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Carbonucleosides has extensively been studied as a promising anti-viral agents having chemical and metabolical stability. As yet there are no rules relating the structures of carbocyclic nucleosides to their therapeutic activity, although trends among certain kinds of structure have been tentatively put forward. In our research program for discovery of anti-viral drugs, the novel cyclobutyl nucleosides can be expected to be potential antiviral drugs as analogues of cyclobut-A, anti-HBV agent. The key cyclobutyl intermediate synthesized by ring contraction reaction using zirconium complex, was condensed with purine base for synthesis of the novel carbocyclic nucleosides.

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

Syntheses of Aminoalcohols with Alkenyl Substituents for the Development of Tissue Factor Inhibitors and Their in vitro Nanomolar Level-Activities

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Tissue Factor (TF), a principal initiator of the veterbrate coagulation cascade is known to to induced in endothelial cells, monocytes and macrophages by inflammetry stimuli and in many pathological conditions. Through our synthetic efforts to develop new TF inhibitors, seventeen N-C-18 alkenyl group (9-octadecenyl or 9,12-octadecadienyl) substituted aminoalcohols (2-aminoethanol, 1-amino-2-propanol and 3-amino-1-propanol) were prepared and their in vitro TF inhibitory activities were examined. Except one case, they all exhibit nanomolar level activities (1.1~7.7×10^-9 mole/TF unit). Details of the studies will be discussed.

[PD1-17] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Synthesis and Biological Activity of 1β-Methyl-2-[5-(2-N-Substituted aminoethylcarbamoyl)pyrrolidin-3-ylthio]carbapenem Derivatives.

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The synthesis of a new series of 1β-methylcarbapenems having the substituted aminoethyl-carbamoylpyrrolidine moiety is described. Their in vitro antibacterial activities against both Gram-positive and Gram-negative bacteria were tested and the effect of substituent on the pyrrolidine ring was investigated. In particular, the compound 11g having piperazinyl urea moiety showed the most potent antibacterial activity.

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

Stereoselective synthesis of carbocyclic analogue of Nucleocidin

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Among 4'-substituted nucleosides, Nucleocidin, 4'-azido thymidine (ADRT), 4'-fluorinated carbocyclic nucleoside, and 3'-fluoro oxetanosin analogue have demonstrated a variety of biological activities. Since the cyclopentane ring of carbocyclic nucleosides can emulate the furanose moiety, a number of these compounds exhibit interesting biological activity, particularly in the areas of antiviral and anticancer chemotherapy.
Encouraged by these interesting structures and antiviral activities, novel class of nucleoside comprising branched carbocyclic nucleosides with an additional fluorine atom at 4'-position was synthesized. The synthetic procedure and biological activity will be discussed in the meeting.

[PD1-19] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

A Novel and Highly Potent Non-vanilloid VR Antagonist

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The vanilloid receptor VR has attracted great interest as a sensory transducer for capsaicin, protons, and heat, and as a therapeutic target.
On the basis of the previous studies on vanilloid agonists and antagonists, we have looked for non-vanilloid VR antagonists by developing ideal vanilloid equivalents, which might provide the perfect analgesic effects without the side effects caused by vanilloid receptor agonists
Initially, we examined the in vitro activities of more than eight hundred synthetic compounds, which were designed based on the structures of the reported natural and unnatural agonists and antagonists.
In particular, our work focused on the development of novel vanilloid equivalents, which function as both hydrogen bonding donors and acceptors, like the vanilloid moiety of capsaicin. Here we present novel non-vanilloid VR antagonists, N-(4-t-butylbenzyl)-3,4-disubstituted benzylthiourea derivatives, with enhanced activities in both capsaicin single channel and calcium uptake assays compared with capsazepine.

[PD1-20] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Studies on the Regioselective and Diastereoselective Amination using Chlorosulfonyl Isocyanate (CSI)

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We have recently described the novel synthetic method for N-protected amines from various ethers using chlorosulfonyl isocyanate(CSI) and found that the mechanism of our CSI reaction is a competitive reaction of SN1 and SNi mechanism according to the stability of carbocation intermediate. Forthermore, we developed the regioselective and diastereoselective one-pot