Pergamon

Tetrahedron Letters, Vol. 35, No. 21, pp. 3469-3472, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

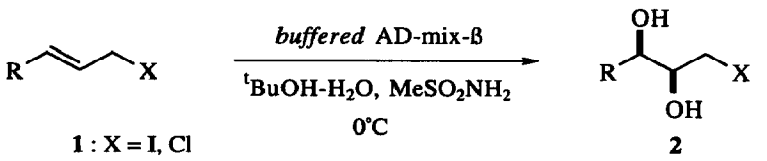
0040-4039(94)E0653-F

Asymmetric Dihydroxylation of Primary Allylic Halides and a Concise Synthesis of (–)-Diepoxybutane

Koen P. M. Vanhessche[1], Zhi-Min Wang and K. Barry Sharpless*
Department of Chemistry, The Scripps Research Institute, 10666 N. Torrey Pines Road, La Jolla, CA 92037, USA

Abstract: *The asymmetric dihydroxylation (AD) of primary allylic halides is described. Enantiomeric excesses range from 40 to 98%. Subsequent base treatment gives epoxy alcohols in high yields. This strategy is further illustrated by the synthesis of (–)-diepoxybutane, an important C_4-chiral building block.*

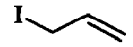
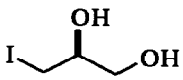
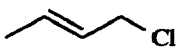
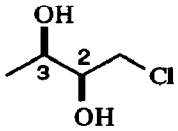
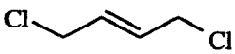
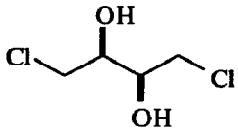
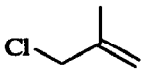
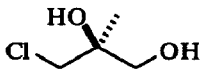
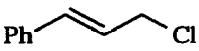
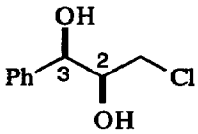
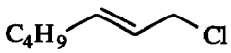
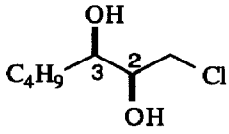
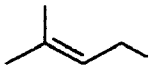
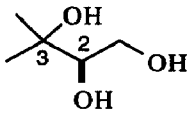
Aiming to expand the scope of the AD-reaction[2,3] we present here the results of its application to some readily available allylic halides (except for **1a**, all are chlorides). In order to suppress both the hydrolysis of the starting halide and the closure of the diol to the epoxy alcohol, the so-called *buffered* AD-mix (containing 3 eq. of $NaHCO_3$ in addition to the 3 eq. of K_2CO_3) was used in all entries.[4]



1 : X = I, Cl **2**

The AD of C_3-allylic substrates such as allyl chloride, bromide and tosylate has been previously reported.[5] Because of the moderate enantioselectivities (40-72% ee) that were obtained, we investigated the reaction of allyl iodide using $(DHQD)_2$-PHAL which afforded the iodo diol **2a** with 62% ee (70% yield). The enantioselectivity was increased to 70% ee with the recently developed pyrimidine ligand $(DHQD)_2$-PYR.[2b] Unfortunately, attempts to increase the optical purity by recrystallization failed.

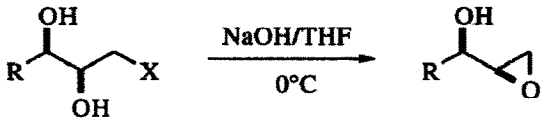
Table : Results for the AD of primary allylic halides[6]

entry	olefin	diol[a,b]	% ee[c]	yield	abs. conf.[d]
a			70	70%	2S
b			95	75%	2S,3R
c			94	88%	2S,3S
d			40	70%	2S[e]
e			98	80%	2S,3R
f			94	89%	2S,3R
g			12	50%	2R[e]

