SYNTHETIC STUDIES ON THE POLYETHER ANTIBIOTICS (PART I)

A NEW METHOD FOR THE SYNTHESIS OF FUNCTIONALIZED TETRAHYDROFURANS

AND TETRAHYDROPYRANS

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In the course of studies on the tatal synthesis of polyether antibiotics such as salinomycin and iso-lasalocid A, we planned to develop a new and useful synthetic method for building up the functionalized tetrahydrofurans and tetrahydropyrans which constitute structural unit of polyether antibiotics. Our initial studies in this area involved the synthesis of relatively complex, chiral tetrahydrofuran and tetrahydro-pyran systems <u>via oxidative cyclization by DDQ.</u>

When the compounds <u>Ia,b</u> and <u>IIIa,b</u> were treated with DDQ in CH_2Cl_2 at room temperature, the corresponding <u>IIa,b</u> and <u>IVa,b</u> were isolated in 20-30 % yields. The diastereomer ratio varies in the range from 1.8 : 1 to 4 : 1, and it was found that DDQ reacts only with E-olefin, and Z-isomer can be recovered unchanged. The factors which determine the reactivity of the olefins toward DDQ are not well understood. As the low yield of the reaction is due to unreactive Z-olefin contained in the starting material(E/Z=1:1), selective synthesis of E-olefin is under investigation.

Next, this reaction was applied to the consturction of six-membered ring systems. The reaction of <u>V</u> with DDQ in CH_2Cl_2 gave tetrahydropyran derivatives <u>VI</u>, and <u>VII</u> in a ratio of 2.3 to 1. When the pure E-olefin <u>VIII</u> was treated with DDQ, <u>IX</u> was pro-duced in favor of one diastereoisomer, although of which stereochemical assignment on the newly formed asymmetric center is not confirmed yet.