

by substituting triflic acid for tetrafluoroboric acid and the both iodonium compounds served for the purpose.

As can be seen in Table 1, excellent yields of diphenylsulfonium salts were obtained from readily available starting materials. The mechanism of the present reaction may only be tentative, but it is tempting to speculate that the course of reaction was governed by oxidative addition–reductive elimination chemistry. Further efforts for the utility of the ylides generated from the above sulfonium salts are being planned.

References

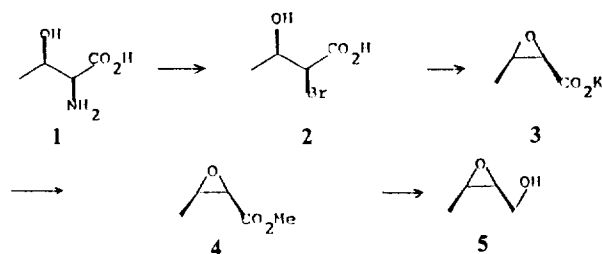
- (1) Undergraduate Research Participant, 1982–83, Present Address; Department of Chemistry, Korea Advanced Institute of Science and Technology, Seoul, Korea.
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Preparation of *cis*-(2S, 3R)-Epoxy-1-butanol; The Unexpected Regiocontrol

Jahyo Kang,¹ Min Park, Hyun Tae Shin and Jae Kook Kim

Department of Chemistry, Sogang University, Seoul 121, Korea (Received July 15, 1985)

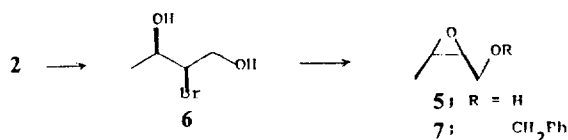
For on-going projects in these laboratories, large quantities optically active (2S, 3R)-epoxy-1-butanol was required, the preparation of which seemed to be quite straightforward in view of the well established asymmetric epoxidation by Sharpless.¹ Unfortunately, even with modified work-up available for water-soluble epoxy alcohols,² the chemical yield in large-scale reactions was not so high to be synthetically useful. Consequently, recourse was made to utilize other chiral C-4 fragments. In this regard L-threonine seemed to be appropriate. In fact, it was transformed to the epoxy alcohol by Djerassi *et al.* following the route shown below.³



Thus, L-threonine was diazotized (1.5 equiv NaNO₂ in 2.5 M H₂SO₄) in the presence of 3.5 equiv potassium bromide (1.5 hr at 0°C, 2 hr at rt) to give a 86% yield of bromo acid 2,⁴ which was treated with aqueous KOH to effect cyclization and concurrent formation of the salt 3. Water was stripped off to a white solid of the salt, which was subsequently methylated with a large excess of methyl iodide in DMF. The resulting methyl ester 4 was reduced with sodium borohydride in a 50% aqueous methanol to furnish the *cis* epoxy alcohol in fair yields.³ Indeed, the synthesis worked moderately well with preliminary

small scales, but attempted large-scale reactions encountered three major difficulties: Evaporative drying of the salt 3 from large amount of water was tedious, moreover the methyl ester 4 obtained was often contaminated with its C-2 epimer (NMR(δ) of 4, 1.34 (d, J=7, 3H), 3.75 (S, 3H); of the *trans* isomer of 4, 1.20 (d, J=7, 3H), 3.68 (S, 3H), which would speak for isomerization during salt formation and/or methylation, and finally the reduction of the ester with NaBH₄ was not entirely chemoselective, thus necessitating a premature work-up and chromatography before all the starting ester was consumed.

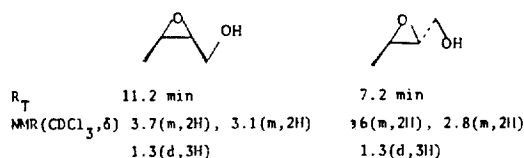
Consequently, the bromo acid 2 was reduced with borane methyl sulfide (2.5 equiv) in THF at rt for 24 hr to give, after aqueous work-up, easily manageable pure diol 6 in 79% yield. The idea here was that after some form of selective protection of the primary OH in 6 ring closure and subsequent deprotection would furnish the *cis*-epoxy alcohol 5. However, direct treatment of the bromo diol 6 with anhydrous K₂CO₃ in methanol (0°C for 1 hr and rt for 7 hr) surprisingly afforded a 65% yield of *cis*-(2S, 3R)-epoxy-1-butanol 5 bp 78–84°C/20 mm (lit. 55–57°C/5 mm).³ Although expensive, 1.5 equiv DBU in THF (0°C for 0.5 hr, rt for 18 hr) was more effective in terms of purity and yield (80%).



