CCLXXXVIII.—*The Application of the Hydrogen Electrode to Organic Bases: Piperidine, and its Use as an Alkaline Buffer.*

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The dissociation constants of organic bases rest on conductivity determinations alone, whilst the hydrogen-ion concentrations of their partly neutralised solutions are either calculated from these constants or determined by colorimetric methods. It would seem desirable to test these results with the hydrogen electrode, as has been done in the case of acids. It has long been known that this electrode is untrustworthy with ammonia and some amines (Bottger, *Z. physikal. Chem.*, 1899, **24**, 253), and it has also been stated (Kolthoff, *Biochem. Z.*, 1925, **162**, 289) that the alkaloids are susceptible to catalytic reduction at the surface of a hydrogen electrode. The possibility of carrying out an electrometric titration on hydrazine has, however, been established by Gilbert (*J. Amer. Chem. Soc.*, 1924, **46**, 2648). This base is unstable in most respects, but is resistant to reducing agents. Although the numerical results were not given in the paper, one can infer that the first constant was in fairly good agreement with the value, 3×10^{-6}, based on Bredig's measurements of conductivity.

Piperidine seemed to be eminently suitable for testing the constant derived from conductivity, since it is a moderately strong base which obeys the dilution law, and it was deemed to be stable towards platinum–hydrogen. The dissociation constant according to Bredig is $1{\cdot}6 \times 10^{-3}$, and $\lambda_0 = 216$, expressed in modern units (*Z. physikal. Chem.*, 1894, **13**, 191). The value used by Hantzsch and Sebaldt (*ibid.*, 1900, **33**, 129) is 232 at 25°. In the case of the hydrochloride, at $v = 1024$, $\lambda = 110$; if 2·5 units be added, according to the usual rule, $\lambda_0 = 112{\cdot}5$; since the mobility of the chlorine ion is 75·5, that of the piperidinium ion is 37·0, and, that of the hydroxyl ion being 196, λ_0 for piperidine is found to be 233. On combining this with the λ values of Bredig (converted into ohms) for $v = 32$ and 256, one finds $K = 1{\cdot}42 \times 10^{-3}$ and $1{\cdot}30 \times 10^{-3}$, respectively. These are rather higher than the constants of Hantzsch and Sebaldt (*loc. cit.*), *viz.*:

Temp. =	15°	20°	25°
10^3K =	1·11	1·15	1·20

from which, by interpolation, the constant at 18° is $1{\cdot}14 \times 10^{-3}$, $p_K = 2{\cdot}94$. We consider this constant to be a more satisfactory basis for calculations than the uncorrected constant of Bredig. We have tested its validity for expressing the p_H values obtained during neutralisation by (*a*) a potentiometric and (*b*) a colorimetric titration.

(a) *Electrometric Titration.*—The usual circuit for potentiometric titrations was set up, containing a cadmium cell, which was checked against an N.P.L. Standard, a capillary electrometer, and a metre slide wire, which had been calibrated against an accurate resistance box. A platinised platinum–hydrogen electrode of the Hildebrand type dipped into an open beaker which contained the solution of piperidine. The other half-cell was an $N/10$-potassium chloride–calomel electrode, the two solutions being connected by a salt bridge of saturated potassium chloride–agar.

To the $N/10$-piperidine solution, N-hydrochloric acid was added with stirring. The balance point on the bridge-wire became steady at once, and readings were taken after each addition of acid. The *E.M.F.*, E_c in table, of the hydrogen half-cell against an electrode in N-hydrogen ion is equal to the *E.M.F.*, E in table, corresponding to the balance-point minus 0·338. The readings are given as c.c. of hydrochloric acid added to a given volume of piperidine:

c.c. =	2·1	2·45	2·75	3·0	3·2	3·4
E =	0·962	0·943	0·914	0·845	0·502	0·461
E_c =	0·624	0·605	0·576	0·507	0·164	0·123

$\Delta E/\Delta C$ assumes a high value between 3·0 and 3·2 c.c.; the subsequent readings correspond to solutions beyond the equivalence point.

The possibility of a satisfactory electrometric titration is thus demonstrated. Some of these results were used in determining p_K (see below), the following p_H values being calculated from $E_c/0{\cdot}058$:

E_c =	0·624	0·605	0·576	0·507	0·164	0·123
p_H =	10·75	10·45	9·92	8·73	2·84	2·12

Electrometric Determination of K.—Since the middle part of the neutralisation is of particular importance in determining K, another experiment was carried out (with a different volume of piperidine) from an earlier stage in the neutralisation and with 0·55N-acid, in order to obtain a greater accuracy in the values of x, the fraction of base neutralised. The values of p_K are calculated from the equation

$$p_K = \log (1 - x)/x + p_{K_W} - p_H,$$

where p_{K_W} has its usual significance and is equal to 14·13 at 18°.

The potentiometric titration of 0·1N-piperidine with 0·55N-hydrochloric acid.

