Tetrahedron Letters,Vol.27,No.41,pp 4987-4990,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

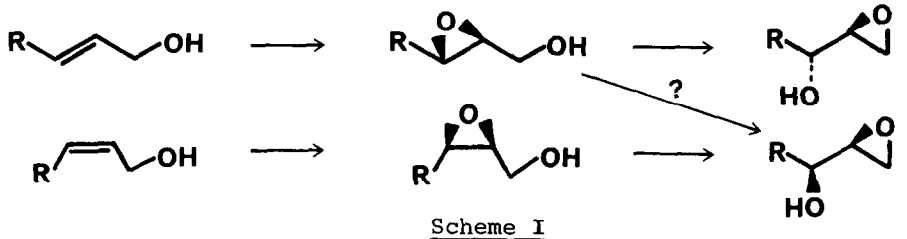
GENERAL METHOD TO TRANSFORM CHIRAL 2,3-EPOXYALCOHOLS INTO ERYTHRO OR THREO 1,2-EPOXYALCOHOLS WITH TOTAL STEREOCHEMICAL CONTROL

J.M. Palazón, B. Añorbe and V.S. Martín*
Instituto Universitario de Química Orgánica
Universidad de La Laguna, Tenerife, Spain

Abstract: The isomerization of chiral 2,3-epoxyalcohols from E-allylic alcohols to chiral erythro or threo 1,2-epoxyalcohols has been accomplished with good yields, perfect stereochemical control and a very high grade of generality.

Epoxides are very well known intermediates in organic synthesis mainly because of their special reactivity under a wide range of reaction conditions. Special attention has been focussed, in the last few years, on this functional group due to the possibility of building chiral 2,3-epoxyalcohols from suitable allylic alcohols, in most cases with a very high grade of enantioselectivity[1].

In our current syntheses on marine natural products we were very interested in chiral 1,2-epoxyalcohols with either erythro or threo stereochemistry as precursors of vicinal groups with an absolute configuration control. This prompted us to attempt the isomerization of 2,3 to 1,2-epoxyalcohols (Scheme I)



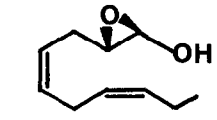
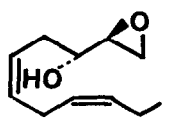
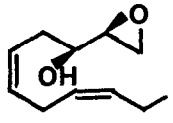
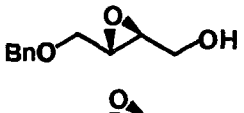
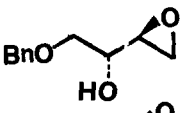
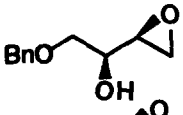
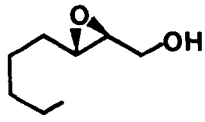
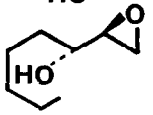
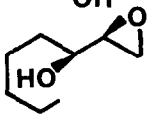
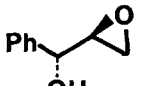
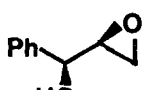
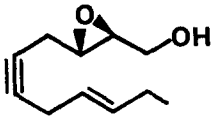
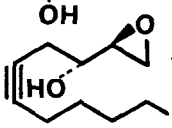
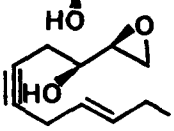
Scheme I

Since Z-allylic alcohols are not ideal substrates for enantioselective epoxidation[2], it seemed reasonable to try to use epoxyalcohols from E-olefins as a source of either erythro or threo 1,2-epoxyalcohols[3]. In this paper we report an easy and general method to achieve this isomerization with perfect stereochemical control, that nicely complements the one reported by Sharpless and co-workers using Payne's rearrangement and sulphide opening on epoxides with an alkoxy substituent at C-4[4].

