76-8296

RINGEN, John Charles, 1946-
POLAROGRAPHIC STUDY OF METAL CHELATES
OF PYRAZINE CARBOXYLIC ACIDS AND
RELATED COMPOUNDS.

The City University of New York
Ph.D., 1976
Chemistry, analytical

Xerox University Microfilms, Ann Arbor, Michigan 48106

POLAROGRAPHIC STUDY OF METAL CHELATES OF PYRAZINE CARBOXYLIC ACIDS AND RELATED COMPOUNDS

by

JOHN C. RINGEN

A dissertation submitted to the Graduate Faculty in Chemistry in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York.

1975

This manuscript has been read and accepted for the Graduate Faculty in Chemistry in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

Nov. 3, 1975
Date

Robert E. Kirby
Chairman of Examining Committee

November 11, 1975
Date

Leonard H. Schwartz
Executive Officer

W F Berkowitz

Joseph Gerstein

David C. Locke

Supervisory Committee

The City University of New York

Abstract

POLAROGRAPHIC STUDY OF METAL CHELATES OF PYRAZINE CARBOXYLIC ACIDS AND RELATED COMPOUNDS

by

John C. Ringen

Adviser: Professor Robert E. Kirby

Although much work has been performed to study metal complexes of pyridine carboxylic acids, only recently have diazine carboxylic acids (i.e. pyrazine, pyrimidine, and pyridazine carboxylic acids) been studied for possible use as chelating agents, and no stability constants of chelates of these acids have yet been determined.

In this investigation, the polarographic method has been used to study the polarographic reduction of four diazine carboxylic acids and their copper chelates. In addition, the lead-picolinic acid chelates have been reexamined in order to resolve some difficulties which had come up in previous work.

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CHAPTER I

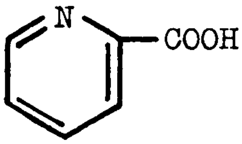
INTRODUCTION

It is well known that pyridine carboxylic acids form complexes with a wide variety of metal ions; many workers have obtained stability constants of metal chelates of these acids using a number of techniques including spectrophotometry, potentiometry, and polarography.[1,2]

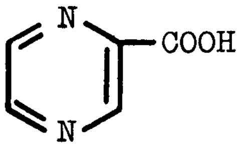
The red color obtained when pyridine carboxylic acids are added to solutions of ferrous salts is due to the formation of a chelate between the two compounds, and this color formation is the basis for the Skraup test for pyridine-2-carboxylic acids.[3,4]

Ley, Schwarte, and Münnich[5] determined absorption spectra of ferrous complexes of various carboxylic acids including picolinic acid and pyrazine-2,3-dicarboxylic acid. Other workers had reported that red colors are obtained when ferrous salts are added to solutions of pyrazinoic acid[6], pyrimidine-4-carboxylic acid[7], and pyridazine-3-carboxylic acid[8].

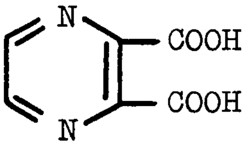
The structures of these acids are as follows:



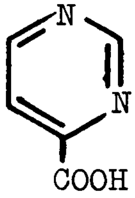
Picolinic acid
(Pyridine-2-carboxylic acid)



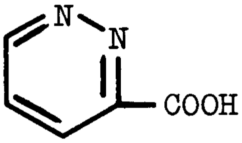
Pyrazinoic acid
(Pyrazine-2-carboxylic acid)



Pyrazine-2,3-dicarboxylic acid

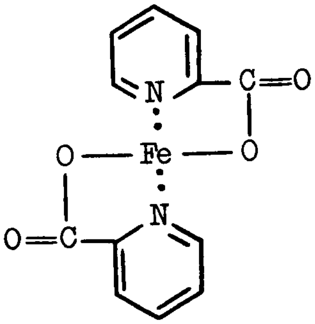


Pyrimidine-4-carboxylic acid



Pyridazine-3-carboxylic acid

The red color formed when these acids react with ferrous ions was attributed to the formation of a cyclic complex in which iron is coordinated with the unshared electron pair of the nitrogen atom:[9]



This color reaction has a number of practical applications; an interesting one is the use of solutions of ferrous sulfate as a detection reagent in paper chromatography and thin-layer chromatography. Dietrich and Mercier[10] have used this method with pyrazine carboxylic acids, and Morimoto and Furuta[11] then used essentially the same technique with pyridine carboxylic acids.

Allen et. al.[12] found that the pyrazinamide content of blood and urine could be determined spectrophotometrically by hydrolyzing the pyrazinamide to pyrazinoic acid, adding ferrous ammonium sulfate, and using the resulting orange-red color of the ferrous-pyrazinoic acid chelate to determine the amount of pyrazinamide originally present by the use of a calibration curve. Kajiwara and Sunada[13] then modified this procedure, using sodium pentacyanoammine ferroate as the source of ferrous ions; this reagent was said to be a more sensitive detection reagent than ferrous ammonium sulfate.

Although much research has been done on metal chelates of pyridine carboxylic acids and many stability constants have been obtained, no one has yet determined any stability constants of chelates of carboxylic acids which have two ring nitrogen atoms. In fact, only in recent years have people begun to study extensively the chelates between various metal ions and pyrazine carboxylic acids.

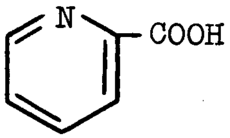
Hartkamp[14] developed a spectrophotometric method of determining small amounts of molybdenum using pyrazine-2,3-dicarboxylic acid as the chelating agent. Dutta and Ghosh[15] have studied vanadium complexes of pyrazine-2,3-dicarboxylic acid, and have concluded that this complex has a polymeric structure since the ligand:metal ratio is 1:1. Similar polymers for chelates of this acid have been reported by Berenblyum et. al. [16-19]; Richard, Duc, and Bertraut[20]; and Matthews and Walton[21]. On the other hand, Tenhumen[22] reported that the cobalt and zinc complexes of this acid have a ligand:metal ratio of 2:1.

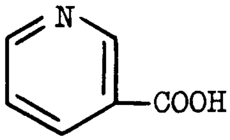
Polymers are not possible in the case of pyrazinoic acid, and the problem of structure determination is much simpler. Tenhumen[23] studied the crystal structure of bis(pyrazine-2-carboxylato)cobalt(II) dihydrate and bis(pyrazine-2-carboxylato)zinc(II) dihydrate, and obtained IR spectra of both salts. Matthews and Walton[21] studied the copper and silver compounds of this acid, and also obtained a ligand:metal ratio of 2:1.

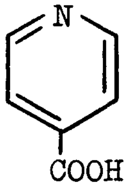
Although these articles have appeared in recent years, there evidently has been no attempt to determine the stability constants of any chelates of pyrazine carboxylic acids, or to study the chelates of two similar carboxylic acids: pyrimidine-4-carboxylic acid and pyridazine-3-carboxylic acid.

This research has therefore been undertaken for the main purpose of studying some metal chelates of pyrazine, pyrimidine, and pyridazine carboxylic acids in order to determine their structure and stability constants. This information would then be evaluated to see if there are any correlations between the dissociation constants or structures of the carboxylic acids and the stability constants of their chelates.

In order to select what acids are to be studied, it became necessary to look at the structures of the acids to see which ones would be expected to form chelates. For example, there are three different pyridine monocarboxylic acids:

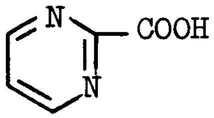

Picolinic acid


Nicotinic acid

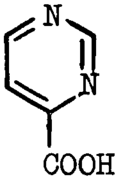

Isonicotinic acid

Picolinic acid readily forms chelates; consequently, much research has been done using this acid. There is some dispute as to whether or not any chelates are formed for nicotinic acid complexes, and it is highly improbable for isonicotinic acid to form any chelates at all because of the extremely unfavorable steric factors.

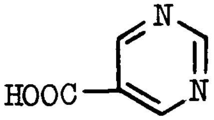
There is no problem with pyrazine: only one monocarboxylic acid is possible since the two ring nitrogen atoms are opposite each other. However, three pyrimidine monocarboxylic acids exist:



Pyrimidine-2-CA



Pyrimidine-4-CA



Pyrimidine-5-CA

Of these three acids, pyrimidine-5-carboxylic acid would probably not form any chelates since its structure is similar to that of nicotinic acid. Pyrimidine-2-carboxylic acid was first synthesized in 1954 by Holland[24]; this synthesis is difficult and the acid was obtained in milligram amounts only. On the other hand, pyrimidine-4-carboxylic acid is readily available and can be purchased from various chemical companies. For these reasons, pyrimidine-4-carboxylic acid was chosen for this investigation.

Only one pyridazine monocarboxylic acid, pyridazine-3-carboxylic acid, would be expected to form any chelates. Although this acid is not commercially available, it was found that this acid can readily be synthesized from 3-methylpyridazine.

Finally, in addition to the three monocarboxylic acids previously chosen (pyrazinoic acid, pyrimidine-4-carboxylic acid, and pyridazine-3-carboxylic acid), pyrazine-2,3-dicarboxylic acid was included in this investigation since it was commercially available and a number of chelates of this acid have already been studied by other workers.

Once the chelating agents have been selected, a specific method must be chosen to determine the structures and stability constants of the chelates. By far, the most common method used to study chelates of pyridine carboxylic acids has been the potentiometric method developed by Bjerrum.[25] Although this method has been widely used, it has been criticized as being inaccurate in the case of picolinic acid chelates for the following reasons:

(1) In calculating $\bar{n}$, it is assumed that the picolinic acid is either chelated or entirely free from the metal; this assumption is not true since at low pH values simple complexes between the metal ion and the undissociated picolinic acid molecules would occur.[26] (Here the coordination would occur through the ring nitrogen atom of picolinic acid only.)

(2) Since complexation occurs at low pH values, a small error in the pH reading will cause a relatively large error in the value of $\bar{n}$, and therefore in the stability constants also.[27]

(3) Similarly, considerable error will result if the pK_a values of the carboxylic acids are not determined precisely.[27]

(4) It is often impossible to determine the complete formation curve because of precipitate formation at high pH values.[28] If this occurs, approximate methods are used to obtain some formation constants.