HCl (c.c.).	E_c.	p_H.	100x.	p_K.
0·65	0·682	11·8	17·8	2·99
0·95	0·672	11·6	26·0	2·98
1·24	0·665	11·43	33·9	2·99
1·60	0·652	11·23	43·7	3·00
1·85	0·645	11·1	51·0	3·01
1·95	0·640	11·05	53·4	3·02
2·10	0·637	10·95	57·4	3·05
2·40	0·620	10·75	66·0	3·09
2·65	0·607	10·55	73·3	3·14
	0·605	10·45	80	3·09
	0·576	9·92	90	3·26

Thus the potentiometric constant is distinctly lower (p_K higher) than that derived from conductivity results; the constancy is very satisfactory, the trend up to $x = 0{\cdot}50$ being very slight, less indeed than in the case of most acids. Thus it has been shown by Michaelis and Kruger (*Biochem. Z.*, 1921, **119**, 307) that the p_K of acetic acid when 50% neutralised is 4·665, whilst that of the free acid is 4·733; there is therefore a decrease of 0·068 in p_K, or an increase in the constant. Although it is not possible to determine the potentiometric p_K with sufficient accuracy on aqueous solutions of free piperidine, we do know that the change of p_K over a large range of neutralisation is only about 0·02. If, however, p_K of the pure base is 2·94, the difference between this and the value prevailing at 50% neutralisation is 0·07—of the same order as the difference for acetic acid, but in the opposite direction. While, therefore, the constant increases during neutralisation in the case of typical weak acids, it decreases in the case of this weak base. It is intended to test other bases, in order to find whether this behaviour is characteristic of the class.

The increases in the constants of acids may be plausibly attributed to the presence of the increasing amount of salt formed during the neutralisation, since the addition of sodium chloride, or other neutral salt, has a marked effect in the same direction (Michaelis and Kruger, *loc. cit.*).

The present effect, however, is not a salt effect, as was proved by the following experiments. Sodium chloride was added to the solutions under investigation so as to preserve a constant concentration of chloride, equal to that which would have been attained at the end of the neutralisation. Had the drift in the constant been a salt effect, the balance point would have been altered in the first stages of neutralisation, so as to give a constant p_K equal to the slightly higher value obtained in the nearly neutralised solution.

Addition of NaCl to 30 c.c. of piperidine at various degrees of neutralisation.

100 *x*.	Balance point on bridge, without NaCl.	Weight of NaCl added (g.).	Balance point in presence of NaCl.
10	51·2	0·158	51·2
30	49·7	0·117	49·8
50	48·7	0·088	48·7
80	46·4	0·035	46·5

Hence the *E.M.F.*'s and the p_H values are not affected by moderate amounts of neutral salt, the presence of which, therefore, does not account for the slight trend in K in the case of solutions which are more than 50% neutralised.

(b) *Colorimetric Titration.*—It is clear from the above results that the calculation of p_H during neutralisation from the constant which is based on conductivity will give numbers about 0·2 unit higher than those determined by the hydrogen electrode. It remains to be found whether these latter p_H values have the same effect on indicators as those derived from known buffer solutions.

We have selected the buffers of Ringer: $0{\cdot}15N\text{-Na}_2\text{HPO}_4 + 0{\cdot}1N\text{-NaOH}$ (p_H 11—12), and one of Sörensen's: $0{\cdot}2N\text{-Na}_2\text{B}_4\text{O}_7 + 0{\cdot}1N\text{-NaOH}$ or HCl (p_H 11—8). These solutions were matched against the piperidine at various stages of neutralisation, by using the B.D.H. "universal indicator," which can be made to show changes within 0·1 in p_H over the range involved. To 10 c.c. of the $N/10$-piperidine solution were added counted numbers of drops of the $0{\cdot}55N$-hydrochloric acid, from a dropping pipette, 22 drops of which were equal to 1 c.c. When the colour matched that of the buffer solution containing the same concentration of indicator, the % of neutralisation was recorded.

No. of drops.	p_H of buffer.	100x.	p_K.	No. of drops.	p_H of buffer.	100x.	p_K.
9	11·74	22·5	2·93	35	10·05	87·5	3·23
18	11·19	45	3·02	36	9·84	90	3·33
22	11·01	55	3·03	37	9·50	92·7	3·53
33	10·33	82·5	3·12	38	9·41	95·0	3·43
34	10·15	85·0	3·23	39	9·21	97·5	3·33

The values determined by the hydrogen electrode are therefore confirmed, and the slight trend in K_B is again found, the values of p_K rising more sharply when neutralisation is nearly complete.

In all the middle part of its neutralisation interval, piperidine will make an excellent buffer solution : the p_H values may be calculated from $p_K = 3·00 \pm 0·02$ between 15 and 55% neutralisation. In an N/10-solution of piperidine which has been 50% neutralised by 0·5N-hydrochloric acid, p_K is found, both by the hydrogen electrode and by indicators, to be 11·10 ± 0·05. This is an accurately defined reference point for the measurement of acidity.

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