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Photochemistry of Some Pteridine *N*-Oxides[1]

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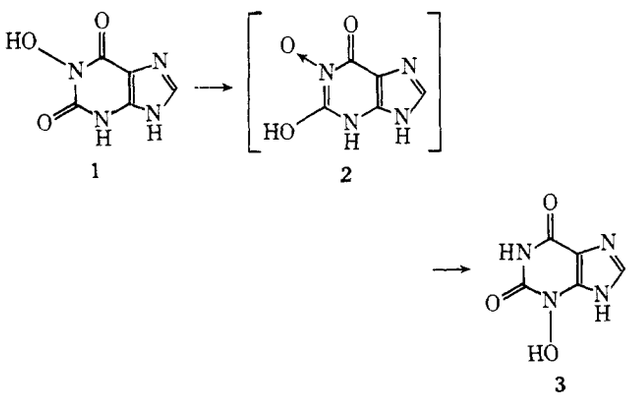
Purine *N*-oxides, like many heterocyclic aromatic *N*-oxides,[2] undergo deoxygenation and migration of the oxygen to the adjacent carbon under the influence of ultraviolet light.[3-6] 1-Hydroxyxanthine (**1**), which has an *N*-hydroxyimide structure, shows the expected photoreduction, but it also undergoes an unusual 1:3 isomerization of the 1-hydroxyl group to afford 3-hydroxyxanthine[7] (**3**). It was suggested that the isomerization of **1** to **3** proceeds via the enol nitrone (**2**) and two successive oxazirane migrations (Scheme I).

Recently, the pteridine analogues of **1** and **3**, i.e., 3-hydroxy-2,4-dioxo-1,2,3,4-tetrahydropteridine (**4**) and its 1-hydroxy isomer **6**, were reported.[8,9] To investigate whether a pteridine would undergo the unusual *N*-hydroxy rearrangement, we examined the possible photochemical conversion of **4** to **6**. However, the main photoproduct from **4** over the pH range 2 to 12 (Figure 1) was the reduction product **5**, together with a trace of ring-opened compound. Under the same conditions of irradiation, the possible rearrangement product **6** showed little change, although with prolonged ir-

Scheme I



1 **2** **3**

Table I. 3-Hydroxy-2,4-dioxo-1,2,3,4-tetrahydropteridine

pH	Species	λ_{max}, nm, $\epsilon \times 10^{-3}$	pK_a
		231 (13.7)	
2	0		
		322 (7.4)	
			5.61 ± 0.1[a]
		217 (15.7)	
6.8	−1		
		243 (8.7)	
		327 (8.0)	
		338[b] (7.5)	
			9.0 ± 0.3
12	−2	217 (17.5)	
		261 (19.0)	
		356 (8.4)	

[a] pK_as calculated at isosbestic points of isosbestic spectra. [b] Shoulder.

radiation it could be slowly reduced to **5** (Φ 5.9 × 10^{-5} at pH 7.0). The hydroxyl isomerization of **1** was deduced to occur via the singlet state.[5] The lack of *N*-hydroxyl isomerization by the pteridine **4** indicates that the apparent structural similarity of the pyrimidine ring in **1** and **4** is not paralleled by the formation of a tautomer in the excited singlet comparable to **2**. The absence of this tautomer in the excited state precludes *N*-hydroxyl isomerization and the only photoprocess then observed is deoxygenation via the triplet, i.e., **4** to **5**. That process is quite sensitive to change in pH (Figure 1). Changes in pH from 3 to 8 did not affect the quantum yield for the conversion of **4** to **5**. Decreasing the pH from 3 to 1 caused a steep decline in the quantum yield for photoreduction of **4**, and at pH 1 there was no reduction of **4**. This effect of acid is similar to that on the photoreactions of quinoline *N*-oxide[10] and isoquinoline *N*-oxide.[11] Between pH 8 and 10 the quantum yield of reduction of **4** decreased, and then remained unchanged with further increases in pH. Significantly, the inflection in the curve in Figure 1 at pH 9.0 coincides with one of the pK_as of **4**. In contrast to the relatively small spectral changes accompanying the first ionization of **4** (pK 5.6), the second ionization (pK 9.0) is associated with the appearance of a band of high extinction at 261 nm. These data indicate that the sequence of ionization of **4** is N-1 H to **4a**, and then N-3 OH to **4b**. This ionization sequence parallels that of **1**[12,13] (N-3 H, N-1 OH). The close correspondence of the inflection point in Figure 1 with the second ionization pK_a to **4b** would accord with the assignment of positions of ionization and indicates that photoreduction of the *N*-hydroxy species, **4** or **4a**, has a higher quantum efficiency than does that of the enolate anion **4b**. In contrast to the relatively large effects of changes in pH and ionic form on the quantum efficiency for photoreduction observed with **4**, changes in the ionic form of **6** (pK_as 6.50 and 9.35)[9] did not greatly affect the quantum yield for the appearance of **5**.

