Inhibitory effects of synthetic 2-hydroxychalcone derivatives on rat lens aldose reductase(RLAR) and on platelet aggregation were investigated for the prevention or the treatment of chronic diabetic complications.
5-chloro-4,2-dihydroxychalcone and 5-chloro-3,2-dihydroxychalcone exhibited a potent inhibitory effects on rat platelet aggregation induced by ADP(IC_{50}=0.10 and 0.06 mg/ml, respectively.) and collagen(IC_{50}=44 and 16 μg/ml, respectively.) but showed relatively weak inhibitory activities on RLAR. 2,4,2,4-Tetrahydroxychalcone, 3,4,2,4-tetrahydroxychacone, 5-chloro-2,4,2-trihydroxychalcone and 5-chloro-3,4,2-trihydroxychalcone possessing o-dihydroxy or m-dihydroxy moiety exhibited relatively potent inhibitory activities in both systems.

[PD1-3] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Stereoslective trans-oxazoline formation via Pd(0)-catalyzed cyclization of isopropenyl acetate.

Lee YS, Oh CY, Lee KY, WH Ham

College of Pharmacy, Sungkyunkwan University, Suwon 440-746

Palladium(0)-catalyzed intramolecular cyclization of benzamide via p-allylpalladium complex is useful tool for the synthesis of highly functionalized compounds. Ongoing program for the formal total synthesis of (+)-lactacystin, which is remarkably selective and potent inhibitor of the 20S proteasome, we applied the newly developed Pd(0)-catalyzed cyclization reaction to the highly stereoselective synthesis of trans-oxazoline, which is key intermediate of (+)-lactacystin. The requisite cyclization precursor, isopropenyl acetate, was straightforwardly prepared from the L-serine by a seven-step sequences (overall 61%).

[PD1-4] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Synthesis and In vitro evaluation indandione-2-carboxamides.

Lee H*, Lee J, Hong SS, Yang SI#

College of Pharmacy, Chungbuk National University, #College of Medicine, Kunkuk University

6-(2-Dimethylaminoethylamino)-3-hydroxyindeno[2,1-c]quinoline-7-one (TAS-103) is a dual topoisomerase I and II inhibitor with preclinical efficacy in a broad spectrum of tumors and in multidrug-resistant tumor cell lines. It is currently in Phase I clinical trials in the U.S. It could be useful as a lead compound for development of new drugs.
In this study, we presented the synthesis and cytotoxicity of indandione-2-carboxamides. These were designed as an open form of tetracyclic TAS-103. The cytotoxicities of TAS-103 analogs against various tumor cell lines were worse than that of Doxorubicin and Mitomycin-C. The compounds containing methyl substituents were more potent than other compounds in this result

[PD1-5] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Synthesis and Structure Activity Relationships of a series of 7-acylamino-3-(isoxazolylmethylthio)-3-cephem exhibiting activity against MRSA.

Chang KY, Kim SH, Nam GS, Seo JH, Kim JH, Ha DC

Biochemicals Research Center, Korea Institute of Science and Technology. Department of Chemical, Korea University

7-Acylamino-3-(isoxazolylmethylthio)-3-cephem-4-carboxylic acids or their pharmacologically acceptable salts were synthesized and their antibacterial activities against Gram-positive and Gram-negative were inspected. We discovered that their analogs exhibited a wide spectrum against Gram(+) and Gram(-) including MRSA.
We will describe the relationships between the structure and activity of these novel Cephalosporins with 3-isoxazolylmethylthio Derivatives.

[PD1-6] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

The Development of New Carbacephem Antibiotics

Pyun SJ, Kim YH, Lee YS, Ham WH

College of Pharmacy, Sungkyunkwan University, Suwon 440-746

Carbacephem is one of β-lactam antibiotics having a broad spectrum of antibacterial activity. So numerous methods for constructing carbacephems have been reported. In this study, we describe a new route to the synthesis of trans-carbacephem moiety and derivatives. The total synthesis of trans-carbacephem was starting from trans-oxazoline. Key stages in the strategy involved (i) the use of hydrogenation gave a cleavage of trans-oxazoline (ii) formation of β-lactam ring was prepared using the Mitsunobu reaction (iii) six-membered ring of carbacephem was prepared by a Dieckmann-condensation.

[PD1-7] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Synthesis and antiviral activity of novel exomethylene cyclopropyl nucleosides

Kwak EY[o1], Choi BG[1], Hong JH[2], Lee CK[3]

[1]College of Pharmacy Chonnam National University, Kwangju 500-757,[2]Department of Medicinal Chemistry, College of Pharmacy Ewha Womans Univ., Seoul 120-750, [3] Korea Res. Institute of Chem. Technology, Taejon Korea.

Some novel exomethylene cyclopropyl nucleosides were synthesized as analogues of Synadenol derivatives to find potent antiviral agents. The intermediate, Feist's acid was prepared from α-ethy acetoacetate by three steps. The key cyclopropyl compound was obtained via esterfication, reduction, and the partial protection by using TBDPS-Cl, bulky protecting group which was activated by tosylation. Its condensation with pyrimidine and purine bases in the presence of potassium carbonate and a crown compound and its deprotection by using n-Bu4NF gave their corresponding cyclopropyl nucleosides. All the synthesized compounds were evaluated for antivira activity. However, none of them showed any antiviral activity against HSV-1, HSV-2, HCMV, HIV-1, HIV-2, and HBV up to 100 μM.

[PD1-8] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Synthesis and Biological Properties of 7H -Pyrazolo[3,4-d]pyrimidine-Derived Antifolates As Antitumor Agents

Jahng, Y, Park, JG, Yu JW, Kim, HH, Yang, SI.