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[Lab. of Medicinal Chemistry]

A Convenient Method for the Preparation of *N*²-Ethylguanine Nucleosides and Nucleotides.

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*N*²-Et-*d*GTP has been documented to be efficiently incorporated in place of *d*GTP as a substrate for *Escherichia coli* DNA-polymerase I to give the corresponding full-length oligodeoxyribonucleotides. And also, an *N*²-Et-3'-*d*GMP moiety has been reported to be involved in the granulocyte and lymphocyte DNA of alcohol abusers at a high level as the ultimate DNA-adduct of acetaldehyde which is formed as a primary product during the metabolic oxidation of ethanol in the liver. These facts are of interest in relation to the occurrence of cancers of the pharynx, esophagus, and liver in alcohol abusers. To study the molecular mechanisms explaining the carcinogenic effects of the primary metabolite of ethanol, a convenient preparative method for a variety of *N*²-ethylguanine derivatives, involving the regio-selective ethylation of appropriate guanosines by the use of an acetaldehyde-NaBH₃CN system in aqueous methanol and subsequent purification with a reversed phase column at atmosphere pressure, was developed. The present method is applicable to the syntheses of other *N*²-alkylated guanosine derivatives.

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[Lab. of Medicinal Chemistry]

A Facile Synthetic Method for ¹⁵N⁴-Labeled Cytosine Nucleosides.

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Recent advances in heteronuclear NMR spectroscopic techniques on isotopically labeled DNA and RNA oligonucleotides have made it possible to obtain valuable information regarding the dynamic structural features of nucleic acids and their interactions with proteins or xenobiotics in the solution state. Along this line, a variety of methods for the regio-selective ¹⁵N-labeling of purine nucleosides has been developed. On the other hand, the preparative methods for regio-selectively ¹⁵N-labeled pyrimidine nucleosides were still unsatisfactory to use. In the course of our investigations on the chemical modification of purine and pyrimidine nucleosides, the syntheses of ¹⁵N⁴-labeled cytidine and 2'-deoxycytidine were accomplished using the silylation-benzylamination of appropriate uridine derivatives followed by oxidative *N*-debenzylation of the resulting ¹⁵N⁴-labeled *N*-benzylcytidine derivatives with ammonium persulfate in a pH 7.0 buffer solution.

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[Lab. of Medicinal Chemistry]

Highly Increased Cellular Accumulation of Vincristine, a Useful Hydrophobic Antitumor-drug, in Multidrug-resistant Solid Cancer Cells Induced by a Simply Reduced Taxinine.

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Current attention is centered on the rapid emergence of multidrug-resistant (MDR) cancer cells in the chemotherapeutic treatment for various types of advanced solid cancers. This is mainly caused by the over-induction of P-glycoprotein, a cell-membrane transporter for a variety of hydrophobic substrates, during the course of the clinical use of vincristine, paclitaxel, and etoposide which are very useful hydrophobic antitumor-drugs for cancer chemotherapy. After our searches for potent inhibitors of the P-glycoprotein efflux-function to improve the cancer chemotherapy, 5-*O*-phenylpropionylated taxinine A prepared with ease by the catalytic hydrogenation of taxinine, a taxane diterpenoid readily obtainable from the needles of a Japanese yew (*Taxus cuspidata*), was found to be highly effective in increasing the cellular accumulation of vincristine in the MDR human ovarian cancer cells compared with the cases of verapamil, a typical functional inhibitor of the P-glycoprotein, and the previously reported taxoids.

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[Lab. of Pharm. Synthetic Chemistry]

Two Novel Chiral Rhodium Complexes as Catalysts for the Enantioselective Allylation of Arylaldehydes.

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Two novel chiral rhodium complexes were successfully synthesized from the reaction of a new class of bidentate nitrogen ligands with RhCl₃·3H₂O in ethanol under reflux. The crystal structure of **4a** was unambiguously established by X-ray analysis. Their corresponding cationic metal complexes prepared *in situ* from the reaction of **4a** or **4b** with AgBF₄ catalyze the enantioselective allylation of arylaldehydes with allylstannane in 5-50% ee.