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The Photochemistry of Heterocyclic Compounds. IV. The Mechanism of the Photodecomposition of Alloxan Monohydrate. The Effects of Solvents

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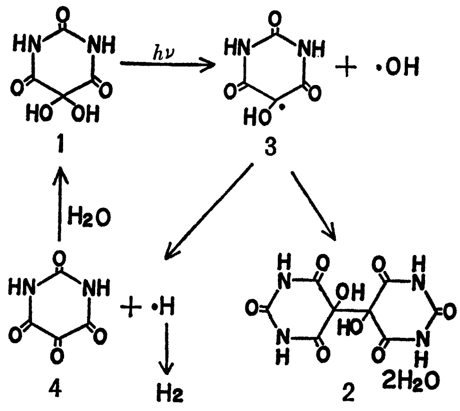
The photolyses of alloxan monohydrate (**1**) were carried out in water, 2-propanol, and dioxane. Irradiation in water produced alloxantin dihydrate (**2**), glyoxal (**5**), oxaluric acid (**6**), parabanic acid (**7**), and oxalyl diureide (**8**). However, when the photolyses were conducted in 2-propanol and dioxane, **2** and **5** were isolated as the main products. A detailed examination of the changes in the product distributions in the three solvents led to the conclusion that **2** and **5** are produced through the pathways involving the radical fission of the C–OH and C–CO bonds in **1**. On the other hand, **6**, **7**, and **8** were supposed to be produced by the pathways involving the photochemical hydrolysis of **1** to alloxanic acid (**13**).

In the previous papers of this series, we have reported the results of the photolyses of alloxan monohydrate (**1**) and its derivatives in aqueous solutions.[1,2] The irradiation of an aqueous solution of **1** with ultraviolet light afforded hydrogen, hydroxyl radical, alloxantin dihydrate (**2**), and other decomposition products. The processes for the formation of the former three products have been accommodated mechanistically by invoking the water-decomposition pathways illustrated in Scheme 1.



Scheme 1

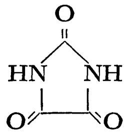
This photochemical reaction was, therefore, of considerable interest in view of the fact that **1** might serve as a useful catalyst of the photochemical decomposition of water. However, the efficiency of **1** as a catalyst was low because of the participation of decomposition pathways other than those indicated in Scheme 1.

The present study was undertaken in order to obtain more information about the mechanism of the photolysis of **1**. Specifically, the solvent effect on the pathways of the photolysis was examined in detail in the hope of elucidating the nature of the excited state(s) involved. The retults will be presented in this paper.

Results

*Photolyses of Alloxan Monohydrate (**1**).* When a dilute solution (3.1×10^{-2} M) of **1** in water was irradiated with a low-pressure mercury lamp under nitrogen at room temperature,[3] **2**, glyoxal (**5**), oxaluric acid (**6**), parabanic acid (**7**), and oxalyl diureide (**8**) were isolated from the reaction mixture.[4] The relative yields of these products were dependent upon the irradiation time. The yield of **2** decreased, and that

$$\mathbf{1} \xrightarrow[H_2O]{h\nu} \mathbf{2} + \underset{\mathbf{5}}{OHCCHO} + \underset{\mathbf{6}}{H_2NCONHCOCO_2H}$$

+  + $H_2NCONHCOCONHCONH_2$

7 **8**

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[1] Y. Otsuji, S. Wake, and E. Imoto, *Tetrahedron*, **26**, 4139 (1970).

[2] Y. Otsuji, S. Wake, and E. Imoto, *ibid.*, **26**, 4293 (1970).

[3] Unless otherwise noted, all the irradiations were carried out with a 15-W low-pressure mercury lamp under a nitrogen atmosphere.

[4] The evolution of a gas consisting of H_2, CO, and CO_2 was observed during the irradiation of **1**, as has previously been reported.[1] However, in this investigation no detailed analysis of the gas was attempted.

