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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 prostrate 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-

2,3,6-trimethoxy-phenanthrene and (R)-(E)-4-(tributylstannanyl)but-3-en-2-ol, Overmann rearrangement of imidate, and RCM(ring-closing metathesis) for construction of pyrrolidine.

[PD1-36] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Studies on the Regioselective of Chlorosulfonyl Isocyanate with Cyclic ethers

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The synthesis of various cyclic carbamate compounds and amino alcohols has attracted attention in the past because of their potential as antibiotics, antitumor, analgenics, anticonvulsants. Several methods for the preparation of cyclic carbamate compounds have previously been reported including the use of heterocumulenes. 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 S_N1 and S_Ni mechanisms according to the stability of carbocation intermediates. In the present, we developed the regioselective one-pot synthetic method for the corresponding cyclic carbamates from various cyclic ethers using CSI. This presentiton, we will describe the CSI reaction with three, four, five-membered cyclic ethers to give five, six, seven-membered cyclic carbamates, which can be converted to various amino alcohols.

[PD1-38] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Synthesis of 2-Oxo-4-quinolines Using One-pot Reaction for Novel Flavonoid Derivatives

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We report the synthesis of 3,4-dihydro-2-oxo-4-quinolines 5a-e for the development novel flavonoid derivatives with potential antiinflammatory activity and propose a mechanism of the one-pot reaction. The various amines (1a-e) for this work were commercially available. We isolated that ester (2a-e) were formed by nucleophilic attraction using ethyl benzoylacetate. The C-N bond formation proceeded at refluxing in toluene with catalytic amount of p-toluenesulfonic acid and a removal of water and ethanol was important in this reaction. Esters 2a-e were converted to 2-oxo 4-quinolines (3a-e) in toluene after removal of water using Dean-Stark apparatus. Synthetic process from amine (1a-e) to 3,4-dihydro-2-oxo-4-quinolines 5a-e could be carried out in one-pot without isolation of intermediate (2a-e) and 2-oxo 4-quinolines 3a-e. 3,4-Dihydro-2-oxo-4-quinolines 5a-e were generated during the standing at rt or recrystallization. One-pot condensation with dehydration could be convenient synthetic method, gives 3,4-dihydro-2-oxo-4-quinolines 5a-e.

[PD1-39] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

First Total Synthesis of (-)-Antofine by Using Catalytic Phase Transfer Alkylation.

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Phenanthroindolizidine alkaloid, (-)-antofine has attracted attention because of its extremely potent inhibition of cancer cell growth (Its IC_{50} values have the low nanomolar range). The frist asymmetric total synthesis of (-)-antofine is described. An important feature of this synthesis is the creation of a stereogenic center by enantioselective alkylation using the phase transfer catalyst (PTC) and ring-closing metathesis (RCM) for pyrrolidine ring construction. This synthesis is efficient to allow the asymmetric preparation of other naturally occurring phenanthroindolizidine and phenanthroquinolizidine alkaloid.