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 acycic nucleosides and synthesized a series of methyl-C-branched-chain cyclopropyl nucleosides. To synthesized the targeted nucleosides, D-isoproylidene glyceradehyde was reacted under Witig 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 CH_2Cl_2. Its isopropylidene group was removed by CH_3COOH/MeOH to give the diol nucleoside which was reacted with $NaIO_4$ 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 Peptydyl 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 bulding blocks was introduced stepwise at the N-terminal site of these α-hydroxyesters. The resulting tetra-peptidyl α-hydroxyesters were oxidized to generate tetra-peptidy α-ketoesters.