

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 IC₅₀ 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 Troviridine analogs

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Simple thiourea analogs have been recently focused as potent HIV nonnucleoside reverse transcriptase inhibitors. Troviridine 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 troviridine

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