Studies on the Synthesis and Antibacterial Activities of 4-Pyrrolidinylthio Carbapenems: 2-Alkyl Substituents Containing Heteroaromatics Linked Via a C-N Bond

Cho hanWon°[2], Oh ChangHyun[1], Choi JungHoon[2], Cho JungHyuck[1]

[1] Medicinal Chemistry Research Center, Korea Institute of Science and Technology, [2] Chemistry Department, Hanyang University

The synthesis and biological activity of series of 2-alkyl-4-pyrrolidinylthio-β-methylcarbapenems containing a variety of heteroaromatic substituents is described. These compounds were synthesized via several step from *trans*-4-hydroxy-*L*-proline and β-methylcarbapenem by the general route. Antibacterial activities of the prepared compounds were tested.

[PD1-4] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Preparation and Application of New Friedlaender Synthon for the Synthesis of 2-Substituted Pyrido[3,2-c]acridines

Kim Seung ill°, Son JaeKeun, Jahng Yurngdong

College of Pharmacy, Yeungnam University, Kyongsan 712-749

The increasing interests on pyrido[3,2-*c*]acridine and its related derivatives stem from their properties not only of showing a broad spectrum of biological properties such as antileukemic, antithrombic, and anticancer activities, but also of acting as ligands for small molecules and transition metals. The synthetic methods, however, are limited only to the Skraup reaction of 4-aminoacridine and the Friedel-Craft reaction of 7-acyl-8-arylaminoquinolines.
In connection with our interests in the design and synthesis of new polydentates and in the development of new synthetic method for the preparation of cytotoxic heterocycles, we herein described preparation of a new Friedlaender synthon, 4-aminoacridine-3-carbaldehyde and its application toward pyrido[3,2-*c*]acridines.

[PD1-5] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Stereoselective synthesis of novel 4'-hydroxy-carbocyclic nucleosides

Hong JoonHee°, Shim MyungJung, Kim KwanWoo, Ko OkHyun

College of Pharmacy, Chosun University, Kwangju 501-759, Korea

The resistance of glycosidic bond to enzymatic hydrolysis catalyzed by nucleoside phosphorylase is one of the critical points in nucleoside antiviral chemotherapy. In order to avoid such enzymatic degradation as well as to improve the antiviral activity, a great number of structural modifications have been carried out on both the sugar and the heterocycle moiety of nucleosides. One strategy has been to replace the oxygen of the furanose ring by a methylene group, which gives rise to carbocyclic nucleosides.
Recently, much attention has been paid to 4'-substituted nucleosides such as 4'-cyano-thymidine 4'-azido-thymidine, and 4'-methoxy-nucleoside as potent antiviral agents. However, only a few examples of 4'-substituted nucleosides of defined absolute stereochemistry are reported in literature. The scarcity of examples of 4'-substituted nucleosides may be due to the synthetic difficulties for elaborating a necessary tertiary carbon center. Therefore it was great important to develop efficient methodology for the synthesis of furanosyl or cyclopentane ring containing stereochemically defined tertiary carbons.
Based on promising biological activities of carbocyclic and 4'-substituted nucleosides, we designed novel 4'-hydroxy carbocyclic nucleosides from very cheap and commercially available D-lactose, which can combine the chemical and biological properties of 4'-substituted furanose nucleosides and enzyme resistant carbocyclic nucleosides.
Here, we would like to present the synthetic route of 4'-hydroxy substituted various types of novel

carbocyclic nucleosides using sequential Grubbs' ring closing metathesis and Trost allylic alkylation reaction as key reactions.

[PD1-6] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Cyclopropyl Intermediate for Synthesis of Novel Carbocyclic Nucleosides, Potential Antiviral Agents

Kook MinChul°, Park JeKyung, Choi BoGil

College of Pharmacy, Chonnam National University

Carbocyclic nucleosides has extensively studied as a promising antiviral agents having chemical and metabolical stability. In our research program for discovery of antiviral drugs, some novel dimethylcyclopropyl nucleosides possessing additional methyl spacer between the base and the ring were synthesized. The important intermediate, dimethylcyclopropyl compound was synthesized from ethyl chrysanthemate via its ozonolysis, isomerization, reduction and protection by protecting group. The ethyl ester was reduced by LiAlH4 to give the cyclopropyl intermediate which was activated by tosylation for using condensation with purine bases.

[PD1-7] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Total Synthesis of Cyclictetrapeptide Analogues of Apicidin

Jin ChengHua°, Park Hyun-Ju, Jung YoungHoon

College of Pharmacy, Sungkyunkwan University, Suwon 440-746

The antiparasitic agent apicidin, which was recently isolated from cultures of Fusarium Pallidoroseum, belongs to a rare group of cylic tetrapeptiol fungal metabolites. Apicidin inhibits protozoal HADC and is orally active against Plasmodium berghei malaria in mice. The biological activity of apicidin appears to be attributable to inhibition of apicomplexan HADC at low nanomolar concentrations.
In the present, we have worked about the synthesis of new apicidin derivatives and discovered that apicidin and some derivatives have mild antiumor activity. It caused the change of tumor cells to normal ones morphology.
As part of our program toward the development of new antitumor agents, we designed and synthesized several cyclictetrapeptide compounds. In this presentation, we will report the total synthesis of these Apicidin analogues.

[PD1-8] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

A Convenient Synthesis of Chelerythrine via Intramolecular Cyclization Reaction

Le NguyenThanh° Chung ByungHo Cho WonJea

College of Pharmacy, Chonnam National University

The benzophenanthridine alkaloids constitute a large group of metabolites which occur in the Fumariaceae, Papaveraceae, and Rutaceae and posses, in many cases, strong pharmacological activities. Thus, nitidine and fagaronine have been shown to have a antitumor activity in animal models, an activity which could be related to inhibition of DNA topoisomerase. The toxicological problems associated with the most active members of this group have led to develop new synthetic methods of these compounds, in order to study the structure-activity relationship.
There are many classical methods by which this heterocyle can be constructed and especially attractive are