494. *Pteridine Studies. Part XXI.*[1] *Kinetics of the Reversible Addition of Water to, and Ring-opening of, Pteridine and its Methyl Derivatives.*

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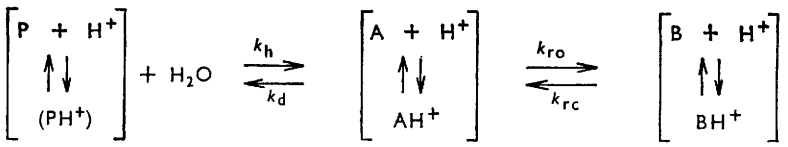
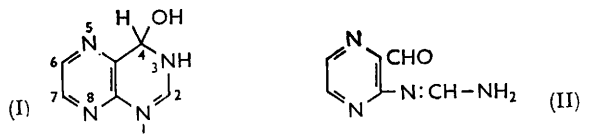
Pteridine and its 2-, 4-, and 7-methyl derivatives add a molecule of water, reversibly, across the 4,3-double bond to form the corresponding 3,4-dihydro-4-hydroxy-compounds. First-order rate constants at 20° for the reaction, which shows general acid–base catalysis, have been evaluated by using a rapid-reaction spectrophotometric method. Ring-opening of the cation of 3,4-dihydro-4-hydroxypteridine and its methyl derivatives, catalysed by hydronium ions has also been investigated.

A kinetic study of the reversible, acid–base-catalysed hydration of 2-hydroxypteridine [2] has now been extended to pteridine and its methyl derivatives, all of which add water reversibly across the $C_{(4)},N_{(3)}$-double bond. The annexed scheme for pteridine shows the reactions and equilibria involved in acid and neutral solutions,[3] where P denotes pteridine, A is 3,4-dihydro-4-hydroxypteridine (I), and B is 2-aminomethyleneamino-3-formylpyrazine (II). Also, in sufficiently alkaline solutions, the base A forms an anion (pK_a 11·2).[3] The portions inside the square brackets exist in dynamic equilibrium (except that



the cation of pteridine has never been characterised), while the rate constants, k_h and k_d, for hydration and dehydration, respectively, and k_{ro} and k_{rc}, for the ring-opening and ring-closing, respectively, are small enough to be obtained from spectrophotometric measurements. Ring-opening is much slower than hydration, and at equilibrium [B] is much less than [A].[3] Also, the equilibrium ratio, $[P]_{eq} : [A]_{eq}$ is 3·5 : 1 in neutral aqueous solutions at 20°. These circumstances make it possible to study hydration and ring-opening separately. Similar considerations apply to 2-, 4-, and 7-methylpteridine for which, at



20°, the equilibrium ratio $[Me\text{-pteridine}]_{eq} : [Me\text{-A}]_{eq}$ is 2·8 : 1 (ref. 3), 36 : 1 (present work), and 25 : 1 (ref. 3), respectively. The remaining isomer, 6-methylpteridine, is unknown. We have found that, as in hydration of 2-hydroxypteridine,[2] at constant wavelength and constant pH, optical density changes due to the reactions in the above scheme obey first-order rate equations.

Experimental

Materials.—We are indebted to Professor A. Albert for providing the pteridine [4] and its methyl derivatives.[5] 2-Methylpteridine was stable but pteridine and 4- and 7-methylpteridine were sublimed *in vacuo* immediately before use. Buffer solutions in the pH range 3·4—6·2 were prepared by mixing 0·05M-sodium borate and 0·05M-succinic acid. Similarly, for the

[1] Part XX, Inoue and Perrin, *J.*, 1962, 2600.
[2] Inoue and Perrin, *J. Phys. Chem.*, 1962, **66**, 1689.
[3] Perrin, *J.*, 1962, 645.
[4] Albert, Brown, and Cheeseman, *J.*, 1951, 474.
[5] Albert, Brown, and Wood, *J.*, 1954, 3832.

ranges pH 6·3—9·2 and 9·4—10·6, 0·05M-sodium borate was added to 0·1M-potassium dihydrogen phosphate and 0·1M-sodium carbonate, respectively. For work at pH >10·6, 0·1M-sodium hydroxide was added to 0·1M-disodium hydrogen phosphate.

