

almost comparable cytotoxicity to adriamycin and (E)-methyl/ethyl 3-[2-(1,4-dimethoxy-5,8-dione)naphthalenyl]-2-propenoates showed strong cytotoxicity against various solid tumor cell lines.

[PD1-6] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Cinmetacin유도체의 합성과 진통항염활성

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Nine cinmetacin derivatives as potential nonsteroidal analgesic and antiinflammatory compounds were prepared and their analgesic-antiinflammatory activity was compared with cinmetacin. Salicylic acid and phenols were reacted with DCC to give phenyl saicylates. Cinmetacin was treated with DCC and phenol derivatives to yield cinmetacin esters. Some of compounds showed stronger analgesic activity than cinmetacin, but only one compound showed comparable antiinflammatory activity to cinmetacin.

[PD1-7] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Design and Synthesis of Isoindoloquinoline Derivatives as Potential Antitumor Agents

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The azaanthraquinones are a new class of antitumor agents that exhibit promising in vitro and in vivo activity against a wide spectrum of tumor cell lines. In an effort to develop novel antitumor intercalating agents that could overcome the shortcoming of anthracyclines, we recently reported the synthesis and biological evaluation of some azaanthraquinone derivatives and continued our efforts to design the related compounds.

In this study, we describe synthesis of a series of isoindoloquinoline derivatives. These were designed based on the structure-activity relationship of azaanthraquinones and structural analysis of products which are fitted with doxorubicin. A Diels-Alder reaction and a high temperature and pressure oxidative reaction were used as key synthetic steps.

[PD1-8] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Formation of Carbamates: Comparison of the Stability of Various Carbocations via CSI Reaction

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The cinnamyl alkyl ethers were treated with chlorosulfonyl isocyanate (CSI) to afford the corresponding N-protected allylic amines as a mixture of regioisomers. However, in the case of cinnamyl t-butyl ether, the corresponding allyl carbamate was obtained rather than N-allylcarbamates as a single product. These results may be rationalized by suggesting that the reaction pathways are determined in accord with the stability of carbocations obtained during the reaction process. From these results, we

developed novel technique to determine the stability of carbocations in solution phase by simple CSI reaction and set up the stability order of carbocations. And also various N-protected amines (carbamates) have been synthesized from ethers using CSI reaction in one pot.

[PD1-9] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Synthesis and antiviral activity of novel C-methyl-substituted cyclopropyl nucleosides

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Recently, new classes of nucleoside analogues framed of core cyclopropyl backbone, such as synadenol, synguanol, and trisubstituted cyclopropyl nucleoside (A-5021) was found to be potential antiviral agents by Zemlick et al and Sekiyama et al, respectively. On the basis of these findings, we became interested in the antiviral activities of C-carbon-substituted acyclic nucleosides and synthesized a series of methyl-C-branched-chain cyclopropyl nucleosides. To synthesized the targeted nucleosides, D-isopropylidene glyceradehyde was reacted under Wittig reaction using triethyl phosphonopropionate to give (E)- α,β -unsaturated methyl ester. The ester was reduced to ethanol and reacted with TBDPS-Cl to protect hydroxyl group and followed by Simonns-Smith reaction to give the desired cyclopropyl derivatives in high yield. The cyclopropyl intermediate was deprotected to give free alcohol which was activated by tosylation and followed to S_N2 reaction with purine bases in the presence with potassium carbonate and crown ether in CH₂Cl₂. Its isopropylidene group was removed by CH₃COOH/MeOH to give the diol nucleoside which was reacted with NaIO₄ and followed by the reduction to give an alcohol in high yield.

The antiviral activities of the nucleosides against HSV-1, HSV-2 and HIV-1 were also examined in vitro. Among the synthesized nucleosides, only adenine nucleosides was moderate active against HIV-1 without showing significant toxicity to the host cell.

[PD1-10] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Synthesis of Peptidyl α -Ketoesters as Inhibitors of Proteases

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It has been reported that the compounds containing electrophilic carbonyl group could form a stable tetrahedral intermediate with the residue in the active site of the proteases. Recently, it has been reported that peptidyl α -ketoesters showed potent inhibitory activity on HCV NS3 protease, belonging to serine protease family. In order to be a potent and specific HCV NS3 protease inhibitor, the binding residues of an inhibitor should be carefully designed based on the structure of substrate recognition unit (S1~S4).

In this presentation, we will discuss on the preparation of tetra-peptidyl α -ketoester library in an attempt to discover a potent and specific inhibitor for HCV NS3 protease. The diversity was obtained by introducing various building blocks such as natural and non-natural α -amino acids as P2~P4 unit and β -amino- α -ketoesters as P1 unit. A series of β -amino- α -hydroxyesters were synthesized from α -aminoacid, and then P2~P4 building blocks was introduced stepwise at the N-terminal site of these α -hydroxyesters. The resulting tetra-peptidyl α -hydroxyesters were oxidized to generate tetra-peptidyl α -ketoesters.