CHAPTER IV

CONCLUSION

We have found that the effect of protic solvent can increase the reaction rate of epoxide ring opening with neutral nucleophiles such as amines. With anionic nucleophiles such as azide or phthalimide anions, the effect of polar aprotic solvent is more likely to become more productive while protic solvents are beneficial for reactions with neutral nucleophiles. The differentiation of the solvent effect between two kinds of nucleophile on reactivity of styrene oxide ring opening can be concluded by the fact that the electrostatic solvent effect on stabilizing charge separation of the epoxide ring opening with both nucleophiles is probably favored by polar solvent. For azide or phthalimide anions, their nucleophilicity is reduced by forming hydrogen bond to protic solvent, so that the reaction of styrene oxide ring opening with the nucleophiles should work well in polar aprotic solvent, specifically for DMF. The reactivity of the azide can be increased by a phase transfer catalyst but the yield was still low due to its purification process. The reactivity of styrene oxide ring opening with amines in protic solvents largely depends on the acidity of the protic solvents determined by pK_a of the solvents to activate the epoxide ring opening, increasing reactivity of the reaction. However, at the same time, deactivation of the amines also occurs. As a result, the acidity of the protic solvents for aminolysis of styrene oxide ring opening must not be too high relative to the basicity of amines. The reactivity with amines depends on their nucleophilicity with the relatively increasing order by aromatic amines < primary alilphatic amines < secondary aliphatic amines in EtOH and TFE. In HFIP which is more acidic, the highly nucleophilic

acidic, the highly nucleophilic primary aliphatic amines and secondary aliphatic amines without other heteroatoms provide low yield or no products at all.

The regioselectivity of styrene oxide ring opening with anionic nucleophiles was in high preference of beta to alpha regioisomers for phthalimide but about the same ratio for azide probably due to the steric effect. However, its regioselectivity with azide can be improved by using crown ether to obtain a better ratio of beta to alpha product. In addition, the regioselectivity of styrene oxide ring opening with amines depends on the nucleophilicity of amines. The more nuclephilic the amines are, the more beta product occurs. It also depends on acidity of the solvents. The more acidic the solvents are, the more α-attacked product occurs. Furthermore, it depends on the type of epoxides. Styrene oxide and β-naphthyloxirane ring opening with amines is more subjected to obtain both α and β regioisomers, but benzyl glycidyl ether afforded only β product.

The condition from this study can be applied for regioselective synthesis of vicinal amino alcohols. The reaction conditions are simple and require no metal salts or catalysts. The ratio of regioisomers can be controlled by selection of a suitable solvent and reactants.

From stereospecificity of optically active (*R*)-styrene oxide ring opening with the amine in the alcoholic solvents the reaction mechanism is mainly through S_N2, since stereochemical integrity of the starting epoxide was almost completely preserved. This advantage can be possible to benefit for stereospecific synthesis of both alpha and beta regioisomers of vicinal amino alcohols in optically active forms.