TABLE 1. THE PRODUCTS OBTAINED UPON IRRADIATION OF ALLOXAN MONOHYDRATE (**1**)[a]

Solvent	Irrad. time (hr)	Recovered starting material (%)	Alloxantin · $2H_2O$ (**2**)	Yield of products (%)[c]			
				Glyoxal (**5**)	Oxaluric Acid (**6**)	Parabanic acid (**7**)	Oxalyl diureide (**8**)
Water	3	61	8	0	2.4	—	0
	7	45	16	0.3	2.4	—	0
	20	18	8	1.0	0	47	0
	100[b]	0	0	—	0	28	3.8
2-PrOH	3	39	37	0.3	—	—	0
	7	15	40	0.8	—	—	0
	20	3	0	1.0	—	—	0
Dioxane	1.5	43	17	10	—	—	0
	3.5	26	17	30	—	—	0
	7	13	0	54	—	—	0

a) A 3.1×10^{-2} M solution of **1** was irradiated under N_2 atmosphere.
b) A 6.2×10^{-2} M solution of **1** was irradiated under N_2 atmosphere.
c) Based on total amount of the starting material.

of **5** increased, with an increase in the irradiation time. By 100 hr irradiation, only **7** (28%) and **8** (3.8%) were isolated. The results are summarized in Table 1.

The products were satisfactorily isolated by means of careful fractional crystallizations, as is presented in detail in the Experimental section. The unreacted starting material was separated from the reaction mixture as its semicarbazone (**9**). Glyoxal (**5**) was isolated as its 2,4-dinitrophenylhydrazone (**10**). It must be noticed here that **10** was obtained only when the reaction mixture was heated with an excess of a solution of 2,4-dinitrophenylhydrazine in 2 N hydrochloric acid on a boiling water bath for 3 hr or more. This result implies that **5** is produced by the acid hydrolysis of its precursor, which is presumably an acetal of **5** (**5** itself immediately forms **10** upon treatment with an acidic aqueous solution of 2,4-dinitrophenylhydrazine at room temperature).

The photolyses of **1** were also conducted in dioxane and 2-propanol under conditions similar to those employed for the photolyses in water. In these cases, **2** and **5** were isolated from the reaction mixture, the yields depending also on the irradiation time. The results are included in Table 1. The total yields of the isolated products for the photolyses of **1** in the organic solvents were better than those in water.

*Photolysis of **1** in the Presence of Urea.* We have recently found that, when the photolysis of an aqueous solution of **1** was carried out in the presence of urea, the evolution of H_2 completely ceased, although the evolution of CO and CO_2 was still observed. In order to shed light on the mechanism of this, an aqueous solution (6.2×10^{-2} M) of **1** in the presence of an equivalent of urea was irradiated for 7 hr. The subsequent fractional crystallization of the reaction mixture afforded **2** (0.2%), **8** (0.4%), uric acid glycol semihydrate (**11**, 9.1%), and some unidentified product (s) (**12**).

The compounds **11** and **12** thus obtained were also produced by the reaction of **1** with urea in the dark. A careful examination of this dark reaction revealed that the primary product was **11**, which was then gradually converted to **12**.

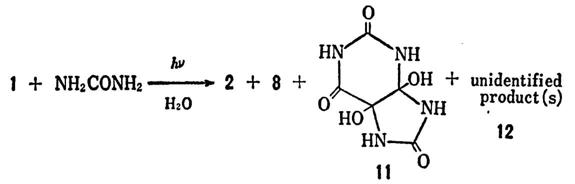
These results clearly suggest that a remarkable decrease in the photochemical reactivity of **1** in the presence of urea is due to the dark reaction between them, and that the **11** or **12** formed by this dark reaction would be photochemically unreactive.

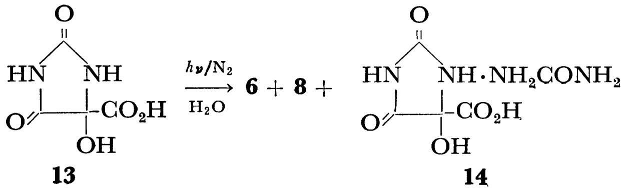
Photolyses of Related Compounds. Since alloxanic acid (**13**) and **7** were supposed to be among the intermediates of the photolysis of **1** in water, their photochemistry was examined briefly.

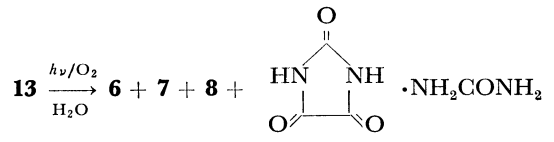
The irradiation of a solution (6.2×10^{-2} M) of **13** in water for 7 hr under nitrogen afforded **6**(3%), **8**(1.3%), and a 1 : 1 adduct(or salt) (**14**, 35%) between **13** and urea, the starting material being recovered in a 49% yield. On the other hand, the irradiation of an aqueous solution of **13** in the presence of air for 7 hr gave **6**(1.8%), **7**(26%), **8**(0.4%), and a 1 : 1 adduct (or salt) (**15**, 3.7%) between **7** and urea along with complex unidentified product(s).