Methods.—Reactions were followed spectrophotometrically in a 1-cm. quartz cell attached to a rapid-reaction apparatus which consisted essentially of two Nylon syringes connected to the cell by a Perspex tap containing a mixing chamber, so that simultaneous depression of the plungers of the syringes led to their contents being mixed and placed in the cell.[2] The hydration–dehydration was followed by adding freshly acidified solutions of pteridine to buffer solutions containing sufficient alkali to neutralise the acid in the other solution. Similarly, the ring opening ($AH^+ \longrightarrow BH^+$) was studied by adding neutral pteridine solutions to moderately concentrated acid solutions. (Under these conditions the initial conversion of pteridine into the hydrated cation, AH^+, is too rapid to be measured: from the pH-rate profile, values of $t_{\frac{1}{2}}$ for the hydration should lie between 10^{-3} and 1 sec. for pH values between 0 and 3.) The known [3] ultraviolet absorption spectra of the reactants permitted choice of suitable wavelengths for following these reactions (330 mμ) and the ring-closure of the neutral species, B (258 mμ).

For hydration–dehydration at constant pH and wavelength, the observed change with time in the optical density of the solution is given by [2] $-dD/dt = k_{obs}(D - D_{eq})$, where $k_{obs} = k_h + k_d$, and, by an argument similar to that used for 2-hydroxypteridine,[2] it may readily be deduced that

$$k_h = \frac{k_{obs}(K_a^A + a_{H^+})}{K_a^A(K + 1) + a_{H^+}}$$

and

$$k_d = \frac{k_{obs}KK_a^A}{K_a^A(K + 1) + a_{H^+}},$$

where $K = [P]_{eq}/[A]_{eq}$, and $K_a^A = (a)_{H^+}[A]/[AH^+]$. Hence, provided that K and K_a^A are known, the experimental results yield k_h and k_d. By making measurements over a range of pH, the pH–rate profile can be obtained. Values of K and K_a^A are available [2] for all except 4-methylpteridine. In the present work, the equilibrium ratio of anhydrous to hydrated neutral species for 4-methylpteridine was obtained as 36 : 1 from measurements on an 0·01M-solution, by using a Selector Tast polarograph (Atlas-Werke, Bremen). At pH 8·0 and 20°, $E_{\frac{1}{2}}$ for the hydrated and the anhydrous species were −1·26 and −0·83 v, respectively (compare −0·87 and −0·49 v for pteridine [6] under the same conditions). The pK_a of "hydrated 4-methylpteridine" (3,4-dihydro-4-hydroxy-4-methylpteridine) was found from rapid spectrophotometric measurements, by using solutions which were freshly acidified and then buffered to known pH values, to be 4·90 at 20°.

Results

Table 1 summarises rate constants, obtained at 20° and an ionic strength of 0·1 (adjusted by addition of sodium chloride), for the reversible hydration of pteridine and the known methylpteridines. In all cases, ~1·6 × 10^{-4}M-solutions in 4 × 10^{-3}M-hydrochloric acid were mixed, within several seconds of preparation, with buffer solutions in the rapid-reaction apparatus and the time-dependent optical-density changes were recorded on a Shimadzu model RS-27 spectrophotometer. Under these conditions, initial conversion into hydrated species is incomplete, especially with 4- and 7-methylpteridine, but, because first-order kinetics are obeyed, this does not affect the rate measurements. The corresponding pH–reaction rate profiles for hydration are shown in Fig. 1. Results for pteridine between pH 6 and 8 are in fair agreement with values obtained by Komenda and Laskafeld [6] who used polarography.

The lines in Fig. 1 are for the equations

$$k_h = \alpha a_{H^+} + \beta + \gamma/a_{H^+},$$

where these constants have the following values:

	α	$10^5\beta$	$10^{13}\gamma$		α	$10^5\beta$	$10^{13}\gamma$
Pteridine	354	2·40	4·06	4-Methylpteridine	191	0·6	0·81
2-Methylpteridine	1079	3·54	1·90	7-Methylpteridine	174	0·90	1·13

Minima in reaction rates occur at pH 7·47, 7·88, 7·69, and 7·59, respectively.

[6] Komenda and Laskafeld, *Coll. Czech. Chem. Comm.*, 1962, **27**, 199.

TABLE 1.

