

[J. Chem. Soc., Perkin Trans. 1, 833-836 (1994)]

[Lab. of Medicinal Chemistry]

**Synthesis of a Novel 5-Deaza-5-thia Analogue of Tetrahydrofolic Acid,
N-(*p*-[(2-Amino-6,7-dihydro-4-oxo-3*H*,8*H*-pyrimido [5,4-*b*] [1,4] thiazin-6-yl) methyl] amino) benzoyl) glutamic Acid.**

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N- (*p* - [(2-Amino-6,7-dihydro-4-oxo-3*H*,8*H*-pyrimido [5,4-*b*] [1,4] thiazin-6-yl) methyl] amino) benzoyl) glutamic acid (1), a deaza-thia analogue of tetrahydrofolic acid, was first synthesized as a diastereoisomeric mixture by the thermal condensation of 5-bromo-6-chloroisocytosine with diethyl *N*- [*p*- [(3-amino-2-mercaptopropyl) amino] benzoyl] glutamate *via* the aliphatic *S-N* type Smiles rearrangement in ethanolic pH 7 phosphate buffer solution followed by smooth alkaline hydrolysis of the ester protecting group. The compound (1) was found to be very cytotoxic to human epidermoid carcinoma KB cells and human nonsmall cell lung carcinoma A 549.

[Nucleosides & Nucleotides, 13, 1239-1246 (1994)]

[Lab. of Medicinal Chemistry]

**A Newly Devised Method for the Debenzylation of *N*⁶-Benzyladenosines.
A Convenient Synthesis of [6-¹⁵N]-Labeled Adenosines.**

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NMR studies employing oligonucleotides regio-selectively labeled with ¹⁵N provide valuable information regarding nucleic acid structures, nucleic acids binding with drugs, and nucleotide-protein interactions. The potential utility of the ¹⁵N-labeled oligonucleotides has led to considerable interest in the development of synthetic routes to the required ¹⁵N-labeled nucleosides. The *N*₁- and *N*⁶- positions of the adenine ring are good candidates for the ¹⁵N-labeling because they can form hydrogen bonds with suitable donors or acceptors in the nucleic acids, drug, and proteins. On this line, [6-¹⁵N]-labeled adenosine was conveniently prepared from inosine by the silylation-benzylamination and subsequent oxidative debenzylation with ammonium peroxydisulfate in a pH 7.2 buffer solution.

[Chem. Pharm. Bull., 42, 179-181 (1994)]

[Lab. of Pharm. Synthetic Chemistry]

**Highly Stereoselective Synthesis and Structural Confirmation of a
Fungal Metabolite, LL-P880 β.**

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A fungal metabolite, LL-P880 β [6*S*-(1'*S*,2'*R*-dihydroxypentyl)-4-methoxy-5,6-dihydropyran-2-one], was synthesized unambiguously from diethyl (*R,R*)-tartrate as a chiral pool *via* highly stereoselective construction of the C7'-asymmetric carbon of the intermediate 6,8-dioxabicyclo-[3.2.1]octane derivative, and the stereochemistry of the C6-chiral center of the metabolite was chemically confirmed as (*S*).