The polarographic method overcomes these disadvantages since:

(1) Before any polarograms are run at different ligand concentrations, the variation of half-wave potential with pH is first investigated. By doing this, it will be seen whether or not it is necessary to use buffered solutions in order to obtain reversible reductions. For metal chelates of picolinic acid (and similar carboxylic acids), three distinct regions of the $E_{1/2}$ vs. pH plot are usually obtained:

a. When $pH < pK_a$, the half-wave potential is a linear function of pH. From the slope of the line, the number of hydrogen ions involved in the reduction can be calculated. As the solution is made more acidic, the half-wave potential of the complex approaches the half-wave potential of the free ion, indicating that little complexation occurs in strongly acidic solutions.

b. When pH > pK_a, the half-wave potential is independent of the pH. The range of this plateau region is usually quite broad (several pH units), indicating that precise control of pH is not required.

c. When pH >> pK_a, the metal ion usually forms either a hydroxyl complex such as $Pb(OH)_3^-$ or a mixed complex between the metal ion, the chelating agent, and hydroxide ions. In either case, the half-wave potential is a function of the pH, and the slope of this line usually permits the formula of the complex to be determined.

(2) After determining the shape of the $E_{1/2}$ vs. pH plot at several ligand concentrations, it is a simple matter to select the pH region in which the half-wave potential is independent of pH. This region usually has a wider range if high ligand concentrations are used. By limiting all polarographic work to this range, the problem of simple complex formation at low pH values presents no difficulty here.

(3) Similarly, since all polarograms are run in the plateau region where pH > pK_a, any error made by previous workers

in determining the dissociation constants of the acid will have no effect whatsoever.

There are two major limitations in the polarographic method. In order for the conventional methods described by Lingane[29] and DeFord and Hume[30] to be used:

(1) the metal ion and the complex must both be reduced reversibly at the dropping mercury electrode, and

(2) the complexing agent must either: (a) not be reduced at all, or (b) be reduced at a more negative potential than the complex, so that the two reduction waves do not interfere with each other.

In spite of these limitations, a considerable amount of work has been done using the polarographic method, especially in recent years. Polarography was first used to study picolinic acid chelates by Thomas in his doctoral research[31]; he used the potentiometric, polarographic, and spectrophotometric methods to study complexes of picolinic acid with a number of metal ions.

The results which Thomas obtained for the lead - picolinic acid chelates contradicted each other. Using the potentiometric method[31,32] he showed that the complex

$Pb(Pic)_3^-$ was formed and he obtained a value of K_3. (Pic^- represents the anion of picolinic acid.) However, using the polarographic method[31,33] he was unable to find any evidence for the existence of this complex and instead concluded that $Pb(Pic)_2$ was the highest-order complex.

Clearly, such important discrepancies should first be examined before the polarographic method is used to examine new chelates never studied before. For this reason, the lead-picolinic acid complexes have been included in this investigation in order to see if the polarographic method can be used to prove the existence of complexes such as $Pb(Pic)_3^-$ and to obtain the corresponding stability constants.

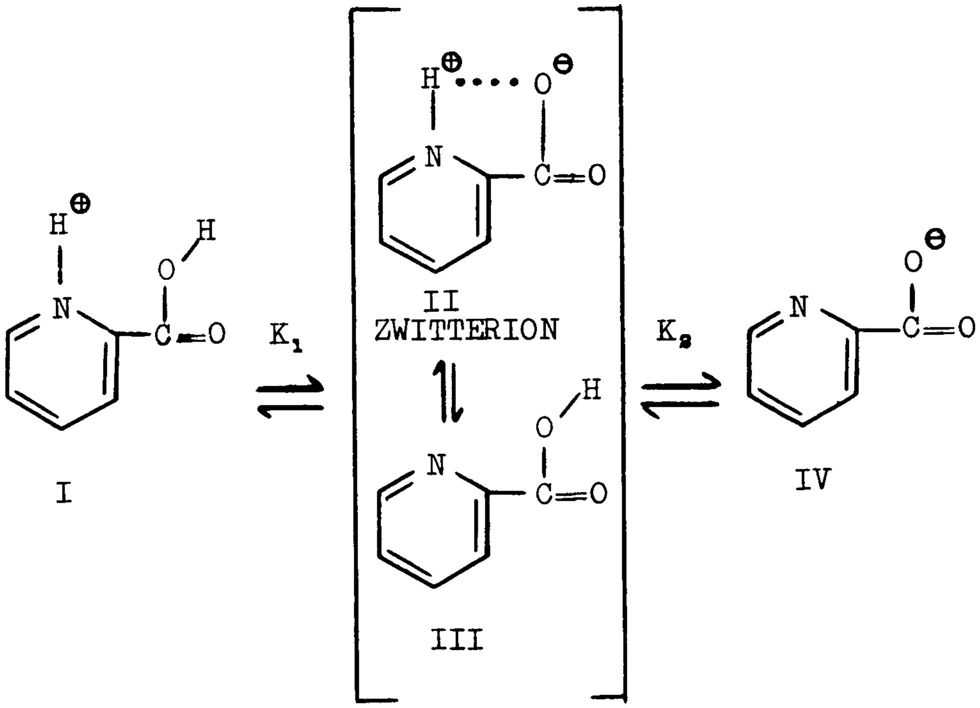
Before the reduction of the metal chelates can be studied, it is first necessary to see if the chelating agents are themselves reduced at the D.M.E., and, if so, whether or not the reduction waves of the chelating agent and the metal chelate overlap with each other. In the case of picolinic acid, the polarographic reduction of this acid has already been studied extensively and the most complete studies have been those of Jellinek and Urwin[34] and Volke and Volkova[35]. For $pH < 9$, Jellinek and Urwin found that the half-wave potential of the acid can be expressed by the equation

$$E_{1/2} = [(-0.081)(pH)] - 0.741 \text{ volts.}$$

Thus at pH = 7.0, $E_{1/2}$ = -1.308 v. Since the reduction wave of the chelating agent (picolinic acid) occurs at a more negative potential than the reduction wave of the lead chelate of picolinic acid, no interference is observed in this case, and the determination of the stability constants can be carried out in the usual manner.

Except for one article dealing with the simultaneous determination of pyrazinamide and pyrazinoic acid[36], no work has been undertaken to study the polarographic reduction of any of the four acids with two ring nitrogen atoms. The first phase of this research was thus directed towards studying the polarographic reduction of these acids, to see how the half-wave potential varies with the pH of the solution and to obtain as much other information as possible. After this work was finished, it was then possible to determine which metal ions could be studied in the second part of the research - the polarographic reduction of the metal chelates.

Before any work is done using these carboxylic acids, it is first necessary to become familiar with their dissociation constants. Extensive work in this area has been done in the case of pyridine carboxylic acids. When dissociation constants of picolinic acid were obtained a number of years ago, it was assumed erroneously that the neutral species (III) was the predominant species in moderately acidic solutions.[37] However, later studies[38] showed that the ratio of zwitterions (II) to neutral molecules (III) is 15. Thus the equilibria are as follows:



Green and Tong[38] obtained the following values:

$pK_1 = 1.01$ $pK_2 = 5.32$

$K_1 = 9.8 \times 10^{-2}$ $K_2 = 4.8 \times 10^{-6}$

Only the fully dissociated acid (IV) would be expected to form any chelates. Carboxylic acids with two ring nitrogen atoms are considerably stronger acids, and only the values of K_2 and pK_2 have generally been reported.

A table showing pK_a and K_a values of these acids appears below.

Acid	Reaction	pK_a	K_a	Ref.
Pyrazinoic acid	$HA \rightleftharpoons H^+ + A^-$	2.92	1.2×10^{-3}	39
Pyrazine-2,3-dicarboxylic acid	$H_3A^+ \rightleftharpoons H^+ + H_2A$	<-2		40
	$H_2A \rightleftharpoons H^+ + HA^-$	0.9	1.3×10^{-1}	40
	$HA^- \rightleftharpoons H^+ + A^=$	2.77	1.7×10^{-3}	39
Pyrimidine-4-carboxylic acid	$HA \rightleftharpoons H^+ + A^-$	2.98	1.05×10^{-3}	41
Pyridazine-3-carboxylic acid	$HA \rightleftharpoons H^+ + A^-$	3.0	1.0×10^{-3}	42

Thus the pK_a values of the monocarboxylic acids listed above are all between 2.9 and 3.0, indicating that there is no large variation in acidity in the group. Potentiometric titrations performed in this laboratory showed that the above values for the monocarboxylic acids were accurate to about ±0.1 pH unit.

Footnotes - Chapter I

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CHAPTER II

THEORY

(a) Polarography - General

Once a polarographic wave is obtained for a given compound, it is necessary to determine what kind of wave it is. There are four important types of polarographic currents:[42a]

(1) DIFFUSION CURRENT: the limiting current is determined by the rate of diffusion of the electroactive substance to the electrode. The well-known Ilkovic equation gives the formula for calculating the magnitude of this diffusion current:[43]

$$i_d = 706\ n\ C\ D^{1/2}\ m^{2/3}\ t^{1/6}$$

where: i_d = diffusion current (maximum current using the tops of the recorder oscillations)

n = number of electrons involved in the electrode reaction

C = concentration of the substance in millimoles/liter

D = diffusion coefficient of the substance in cm^2/sec

m = rate of flow of mercury in mg/sec

t = drop time of mercury in sec

If the mean current is used in the above formula, instead of the maximum current, the constant in the Ilkovic equation then is 607.

At any point along the rising part of the wave, the following relationship holds:[44]

$$E_{d.e.} = E_{1/2} - \frac{0.05915}{n} \log\left(\frac{i}{i_d - i}\right)$$

where: $E_{d.e.}$ = potential of the dropping electrode

$E_{1/2}$ = half-wave potential

n = number of electrons in the reaction

i = current at a point on the polarographic wave (corrected for residual current)

i_d = diffusion current (corrected for residual current)

This equation is valid whenever the reduction is reversible (i.e. the electron transfer reaction is very rapid). Then a plot of $E_{d.e.}$ vs. log $(i/i_d - i)$ is a straight line whose slope is $(-0.05915/n)$.

In the case of an irreversible wave - in which the electron transfer reaction is relatively show - the above equation becomes:[45]

$$E_{d.e.} = E_{1/2} - \frac{0.05915}{\alpha n} \log \frac{i}{i_d - i}$$

where α is the transfer coefficient; it has a value between 0 and 1. Here the plot of $E_{d.e.}$ vs. log $(i/i_d - i)$ is a straight line whose slope is $(-0.05915/\alpha n)$.

