carboxylic acid methyl ester 1,1-dioxide (1) for this work was prepared by the literature method. Its tautomer (2) was oxidized to 3 by silver(I) oxide. The oxidation proceeded at room temperature, and solvent purity was important to the reaction. Compounds 3 were converted to 3-methoxy-2H-4-oxo-1,2-benzothiazine-3- carboxylic acid methyl ester 1,1-dioxide (4a-c) in methanol, 3-ethoxy compound 4d in ethanol and 3-propoxy compound 4e in propanol. The unsymme- trical dimer (5) formed through the intermolecular dehydration between the 4-hydroxyl group of the enol form and the 3-hydroxyl group of the oxidized keto form are generated during the proloned reaction time. The reaction mechanism of the formation of the 3-alkoxy compound (4a-e) and the dimer (5) involves the dehydration between two alcohols.

[PD1-14] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Efficient Macrocyclization for Making Cyclic Peptide

Hong Il-Khee, Mun Han-Seo°, Yoon Chang No*, Jeong Jin-Hyun

College of Pharmacy, Kyung Hee University, Dongdaemoonku, Hoegidong #1 Seoul 130-701, Korea. *Korea Institute of Science and Technology

We can see that there are many spotlights on peptide drugs by examining the recent trend in drug development. For example, drugs like cyclosporin shows striking activity as an autoimmune suppressor. Especially, cyclic peptides stands out among all other peptides as a good drug. That is why we are trying to develop more effective cyclization process.
There are three ways to cyclize certain sequences of amino acids such as Gly-Met-Ile-Phe-Gly. First is head-to-tail cyclization method, linking between N-terminal and C-terminal. Second method utilizes amino acid side chain such as thiol functional group in Cys, making a thioether bond. The last one includes an application of resin-substituted amino acids in solid phase reaction. Among the three methods, solid phase reaction showed the greatest yield.

[PD1-15] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Studies on the Stereoselective Synthesis of Oxazine using a Pd-catalyzed Intramolecular Cyclization

Joo JE, Shin YH, Pyun SJ, Ham WH

College of Pharmacy, Sungkyunkwan University, Suwon 440-746

Palladium(0)-catalyzed intramolecular cyclization of benzamide via p-allylpalladium complex is useful for the synthesis of highly functionalized compounds, particularly when chirality transfer is involved. Therefore, we investigated a new method for oxazine formation reaction catalyzed by palladium(0).
The transformation of acyclic homoallyl benzamide to vinyl oxazine was intensively studied. The stereochemistry of major product was determined to be trans by using NOE experiment.

[PD1-16] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

5,8-QUINAZOLINEDIONES AS POTENT INHIBITORS OF ENDOTHELIUM-DEPENDENT VASORELAXATION

Ko KM°, Shin KH, Sun YJ, Song EH, Seo JH, Kim HJ, Ryu CK