Synthesis and Antiviral Activity of D-2'-azido-2',3'-dideoxy-arabinofuranosyl-4'-thiopyrimidines and purines

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Since the efficient synthesis of 4-thiosugar has recently been developed, many 4'-thionucleoside analogues have been synthesized and evaluated for antiviral and antitumor activities. From the conformational analysis of 4'-thionucloesides by X-ray or molecular modeling, their conformations were found to be very similar to those of the 4'-oxonucleosides. Based on these findings, we synthesized various 2'-azido-2',3'-dideoxy-4'-thiopyrimidine and purine nucleosides via 2'-azido-2',3'-dideoxy-4'-thiosugar acetate as a key intermediate from L-xylose because 2'-azido-2',3'-dideoxy-4'-oxonucleosides gave been reported to show very potent antiviral activities. Introduction of the azido group was achieved using a Mitsunobu reaction and anomeric acetate was obtained from a Pummerer rearrangement. Synthesis and antiviral activities of the target nucleosides will be presented in detail in the symposium.

[PD1-27] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthesis, Biological Activity and Comparative Analysis of Cytotoxicities and Human Topoisomerase I Inhibitory Activities of Isoquinoline Compounds

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Topoisomerase I promote the relaxation of DNA superhelical tension by introducing a transient single-stranded cleavage in DNA and are essential for the processes of replication, transcription, and recombination. Recently, the crystal structure of this enzyme revealed the core domain and the first eight residues of the carboxyl-terminal domain of the enzyme, including the active site nucleophile tysosine-723 share significant structural similarity with the DNA integrase. A binding mode of action for the anticancer 3-arylisoquinolines was proposed on the basis of chemical and biochemical information combined with the structure of topoisomerase I - DNA complex. We performed the synthesis of 3-arylisoquinolines as a topoisomease I inhibitors and compared the cytotoxic activities against human tumor cell lines.

[PD1-28] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Chiral Supply for Functionalized Four Carbon Unit from The Enzymatic Resolution

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We prepared isomers of functionalized four carbon unit by biotransformation as a key step3-Benzyloxylmethyl-oxiramylmethanol was prepared from 2-butene-1,4-diol.Acetate-protected 3-benzyloxymethyl-oxiranylmonomethyl ester was obtained by biotransformation with lipase in organic solvent(toluene, etc). We also prepared an aldehyde, 4-benzyloxy-but-2-enal from (3-benzyloxymethyl-oxiranyl)-methanol with oxidative reagents. In this oxidative stage cis-olefine was isomerized to be turned out as trans-olrefin. We can easily gain four functionalized carbon compounds which can be used for futher complicated chiral compound synthesis.