Polarographic Studies on Heterocyclic Compounds. I. Kinetic Current of Isonicotinic Acid

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Introduction

Polarographic studies of pyridine derivatives have been made by several scholars. The reduction mechanism of picolinic, nicotinic and isonicotinic acids, which are monocarboxylic acid of pyridine, have been studied by Tompkins and others[1-6].

The present authors investigated the limiting current of isonicotinic acid.

Experimental Part

A specimen of isonicotinic acid is offered by Prof. Dr. T. Takahashi (the Department of Pharmacy, Faculty of Medicine, Kyoto University).

The concentration of isonicotinic acid in the electrolytic solution, in which 0.1-N potassium chloride is involved as an indifferent electrolyte, is in the range of 10^{-4} to 10^{-3} mol per liter. The *p*H of electrolytic solution is changed by using the various kinds of buffer solutions, which are Mc Ilvain's phosphate buffer, Kolthoff's buffer, and Sörensen's borate buffer. The volume of buffer solution contained in the electrolytic solution corresponds to 80 vol. % of the whole solution.

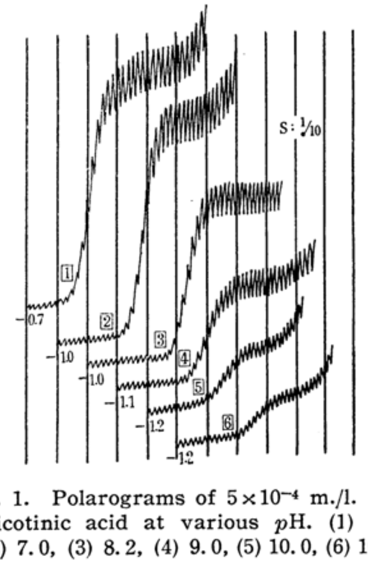

Fig. 1. Polarograms of 5×10^{-4} m./l. isonicotinic acid at various *p*H. (1) 2.2, (2) 7.0, (3) 8.2, (4) 9.0, (5) 10.0, (6) 10.8.

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1) M. Shikata and I. Tachi *Chem. News.* **137**, 126 (1928).

2) P. C. Tompkins and C. L. Shmidt *J. Biol. Chem.*, **143**, 643 (1942).

3) P. C. Tompkins and C. L. Schmidt, *Univ. California Pub., Physiol.*, **8**, 229 (1943).

4) P. C. Tompkins and C. L. Schmidt, *Uuiv. California Pub., Physiol.*, **8**, 237 (1943).

5) P. C. Tompkins and C. L. Schmidt, *Univ. California Pub. Physiol.*, **8**, 247 (1943).

6) E. Knobloch, *Collection*, **12**, 407 (1947).

The Yanagimoto Type Polarograph is used and the normal calomel electrode is connected with the electrolytic solution as a reference electrode. The sensitivity of the galvanometer is 3×10^{-9} Amp./mm./m. The rate of the flow of mercury from the capillary, *m*, and drop time *t*, at −1.6 volt vs. N.C.E. are 1.202 mg./sec. and 4.26 sec. at 20°C., respectively.

Experimental Results

(1) Effects of the *p*H on the Half-wave Potential and the Limiting Current.

The polarograms obtained with 5×10^{-4} m./l. isonicotinic acid solution of various *p*H values show a so-called well-defined single reduction wave in the whole *p*H range (Fig. 1). The relationship between *p*H, the half-wave potential, and the limiting current is shown in Table I. As shown by curve (1) in Fig. 2, the half-wave potential shifts to more negative value with increasing *p*H value and in the range of *p*H greater than 10 it remains nearly constant.

TABLE I

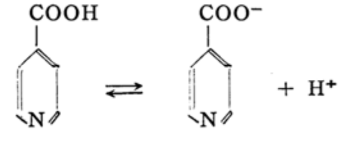
RELATIONSHIP BETWEEN THE *p*H, $E_{1/2}$, AND THE LIMITING CURRENT OF THE REDUCTION WAVE OF 5×10^{-4} m./l. ISONICOTINIC ACID

Temperature: 20°C.