The opening of 2,3-epoxyalcohols from E-olefins assisted by titanium (IV) iso-propoxide[5] and benzoic acid as nucleophile has proved to be general

in both regio- and stereo-selectivity (Scheme II). In the reported cases (Table I) the regioselectivity has been, at least, 100:1 (C-3 vs. C-2 attack) with virtually complete inversion at C-3[6]. The reaction mixture was tosylated with 1.1 equiv. of tosyl chloride, in pyridine, at 0°C, for 16 hrs. and treated with sodium hydride in dichloromethane, adding a catalytic amount of DMSO to give, after chromatographic purification, the 1,2-epoxybenzoates 3. The free 1,2-epoxyalcohols 4 were liberated with sodium methoxide generated in situ by adding an equivalent amount of methanol to a solution of 3 in THF containing sodium hydride[7]. An alternative way to cleave the benzoates, without isomerization to the 2,3-epoxyalcohols, is by using an equivalent amount of DIBAL and acidic hydrolysis. Other methods such as potassium carbonate in methanol, or sodium hydroxide treatment in THF gave substantial amounts of the isomerized products.

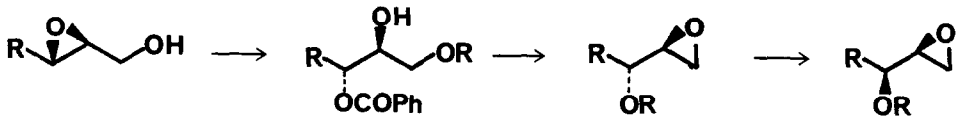
Table I

Entry	Starting 2,3-EA[a,b]	$\lvert\alpha\rvert_D^{25}$[c]	Erythro 1,2-EA[b]	$\lvert\alpha\rvert_D^{25}$[c]	%[d]	Threo 1,2-EA[b]	$\lvert\alpha\rvert_D^{25}$[c]	%[d]
1		-16.8° (2.8)		-28.4° (2.46)	60		-11.7°[e] (2.63)	48
2		-19.9° (2.66)		-10.6° (2.46)	55		+12.2° (3.04)	47
3		-35.6° (2.35)		-22.8° (2.46)	62		+3.5° (2.68)	50
4		-10.7° (2.45)		-100.2° (2.31)	57		+7.6° (2.74)	52
5		-10.0° (2.28)		-28.6° (2.31)	50		+9.1° (1.81)	42

a) The 2,3-epoxyalcohols were synthesized using the E-allylic alcohol by the standard procedure of asymmetric epoxidation[1]; **b)** Optical purities were in all cases above 95% ee, except in entry 5 which was 88% ee, checked by NMR of the corresponding acetates using Eu(hfbc)$_3$ as chiral shift reagent and/or Mosher's esters; **c)** The reported optical rotations were measured at 25°C, in $CHCl_3$ at the concentration shown in parentheses in g/100 mL; **d)** Isolated yields from 2,3-epoxyalcohols; **e)** Optical rotation measured in ether (in $CHCl_3$ it is close to zero).

The isolation of 3 is critical to avoid loss of enantiomeric purity since the small amount of the C-2 opened product does not give any epoxide, but if the tosylated mixture is treated with sodium methoxide in THF, both the C-2 and C-3 products give the enantiomeric 1,2-epoxyalcohols (Scheme III).

