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7-Acylamino-3-(isoxazolylmethylthio)-3-cephem-4-carboxylic acids or their pharmacologically acceptable salts were synthesized and their antibacterial activities against Gram-positive and Gram-negative were inspected. We discovered that their analogs exhibited a wide spectrum against Gram(+) and Gram(-) including MRSA.
We will describe the relationships between the structure and activity of these novel Cephalosporins with 3-isoxazolylmethylthio Derivatives.

[PD1-6] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

The Development of New Carbacephem Antibiotics

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Carbacephem is one of β-lactam antibiotics having a broad spectrum of antibacterial activity. So numerous methods for constructing carbacephems have been reported. In this study, we describe a new route to the synthesis of trans-carbacephem moiety and derivatives. The total synthesis of trans-carbacephem was starting from trans-oxazoline. Key stages in the strategy involved (i) the use of hydrogenation gave a cleavage of trans-oxazoline (ii) formation of β-lactam ring was prepared using the Mitsunobu reaction (iii) six-membered ring of carbacephem was prepared by a Dieckmann-condensation.

[PD1-7] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Synthesis and antiviral activity of novel exomethylene cyclopropyl nucleosides

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Some novel exomethylene cyclopropyl nucleosides were synthesized as analogues of Synadenol derivatives to find potent antiviral agents. The intermediate, Feist's acid was prepared from α-ethy acetoacetate by three steps. The key cyclopropyl compound was obtained via esterfication, reduction, and the partial protection by using TBDPS-Cl, bulky protecting group which was activated by tosylation. Its condensation with pyrimidine and purine bases in the presence of potassium carbonate and a crown compound and its deprotection by using n-Bu4NF gave their corresponding cyclopropyl nucleosides. All the synthesized compounds were evaluated for antivira activity. However, none of them showed any antiviral activity against HSV-1, HSV-2, HCMV, HIV-1, HIV-2, and HBV up to 100 μM.

[PD1-8] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Synthesis and Biological Properties of 7H -Pyrazolo[3,4-d]pyrimidine-Derived Antifolates As Antitumor Agents

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Although methotrexate (MTX) has been in clinic for decades, its side effects limit its usefulness in cancer chemitherapy. Efforts to reduce such unfavorable effect include structural modifications on pteridine nucleus and 1,4-disubstituted benzene moiety of MTX. In addition to such modifications, a new model was introduced as a nonclassical antifolate which does not retain glutamic acid moiety in MTX. Recently, a combination of two strategies resulted in trimetrexate (Neutrexin) and piritrexin (PTX) which showed promising results in clinical trials. The anticancer activity of the latter two stems from the inhibition of thymidylate synthase in nucleotide synthesis while that of MTX comes from the inhibition of dihydrofolate reductase. We herein desribe the design, synthesis and biological activities of 7H-pyrazolo[3,4-d]pyrimidine-based antifolate as potential antitumor agents.

[PD1-9] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Synthesis of [1,2,5]thiadiazole-1,1-dioxides and their cytotoxicities

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Arylsulfonylimidazolidinones 1 have been reported to be potential antitumor agents. According to the study of the structure activity relationship of these compounds, 4-phenyl-1-phenylsulfonylimidazolidinone moiety has been identified as a pharmacophore. However the necessity of planar ureido moiety for their activity has not been fully tested. Therefore, a tetrahedral sulfamide in place of ureido group of 1 was introduced to vary the stereochemistry of their position. Accordingly compounds 2 and 3 were synthesized and tested against human cancer cell lines.

[PD1-10] [10/20/2000 (Fri) 11:30 - 12:30 /[Hall B]]

Optimal Synthesis Condition of Magnesium Trisilicate

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Magnesium trisilicate was prepared by reacting Magnesium chloride solution with Sodium silicate solution in this study. The optimum synthesis conditions base on the yield of the product were established by applying Box-Wilson experimental design. It was found that the optimum synthesis condition of Magnesium trisilicate were as follows; Reacting temperature: 57~90℃ Concentration