to find highly potent 4-phenyl-1-(N-acylindoline-5-sulfonyl)imidazolidinones. Among them, 4-phenyl-1-[N-(p-aminobenzoyl)indoline-5-sulfonyl]imidazolidinone (PA) was proved to have good pharmacological profile. Without any significant change of body weight, PA shows 84.3%, 55.6%, 67.0%, and 87% suppression of tumour growth for murine tumor 3LL, Colon26, and human xenograft NCI-H23, and SW620, respectively (at dose of 65mg/kg/2day x 5 perorally). Although this compound has excellent activity in mice, the results of pliclinical toxicological study with dog hampers the further development. To find out the better derivatives, modification of indoline moiety of PA has been attempted. As a result, many analogs shows better pharmacological profiles compared to PA. Especially 4-acylamino-3-alkyl(or halogeno)benzenesulfonyl-4-phenylimidazolidinones show outstanding cytotoxicity against human solid cancer cell lines. Structure activity relationship of this series will be discussed.

[PD1-18] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Synthesis of 2,6-Diaromatic Substituted Pyridine Derivatives and Their Antitumor Activities

Moon YoonSoo○, Lim HyunTae, Zhao LongXuan, Basnet Arjun, Lee EungSeok

College of Pharmacy, Yeungnam University, Kyongsan 712-749, Korea

α-terthienyl the first isolated from natural products shows potent antitumor activity, which encouraged us to study terpyridine and its biological properties. Terpyridine has also been reported as having carcinogenicity, and it's derivatives showed high cytotoxic activities against several human cancer cell lines and topoisomerase I inhibitory activity. Mannich free base from condensation reaction was allowed to react with pyridinum salts to give diaromatic substituted pyridine. In the present study, twenty 2,6-diaromatic substituted pyridine derivatives including phenyl, furyl, thienyl or pyridyl units were prepared. We have also tried to introduce monoaldehyde, dialdehyde, monohydroxymethyl and dihydroxymethyl functional groups in substituted moiety. Prepared compounds were evaluated their antitumor activities. Most of prepared compounds displayed moderate cytotoxic activities against several human cancer cell lines compared to doxorubicin, although they did not have significant inhibitory activities against topoisomerase I.

[PD1-19] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Stereoselective synthesis of novel 4'α-C-methyl branched novel carbocyclic nucleosides

Kim Jihee○, Ko OkHyun, Hong JoonHee*

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

Recently, 4'α-C homologated furanose nucleosides, especially alkyl branches, are molecules of considerable current interest. One of reasons for this prominence arises from the notable biological activities as antiviral and antitumor agents, as shown in 4'α-C-methyl-2-deoxythymidine (EC_{50} = 7.2μM against HIV in MT-4 cell), 4'α-C-fluoromethyl-2-deoxycytidine, 4'α-C-hydroxymethylthymidine and 4'α-C-azidomethyl-thymidine. Furthermore, recently, we have reported synthetic routes of a series of novel 4'α-C-alkyl branched nucleosides having diverse functionality and stereochemistry employing versatile [3,3]-sigmatropic rearrangement as key reaction. As a part of our drug discovery program for antiviral agents, herein we report stereoselective synthetic route of novel carbocyclic nucleosides having methyl group at 4'α-position employing our versatile three step sequences ([3,3]-sigmatropic rearrangement, ring-closing metathesis, and Pd(0)-catalyzed allylic alkylation) from very simple acyclic precursor 'acetol'.

[PD1-20] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Diastereoselective Synthesis of (+)-Frontalin

Jung JungHwa○, Kim HeeDoo

College of Pharmacy, Sookmyung Women's University

In connection with the asymmetric synthesis of chiral 1,2-diol, we report here the total synthesis of (+)-frontalin using diastereoselective alkylation featuring tridentate chelation-controlled asymmetric alkylation of a-hydroxyketone, in which the chiral auxiliary is attached to the hydroxyl group as ether linkage. The starting D-glyceraldehyde acetonide was converted (S)-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl](4-methoxyphenyl) methanol. Then, the methanol was successively transformed to frontalin in 3 steps *via* alkylation, ozonolysis and deprotection.

[PD1-21] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Lead Discovery and Optimization towards FXR Specific Compounds

Jeon Raok[O]

College of Pharmacy, Sookmyung Women's University

FXR (farnesoid X-activated receptor) is a member of nuclear steroid hormone receptor superfamily and especially a orphan receptor, which are able to control mevalonate pathway upon activation by binding of the specific ligands. We have launched our study for development of FXR specific ligands getting on in lead discovery. A promising lead, stilbene analog was obtained through the screening of a set of library compounds, which was previously targeted for other nuclear receptors. And then synthetic modification of the lead was performed. In addition, fishing a new pharmacophore was tried by UNITY search, which brought new structural features.

[PD1-22] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

The first synthesis of 4'α-C aryl branched carbocyclic nucleosides

Xu XiangShu[O], Ko OkHyun, Hong JoonHee*

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

Recently, several branched-nucleosides have been synthesized and evaluated as potent antitumor or antiviral agents. Among them, 4'α-C-ethenyl and 4'α-C-ethynyl nucleosides which having an additional double or triple bond at 4'-position were reported to be as potent antiviral and antitumor activities.
Encouraged by these interesting structures and antiviral activities, it was determined to synthesize novel classes of nucleosides comprising branched carbocyclic nucleosides with an additional aryl group at 4'α-position using versatile reiterative three-step sequences from simple acyclic precursor '2-hydroxyacetophenone'. Our efforts toward the synthesis of novel nucleosides analogues are reported herein.

[PD1-23] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Synthesis and Characterization of Polyamines and Their Metal Complexes

Jang GyuHwan[O], Kim Yang, Lee ManKil

고신대학교 화학과

The polyamine pathway represents a logical target for chemotherapeutic intervention, since depletion of polyamines results in the disruption of a variety of cellular functions, and may in specific cases result in cytotoxicity. Polyamine interaction with DNA has also long been thought to be an important function of the natural polyamines and as more is learned about the specific interactions and the resultant conformational changes which can be influenced by the polyamine binding to DNA the potential for regional and gene-specific changes are becoming more evident. We have prepared the elaborate polyamines by the reaction of simpler polyamines with polyalkylating agents. Synthesized polyamines were separated and purified by metal complex formation and ion-exchange chromatography. They were characterized by X-ray crystal structure determinations of their metal complexes.