First-order rate constants (sec.$^{-1}$) for hydration and dehydration at 20° and $I = 0{\cdot}1$.

pH	10^4k_{obs}	10^4k_h	10^4k_d	pH	10^4k_{obs}	10^4k_h	10^4k_d	pH	10^4k_{obs}	10^4k_h	10^4k_d
					Pteridine						
3·69	1060	841	219	6·75	4·41	0·989	3·42	9·14	30·0	6·68	23·3
3·97	790	541	249	7·17	2·88	0·646	2·23	9·30	48·9	10·9	38·0
4·02	509	338	171	7·35	2·58	0·575	2·00	9·50	67·8	15·1	52·7
4·36	385	198	187	7·79	2·62	0·569	2·05	9·69	96·6	21·5	75·1
4·55	271	75·0	196	8·04	3·06	0·682	2·38	9·85	141	31·4	110
4·76	165	61·4	104	8·41	6·46	1·26	5·20	10·05	210	46·8	163
4·94	126	41·4	84·6	8·77	13·3	2·97	10·3	10·19	274	61·1	213
5·14	86·6	25·3	61·3	8·98	21·3	4·74	16·6	10·37	428	95·3	333
5·86	23·6	5·61	18·0					10·50	584	130	454
6·35	9·47	2·14	7·33					10·60	770	172	598
					2-*Methylpteridine*						
4·36	661	546	115	7·57	2·74	0·726	2·01	9·85	92·6	24·4	68·2
4·55	427	325	102	7·79	2·59	0·686	1·90	10·05	136	35·8	100
4·76	333	225	108	8·22	2·90	0·764	2·14	10·19	123	33·1	89·9
4·94	205	124	81	8·58	5·00	1·32	3·68	10·37	193	50·8	142
5·14	116	60·4	55·6	8·77	8·13	2·14	5·99	10·50	277	73·0	204
5·86	44·0	14·6	29·4	8·98	12·0	3·16	8·84	10·62	324	85·3	239
6·35	19·2	5·51	13·7	9·14	17·5	4·60	12·9	11·00	855	225	630
6·75	11·4	3·12	8·28	9·30	26·9	7·08	19·8	11·24	1380	363	1017
7·15	4·40	1·18	3·22	9·50	41·7	11·0	30·7	11·43	2030	535	1495
7·35	3·78	1·01	2·77	9·69	62·0	16·3	45·7	11·63	3080	811	2269
					4-*Methylpteridine*						
4·36	~800	~88·3	~712	7·35	9·65	0·262	9·39	9·30	66·4	1·81	64·6
4·76	498	31·2	467	7·79	5·39	0·146	5·24	9·50	82·9	2·26	80·6
5·14	333	14·0	319	8·04	5·84	0·159	5·68	9·69	122	3·32	119
5·86	127	3·83	123	8·20	6·79	0·185	6·60	9·85	176	4·79	171
6·55	42·5	1·18	42·4	8·58	14·5	0·395	14·1	10·05	326	12·5	313
6·75	29·3	0·807	28·5	8·98	31·1	0·847	30·3	10·37	595	16·2	579
6·95	19·1	0·522	18·6	9·14	47·0	1·23	45·8	10·50	1010	27·5	982
					7-*Methylpteridine*						
4·36	692	107	585	7·58	4·40	0·169	4·23	10·19	608	23·4	585
4·55	617	71·9	545	7·79	4·57	0·176	4·39	10·37	544	20·9	523
4·76	343	30·2	313	8·22	6·68	0·257	6·42	10·50	708	27·2	681
4·94	281	20·1	261	8·58	13·4	0·515	12·9	10·62	1050	40·5	1009
5·14	214	12·7	201	8·98	35·2	1·36	33·8	11·00	2320	89·3	2231
5·86	71·7	3·08	68·6	9·30	72·3	2·78	69·5	11·24	3730	144	3586
6·35	30·0	1·19	28·8	9·50	126	4·84	121·2	11·43	5570	214	5356
6·75	13·6	0·532	13·1	9·85	262	10·1	252	11·63	7100	273	6827
6·95	10·5	0·406	10·1	10·05	379	14·6	364	11·79	8790	338	8452
7·15	6·29	0·244	6·05								

TABLE 2.

Catalysis of the hydration–dehydration of pteridine at 20° in 4-ethylmorpholine buffers.

