Tetrahedron: Asymmetry Vol. 4, No. 7, pp. 1533-1536, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00
Pergamon Press Ltd

One-pot Synthesis of α,β-dihydroxy Sulfides via Titanium-promoted Oxirane Ring Opening

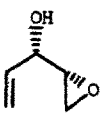
Guo-qiang Lin*, Zhi-cai Shi, and Chun-ming Zeng

Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences
345 Lingling Lu, Shanghai 200032, China

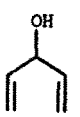
(*Received in Japan* 5 *March* 1993; *accepted* 5 *April* 1993)

Abstract: The one-pot synthesis of α,β-dihydroxy sulfides via titanium-promoted oxirane ring opening of (2R,3S) 1,2-epoxy-4-penten-3-ol by various thiols is described.

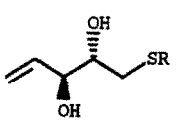
The oxirane ring opening with various nucleophiles is an important access to a large number of intermediates required for the synthesis of natural products.[1] We have recently reported an one-pot aminolysis procedure for the ring opening of the oxirane-(2R,3S)-1,2-epoxy-4-penten-3-ol (**1**) mediated by $Ti(OPr^i)_4$.[2] In this work we wish to report the mercaptanolysis of **1**, which was prepared according to Sharpless asymmetric epoxidation of **2**[3], with various thiols. The results are summarized in Table 1.



1



2



3

a: R=$PhCH_2$
b: R=Ph
c: R=*o*-$NH_2C_6H_4$-
d: R=$CH_2CH_2CH_2SH$
e: R=PhCO-
f: R=*o*-$HOCH_2C_6H_4$-

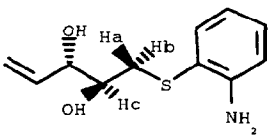
The one-pot ring-opening of **1** required the presence of 1.5eq. $Ti(OPr^i)_4$ in order to promote the process of nucleophilic addition. In our cases, **1** was treated one-pot with thiols in the presence of 1.5eq $Ti(OPr^i)_4$ at room temperature overnight. Usual work-up yielded α,β-dihydroxy sulfides **3** in satisfactory yields.

In the case where two nucleophilic function groups co-occured in a substrate, for example, -SH and $-NH_2$ in Entry c, -SH and -OH in Entry e, since the nucleophilicity of the sulfur atom was higher than that of the nitrogen and oxygen atoms, sulfur dominantly attacked the less hindered side of the epoxy ring providing **3c** and **3e** as the only products as proved by 600 MHz ^1H NMR analysis. 600 MHz ^1H NMR spectra of **3c** showed clearly two d.d splitting of Ha and Hb (Ha, 2.70 ppm, Jab=9.3 Hz and Jac=13.8 Hz; Hb, 2.95 ppm, Jab=9.3 Hz, Jbc=3.3 Hz).

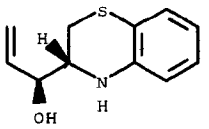
Table 1. Results of the one-pot ring-opening of **1** by thiols

Entry	Nucleophiles	Yield of **3** from **2** via **1**[a]	$[\alpha]_D^{25}$ [b]
a	$C_6H_5CH_2SH$	72.2%	+18.8 [c]
b	C_6H_5SH	72.4%	+12.4
c	*o*-$NH_2C_6H_4SH$	78.4%	+37.5
d	$HS(CH_2)_3SH$	56.8%	+1.4
e	C_6H_5COSH	68.1%	-3.4
f	*o*-$HOCH_2C_6H_4SH$	60.3%	+2.1

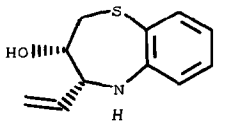
a: The yield was not optimized. b: The specific rotation was determined as a solution in $CHCl_3$ unless mentioned elsewhere. c: Measured in CH_2Cl_2.



3c



4a



4b

Furthermore, when **3c** was treated with an equimolecular amount of PPh_3 and DEAD at r.t. for 8 hrs, a mixture of **4a** and **4b** (1:1) was obtained in 68.3% yield. This supports the structure of **3c**. Thus this one-pot ring opening mercaptanolysis provides a convenient way of synthesizing α,β-dihydroxy sulfides. We are continuing to explore the applications of these α,β-dihydroxy sulfides which contain a terminal double bond.

EXPERIMENTAL

^1H NMR spectra were obtained on Bruker AM-300 (300 MHz) or Bruker AMX-600 (600 MHz) spectrometers, using $CDCl_3$ as solvent and TMS as an internal standard. IR spectra were taken on a IR-440 spectrometer, and main absorption frequencies were given in cm^{-1}. MS spectra were recorded with Finnigan 4021 spectrometer. The specific rotations were measured with PERKIN-ELMER 241 polarimeter.

General procedure and identifications of the α,β-dihydroxy sulfides 3a-f.