The photolysis of a 6.4×10^{-2} M solution of **7** in water for 3 hr under nitrogen produced **8** (1.4%) and complex unidentified product(s), the starting material being recovered in a 35% yield.

Finally, a solution of **2** in dioxane was photolyzed for 3.5 hr under nitrogen to give **5** in a 40% yield.







$$13 \xrightarrow[H_2O]{h\nu/O_2} 6 + 7 + 8 + \cdot NH_2CONH_2$$

15

$$7 \xrightarrow[H_2O]{h\nu/N_2} 8 + \text{unidentified product(s)}$$

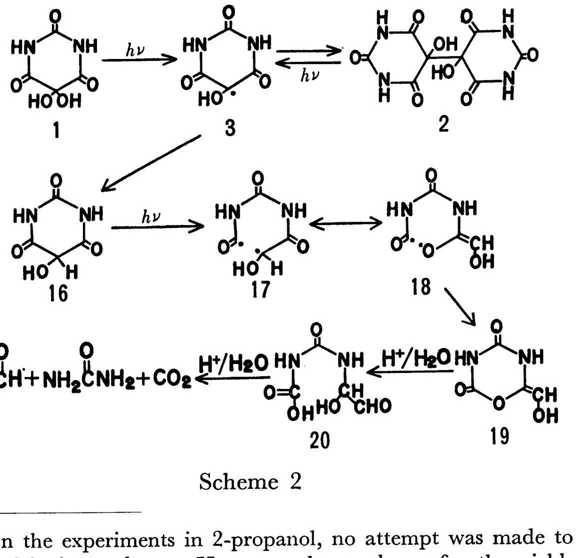
$$2 \xrightarrow[\text{dioxane}]{h\nu/N_2} 5$$

Discussion

A striking observation of this investigation concerns the effects of solvents on the product distributions in the photolyses of **1**. Experimental difficulties prevented us from making complete analyses of the products, specifically in the photolyses in hydroxylic solvents, and so no detailed discussion can be given at the present time; nevertheless, the following important conclusions can be drawn from the data in Table 1: (1) the products **2** and **5** are those derived from a radical intermediate, (2) the pathways leading to **2** and **5** are closely related to each other and **2** is converted to **5**, and (3) the products **6**, **7**, and **8** are those produced through the pathways involving ionic reactions of **1** or **2** with water.

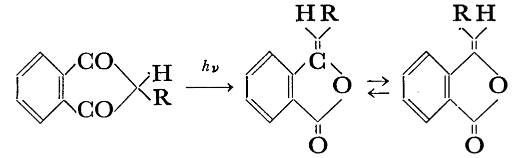
Dioxane does not react to **1** in a manner characteristic of a nucleophilic reagent. Only the radical reactions are, therefore, expected to take place in this medium. Indeed, **6**, **7**, and **8** could not be isolated in detectable yields by the photolyses in dioxane. On the other hand, in water, which possesses a nucleophilic reactivity toward **1**, ionic products, **6**, **7**, and **8**, were formed, making the photochemical reaction a complex one.[5]

On the basis of these considerations as well as other experimental observations, we now propose a probable mechanism for the formation of **2** and **5** (Scheme 2).



Scheme 2

Evidence that the process **1**→**3** really takes place probably through the $n \to \pi^*$ state of **1** has been presented in a previous paper.[1] The combination of two of the radical **3** gives **2**. The irradiation of **2** also produces **3**, as may be inferred from the fact that the photolysis of **2** in dioxane gave **5** in a high yield. The disproportionation of **3** or the abstraction of hydrogen atom from solvent by **3** affords dialuric acid (**16**). The cleavage of the C—C bond α to the carbonyl in **16** would produce the lactone **19** *via* **17** and **18**. The process **16**→**19** can be induced by the photoexcitation of **16**. That this kind of reaction really occurs has been established in the photochemistry of cyclic β-diketones. For example, 2-substituted 1,3-indanedione (**21**, R=alkyl or aryl) isomerizes to the phthalide **22** or **23** through the $n \to \pi^*$ state of **21**[6] upon irradiation with ultraviolet light.