The photoreactivity of 1-hydroxy-2-oxo-1,2-dihydropteridine (**7**)[9] was also examined. In contrast to the facile photoreduction of 3-hydroxy-2-oxopurine,[14] neither the anion nor the neutral molecule of **7** yielded the anticipated photoreduction product, 1,2-dihydro-2-oxopteridine (**10**). Instead, both produced the C-4 oxidation product **5** in 9 and 38% yields, respectively, as the only UV-absorbing product after irradiation (Corex filter) for 4 h. Irradiation of the neutral molecule of **10** under the same conditions also produced **5** (18%). This indicates that the deoxygenation process at N-1 of **7** is not correlated with oxidation at C-4. Both **7** and **10** form stable hydrates, **8** and **9** (Scheme II), in solution, and air oxidation of **9** is known to yield **5**.[15] These observations suggest that the photochemical formation of **5** probably proceeds via the hydrate **9**. No oxidation of **8** and **9** to **5** occurred under the ex-

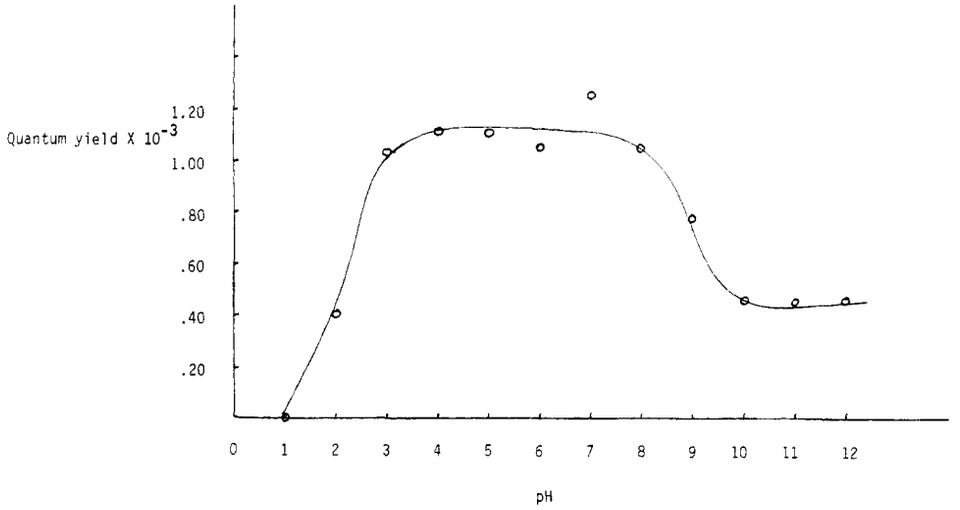
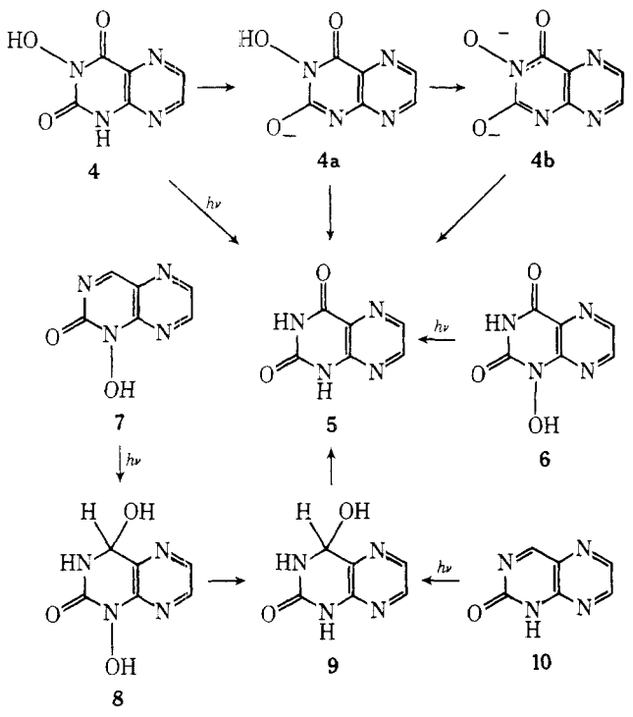


Figure 1. Effect of pH on quantum yields of formation of 2,4-dioxo-1,2,3,4-tetrahydropteridine from 3-hydroxy-2,4-dioxo-1,2,3,4-tetrahydropteridine.

Scheme II



perimental conditions without irradiation. Hence, this represents a novel photochemical oxidation that has not been previously described for pteridines.

Experimental Section

Photolysis. Method A. A sample of compound (~1.0 mmol) was dissolved in 350 mL of H_2O or buffer solution. The solution was degassed and irradiated in an immersion-type apparatus equipped with a 450-W Hanovia high-pressure Hg lamp with a pyrex or corex filter. The disappearance of the starting material was monitored by change in the UV absorption. After the photolysis was discontinued, the solution was then reduced to a small volume in vacuo. The products were then separated and isolated by chromatography over a Bio-Rad AG-50 × 8 (H^+), 200–400 mesh column (9 × 450 mm). Yields of reaction products were calculated from their known ϵ_{max}.

Method B. The quantum-yield study was performed in a Rayonet photochemical reactor equipped with 2537 A and 3000 A and a merry-go-round apparatus. Potassium ferrioxalate was used as the chemical actinometer.[16]

Chromatography. For routine quantitation, a 2.0 × 1000 mm analytical high-pressure liquid chromatography column of Bio-Rad A-6 resin eluted with 0.4 M NH_4OOCH buffer of pH 4.7 and a Laboratory Data Control (LDC) UV monitor were used. The volume values (mL) of compounds **4**, **6**, **5**, **7**, and **10** were found to be 10.5, 10.1, 11.1, 8.0, and 9.0, respectively. The column's temperature was maintained at 50 °C with a flow rate of 16.6 mL/h.

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Registry No.—**4**, 10579-28-9; **5**, 487-21-8; **7**, 37440-31-6.

References and Notes

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5,5,6,6,11,11,12,12-Octamethylcyclododeca-1,3,7,9-tetrayne

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3-Chloro-3-methyl-1-butyne (**1**) has been used in C, O, and N alkylations[1,2] as a convenient method for introducing the 1,1-dimethyl-2-propynyl group. It has also been employed as a precursor of dimethylvinylidene carbene (**2**).[3] Recently, when studying the alkylation of amines with **1**, a crystalline