To a mixture of 4A molecular sieves (150mg) and dried CH_2Cl_2 (8ml), was added subsequently (142 mg) L(+)-DIPT (0.6 mmol), TBHP (1.3 ml, 6.7 M in CH_2Cl_2), 143 mg $Ti(OPr^i)_4$ (0.5 mmol) at -20°C under positive N_2 pressure. After stirring for 0.5 hr, 420 mg **1** (0.5 mmol) was added via syringe. The mixture was kept in refrigerator at -20°C for 2 days until completion of the reaction showed by the disappearance of **1** on TLC. $P(OEt)_3$ (0.5 ml) was then added at -20°C, stirring was continued for 0.5hr followed by the addition of $Ti(OPr^i)_4$ (2.3 ml) together with RSH (0.75 mmol). The mixture was stirred overnight at r.t. Then $CHCl_3$

(20 ml) and 10% NaOH in brine (5 ml) were added and stirred for 3 hrs. The organic layer was separated and dried over anhydrous Na_2SO_4. After usual workup the residue was subjected to flash column chromatography to furnish **3a-f**. Identifications of **3a-f** were based upon their ^1H NMR (300 MHz or 600 MHz) IR, HRMS and MS.

3a: $[\alpha]_D^{25}$ + 18.8 (c 0.36, CH_2Cl_2)
IR (film) ν_{max}: 3400 cm^{-1}(strong), 3050, 2950, 2900, 1645, 1610, 1450, 1560 cm^{-1}. ^1H-NMR: 5.82 (m, 1H), 5.26 (m, 2H), 4.49 (s, 1H), 4.25 (dd, J=5.7 and 4.5Hz, 1H), 3.67(m, 1H), 3.09 (s, 1H), 2.60 (m, 2H), 1.55 (b, 2H) ppm. m/z: 225 (M+1, 1.60%), 206 (M-H_2O, 9.9%), 137 (-CH_2SCH_2Ph, 8.9%), 124(-SCH_2Ph, 43.2%), 91(-CH_2Ph, 100%). HRMS: M-H_2O, Calcd for $C_{12}H_{14}OS$: 206.0766; Found: 206.0722.

3b: $[\alpha]_D^{25}$ +12.4 (c 1.45, $CHCl_3$)
IR (film) ν_{max}: 3400, 3040, 2950, 2900, 1630, 1600, 1550 cm^{-1}. ^1H-NMR : 7.30 (m, 5H), 5.78 (m, 1H), 5.30 (m, 2H), 4.50 (m, 2H), 3.05 (dd, 2H), 2.55 (b, 2H) ppm. m/z: 210 (M^+, 12.45%), 192(M-H_2O, 7.98%), 135(M-Ph+2H, 100%), 109(SPh, 87.3%). HRMS: Calcd for $C_{11}H_{14}O_2S$: 210.0678; Found: 210.0674.

3c: $[\alpha]_D^{25}$ +37.5 (c 1.35, $CHCl_3$)
IR (film) ν_{max}: 3400, 3050, 2950, 2900, 1645, 1610, 1580, 1450 cm^{-1}. ^1H-NMR: 5.83 (m, 1H), 5.29 (dd, J=17.3 and 1.5Hz, 1H), 5.20 (d, d, J=10.6 and J=1.5Hz, 1H), 4.19 (m, 1H), 4.10 (m, 1H), 2.95 (dd, J=13.8 and 3.3 Hz, 1H), 2.73 (dd, J=13.8 and 9.3 Hz, 1H), 3.70 (b, 2H), 7.39 (dd, J=7.7 and 1.5 Hz, 1H), 7.12 (dt, J=7.3 and 1.5 Hz, 1H), 6.73 (dd, J=8.0 and 1.2 Hz, 1H) 6.70 (dt, J=7.5 and 1.3Hz, 1H) ppm. m/z: 226 (M+1, 30%), 225 (M, 42%), 124 (-S-$C_6H_4NH_2$, 40%), 138 (CH_2S-$C_6H_4NH_2$, 20%). HRMS: Calcd for $C_{11}H_{15}NO_2S$: 225.0824; Found: 225.0807.

3d: $[\alpha]_D^{25}$ +1.4 (c 1.08, $CHCl_3$)
IR (film) ν_{max}: 3350, 2950, 2900, 2495, 1640, 1479 cm^{-1}. ^1H-NMR: 5.93 (m, 1H), 5.39 (d, J=18 Hz, 1H), 5.30 (d, J=12 Hz, 1H), 4.30 (m, 1H), 3.76 (m, 1H), 2.20 (b, 3H). 2.75--2.65 (m, 6H), 1.92 (m, 2H) ppm. m/z: 210 (M+2H, 0.8%), 208 (M, 0.7%), 150 (M-CH_2CH_2SH+2H, 19.0%), 136 (M-$CH_2CH_2CH_2SH$+2H, 24.3%). HRMS: Calcd for $C_8H_{16}O_2S_2$: 208.0548; Found: 208.0541.

