Jang Jinhee°, Sin Kwanseog, Tran ThanhDao, Park Haeil

College of Pharmacy, kangwon National University

A convenient pathway for synthesis of trans-metanicotine analogues was developed. trans-Metanicotine, a subtype(alpha4beta2)-selective ligand for neuronal nicotinic acetylcholine receptor, is under clinical phase for Alzheimer's disease. Allylation of N-methyl aldimines with allylmagnesium bromide yielded methyl-(1-aryl-but-3-enyl)amines. Protection of the amines with Boc group and followed by Heck reaction with 3-bromopyridine gave methyl-(1-aryl-4-pyridin-3-yl-but-3-enyl) carbamic acid tert-butyl esters. Following deprotection of N-Boc group provided methyl-(1-aryl-4-pyridin-3-yl-but-3-enyl)amines in good yields. Thus, trans-metanicotine analogues modified at the α-position of the methylamino group with various aryl groups can be obtained in 5 steps.

[PD1-11] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthesis of Novel TNF-α Production Inhibitors. 2-[3-(Cyclopentyloxy)-4-methoxyphenyl]-substituted-1-isoindolinone derivatives

Park Joon Seok°, Moon Seong Cheol, Byun Young Seok

Institute of Bioscience & Biotechnology, Daewoong Pharm. Co., Ltd.

This study describes the synthesis and in vitro evaluation of 2-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-isoindolinone derivatives substituted on benzene moiety of isoindoline ring for the inhibition of TNF-α production. From this study, we have found the 6-C position on isoindolinone ring is an optimal derivatization site. Among the compounds synthesized, 6-amino-2-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-isoindolinone (6) was the most potent in inhibitory activity of TNF-α production in LPS-stimulated RAW264.7 cells.

[PD1-12] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthesis of Chelerythrine, Natural Benzo[c]phenanthridine Alkaloid

LeNguyen Thanh°, Cho WonJea

College of Pharmacy, Chonnam National University

Benzo[c]phenanthridines are naturally occurring alkaloids which have demonstrated numerous biological activities. Among these structures, fagaridine, nitidine and fagaronine have solicited much attention as antitumor drugs. Many synthetic approaches to benzo[c]phenanthridine alkaloids leading to natural products have been reported, but relatively few studies of synthetic analogues have been described. These alkaloids have also demonstrated binding affinities to DNA, have been presumed to be intercalators and have been shown to be inhibitors of DNA topoisomerase I and II, the well known targets for clinically important and emerging antitumor drugs.
As part of our endeavor to develop potential antitumor agents, we have tried to synthesize benzo[c] phenanthridine alkaloids. Our strategy is based on the synthesis of substituted 3-arylisoquinolines which is a crucial intermediates for the formation of C ring of these alkaloids. The synthesis of chelerythrine and other derivatives will be described.

[PD1-13] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Pimarane Cyclooxygenase 2 (COX-2) Inhibitor and its Structure-Activity Relationship