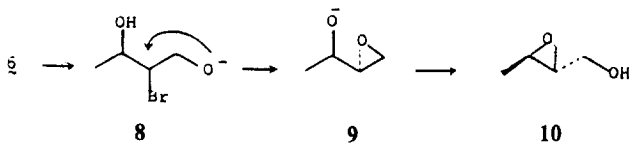
Optical rotation of the alcohol 5 was erratic with variation of water contents in the sample but that of the corresponding ben-

zyl ether **7** (NaH, PhCH₂Br, Cat. *n*-Bu₄NI)⁵ (+16.8° (c=1.0, CHCl₃)) indicated that the alcohol **5** was at least 95% enantiomerically pure (lit. +17.7° (c 1.0, CHCl₃)).⁶

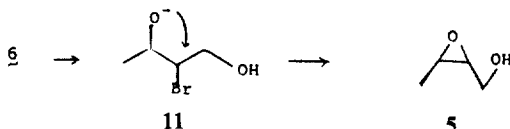
The chemical identity of the alcohol **5** was further confirmed by gas chromatography (a 6 ft. × 0.125 in. 10% Carbowax 20 M at 125° isothermal), which showed it to be at least 99.1% pure (Retention times for *cis* epoxy alcohol 11.2 min; for *trans* epoxy alcohol 7.2 min): The individual racemic stereoisomeric 2,3-epoxy-1-butanols were prepared independently from the corresponding allylic alcohols and mCPBA.



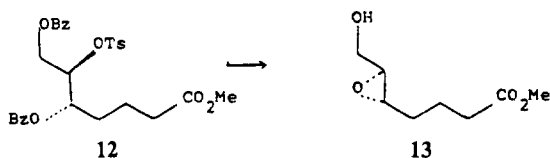
The mechanism of this reaction is highly intriguing. Initial alkoxide generation at C-1 (*ie.* **8**) and ring closure followed by Payne rearrangement^{1,7} would generate *trans* alcohol **10** as a result of double inversion of configuration at C-2. But that was not the case.



Alternatively, for some unknown reasons it was only the alkoxide at C-1 that was capable of undergoing direct epoxide-forming reaction (*ie.* single inversion of configuration).



To the best of our knowledge, the closest precedent could be found in the SRS synthesis by Corey.⁸ Thus, even identically substituted 1,3-benzoate **12** undergoes exclusive oxirane formation from C-3 alkoxide attack.



In summary, a simple method for *cis*-(2*S*, 3*R*)-epoxy-1-butanol was developed (3 steps, 54%), which is also suitable for large-scale preparation (~1 mole).

(2*R*)-Bromo-(3*R*)-butane-1,3-diol (**6**). To a solution of 31.5g (172 mmol) of the acid (**2**)⁴ in dry THF (570 ml) was added dropwise 40.81 ml (430 mmol) of 10M solution of BMS in THF at 0°C. The reaction mixture was allowed to warm up to rt and stirred for a day at room temperature. After complete reaction (TLC), the reaction mixture was cooled to 0°C and 40 ml of water was added. The aqueous layer was extracted with ether (50 ml × 5), and the combined extracts were dried over anhydrous MgSO₄. Evaporation of the solvent on a rotary evaporator afforded 22.7g (79% yield) of viscous liquid (**6**) which was almost pure.

TLC R_f 0.39 (5% MeOH in CH₂Cl₂)

NMR (CDCl₃; Si (CH₃)₄ ref.) 4.2-3.9 (m, 3H), 1.3 (d, 3H)

(2*S*, 3*R*)-Epoxybutanol-1 (**5**). To a solution of the diol (**6**; 24g, 143 mmol) in MeOH (230 ml) was added 39.5g (286 mmol) of K₂CO₃ at 0°C. The reaction mixture was stirred for 1 hr at 0°C and for 7 hrs at rt. The mixture was cooled to 0°C and precipitated K₂CO₃ was removed by filtration with ether washing. The filtrate was evaporated until 1/3 of the volume remained and then 10 ml of H₂O was added. The aqueous layer was extracted with ether (30 ml × 10) and dried over anhydrous K₂CO₃. The ethereal solution was concentrated on rotary evaporator, and the residue was distilled to give 8.15g (65% yield) of the epoxy alcohol (**5**) at reduced pressure, bp 78-84°C/20 mmHg (lit. 55-57°C/5 mmHg).³

TLC R_f 0.33 (5% MeOH in CH₂Cl₂)

NMR (CDCl₃; Si (CH₃)₄ ref.) 3.7 (m, 2H), 3.1 (m, 2H), 1.3 (d, 3H).

To determine the ratio of *cis* and *trans*, the authentic samples were prepared. The *cis*-epoxy alcohol was prepared from *cis*-buten-1-ol by oxidation with mCPBA. Also the *trans*-epoxy alcohol was prepared from *trans*-2-buten-1-ol derived from 2-butyne-1-ol by reduction with LAH. The *cis/trans* ratio was determined by GC analysis (10% Carbowax 20M column, 6ft × 0.125 inch, 120°C const.) The response of *cis*- and *trans*-epoxy alcohol was identical, and the retention times of *cis* and *trans* were *cis* = 11.2 min, *trans* = 7.2 min, sample = 11.2 min. So the ratio was *cis/trans* = 127; *cis* = 99.2%, *trans* = 0.8%. Also the *cis*- and *trans*-epoxyalcohol differed on NMR data, and our sample was identical with the authentic *cis*-epoxy alcohol and differed from the *trans*-epoxy alcohol. The NMR data of authentic samples were listed in the text.

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References and Notes

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