Suh YoungGer[1], Chae HeeSung[O1], Kim SukHo[1], Min KyungHoon[1], Park MiHyoun[2], Kim YoungHo[2], Park HyungSup[3]

[1]College of Pharmacy, Seoul National University, San 56-1, Shinrim-Dong, Kwanak-Gu, Seoul 151-742, Korea, [2]College of Pharmacy, Chungnam University, Taejon 305-764, South Korea, [3]College of Medicine, Ulsan University, Seoul 138-040, South Korea.

Recently, we have reported the isolation of a novel pimarane diterpene, acanthoic acid, from the Korean medicinal plant which has been traditionally used for treating rheumatism. In particular, acanthoic acid turned out to be biologically attractive because it has been showned to exhibit an excellent suppression of interleukin-1(IL-1) and tumor necrosis factor-α(TNF-α) at low level which are major proinflammatory cytokines.
More recently, the COX-2 inhibitory activities of acanthoic acid have also been investigated by us as an extension of the stuies on its anti-inflammatory effects as well as therapeutic utilities.
We herein report acanthoic acid and its analogues as a novel COX-2 inhibitor as well as structure-activity relationship of acanthoic acid.
In addition, the interaction mode of acanthoic acid with the COX-2 active site and antiinflammatory effects of the highly bioactivity-enhanced acanthoic acid analogues will be presented.

[PD1-14] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Asymmetric Synthesis of (1R, 2S)-1-Allyl-2-Silanyloxy Carbamates using CSI reaction

Kim JiDuck[O]:Jung YoungHoon

College of Pharmacy, Sungkyunkwan University

A plethora of pharmaceutically and biologically valuable compounds comparise 1, 2-amino hydroxy functional groups. The substances are usually involved in exhibiting a variety of biological activities. The representatives are the glycosidase inhibitors (-)-swainsonine, (+)-castanoper-mine and azasugars, and (-)-statine as the key constituent of the aspartic protease inhibitor pepstatin. In addition, others include the neurotrophic agent (+)-lactacystin, the antibiotic (-)-furanomycin, the antifungal agent (-)-anisomycin and so forth.
We have recently described synthetic method for N-protected allylic amines from allyl ethers using chlorosulfonyl isocyanate(CSI) via the stable allylic carbocation.
In this presentation, we will report asymmetric synthetic method for (1R, 2S)-1-allyl-2-silanyloxy carbamates (1, 2-amino alcohol) by the simple CSI reaction which we developed with various allyl ethers and discuss mechanism of these reactions.

[PD1-15] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthesis of Ester Type Derivatives as Inhibitors of Acetylcholinesterase

Kang JeongHo[O], Lee HwaJung, Lee SangJae, Kwon Young-Ee

New Drug R&D Institute, STC Life Science Center

We have known that acetylcholinesterase inhibitiors are effective in enhancing cholinergic activity and useful in improving the memory of Alzheimer's patients. By structure-activity relationship studies and structural analysis, we have focused on the discovery of potent inhibitors of acetylcholinesterase and synthesized a series of 4-[4-(benzhydryloxy)piperidino]butyl benzoate's derivatives from reaction 4-[4-(benzhydryloxy)piperidino]-1-butanol with some para substituted benzoic acid by 1-ehtyl-3-(3-dimethylaminopropyl)carbodiimide and 4-dimethylaminopyridine coupling. Also,4-[4-(benzhydryloxy)-

piperidino]-1-butanol was converted from 4-hydroxypiperidine through several steps. Some of ester derivatives have a potent inhibition activity with the IC50 value of μM against acetylcholinesterase. Specially, IC50 value of 4-[4-(benzhydryloxy)piperidino]butyl 4-chlorobenzoate was found to be 300nM, against acetylcholinesterase.

[PD1-16] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Total Synthesis of (+)-Hernandulcin

Kim JungHun°, Cheon SeungHoon

College of Pharmacy, Chonnam National University

(+)-Hernandulcin was isolated as a sweet bisabolane sesquiterpene constituent of the Mexican plant Lippia dulcis Trev. (Verbenaceae) and has shown to be 1,000-1,500 times as sweet as sucrose. The structure and relative stereochemistry of this sesquiterpene were proposed by Kinghorn and the absolute configuration was determined by Mori and Kato in 1985 by a total synthesis. They established that the absolute configuration of naturally occuring hernandulcin is 6S, 1'S enantiomer and found that (+)-isomer is the only sweet compound.
A concise synthesis of (+)-hernandulcin((6S,1'S)-(+)-6-(1'-Hydroxy-1',5'-dimethyl-4'-hexenyl)-3-methyl-2-cyclohexenone) from (-)-isopulegol is reported here. Selective epoxidation followed by opening of the epoxide with prenyl Grignard, which was prepared from prenyl chloride and magnesium in the presence of purified cuprous iodide, was afforded the tertiary alcohol with correct stereochemistry. Oxidation of the secondary alcohol to ketone was accomplished by using TPAP and N-methylmorpholine N-oxide. Finally, phenylselenide formation followed by oxidative elimination provided the final product.

[PD1-17] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Macrolactonization of ω-Hydroxy Esters from Selenoester Intermediate

Shen Liu-Lan°, Jeong Jin-Hyun

College of Pharmacy, Kyung Hee University

A new method of macrolactonization of ω-hydroxy methyl esters has been studied. Dimethylaluminum methaneselenolate($Me_2AlSeMe$) converts methyl esters to the corresponding esters of methaneselenol in a high yield. These will function as extremely reactive acyl transfer agents for macrolide in the condition of medium-diluted system.

[PD1-18] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthesis of new Apicidin derivatives as a potential antitumor agents.

Kang HyunOk°:Jin ChengHua, Han JeongWhan, Lee HyangWoo, Lee HoiYoung*, Lee YinWon**, Zee OkPyo, Jung YoungHoon

College of Pharmacy Sungkyunkwan University,*College of Medicine Konyang University,**College of Agriculture & Life Siences Seoul National University

Apicidin [cyclo(N-O-methyl-L-tryptophanyl-L-isoleucinyl-D-pipecolinyl-L-2-amino-8-oxodecanoyl)] is a fungal metabolite shown to exhibit antiparasitic activity by the inhibition of histone deacetylase (HDAC).