Pergamon

Tetrahedron: *Asymmetry* 9 (1998) 1843–1846

TETRAHEDRON: *ASYMMETRY*

A convenient resolution of long-chain alkyl epoxides with Jacobsen's salen(Co)III(OAc) catalysts †

Prashant S. Savle, Marika J. Lamoreaux,‡ John F. Berry‡ and Richard D. Gandour *

Department of Chemistry, Virginia Tech, Blacksburg, VA 24061-0212, USA

Received 17 April 1998; accepted 20 April 1998

Abstract

Non-racemic terminal long-chain alkyl epoxides are prepared from racemic epoxides and 1 mol% (*R,R*)- and (*S,S*)-salen(Co)III catalysts following a modified procedure for kinetic resolution. The ee's for all epoxides (C-10, C-12, C-14, C-16, C-18, C-20) exceed 95% and the chemical yields range from 85% to 95%.

Our interest[1] in designing mimetics of molecules that comprise biomembranes has led us to prepare non-racemic long-chain 2-alkyloxiranes. Many pioneering methods focus on converting long-chain alkenes[2–4] and long-chain alkyl chirons[5–10] into non-racemic epoxides; other methods use enzymatic resolution[11] to isolate non-racemic epoxides and precursors to epoxides. In our hands, such methods[12] have limitations with long-chain (>C-10) compounds. To date, large-scale syntheses of non-racemic long-chain 2-alkyloxiranes have required multiple steps. The recent, hydrolytic kinetic resolution of 2-hexyloxirane with a chiral salen(Co)III catalyst[13] has prompted us to evaluate this procedure for resolving long-chain 2-alkyloxiranes.

Non-racemic long-chain 2-alkyloxiranes are used in syntheses for natural products, *e.g.*, (*R*)-[14,15] and (*S*)-4-dodecanolide,[16] (*R*)- and (*S*)-5-dodecanolide,[17–19] (*R*)-[20] and (*S*)-8-hydroxydecanoic acid,[21] (2*R*,2*S*′)-1-*O*-(2′-hydroxyhexadecyl)glycerol,[22] and 6-alkyl-δ-lactones,[23] and non-natural products, *e.g.*, chiral stationary phase,[24] liquid crystals,[25] chirons,[26,27] and chiral dopants.[28] Because of this usage, we report herein the success of Jacobsens's chiral salen(Co)III catalysts in resolving six even-numbered homologues. With 2-octyl-, 2-decyl-, 2-dodecyl-, 2-tetradecyl-, 2-hexadecyl-, and 2-octadecyloxirane,[29] we find >95% ee for both enantiomers and excellent chemical yields (Table 1). We have not fully optimized these resolutions, but we present these results to inform the chemical community of a convenient resolution of these compounds (Scheme 1).

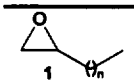
* Corresponding author. E-mail: gandour@vt.edu

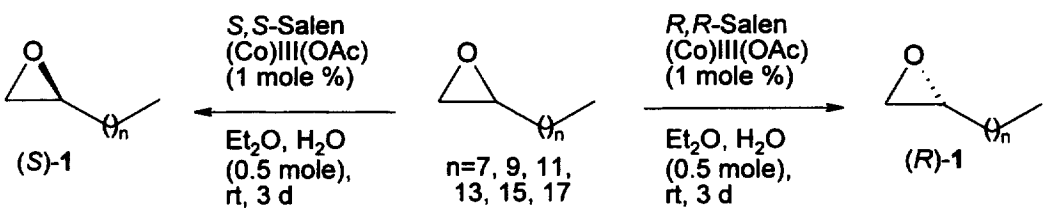
† Keywords: asymmetric reactions; epoxides; resolution; enantiomeric purity.

‡ Undergraduate research participant.

0957-4166/98/$19.00
PII: S0957-4166(98)00175-X

Table 1
Comparison of chiroptical properties

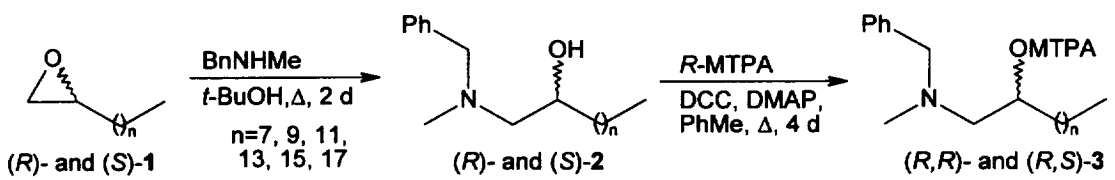
	Yield	Enantiomer	Enatiomeric excess.	[α], c g/dL $CHCl_3$ Obsv.	Solvent: [α], c g/dL
n=7	86%	R	>95%	+8.29 , 1.35	Et_2O: +15.0 ,0.98;[14] +14.2 , 1.02;[15] +14.6 .[36] $CHCl_3$: +7.4 , 1.0;[23] +9 .[5]
n=7	88%	S	>95%	-8.12 , 1.54	Et_2O: -14.7 , 1.44 ;[16] -13.9 , 1.2;[6] -12.9 , 1.07;[21] -14.1 , 1.11;[15] -14.5 , 0.47.[33] $CHCl_3$: -8.1 , 1.0;[23] -9.2 .[5]
n=9	90%	R	>95%	+6.92 , 1.04	No data found.
n=9	95%	S	>95%	-6.55 , 1.10	No data found.
n=11	94%	R	>95%	+4.31, 1.42	No data found.
n=11	91%	S	>95%	-4.47, 1.34	No data found.
n=13	85%	R	>95%	+4.84 , 2.8	Hexanes: +10.2 , 1.76;[37] +9.64, 3.71.[2]
n=13	87%	S	>95%	-4.71 , 2.7	$CHCl_3$: -4.49 , 2.[22]
n=15	88%	R	>95%	+4.28 , 1.09	No data found.
n=15	89%	S	>95%	-4.31 , 2.57	No data found.
n=17	90%	R	>95%	+2.99, 1.87	No data found.
n=17	88%	S	>95%	-2.89, 1.91	No data found.



