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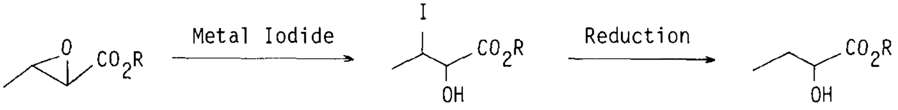
A HIGHLY STEREOSELECTIVE CONVERSION OF α,β-EPOXY ESTERS TO α-HYDROXY ESTERS. AN EFFICIENT ROUTE TO OPTICALLY ACTIVE α-HYDROXYESTERS[1)]

Kenji Otsubo, Junji Inanaga,* and Masaru Yamaguchi
Department of Chemistry, Kyushu University 33,
Hakozaki, Higashi-ku, Fukuoka 812, Japan

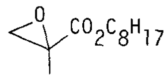
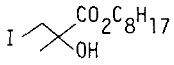
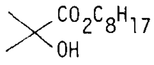
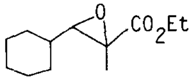
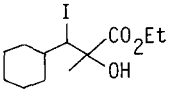
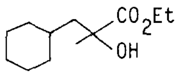
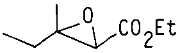
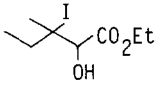
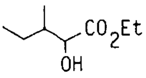
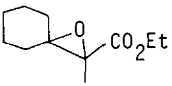
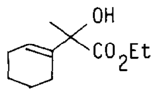
Summary: α,β-Epoxy esters were cleanly converted to α-hydroxy esters with retention of the configurations at the α-carbon atoms via MgI_2-promoted regioselective oxirane ring-opening followed by tributyltin hydride-reduction.

α-Hydroxy esters are frequently encountered in natural products and also serve as useful intermediates in organic synthesis. Although α,β-epoxy esters (**1**) seem to be good precursors for α-hydroxy esters (**3**), there have been few examples for the regioselective reduction of the oxirane ring to provide **3**. In this paper we wish to describe the two-step conversion of **1** to **3**, which includes regioselective ring-opening by metal iodide and subsequent reduction of the resulting iodohydrins (**2**).



1 **2** **3**

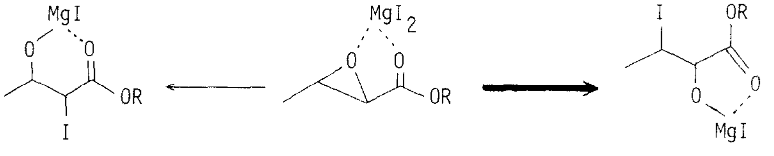
Table. Two-step Conversion of α,β-Epoxy Esters to α-Hydroxy Esters by Using MgI_2-Bu_3SnH Sequence

Epoxy ester	Iodohydrin[a)]	Ratio[b)] (α-OH : β-OH)	α-Hydroxy ester[c)]	Yield(%)[d)]
		200 : 1		95
		200 : 1		91
		200 : 1	 e)	77
	----- f)	-----	 f)	92

a) Obtained instantaneously by stirring with a MgI_2-Et_2O solution (1.6 mol dm^{-3}, 1.5 eq) at room temperature. b) Determined by ^1H NMR (400 MHz) analysis. c) Obtained by stirring with Bu_3SnH (1.1 eq) in hexane for 5 min. d) Isolated overall yield. e) erythro : threo ≈ 1 : 1. f) The corresponding iodohydrin was not detected, but the dehydroiodination product was isolated as a single product.

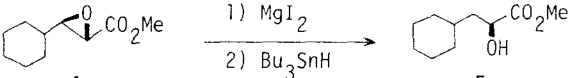
After a brief screening of metal iodides under various conditions,[2] an excellent selectivity of 200 : 1 was attained by using MgI_2 in ether,[3] affording the iodohydrin (**2**, R=Et) quantitatively. Tributyltin hydride reduction of **2** proceeded smoothly at room temperature to afford the desired α-hydroxy ester (**3**) in good yield. Thus, as shown in the Table, a variety of epoxides were cleanly converted to α-hydroxy esters regardless of the substitution pattern.

The highly regioselective C-O bond-cleavage observed here may be explained in terms of kinetic control, where the much favored five-membered chelate structure **A** of the product over the six-membered **B**, is reflected upon the transition state.[4]

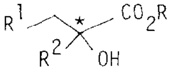


B **A**

As expected, an optically pure α,β-epoxy ester (**4**)[5] was converted to the α-hydroxy ester (**5**) with complete retention of the configuration at α-carbon atom.[6] Therefore, the present method with the combination of the Sharpless process[5] will provide an efficient route to optically active α-hydroxy esters, especially for the ones having tert-hydroxyl group on the asymmetric carbon, such as **6**, which has been difficult to access by the conventional methods.[7]



4 **5**



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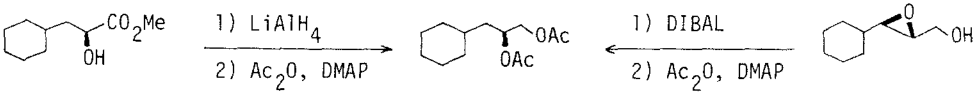
References and Notes

1) Presented at the 53rd National Meeting of the Chemical Society of Japan, Nagoya, Oct 1986.
2) A suspension of ZnI_2 in ether also gave satisfactory selectivity (150:1) but required longer reaction time (~1 day).
3) P.Coutrot, C.Legris, Synthesis, 118 (1975).
4) $Ti(O\text{-}\underline{i}\text{-}Pr)_4$-mediated oxirane ring-opening reaction of epoxy alcohols and epoxy acids has been discussed: M.Caron and K.B.Sharpless, J. Org. Chem., **50**, 1557 (1985); J.M.Chong and K.B.Sharpless, ibid., **50**, 1560 (1985).
5) Prepared from the corresponding allylic alcohol according to the Sharpless process: See J.M.Chong and K.B.Sharpless, Tetrahedron Lett., **26**, 4683 (1985).
6) According to the following scheme, the hydroxy ester (**5**) and the epoxy alcohol (**8**) were reduced and acetylated to give the corresponding diacetates (**7**) and their optical purities were determined by ^1H NMR (400 MHz) analyses with a chiral shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-d-camphorato]europium(III), by comparing with the dl-diacetate (**7**).



(>98% ee) (>98% ee)

5 **7** **8**

7) For example: See G.Solladié, "Asymmetric Synthesis," ed by J.D.Morrison, Academic Press, New York (1983), Vol 2, p 157..

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