

[*Nucleosides & Nucleotides*, 17, 1333-1345 (1998)]

[Lab. of Medicinal Chemistry]

**A Convenient Synthesis of Acyclic Adenosines with an Unsaturated Side Chain
by Modification of 9-(2,3-*O*-Isopropylidene-D-ribose)adenine.**

Kosaku HIROTA,* Yasunari MONGUCHI, Hironao SAJIKI, Chizuko YATOME,
Akio HIRAOKA and Yukio KITADE

In expectation of discovering their antiviral activity, acyclic adenosine derivatives were designed as analogs of neplanocin A (NPA) and L-eritadenine which are strong inhibitors of *S*-adenosyl-L-homocysteine hydrolase. The 1',5'-*seco*-analog of 4'-deoxymethyl-NPA (DHCA) was synthesized by didecyclogenation of 9-(2,3-*O*-isopropylidene-D-ribose)adenine. Acyclic DHCA analogs were obtained by Wittig reaction of the aldehyde with $\text{Ph}_3\text{P}=\text{CHCO}_2\text{Et}$ and $\text{Ph}_3\text{P}=\text{CHCN}$, respectively. Hydrolysis of the ester afforded a vinyllog of L-eritadenine. The synthesized acyclic nucleosides were evaluated for antiviral activity, however, none of them showed any significant antiviral activity.

[*Heterocycles*, 47, 871-882 (1998)]

[Lab. of Medicinal Chemistry]

Convenient Synthesis of Pyrido[4,3-*d*]pyrimidine-2,4 (1*H*,3*H*)-diones.

Kosaku HIROTA,* Yukio NAKAZAWA, Yukio KITADE and Hironao SAJIKI

A convenient synthesis of pyrido[4,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones is described. Treatment of 5-formyl-1,3-dimethyl-6-(2-dimethylamino)vinyluracil with ammonia and hydrazines affords the corresponding pyrido[4,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones, respectively. Similar reaction of 5-cyano- and 5-ethoxycarbonyluracils with ammonia led to formation of 5-amino- and 5-hydroxypyrido[4,3-*d*]pyrimidine-2,4(1*H*,3*H*), respectively. Among the compounds synthesized here, 5-amino-1,3-dimethylpyrido[4,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione exhibited greater inhibitory activity against cyclic AMP phosphodiesterase than theophylline.

[*Heterocycles*, 49, 475-479 (1998)]

[Lab. of Medicinal Chemistry]

**Reduction of Uracil Derivatives with an NADH Model, 1-Benzyl-1,4-
Dihydronicotinamide.**

Kosaku HIROTA,* Keiko KUBO, Yukio KITADE and Hironao SAJIKI

Among various *C*(5)-, *N*(1)-, and *N*(3)-substituted uracils, 1-substituted 5-nitrouracil derivatives were reduced by an NADH model, 1-benzyl-1,4-dihydronicotinamide, to give 5,6-dihydro-5-nitrouracil derivatives, the formation of which was accelerated to a large extent by the use of Mg^{2+} as a catalyst.

[*J. Chem. Soc., Perkin Trans. 1*, 941-946 (1998)]

[Lab. of Medicinal Chemistry]

**Novel Synthesis of Purine Acyclonucleosides Possessing a Chiral 9-
Hydroxyalkyl Group by Sugar Modification of 9-D-Ribityl Purines.**

Kosaku HIROTA,* Yasunari MONGUCHI, Hironao SAJIKI, Magoichi SAKO and Yukio KITADE

A novel approach for the synthesis of purine acyclonucleosides having chiral carbons in the *N*₉-hydroxyalkyl chain was achieved by using 9-(2,3-*O*-isopropylidene-D-ribose)purines, which were readily prepared from commercially available purine nucleosides. 9-[(2*S*,3*R*)-2,3,4-Trihydroxybut-1-yl]purines, 9-[(2*S*,3*S*)-2,3,4-trihydroxybut-1-yl]purines, L-eritadenine, and its analogue were conveniently synthesized *via* key intermediates, (2*S*,3*S*)-2,3-dihydroxy-2,3-*O*-isopropylidene-4-(purin-9-yl)butanals prepared by NaIO_4 oxidation of 9-(2,3-*O*-isopropylidene-D-ribose)purines.