

[Synthesis, 1993, 213-215]

[Lab. of Medicinal Chemistry]

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

KOSAKU HIROTA,* YUKIO KITADE, YOSHITAKE KANBE,
YOSHIKI ISOBE, YOSHIFUMI MAKI

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.

[Heterocycles, 35, 325-337 (1993)]

[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.**

YOSHIFUMI MAKI,* TORU MAKINO, KOSAKU HIROTA, MAGOICHI SAKO

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.

[J. Chem. Soc., Chem. Commun., 750-751 (1993)]

[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.**

MAGOICHI SAKO, KATSUYUKI NAGAI, YOSHIFUMI MAKI*

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.