

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 $\alpha$ -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  $\alpha$ -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  $\alpha$ -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  $\alpha$ -

methyltoluamide with *o*-hydroxymethylbenzotrile might afford 3-arylisoquinoline which could be transferred to the aldehyde. Indeno[1,2-*c*]isoquinolines can be formed by an intramolecular ring cyclization method. Various derivatives of this compound including 11-alkoxy-6-methyl-6H,11H-indeno[1,2-*c*]isoquinolin-5-one and biological activity will be presented with the docking model with topoisomerase I enzyme.

[PD1-7] [ 10/17/2002 (Thr) 09:30 - 12:30 / Hall C ]

### Design and Synthesis of Apio Nucleosides with Exocyclic Methylene Substituent

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Apio nucleosides belong to unique classes of nucleosides in that 4'-hydroxymethyl group moves to 3'-position. Among these compounds, we found that apio dideoxyadenosine (apio-ddA) exhibited potent antiviral activity and apio-d4A showed potent anti-HCMV activity. Based on these findings, it was of great interest to design and synthesize apio nucleoside analogues with various substituents such as fluoro or azido group. In order to synthesize apio analogues, the glycosyl donor, D-, and L-apio sugar acetates were first synthesized, starting from D-galactose, condensed with silylated N4-benzoylcytosine, and then converted to the final D- and L-nucleosides. Synthesis of the D- and L-apio nucleosides will be presented in detail at the meeting.

[PD1-8] [ 10/17/2002 (Thr) 09:30 - 12:30 / Hall C ]

### Solution-Phase Synthesis of a Library of Biaryl Amides Using Girard's reagent T as an Acid Chloride Scavenger

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An efficient process for the solution-phase synthesis of biaryl amides has been developed. Girard's reagent T, an inexpensive scavenger, was found to be very efficient in trapping excess aromatic acid chlorides, resulting in water soluble by-products, which were easily removed from the products by liquid-liquid extraction. The ease of use, and the excellent purity of the amide libraries obtained are important features of this protocol.

[PD1-9] [ 10/17/2002 (Thr) 09:30 - 12:30 / Hall C ]

### Regio- & Stereoselective Synthetic Method for Polyhydroxyamines using Chlorosulfonyl Isocyanate

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The interest in polyhydroxyamines is based in their biological activity as enzyme inhibitors, and as starting materials in the synthesis of more complex compounds.

Polyhydroxyamines is that amine group is continuing structurally with hydroxy groups and has become important target of the synthesis strategy because of the chirality control of amine group and each hydroxy groups.

Polyhydroxyamines is a structural unit present in some biologically important compounds such as polyoxamic acid, codonopsinine, deoxynojirimycin, castanospermine, detoxinine. They belong to the class of compounds known as polyhydroxylated amino sugars, which proved to be highly effective glycosidase inhibitors.

We have recently described synthetic method for N-protected allylic amines from allyl ethers using chlorosulfonyl isocyanate(CSI) and found that the mechanism of this reaction is based on the stability of carbocation.

Furthermore, we investigated the reactions of various polybenzylethers and CSI, and developed the stereocontrolled CSI reaction condition of various polybenzylethers by varying the solvents and temperature.