

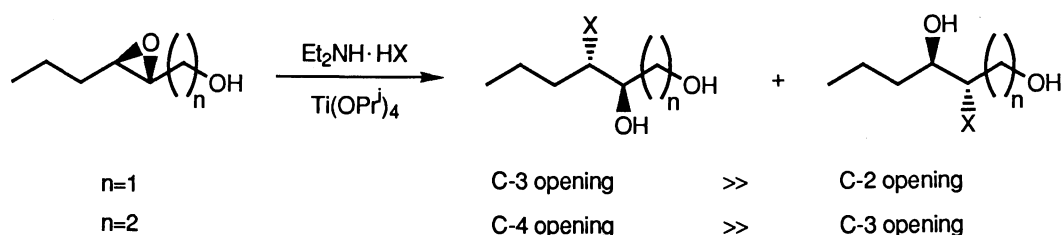
Solvent Dependency in Regioselective Ring Openings of 3,4- and 2,3-Epoxy Alcohols with Diethylamine Hydrohalides

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Titanium-mediated ring openings of 3,4-epoxy-1-ols at the 4-position with diethylamine hydrohalides proceeded efficiently in dichloromethane, while the requisite openings of 2,3-epoxy-1-ols at the 3-position in benzene.

Recently, we have reported that diethylamine hydrohalides are much more effective as sources of halide nucleophiles for titanium-mediated ring openings of 2,3-epoxy-1-ols at the 3-position.¹⁾ In the course of synthetic studies on halogenated marine natural products, we have extended our procedure to the system of 3,4-epoxy-1-ols and found that dichloromethane (CH₂Cl₂) is much more effective solvent for stereoselective opening at the 4-position. A general procedure is as follows: Ti(O-*i*-Pr)₄ (2.6 mmol) and diethylamine hydrohalide (5.2 mmol) were stirred in CH₂Cl₂ (6 ml) under argon at 20 °C for at least 30 min, until the solution became clear. A solution of 3,4-epoxy alcohol (1.7 mmol) in CH₂Cl₂ (4 ml) was added and the solution was stirred at 20 °C for 20 h or 36 h. The reaction was quenched with aq. tartaric acid solution and the mixture was diluted with ethyl acetate, washed with water, aq. NaHCO₃, and satd brine. The residue was acetylated to give a mixture of the diacetates, in which the ratio of C-4 to C-3 opening in a S_N-2 fashion was estimated by ¹H NMR. The results were summarized in Table 1. The data are in contrast to the cases of 2,3-epoxy-1-ols. It is to be



noted that, while in the latter cases the stereoselectivity in the ring openings at the 3-position were more preferential in benzene, CH₂Cl₂ was more efficient for the C-4 openings in the former cases. The detailed reason of these solvent dependencies has not yet been clarified. These new reaction conditions were efficiently applied to the preparation of the more complicated halo-diols as depicted below.

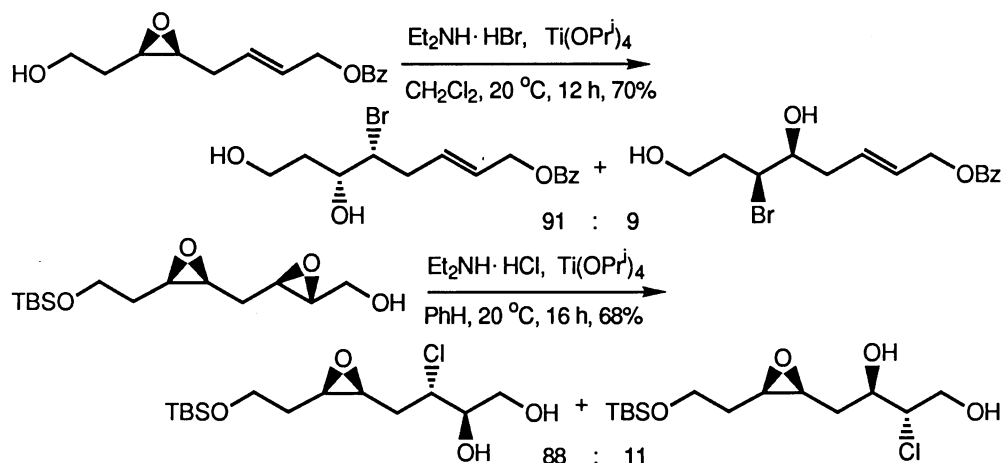


Table 1. Ring Openings of 3,4- and 2,3-Epoxy Alcohols

Epoxy alcohol	Et ₂ NH-HX	Solvent	Time h	Regioselectivity (C-4/C-3) ^a (C-3/C-2) ^a	Yield %
	X=Cl	CH ₂ Cl ₂	36	91/9	84
		PhH	60	72/28	52
	X=Br	CH ₂ Cl ₂	20	97/3	71
		PhH	60	83/17	62
	X=Cl	CH ₂ Cl ₂	36	79/21	71
		PhH	60	70/30	55
	X=Br	CH ₂ Cl ₂	20	95/5	77
		PhH	60	86/14	65
	X=Cl	CH ₂ Cl ₂	10	94/6	90
		PhH	12	99/1	91
	X=Br	CH ₂ Cl ₂	10	88/12	88
		PhH	12	93/7	93
	X=Cl	CH ₂ Cl ₂	12	92/8	85
		PhH	36	95/5	78
	X=Br	CH ₂ Cl ₂	12	88/12	75
		PhH	36	91/9	83

a) The ratio was based determined by ¹H NMR (400 MHz) after peracetylation.

References

- 1) L.-x. Gao and A. Mural, Chem. Lett., **1989**, 357, and references cited therein: recently, the new paper on the related reactions has been published. cf., E. Alvarez, M. T. Nunez, and V. S. Martin, J. Org. Chem., **55**, 3429 (1990).

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