[PD1-8] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

The synthesis of aminocarbocyclics from glucose

Shin Dong-Hyouk°, Jeong Jin-Hyun

College of Pharmacy, Kyung Hee University

The abundance of carbohydrates in nature with diverse roles in biological systems makes them a subject of considerable interest.
They exhibit biological effects, ranging from cellular regulation to the selective inhibition of enzymes with key roles in living organisms.
A wide range of carbocyclic polyhydroxyls has significant therapeutic effects, examples of which include cyclohexane hexitols, such as inositols, and pseudo-sugars, such as cyclophellitol and valienamine. Structural analogues of valienamine include adiposin, trestatin, amylostatin and most constituents of aminoglucoside antibiotics.
Many chemical synthetic methods have been developed to obtain pure optically analogues of these compounds.
Enzymatic reactions have proved to be efficient and give good yields with high stereoselectivity and regioselectivity.
To first synthesize valienamine from glucose and partially protected glucose using the Nozaki-Kishi reaction.
Glucose is being used because of the fixed stereochemistry that is identical to the valienamine structure.
Synthesize intermediate compounds for transformation into carbocyles using both chemical and enzymatic methods.
Use organometallic reagents of identical mechanism.

[PD1-9] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Synthesis and Inhibitory Activity against COX-2 Catalyzed Prostaglandin Production of Flavone Analogs

Tran ThanhDao°, Chi YeonSook, Kim JeongSoo, Kim HyunPyo, Kim SangHee, Park Haell

College of Pharmacy, Kangwon National University;College of Pharmacy, Seoul National University

To decipher the structure-activity relationships of flavones for the inhibition of cyclooxygenase-2 catalyzed prostaglandin production, we synthesized 7-methxoyflavones, 7-hydroxyflavones, 5-methxoyflavones, 5-hydroxyflavones and flavones without any phenol group on A ring. Methoxyflavones were prepared from 2,6- and 2,4-dihydroxyacetophenones in 3 steps. Most of the methxoyflavones were converted to the corresponding hydroxyflavones by the reaction with BBr3 in good yields. Flavones without any phenol group on A ring were synthesized from 2-hydroxyacetophenone in 2 steps.
The inhibitory activity of the synthetic flavones against prostaglandin production from lipopolysaccharide-treated RAW 264.7 cells was measured. 3',4'-Dichloroflavones exhibited good inhibitory activity of prostaglandin production.

[PD1-10] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

A synthesis of sugar-modified S-adenosyl-L-homocysteine(AdoHcy) analogues as

inhibitors of AdoHcy hydrolase via the coupling sugar-modified adenosine analogues with L-homocysteine sodium salt.

Kim BeomTae°, Kim SeungKi, Ryu JeongHyun, Hwang KiJun

Department of Chemistry, and Research Center of Bioactive Materials, College of Natural Science, Chonbuk National University, Dukindong 664-14, Chonju, S. Korea 561-756

S-adenosyl-L-homocysteine(AdoHcy) is the product of all biological methylation in which S-adenosyl-L-methionine (AdoMet) is utilized as a methyl donor and is reversibly hydrolyzed to L-homocysteine and adenosine by AdoHcy hydrolase physiologically. Inhibition of this enzyme results in intracelluar accumulation of AdoHcy leading to a feedback inhibition of AdoMet-dependent methylation reactions which are essential for viral replication. Therefore AdoHcy hydrolase has become an attractive target for the molecular design of broad-spectrum antiviral agents. While the majority of the synthetic efforts has been focused on the Neplanocine A or aristeromycin-derived nucleosides, there has been very few studies on the AdoHcy analogues and evaluation of their activities. So, it was interesting to us to synthesize sugar-modified AdoHcy analogues and to investigate the role of amino acid portion of AdoHcy and the effect of functionality in sugar moiety on their inhibitory activity. A series of sugar-modified nucleosides were synthesized from adenosine via conventional protocols and converted to 5'-chloroadenosine analogues. The required L-homocyteine sodium salt was prepared via Birch reduction of L-methionine. Finally, AdoHcy analogues were prepared in moderate yields via the coupling 5'-chloroadenosine analogues with L-homocysteine sodium salt. The activity test against some kind of viral species is in progress. The synthetic details will be discussed in the meeting.

[PD1-11] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

A Novel Photonuclease; Bromofluoroacetophenone-Pyrrolecarboxamides

Jeon Raok°

Sookmyung Women's University

Bromofluoroacetophenone derivatives which produce fluorine substituted phenyl radicals that cleave DNA upon excitation were investigated as a novel photonuclease. Pyrrolecarboxamide-conjugated bromofluoroacetophenones; 4'-bromo-2'-fluoroacetophenone and 2'-bromo-4'-fluoroacetophenone were synthesized and their DNA cleaving activities and sequence selectivities were determined. Bromofluoroacetophenone-pyrrolecarboxamide conjugates were found to be effective DNA cleaving agent upon irradiation in concentration dependent manner based on plasma relaxation assay. The DNA cleaving activities of 2'-bromo-4'-fluoroacetophenone derivatives were larger than those of 4'-bromo-2'-fluoroacetophenone derivatives.

[PD1-12] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Topoisomerase I inhibition of 2-substituted 5-nitrobenzimidazoles

Kwon MinJin°, LaVoie Edmond J., Kim JungSun

Dept. of Biotechnology, Dongseo University, Busan 617-716, Korea and College of Pharmacy, Rutgers the State University of New Jersey, USA