Buffer concn. (M)	Added electrolyte	I	pH	10^4k_{obs}	10^4k (predicted *)
0·042	—	0·025	7·58	1·67	(1·67)
0·042	0·375M-Boric acid	0·084	7·84	7·41	1·95
0·042	0·375M-$NaHCO_3$	0·400	7·84	134·5	2·03
0·042	0·0375M-$NaHCO_3$	0·063	7·85	13·7	1·94
0·042	0·417M-Phosphate †	1·09	7·38	10·3	2·02
0·042	0·417M-NaOAc	0·442	7·74	2·64	1·84
0·042	0·417M-NH_4Cl	0·442	7·68	2·34	1·83
0·833	—	0·525	7·77	6·81	1·95

* From value in parentheses by using $\log k_{obs} = \log k_0 + 0{\cdot}06I$, and correction for differences in pH. † $[KH_2PO_4] : [K_2HPO_4] = 2 : 7$.

Similar measurements were made on acidified pteridine solutions adjusted near to pH 7·9 by means of a 0·1M-4-ethylmorpholine buffer which contained sodium chloride to vary the ionic strength from 0·21 to 0·97. The value of k_{obs} showed only a slight dependence on ionic strength, the best straight lines through the experimental points being given by $\log k_{obs} = \log k_0 + 0{\cdot}06I$. A comparable small primary salt effect was found for hydration of 2-hydroxypteridine.[2] However, much larger effects were observed when sodium chloride was replaced by some other

electrolytes. The results summarised in Table 2, especially those for bicarbonate and phosphate ions, boric acid, and 4-ethylmorpholine, indicate that the reaction shows general acid–base catalysis. Catalysis by boric acid and bicarbonate ion has been observed in similar studies of 2-hydroxypteridine.[2]

The Ring-opening, $AH^+ \longrightarrow BH^+$.—Table 3 summarises results of measurements of reaction rates for hydrated pteridine and its methyl derivatives. These indicate that the ring-opening is strongly catalysed by hydronium ion, but the rate does not vary directly with the hydrochloric

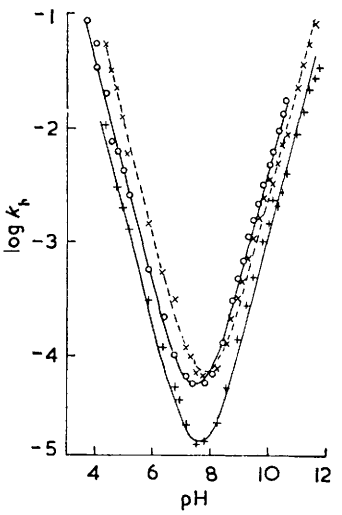


FIG. 1. pH–reaction rate profiles at 20° and $I = 0{\cdot}1$ for the reversible hydration of (○) pteridine, (×) 2-methylpteridine, and (+) 7-methylpteridine.

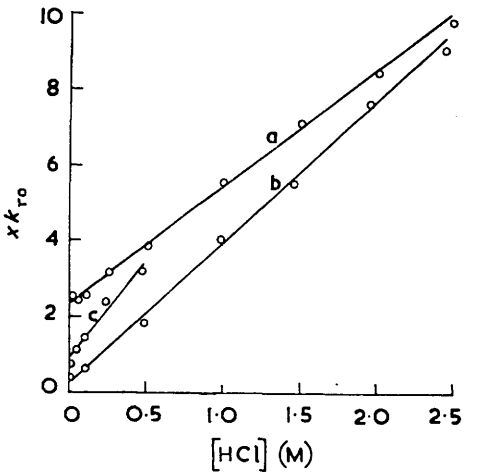


FIG. 2. Variation of k_{ro} with hydrochloric acid concentration, at constant ionic strength ($I = 2{\cdot}50$ by addition of sodium chloride) and at 20·0° ± 0·2°, for hydrated forms of (*a*) pteridine ($x = 10^4$), (*b*) 2-methylpteridine ($x = 5 \times 10^3$), and (*c*) 4-methylpteridine ($x = 10^2$).

TABLE 3.

First-order rate constants (sec.$^{-1}$) for the ring-opening of hydrated pteridine and its methyl derivatives.