Finally, it is possible that the plot of $E_{d.e.}$ vs. log (i/i_d-i) is curved; this results when the electrode reaction is neither so relatively slow as to be completely irreversible, nor so fast as to appear reversible. These reactions have been called "quasi-reversible"[46,47] and it is possible, using various electrochemical techniques including polarography, to determine the rate constants for the electrode reaction.

(2) KINETIC CURRENT: the electroactive substance is formed by a chemical reaction in the vicinity of the electrode; thus the magnitude of the limiting current depends upon the rate at which this substance is produced.

(3) ADSORPTION CURRENT: particles of the electroactive substance are adsorbed onto the mercury surface by either physical, chemical, or electrical forces.

(4) CATALYTIC CURRENT: a substance, acting as a catalyst, is added to a solution containing an electroactive substance and it causes a shift in the reduction of that electroactive substance to more positive potentials. A common example of this effect occurs in catalytic hydrogen currents in which the addition of a substance (such as pyridine carboxylic acids) displaces the reduction potential of hydrogen ions to more positive

values. The result is a small catalytic wave occurring about 0.2 v more positive than the main hydrogen wave.

A number of techniques are available to determine the type of reduction wave which is obtained; the usual procedure, as described by Heyrovsky and Zuman[42a], consists of observing how the limiting current varies as a function of concentration of the electroactive substance, mercury height, temperature, etc. For example, if the limiting current is proportional to the square root of the mercury height, this indicates a diffusion current. If the limiting current is proportional to the mercury height itself, it is an adsorption current, and if the limiting current does not vary with the mercury height at all, it is a kinetic current. If the limiting current happens to be a catalytic current, it sometimes varies with the mercury height but this is not necessarily the case according to Heyrovsky and Zuman.

Similarly, the height of a diffusion-controlled wave increases 1.6% per degree centigrade, while for kinetic currents the effect is much larger: about 5-20% per degree. Varied results are obtained in the case of adsorption and catalytic waves.

After considering these various effects, it usually is possible to identify the nature of the reduction wave without much difficulty.

(b) Polarographic Reduction of Carboxylic Acids

The general equation for the dissociation of a weak acid is:

$$HA \underset{k_r}{\overset{k_d}{\rightleftharpoons}} H^+ + A^-$$

where: k_d = dissociation rate constant

k_r = recombination rate constant

so that:

$$K_a = \frac{[H^+][A^-]}{[HA]} = \frac{k_d}{k_r}$$

and $$pK_a = -\log K_a$$

Let us assume that both the free acid (HA) and the anion (A^-) are reduced at the dropping mercury electrode. When $pH < pK_a$, only the undissociated acid is present, and a single reduction wave is observed due to the reduction of the free acid:

$$HA + p_1H^+ + n_1e^- \rightarrow \text{product}_1$$

where: p_1 = number of hydrogen ions involved in the reduction

n_1 = number of electrons involved in the reduction

When pH >> pK_a, only the anion is present, and a single reduction wave is observed due to the reduction of the anion:

$$A^- + p_2H^+ + n_2e^- \rightarrow \text{product}_2$$

Generally, the value of $E_{1/2}$ for the reduction wave of the free acid occurs at a more positive potential than the value of $E_{1/2}$ for the wave of the anion (i.e. the undissociated acid is reduced more easily than the anion).

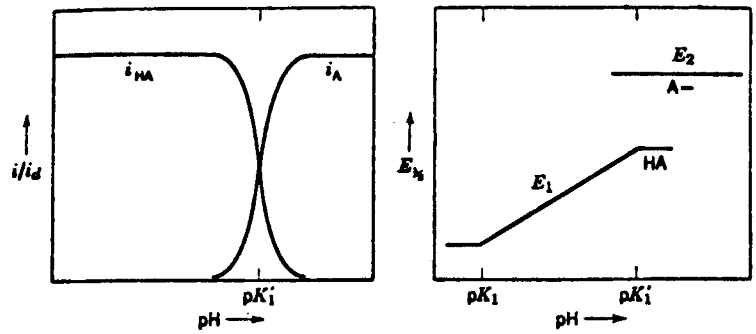
It might be expected that when pH = pK_a, two reduction waves of equal height would be obtained—one for the acid and one for the anion—since both the acid and the anion are present in equal concentrations. Actually, only one wave is obtained; it is the reduction wave of the undissociated acid.

It is only later, when the pH is several pH units larger than the pK_a, when the two reduction waves are equal in height. The pH at which this occurs is called the pK' and K' is called the polarographic dissociation constant.

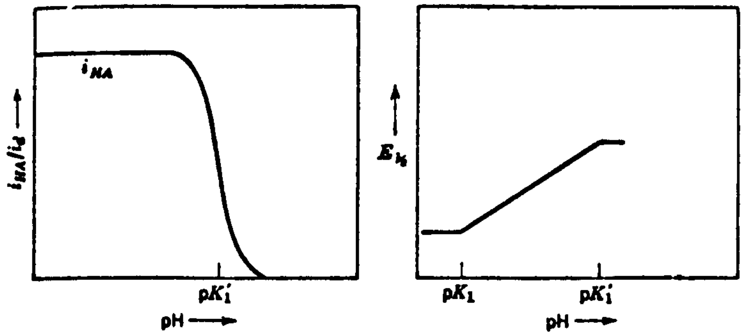
In the intermediate region, in which (pK'-1) < pH < (pK'+1), two reduction waves are obtained - one for the anion and one for the free acid.

The reason why pK' is several pH units higher than the pK_a is the fact that in the vicinity of the D.M.E., anions of the acid combine with proton-donating species such as free protons, solvent molecules, or buffer components to form the free acid, which is then reduced at the D.M.E.

In the ideal case where both the acid and the anion are reducible at the D.M.E., the variation of the diffusion current and $E_{1/2}$ with pH are shown in the following graphs:[48]



In the analagous case in which the anion A^- is not reduced at the D.M.E., the plots look like this:[49]



The value of the rate constant for the recombination of anions with protons, k_r, can be determined using the following equation:[50]

$$k_r = \frac{1}{K'^2} \cdot 1.31 \cdot \frac{K_a}{t_1}$$

where t_1 = drop time

In the case of a dibasic acid - e.g. pyrazine-2,3-dicarboxylic acid - the equations are more complicated. If the three species (H_2A, HA^-, and $A^=$) are all reduced at the D.M.E., then three equations for reductions must be written:

$$H_2A + p_1H^+ + n_1e^- \rightarrow \text{product}_1$$
$$HA^- + p_2H^+ + n_2e^- \rightarrow \text{product}_2$$
$$A^= + p_3H^+ + n_3e^- \rightarrow \text{product}_3$$

and three reduction waves would be observed with the values of the diffusion currents and half-wave potentials varying with the pH in a similar manner as with the monocarboxylic acids.[50]

From the general equation for the reduction

$$Ox + p\,H^+ + n\,e^- \rightleftarrows H_pRed$$

it can be shown[51] that:

$$\frac{d(E_{1/2})}{d(pH)} = -\frac{0.05915}{\alpha n}\,p$$

Thus from the slope of a plot of $E_{1/2}$ vs. pH it is possible to calculate the number of hydrogen ions involved in the reduction.

(c) Polarographic Reduction of Metal Complexes

The overall reaction between a metal ion, M, and a complexing agent, X, can be written as:

$$M + n\,X \rightleftarrows MX_n$$

The complete reaction normally occurs in several steps, each being identified with a stepwise stability constant:[52]

$$M + X \rightleftarrows MX \qquad K_1 = \frac{[MX]}{[M][X]}$$

$$MX + X \rightleftarrows MX_2 \qquad K_2 = \frac{[MX_2]}{[MX]\,[X]}$$

$$MX_2 + X \rightleftarrows MX_3 \qquad K_3 = \frac{[MX_3]}{[MX_2][X]}$$

$$\vdots \qquad\qquad\qquad \vdots$$

$$MX_{n-1} + X \rightleftarrows MX_n \qquad K_n = \frac{[MX_n]}{[MX_{n-1}][x]}$$

Similarly, equations can be written to represent the overall formation in one stage of each complex species; in such a case, each equation is identified with a corresponding overall stability constant:

$$M + X \rightleftarrows MX \qquad \beta_1 = \frac{[MX]}{[M]\ [X]}$$

$$M + 2\,X \rightleftarrows MX_2 \qquad \beta_2 = \frac{[MX_2]}{[M]\ [X]^2}$$

$$M + 3\,X \rightleftarrows MX_3 \qquad \beta_3 = \frac{[MX_3]}{[M]\ [X]^3}$$

$$\vdots \qquad\qquad \vdots$$

$$M + n\,X \rightleftarrows MX_n \qquad \beta_n = \frac{[MX_n]}{[M]\ [X]^n}$$

A simple relationship exists between a given overall stability constant - e.g. β_2 - and the corresponding stepwise stability constants. The general formula is:

$$\beta_n = (K_1)(K_2)(K_3)\ \ldots\ (K_n)$$

and this can be illustrated using the above definitions of β_2, K_1, and K_2:

$$\beta_2 = (K_1)(K_2)$$

$$\frac{[MX_2]}{[M][X]^2} = \frac{[MX]}{[M][X]} \cdot \frac{[MX_2]}{[MX][X]}$$

Thus the overall stability constant is equal to the product of the stepwise stability constants.

The polarographic method of studying metal complexes is based on the fact that the half-wave potential of a metal ion is shifted to more negative potentials if a complexing agent is present. In general, the metal complex is more difficult to reduce than the simple metal ion, and by measuring the shift of the half-wave potential as a function of the complexing agent concentration, it is possible to determine the formula of the complex and its stability constant.