*p*H	Buffer	$E_{1/2}$ (vs. N.C.E.)	$i(\mu A)$
2.2	Mc Ilvain's buffer	−0.910 v.	2.30
3.0	,,	−0.970	2.30
4.0	,,	−1.030	2.31
5.0	,,	−1.120	2.40
6.0	,,	−1.180	2.40
7.0	,,	−1.280	2.10
6.2	Kolthoff's buffer	−1.190	2.30
7.1	,,	−1.260	2.04
7.5	,,	−1.290	1.83
8.2	,,	−1.330	1.56
8.5	,,	−1.360	1.35
9.0	,,	−1.410	0.93
9.2	Sörensen's buffer	−1.420	0.72
9.5	,,	−1.440	0.48
10.0	,,	−1.460	0.26
10.8	,,	−1.470	0.18
12	,,	−1.470	—
13	in 0.1-N NaOH	—	—

While the limiting current shows a constant value in the *p*H range from 2 to 6, it decreases gradually with increasing *p*H value in the range of *p*H greater than 7 until it diminishes at *p*H 12.

Isonicotinic acid is a weak mono-basic acid and dissociates as follows:



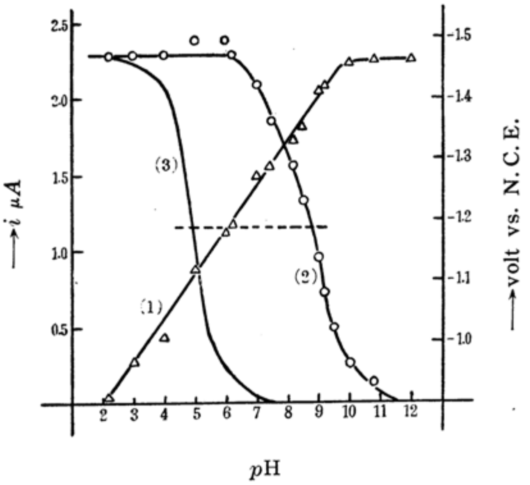


Fig. 2

(1)......$E_{1/2}$-*p*H curve
(2)......*i*-*p*H curve
(3)......Dissociation curve

Its dissociation constant, *K*, is equal to 1.09×10^{-5}[7]. Curve (3) in Fig. 2 represents the dissociation curve of isonicotinic acid and the course of *i*-*p*H curve (curve (2) in Fig. 2) runs similarly to it. Therefore, provided the reduction wave is due to the reduction of undissociated molecules of isonicotinic acid, curve (2) is to be regarded to show the apparent polarographic dissociation curve.

(2) Effect of the Concentration of Isonicotinic Acid on the Limiting Current.

The relationship between the concentration of isonicotinic acid, the half-wave potential, and the limiting current at *p*H 5.0 at 22°C. is shown in Table II. As shown in column 4 (Table II) and Fig. 3 the limiting current is

TABLE II

RELATIONSHIP BETWEEN THE CONCENTRATION OF ISONICOTINIC ACID AND ITS LIMITING CURRENT AT *p*H 5.0

Temperature: 22°C.

Conc. ($\times10^{-4}$ m./l.)	$E_{1/2}$ (vs. N.C.E.)	$i(\mu A)$	i/Conc.
9	−1.050 v.	4.56	0.506
8	−1.040	4.11	0.512
7	−1.030	3.54	0.505
6	−1.040	3.06	0.510
5	−1.030	2.52	0.504
4	−1.030	2.04	0.510
3	−1.020	1.56	0.520
2	−1.020	1.02	0.510
1	−1.030	0.54	0.540

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[7] H. Scudder, "Conductivities and Ionization Constants of Organic Compounds", 267 (1914).

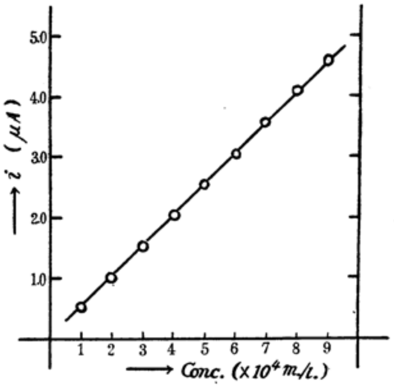

Fig. 3

proportional to the concentration of isonicotinic acid. Hence the quantitative analysis of isonicotinic acid is possible at *p*H 5.0 in the range from 10^{-4} to 10^{-3} mol per liter. The half-wave potential is hardly influenced by the change of concentration (Column 2 in Table II).

(3) Effect of the Height of Mercury Reservoir on the Limiting Current.

