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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

of reactant solution: 19.1~29.0% Molar concentration ratio of two reactant: [Sod. silicate]/[Mag. sulfate]:1.47~1.80 Temperature of Washing water: 45~48℃ Drying temperature: 65~82℃ The physical and chemical properties of Magnesium trisilicate as medicine were studied by use of chemical analysis and acid consuming capacitiy mesurements.

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

Synthesis of benzastatin derivatives as plausible antioxidants

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Oxygen is essential for life as the terminal oxidant in cell respiration except for some anaerobic microorganism. The oxygen molecule is usually stable in a normal condition, however it can be converted to the reactive species such as hydroxyl radical, hydrogen peroxide and singlet oxygen under certain chemical or physical conditions. It is well known that reactive oxygen molecule causes cell injury by destruction of cell components. For therapeutic treatment against diseases caused by oxidative damage the lipid peroxidation inhibitors with antioxidative activity and free radical scavenging activity have been used.
Recently, seven benzastatins which have been found to show inhibitory activity against glutamate toxicity and lipid peroxidation in rat liver microsomes were isolated from the culture broth of *Streptomyces Nitrosporeus* 30643. Aiming at the study of structure-activity relationship of benzastatins, we have tried to develop an efficient synthetic method. A novel synthetic process of benzastatin analogs will be presented.

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

Enantioselective synthetic method for 3-hydroxyflavanones: an approach to (2R, 3R)-3',4'-O-dimethyltaxifolin

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A new enantioselective synthetic method for (2R,3R)-3-hydroxyflavanone(1a) was developed via asymmetric dihydroxylation(ADH) and intramolecular Mitsunobu reaction as key reactions and the application to synthesis of (2R, 3R)-3',4'-O-dimethyltaxifolin (1b) is described. By this new synthetic method, (2R, 3R)-3',4'-O-dimethyltaxifolin was prepared from methyl 3,4-dimethoxycinnamate in seven steps(8%, 99% ee).

[PD1-13] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Synthesis of Novel 3-Alkoxy-4-oxo-1,2-benzothiazine Derivatives for COX-2 Inhibitors

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We report the synthesis of key intermediates for dimerization and several 3-alkoxy derivatives and propose a mechanism of the dehydration of alcohols. The 4-hydroxy-2H-1,2-benzothiazine-3-