[PD1-29] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthesis and Cytotoxicity of 3,4-Diaryl-2(5H)-Furanone Derivatives

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2(*5H*)-Furanone is a common moiety incorporated in a number of drugs with diverse biological activities such as antitumor, antifungal, antibacterial and antiinflammatory. One of them, a 3,4-diaryl-2(*5H*)-furanone analogues, in which the two aromatic rings are tethered directly into the 2(*5H*)-furanone ring, a biomoiety found in a number of drugs with diverse biological activities were synthesized and evaluated against for their cytotoxicity in a small panel of cancer cell lines. Four of ten compounds in this series, e.g. 3-(3,4,5-trimethoxyphenyl)-4-(4-methoxyphenyl)-, 3-(3,4,5-trimethoxyphenyl)-4-(3-hydroxy-4-methoxyphenyl)-, 3-(3,4,5-trimethoxyphenyl)-4-(3-amino-4-methoxyphenyl)-, and 3-(3,4,5-trimethoxyphenyl)-4-(2-naphthyl)-2(*5H*)-furanones, were found to have potent cytotoxic activities with ED_{50} values of less than 20 nM in most of the cell lines tested.

[PD1-30] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Epoxidation of [25R]-1,4,6-Spirostatriene-3-one

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The [25R]-5-spirosten-3β-ol was oxidized with dichlorodicyanobenzoquinone(DDQ) to give [25R]-1,4,6-spirostatriene-3-one. Treatment of the triene with alkaline hydrogen peroxide afforded the [25R]-1,2-epoxy-4,6-spirosta
dien-3-one. Epoxdation of the triene with m-chloroperoxybenzoic acid produced the[25R]-6,7-epoxy-1,4-spirostadien-3-one. These products were reduced with litium metal and ammonium chloride in liquid ammonia, to yield [25R]-6-spirosten-1,3-diol and [25R]-1-spirosten-3,6-diol, respectively. [25R]-1,2-epoxy-4,6-spirostadien-3-one was reduced with lithium metal in absolute ethanol to give [25R]-1-ethoxy-4,6-spirostadien-3-one.

[PD1-31] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Aminoacyl adenylate analogues as inhibitors of aminoacyl-tRNA synthetase

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The emergence of drug resistant *Staphylococcus aureus* poses a significant health treat to human. Thus there is a critical need to develop new antimicrobial agents with novel mode of action. Aminoacyl-tRNA synthetases(ARSs) are essential in protein biosynthesis, catalyzing the attachment of amino acids to their cognate tRNA prior to the ribosome. Selective inhibition of bacterial ARS has proved to be a successful strategy for the production of antibacterial compounds. Pseudomonic acid(generic name: mupirocin) is a potent inhibitor of isoleucyl-tRNA synthetase. Recently, structure-activity relationship

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.