There are two widely-used methods of obtaining complex stability constants using polarography. The first method, developed by Lingane[29], is used when a single complex is present in a given concentration range. The equation given by Lingane is:

$$(E_{\frac{1}{2}})_c - (E_{\frac{1}{2}})_s = \frac{0.0591}{n} \log\left(\frac{K_c f_c k_s}{f_s k_c}\right) - p\,\frac{0.0591}{n} \log C_X f_X$$

where: $(E_{\frac{1}{2}})_c$ = half-wave potential of the complex ion

$(E_{\frac{1}{2}})_s$ = half-wave potential of the simple, uncomplexed metal ion

n = number of electrons involved in the electrode reaction

K_c = "dissociation constant of the metal complex" (term used by Lingane) (This is the reciprocal of the overall complex stability constant β_n and should not be confused with the stepwise stability constants defined earlier)

f_c = activity coefficient of the complex ion

k_s = capillary constant ($m^{2/3}\ t^{1/6}$) of the simple ion

f_s = activity coefficient of the simple metal ion

k_c = capillary constant of the complex ion

p = number of ligands coordinated to the metal ion (coordination number)

C_X = concentration (molarity) of the complexing agent

f_X = activity coefficient of the complexing agent

To eliminate the confusing notation involving K_c, the equation can be rewritten as follows:

$$(E_{\frac{1}{2}})_c - (E_{\frac{1}{2}})_s = -\frac{0.0591}{n} \log\left(\frac{\beta_n f_s k_c}{f_c k_s}\right) - p\,\frac{0.0591}{n} \log C_X f_X$$

where β_n is the overall complex stability constant, defined earlier.

Inasmuch as all of the polarograms involving metal chelates were run at a constant ionic strength (μ = 1.0), the ratio (f_s/f_c) is assumed to be equal to 1.00. In addition, the ratio (k_c/k_s) can be simplified as follows:

$$\frac{k_c}{k_s} = \left(\frac{D_c}{D_s}\right)^{1/2} = \frac{i_{d(c)}}{i_{d(s)}} = \frac{I_C}{I_M}$$

where D is the diffusion coefficient, i_d is the diffusion current, and I is the diffusion current constant = 607 n $D^{1/2}$. Finally, it is generally assumed that $f_X \approx 1$ (since precise values are usually not available). Making these substitutions, and solving for log β_n yields the following equation:

$$\log \beta_n = \frac{E_{1/2(s)} - E_{1/2(c)}}{0.0295} + \log \frac{I_M}{I_C} - p \log [X]$$

since n = 2 in these reductions. (Please see note below.)

From the original equation given by Lingane, it can be shown that:

$$\frac{\Delta E_{1/2(c)}}{\Delta \log (C_X f_X)} = -\frac{0.0591}{n} p$$

Thus a plot of $E_{1/2(c)}$ vs. $\log (C_X f_X)$ would be a straight line of slope (-0.0591 p/n).

In practice, the activity coefficients of the chelating agents probably have not yet been determined, so it is necessary to use $\log C_X$ in the denominator instead of $\log (C_X f_X)$. This substitution causes no error insofar as the determination of p is concerned, since the effect of neglecting $\log f_X$ in the plot is to shift the entire straight line so that it has a different intercept, but the slope - and thus the value of p is unchanged.

NOTE: Two different symbols are used throughout this dissertation to refer to the number of hydrogen ions involved in the reduction. When referring to the reduction of carboxylic acids, the symbol p is used; however, when referring to the reduction of metal chelates, q is used to refer to the number of hydrogen ions, since p has already been used to refer to the number of ligands per metal ion (the coordination number). This terminology, though not internally consistent, is consistent with the symbols used by the authors in these fields.

Thus the plot of $E_{1/2(c)}$ vs. log [X] is the easiest method of determining the formula of the complex - provided that the plot yields one straight line.

If the reduction wave of the chelate is irreversible, then the plot of $E_{1/2(c)}$ vs. log [X] would still be a straight line, but the slope would be equal to $(-0.0591\ p/\alpha n)$. Since the value of αn is obtained directly from the log plot, such an irreversible reduction would present no problem here.

There are many cases in which a plot of $E_{1/2(c)}$ vs. log [X] is not a straight line. If this happens, there are two possibilities:

(1) The plot of $E_{1/2(c)}$ vs. log [X] consists of two or more straight lines in different ligand concentration ranges. In this case, the Lingane method is used to obtain the formula and stability constant of each individual complex.

(2) The plot of $E_{1/2(c)}$ vs. log [X] is a curve instead of a straight line. Here is not possible to use Lingane's method, and a more recent method developed by DeFord and Hume is used instead.

In the DeFord-Hume method[30], a number of different functions are calculated:

$$F_0[X] = \exp\left\{ \frac{nF}{RT} \left[E_{1/2(s)} - E_{1/2(c)} \right] + \ln \frac{I_M}{I_C} \right\}$$

$$F_1[X] = \frac{F_0[X] - 1}{[X]}$$

A plot of $F_1[X]$ vs. $[X]$ is prepared and extrapolated to $[X] = 0$ to obtain the value of β_1. This value of β_1 is then used to calculate the values of $F_2[X]$:

$$F_2[X] = \frac{F_1[X] - \beta_1}{[X]}$$

Extrapolation of the plot of $F_2[X]$ vs. $[X]$ to $[X] = 0$ similarly yields the value of β_2. This value of β_2 is then used to calculate the values of $F_3[X]$:

$$F_3[X] = \frac{F_2[X] - \beta_2}{[X]}$$

and the value of β_3 is obtained using the same extrapolation technique.

This procedure gets repeated until for some value of n, the plot of $F_n[X]$ vs. $[X]$ is a straight line parallel to the x-axis. This indicates that MX_n is the highest-order complex and the y-intercept then gives the value of β_n.

In addition, the DeFord-Hume method makes it possible to determine easily the value of $\bar{n}$, known as the ligand number or degree of formation. The value of $\bar{n}$ can be regarded as the average composition, $MX_{\bar{n}}$, of the complex species then present in solution, and it is given by the equation

$$\bar{n} = \frac{d\,\{\log F_0[X]\}}{d\,\{\log [X]\}}$$

Thus if a plot of log $F_0[X]$ vs. log $[X]$ is made, the slope at any point equals the value of $\bar{n}$ at that ligand concentration.

Footnotes - Chapter II

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CHAPTER III

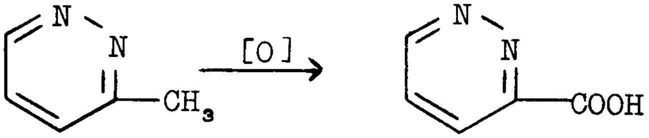
EXPERIMENTAL

a. Chemicals - Sources

Picolinic acid, pyrazinoic acid, and pyrazine-2,3-dicarboxylic acid were obtained from the Aldrich Chemical Company. Pyrimidine-4-carboxylic acid was obtained from two sources: Krishell Laboratories, Inc., and Nutritional Biochemicals, Inc.

One of the chelating agents—pyridazine-3-carboxylic acid—was not commercially available, and published methods of synthesis are quite complicated. Rosseels[53] wrote an article explaining six different ways in which the acid could be synthesized; each method required either five or six individual reactions. Clearly, it was desirable to synthesize the acid using a new process which required either one or two steps—if, in fact, such a process were feasible.

Inasmuch as 3-methylpyridazine was readily available (Aldrich Chemical Company), pyridazine-3-carboxylic acid would be obtained if the methyl group could be oxidized to a carboxyl group:



Poppenberg[54] attempted such an oxidation in 1901, using aqueous potassium permanganate, and he reported that he was unable to produce any significant amounts of the carboxylic acid. In order to develop alternate ways of oxidizing the methyl group to the carboxyl group, published methods of synthesis for pyrazine and pyrimidine carboxylic acids were consulted. Two alternate methods of obtaining the carboxylic acids were found:

(1) Use of selenium dioxide as the oxidizing agent instead of potassium permanganate. Gainer[55] found that he could obtain a 64% yield of pyrazinoic acid from methylpyrazine if he used either selenium dioxide (SeO_2) or selenius acid (H_2SeO_3) as the oxidizing agent.

(2) Conversion of the methyl group into a styryl derivative which is then oxidized to the acid using $KMnO_4$. Holland[56,57] developed the first synthesis of pyrimidine-2-carboxylic acid in 1954. He first reacted 2-methylpyrimidine with benzaldehyde in the presence of zinc chloride in a sealed tube to yield 2-styrylpyrimidine. This intermediate was then dissolved in aqueous pyrimidine,

and potassium permanganate was then added to oxidize the styryl group to yield pyrimidine-2-carboxylic acid.

Although the above two methods have been used to synthesize pyrazine and pyrimidine carboxylic acids, no attempt has evidently been made to synthesize pyridazine-3-carboxylic acid using either of these two methods. Inasmuch as method #1 appeared to be the simpler method, it was tried and it yielded satisfactory amounts of the desired acid.

Synthesis of pyridazine-3-carboxylic acid

In a 500 ml three-neck distilling flask were placed 114 ml of pyridine, 33 g H_2SeO_3, 11 ml H_2O, and 10 g 3-methylpyridazine (Aldrich Chemical Company). The mixture was refluxed with stirring for about 10 hr, during which time selenium was produced and it precipitated out of solution. After cooling, the mixture was filtered (ultra fine fritted glass Büchner funnel) and the filtrate was evaporated *in vacuo*. Then 68 ml of 2.5 N NaOH were added, charcoal was added, and the mixture was stirred overnight. The next day 20 ml of 12 N HCl were added; the acid precipitated out of solution and was filtered and dried, yielding 4.2 g of impure acid. The acid was then dissolved in alkali (25 ml of 2.5 N NaOH), charcoal was added, and subsequent acidification yielded the purified acid which was collected and dried. Yield 2.2 g (16.7%).

It is possible that a larger yield would be obtained if some modifications are made in the reflux time or other experimental conditions, but this possibility was not examined further.

Lead perchlorate, cupric perchlorate, and sodium perchlorate were obtained from the G. Frederick Smith Chemical Company. Triton X-100 was donated by Rohm and Haas. Sodium diethylbarbiturate (veronal sodium) was obtained from Pfaltz & Bauer, Inc.

b. Preparation of Solutions

Stock solutions of the sodium salts of the carboxylic acids were needed when studying the metal chelates. These solutions were prepared by weighing out the calculated amount of the free acid, adding the same number of moles of solid NaOH pellets (or twice the number of moles, in the case of pyrazine-2,3-dicarboxylic acid), and then dissolving and diluting the mixture to the correct volume with distilled water.

Constant ionic strength McIlvaine buffer solutions were prepared according to the instructions given by Elving, Markowitz, and Rosenthal.[58] Veronal buffer solutions were prepared as described by Michaelis.[59]

c. Apparatus and Procedure

All polarograms were recorded using a Beckman Electroscan 30 Electroanalytical System. A damping setting of 0.5 second was used in recording the polarograms. It was necessary to use an external means of measuring the potential applied to the dropping mercury electrode, and a Sargent NX Digital pH meter was used for this purpose.