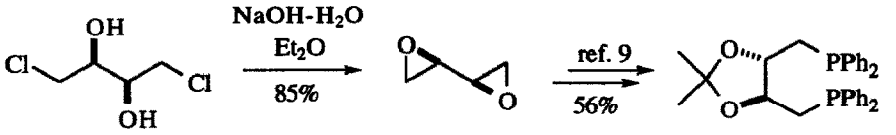
a) No methanesulfonamide was added for entries **1a** and **1d**. b) Except for **2g**, due to hydrolysis of the chloride prior to AD-reaction. c) Enantiomeric excesses were determined by HPLC analysis of the diol **2a**, the 1-mono-MTPA-ester of **2d**, the 1,2-bis-MTPA-ester of **2g** and the 2,3-bis-benzoate of **2f** on a Chiralcel® OD-H column (Daicel Chemical Industries, LTD). The enantiomeric excess of diol **2e** was determined on a Chiralcel® OB column (D.C.I., LTD.). Enantiomeric excesses of **2c** and **2d** were determined by GLC analysis of the mono-MTPA-ester of the corresponding epoxyalcohols **3c** and **3d** on a DB-5 column (J&W Scientific). d) The absolute configuration of **2c** was determined by its transformation to (–)-diepoxybutane (**4**) and comparison with the known (+)-**4**.[7] For the other diols, the absolute configurations are assigned according to the AD face-selection rule.[2a] e) The low ee renders the configurational assignment (based in this case on the AD face-selection rule) highly uncertain.

All *trans*-disubstituted olefins gave ee values greater than 94%, whereas the yields range from 80 to 90%. The ee for **2c** is readily increased from 94% to >98% upon recrystallization from toluene. On the other hand, 3-chloro-2-methylpropene (**1d**) gave only 40% ee whereas 1-chloro-3-methyl-2-butene (**1g**) hydrolyzed rapidly, giving rise to a mixture of the corresponding isomeric allylic alcohols, prenyl alcohol and 3-methyl-1-buten-3-ol, prior to the AD-reaction. According to the AD-mnemonic[2a], these two allylic alcohols give opposite face-selectivities, accounting for the very low ee observed for triol **2g**.

Treatment of the chlorodiol **2** with pulverized sodium hydroxide (2 eq.) in THF at 0°C gives gives the corresponding epoxy alcohols **3** in 80-90% yield.



2 : X = Cl **3**



2c **4** **(+)-DIOP**

(S,S)-Dichlorodiol **2c** (>98% ee), pulverized sodium hydroxide and methanol (1 eq.) were stirred for 1 hour to produce (R,R)-(–)-diepoxybutane (**4**) {$[\alpha]_D = -24°$ (c 4, CCl_4)} in 85% isolated yield. This bisepoxide[8] is an important C_4-chiral building block, e.g. serving as a key intermediate in the synthesis of DIOP[9] and various modifications thereof.[10] The described two-step procedure provides a fast and facile route to **4** compared to the previously reported 5-step synthesis starting from tartaric acid.[7, 11]

In summary, the catalytic asymmetric dihydroxylation of primary allylic halides under buffered conditions followed by base-mediated epoxide formation gives easy access to *threo*-1,2-epoxy-3-ols.[12] High overall enantioselectivities are obtained with *trans*-disubstituted olefins. Applying this protocol, a very short synthesis of enantiomerically pure (–)-diepoxybutane was achieved in high overall yield.

Acknowledgment: K. P. M. V. thanks the Belgian National Fund for Scientific Research and the NATO for a postdoctoral fellowship. Financial support was provided by the National Institutes of Health (GM-28384).

