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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

synthetic method for 1,2-amino alcohol, through the reaction of di- and tribenzyl ethers with CSI, and invetigated its mechanism.
The regioselectivity of dibenzyl ethers with CSI depends on the stability of carbocation intermediate. The diastereoselectivity of dibenzyl ethers with CSI is as follows: The treatment of anti-1,2-dibenzyl ether in toluene afforded the anti-N-benzylcarbamate with the highest diastereoselectivity (46:1, 98%ds). The anti-selectivity can be explained by the modified Felkin-Ahn model. On the other hand, the treatment of syn-1,2-dibenzyl ether with CSI in hexane afforded the syn-N-benzylcarbamate with high diastereoselectivity (25:1, 96%ds). This syn-selectivity can be explained by the neighboring group effect.
This new synthetic strategy involving our regioselective and diastereoselective CSI reaction can be widely applicable to the total synthesis of other alkaloidal sugar mimics(Azasugars) with a nitrogen in the ring.

[PD1-21] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Synthesis of Novel 1-(4-Halophenyl)-5-arylhydantoins as Selective COX-2 Inhibitors

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Nonsteriodal antiinflammatory drugs(NSAIDs) are widely used to treat pain, fever, and inflammatory conditions including osteoarthritis. However, gastrointestinal (GI) and renal toxicity were related to common NSAIDs limits their usefulness because NSAIDs inhibit not only COX-2 associated with anti-inflammatory activity, but also COX-1 accompanied with side effects in the stomach and kidney. On the basis of this fact, specific COX-2 inhibitors such as celecoxib and rofecoxib are introduced in the drug market. The distinguished feature of these drugs is that the 5-membered heterocycle ring is substituted with two aryl groups. Therefore, in this study, we designed a new hydantoin derivatives via the reaction of methyl α-(p-methoxyanilino)-(p-halo) phenylacetates as selective COX-2 inhibitor candidates. These compounds were prepared through esterification, bromination, α-substitution and cyclization from commercially available (p-halo)phenylacetic acid. Especially, N-aralkylgroups could be introduced in 3-position of hydantoin ring by one-pot reaction of methyl α-(p-methoxyanilino)-(p-halo)phenylacetates with aralkyl isocynate.

[PD1-22] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

A Model Study toward the Synthesis of Xestoquinone and Halenaquinone

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A strategy for synthesis of the furan-fused tetracyclic core of
xestoquinone and halenaquinone was explored through a model study.
Methyl 8-oxo-4-methyl-4-phenyl-2,7-nonadiynoate was prepared from hydratroponitrile and 3-butyn-1-ol as starting materials.
The intramolecular cycloaddition of this intermediate as a key step will be involved.