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[Lab. of Medicinal Chemistry]

Synthesis and Biological Evaluation of CX-659S and its Related Compounds for their Inhibitory Effects on the Delayed-Type Hypersensitivity Reaction.

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In order to find novel nonsteroidal compounds possessing an inhibitory activity against delayed-type hypersensitivity (DTH) reactions, we conducted random screening using a picryl chloride (PC)-induced contact hypersensitivity reaction (CHR) in mice, and found 6-amino-5-(N-substituted carboxamido)-3-methyl-1-phenyluracil as a lead compound. Then we synthesized and evaluated an extensive series of 5-carboxamidouracil derivatives focused on both the uracil and the antioxidative moieties. Among them, we found that the hindered phenol moiety was necessary to exhibit the activities; especially, the corresponding derivative (**A**) having the partial structure of vitamin E at the 5-carboxamido group were found to exert potent activities against the DTH reaction by both oral and topical administration. And compound **A** showed antioxidative activity against lipid peroxidation with an IC_{50} of 5.9 μ M. Compound **A** (CX-659S) was chosen as a candidate drug for the treatment of cutaneous disorders such as atopic dermatitis and allergic contact dermatitis.

[*Heterocycles*, **52**, 1329-1336 (2000)]

[Lab. of Medicinal Chemistry]

Reactivity of 2',3'-Anhydropyrimidine nucleosides toward Trimethylaluminum.

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Treatment of 2',3'-anhydro pyrimidine nucleoside derivatives (**1**) with trimethylaluminum afforded 1-(3-deoxy-3-methyl- β -D-arabinofuranosyl)pyrimidine derivatives (**2**) and 1-(2-deoxy-2-methyl- β -D-xylofuranosyl)pyrimidine derivatives (**3**) as a mixture in approximately 2 : 1 – 3 : 1 ratio *via* ring-opening of the epoxide involving the nucleophilic attack of trimethylaluminum at the 3' or 2'-position of **1**.

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[Lab. of Medicinal Chemistry]

Highly Chemoselective Hydrogenation Retaining the Epoxide Function Using a Heterogeneous Pd/C-ethylenediamine Catalyst and THF.

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In general, palladium carbon (Pd/C) catalyzed hydrogenation of epoxides affords the corresponding primary and secondary alcohols as a mixture. It has been found that the catalytic activity of a Pd/C-ethylenediamine complex catalyst [Pd/C(en)] toward the hydrogenolysis of epoxide functions is drastically reduced. This paper describes a mild and chemoselective hydrogenation method of olefin, nitro and azide functions retaining the epoxide function. The chemoselective method was accomplished by using a combination of 5% Pd/C(en) and THF as the solvent. With 5% Pd/C(en) in MeOH a significant drop in the chemoselectivity of the hydrogenation is observed. These results reinforce the utility of epoxides as important precursors of alcohols in synthetic chemistry.

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The Undesirable Lability of *tert*-Butyldimethylsilyl Ethers under Pd/C-catalyzed Hydrogenation Conditions and Solution of the Problem by Using Pd/C(en) Catalyst.

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The frequent and unexpected loss of the TBDMS protective group of a variety of hydroxylic functions was demonstrated under neutral and mild hydrogenation conditions using 10% Pd/C. Moreover, we have found the use of the 10% Pd/C(en) catalyst totally suppressed the hydrogenolysis of the TBDMS ether and also applied the catalyst to develop a reliable and chemoselective hydrogenation method of olefin and nitro functionalities in the presence of the TBDMS ether. These findings further reinforce the versatile potential of TBDMS ethers as one of the most popular protective groups in organic synthesis.