Scheme 1.

To decrease reaction times, we slightly modified the reported[13] procedure by increasing the amount of catalyst[30] from 0.2 to 1.0 mol% and using ethyl ether[31] as a solvent. With 2.0 mol% catalyst, we detected the formation of alkene, which likely resulted from (Co)II-catalyzed deoxygenation of the epoxide.[32] We recovered the non-racemic epoxide and isolated the non-racemic diol in certain cases.[33] This procedure gave modest % ee's, however, in an attempted resolution of 2-eicosyloxirane (C-22 epoxide).

We determined the % ee of the Mosher's ester of **2**, which formed in the reaction of (*R*)- and (*S*)-**1** with *N*-benzylmethylamine (Scheme 2). We used this amine because it: (a) favors attack on terminal epoxy carbon, (b) imparts UV activity in the products, and (c) produces a norbenzalkonium spermicidal[34] analogue. In all cases, signals in ^1H and ^{19}F NMR spectra for the opposite enantiomer were absent.[35]



Scheme 2.

In summary, the kinetic resolution of long-chain 2-alkyloxiranes proceeds smoothly with Jacobsen's salen(Co)III catalysts to give excellent chemical yields and high % ee's. Many groups will find these chirons valuable in the synthesis of natural products, biomimetic molecules, chiral lipids, and surfactants.

Acknowledgements

We thank Dr. John Schwab for suggesting this procedure and Professor Eric N. Jacobsen and Mr. Scott E. Schaus of Harvard University for helpful discussions. We also thank Atochem of North America for their generous gift of C-10 to C-18 epoxides.

References

1. Hubieki, M. P.; Gandour, R. D.; Ashendel, C. L. *J. Org. Chem.* **1996**, *61*, 9379–9384.
2. Ohta, H.; Tetsukawa, H. *J. Chem. Soc., Chem. Commun.* **1978**, 849–850.
3. Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974–5976.
4. Zhang W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1991**, *112*, 2801–2803.
5. Solladié, G.; Demailly, G.; Greck, C. *Tetrahedron Lett.* **1985**, *26*, 435–438.
6. Oppolzer, W.; Dudfield, P. *Tetrahedron Lett.* **1985**, *26*, 5037–5040.
7. Pirkle, W. H.; Rinaldi, P. L. *J. Org. Chem.* **1978**, *43*, 3803–3807.
8. Chen, C.-S.; Liu, Y.-C. *Tetrahedron Lett.* **1989**, *30*, 7165–7168.
9. Eisenberg, C.; Knochel, P. *J. Org. Chem.* **1994**, *59*, 3760–3761.
10. Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483–2547.
11. Archeals, A.; Furstoss, R. *Annu. Rev. Microbiol.* **1997**, *51*, 491–525.
12. In our hands, the following reactions produced moderate to poor results: Sharpless asymmetric epoxidation and asymmetric dihydroxylation of 1-heptadecene (ee<80%); lipase PS-30 catalyzed acetylation of 1-bromo-2-hydroxyhexa- and octadecane (ee<60%); chiral reduction of 1-bromooctadecan-2-one with DIP-Cl (ee<20%). Attachment of a long chain to an enantiopure glycerol equivalent *via* nucleophilic displacement gave no or low yield of the desired products. The literature contains many examples of Wittig homologation of glyceraldehyde derived from D-mannitol and L-ascorbic acid to introduce a long chain.
13. Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science*, **1997**, *277*, 936–938.
14. Kakeya, H.; Sakai, N.; Sugai, T.; Ohta, H. *Agric. Biol. Chem.* **1991**, *55*, 1877–1881.
15. Sugai, T.; Mori, K. *Agric. Biol. Chem.* **1984**, *48*, 2497–2500.
16. Chattopadhyay, S.; Mamdapur, V. R.; Chadha, M. S. *Tetrahedron* **1990**, *46*, 3667–3672.
17. Coke, J. L.; Richon, A. B. *J. Org. Chem.* **1976**, *41*, 3516–3517.
18. Mori, K.; Otsuka, T. *Tetrahedron* **1985**, *41*, 547–551.
19. Chattopadhyay, S.; Mamdapur, V. R.; Chadha, M. S. *Bull. Soc. Chim. Fr.* **1990**, 108–111.
20. Sugai, T.; Mori, K. *Agric. Biol. Chem.* **1984**, *48*, 2155–2156.
21. Masaoka, Y.; Sakakibara, M.; Mori, K. *Agric. Biol. Chem.* **1982**, *46*, 2319–2324.
22. Baskaran, S.; Baig, M. H. A.; Banerjee, S.; Baskaran, C.; Bhanu, K.; Deshpande, S. P.; Trivedi, K. T. *Tetrahedron* **1996**, *52*, 6437–6452.
23. Haase, B.; Schneider, M. P. *Tetrahedron: Asymmetry* **1993**, *4*, 1017–1026.
24. Martens, J.; Lübben, S. *Tetrahedron* **1990**, *46*, 1231–1234.
25. Nohira, H.; Nakamura, S.; Kamei, M. *Mol. Cryst. Liq. Cryst.* **1990**, *180*, 379–388.
26. Takaki, K.; Tanaka, S.; Beppu, F.; Tsubaki, Y.; Fujiwara, Y. *Chem. Lett.* **1990**, 1427–1430.
27. Toshimitsu, A.; Hirosawa, C.; Tanimoto, S. *Tetrahedron Lett.* **1991**, *32*, 4317–4320.
28. Kusumoto, T.; Sato, K.; Hiyama, T.; Takehara, S.; Ito, K. *Chem. Lett.* **1995**, 537–538.
29. 2-Octyl-, 2-decyl-, 2-dodecyl-, 2-tetradecyl-, and 2-hexadecyloxiranes, obtained from Atochem North America, Inc., Philadelphia, PA 19102, USA, were used as received. As the commercial product is a blend of C-20, C-22 and C-24 epoxides, 2-octadecyloxirane was prepared in $CHCl_3$ by oxidation of eicosene with 3-chloroperoxybenzoic acid in 87% yield (Muzart, J.; Riahi, A. *J. Organomet. Chem.* **1992**, *433*, 323–336).
30. Catalysts (Aldrich Chemical Co. catalogue numbers for *R,R*-: 47,459-2 and for *S,S*-: 47,460-6) were used as received.

