

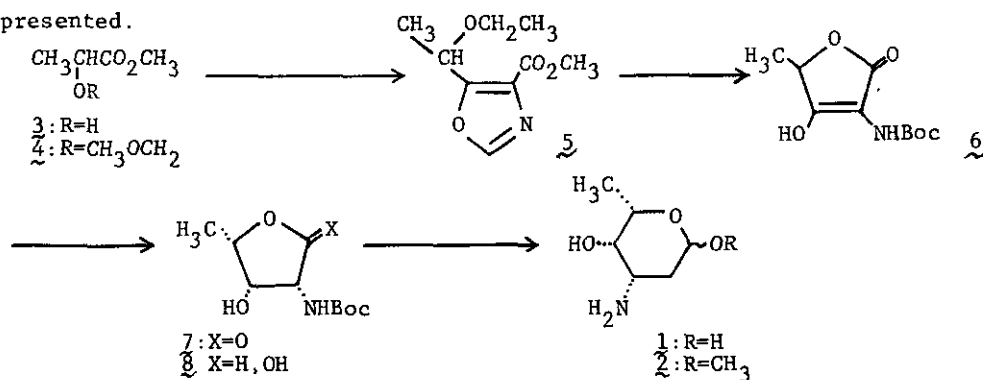
A STEREOSELECTIVE SYNTHESIS OF DAUNOSAMINE UTILIZING OXAZOLE DERIVATIVES

Akiyoshi Kawai, Yasumasa Hamada, and Takayuki Shioiri

Faculty of Pharmaceutical Sciences, Nagoya City University,
Tanabe-dori, Mizuho-ku, Nagoya 467, Japan

Recent publication from our laboratories has disclosed¹⁾ that optically active 5-substituted 4-methoxycarbonyloxazoles can be efficiently prepared from optically active carboxylic acids and methyl isocyanoacetate by the direct C-acylation using diphenyl phosphorazidate (DPPA, $(\text{PhO})_2\text{P}(\text{O})\text{N}_3$). As an application of this oxazole synthesis, we described a facile synthesis of 2,4-diamino sugar antibiotic, prumycin.²⁾ Further investigation along this line achieved a stereoselective synthesis of daunosamine (1), the amino sugar constituent of the antitumor antibiotics daunomycin and adriamycin, in the form of its rac-methyl glycoside (2).

Methyl (O-methoxymethyl)lactate (4), prepared from methyl DL-lactate (3) and chloromethyl methyl ether, was hydrolyzed with lithium hydroxide. The resulting lithium salt was treated with DPPA, followed by methyl isocyanoacetate to give the 4-methoxycarbonyloxazole 5 in good yield. Treatment of 5 with hydrogen chloride in methanol followed by di-tert-butylidicarbonate afforded the α,β -unsaturated lactone 6. Stereoselective catalytic reduction of 6 over rhodium on alumina gave the saturated lactone 7, which was converted to the lactol 8 with diisobutylaluminum hydride. The Wittig reaction of 8 with methoxymethylenephosphorane followed by the treatment with methanolic hydrogen chloride afforded methyl DL-daunosaminide hydrochloride (2). Preparation of L-daunosamine started from L-lactic acid will also be presented.



1) Y. Hamada and T. Shioiri, *Tetrahedron Lett.*, **23**, 235 (1982).

2) Y. Hamada and T. Shioiri, *Tetrahedron Lett.*, **23**, 1193 (1982).