Two different methods were used to determine the value of the half-wave potential. In obtaining the $E_{1/2}$ vs. pH plots for some of the metal chelates, the "direct" method[60] was used: after running the polarograms, the potential was varied manually until the current was one-half of the diffusion current; the pH meter was then connected, and the potential was read off. The pH meter was not connected while running the polarograms since it had a slight damping effect on the oscillations. This method yields values of $E_{1/2}$ to within ± 2 mv.

It was usually necessary to get more accurate values of the half-wave potential. In such cases, the "direct" method was first used to get the approximate value of $E_{1/2}$. The potential was then set to a value about 30-35 mv more positive than the half-wave potential, and, keeping the potential constant, about five oscillations of the pen were recorded. The potential was then set to a value 5 mv more negative, more pen oscillations were recorded, and this process was repeated until the potential was about 30-35 mv more negative than the half-wave potential. The total potential range was thus about 65 mv and this range was chosen so that the values of log (i/i_d-i) varied from about -1.1 to +1.1. The resulting values of $E_{1/2}$ (see "Calculations," page 43) were estimated to ± 0.1 mv, and the actual reproducibility was about ± 1.0 mv.

A Beckman Digital pH meter and a Thomas combination pH electrode (pH 0-14) were used to measure the pH. The pH meter was standardized using two Beckman buffer solutions, usually pH 4.01 and pH 7.00, and readings were generally accurate to ± 0.02 pH unit.

A constant-temperature bath (Wilkens-Anderson Co.) was used to maintain a temperature of (25.0 ± 0.1) °C. A Small Volume Titration Cell (Beckman #563218) was used as the electrolysis cell and a pump from the water bath circulated water throughout the outer jacket of the call. A rubber beaker cap (Beckman #101253) was used to hold the electrodes and the purge probe. The purge probe (Beckman #130845) was used in deaerating the solution and blanketing it with nitrogen. The prepurified nitrogen was saturated with water vapor at 25°C before use.

No iR correction was required since a three-electrode system was used. The dropping mercury electrode apparatus was essentially the same as that described by Meites[61]; a stand tube was connected to a meter stick so that the mercury height could easily be measured. A Sargent D.M.E. capillary (6-12 sec., stock no. S-29417) was cut to a 10.5 cm length. A mercury height of 50 cm was used at all times. In 1 M $NaClO_4$ at 25°C and at an applied potential of -0.500 volt (vs. S.C.E.), the capillary characteristics were: $\underline{m} = 1.897$ mg/sec and $\underline{t} = 4.22$ sec.

The platinum auxiliary electrode (Beckman #39017) was connected to a fritted glass tube with a $NaNO_3$-agar salt bridge and a saturated $NaNO_3$ solution above it.

Two different reference electrodes were used, depending upon the solution being analyzed. When polarograms of the various carboxylic acids were being run, a conventional saturated calomel electrode of the type used in pH meters was used as the reference electrode. When polarograms of the metal chelates were being run, it was found that this electrode could not be used because irreproducible results occurred due to the precipitation of potassium perchlorate at the interface. To remedy this situation, a calomel electrode saturated in sodium chloride (rather than potassium chloride) was used.[62-64] A small

$NaNO_3$-agar plug was put at the tip of this electrode so that chloride ions could not diffuse into the solution and cause erroneous values of the half-wave potential to be obtained when polarograms of the uncomplexed metal ions were run. The same modified calomel electrode was used for all polarograms involving metal chelates.

d. Calculations

(1) Determination of the half-wave potential

The usual procedure of obtaining accurate $E_{1/2}$ values consists of making a plot of log $[i/(i_d-i)]$ vs. $E_{d.m.e.}$; the value of $E_{1/2}$ then is the potential at which the log term is equal to zero. From the slope, the number of electrons involved in the reduction (n) can be calculated.

Statistically, the best method of determining the value of the half-wave potential and slope is to fit the E_{dme} and log $[i/(i_d-i)]$ data to a straight line of the type $y = mx + b$ using the method of least squares. A least-squares program for use with Wang calculators was made available by Prof. Gerald Koeppl of the Chemistry Department of Queens College; this program was used in all of the calculations in order to determine the values of $E_{1/2}$ and n.

(2) DeFord-Hume method - Determination of $F_0[X]$ and $F_1[X]$

A similar program for use with the Wang calculator was developed by the author for the purpose of calculating the values of $F_0[X]$ and $F_1[X]$ in the DeFord-Hume method of obtaining chelate stability constants.

Footnotes - Chapter III

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CHAPTER IV

POLAROGRAPHIC REDUCTION OF THE CHELATING AGENTS

(a) Pyrazinoic Acid

Of the four diazine carboxylic acids being investigated at this time, pyrazinoic acid is the only acid for which some research has already been performed involving the polarographic reduction of the acid. Svoboda[36] developed a polarographic method for determining the concentrations of pyrazinoic acid and pyrazinamide (an anti-tubercular drug) in human blood serum or plasma. In the course of developing this analytical method, Svoboda first studied the variation of $E_{1/2}$ with pH and found that the half-wave potential varies linearly with pH in the pH range of 1.5 to 7.0, after which the half-wave potential of pyrazinoic acid no longer exhibits such a linear relationship, and the wave becomes poorly defined. Svoboda mentioned that the value of $E_{1/2}$ at pH 1.5 is -0.362 v, but no other values are given and the results are summarized on a graph. From the graph, the following approximate relationship can be obtained:

$$E_{1/2} = [(-0.223) - (0.091)(\mathrm{pH})] \text{ volts}$$

In addition, at pH 1.5, the diffusion current of pyrazinoic acid varies directly with the concentration in the range studied (2 to 50 mcg/ml). This is equivalent to 1.61×10^{-5} M to 4.03×10^{-4} M. (This statement by Svoboda does not necessarily mean a non-linear relationship exists if the concentrations are outside this range; a more likely explanation is the idea that Svoboda expected all concentrations to fall within that range, and it was unnecessary for him to study the effects of using different concentrations.)

Svoboda also determined that two electrons are involved in the reduction; however, no mention was made as to whether or not the reduction is reversible, and specific information as to the types of waves obtained in basic solutions was not given.

Although some limited information dealing with the polarographic reduction of pyrazinoic acid was given in Svoboda's article, it was insufficient for the purposes of this investigation. Accordingly, polarograms of pyrazinoic acid were run at a number of pH values; the results are shown on the following page.

Values of the half-wave potential from pH 5.80 to 8.11 are recorded only to the nearest hundredth of a volt because the polarographic reduction waves are poorly defined in this region.

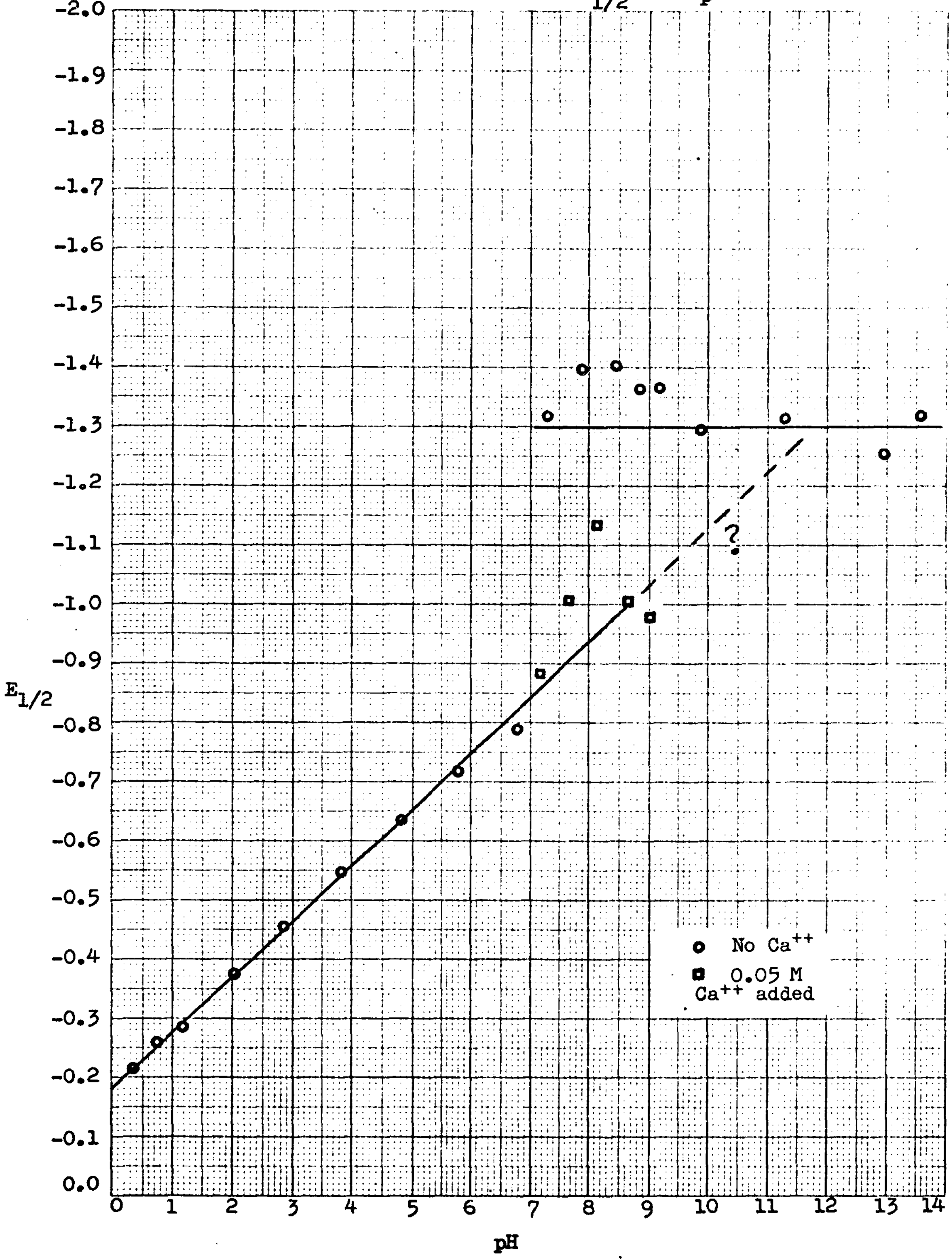
Only one reduction wave is obtained throughout the entire pH range. A plot of $E_{1/2}$ vs. pH appears on page 48.