TABLE III

DEPENDENCE OF THE HEIGHT OF MERCURY RESERVOIR ON THE LIMITING CURRENT OF 5×10^{-4} m./l. ISONICOTINIC ACID

Temperature: 20°C.

h	$\sqrt{h}$	*p*H 9.5 i	*p*H 3.0 i	 $i/\sqrt{h}$
60 cm.	7.75	0.495 μA	2.400 μA	0.31
55	7.42	0.495	2.280	0.31
50	7.07	0.510	2.265	0.32
45	6.71	0.510	2.175	0.33
40	6.33	0.510	2.070	0.33
35	5.92	0.499	1.950	0.33
30	5.48	0.495	1.830	0.33
25	5.00	0.510	1.665	0.33

Table III represents the relationship between the mercury reservoir height, *h*, and the limiting current at *p*H 3.0 and 9.5. The fact that the limiting current at *p*H 3.0 is proportional to $\sqrt{h}$ (column 5 in Table III) means that this current is controlled by a diffusion process as shown by the Ilkovič theory[8]; whilst, the limiting current at *p*H 9.5 is independent of *h*, i.e., it can be concluded that the limiting current at *p*H 9.5 shows the characteristics of kinetic current[9,10].

TABLE IV

INFLUENCE OF THE TEMPERATURE ON THE LIMITING CURRENT OF 5×10^{-4} m./l. ISONICOTINIC ACID

*p*H 3.0 t°C.	 i	 Temp.-Coeff.	*p*H 9.5 t°C.	 i	 Temp.-Coeff.
22.4	2.40 μA		21.2	0.548 μA	
26.4	2.58		25.2	0.630	3.19%
30.0	2.70		30.5	0.705	2.67%
35.7	2.97	Av.	36.2	0.774	2.27%
41.0	3.24	1.62%	39.4	0.819	1.92%
45.5	3.48		45.0	0.870	1.89%
50.5	3.78		50.5	0.910	1.80%
55.2	4.08		55.5	0.975	1.63%

(4) Effect of the Temperature on the Limiting Current.

The relationship between the temperature and the limiting current at *p*H 3.0 and 9.5 is shown in Table IV. The temperature coefficient of the limiting current which is expressed by $\left(\frac{1}{i}\frac{di}{dT}\right)\times100\%$ is about 1.6% per degree at *p*H 3.0 and it is equal to that of the diffusion current[11]. The coefficient at *p*H 9.5 is greater than at *p*H 3.0 (Column 6), but it decreases gradually with rising temperature. This tendency seems to be opposite to the general one concerning the temperature coefficient. The reason why such a phenomenon presents itself cannot be interpreted and must to be investigated furthermore.

Discussion

As the limiting current at *p*H 3.0 is controlled by diffusion process, the theoretical diffusion current can be calculated from Ilkovič's equation[8]

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[8] D. Ilkovič *Collection*, **6**, 498 (1934).

[9] R. Brdička and K. Wiesner, *Collection*, **12**, 138 (1947).

[10] J. Koutecký and R. Brdička, *Collection*, **12**, 337 (1947).

[11] D. Ilkovic, *Collection*, **10**, 249 (1938).

$$i_d=0.605nFCD^{1/2}m^{2/3}t^{1/6} \qquad (1)$$

where i_d denotes the diffusion current, n electron number involved in the reduction, F Faraday's constant, C the concentration of the depolarizer, D its diffusion coefficient, m the rate of flow of mercury from the capillary, and t drop time. Employing the following numerical values: $C=5\times10^{-4}$ m./l., $D=8.86\times10^{-6}$ (assuming that the diffusion coefficient of isonicotinic acid is equal to that of benzoate[12]), $m=1.201$ mg./sec., $t=4.26$ sec., and supporting that $n=2$, we obtain the result $i_d=2.514\ \mu$A. Hence the experimental value agrees nearly with the calculated value within experimental error. Therefore, the reduction of isonicotinic acid seems to correspond to the two electron reduction.

Next, as the result of the wave analysis, the reduction process of isonicotinic acid is found to be irreversible; and this conclusion is also confirmed from the standpoint of A. C. polarography, in which A.C. voltage of an arbitrary amplitude is superposed on the D.C. voltage of polarograph, and A.C. component of the pulsating current resulting electrolysis shows a peak at the half-wave potential of polarographic wave in the case of reversible system, while such a peak does not appear in the case of irreversible system[13,14].

The kinetic current due to the recombination of the dissociated anion with proton was for the first time studied theoretically by R. Brdička and K. Wiesner[9]. Later, J. Koutecký and R. Brdička[10] cleared it up mathematically.