3e: $[\alpha]_D^{25}$ -3.4 (c 1.94, $CHCl_3$)
IR (film) ν_{max}: 3400, 3050, 2990, 2900, 1720, 1660, 1480, 1450, 790, 690 cm^{-1}. ^1H-NMR: 8.0 (d, J=9.0Hz, 2H), 7.60 (m, 1H), 7.50 (m, 2H), 6.04 (m, 1H), 5.48 (m, 1H), 5.37 (m, 1H), 4.28 (m, 1H), 3.90 (m, 1H), 3.34 (m, 2H), 2.60 (b, 2-H) ppm. m/z: 239(M+1, 0.20%), 181(9.21%), 138(-COPh+H, 2.49%), 105(-COPh, 100%), 77 (Ph, 38.34%). HRMS: fragment $CH_3CH(OH)CH_2SCOPh$ Calcd for $C_9H_9O_2S$: 181.0323; Found: 181.0371.

3f: $[\alpha]_D^{25}$ +2.1 (c 0.29, $CHCl_3$)
IR (film) ν_{max}: 3350, 3040, 2960, 2900, 1440 cm^{-1}. ^1H-NMR: 7.43 (m, 4H), 5.90 (m, 1H), 5.34 (d, J=17.5 Hz, 1H), 5.24 (d, J=12 Hz, 1H), 4.7 (m, 2H), 4.2 (m, 1H), 3.68 (m, 1H), 3.15 (m, 2H), 2.74 (b, 3H) ppm. m/z: 241 (M, 2.01%), 171 (15.58%), 137 (100%),

4a: $[\alpha]_D^{25}$ -37.3 (c 0.69, CH_2Cl_2)
IR (film) ν_{max}: 3400, 3040, 2950, 1485, 1400 cm^{-1}. ^1H-NMR: 7.40 (m, 1H), 7.15 (m, 1H), 6.65 (m, 2H), 5.49 (m, 1H), 5.20 (m, 2H), 4.25 (b, 3H), 3.0 (m, 1H), 2.9 (m, 1H), 2.75 (m, 1H) ppm. m/z: 207

(M^+, 21.27%), 208 (M+1, 9.59%), 163 (42.69%), 136 (100%). HRMS: Calcd for $C_{11}H_{13}NOS$: 207.0718; Found: 207.0721.

4b: $[\alpha]_D^{25}$ -6.2 (c 0.60, CH_2Cl_2)
IR (film) ν_{max}: 3350, 3020, 2950, 2900, 1465, 1400 cm^{-1}. ^1H-NMR: 7.45 (d, J=7.4 Hz, 1H), 7.15 (m, 2H), 7.00 (t, J=6.5 Hz, 1H), 5.55 (m, 1H), 5.45 (dd, J=17.0Hz and 9.8Hz, 1H), 5.30 (dd, J=11.0Hz and 3.1 Hz, 1H), 4.30 (m, 1H), 4.20 (m, 1H), 4.05 (b, 2H), 2.85 (dd, J=14.8 and 4.1Hz, 1H) ppm. m/z: 208 (M+1, 9.44%), 207 (M^+, 14.04%), 163 (45.11%), 136 (100%). HRMS: Calcd for $C_{11}H_{13}NOS$: 207.0718; Found: 207.0721.

Acknowledgment: We are grateful to the National Sciences Foundation of China for financial support.

REFERENCES:

[1] a. Hayashi, M.; Tamura, M.; Oguni, N. *SynLett.* **1992**, 663.
b. Jager, V.; Hummer, W. *Angew. Chem. Int. Ed Engl.* **1990**, 1171.
c. Chini, M.; Crotti, P.; Macchia, F. *Tetrahedron Lett.* **1990**, 31, 4661.
d. Hayashi, M.; Kohmura, K.; Oguni, N. *Synlett.* **1991**, 774.
e. Jager, V.; Schroter, D.; Koppenhoefer B. *Tetrahedron* **1991**. 47, 2195.
f. Canas, M.; Poch, M.; Verdaguer, X.; Moyano, A.; Pericas, M.A.; Riera, A. *Tetrahedron Lett.* **1991**. 32, 6931.
g. Chini, M.; Crotti, P.; Flippin L.A.; Macchia, F.; *J. Org. Chem.* **1991**, 56, 7043.
h. Ader, U.; Schneider, M.P. *Tetrahedron: Asymmetry* **1992**, 3, 205.
i. Chini, M.; Crotti, P.; Giovani, E.; Macchia, F.; Pineschi, M. *Synlett.* **1992**, 303.
[2] Lin, G.-Q.; Zeng, C.-M. *Chinese J. Chem.* **1991**, 9(4), 381.
[3] Schreiber, L.S.; Schreiber, T.S.; Smith, O. B. *J. Am. Chem. Soc.* **1987**, 109, 1526.