POLAROGRAMS OF PYRAZINOIC ACID

Buffer Solution Used	pH	$E_{1/2}$, v	i_d, μA
1 M H_2SO_4	0.37	-0.218	8.48
0.2 M HCl - 0.8 M KCl	0.75	-0.269	8.34
0.1 M HCl - 0.9 M KCl	1.20	-0.289	7.27
McIlvaine Buffer Solutions: 0.2 M Na_2HPO_4 and 0.1 M citric acid	2.05	-0.377	7.83
	2.87	-0.458	7.81
	3.84	-0.550	7.88
	4.81	-0.637	7.86
	5.80	-0.72	6.44
	6.82	-0.79	7.13
Veronal Buffer Solutions: Sodium diethylbarbiturate and 0.1 N HCl (No Ca^{++} added)	7.27	-1.18	5.22
	7.90	-1.39	4.93
	8.39	-1.43	5.85
	8.83	-1.37	5.05
	9.20	-1.37	5.54
Veronal Buffer Solutions: Sodium diethylbarbiturate and 0.1 N HCl (0.05 M Ca^{++} added)	7.14	-0.88	4.59
	7.68	-1.04	5.68
	8.11	-1.13	5.75
	8.64	-1.004	6.04
	9.00	-0.979	5.95
0.5 M $KHCO_3$ and K_2CO_3	9.90	-1.297	6.43
0.25 M Na_2HPO_4 and Na_3PO_4	11.30	-1.315	5.97
0.1 M KOH	12.98	-1.256	6.30
1.0 M KOH	13.60	-1.320	6.93

All values of i_d were recorded with the mercury height at 50 cm. The plot of $E_{1/2}$ vs. pH appears on the next page.

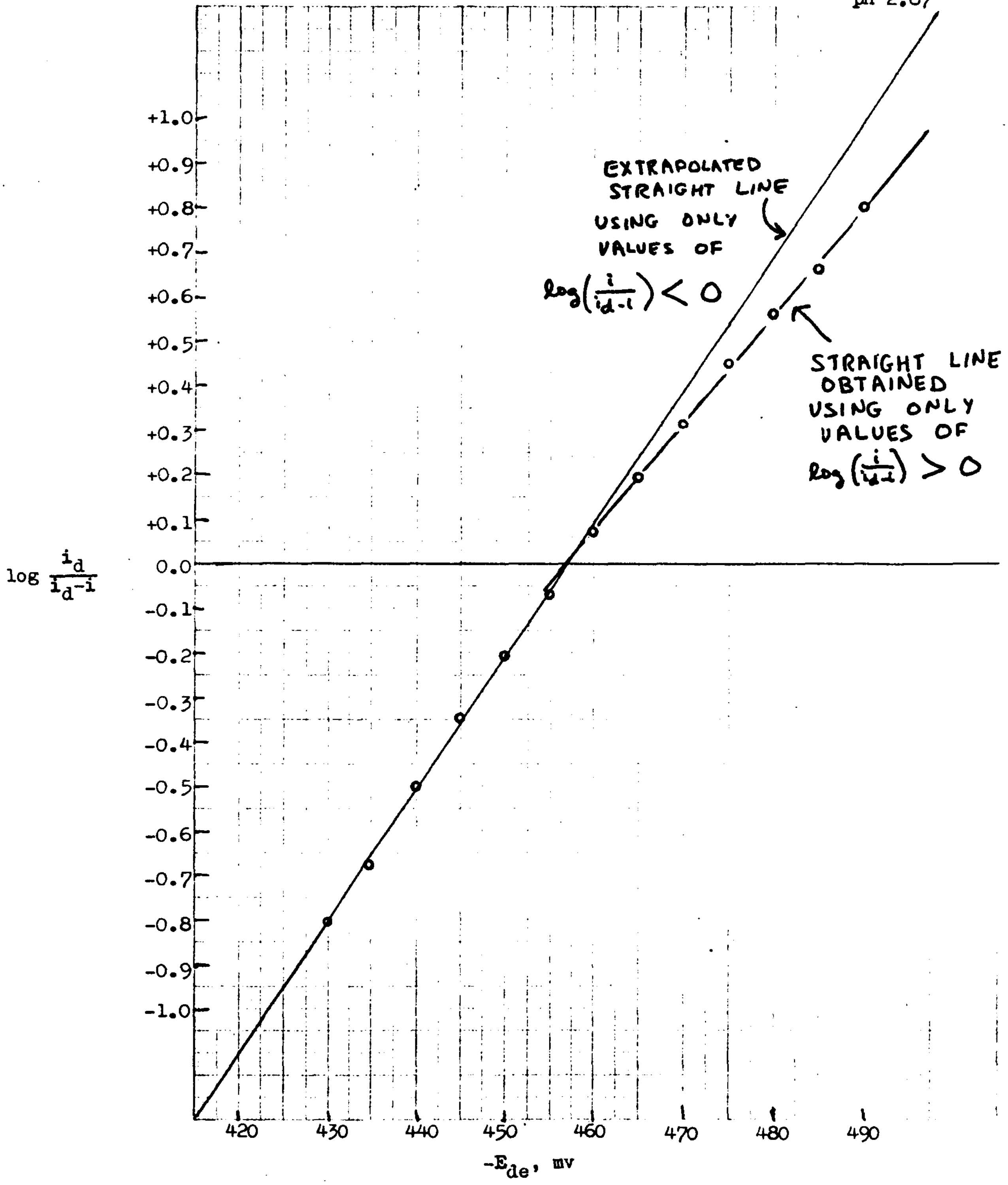
PYRAZINOIC ACID: VARIATION OF $E_{1/2}$ WITH pH



It was found that well-defined polarographic waves were obtained in acidic solutions. When plots of log $[i/(i_d-i)]$ vs. E_{dme} were made, it was found that curves, instead of straight lines, were generally obtained. A typical case (using a McIlvaine buffer, pH 2.87) is shown on the next page. Here a straight line was obtained when the log term was equal to a negative number, but when the log term was positive, a noticeable deviation from the straight line was clearly evident. In view of the fact that very good straight lines were obtained in other phases of the research (such as in the polarograms of the metal chelates), such a deviation could not be attributed here to "experimental error" or some other factor; instead, this curvature indicated that the electrode reaction was quasi-reversible.

In very basic solutions (pH>10), the value of $E_{1/2}$ is reasonably constant and independent of pH. ($E_{1/2} = -1.3 \pm 0.1$ v) However, very poor results are obtained in mildly alkaline solutions (pH between 7 and 10). It is interesting to note the effect of adding 0.05 M Ca^{++} to solutions in this pH region; this method was first used by Volke in his studies involving the polarographic reduction of pyridine carboxylic acids.[35,65] When 0.05 M Ca^{++} is added to solutions of pyrazinoic acid in the pH range of 7 to 10, the half-wave potential is shifted abruptly to more positive values - as much as 0.4 v more positive than the same solution without Ca^{++}. The values

Typical log plot - pyrazinoic acid (1.0 x 10^{-3} M) in McIlvaine buffer pH 2.87



of the half-wave potential in the table are those obtained in one run, and are not meant to imply that the values are necessarily very reproducible. For example, the same solution containing 0.05 M Ca^{++} at pH 7.14 was used to run five different polarograms - one after another, under the same conditions - and the values of the half-wave potential were: -0.79 v, -0.91 v, -0.87 v, -0.90 v, and -0.97 v. The value reported in the table, -0.87 v, is very close to the average value of the five half-wave potentials (-0.888 v). Thus irreproducible values of $E_{1/2}$ and very poorly defined polarograms were obtained in this pH range. (The reproducibility of the half-wave potential and the shape of the polarograms was very good in acidic solutions).

It is possible that there might be a variation in $E_{1/2}$ with Ca^{++} concentration in the pH range of 7 to 10, but a study to investigate this aspect further would have been outside the scope of this work.

In the graph on page 50, log (i/i_d-i) is plotted as a function of $E_{d.e.}$; thus the slope equals $(-\alpha n/0.05915)$. The value of αn is therefore calculated using the equation

$$\frac{\Delta Y}{\Delta X} = - \frac{\alpha n}{0.05915}$$

Here there is a problem in determining the value of αn due to the fact that the reduction is quasi-reversible, resulting in the curve on page 50. One approach is to use only the values of log (i/i_d-i) less than 0.0; this results in the first straight line of slope -29.85, yielding a value of $\alpha n = 1.77$. The second approach is to use only those values of log (i/i_d-i) greater than zero; here the slope equals -23.98 and $\alpha n = 1.42$. Finally, all of the values might be used resulting in a straight line with intermediate slope (not shown in the graph on page 50); this line results in a value of $\alpha n = 1.59$.

In all three cases it may be assumed that n = 2 (as reported by Svoboda[36]) but the uncertainty in αn creates a problem when the value of p is calculated using the graph on page 48:

(a) Using the first straight line, $\alpha n = 1.77$, and:

$$\frac{\Delta E_{1/2}}{\Delta \text{pH}} = - \frac{0.05915}{\alpha n} p = - \frac{0.05915}{1.77} p = -0.0334 p$$

$$- 0.0946 = - 0.0334 p$$

$$p = 2.83 \approx 3$$

(b) Using the second straight line, $\alpha n = 1.42$, and:

$$\frac{\Delta E_{1/2}}{\Delta\ pH} = -\frac{0.05915}{\alpha n}\, p = -\frac{0.05915}{1.42}\, p = -\ 0.0417\ p$$

$$-\ 0.0946 = -\ 0.0417\ p$$

$$p = 2.27 \approx 2$$

Thus the uncertainty in the value of αn makes it impossible to determine whether the correct value of $\underline{p}$ is 2 or 3 in this case.

Although the reduction wave of pyrazinoic acid was quasi-reversible in acidic solutions, it is definitely irreversible in basic solutions. On the next page is the log plot obtained from a polarogram of pyrazinoic acid in 0.1 N KOH, pH 12.98.

