

Photosensitized Oxidation of Hydroxylated Purines¹

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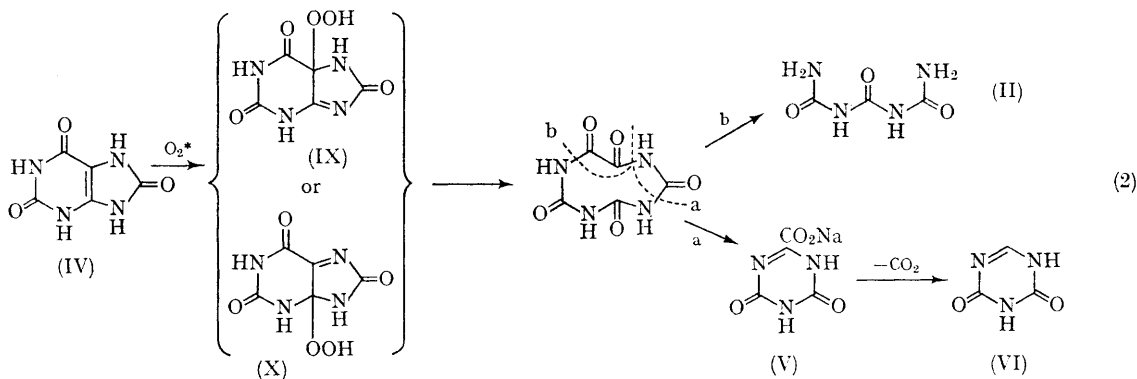
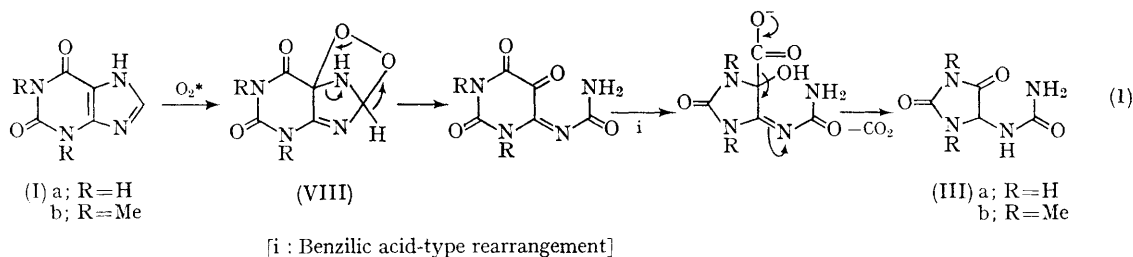
IN connection with the photodynamic inactivation of deoxyribonucleic acid, photosensitized oxidation of guanine and related purine derivatives has recently received much attention. Irradiation of such compounds by visible light in the presence of sensitizing dyes and oxygen usually causes considerable destruction of the molecule to give various products,² and details of the pathway remain unknown. We now report results obtained with some hydroxylated purines.

In a typical run, a solution (pH 11.7) of xanthine (Ia) (1 g.) and Rose Bengal (20 mg.) in aqueous sodium hydroxide (0.5 mole equiv.) (150 ml.) was irradiated with a 100w high-pressure mercury lamp with a Pyrex cooling jacket at room temperature under bubbling oxygen. After 1.05 mole equiv. of oxygen had been consumed, the mixture (final pH 8.8) was adjusted to pH 2.0 with 2*N*-hydrochloric acid. Carbon dioxide (1.0 mole equiv.) liberated was determined by converting into barium carbonate. From the acidified mixture two

crystalline products, triuret (II) (5%) and allantoin (IIIa) (41%),[†] were obtained.

Uric acid (IV) also consumed oxygen (1.1 mole equiv.) under similar conditions. Isolation of the products at pH 2.0 yielded triuret (II) (20%), sodium oxonate (V) (30%), allantoxaidin (VI) (15%), and carbon dioxide (85%). When the isolation was made at pH 5.0, the yield of sodium oxonate (V) was increased up to 40% at the expense of carbon dioxide (25%) and no allantoxaidin (VI) was obtained. It is, therefore, concluded that alloxaidin is the secondary product which was formed in the course of isolation.³ Photo-oxidation of uric acid in the presence of a large excess of alkali followed by the isolation of the products at pH 5.0, yielded triuret (II) (8%), sodium oxonate (V) (69%), and carbon dioxide (10%).

Photosensitized oxidation (0.95 mole equiv. oxygen) of 8-methylxanthine (VII) in aqueous sodium hydroxide (1.1 mole equiv.) resulted in a

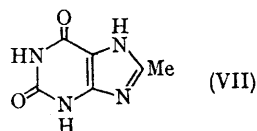


[†] All products were identified by comparison with authentic samples.

complex mixture, which was found, by paper chromatography, to consist of at least six compounds. Among them, acetamide (6%), sodium oxonate (V) (25%), and carbon dioxide (53%) were obtained.

In the absence of the sensitizer, none of the substrates reacted with oxygen on irradiation. Furthermore, no spectroscopic evidence was obtained for the formation of a charge-transfer complex between Rose Bengal and any of the substrates. It appears that the attack of reactive oxygen, either in singlet excited state⁴ or in a complex form with the excited sensitizer,⁵ on the ground-state substrate molecule results in a peroxide intermediate which then spontaneously decomposes to the products. Peroxide intermediates, such as a cyclic peroxide (VIII) and hydroperoxides (IX) and (X), have been postulated in the photo-oxidation of nitrogen heterocycles.⁶

The formation of 1,3-dimethylallantoin (IIIb) in the photosensitized oxidation of theophylline (Ib)⁷ is quite analogous to our results obtained with xanthine (Ia). Possible sequences for the transformation of (I) to (III) are indicated in Equation 1. We also formulate possible sequences for the photo-oxidation of (IV) to (II), (V), and (VI) involving hydroperoxide, (IX) or (X),[†] as shown in Equation 2. Such a mechanism can be also applied for the formation of (V) and acetamide from (VII).



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[†] A cyclic peroxide [*e.g.*, (VIII)], derived from the 8,9-enolic form of (IV), can be also considered as a possible intermediate.

¹ Previous Paper in this series: K. Omura and T. Matsuura, submitted to *Tetrahedron*.

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