

[Synthesis, 1993, 213-215]

[Lab. of Medicinal Chemistry]

Facile Synthesis of Thymidine Derivatives by Cross-Coupling of
5-Halogenouridine Derivatives with Trimethylaluminum.

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An efficient method for the introduction of a methyl group in the 5-position of uracil derivatives is described. This method involves three steps: protection of 5-halogenouridines with hexamethyldisilazane, a palladium-catalyzed cross-coupling of the pertrimethylsilylated nucleosides with trimethylaluminum, and subsequent deprotection to afford the corresponding thymidine derivatives in high overall yields. This method was applied to synthesis of 5-(*trans*-1-octenyl)uridine by the reaction of 5-bromouridine with diisobutyl-*trans*-octenyluridine.

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[Lab. of Medicinal Chemistry]

**Distinct Solvent-dependence in the Photoreactions of Purine
Nucleosides with Pyrimido[5,4-*g*]pteridinetetrone *N*-Oxide :
Possible Generation of Hydroxyl Radical from the Excited
N-Oxide in Alcohols.**

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Photoreaction of 2',3',5'-tri-*O*-acetyladenosine (**2**) with pyrimido[5,4-*g*]pteridinetetrone *N*-Oxide (**1**) in acetonitrile gave *N*⁶-cyanomethyl-2',3',5'-tri-*O*-acetyladenosine *via* coupling of adenosyl radical with cyanomethyl radical generated by the mediation of **1**. Under the analogous conditions, *N*²-benzoyl-2',3',5'-tri-*O*-acetylguanosine (**3**) underwent oxidative degradation of the guanine skeleton by **1**. In sharp contrast, photoreaction of **2** and **3** with **1** in *tert*-butanol resulted in the formation of the corresponding 8-hydroxypurine nucleosides, respectively. These facts and other observations suggest that **1** could generate hydroxyl radical upon irradiation in alcohols.

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[Lab. of Medicinal Chemistry]

**Facile Generation of Hydroxyl Radical by Photolysis of Pyrimido-
[5,4-*g*]pteridinetetrone *N*-Oxides in Aqueous Solution. A New Efficient
DNA-photocleaving Agent.**

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Photolysis of 1,9-di (methoxymethyl)-3,7-dimethylpyrimido[5,4-*g*]pteridine-2,4,6,8 (1*H*,3*H*,7*H*,9*H*)-tetrone 5-oxide (**1**) in water with UV-VIS light (>355 nm) provides a convenient and efficient method for the clean generation of hydroxyl radicals, which are useful as DNA-cleaving agents. Synthesis of ¹⁸O-labeled *N*-oxide (**1**) resulting in the generation of ¹⁸O-labeled hydroxyl radical was achieved by using a 6-amino-5-¹⁸O-labeled nitrosouracil derivative as starting material, prepared by the nitrosation of the corresponding 6-aminouracil derivative with nitrosonium tetrafluoroborate pretreated with ¹⁸O-labeled water in dry acetonitrile.