The transfer coefficient, α, is calculated from the slope as follows:

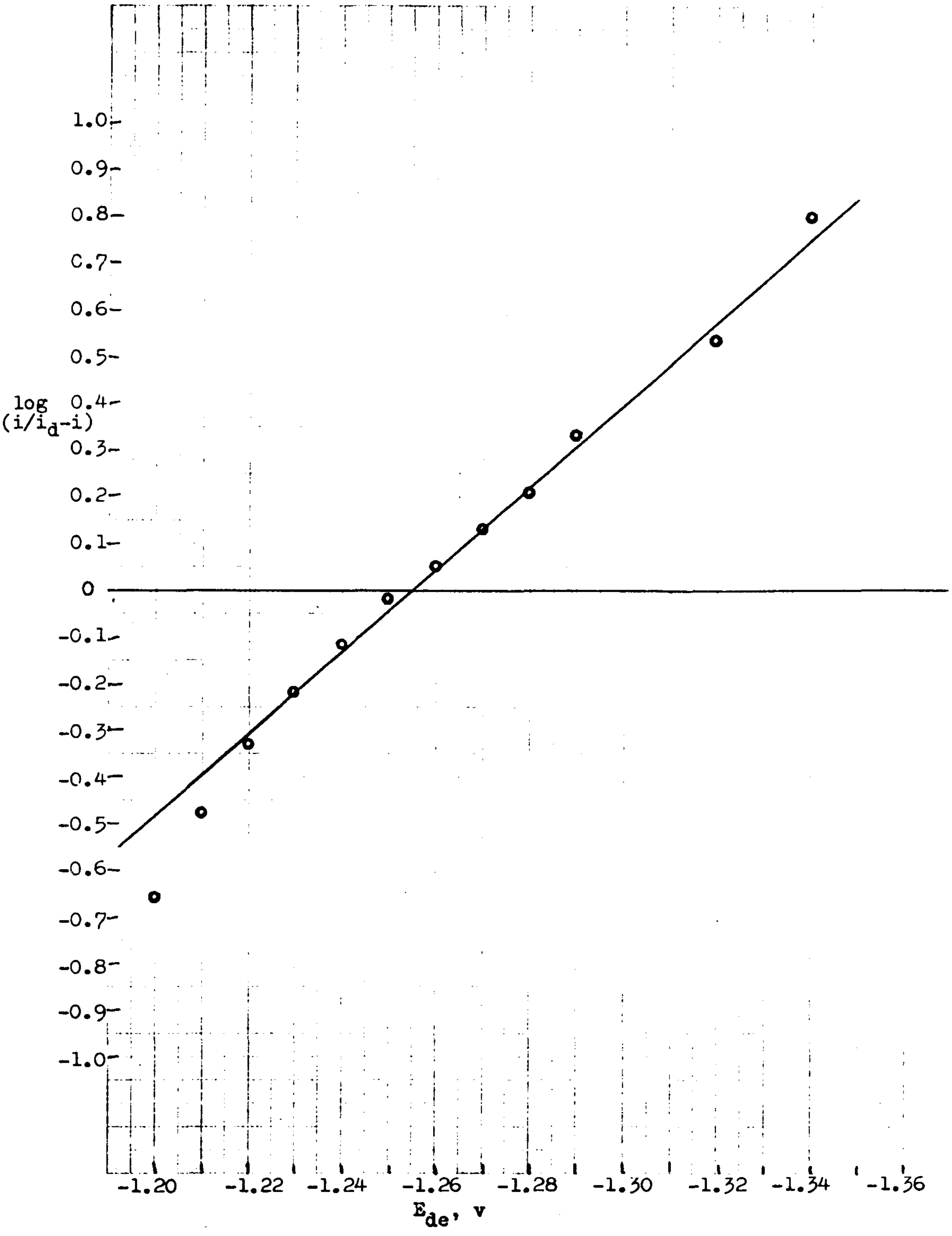
$$\frac{\Delta Y}{\Delta X} = \frac{1.00}{-0.114} = -8.77 = -\frac{\alpha n}{0.05915}$$

$$\alpha n = 0.519$$

$$\alpha = (0.519/2) = 0.259$$

Here it was assumed that n=2 as before, primarily because there is no significant change in the diffusion current in going from acidic solutions (where it can conclusively be shown that n=2) to basic solutions.

Log plot: pyrazinoic acid (1×10^{-3} M) in 0.1 N KOH (pH 12.98)



One would expect that as the pH is increased (going from acidic to neutral), the value of the diffusion current should decrease considerably in the vicinity of pK' as is explained on pages 21-25. However, this expected behavior does not occur, and the value of the diffusion current is fairly constant throughout the entire pH range.

This might be explained in several different ways; the most likely explanation is the possibility that wave #1 (reduction wave of the free acid) and wave #2 (reduction wave of the anion) have such similar half-wave potentials that the two waves actually overlap, making it impossible to distinguish between the two waves in the neutral pH region.

One method of investigating this possibility would be to use a polarographic instrument which automatically records the derivative (di/dt) as a function of applied voltage. One peak would be obtained if a single substance is reduced, while two peaks would be obtained if two reduction waves were overlapping with each other.[66] Another method which gives similar results is a.c. polarography.[67] Unfortunately, such an investigation was not possible and as a result no definite information was available to determine whether the wave in neutral solutions is one reduction wave or two overlapping waves.

It is also possible that the reduction wave in acidic solutions might be diffusion-controlled, while the wave in basic solutions might be a kinetic, adsorption, or catalytic wave. In order to obtain more information about the nature of the wave, a number of polarograms were run at different mercury heights and different temperatures. Three such sets of trials are shown below:

(1) 1.00 x 10^{-3} M pyrazinoic acid in McIlvaine buffer, pH 2.05

$\underline{h}$, cm	$\underline{t}$, °C	$\underline{i}_d$, µA	$\underline{h}_{corr}$	$(\underline{h}_{corr})^{1/2}$
50	25.0	7.83	48.45	6.96
30	25.0	6.15	28.45	5.33
70	25.0	9.40	68.45	8.27
50	57.2	14.08	48.45	6.96

(2) 1.00 x 10^{-3} M pyrazinoic acid in McIlvaine buffer, pH 4.81

$\underline{h}$, cm	$\underline{t}$, °C	$\underline{i}_d$, µA	$\underline{h}_{corr}$	$(\underline{h}_{corr})^{1/2}$
50	25.0	7.86	48.45	6.96
30	25.0	5.94	28.45	5.33
40	25.0	7.01	38.45	6.20
60	25.0	8.72	58.45	7.65
70	25.0	9.36	68.45	8.27
50	54.0	12.31	48.45	6.96

(3) 1.00 x 10^{-3} M pyrazinoic acid in 0.1 M KOH, pH 12.98

$\underline{h}$, cm	$\underline{t}$, °C	$\underline{i}_d$, µA	$\underline{h}_{corr}$	$(\underline{h}_{corr})^{1/2}$
50	25.0	6.30	48.45	6.96
30	25.0	5.24	28.45	5.33
40	25.0	5.88	38.45	6.20
60	25.0	6.43	58.45	7.65
70	25.0	6.50	68.45	8.27
50	59.5	9.52	48.45	6.96

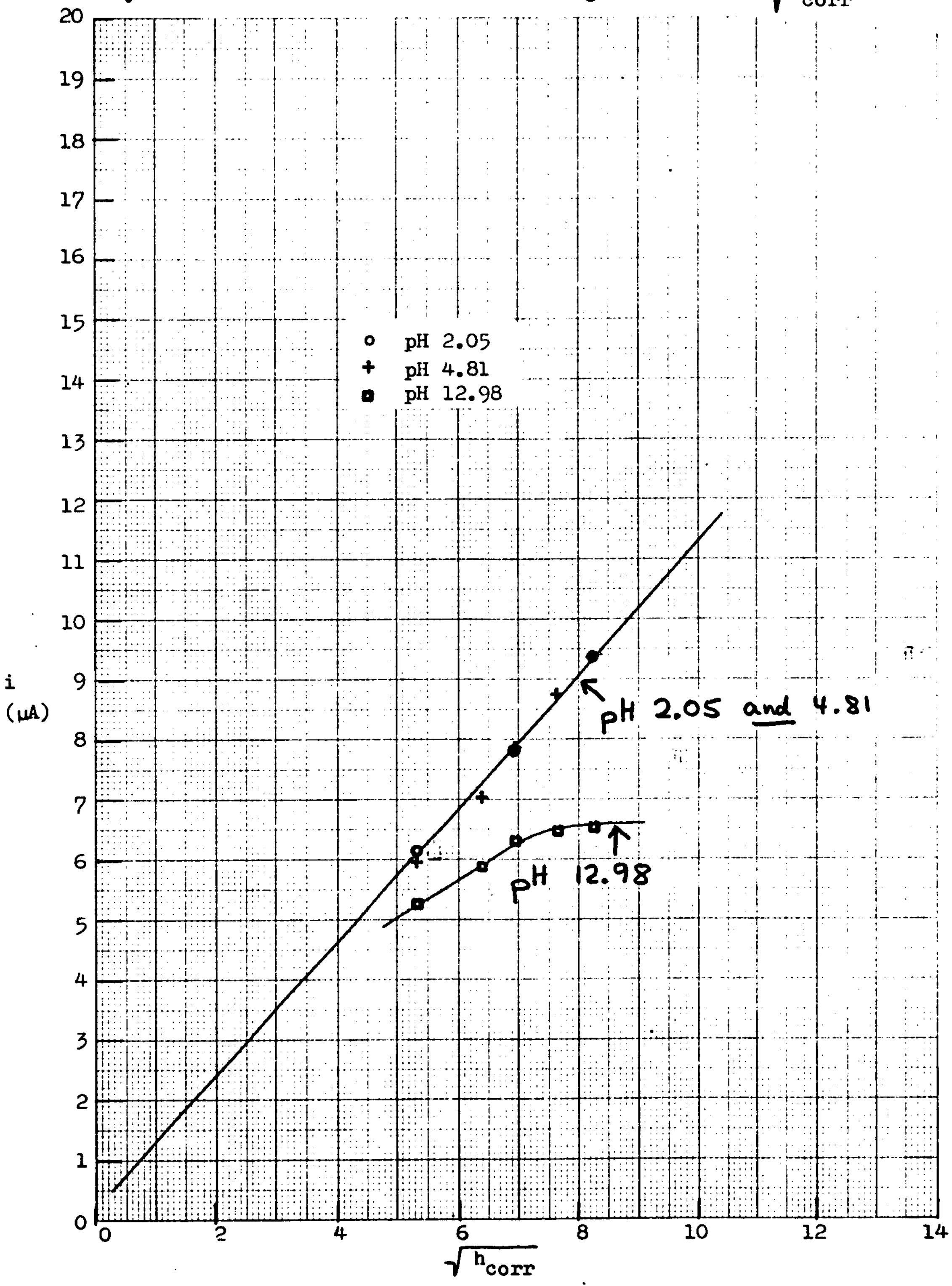
In plotting the variation of limiting current with the square root of the mercury height (to determine whether or not the reduction is diffusion-controlled, the "corrected height" must be used to take into account the back pressure of the mercury.[68]

$$h_{corr} = h - \frac{3.1}{(mt)^{1/3}}$$

Since $\underline{m}$ = 1.897 mg/sec and $\underline{t}$ = 4.22 sec, $\underline{mt}$ = 8.005 mg and $(mt)^{1/3} = 2.00$. Thus the back pressure is equal to (3.1/2.00), or 1.55 cm of Hg.

