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PHOTO-INDUCED REACTIONS. XV. THE NATURE OF PEROXIDE INTERMEDIATES IN THE PHOTOSENSITIZED OXYGENATION OF PURINE DERIVATIVES[1]

Teruo Matsuura and Isao Saito
Department of Synthetic Chemistry, Faculty of Engineering
Kyoto University, Kyoto, Japan

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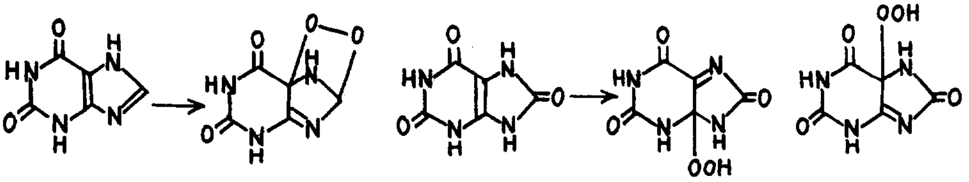
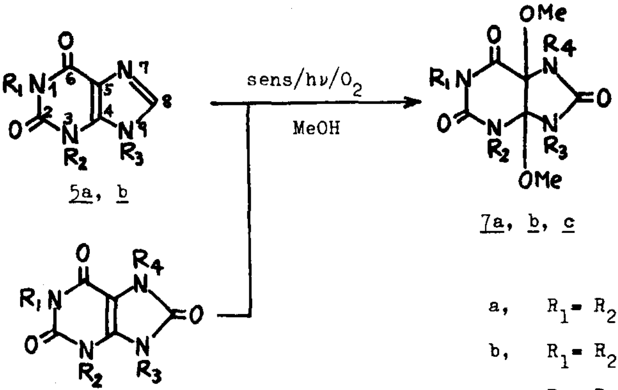
In our previous communication[2] it has been shown that photosensitized oxygenation of hydroxylated purines, including xanthine (1) and uric acid (2), give various degradation products which are possibly formed via peroxide intermediates. These intermediates include two types of peroxides 3 and 4a (or 4b), analogous to photoperoxides from cyclic conjugated dienes[3] and from olefins[4] having allylic hydrogen, respectively. We now report some evidences which indicate the intermediary formation of other types of peroxides 13 and 14, in the photosensitized oxygenation of certain N-substituted hydroxypurines.



1 3 2 4a 4b

When a methanol sclution of xanthine derivatives 5a and 5b and uric acid derivatives 6a, 6b, and 6c was submitted to photosensitized oxygenation[5] in the presence of rose bengal, about one mole of oxygen was consumed and a 4,5-dimethoxyuric acid 7 was found to be the major product in most cases. Thus, 5a, 5b, 6a, 6b, and 6c gave 7a (58%), 7b (23.3%), 7a (46%), 7b (2.1%), 7c[6] (35%), respectively. Other products 8 (11.4%) and allocaffeic acid[7] (5%) were obtained from 6b and 6c, respectively. Methylation of 7a with diazomethane yielded 7b. Structure 7b was confirmed by an independent synthesis using the known method for the synthesis of 7c[6]. On the basis of the nmr data which are shown in figure (τ value) structure 8 was assigned for compound 8. This structure was supported by the fact that partial hydrolysis of 7b with 2N HCl gave 8.

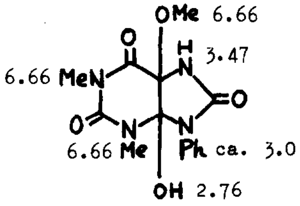
On the other hand, photosensitized oxygenation of fully N-alkylated uric acids in chloroform in the presence of methylene blue resulted in the formation of different types of products. Thus, 1,3,7,9-tetramethyluric acid (6c) gave 1,3,7-trimethylcaffolide (9c) in 18% yield and 1-ethyl-3,7,9-trimethyluric acid (6d) gave 1,3-dimethyl-7-ethylcaffolide (9d), N,N'-dimethylparabanic acid, and a compound $C_{10}H_{14}N_4O_5$ (10d) in 12, 8, and 22% yields, respectively. The structures of 9c and 9d were confirmed by their syntheses.[8] The results clearly indicate that the 3-N-methyl group was expelled in the course of the formation of 9c and 9d from 6c and 6d. Molecular formula for compound 10d was confirmed by the appearence of the parent peak m/e 270. IR spectrum shows a broad band at 1750-1650cm^{-1} but neither NH or OH band. Nmr spectrum consists of three singlets at τ 6.85, 7.01, and 7.10, assigned for three N-methyl groups, a quartet (J=7cps) at τ 6.32, and a triplet (J=7cps) at τ 8.17. The latter two signals were assigned for anN-ethyl group. Hydrolysis of 10d afforded N,N'-dimethyl- and N-ethyl-N'-methylparabanic acids. These data led us to give structure 10d for this compound.



