

[PD1-29] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Ring enlargement reaction of 5,6-dimethoxyindan-2-one

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2-Aminoindan derivatives has been shown the serotonergic activities. In order to find new serotonergic agent, we tried to enlarge the indan ring. 3,4-Dimethoxybenzaldehyde, used as starting material was condensed with malonic acid, piperidine to form 3,4-dimethoxycinnamic acid. It was catalytically hydrogenated and subsequently cyclized by Friedel-Crafts acylation reaction to yield 5,6-dimethoxyindanone. This compound was reacted with pyrrolidine and then acrylamide to be synthesized the 3-membered ring. Whereas, indanone was converted to oxime, and oxime was reduced with H₂ in the presence of 10% Pd-C to obtain cis and trans isomer mixture of 2-amino-1-indanol. It was reacted with benzaldehyde, and then reduced with sodium borohydride to yield N-benzyl-2-amino-indan-1-ol derivative. It was cyclized by Friedel-Crafts intramolecular alkylation to synthesize the 4-membered rings.

[PD1-30] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Synthesis of 1,2,3-and 1,2,4-Triazole Isonucleosides as Potential antiviral agents

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Inosine monophosphate dehydrogenase (IMPDH) catalyzes the NAD⁺-dependent oxidation of IMP to XMP, the rate limiting step in the de novo biosynthesis of guanine nucleotide. Its critical role at the metabolic branch point in purine nucleotide biosynthesis makes it a useful target in the development of drugs for antiviral and anticancer chemotherapy and in immunosuppressant area. Several compound with antiviral activity have been found to be inhibitors of IMPDH. For example, ribavirin, a competitive inhibitor of IMPDH, has broad spectrum antiviral activities against DNA and RNA viruses. Isonucleosides are a novel class of nucleosides in that base is transposed from the natural 1'-position to the isomeric 2'-position. Isonucleosides have attracted great interest because of higher stability towards acids and enzymatic deamination. It has been reported that both D- and L-isonucleosides exhibit some activity against a broad spectrum of viruses and tumor cell lines. In view of these interesting biological activity of isonucleosides as well as triazole nucleosides, it was great interest to design and synthesize triazole (2S,4S)-isonucleosides. Here we report the synthesis of novel 1,2,4- and 1,2,3-triazole isonucleosides, starting from D-ribose and D-xylose, respectively.

[PD1-31] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

3D-QSAR (CoMFA, CoMSIA) study of PPAR- γ agonists.

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Comparative molecular field analysis (CoMFA) and comparative molecular similarity indices analysis (CoMSIA) were performed on 60 PPAR- γ agonists. Partial Least Squares (PLS) analysis produced good predicted models with q^2 value of 0.62 (SDEP=0.33, F value=93.22, $r^2=0.92$) and 0.56 (SDEP=0.47 F value=27.65, $r^2=0.86$), respectively. The key spatial properties were detected by careful analysis of the isocontour maps.

[PD1-32] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Synthesis of 6-Formyl-pyridine-2-carboxylate Derivatives and their Telomerase Inhibitory Activities

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Telomeres are DNA-protein complexes at the ends of chromosomes, which play an essential protective role against DNA degradation and aberrant recombination during cell divisions. Several telomerase inhibitors have been reported as candidates for new antitumor drugs. Among them, 2-thiobenzylpyridines, developed by Geron. Co. Ltd. as a telomerase inhibitor, were chosen as lead compounds. Twenty-one pyridine-2-carboxylate derivatives were prepared by the coupling of 6-formyl-2-carboxylic acid with the corresponding phenol, thiophenol, and aniline, substituted with various functional groups. Among them, the 3,4-dichlorothiophenol ester showed the highest in vitro telomerase inhibitory activity and quite significant in vivo tumor suppression activity.

[PD1-33] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Synthesis of Selenoflavonoids

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Flavonoids with oxygen atoms are known to have potent biological effect. They have been studied long as major antioxidants which protect cell membranes. Recent medical surveys show that increased intake of selenium decreases the risk of breast, colon, lung and prostate cancer by preventing free radical generation. The flavonoids, isoflavonoids, and coumarins which form the bulk of these compounds are very polar and have limited use as drugs which have to pass through BBB (Brain Blood Barrier). The non-polar property is increased by exchange oxygen to selenium as a part of heterocyclic compound. Our group is focused on synthesizing selenoheterocyclic compound with the above property. Several compounds have been synthesized and monitored.

[PD1-34] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Synthesis and biological evaluation of 4,7-benzimidazolediones that inhibit vascular smooth muscle cell proliferation

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The abnormal proliferation and migration of vascular smooth muscle cell (SMC) play an important role in the pathology of coronary artery atherosclerosis and restenosis. Platelet-derived growth factor (PDGF) is one of the most potent promoters of the proliferation and migration of the SMC. The heterocyclic quinones represent an important class of biologically active molecules. However, the inhibitory activity of quinone classes on the proliferation of the SMC has not been reported. Therefore, we synthesized and tested various quinone derivatives to elucidate their contribution to the antiproliferative effects on PDGF-stimulated SMC proliferation. Among the quinones tested, 4,7-benzimidazoledione derivatives showed the potent antiproliferative activity.

[PD1-35] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Efficient Total Synthesis of (-)-Antofine by Using (R)-(E)-4-(tributylstannanyl)but-3-en-2-ol as a Chiral building block

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(-)-Antofine is phenanthroindolizidine alkaloid being isolated from *Cynanchum vincetoxicum*. It has powerful cytotoxicity toward drug-sensitive KB-3-1 and multidrug resistant KB-V1 cancer cell line. We have successfully accomplished stereoselective total synthesis by using palladium catalyzed Stille coupling of 10-bromomethyl-