In the present work about the synthesis and biological activities of new apicidin derivatives which are analogues of apicidin isolated from Fusarium sp., we have discovered that some apicidin and derivatives have mild antitumor activity, which caused the change of tumor cells morphology to return to normal cells. As part of our program toward the development of new antitumor agents, we established its efficient synthetic route, synthesised its derivatives systemically, and then studied their structure-activity relationships. At present, we modified the ketone moiety of apicidin to various imine derivatives. Synthesis and biological activities of our new apicidin derivatives will be presented in detail.

[PD1-19] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Enantioselective synthesis of (S)-N,N-diethyl-2-formyl-2-(methoxymethoxy) butyramide, a key intermediate for 20(S)-camptothecin analogues, via asymmetric bromolactonization

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A new enantioselective synthetic method for enantiomerically pure (S)-N,N-diethyl-2-formyl-2-(methoxymethoxy)butyramide, a versatile key intermediate of camptothecin has been developed employing asymmetric bromolactonization using (S)-proline as the chiral auxiliary.

[PD1-20] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

One-Pot Synthesis of Cinnamylamines with various Protecting Groups from Cinnamyl Ethers

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Carbamates have been widely used in peptide and protein synthesis as a protective group of the amines, and also used as biologically active compounds in the field of medicine and pharmaceutical industry. Especially, carbamate moiety is frequently introduced for the derivatization of lead compound in medicinal chemistry. Representative protecting groups for this purpose are the Boc, the Cbz, the Moc, the iPoc, the Pnz, the Moz), the Troc and the Aloc group. Because of their important roles, continuous efforts have been made to obtain carbamates through simple and efficient methods.
Our studies are based on the observation that various carbamates are formed from cinnamyl alkyl ethers using CSI in accord with the alkyl moiety of the cinnamyl alkyl ethers.
The reaction of various cinnamyl alkyl ethers with CSI afforded the corresponding cinnamylamines with various protecting groups, such as -NHMoc, -NHiPoc, -NHCbz, -NHPnz, -NHTroc and -NHAloc. In the case of cinnamyl t-butyl ether and cinnamyl p-methoxybenzyl ether, the corresponding cinnamyl carbamates were formed via a different reaction pathway from the above.

[PD1-21] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

The Synthesis and Antibacterial Activity of Mansonone F, a Potent Anti-MRSA Sesquiterpenoid Quinone, and its structural analogues

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During the last two decades, the increasing prevalence of antibiotic-resistant bacteria has had an enormous impact on infection control policies. In particular, the resistances to multiple antibiotics of strains of Gram-positive Staphylococci, methicillin-resistant Staphylococcus aureus (MRSA), are now significant clinical problem. Even though vancomycin and teicoplanin, a class of glycopeptide antibiotics, are widely used clinically in the treatment of MRSA infections, the structural complexity and toxic side effects of these antibiotics have prompted increased efforts to find and investigate new and effective antibiotics.

Towards this end, we have recently reported the isolation of a potent anti-MRSA sesquiterpenoid ortho-quinone, mansonone F, from the Korean medicinal plant which has traditionally been used to treat infectious diseases. It has been shown to have antibacterial activities against Gram-positive bacteria and, in particular, MRSA (with an MIC90 of 2 mg/ml in vitro), comparable to vancomycin. Mansonone F is structurally simple and unique ortho-naphthoquinone with conjugated tricyclic ring skeleton, and its energy-minimized structure turned out to be complete flat and highly strained.

In continuation of pharmacophore identification and investigation into the structure-anti-MRSA activity relationship of sesquiterpenoids based on the natural mansonone F, the systemically modified analogues of mansonone F were synthesized and assayed against MRSA strains.

Consequently, we have established the partial structure-activity relationship of mansonone F.

[PD1-22] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthesis and in vitro Antibiotic Activity of C-9 modified Derivatives of Erythromycin A.

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Since its discovery by Mcgurie et al. in 1952, erythromycin A (EM-A) has been the most widely used against many diseases, owing to its safety and effectiveness, especially respiratory tract infections. A major drawback to erythromycin is its instability in the acidic medium of the stomach. To minimize the acid instability and improve the activity, C-9 modified derivatives of erythromycin A were designed. The improvement of activity of erythromycin 9-oxime against gram-positive bacteria by introducing phenyl groups and isoxazole groups into the aliphatic chain was attempted. And also phenyl substituents were introduced at the C-9 position of erythromycin for forming C=C bond instead of C=O bond. Thus, prepared antibiotics were evaluated biologically by measuring the minimum inhibitory concentrations (MIC) against various bacterial strains. This new class of macrolide antibiotics showed reduced MIC value compared with those of erythromycin A and clarithromycin.

[PD1-23] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Lupane Derivatives Bearing Aminoacetyl Moiety

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Lupane derivatives showed good cytotoxic activity and it was reported that their cytotoxic activity mainly