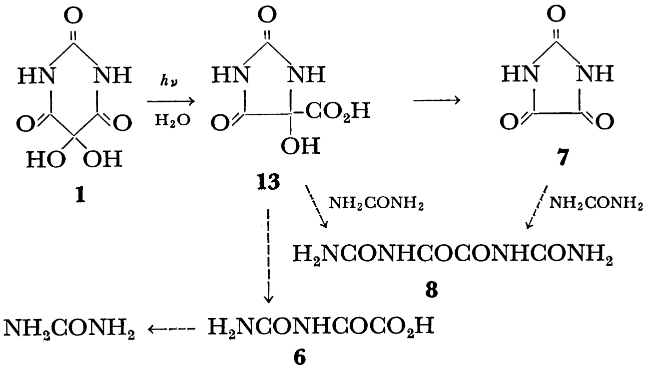
21 **22** **23**

The acid hydrolysis of **19** affords **5**. The presence of the intermediate **19** in the reaction mixture, in which the aldehyde function of **5** is protected, accords with the experimental finding that heating with acid was neccessary to obtain **5**.

The solvent effects observed in this study are also consistent with the mechanism depicted in Scheme 2 if the reaction is initiated by the $n \to \pi^*$ excited states of **1**, **2**, and **16**. As is well established, the $n \to \pi^*$ excited state of a carbonyl group can be brought about in a higher probability in non-hydroxylic solvents such as dioxane than in hydroxylic solvents, such as water or 2-propanol. Indeed, our results (Table 1) indicate that **1** was photolyzed much more rapidly in dioxane than in water.

The mechanism of the formation of **6**, **7**, and **8** will now be only briefly discussed. A speculative mechanism which accommodates our results is shown in Scheme 3, although the real pathways must be much more complex.

The process **1**→**13** has been known to be achieved



Scheme 3

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[5] In the experiments in 2-propanol, no attempt was made to isolate of ionic products. However, the tendency for the yields of the products **2** and **5** to vary with the irradiation time in 2-propanol was parallel to that in water, supporting the view that the ionic products are being also formed in 2-propanol.

[6] J. Rigaudy and P. Derible, *Bull. Soc. Chim. Fr.*, **1965**, 3047, 3055, 3061.

by the action of alkali on **1**[7] in the dark, but **1** was stable under the conditions of our photochemical reactions. Hence, this process must be of photochemically-accelerated. Our previous work has shown the possibility of this sort of ionic photochemical reaction. Barbital (**24**) has been found to be hydrolyzed to diethylacetylurea by the attack of the hydroxide ion on the carbonyl carbon at the 4-position upon the irradiation of its aqueous solutions through the singlet excited state.[8] The close similarity between the structure of **1** and that of **24** suggests that the similar ionic reaction, which should lead to **13**, might be accelerated by the irradiation. Although the oxidation of **13** has been known to give **7**,[9] this oxidation must be carried out by the hydroxyl radical, which is generated by the irradiation of **1**, in our photochemical reaction. This view is further supported by the fact that the irradiation of **13** in the presence of oxygen caused a remarkable increase in the yield of **7** as compared with that in photolysis under a nitrogen atmosphere. That the other isolated products could, in fact, be produced from **7** and **13** was shown by the photolyses of their aqueous solutions.

Experimental

The melting points are uncorrected. The UV spectra were determined on a Hitachi EPU-2U recording spectrophotometer. The IR spectra were determined on a Hitachi-EPI-S2 infrared spectrophotometer. The microanalyses were performed with a Yanagimoto MT-1 CHN Corder. Irradiation was carried out with a 15 W Taika low-pressure immersion mercury lamp at room temperature.

Materials. Alloxan monohydrate (**1**), alloxantin dihydrate (**2**), and parabanic acid (**7**) were prepared by the methods described in a previous paper.[1] Alloxanic acid (**13**) was prepared from Barium alloxanate[10] by the method of Biltz and Kobel[11] and was purified by means of column chromatography using Amberlite CG-120 Type 1 as the adsorbent and ether as the eluent; mp 153—157°C (decomp.). (Found: C, 30.24; H, 2.71; N, 17.30%. Calcd for $C_4H_4N_2O_5$: C, 30.01; H, 2.52; N, 17.50%).

