

[PD1-1] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

A New Synthesis of Hydantoin derivatives by the Reaction of Unnatural Amino acids with Potassium Isocyanate

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Since two selective COX-2 inhibitors, celecoxib and rofecoxib, showed good biological activity as antiinflammatory agents, many medicinal chemists are interested in specific COX-2 inhibitors. The distinguished feature of these drugs is that the 5-membered heterocycle ring is substituted with two aryl groups. Therefore, in this study, we designed a new hydantoin derivatives via the reaction of unnatural amino acids as selective COX-2 inhibitors. In systematically steps, 5-phenyl-1(or substituted) hydantoin derivatives were prepared through esterification, bromination, C-N bond formation, cyclization from phenyl acetic acid. Particularly, a novel hydantoin ring was converted from unnatural amino acids with potassium isocyanate. In last step, the final analogs were synthesized the substitution at 3-position with alkyl reagents.

[PD1-2] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Template Synthesis of New Polyazamacrocycles

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Interest in the synthesis and chemistry of multidentate macrocyclic ligands is currently very high. Synthetic macrocycles arise from the fact that many biologically important molecules are metal complexes of macrocyclic organic systems; and in order to understand the mechanism of action of the naturally occurring complexes, chemists have resorted to the synthesis and study of so-called model systems. Macrocyclic ligands and their metal complexes can be used as models for protein-metal binding sites in a substantial array of metalloproteins in biological systems, as synthetic ionophores, as models to study the magnetic exchange phenomena, as therapeutic reagents in chelate therapy for the treatment of metal intoxication, and as cyclic antibiotics that owe their antibiotic actions to specific metal complexation. We represent several kinds of new synthetic macrocyclic complexes and their X-ray crystal structures.

[PD1-3] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Design and Synthesis of Thioureas as Capsaicin Receptor Antagonist

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Capsaicin is hot taste ingredient of chili pepper and was isolated in 1876 and in 1919 its structure is sympathized compound, induces pain and when persistently dosed, the fact will bring insensible condition to other chemical and mechanical thermal stimulation by incapacitating sensory neuron is known. The analgesic effect by desensitization of such capsaicin is differ from the mechanism by analgesic action by opiate receptor of the existing analgesia or by prostaglandin mediation and the efficacy was known as similar with morphine. Since therefore, the analgesic action of capsaicin is local and may become a good pioneer substance for development of non-narcotic analgesia having more excellent analgesic efficacy with new mechanism may overcome limit of the existing non-narcotic analgesia which is weak. However, in case of agonist to bind with VR1 and will result extinction of sensory neuron due to persistent depolarization and so, development of capsaicin receptor antagonist is seriously required. Therefore, in this study designed and synthesized a series of compounds which have thiourea group through the

structural formula of compound shown activity of antagonist by continuation of study of capsaicin receptor antagonist which has been progressed in the laboratory in the meantime.

[PD1-4] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Structure-Activity Relationship Study of Asiatic Acid Derivatives for New Wound Healing Agent

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Centella asiatica is an herbal plant used on different continents by diverse ancient cultures and tribal groups. Historically, the extract has been used as a wound healing agent. The extract has three different triterpenoid ingredients: asiaticoside, asiatic acid, and madecassic acid. It has been reported that its wound healing activity is associated with the modulation of collagen synthesis in the skin dermis. The wound healing property of the extract has led to its commercial introduction under the trade name, Madecassol. As part of our program toward the development of new wound healing agents, structure activity relationship (SAR) studies have been performed by modifying asiatic acid. In this communication, the SAR study of asiatic acid for the development of an efficient wound healing agent is reported.

[PD1-5] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

The versatile conversion of lactam to the α -alkylated amines via cyclic N,O-acetal TMS ether

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As a part of our continuing studies directed toward the synthesis of the medium to macrolactam alkaloids, we have been interested in the versatile functionalization of the lactam carbonyl. Synthetic routes involving cyclic N-acyliminium ions are generally useful strategies that have been applied for a wide variety of synthetic transformation. Especially, the use of α -alkoxy azacycles as precursors to cyclic N-acyliminium ions was well reviewed. Despite significant progress made in preparation of these intermediate, however, most of these methods have a limitation that it is applicable only to the 5 or 6-membered azacycles, and rarely 7-membered azacycle. In fact, the synthesis of the medium to large sized α -alkoxy azacycle from the corresponding lactam has not been successful due to the considerable difficulty in manipulation of their lactam functionality and the instability of the reaction intermediate. In light of the result that aluminum alkoxide of hemiacetal prepared by DIBAL reduction of esters is more stable than the free hemiacetal, we were able to reduce the medium-sized lactam without lactam ring-opening and trap the resulting N,O-hemiacetal. We herein report a novel and versatile method for the preparation of the stable N,O-acetal TMS ether as an excellent precursor of cyclic acyliminium ions. Moreover, the facile nucleophilic additions of various carbon nucleophiles to the resulting N,O-acetal TMS ether in the presence of the Lewis acid are also reported.

[PD1-6] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Synthesis of Indeno[1,2-c]indenoisoquinoline Derivatives as Potential Topoisomerase I Inhibitors

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During the research for the development of antitumor agents, we found the 3-aryloisoquinoline derivatives exhibited potent cytotoxicity against human tumor cell lines. For extending our study on these compounds, indeno[1,2-c]isoquinolines were chosen as the next research target due to previous studied data of the compounds that showed potent topoisomerase I inhibition activity as well as cytotoxicity against many kinds of tumor cell lines. Retrosynthetic consideration of indeno[1,2-c]isoquinolines indicates that the coupling of α -