152. *The Dissociation Constants of Benziminazole and Certain Purine Derivatives.*

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The pK_a' values of the compounds listed in the table have been determined, and their significance is briefly discussed.

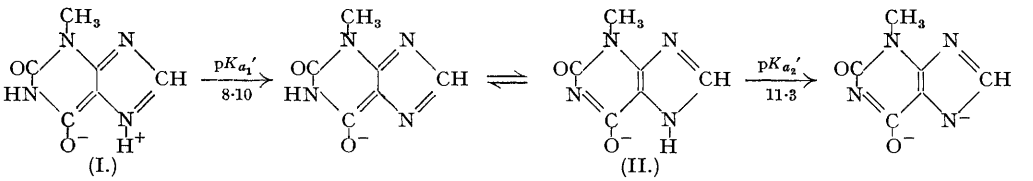
The pK_a' values of benziminazole, adenine, guanine, and certain monomethylxanthines have been determined by electrometric titration in aqueous solution at 25° using the hydrogen electrode, and the values obtained are given below. It will be seen that the pK_{a_1}' values for the monomethylxanthines are in fair agreement with those determined at 18° by Ogston (*J.*, 1935, 1376), whose data are given in parentheses. No dissociations other than those given could be detected from electrometric titrations over the pH range 1·5—12·5.

	pK_a' Values.	
Benziminazole	5·30 *	12·3
Adenine	4·15 *	9·80
Guanine	3·3 † * 9·2 †	12·3 †
1-Methylxanthine	* 7·70 (7·7)	12·0
3-Methylxanthine	* 8·10 (8·5)	11·3
7-Methylxanthine	* 8·30 (8·5)	
9-Methylxanthine	* 6·25 (6·3)	

* Denotes the relative position of the iso-ionic point.
† Approximate values.

The first and second pK_a' values of benziminazole must represent the dissociation of $-\overset{+}{N}H=$ and $-NH-$ groups respectively. The value 5·30 may be compared with that of 7·1 given by Dedichen (*Ber.*, 1906, **39**, 1831) for iminazole (glyoxaline). The value 12·3 is of the same order as those of the weakest acid dissociations of guanine, 1- and 3-methylxanthine, all of which are unsubstituted in the iminazole ring; as would be expected, 7- and 9-methylxanthine show no dissociation in the pH range 11·0—12·5. Analogous results were obtained by Tafel and Dodt (*Ber.*, 1907, **40**, 3757) for the 6-deoxyxanthines.

The basic associations of adenine and guanine may be attributed to the 6-amino- and the 2-amino-group, respectively. The acid dissociation constant of guanine having pK_a' 9·2 and the first acid dissociations of the monomethylxanthines (pK_a' 6·25—8·30) are most probably associated with the presence of an oxygen atom in the 6-position. Ogston (*loc. cit.*) has concluded that enolisation involving the 1-position must be excluded, and that in 3-, 7-, and 9-methylxanthine the zwitterionic form predominates, the acid dissociation being represented as that of an $-\overset{+}{N}H=$ group in the iminazole ring (I, for the case of 3-methylxanthine). If this theory is correct, dissociation of the second hydrogen atom in the iminazole ring must be preceded by a tautomeric change to form the ion (II) since, according to Ogston, the $-NH-$ group in the 1-position does not appear to show acid properties.



In the case of adenine, the dissociation having pK_a' 9·80 can only be due to the $-NH-$ group of the iminazole ring, a fact which is confirmed by the absence of any such dissociation in adenosine, in which the 9-position is substituted (Levene and Simms, *J. Biol. Chem.*, 1925, **65**, 579). The abnormal strength of this group cannot be explained on the basis of the data available.

Experimental.

The experimental procedure was similar to that described by Fletcher, Gulland, and Jordan (*J.*, 1944, 33), and the results were calculated by the method of Jordan and Taylor (*J.*, 1946, 994). The pK_a' values are based on the pH standard of 3·97 for 0·05M-potassium hydrogen phthalate solution.

The concentrations of the solutions titrated lay between 0·0012M and 0·007M, except in the case of benziminazole when solutions of approximately 0·035M were used. The guanine was brought into

approximately 0·0015M-solution at pH 11—12 and back-titrated rapidly with acid, supersaturated solutions being obtained.

The benziminazole was the sample used by Jordan and Taylor (*loc. cit.*). The adenine and guanine were obtained in the form of hydrochlorides from Mr. C. J. Threlfall, B.Sc., and were recrystallised from dilute hydrochloric acid. The methylxanthines, samples of which were supplied by (the late) Professor J. M. Gulland, F.R.S., and Dr. F. G. Mann, F.R.S., were recrystallised twice from aqueous alcohol.

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