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

hydroxyl moiety but also the stability of carbocation intermediate affect the diastereoselectivity and established that our CSI reaction is a competitive reaction of S_Ni and S_N1 reaction according to the stability of carbocation intermediate.
Namely, the less stable the carbocation intermediate, the greater is the proportion of S_Ni reaction (retention of configuration). And, the more stable the carbocation intermediate, the proportion of the S_N1 reaction (racemisation) increases.

[PD1-28] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

A new synthesis route to nucleoside: Two-directional synthesis of carbocyclic nucleoside using double [3,3]-sigmatropic rearrangement and double RCM

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Extensive efforts in the search of therapeutically useful carbocyclic nucleosides have resulted in a wealth of their synthetic methodologies in racemic and optically active forms. The classical one-directional methods such as linear synthesis and convergent synthesis are the approaches most frequently seen in the literature for the preparation of carbocyclic nucleosides, and their advantages and limitations are well known. The other strategy, two-directional synthesis by simultaneously homologation, has received considerable attention over the last few years. When applied to appropriate target molecules, namely those with a significant element of symmetry, this strategy offers a highly efficient synthetic route to stereochemically pure products in relatively few steps, compared with the one-directional strategy. Although several efficient synthetic procedures for nucleosides have been developed on the basis of one-directional strategy, no attempt has been made for the preparation of nucleosides using more efficient two-directional strategy thus far. In this conference, we would like to disclose the pioneering synthetic example of carbocyclic nucleoside with use of the two-directional synthetic strategy by simultaneous homologation starting from C2-symmetric chiral template.

[PD1-29] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

The Structure-Activity Relationship of Mansonone F, a Potent Anti-MRSA Sesquiterpenoid Quinone: Insights into Minimum Structural Requirements and SAR of C3 position

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The resistances to multiple antibiotics of strains of Gram-positive Staphylococci, methicillin-resistant Staphylo coccus aureus (MRSA), are now significant clinical problem. One of the major efforts of our laboratory has been the search and design and synthesis of novel lead compound for the purpose of obtaining highly potent anti-MRSA drug. Towards this end, we have recently reported the isolation of a potent anti-MRSA sesquiterpenoid ortho-quinone, mansonone F, from the Korean medicinal plant which has traditionally been used to treat infectious diseases. It has been shown to have antibacterial activities against Gram-positive bacteria and, in particular, MRSA (with an MIC90 of 2 mg/ml in vitro), comparable to vancomycin.
For the identification of pharmacophore and our systemic investigation into the relationship between the structures of quinoid compounds based on the natural product mansonone F and