diastereomeric mixtures.

[PD1-5] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthesis and Antitumor Activity of 4'-O-Aminoacyl-, Carbamate-, and Carbonate Prodrugs of 4'-Demethyl-1-Deoxypodophyllotoxin

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Deoxypodophyllotoxin (DPT), first isolated from *Anthricus sylvestris* is a potent inhibitor of mitosis, and showed a potent cytotoxic activity against a wide variety of cancer cell lines. But, DPT still did not show a potent antitumor activity comparable to its potent cytotoxic activity. This was considered to be due to poor aqueous solubility and bioavailability of DPT. To obtain compounds with pharmaceutically acceptable properties and improved antitumor activity, we designed 4'-demethyl-1-DPT derivatives in which the methyl group at 4'-position was replaced with various aminoacyl, carbamoyl, oxycarbonyl groups. Among them, 4'-demethyl-4'-*O*-(8-aminooctanoyl)-1-DPT, 4'-demethyl-4'-*O*-(2-hyroxyethylcarbamoyl)-1-DPT, and 4'-demethyl-4'-*O*-(2-chloroethylcarbonyl)-1-DPT showed inhibition ratio (IR) of 87%, 95%, and 89%, respectively, much higher than the IR (78%) of etoposide which was used as positive control.

[PD1-6] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Stereoselective synthesis hydroxylated cyclopentane carbocycle for nucleosides via sequential Claisen rearrangement and RCM reaction

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Extensive efforts in the search of chemotherapeutic agents against viral infection and cancers have led to the discovery of a variety of biologically active nucleoside analogs, including carbocyclic nucleosides (i.e. abacavir).
As part of our drug discovery program, we have determined to synthesize carbocyclic nucleosides with hydroxy group at 5'-position. Herein, We would like to introduce synthetic method of cyclopentane carbocycle intermediate for the synthesis of 5'-hydroxy carbocyclic nucleosides using sequential Claisen rearrangement and ring closing metathesis from D-mannitol.

[PD1-7] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthetic Approaches to the Generation of New COX-2 Inhibitor through the Modification of Indomethacin

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All nonsteroiddal antiinflammatory drugs(NSAIDs) inhibit coclooxygenase(COX) isoenymes to different extents, which accounts for their antiinflammatory and analgesic activities and their gastrointestinal(GI)