5a, b

6a, b, c, d

7a, b, c



8

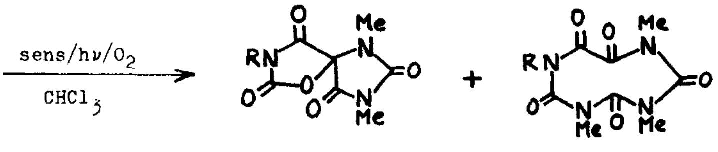
a, $R_1 = R_2 = R_4 = H$, $R_3 = Ph$

b, $R_1 = R_2 = Me$, $R_3 = Ph$, $R_4 = H$

c, $R_1 = R_2 = R_3 = R_4 = Me$

d, $R_1 = Et$, $R_2 = R_3 = R_4 = Me$

6c and 6d

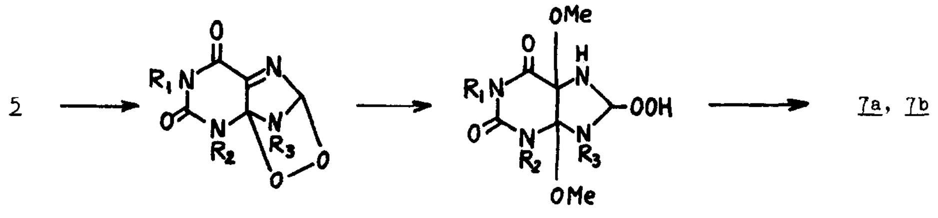


9c R = Me

9d R = Et

10d R = Et

Although both 5 and 6 afford 7, different mechanisms must be applied for the formation of 7. As shown in Scheme 1, the initially formed endo-peroxide 11 analogous to 3 could be solvolized by methanol to dimethoxy hydroperoxide 12 which is then dehydrated to give 7. A similar dimethoxy hydroperoxide has been proposed for the photosensitized oxygenation of 2-methyl-5-phenyloxazole.[9] On the other hand, a hydroperoxide analogous to 4a may be considered to account for the formation of 7 from 6a and 6b having -C=C-NH- moiety, but in the case of 6c such a hydroperoxide intermediate is not possible. We, therefore, propose a zwitterion peroxide 13 to the first step intermediate in the photosensitized oxygenation of compounds 6.[10]

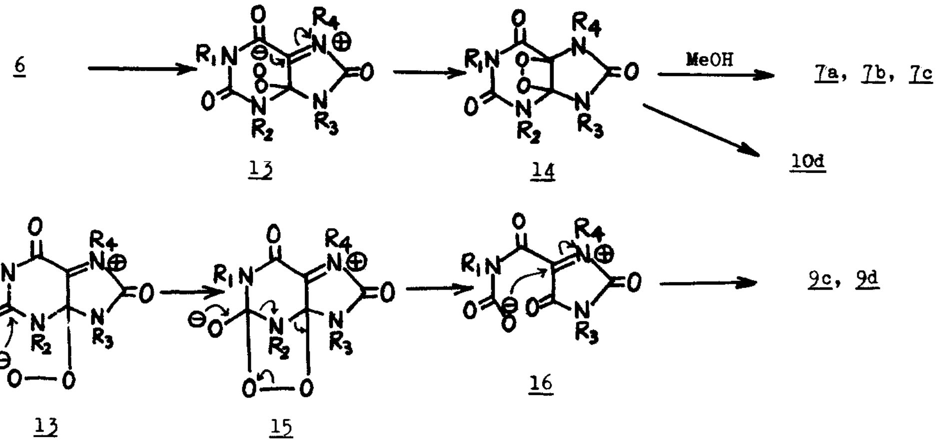


11 12

Scheme 1

The decomposition process of 13 may depend upon its surroundings and its substituents. As shown in Scheme 2, the polar peroxide 13 could rearrange to a four-membered cyclic peroxide 14[11] which, in the presence of methanol, undergoes reductive cleavage to give a dimethoxyuric acid 7a, 7b, or 7c. Such a process involving reductive cleavage of a cyclic peroxide has analogy in the photooxygenation of a cyclophane derivative.[12] 4,5-Bond fission leading to compound 10d may occur either from 14 stepwise or from 13 concertedly. Finally, the formation of caffolides 9 strongly supports our mechanism involving the zwitterion peroxide 13. The cyclic tautomer (15) of the peroxide 13 could lose an N-methyl group to give an intermediate 16 which then cyclizes to 9c or 9d. The loss of an N-methyl group has been also observed in the photooxygenation of 1,3-diphenyl-2-methylisoindole leading to o-dibenzoylbenzene.[13]

Reaction of 5a with hypochlorite and hydrogen peroxide in methanol[14] afforded a complex mixture of products, from which 7a was isolated as a minor product. This may be due to instability of 7a under conditions employed. However, it is probable that singlet oxygen[14] is involved in the present photosensitized oxygenation. Satisfactory elemental analyses and spectral data were obtained for all new compounds. Preparation of the starting materials will be described in datails in the forthcoming papers.



Scheme 2

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