# DIANION FORMATION BY 2- AND 6-HYDROXYPTERIDINE*

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Both 2- and 6-hydroxypteridine (I and III) add water reversibly so that their neutral molecules exist predominantly as the covalently hydrated species, (II) and (IV). In weakly alkaline solutions the "anhydrous" monoanions are favoured, the equilibrium ratios of monoanions derived from (II) and (I), and from (IV) and (III), being 0·14 and 0·045, respectively.[1]

(I) (II) (III) (IV)
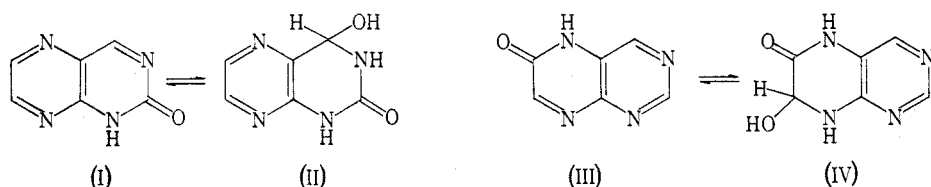
Although the equilibrium acidic pK_a values of 2- and 6-hydroxypteridine are 10·15 and 8·55, we have found that at higher pH values further ionization occurs. From the pH dependence of ultraviolet spectral changes, pK_a values of $14·11 \pm 0·03$ and $14·24 \pm 0·02$ for 2- and 6-hydroxypteridine, respectively, were obtained at 20° (Table 1). Because the "anhydrous" monoanions from (I) and (III) lack ionizable protons, there seems little doubt that these pK_a values relate to dianion formation by the anions of (II) and (IV).

TABLE 1

pK_a VALUES FOR DIANION FORMATION AT 20°

Compound	pK_a	Concn. (M)	$\lambda_{anal.}$ (mμ)	pH Range
"Hydrated 2-hydroxypteridine"				
pK_a	$13·03 \pm 0·03$	$7·5 \times 10^{-5}$	258	12·2–13·6
pK_a^{eqm}	$14·11 \pm 0·03$	$1·1 \times 10^{-4}$	377	13·4–15·0
"Hydrated 6-hydroxypteridine"				
pK_a	$12·70 \pm 0·03$	$1·0 \times 10^{-4}$	323	12·2–13·6
pK_a^{eqm}	$14·24 \pm 0·02$	$8·2 \times 10^{-5}$	300	13·4–15·0

Using rapid reaction techniques, in which solutions of the hydrated neutral molecules were made alkaline and the initial optical densities were recorded, the true pK_a values for the dianion formation from (II) and (IV) were obtained as 13·03±

1 Inoue, Y., and Perrin, D. D., J. Chem. Soc., 1962, 2600.

$0\cdot03$ and $12\cdot70\pm0\cdot03$, respectively. These pK_a values are related to the equilibrium values by the identity

$$pK_a^{eqm} = pK_a + \log\{(k+1)/k\},$$

where k is the equilibrium ratio of hydrated to anhydrous monoanions. Insertion of the published[1] values of k gives

$13\cdot03 + \log(1\cdot14/0\cdot14) = 13\cdot94$, for 2-hydroxypteridine, and

$12\cdot70 + \log(1\cdot045/0\cdot045) = 14\cdot07$, for 6-hydroxypteridine,

in reasonable agreement with the experimental results.

The ultraviolet spectra of the various mono- and di-anions are summarized in Table 2. The previously published[1] spectrum of the hydrated monoanion of 2-hydroxy-

TABLE 2

PHYSICAL PROPERTIES OF HYDROXYPTERIDINE ANIONS IN WATER AT 20°

EMA, equilibrated monoanion (mainly anhydrous); HMA, hydrated monoanion; DA, dianion

Species	pK_a		λ_{max} (mμ)	$\log \epsilon$	pH
2-OH Pteridine	EMA[1]	$10\cdot15$*	224, 265, 375	$4\cdot31, 3\cdot82, 3\cdot83$	$11\cdot8$
	HMA	$11\cdot05$†	230, 267, 313	$3\cdot96, 3\cdot83, 3\cdot76$	$12\cdot0$
	DA	$13\cdot03,$† $14\cdot11$*	266, 339	$3\cdot95, 3\cdot81$	$15\cdot0$
6-OH Pteridine	EMA[1]	$8\cdot55$*	222, 256, 358	$4\cdot27, 3\cdot88, 3\cdot74$	$12\cdot0$
	HMA[1]	$9\cdot90$†	236, 294	$3\cdot39, 4\cdot03$	$11\cdot3$
	DA	$12\cdot70,$† $14\cdot2$*	303	$3\cdot94$	$15\cdot0$

* Equilibrium pK_a.   † True pK_a.

pteridine was obtained by rapid reaction measurements at pH 13, beginning with the hydrated neutral molecule. From the present results, such a solution is seen to be a mixture of almost equal parts of the hydrated mono- and di-anions. The spectrum of the hydrated monoanion has been redetermined at pH 12, but even at this optimum pH value 9% is present as the hydrated neutral molecule and 8% as the dianion.

Dianion formation was not found in aqueous solutions of 4- and 7-hydroxypteridine. This is as expected, because there is no evidence that the monoanions of these substances undergo covalent hydration. Conversely, we predict that dianion formation can occur with 2- and 6-mercaptopteridine, which are known to add water reversibly to their neutral molecules.[1,2] This ability to form an anion by ionization of covalently bonded water explains the equilibrium acidic pK_a of $11\cdot86$ for pteridine,[3] and similar values for species such as 1-methyl-2-pteridone[4] and 5-methyl-6-pteridone.[4] For the same reason, 6-chloro- and 7-chloro-pteridine[5] should also form anions.

[2] Albert, A., and Clark, J., *J. Chem. Soc.*, 1965, 27.

[3] Perrin, D. D., *J. Chem. Soc.*, 1962, 645.

[4] Brown, D. J., and Mason, S. F., *J. Chem. Soc.*, 1956, 3443.

[5] Albert, A., and Clark, J., *J. Chem. Soc.*, 1964, 1666.

Experimental

Equilibrium pK_a values were obtained spectrophotometrically by the method of Albert and Serjeant,[6] with a Hilger Uvispek spectrophotometer. This instrument was also used to measure the absorption maxima of stable species. The pH values of potassium hydroxide solutions were calculated from activity coefficient data,[7] taking $pK_w = 14 \cdot 17$ at $20°$. The plot of $(D_{ma} - D)[H^+]$ against D, the optical density, afforded K_a as the slope of the line and D_{da} as the intercept when $(D_{ma} - D)[H^+]$ was equal to zero. (D_{ma} and D_{da} are the optical densities of pure mono- and di-anion, respectively.) The pK_a values and spectra of unstable species were obtained with a Shimadzu RS 27 recording spectrophotometer, using the rapid reaction apparatus described previously.[8] Solutions of the dianions of 2- and 6-hydroxypteridine decomposed slowly during several days.

[6] Albert, A., and Serjeant, E. P., "Ionization Constants of Acids and Bases." (Methuen: London 1962.)

[7] Harned, H. S., and Cook, M. A., *J. Am. Chem. Soc.*, 1937, **59**, 496.

[8] Inoue, Y., and Perrin, D. D., *J. Phys. Chem.*, 1962, **66**, 1689.