[HCl] (M)	Temp.	$10^4 k_{ro}$	[HCl] (M)	Temp.	$10^4 k_{ro}$
		Pteridine			
0·050	12·2°	0·971	0·495	11·4°	0·983
1·261	13·2	2·19	2·491	11·4	3·12
4·638	12·5	20·7			
0·010	20·5	3·05	0·050	19·8	2·89
0·100	20·2	2·96	0·245	20·0	3·08
0·495	20·2	3·54	0·996	20·2	4·18
1·261	19·8	4·82	1·892	20·0	6·64
2·491	19·8	9·75	2·989	20·3	15·0
3·865	20·6	31·7	4·638	20·3	58·5
5·797	20·1	137			
0·050	32·3	13·1	0·495	30·7	12·8
1·261	30·3	17·0	2·491	30·5	34·4
4·638	26·8	142			
0·495	36·7	25·0	2·491	36·5	70·4
		2-Methylpteridine			
0·495	10·7	0·309			
0·010	20·4	0·96	0·100	19·5	0·93
0·495	20·6	1·98	1·261	20·2	5·25
2·491	20·3	15·7	3·865	19·9	52·0
0·495	39·8	24·5			

[HCl] (M)	Temp.	$10^4 k_{10}$	[HCl] (M)	Temp.	$10^4 k_{ro}$
		4-Methylpteridine			
0·495	8·0°	53·9	0·495	9·7°	65·0
0·495	11·5	65·3	0·495	12·2	69·1
0·010	14·0	30·0	0·100	14·7	44·2
0·495	14·7	91·6	1·261	14·5	156
0·010	19·7	71·5	0·050	20·1	91·8
0·100	20·1	116	0·245	20·2	149
0·996	20·3	364	1·261	20·1	457
0·495	24·7	266			
		7-Methylpteridine			
0·495	7·7	3·82			
0·495	15·5	11·5			
0·010	20·1	10·5	0·100	19·9	13·4
0·495	19·9	17·3	1·261	19·9	40·0
2·491	19·9	106			
0·495	29·1	48·1			
0·495	35·4	98·5			

acid concentration unless the ionic strengths of the solutions are kept constant. When this is done, by addition of an " inert " electrolyte, a linear relation is found (Fig. 2). Similarly, the results in Table 3 show that, in the absence of added salt, the logarithms of the rate constants vary linearly with the Hammett acidity function, H_0, if correction is made for the uncatalysed component of the rate constants. Relevant data are summarised in Table 4.

TABLE 4.

Dependence on H_0 of rate constants for ring-opening. Values of a and b relate to the equation, $10^4k_{ro} = a + bh_0$, where $h_0 =$ antilog $(-H_0)$.*

	a	b	Temp.
Pteridine	1·00	0·458	12·5°
Pteridine	3·00	1·24	20·3 ± 0·2
Pteridine	10·8	3·03	30·5 ± 0·2
2-Methylpteridine	0·90	2·22	20·1 ± 0·2
4-Methylpteridine	35	56	14·4 ± 0·3
4-Methylpteridine	90	173	20·2 ± 0·1
7-Methylpteridine	11	13·0	19·9

* Values of H_0 for hydrochloric acid solutions are as given by Paul and Long (*Chem. Rev.*, 1957, **57**, 1).

In the conditions of the measurements, the hydrated species are protonated, so that the values of a for the uncatalysed reaction relate to the cations. There is no evidence that the neutral molecules undergo this reaction: instead, the ring-opened species B slowly cyclises to A. Approximate values for the first-order rate constant, k_{rc}, for the latter reaction at 20° are $1·04 \times 10^{-4}$, $1·01 \times 10^{-4}$, $2·37 \times 10^{-4}$ sec.$^{-1}$, at pH 5·26, 7·58, and 8·95, respectively. These constants have been obtained from changes with time in the optical density at 258 mμ of a pteridine solution in 0·01M-hydrochloric acid, which, after being kept for 4½ hr., was added to appropriate buffers. No corrections have been applied for the effect of partial protonation of B at pH 5·26 or for the fact that, at pH 7·58, k_{obs} is comparable with the rate constant for the reaction, A $\rightleftharpoons$ P.

