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

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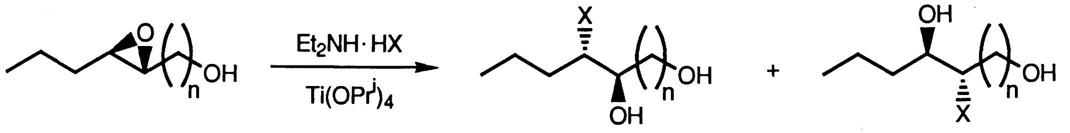
Titanium-mediated ring openings of 3,4-epoxy-1-ols at the 4-position with diethylamine hydrohalides proceeded efficiently in dichloromethane, while the requisite openings of 2,3-epoxy-1-ols at the 3-position in benzene.

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 (CH_2Cl_2) 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 CH_2Cl_2 (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 CH_2Cl_2 (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. $NaHCO_3$, 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 SN-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 prefential in benzene, CH_2Cl_2 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.



n=1	C-3 opening	>>	C-2 opening
n=2	C-4 opening	>>	C-3 opening

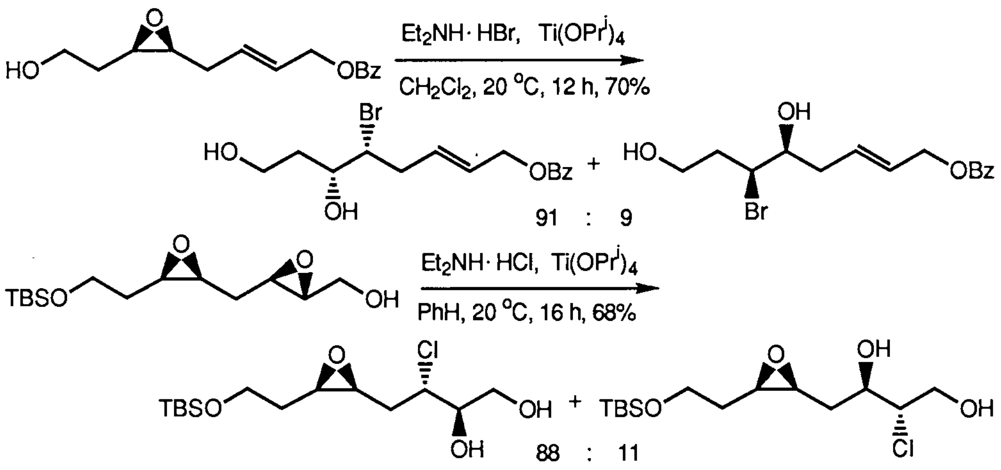
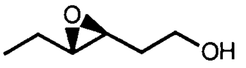


Table 1. Ring Openings of 3,4- and 2,3-Epoxy Alcohols

Epoxy alcohol	Et_2NH-HX	Solvent	Time h	Regioselectivity (C-4/C-3)[a]	(C-3/C-2)[a]	Yield %
	X=Cl	CH_2Cl_2	36	91/9		84
		PhH	60	72/28		52
	X=Br	CH_2Cl_2	20	97/3		71
		PhH	60	83/17		62
	X=Cl	CH_2Cl_2	36	79/21		71
		PhH	60	70/30		55
	X=Br	CH_2Cl_2	20	95/5		77
		PhH	60	86/14		65
	X=Cl	CH_2Cl_2	10		94/6	90
		PhH	12		99/1	91
	X=Br	CH_2Cl_2	10		88/12	88
		PhH	12		93/7	93
	X=Cl	CH_2Cl_2	12		92/8	85
		PhH	36		95/5	78
	X=Br	CH_2Cl_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. Murai, 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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