Scheme II

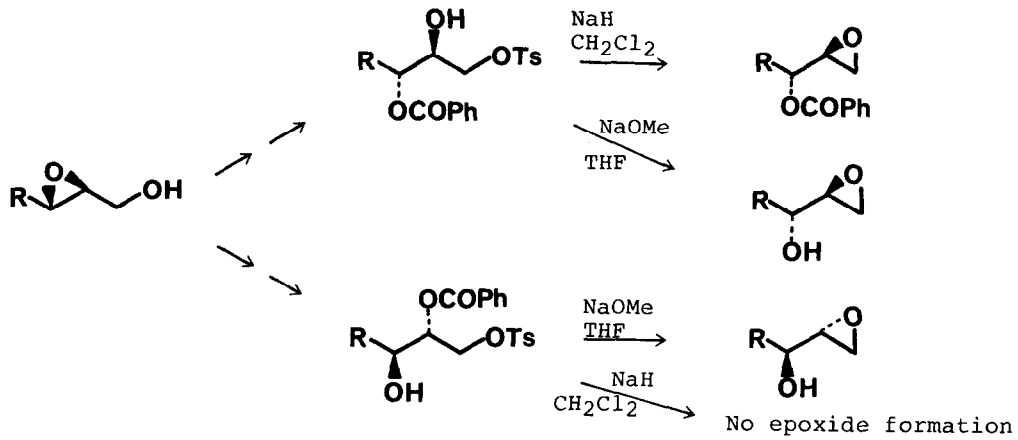


1, R=H
2, R=Ts

3, R=Bz
4, R=H

5, R=Bz
6, R=H

Scheme III



The threo 1,2-epoxyalcohols 6 were obtained from the erythro-products by epimerization of the alcoholic centre by the Mitsunobu procedure[8] using benzoic acid as nucleophile (Ph_3P, DEAD, PhCOOH, CH_2Cl_2, 0°C, 2 hrs.) and generation of the free epoxyalcohols was achieved by treatment with sodium methoxide generated in situ as described before.

It is very interesting to mention that the procedure is also useful in epoxyalcohols with an alkoxy substituent at C-4 (Entry 2) where Payne's rearrangement-sulphide procedure works cleanly[4].

The procedure does not work with epoxides from Z-allylic alcohols because the main product in the opening step is that corresponding to the elimination between C-3 and C-4[9]. This fact combined with the poor enantioselectivity in some Z-allylic alcohols[2] suggests the described epimerization as the

optimal solution to obtaining threo epoxyalcohols.

Under the mild conditions described a wider application of the asymmetric epoxidation in terms of generality, yield and enantioselectivity is achieved.

Acknowledgement: This research was supported by a grant from the CAICYT (MEC) of Spain, nº 3064-83. JMP and BAD thank the MEC for a FPI fellowship.

References and notes:

1) a) Katsuki,T.; Sharpless, K.B.; J. Am. Chem. Soc., 1980, 102, 5974.
b) Martín, V.S.; Woodard, S.S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K.B.; J. Am. Chem. Soc., 1981, 103, 6237.

3) Sharpless, K.B.; Behrens, C.H.; Katsuki, T.; Lee, A.W.M.; Martín, V.S.; Takatani, M.; Viti, S.M.; Walker, F.J.; Woodard, S.S.; Pure Appl. Chem., 1983, 55, 589.

3) A similar idea was used to synthesize erythro or threo diols. See: Lee, A.W.M.; Martín, V.S.; Masamune, M.; Sharpless, K.B.; Walker, F.J. J. Am. Chem. Soc., 1982, 104, 3515.

4) Behrens, C.H.; Ko, S.Y.; Sharpless, K.B.; Walker, F.J.; J. Org. Chem., 1985, 50, 5687.

5) Caron, M.; Sharpless, K.B.; J. Org. Chem., 1985, 50, 1557.

6) See experimental details in Ref. 5. In all cases the work-up was done by adding 15% tartaric acid aqueous solution, stirring until clear phases were reached followed by extraction with dichloromethane.

7) A clean work-up of this reaction require the addition of a few drops of acetic acid, at -20°C, to the reaction mixture in order to destroy the sodium hydride excess, before water is added. If this step is omitted a substantial degree of benzoate hidrolysis can occur.

8) Mitsunobu, O.; Synthesis, 1981, 1; Hungerbüler, E.; Seebach, D.; Wasmuth, D.; Angew. Chem., Int. Ed. Engl., 1979, 18, 958; Roush, W.R.; Brown, R.J.; DiMare, M.; J. Org. Chem., 1983, 48, 5083.

9) Morgans, D.J.; Sharpless, K.B.; Traynor, S.G.; J. Am. Chem. Soc., 1981, 103, 462.

(Received in UK 23 June 1986)