The Friedlaender reaction was first introduced in 1882 for the preparation of quinoline from *o*-aminobenzaldehyde and acetaldehyde and has long been employed for the construction of quinoline nucleus in a variety of polyaza cavity-type molecules, as well as biologically important molecules. Even such a variety of applicability, the scope of the Friedlaender reaction is somewhat limited for the preparation of some substituted quinolines such as hydroxyquinolines and quinoline carboxylic acids. The Niementowski reaction, a reaction of anthranilic acid with a ketone to form a 4-hydroxyquinoline ring, thus introduced to overcome such a limitation. Additionally, the Niementowski reaction can also apply for the the construction of quinazoline nucleus by using lactam instead of ketone. Although many variations of reagent and reaction condition have been introduced to extend the applicability of the Niementowski reaction, the scope of the Niementowski reaction still remained limited presumably due to the severe reaction condition.
As a part of our interests to develop an efficient procedure for the synthesis of heterocycles, we reinvestigate the Niementowski reaction. We herein describe a modified procedure that may have general pplicability for the synthesis of 4-hydroxyquinoline as well as quinazoline derivatives.

[PD1-38] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Deoxypodophyllotoxin Derivatives With Potent Antitumor Activity

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Etoposide, developed from podophyllotoxin (PT), is an antitumor drug available in the clinic. Deoxypodophyllotoxin (DPT), demethylated form of PT, shows very strong cytotoxic activity in vitro but it exhibits a weak activity in vivo. The weak water solubility and the higher possibility by first pass metabolism might be the problems to be overcome.
Three group of thirty five DPT derivatives were synthesized with an anticipation that the esters with bulky group could be durable against esterases in the body resulting in the reduction of first pass metabolism: thirteen alkyl esters, six carboxyalkyl ester, and sixteen alkenoyl esters, The cytotoxic activities against two cancer cell lines, SK-MEL-2 and A-549, and in vivo antitumor activity on LLC in BDF1 mice as solid tumor model were evaluated.
As a results, the alkyl esters showed potentiated cytotoxic activity with some increase in antitumor activity. The striking increase in antitumor activity was observed by alkenoyl esters with easier solublization in injection medium (DMSO/cremophore/water, 5:25:70): DFE12, 4'-O-(all-cis-11,14-eicosadienoyl)-DPT, was selected for more studies due to better antitumor activity than positive control, etoposide, without toxicity.

[PD1-39] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Asymmetric Synthesis of Amino-Substituted Apio Dideoxynucleosides as Potential Anti-HBV Agent

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Apio dideoxynucleosides in which 4'-hydroxymethyl group moves to C3' position exhibit interesting biological activity like anti-HIV activity. Recently, we have reported the synthesis of racemic amino or azido substituted apio dideoxynucleosides as potential antiviral agents, among which adenine derivative, (±)-LJ-45 was found to be active against hepatitis B virus (HBV). Since biological activity of racemic mixture generally resides in one enantiomer, it was of interest to synthesize each enantiomeric pure form of (±)-LJ-45 and to find out which enantiomer is responsible for anti-HBV activity of (±)-LJ-45. For the synthesis of enantiomeric pure stereoisomer, we utilized Seebach's chemistry to fix the