SYNTHESIS OF OPTICALLY ACTIVE SYNTHONS FOR THE TOTAL SYNTHESIS OF MACROLIDE- AND β-LACTAM-ANTIBIOTICS

Yoshimitsu Nagao,[1] Takehisa Inoue,[2] Yuichi Hagiwara,[1] Masahito Ochiai,[1]
Keiji Hashimoto,[2] and Eiichi Fujita[1]
Institute for Chemical Research, Kyoto University, Uji, Kyoto 611, Japan[1]
and Kyoto College of Pharmacy, misasagi, Yamashina-ku, Kyoto 607, Japan[2]

Recently, we reported a novel method for the highly diastereo-selective chiral induction into prochiral and symmetrical dicarboxylic acids 2a - d utilizing an optically active heterocycle, 4(R)-MCTT(1). We also reported orally a highly diastereo-selective aldol condensation reaction utilizing two chiral 1, 3-oxazolidine-2-thione derivatives, 4(R), 5(S)-MPOT (3) and 4(S)-EOT(4) as the chiral auxiliary.

As application of the both new reactions, we are carrying out a total asymmetric synthesis of 6-deoxyerythronolide-B(5) employing the optically active five-membered heterocycles. We have succeeded in a chiral synthesis of compound 6 which was a desired important intermediate of the total synthesis of 5. The stereochemistry of 6 was confirmed by its chemical conversion into the Prelog-Djerassi lactonic acid methyl ester.

Very recently, we have prepared optically active 1, 3-thiazolidine-2-thione derivatives 7 - 10 from the corresponding optically active aminoalchols, respectively. We are investigating the availability of these heterocycles 7 - 10 as the chiral auxiliary of asymmetric aldol reaction. We are also trying preparation of useful chiral synthons for the total synthesis of thienamycin (11) utilizing 7 and 10.