SUMMARY OF Ph.D. DISSERTATION

School Keio University	Student Identification Number	SURNAME, First name Ohgiya, Tadaaki

Title

Chemical Studies on Useful Substances Utilizing Inductive Effect of Substituents

Abstract

2-Bromo-1-alkenes have been recognized as one of useful functional groups for preparation of vinyl lithiums and vinyl Grignard reagents, for coupling partners in a wide range of transition metal-mediated coupling reactions, substrates of radical reaction, and precursors of α-haloketones. Selective elimination reaction of 1,2-dibromoalkanes possessing 3-*O*-aryl or 3-*O*-acyl groups at C-3 position into 2-bromo-1-alkenes under basic conditions such as NaOAc, NaOPiv, and DBU, was founded. It can be explained that this regioselective elimination is controlled by a high acidity of a hydrogen atom at the C-2 position by electron-withdrawing effect of the oxygen functional group at the C-3 position.

Application of this regioselective elimination reaction to natural products synthesis was achieved as follows.

1. Total synthesis of tremetones

Recently, 12-hydroxy-tremetone, isolated from *Helichrysum stoechs*, was observed to possess inhibitory activity against myeloperoxidase. Total synthesis of 12-hydroxy-tremetone and related natural compounds was accomplished by using the regioselective elimination reaction starting from 2,3-dihydro-2-vinylbenzofuran.

2. Total synthesis of tuliparin B

Tuliparin B, one of the simplest α-alkylidene-γ-lactones, was isolated from bulbs of common tulip *Tulipa gesneriana*. Total synthesis of tuliparin B was achieved by utilizng the regioselective elimination reaction from commercially available substance in 5 steps

3. Total synthesis of tanikolide

(+)-Tanikolide, an antifungal active lactone, was isolated from cyanobacterium *Lyngbia majuscula*, collected in Tanikeli Island, Madagascar. Total synthesis of (+)-tanikolide was carried out by employing the regioselective elimination as key step.

4. Synthetic studies on eranthin

Eranthin, isolated from *Eranthis hiemalis*, is a γ-pyron possessing a benzoxepin structure. During synthetic studies on eranthin utilizing the regioselective elimination reaction was developed, it was found that unexpected bromination of trihydroxybenzene moiety rapidly underwent rather than that of olefin moiety. It was expected that the nucleophilicity of the phenol system might be decreased by adopting trifluoromethanesulfonyl group as a protecting group. To realize this process, mild cleavage condition of aryl triflates was required. Accordingly, selective bromination of the olefin moiety was successfully achieved by employing trifluoromethanesulfonyl group as the protecting group of phenol system of trihydroxybenzene moiety. Finally, production of 2,5-dihydro-1-benzoxepin derivative, a key intermediate for synthesis of eranthin, was accomplishied by using the regioselective elimination reaction.