References

1. Postdoctoral Researcher of the Belgian National Fund for Scientific Research.
2. a) Sharpless, K.B.; Amberg, W.; Bennani, Y.L.; Crispino, G.A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.*, **1992**, *57*, 2768.
   b) Crispino, G.A.; Jeong, K.-S.; Kolb, H.C.; Wang, Z.-M.; Xu, D.; Sharpless, K.B. *J. Org. Chem.*, **1993**, *58*, 3785.
3. Johnson, R.A. and Sharpless, K.B. In *Catalytic Asymmetric Synthesis;* Ojima, I., Ed.; VCH: New York, 1993; pp 227-272.
4. With more lipophilic substrates, buffering is not required.
5. Kolb, H.C.; Bennani, Y.L.; Sharpless, K.B. *Tetrahedron: Asymmetry*, **1993**, *4*, 133.
6. The general procedure: To a well-stirred solution of $(DHQD)_2$-PHAL (8 mg, 1 mol%), $K_2OsO_2(OH)_4$ (1.8 mg, 0.5 mol%), $K_3Fe(CN)_6$ (988 mg, 3 mmol), K_2CO_3 (415 mg, 3 mmol), $NaHCO_3$ (252 mg, 3 mmol) and $CH_3SO_2NH_2$ (95 mg, 1 mmol) in 1:1 *tert*-butyl alcohol-water (10 ml) at 0°C, the appropriate allylic halide (1 mmol) was added. After the reaction was finished (TLC), 1.0 g of $Na_2S_2O_5$ was added and stirring was continued for 30 min. The layers were separated and the aqueous layer was extracted with ethyl acetate (30 mL). The combined organic layers were washed with a 1N KOH, 5% aq. HCl and brine, and then dried over $MgSO_4$ and concentrated. The crude halodiol was purified by flash chromatography on silica gel.
   Physical data for some selected compounds : **2a** : $[\alpha]_D$ +5.6° (*c* 2.1, CH_2Cl_2), ^{1}H-NMR (250 MHz, $CDCl_3$), δ: 3.78 (1H, d, J=11.9 Hz), 3.78 (1H, ddd, J=7.1, 6.3, 4.9, Hz), 3.67 (1H, dd, J=11.9, 7.1 Hz), 3.33 (1H, dd, J=10.3, 4.9 Hz), 3.25 (1H, dd, J=10.3, 6.3 Hz), 2.36 (2H, br. s.) ppm, ^{13}C-NMR (60 MHz, $CDCl_3$), δ : 71.55, 65.30, 8.49 ppm. **2c** : m.p. 68-69°C, $[\alpha]_D$ = −11.7° (*c* 1.5, CH_2Cl_2), ^{1}H-NMR, δ : 3.96 (2H, dd, J=6.6, 5.3 Hz), 3.70 (2H, dd, J=11.3, 5.3 Hz), 3.63 (2H, dd, J=11.3, 6.6 Hz), 2.91 (2H, br.s.) ppm, ^{13}C-NMR, δ : 71.09, 45.79 ppm. **2e** : $[\alpha]_D$ −3.0° (*c* 1.0, EtOH), ^{1}H-NMR, δ : 7.36 (5H, m), 4.72 (1H, dd, J=6.7, 3.2 Hz), 3.89 (1H, m), 3.56 (1H, dd, J=11.5, 3.92 Hz), 3.38 (1H, dd, J=11.5, 5.7 Hz), 2.97 (1H, d, J=3.2 Hz), 2.95 (1H, d, J=4.9 Hz) ppm, ^{13}C-NMR, δ : 139.74, 128.70, 128.43, 126.59, 75.40, 74.69, 46.08 ppm. **2f** : $[\alpha]_D$ +11.0° (*c* 2.6, THF), ^{1}H-NMR, δ : 3.68 (4H, m), 2.57 (1H, m), 2.16 (1H, m), 1.52 (2H, m), 1.35 (4H, m), 0.90 (3H, m) ppm, ^{13}C-NMR, δ : 73.74, 71.53, 46.65, 33.24, 27.66, 22.56, 13.95 ppm. **3f** : $[\alpha]_D$ −3.2° (*c* 1.3, CH_2Cl_2), ^{1}H-NMR, δ : 3.43 (1H, ddd, J=5.6, 5.6, 5.0 Hz), 2.98 (1H, ddd, J=5.0, 4.6, 2.8 Hz), 2.82 (1H, dd, J=4.6, 4.6 Hz), 2.72 (1H, dd, J=4.6, 2.8 Hz), 2.39 (1H, br. s.), 1.60 (2H, m), 1.40 (4H, m), 0.88 (3H, m), ^{13}C-NMR, δ: 71.77, 55.50, 45.16, 33.87, 27.36, 22.57, 13.87 ppm.
7. Seebach, D.; Kalinowski, H.; Bastani, B.; Crass, G.; Daum, H.; Dörr, H.; Dupreez, N. P.; Ehrig, V.; Langer, W.; Nüssler, C.; Oei, H.; Schmidt, M., *Helv. Chim. Acta*, **1977**, *60*, 301.
8. Caution! Diepoxybutane is extremely mutagenic.
9. Zhang, S.; Zhang, S.; Feng, R. *Tetrahedron: Asymmetry*, **1991**, *2*, 173.
10. a) Börner, A.; Ward, J.; Kortus, K.; Kagan, H.B. *Tetrahedron: Asymmetry*, **1993**, *4*, 2219.
    b) Fields, L. B.; Jacobsen, E. N. *Tetrahedron: Asymmetry*, **1993**, *4*, 2229.
11. Mash, E.A.; Nelson, K.A.; Van Deusen, S.; Hemperly, S.B. *Org. Synth.*, **1988**, *68*, 92.
12. The titanium-catalyzed AE process only gives direct access to *erythro*-1,2-epoxy-3-ols.

(*Received in USA* 14 *January* 1994; *revised* 18 *March* 1994; *accepted* 25 *March* 1994)