

Synthesis and Antiviral Activity of Methylene Cyclopropyl Pyrimidine Nucleosides

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Some methylene cyclopropyl pyrimidine nucleosides were synthesized from the intermediate, Feist's acid as a series of purine nucleosides to find potent antiviral agents. The key intermediate 7, cyclopropyl compound was synthesized via esterification, reduction, and the partial protection by using TBDPS-Cl, bulky protecting group which was activated by tosylation. Its condensation with some 5-substituted pyrimidine bases in the presence of potassium carbonate and a crown compound and its deprotection by using $n\text{-Bu}_4\text{NF}$ gave corresponding cyclopropyl nucleosides in low yield, respectively. The thymine nucleoside among the synthesized compounds showed moderate anti-HBV activity.

[PD1-3] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthesis and structure-activity relationship of novel FTase inhibitors containing imidazole and urea moieties

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Ras proteins play an important role in signal transduction process involved in cell proliferation. Mutated Ras proteins have been found in 30% of human cancers including 50% of colon cancer, 90% of pancreas cancer, 50% of lung cancer and thyroid gland cancers. A series of posttranslational modifications are required for its biological function. The first step is alkylation of cysteine residue of its C-terminus with a farnesyl group by farnesyltransferase (FTase), which was identified as a potential target for the discovery of anticancer agents.

Based on the C-terminal CAAX (C: cysteine, A: aliphatic amino acid, X: serine or methionine) box of ras protein, various types of CAAX mimetic FTase inhibitors have been reported.

In this presentation, the synthesis, structure-activity relationship, and biological properties of novel FTase inhibitors containing imidazole group will be described. Cysteine of CAAX box was replaced with imidazole substituent and AAX moiety was replaced with simple urea derivatives. Biological activity was evaluated by FTase assay and MTT based cell growth inhibition assay. Many FTase inhibitors showed potent inhibition against K-ras farnesylation as well as ras-transformed cell growth without showing cytotoxicity.

[PD1-4] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

An Efficient Synthesis of Cyclic α,α -Disubstituted α -Amino Acids

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Development of conformationally constrained amino acid analogues attracts much attention in the design of biologically active compounds such as enzyme inhibitors and receptor agonists/antagonists. It is very important to develop synthetic methodology allowing the ready synthesis of those amino acids. We have devised an efficient method for the synthesis of cyclic α,α -disubstituted α -amino acids such as 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-1-carboxylic acid (Apc), and 4-amino-1-phenylpiperidine-4-carboxylic acid (Appc). Key features of the synthesis involve hydantoin formation, mild hydrolysis of hydantoin and efficient resolution of resulting racemic or