Preparation of Authentic Samples. Oxaluric acid (**6**) and alloxan-5-semicarbazone dihydrate (**9**) were prepared by the methods described in the previous paper.[1] Oxalyl diureide (**8**) was prepared by the method of Biltz and Topp;[12] mp 250°C (decomp.). (Found: C, 27.56; H, 3.54; N, 32.22%. Calcd for $C_4H_6N_4O_4$: C, 27.59; H, 3.47; N, 32.18%). Uric acid glycol semihydrate (**11**) was prepared by the method of Biltz and Heyn;[13] mp 164—165°C (decomp.). The 1 : 1 adduct (or salt) (**14**) between alloxanic acid (**13**) and urea was prepared by adding a solution of 0.8 g (5 mmol) of **13** in 1 m*l* of water to a solution of 0.3 g (5 mmol) of urea in 0.5 m*l* of water. The mixture was then allowed to stand at room temperature for 12 hr. The crystals thus deposited were collected by filtration to give 0.68 g (62%) of **14**; mp 149—150°C (decomp.). An analytical sample was prepared by recrystallization from water; mp 150—153°C (decomp.). (Found: C, 27.34; H, 3.71; N, 25.35%. Calcd for $C_5H_8N_4O_6$: C, 27.28; H, 3.66; N, 25.45%). The 1 : 1 adduct (or salt) (**15**) between parabanic acid (**7**) and urea was prepared by adding a solution of 2.3 g (20 mmol) of **7** in 40 m*l* of water to a solution of 1.2 g (20 mmol) of urea in 2 m*l* of water. The mixture was allowed to stand at 0°C for 12 hr. The crystals thus deposited were collected by filtration and recrystallized from water to give 2 g (27.5%) of **15**; mp 204—206°C (decomp.). (Found: C, 27.73; H, 3.57; N, 32.37%. Calcd for $C_4H_6N_4O_4$: C, 27.59; H, 3.47; N, 32.18%).

Unless otherwise noted, the structures of the photoproducts were identified by a mixed-melting-point test and by a comparison of the IR spectra of the products with those of the corresponding authentic samples.

*Photoreaction of Alloxan Monohydrate (**1**) in Water.* A solution of 1.5 g (9.4 mmol) of **1** in 300 m*l* of water was placed in a cylindrical reaction vessel, and then N_2 was bubbled for 30 min. Irradiation was then carried out under N_2 at room temperature. After irradiation for an appropriate period of time, the solvent was evaporated to dryness under reduced pressure, and the residue was washed thoroughly with water. The residue was identical with **2** in every respect. The aqueous filtrate was again evaporated to dryness under reduced pressure, and then a 10 m*l* portion of water was added to the residue. An insoluble precipitate, which was separated by filtration, was proved to be **6**. To the filtrate we added a solution of 1 g of semicarbazide hydrochloride and 1.5 g of NaOAc in 10 m*l* of water. The filtration of this mixture gave alloxan-5-semicarbazone dihydrate (**9**); mp 231—232°C (decomp.). Finally, an acid solution of 2,4-dinitrophenylhydrazine was added to the above filtrate, after which the mixture was heated for 3 hr on a water bath and allowed to stand overnight. Filtration gave 2,4-dinitrophenylhydrazone of glyoxal (**10**); mp 309—310°C (decomp.).

When a solution of 3 g (18.7 mmol) of **1** in 300 m*l* of water was irradiated for 100 hr, crystals were deposited on the bottom of the reaction vessel. The crystals were separated by filtration to give 0.06 g (3.8%) of **8**; mp 249°C (decomp.).

*Photoreaction of Alloxan Monohydrate (**1**) in Organic Solvents.* A solution of 1.5 g (9.4 mmol) of **1** in 300 m*l* of an organic solvent was irradiated as has been described above. After irradiation, the solvent was evaporated to dryness under reduced pressure, and the residue was washed with 20 m*l* of water. The aqueous filtrate was evaporated to dryness under reduced pressure, and the residue was washed again with 20 m*l* of water. These evaporation and washing operations were repeated three or four times until no more water-insoluble precipitate was obtained. All of the water-insoluble precipitate was proved to be **2**. The aqueous filtrate obtained by the final washing operation was treated with semicarbazide hydrochloride and then with 2,4-dinitrophenylhydrazine in a manner similar to that described above to give **9** and **10** respectively.

*Photoreaction of Alloxan Monohydrate (**1**) in the Presence of Urea.* A mixture of 3.0 g (18.7 mmol) of **1** and 1.1 g (18.3 mmol) of urea in 300 m*l* of water was irradiated for 7 hr under N_2. A precipitate deposited on the bottom of the reaction vessel was collected by filtration; it was proved to be 7 mg (0.4%) of **8**; mp 249°C (decomp.). The filtrate was evaporated to dryness under reduced pressure and the residue was washed with 20 m*l* of water. An insoluble precipitate, which was separated by filtration, was 7 mg (0.2%)

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[7] H. Biltz, M. Heyn, and M. Bergius, *Ann. Chem.*, **413**, 68 (1916).