31. A typical procedure was: To a mixture of (*R,R*)- or (*S,S*)-salen(Co)II (0.17 mmol) in toluene (1 mL), acetic acid (0.34 mmol) was added and the mixture was stirred, open, in air for 1 h. The solvent was removed and the dark brown residue was dried under a high vacuum. The residue was diluted with Et_2O (5 mL), the epoxide (17 mmol) was added, followed by water (8.5 mmol). The dark red–brown mixture was stirred for 3 days at rt. The reaction mixture was concentrated. 2-Octyl-, 2-decyl, (for both bp 80–85 EC/5 mmHg) and 2-dodecyloxiranes (bp 135–140 EC/3 mmHg) were distilled directly from the reaction mixture using Kugelrhor distillation (see Ref. 33). 2-Tetradecyl, 2-hexadecyl, and 2-octadecyloxirane were isolated by column chromatography. The column was eluted with hexanes (300 mL) and then with 5% EtOAc/hexanes (v/v) (300 mL), when epoxide eluted. The diol was eluted by 50% EtOAc/hexanes (v/v), crude yield <20%, contaminated with the catalyst. All epoxides gave satisfactory ^1H and ^{13}C NMR spectra. (*R*)- and (*S*)-2-Tetradecyl-, -2-hexadecyl-, and -2-octadecyloxiranes were isolated as low melting waxy solids, mp <36 EC.
32. Dowd, P; Kang, K. *J. Chem. Soc., Chem. Commun.* **1974**, 384–385.
33. The key to isolation of the diols is the volatility of the epoxide and diol. We have recovered both enantiomers of 1,2-tetradecanediol using the reported[13] procedure in >80% yields; we presume that the enantiomers of 1,2-decane- and -dodecanediol can also be isolated in this manner. The high-boiling 1,2-hexadecane, -octadecane, and -eicosanediols are contaminated with the catalyst after chromatography.[31]
34. Levin, R. J. *Pharmcol. Toxicol.* **1997**, 81, 219–225.
35. Key ^1H NMR (400 MHz) data for (*R,R*)-**3**: 2.19 (s, 3H, N–Me), 3.61 (q, J_{HF}=1.2 Hz, 3H, OMe), 5.35–5.42 (m, 1H, CHOMTPA), ^{19}F NMR (377 MHz) −72.21. Data for (*R,S*)-**3**: 2.15 (s, 3H, N–Me), 3.54 (q, J_{HF}=1.2 Hz, 3H, OMe), 5.27–5.34 (m, 1H, CHOMTPA), ^{19}F NMR −72.67.
36. Ohta, H.; Matsumoto, S.; Sugai, T. *Tetrahedron Lett.* **1990**, *31*, 2895–2898.
37. Jacoby, C.; Braekman, J.-C.; Daloze, D. *Tetrahedron* **1996**, *52*, 10473–10484.