[PD1-23] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Design, Synthesis, And In Vitro Evaluation of Apio Analogs of Neplanocin A and Aristeromycin

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Apio nucleosides whose 4'-hydroxymethyl group moves to 3'-position exhibit interesting biological activity such as antitumor or antiviral activity. On the other hand, neplanocin A and aristeromycin are the representative of the carbocyclic nucleosides and have been recognized as potent inhibitors of S-adenosylhomocysteine hydrolase. Based on these findings, it was of great interest to design apio analogues of neplanocin A and aristeromycin. These nucleosides combine the characteristics of apio nucleosides and carbocyclic nucleosides, neplanocin A and aristeromycin. For the synthesis of the apio carbocyclic analogues, D-ribose was converted to the key intermediate, D-apio cyclopentenol or D-apio cyclopentanol via Grignard reaction, oxidative cleavage, and hydroxymethylation as key steps. The glycosyl donors, D-apio cyclopentenol or D-apio cyclopentanol was condensed with adenine anion to give the final nucleoside after the removal of the protecting group. The final apio neplanocin A and aristeromycin were assayed against S-adenosylhomocysteine hydrolase and found to be much less potent than parent nucleosides. Interesting chemistry encountered during the synthesis and biological activity will be presented in the meeting.

[PD1-24] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Synthesis of Quinolinones for Novel Flavonoid Derivatives

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We report the synthesis of key intermediates for the development novel flavonoid derivatives with potential antiinflammatory activity and propose a mechanism of the one-pot reaction. The various amines (1) for this work were commercially available. Secondary amines (2) were formed by nucleophilic attraction using ethyl benzoylacetate. The C-N bond formation proceeded at refluxing in toluene with catalytic amount of p-toluenesulfonic acid and a removal of water was important in this reaction. Compounds 2 were converted to quinolinones (3) in xylene using Dean-Stark apparatus. Synthetic process from amine (1) to quinolinone (3) could be carried out in one-pot without isolation of intermediate (2), 3 were generated during the proloned reaction time. One-pot condensation with dehydration could be convenient synthetic method, gives quinolinones.

[PD1-25] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Chain-branched Acyclic Phenethylthiocarbamates as Vanilloid Receptor Antagonists

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By acting on vanilloid receptor(VR1), capsaicin excites and then desensitizes a subset of primary neurons involved in nociception, neurogenic inflammation, and a variety of local regulatory functions. Due to this unique biological activity, VR1 is at present one of the most attractive targets for the treatment of pain. However, despite the concentrated effort on agonists, they have been exposed to the side effects such as pungency and/or hypothermia responses. In this context, the possibility of VR1 antagonist as an ideal analgesic has been suggested carefully, and followed by some efforts to discover the novel antagonists in the last decade. Our basic strategy for structural modification is to seek the chain-branched acyclic compounds deviated from coplanar conformation with minimal structural disturbance from cyclic capsazepine. A series of acyclic phenethylthiocarbamate derivatives have been synthesized, and their antagonist effect against vanilloid receptor tested . Chain branching led to a significant change in antagonist activity of the parent molecule. Ethyl-branched compound showed a 6.3 μM of IC_{50} value in $45Ca^{2+}$-influx assay.

[PD1-26] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Evaluation of L-FMUS as a potent anti-HBV agent

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The nucleoside analogue, L-FMUS was synthesized from L-FMAU which has been shown to have significant antiviral activity against hepatitis B virus (HBV). It was prepared by two steps. First, 5'hydroxyl of L-FMAU was substituted by thioacetyl group using diisopropylazodicarboxylate(DIAD), Triphenyl phosphine(PPh3) and thioacetic acid in anhydrous THF. Then, the thioacethylated compound was deacetylated using ammonia-saturated methanol. The anti-HBV activity and toxicity of the L-FMUS was evaluated in HepG2 2.2.15 cells. L-FMUS reduced the secretion of HBsAg in culture media of HepG2 2.2.15 cells. Our finding may have potential to develop as anti-HBV drugs.

[PD1-27] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Retention of Configuration: Mechanism Studies on the Reaction of Chlorosulfonyl Isocyanate with Ethers

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We have developed the novel one-pot synthetic method for regioselective N-protected amines, carbamates as a protective group of amines, through the reaction of various ethers with chlorosulfonyl isocyanate (CSI). This synthetic method provides a simple and convenient alternative for the formation of carbamates, such as -NHMoc, -NHPoc, -NHCbz, -NHPnz, -NHTroc and -NHAloc, by varying the alkyl moiety of ethers. On the basis of this reaction, we also developed a novel regioselective and diastereoselective synthetic approach to the unsaturated 1,2-amino alcohols from the epimeric mixture of optically active allylic ethers having a chiral hydroxyl group using the CSI reaction.
Herein we now describe the examination about the effect of regioisomers, syn- and anti-1,2-protected diols, on the diastereoselectivity, and investigation of the enantioselectivity of CSI reaction with various chiral ethers.
On the ground of these results, we confirmed that not only the stereochemistry of protected