[8] Y. Otsuji, T. Kuroda, and E. Imoto, This Bulletin, **41**, 2713 (1968).

[9] H. Kwart, R. W. Spayd, and C. J. Collins, *J. Amer. Chem. Soc.*, **83**, 2579 (1961).

[10] F. Wöhler and J. V. Liebig, *Ann. Chem.*, **26**, 241 (1838).

[11] H. Biltz and M. Kobel, *Ber.*, **54**, 1802 (1921),

[12] H. Biltz and E. Topp, *ibid.*, **46**, 1404 (1913).

[13] H. Biltz and M. Heyn, *ibid.*, **45**, 1677 (1912); *ibid.*, **47**, 459 (1914).

of **2**; mp 202—203°C (decomp.). The filtrate was evaporated to dryness under reduced pressure. The residue was triturated with 200 m*l* of ethyl acetate and then filtered.[14] The filtrate was evaporated to dryness, and the residue was washed with 10 m*l* of ethyl acetate. The residue was 0.36 g (9.1%) of **11**; mp 170—172°C (decomp.).

*Photoreaction of Alloxanic Acid (**13**).* A solution of 3 g (18.8 mmol) of **13** in 300 m*l* of water was irradiated under N_2 for 7 hr. The filtration of the deposited crystals gave 0.02 g (1.3%) of **8**; mp 218—225°C (decomp.). The filtrate was evaporated to dryness under reduced pressure. The residue was triturated with 200 m*l* of ethyl acetate and then filtered. The evaporation of the filtrate gave 1.47 g (49%) of the starting material. The insoluble solid obtained upon trituration with ethyl acetate was triturated with 5 m*l* of water, after which the water-insoluble crystals were separated by filtration to give 0.075 g (3%) of **6**, mp 172—173°C (decomp.). The evaporation of the aqueous filtrate gave 0.71 g (35%) of the 1 : 1 adduct (or salt) (**14**), which melted at 150.5—151.5°C after recrystallization from water.

*Photoreaction of Alloxanic Acid (**13**) in the Presence of Air.* A solution of 3 g (18.7 mmol) of **13** in 300 m*l* of water was irradiated with bubbling air for 7 hr. The filtration of the deposited crystals gave 6 mg (0.4%) of **8**; mp 224—229°C (decomp.). The filtrate was evaporated to dryness under reduced pressure. The residue was triturated with 80 m*l* of ethyl acetate and then filtered. The evaporation of the filtrate gave 0.56 g (26%) of **7**, which melted at 235—238°C (decomp.) after recrystallization from water. The insoluble solid obtained upon trituration with ethyl acetate was triturated with 5 m*l* of water and the insoluble crystals were separated by filtration. The evaporation of the filtrate gave 1 g of a mixture of complex unidentified products. The recrystallization of the water-insoluble crystals from water gave 45 mg (1.8%) of **6**, mp 193—195°C (decomp.). The mother liquor from the recrystallization was evaporated to dryness, and the residue was recrystallized from water to give crystals (0.06 g) which were identified as the 1 : 1 adduct (or salt), **15**.

*Photoreaction of Parabanic Acid (**7**) in Water.* A solution of 2.2 g (19 mmol) of **7** in 300 m*l* of water was irradiated under N_2 for 3 hr. The filtration of the deposited crystals gave 0.03 g (1.4%) of **8**, mp 238°C (decomp.). The filtrate was evaporated to dryness under reduced pressure, and the residue was washed with 20 m*l* of acetone. The filtration of the insoluble precipitate gave about 0.8 g of a mixture of complex unidentified products. The evaporation of the filtrate gave 0.77 g (35%) of **7**.

*Photoreaction of Alloxantin Dihydrate (**2**).* A solution of 0.5 g of **2** in 300 m*l* of dioxane was irradiated, and then the reaction mixture was treated in a manner similar to that employed for **1** in dioxane.

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[14] The structure of the residue, 1.3 g, mp 159—160°C (decomp.), remains unidentified. However, this residue showed the same IR spectrum as that of the unknown by-product obtained by the treatment of **1** with urea in the dark.