In the dissociation equilibrium of isonicotinic acid

$$HA \underset{k_1}{\overset{k_2}{\rightleftarrows}} H^+ + A^- \qquad (2)$$

where HA, A^-, and H^+ denote the undissociated molecule, dissociated anion, and hydrogen ion, respectively, dissociation constant, K, is given by

$$K=k_2/k_1=[H^+][A^-]/[HA] \qquad (3)$$

where k_1 and k_2 are the recombination and dissociation velocity constant, respectively. In the reduction of acid, the undissociated molecule is generally reduced at the more positive potential than the dissociated anion. The reduction wave in the case of isonicotinic acid is considered to be due to the reduction of undissociated molecules and the anion reduction wave seems to be overlapped with the wave of indifferent cation or hydrogen ion in the electrolytic solution. The difference between the dissociation curve (curve (3) in Fig. 2) and the apparent polarographic dissociation curve (curve (2) in Fig. 2) is clearly caused by the kinetic current due to the recombination of dissociated anion with hydrogen ion.

According to J. Koutecký and R. Brdička[10], the change of the concentration of both molecule and anion with time is represented by the algebraic sum of diffusion and recombination terms; that is

$$\frac{\partial a}{\partial t}=D\frac{\partial^2 a}{\partial x^2}+\rho(b-\sigma a) \qquad (4)$$

$$\frac{\partial b}{\partial t}=D\frac{\partial^2 b}{\partial x^2}-\rho(b-\sigma a) \qquad (5)$$

where a and b the concentration of undissociated molecule and dissociated anion, respectively, and

$$\rho=k_1[H^+], \quad \sigma=K/[H^+]$$

The proper initial and boundary conditions are as follows;

$$\begin{array}{lll} a=a_e, \ b=b_e & \text{for} & t=0, \ x>0 \\ a=0, \ \partial b/\partial x=0 & \text{for} & t>0, \ x=0 \end{array}$$

where a_e and b_e are the equilibrium concentration of a and b, respectively. Eq. 4 can be integrated by means of Laplace transformation, and then the solution is given by

$$\frac{\sqrt{\pi D}}{\alpha}\left(\frac{\partial a}{\partial x}\right)_{x=0}=\frac{1}{(\sigma^2-1)}\Big[t^{-1/2}(\sigma e^{-\rho(1+\sigma)t}-1)$$
$$+2\frac{\rho^{1/2}\sigma^2}{(\sigma^2-1)^{1/2}}e^{\frac{\rho t}{\sigma-1}}\Big\{\int_0^{\sigma\sqrt{\frac{\rho t}{\sigma-1}}}e^{-x^2}dx-\int_0^{\sqrt{\frac{\rho t}{\sigma-1}}}e^{-x^2}dx\Big\}\Big] \qquad (6)$$

where α denotes the analytical concentration of acid. When $\sigma=0$, i.e., dissociation does not take place at all, Eq. 6 is simplyfied to

$$\left(\frac{\partial a}{\partial x}\right)_{x=0}=\frac{a_e}{\sqrt{\pi Dt}} \qquad (7)$$

When $\rho\gg1$ and $\sigma\gg1$, Eq. 6 is reduced to

$$\left(\frac{\partial a}{\partial x}\right)_{x=0}=\alpha\sqrt{\frac{\rho}{D\sigma}}e^{\frac{\rho t}{\sigma}}\Big[1-\Phi\Big(\sqrt{\frac{\rho t}{D}}\Big)\Big] \qquad (8)$$

where

$$\Phi(y)=\frac{2}{\sqrt{\pi}}\int_0^y e^{-y^2}dy$$

and when $\rho\gg1$, $\sigma\gg1$, and $\rho/\sigma\gg1$, Eq. 6 is simplyfied to

$$\left(\frac{\partial a}{\partial x}\right)_{x=0}=\alpha\sqrt{\frac{\rho}{D\sigma}} \qquad (9)$$

Therefore, from Eq. 9 and the surface area

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[12] M. J. Astle and W. V. Mc Connell, *J. Am. Chem. Soc.*, **65**, 35 (1943).

[13] B. Breyer, F. Gutmann and S. Hacobian, *Aust. J. Sci. Res.*, A**3**, 558 (1950).

