methyltoluamide with o-hydroxymethylbenzonitrile 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 thse compounds, we found that apio dideoxyadenosine (apio-ddA) exhibited potent antiviral activity and apio-d4A showed potent anti-HCMV activity. Based on thse findings, it was of great interest to design and synthesize apio nucleoside anlogues 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 scanvenger, 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.

In this presentation, we will report novel regio- and stereocontrolled synthetic method for the precursors of polyhydroxyamines using CSI.

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

Regioselective Substitution of 6,7-Dichloroquinoline-5,8-dione: Synthesis, Cytotoxicity, and X-ray crystal stucture of 4a,10,11-Triazabenzo[3,2-a]fluorene-5,6-diones

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6,7-Dicholroquinoline-5,8-dione reacted with 2-aminopyridine derivatives. Out of the four possible products which could be achieved in this reaction, condensation and rearrangement product, 4a,10,11-triazabenzo[3,2-a] fluorine-5,6-dione was obtained as major product. The definite structure was identified with X-ray crystallographic study. The preparation of ortho-quinones via nucleophilic substitution at C7 position was an unexpected result when considered the para-quinones via substitution at C6 position which prepared in reaction of 6,7-Dicholroquinoline-5,8-dione with ethyl acetoactate in our previous work. The antitumor activity of 4a,10,11-triazabenzo[3,2-a]fluorine-5,6-dione was superior or similar to doxorubicin and much higher than etoposide. Therefore, nucleophilic substitution at C7 position could provide the effective and simple synthetic rout to prepare biologically active ortho-quinone derivatives.

[PD1-11] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Efficient Solid Phase Library Synthesis of 7-Alkoxy-1,3,4,5-tetrahydro-benzo[e][1,4]diazepin-2-one

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The β-turn has been implicated as an important conformation for biological recognition of peptides or proteins. Benzodiazepine classes have been known as one of the nonpeptide β-turn mimic scaffolds. We have developed an efficient approach for the synthesis and derivatization of a scaffold of hydroxytetrahydrodizepinone class in order to screen compound library in various protein targets for new lead generations as well as for structure activity relationships of the scaffold. Amino acid esters and aromatic or alkyl halides for the introduction of amino acid side chains were used for building blocks in the library synthesis. Starting from 5-hydroxy-2-nitrobenzaldehyde, the benzodiazepin-2-one scaffold was synthesized in 4 steps in high yields. The validation of the scheme for the next solid phase derivatization of the scaffold has been expedited in a solution phase synthesis using a solid support mimic group, which was 2,4,6-trimethoxybenzaldehyde. After the validation, the scaffold was loaded in PL-FDMP resin through reductive amination and the alkylations of 7-hydroxyl and amide nitrogen were accomplished. TFA cleavages resulted in the initial 48 members of peptidomimetic library in high yields (50-60% purified yield, for the 4 step solid phase synthesis).

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

Synthesis and hypoglycemic Activity of the Substituted Pyrrolidine Thiazolidinedione Derivatives

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Non-insulin dependent diabetes mellitus (NIDDM) is characterized by hyperglycemia, hyperinsulinemia, and impaired insulin action. Insulin resistance is considered to be the underlying mechanism in the pathogenesis of