studies of isoleucyl adenylate analogue, a intermediate binding more tightly to the enzyme than substrate, have shown that structural modification of adenine moiety provide that with species-selectivity. With an aim to develop novel antimicrobial compounds with selectivity, a series of adenylate analogues have been synthesized and evaluated as inhibitors of their cognate *Staphylococcus aureus* aminoacyl-tRNA synthetases. Some of inhibitors have been identified with IC_{50} values in the range of 4nM to 158nM. However the compounds showed relatively weak antibacterial activity against *Staphylococcus aureus*, indicating poor penetration through the microbial cell wall. The further investigation to improve antibacterial activity is undergoing.

[PD1-32] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

6/7-(Substituted-phenyl)amino-5,8-quinazolinediones as Potent inhibitors of Endothelium-dependent Vasorelaxation

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6/7-(Substituted-phenyl)amino-5,8-quinazolinediones were synthesized by regioselective substitution of 5,8-quinazolinedione in the presence of Ce(III) ions and 7-methoxy-5,8-quinazolinedione with appropriate arylamines. All synthesized 5,8-quinazolinediones showed a potent and efficacious inhibitory effect on the acetylcholine (ACh)-induced vasorelaxation of rat aorta with the endothelium. The quinones, at a low concentration of 0.1 M, reduced the maximal response with increase of EC50 values for ACh. The results indicate that 6/7-(substituted-phenyl)amino-5,8-quinazolinediones are potent inhibitors of endothelium-dependent vasorelaxation.

[PD1-33] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Effective conformation of HIV NNRTI Trovirdine analogs

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Simple thiourea analogs have been recently focused as potent HIV nonnucleoside reverse transcriptase inhibitors. Trovidine has been successfully introduced into the clinical chemotherapy. Later N-thiophenethyl-N'-(5-bromopyridin-2-yl)thiourea was discovered as effective agent against various mutant strain. These compounds are linear and flexible. To find out the effective conformation, rigid conformational analogs were designed and tested against HIV virus. Accordingly, five membered heterocyclic 4-phenyl-1-phenylalkylimidazolidinones and 4-phenyl-[1,2,5]thiazolidine-1,1-dioxides were synthesized.

[PD1-34] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Aziridine analogs of HIV NNRTI trovidine

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Trovidine and its analogs are very effective reversible inhibitors against HIV reverse transcriptase.

Irreversible inhibitor may provide better therapeutic potential to control this viral disease. Since aziridine motif possesses alkylating property, integration of this motif into the backbone of trovidine analogs was attempted. Thus N-(pyridin-2-yl)- carbamoyl-2-phenylaziridines were synthesized and tested against HIV 1
and HIV 2 viruses.

[PD1-35] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Enantiomeric synthesis 3'-hydroxy apionucleosides and 4'-hydroxy carbocyclic nucleosides

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In the search for effective, selective and nontoxic antiviral agents, a variety of strategies have been exploited to design nucleoside analogs, which block viral replication without affecting host cellular process.
Among them 4'-substituted nucleosides have drawn great attention and significant progress have been made in the past several years in the battle against HIV, hepatitis B and other viruses.
As part of our drug discovery program, we have determined to synthesize nucleosides with hydroxy group at 3' or 4'-position. Herein, We would like to introduce very efficient synthetic methods of 2'-deoxy-3'-hydroxy-L-furanosy nucleosides as well as 4'-hydroxy carbocyclic skeleton using metathesis strategy from a-D-lactose.

[PD1-36] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthesis and Biological Activities of Synthetic Flavonoid Libraries

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The flavonoids are a very large and important group of polyphenolic natural product, which exhibit a wide range of biological properties including antimicrobial, antiinflammatory, immunomodulatory, antioxidative, antitumor and so forth. We synthesized series of flavonoid analogues, which can not be isolated from natural resources, to evaluate the biological activities for several therapeutic targets such as inflammation, cancer and others.
Mono and polyhydroxylated 2'-hydroxyacetophenones were reacted with various aromatic aldehydes in methanolic KOH to produce chalcone analogues as key intermediates and further ring formation reaction in iodine-DMSO conditions yielded a large number of synthetic flavonoids as crystalline products. Herein we demonstrate the synthesis and biological activities of synthesized flavonoid libraries for inflammation and some other biological targets.

[PD1-37] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

A Modified Niementowsky Reaction for the Synthesis of 4-Hydroxyquinoline, Qinazoline, and Their Derivatives

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