ER-35786, FR-21818, and IH201 are under clinical or preclinical stage.
We carried out the chemical modification on the pyrrolidine side chain of BO-2727, showing the potent antibacterial activity and high stability to DHP-I. To this end we tried the introduction of cyclic isoxazolidine, isoxazoline, and isoxazole derivatives via 1,3-dipolar cycloaddition reaction of 2-vinylpyrrolidine with nitrone and nitrile oxide instead of acyclic side chain of BO-2727 to give the rigid conformation. It was known that carbapenem derivatives directly linked with isoxazolidine or isoxazoline ring at C-2 position showed potent antibacterial activities.
We describe the synthesis of the 1β-methylcarbapenems containing 5'-isoxazolo-pyrrolidin-3'-ylthio derivatives as C-2 side chain and their biological properties.

[PD1-27] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

The new pyridopyrimidine derivatives as a PDE IV inhibitors

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A novel series of pyrido[2,3-d]pyrimidine compounds exhibiting selective inhibition for phosphodiesterase IV (PDE IV) were designed and synthesized by the reaction of 6-amino-5-iodo-1-methyl uracil with DMF-dimethylaceral, followed by reaction with various olefins in presence of a catalytic amount of Pd(OAc)2and K2CO3 in DMF at 100 oC to give the title compounds. Biological inhibitory potency for these compounds was evaluated as a PDE IV inhibitors. The result will be discussed.

[PD1-28] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

An efficient and selective 1-N-monoethylation of sisomicin : Process development of netilmicn(1-N-ethylsisomicin

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An efficient, newly improved practical synthetic method for the 1-N-ethylsisomicin (Netilmicin), a highly effective antibacterial agent for the refractory Psudomonas aeruginosa infections, was described. Sisomicin in starting material was converted to the 3,2',6'-triacylprotected sisomicin by chelation method, the tri-blocked sisomicin was reacted with mixture of sodium borohydride and acetic acid in methanol, which is a new reagent for selective mono ethylation at 1-aminogroup of sisomicin and new process suitable for mass production of netilmicin under less sensitive to air and moisture. Development efforts focus in optimizing mono-alkylation conditions having little by-product was achived in 87~96% yield. In this presentation, the results will be discussed.

[PD1-29] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Synthesis and Structure-Activity Relationship of Non-peptide FPTase Inhibitors

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