α- and β-amino acids, different alkaloids and carbohydrate derivatives.
Therefore, we developed novel synthetic method for N-protected allyl amines from allyl ethers using chlorosulfonyl isocyanate(CSI) via the stable allylic carbocation and allylic rearrangement.
In this presentation, we will report the regioselective synthesis of allyl carbamates from allyl ethers using CSI.
As one of our results, the reaction of 4-phenyl but-2-enyl methyl ether with CSI afforded methyl N-(4-phenyl but-2-enyl) carbamate and methyl N-(1-benzyl allyl) carbamate in a 1 : 1.1 ratio, on the other hand, (1-benzyl allyl) methyl ether afforded in 4.6 : 1 ratio.

[PD1-6] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Synthesis and in vitro cytotoxic activity of isoindoloquinolines

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Doxorubicin is an important "lead" structure because it possesses broad-spectrum activity against various tumors. This is one of the most widely used intercalating agent since the approval by the FDA in 1974. However several undesirable side effects and the appearance of resistance limit its clinical usefulness.
Twelve isoindolo[5,6-g]quinolines incorporating hydrophobic DNA-interacting or H-bonding functionality were designed based on the structure-activity relationship of azaanthraquinones and structural analysis of products which are fitted with doxorubicin. These compounds were synthesized using a Diels-Alder reaction and a high pressure oxidative reaction as key steps. They were evaluated in vitro against human tumor cell lines. These compounds had less potent cytotoxic activity than the doxorubicin. The cytotoxic activity of the compounds containing substituted aromatic ring substituent are more potent than that containg phenyl substituent or propyl substituent Especially, compounds containing 2-methoxyphenyl substituent are the most potent in this series.

[PD1-7] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Structure-Activity Relationship Study of Asiatic Acid Derivatives Against Beta Amyloid (Ab)-induced Neurotoxicity

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Dementia of Alzheimer's type in the elderly has become the main social problem. Recently it has been reported that the most important pathological hallmark of Alzheimer's disease (AD) is deposition of senile plaques in the brain. The senile plaque consists of diverse molecules but the major component is beta-amyloid (Ab) protein which is concentrated in the plaque core. Based on these results, the abnormal overproduction of Ab has been proposed as a cause of AD. Centella asiatica is one of herbal plants used in different continents by diverse ancient culture and tribal groups. Historically, the extract has been used as a wound healing agent, and brain tonics for the mentally retarded. The extract has three different triterpenoid ingredients; asiaticoside (1), asiatic acid (2), and madecassic acid (3). In this poster, the primary structure activity relationship (SAR) study of asiatic acid against Ab-induced neurotoxicity were reported.

[PD1-8] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Studies On the Synthesis of Antidiabetic Agents

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Type 2 diabetes is commonly called non-insulin-dependent diabete mellitus(NIDDM).
NIDDM is characterized by diminished insulin secretion relative to serum glucose level and by peripheral insulin resistance, both of which can be exacerbated by chronic hyperglycemia and improved by euglycemia.
Rosiglitazone, pioglitazone, and troglitazone, a new class of antihyperglycemic agents, reduce insulin resistance or potentiate insulin action in genetically diabetic animals.
We are in the process of synthesizing troglitazone type of compound in which vitamin E moiety was replaced with catechin.

[PD1-9] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Synthesis of Asiatic Acid Derivatives and their Hepatoprotective Activity

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Hepatopathia has become one of the main social problems in the world. But the considerably effective hepatopreventive agents or drugs for the treatment of hepatic disease have not been introduced. Recently it was reported that some triterpenoids have been extensively studied as hepatopreventive agents. Asiatic acid is one of the triterpenoid isolated from Centella asiatica whose extract was used as a wound healing agent. In our research program for the discovery and development of novel hepatopreventive agents, a series of asiatic acid derivatives was synthesized and evaluated hepatopreventive activities against CCl_4 or galactosamine-induced hepatotoxicity. For the modification of asiatic acid, structure of A or B ring in asiatic acid was modified. Some of the prepared compounds showed better hepatopreventive activity than silybin against CCl_4 or galactosamine-induced hepatotoxicity. The structure-activity relationships of prepared compounds would be further discussed.

[PD1-10] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Synthesis and Structure Activity Relationships of Quaternary Ammonium Cephalosporins with 3-triazolylpyridinium Derivatives.

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The various 3-(triazol-3-yl)pyridine derivatives possessing hydrogen, methyl, thiomethyl, hydroxy, amino group at the C-5 position and hydrogen, methyl, hydroxyethyl group at the C-1 position on triazole ring were synthesized. These novel substitued 3-(triazol-3-yl)pyridine derivatives were coupled with cephalosporin moiety to produce a new series of cephalosporin antibiotic and their antibacterial activity against Gram-positive and Gram-negative was inspected. We discovered that their analogs display comparable antibacterial activity against Gram-positive and Gram-negative bacteria.
We will describe the relationship between the structure and activity of Quaternary Ammonium Cephalosporins with 3-triazolylpyridinium Derivatives tested.