.; Butterworths: London, 1975; p. 237. (b) Trost, B. M. *Acc. Chem. Soc.* **1978**, *11*, 453–461.
4. (a) Corey, E. J.; Clark, D. A.; Goto, G.; Marfat, A.; Mioskowski, C.; Samuelsson, B.; Hammarstrom, S. *J. Am. Chem. Soc.* **1980**, *102*, 1436–1438. (b) *ibid* **1980**, *102*, 3663–3665.
5. (a) Corey, E. J.; Clark, D. A.; Marfat, A.; Goto, G. *Tetrahedron Lett.* **1980**, *21*, 3143–3146. (b) Peach, M. E. In *The Chemistry of the Thiol Group*; Patai, S., Ed.; John Wiley: New York, 1974; Part 3, p. 771.
6. (a) Vougioukas, A. E.; Kagan, H. B. *Tetrahedron Lett.* **1987**, *28*, 6065–6068. (b) Iqbal, J.; Pandey, A.; Shukla, A.; Srivastava, R. R.; Tripathi, S. *Tetrahedron* **1990**, *18*, 6423–6432. (c) Chini, M.; Crotti, P.; Giovani, E.; Macchia, F.; Pineschi, M. *Synlett* **1992**, 303–305.
7. Posner, G. H.; Rogers, D. Z. *J. Am. Chem. Soc.* **1977**, *99*, 8208–8214.
8. (a) Ravikumar, K. S.; Barbier, F.; Bégué, J. P.; Bonnet-Delpon, D. *Tetrahedron* **1998**, *54*, 7457–7460. (b) Ravikumar, K. S.; Bégué, J. P.; Bonnet-Delpon, D. *Tetrahedron Lett.* **1998**, *39*, 3141–3144. (b) Ravikumar, K. S.; Zhang, Y. M.; Bégué, J. P.; Bonnet-Delpon, D. *Eur. J. Org. Chem.* **1998**, 2937–2940. (c) Ravikumar, K. S.; Barbier, F.; Bégué, J. P.; Bonnet-Delpon, D. *J. Fluorine Chem.* **1999**, *95*, 123–125.
9. Kesavan, V.; Bonnet-Delpon, D.; Bégué, J. P. *Synthesis*, in press.
10. Typical experimental procedure: to a solution of cyclohexene oxide (0.098 g, 0.1 ml, 1 mmol) in HFIP (1 ml), thiophenol (0.112 g, 0.1 ml, 1.1 mmol) was added. The solution was kept at reflux under argon atmosphere. The completion of the reaction was ascertained by GC (28 h). After the completion of reaction, the flask was cooled with ice and 1.1 equivalent of 30% hydrogen peroxide (0.14 ml) was added and stirred further for 15 min. The reaction was quenched with sodium sulfite (0.027 g, 0.2 mmol). HFIP was recovered by distillation as an azeotrope. To the flask 10 ml of water was added and the product was extracted with 3×15 ml of diethyl ether. The organic layer was dried over anhydrous $MgSO_4$ and concentrated in vacuum to afford *trans*-2-phenylsulfinyl cyclohexanol (65:35), yield: 0.175 g (84%), ^{1}H NMR (400 MHz) major isomer (1*S**, 2*S**, (*S*) *S**): 1.0–1.45 (m, 5H), 1.70 (m, 2H), 2.10 (m, 1H), 2.74 (ddd, *J*=12.5, 9.5, 4.5 Hz, 1H, C*H*-SO), 4.12 (1H, td, *J*=9.5, 4.9 Hz, 1H, C*H*-OH), 7.5 (m, 3H), 7.7 (m, 2H); minor isomer (1*S**, 2*S**, (*S*) *R**): 1.0–1.45 (m, 5H), 1.70 (m, 2H), 2.10 (m, 1H), 2.68 (ddd, *J*=12.5, 10.5, 4 Hz, 1H, C*H*-SO), 3.9 (td, *J*=10.5, 5 Hz, 1H, C*H*-OH), 7.5 (m, 3H), 7.7 (m, 2H). Crystallisation from acetone afforded pure (1*S**, 2*S**, (*S*) *S**) isomer: mp 154–155°C (Ref. 11, 156–157°C).
11. Carreno, M. C.; Ruano, J. L.; Martin, A. M.; Padregal, C.; Rodriguez, R. A.; Rubio, A.; Sanchez, J.; Solladié, G. *J. Org. Chem.* **1990**, *55*, 2120–2128.