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