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

Synthesis of novel compounds for the inhibition of TNF-α production

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Tumor necrosis factor-α (TNF-α) is an important cytokine produced by activated monocytes/macrophages. If TNF-α is produced in excess and not regulated properly, many diseases like Crohn's disease, toxic shock syndrome, cachexia or rheumatoid arthritis occur. There is a widely accepted belief that inhibition or modification of TNF-α overproduction in different inflammatory diseases would be of benefit in the treatment of some of these conditions. Therefore, inhibitor on TNF-α production is now being studied extensively for therapeutics against the above diseases. This study describes the synthesis, in vitro evaluation and molecular modeling study of novel compounds for the inhibition of TNF-α production. Among these compounds, 2-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-isoindolinone was selected as a lead compound and 3-methyl and 3-azido-2-(3-Cyclopentyloxy-4-methoxy-phenyl)-2,3-dihydro-isoindol-1-one derivatives had comparable inhibitory activity of TNF-α production.

[PD1-4] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Efficient Synthetic Methods for Macrocyclization of polypeptide

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We can see that there are many spotlights on peptide drugs by examining the recent trend in drug development. For example, drugs like cyclosporin shows striking activity as an autoimmune suppressor. Especially, cyclic peptides stands out among all other peptides as a good drug. That is why we are trying to develop more effective cyclization process.
There are three ways to cyclize certain sequences of amino acids such as Gly-Met-Ile-Phe-Gly. First is head-to-tail cyclization method, linking between N-terminal and C-terminal. Second method utilizes amino acid side chain such as thiol functional group in Cys, making a thioether bond. The last one includes an application of resin-substituted amino acids in solid phase reaction. Among the three methods, solid phase reaction showed the greatest yield.

[PD1-5] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Regioselective Synthesis of Allyl Carbamates from Allyl Ethers

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Allylamines are fundamental building blocks in organic chemistry and their synthesis is an important industrial and synthetic goal. The allylamine fragment can be encountered in natural product. Thus allylamines have been used as starting materials for the synthesis of numerous compounds such as

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