[14] I. Tachi, F. Kambara and M. Senda, not published yet.

of mercury drop $q=0.85\,m^{2/3}t^{2/3}$, the average kinetic current, $\bar{i}$, is shown by

$$\bar{i}=\frac{3}{5}\cdot 0.85m^{2/3}t_1^{2/3},nF\alpha\sqrt{\frac{D\rho}{\sigma}} \qquad (10)$$

Since $3/5\times 0.85m^{2/3}t_1^{2/3}$, in Eq. 10 represents the average surface area of the dropping mercury electrode and the product mt_1 is independent of the height of mercury reservoir, when the same capillary is used under the same conditions, the kinetic current shows a constant value independently of the change of the mercury reservoir height. From Eq. 8, the average kinetic current is given by

$$\bar{i}=\frac{0.85m^{2/3}nF\alpha}{t_1}\int_0^{t_1}\sqrt{\frac{D\rho}{\sigma}}e^{\frac{\rho t}{\sigma}}\left[1-\Phi\left(\sqrt{\frac{\rho t}{\sigma}}\right)\right]t^{2/3}dt \qquad (11)$$

when $k_1\rightarrow\infty$, the limiting current has no character of the kinetic current, but corresponds to the diffusion current. Denoting it by $\bar{i}_\infty$, from Eqs. 7 and 11 it is seen that

$$\frac{\bar{i}}{\bar{i}_\infty}\doteq\frac{6}{7\sqrt{\pi}\,y^{7/6}}\int_0^{y_1}F(y)dy=f(y_1) \qquad (12)$$

where

$$F(y)=y^{2/3}e^{y}[1-\Phi(\sqrt{y})]$$
$$y=\rho t/\sigma,\quad y_1=\rho t_1/\sigma \qquad (13)$$

When the kinetic current corresponds to a half of the diffusion current, it can be shown that

$$f(y_1)=0.5$$

and then

$$y_1=0.420(^*)$$

When $K\gg[H^+]$, it follows from Eq. 13 that

$$y_1=\frac{k_1[H^+]}{K}t_1$$

$$\log k_1=2\left(pH+\frac{1}{2}\log y_1\right)-(pK+\log t_1) \qquad (14)$$

The pH value where $f(y_1)=0.5$ in curve (2) (Fig. 2) is 8.8, and $t=4.26$ sec. and

$$K=1.09\times 10^{-5}.$$

Substituting these values into Eq. 14, the recombination velocity constant is equal to

$$k_1=1.22\times 10^{12}\ \text{sec.}^{-1}\ (\text{m./l.})^{-1}$$

Further, it is found that the dissociation velocity constant is

$$k_2=k_1K=1.33\times 10^{7}\ \text{sec.}^{-1}$$

According to J. Koutecký and R. Brdička[10], the thickness of the reaction layer where recombination takes place, μ, is given by

$$\mu=\sqrt{\frac{D}{k_1K}} \qquad (15)$$

Inserting the above mentioned values viz., $D=8.86\times 10^{-6}$, $k_1=1.22\times 10^{12}$ and $K=1.09\times 10^{-5}$ into this equation, it is found that

$$\mu=8.16\times 10^{-7}\ \text{cm}.$$

This value seems to be right in comparison with the other values obtained experimentally concerning some organic acids[17,18].

Summary

(1) Isonicotinic acid shows a single polarographic reduction wave. It is found from the standpoint of the wave analysis as well as of A.C. polarography that the electrode process is irreversible.

(2) The wave height at pH 5.0 is proportional to the concentration of isonicotinic acid in the concentration range from 10^{-4} to 10^{-3} mol per liter.

(3) Since the single reduction wave is considered to be due to the reduction of undissociated molecules, the i-pH curve shows an apparent polarographic dissociation curve.

(4) The kinetic current due to the recombination of dissociated anions with proton is investigated, and the recombination velocity constant and the thickness of reaction layer are determined according to J. Koutecký and R. Brdička's equations.

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[*] According to J. Koutecký and R. Brdička[10], y_1 is equal to 0.400; but J. Koryta[15] points out the error as to this value. M. Senda[16] newly obtains the plot of y_1 vs. f(y_1) from the numerical calculation, and the above value is obtained from this plot.

15) J. Koryta, *Proc. I.Inter. Polaro. Congr. in Prague*, **1** 798 (1951),

16) M. Senda; not published yet.

17) R. Brdička, *Proc. I. Inter. Polaro. Congr. in Prague*, **3** 286 (1952).

18) I. M. Kolthoff and A. Liberti, *J. Am. Chem. Soc.*, **70**, 1885 (1948).