DISCUSSION

The measured rate constants, k_h and k_d, for hydration and dehydration of pteridine and its methyl derivatives are, in principle, composite because of the dynamic equilibrium between corresponding pairs of cations and neutral molecules. However, the pK_a values of the anhydrous species lie so far below the pH range in which hydration is studied that the cation, PH^+, can be neglected in discussing the stoicheiometry of the reaction. Thus, from the results in Table 2 and Fig. 1, the following catalytic coefficients can be found to apply to the hydration of the neutral molecules of pteridine at 20°:

$$k_h = 354[H^+] + 5·9 \times 10^{-7}[H_2O] + 59[OH^-] + 3·5 \times 10^{-2}[NaHCO_3] + 1·5 \times 10^{-3}[H_3BO_3] + 5·1 \times 10^{-4}[\text{4-ethylmorpholine (mixture of cation and neutral molecule in ratio 5 : 3)}]$$

On the other hand, in the dehydration studies, conditions include pH regions where the concentrations of the cation, AH^+, are comparable with, or much greater than, those of the neutral molecule. The levelling-out of values of k_d, but not of k_h, as solutions are made more acid is thus explained if the hydronium-ion catalysis of the reactions proceeds only by formation of the cations, AH^+ and PH^+, respectively: in fact, the pH–reaction rate profiles for k_d enable roughly correct estimates of pK_a^A to be made in this way. Hence, the quantity, $k_d([A] + [AH^+])$, can be expressed as $k_d'[A] + k_d''[OH^-][A] + k_d'''[AH^+]$, where the k's are constants. From $K_a^A = (a_{H^+})[A]/[AH^+]$, this leads to

$$k_d(K_a^A + a_{H^+}) = k_d'''a_{H^+} + k_d'K_a^A + k_d''K_wK_a^A/a_{H^+}.$$

Constants obtained by fitting the data in Table 1 are summarised in Table 5. Results for pteridine, shown in Fig. 3, are typical.

Comparison of the appropriate constants shows that the introduction of a 2-methyl group into pteridine makes only a small difference to the rates of hydration and dehydration of the neutral molecule. A 4- or a 7-methyl group decreases the rate of hydration to about $\frac{1}{4}$ and $\frac{1}{3}$, respectively, while at the same time increasing three-fold the rate of dehydration. Comparable effects are found for 4- and 7-methylpteridine in the rate of dehydration of hydrated cation (increased three-fold) and of the hydroxyl-ion-catalysed hydration (reduced to $\frac{1}{5}$ and $\frac{1}{4}$, respectively) and dehydration (increased 80% and 50%) of the neutral molecule. In all three cases, 2-methylpteridine gives rates roughly one-half of those for pteridine. It is suggested that a 7-methyl group, by its inductometric effect on $C_{(4)}$, helps to stabilise the formation of a carbonium ion, thereby opposing the addition of the nucleophilic hydroxyl group to 7-methylpteridine and facilitating its removal from the hydrated

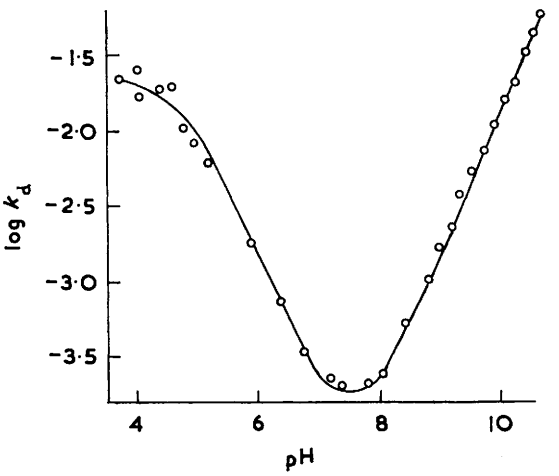


FIG. 3. pH–reaction rate profile for the dehydration of " hydrated pteridine " (3,4-dihydro-4-hydroxypteridine). The solid line is calculated from the constants given in Table 5.

species. A 4-methyl group produces a similar result because of inductive and steric effects, in agreement with the observation that tertiary alcohols ionise more readily to carbonium

TABLE 5.

Rate constants for the dehydration of hydrated pteridine (3,4-dihydro-4-hydroxypteridine) and its methyl derivatives at 20° and $I = 0{\cdot}1$.

	$10^5 k_d'$	k_d''	$10^{-2} k_d'''$
Pteridine	8·45	210	2·36
2-Methylpteridine	9·9	84·9	1·11
4-Methylpteridine	2·25	380	9·1
7-Methylpteridine	22·4	313	6·3

ions than do secondary ones. On the other hand, a 2-methyl group cannot affect interaction at $C_{(4)}$ inductometrically or sterically and its inductive effect would also be quite small. It could, however, interfere sterically if reaction proceeds through a cyclic activated complex of the type postulated for 2-hydroxypteridine,[2] in which case it would reduce to the same extent the rates of the forward- and back-reactions, as found.

The uncatalysed ring-opening for hydrated pteridine showed a negative salt effect, log k_{ro} decreasing by $0{\cdot}05I$ as the ionic strength was varied from 0·01 to 2·8 by addition of sodium chloride. In M-hydrochloric acid, addition of sodium chloride to vary the ionic strength from 1 to 3·0 increased log k_{ro} by $0{\cdot}10I$. Replacement of the sodium chloride by other salts gave increases varying with the cations in the order $Li^+ > Na^+ > K^+ > NH_4^+$. (At $I = 2{\cdot}2$, k_{ro} varied from $1{\cdot}11 \times 10^{-3}$ for lithium bromide to $4{\cdot}84 \times 10^{-4}$ for ammonium

chloride, as against $4{\cdot}21 \times 10^{-4}$ for no added salt. Up to this ionic strength, addition of barium chloride gave a negative salt effect; at higher concentrations the effect was positive.) These differences may reflect changes in H_0 due to variations in f_{H^+} and a_{H_2O}; the latter in particular, may be affected by differences in the hydration numbers of the ions.

Thermodynamic data for the ring-opening of hydrated pteridine and its methyl derivatives in 0·5M-hydrochloric acid have been derived from the temperature effects on the rates, by using the equation,

$$k_{ro} = (\boldsymbol{k}T/\boldsymbol{h}) \exp(-\Delta G^{\ddagger}/\boldsymbol{R}T) = (\boldsymbol{k}T/\boldsymbol{h}) \exp(-\Delta H^{\ddagger}/\boldsymbol{R}T) \exp(\Delta S^{\ddagger}/\boldsymbol{R}),$$

where $\boldsymbol{k}$ is the Boltzmann constant, $\boldsymbol{h}$ is the Planck constant, and $\Delta G^{\ddagger}$, $\Delta S^{\ddagger}$, $\Delta H^{\ddagger}$, are the free energy, entropy, and heat of activation. Results are summarised in Table 6.

The values of $\Delta H^{\ddagger}$ in this Table can be represented to within $\pm 0{\cdot}2$ kcal. mole^{-1} by the equation, $\Delta H^{\ddagger} = 21{\cdot}78 + 0{\cdot}450\Delta S^{\ddagger}$. This linear relationship indicates that the ring-opening is one for which the isokinetic relationship [7,8] holds. The isokinetic temperature is 450°K.

TABLE 6.

Thermodynamic data, calculated at 20°, for the ring-opening of pteridine and its methyl derivatives.

	Temp. range	$\Delta H^{\ddagger}$ (kcal. mole^{-1})	$\Delta S^{\ddagger}$ (cal. deg.$^{-1}$ mole^{-1})
Pteridine	11·4—36·7°	21·8 ± 0·3	0·00 ± 0·06
2-Methylpteridine	10·7—39·8	22·95 ± 0·04	+2·72 ± 0·06
4-Methylpteridine	8·0—24·7	15·7 ± 0·6	−13·25 ± 0·08
7-Methylpteridine	7·7—35·4	18·8 ± 0·7	−7·04 ± 0·08

It was previously suggested [3] that the reported [9] pK_a of 2·94, obtained by direct titration of 4-methylpteridine, is the true pK of 4-methylpteridine. The present results indicate that this is not correct. The value is probably a composite constant involving both hydrated and anhydrous species, in the same way as similar constants for pteridine and its 2- and 7-methyl derivative. Thus the pK of 4-methylpteridine must lie well below 2·9, and that of pteridine (for which a value of 2·6 was suggested) must be still lower. Failure to observe the cation of the hydrated species, 3,4-dihydro-4-hydroxy-4-methylpteridine, was due to its rapid conversion into the ring-opened species, the uncatalysed reaction being 30 times, and the hydronium-ion-catalysed reaction 140 times, as fast as the corresponding reactions for pteridine.

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