A plot of the limiting current vs. $(\underline{h}_{corr})^{1/2}$ is shown on the following page. At pH = 2.05 and pH = 4.81, the plot is a straight line which passes through the origin; this variation of limiting current with the square root of the mercury height shows that the current is diffusion-controlled. However, at pH = 12.98, a curve is obtained; it starts out as a straight line but the current then levels off at about 6.5 μA. At this high pH one would expect a diffusion-controlled reduction wave of the anion; such a conclusion cannot be made in view of the fact that a curve, instead of a straight line, was obtained. It is possible that the wave at pH = 12.98 is an adsorption or a catalytic wave (or that two waves might be superimposed on each other); additional information can be obtained by considering the temperature coefficients at each pH value.

Pyrazinoic acid: Variation of limiting current with $\sqrt{h_{corr}}$



The temperature coefficient is given by the formula:[69]

$$\text{Temperature coefficient} = \frac{2.303}{\Delta T} \log \left(\frac{i_2}{i_1}\right)$$

where: i_1 = limiting current at T_1

i_2 = limiting current at T_2

and $\Delta T = T_2 - T_1$

Using this formula, it was found that the temperature coefficient is 1.825% at pH 2.05, 1.55% at pH 4.81, and 1.68% at pH 12.98. These values are close to the value of 1.6% which is usual for diffusion currents; a temperature coefficient of 5-20% is common for kinetic currents.[70]

These findings confirm the fact that the wave is diffusion-controlled at pH 2.05 and pH 4.81, consistent with the previous findings in the $\underline{i}$ vs. $(\underline{h}_{corr})^{1/2}$ plot. In addition, the temperature coefficient data seem to indicate that the reduction wave is still diffusion controlled at pH 12.98, while the $\underline{i}$ vs. $(\underline{h}_{corr})^{1/2}$ plot gave ambigiuous results.

More information concerning the nature of wave #2 was obtained when the reductions of other acids, especially pyrimidine-4-carboxylic acid, were studied.

(b) Pyrazine-2,3-dicarboxylic acid

Two reduction waves are obtained for this acid; values of $E_{1/2}$ and i_d for these two waves at different pH values are shown in the table on the following page. A graph showing the variation of $E_{1/2}$ with pH for both waves appears on page 62.

WAVE #1

This wave is present only in acidic solutions, and the wave height gradually diminishes with increasing pH. At pH = 7 the wave is completely absent.

The log plots for wave #1 have exactly the same shape as those for the reduction wave of pyrazinoic acid in acidic solutions. The reduction is quasi-reversible, and values of αn from 1.82 to 1.88 were obtained from polarograms in the pH range of 0 to 3.

The number of hydrogen ions involved in the reduction for wave #1 in the pH range of 0 to 3 is calculated as follows (using $\alpha n = 1.85$ at pH 0.36):

$$\frac{\Delta E_{1/2}}{\Delta \text{pH}} = -\frac{0.05915}{\alpha n} p = -\frac{0.05915}{1.85} p = -0.0320 p$$

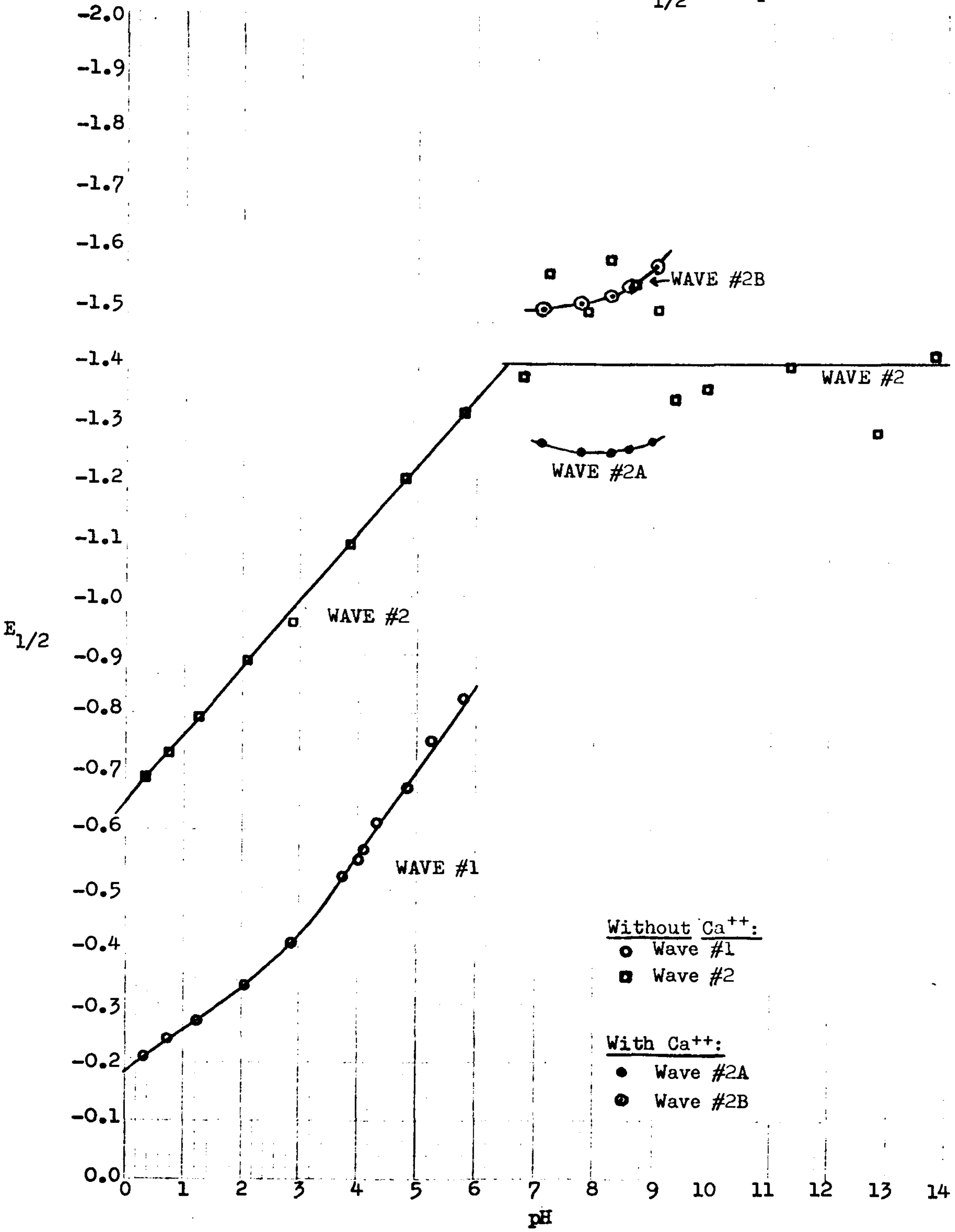
$$-0.071 = -0.0320 p$$

$$p = 2.22 \approx 2$$

POLAROGRAMS OF PYRAZINE-2,3-DICARBOXYLIC ACID
SERIES I

Buffer Solution Used	pH	WAVE #1		WAVE #2	
		$E_{1/2}$, v	i_d, μA	$E_{1/2}$, v	i_d, μA
1 M H_2SO_4	0.36	-0.217	7.18	-0.687	12.36
0.2 M HCl and 0.8 M KCl	0.76	-0.241	7.84	-0.730	13.12
0.1 M HCl and 0.9 M KCl	1.21	-0.273	6.74	-0.791	13.44
McIlvaine buffer sol'ns: 0.2 M Na_2HPO_4 and 0.1 M citric acid	2.07	-0.3341	7.54	-0.8887	13.44
	2.89	-0.4062	7.56	-0.957	13.66
	3.84	-0.507	7.22	-1.083	12.90
	4.80	-0.649	4.34	-1.202	13.28
	5.79	-0.860	2.46	-1.312	11.28
	6.79	absent	absent	-1.378	12.14
	7.72	absent	absent	irrev.	14 ?
Veronal buffer solutions No Ca^{++} added	7.20	absent	absent	-1.545	poor
	7.84	absent	absent	-1.485	poor
	8.30	absent	absent	-1.577	poor
	8.72	absent	absent	-1.535	poor
	9.03	absent	absent	-1.49	poor
Veronal buffer solutions 0.05 M Ca^{++} added	7.10	absent	absent	2A: -1.263 2B: -1.494	3.94 2.35
	7.76	absent	absent	2A: -1.249 2B: -1.501	3.70 4.28
	8.27	absent	absent	2A: -1.246 2B: -1.518	4.87 4.67
	8.56	absent	absent	2A: -1.254 2B: -1.537	4.90 4.90
	8.92	absent	absent	2A: -1.267 2B: -1.563	4.92 4.11
0.5 M NH_3 and 0.5 M NH_4Cl	9.30	absent	absent	-1.337	poor
0.5 M $KHCO_3$ and 0.5 M K_2CO_3	9.89	absent	absent	-1.357	5.10
0.25 M Na_2HPO_4 + 0.25 M Na_3PO_4	11.29	absent	absent	-1.393	5.18
0.1 M KOH	12.95	absent	absent	-1.298	5.98
1.0 M KOH	13.61	absent	absent	-1.404	5.93

PYRAZINE-2,3-DICARBOXYLIC ACID: VARIATION OF $E_{1/2}$ WITH pH



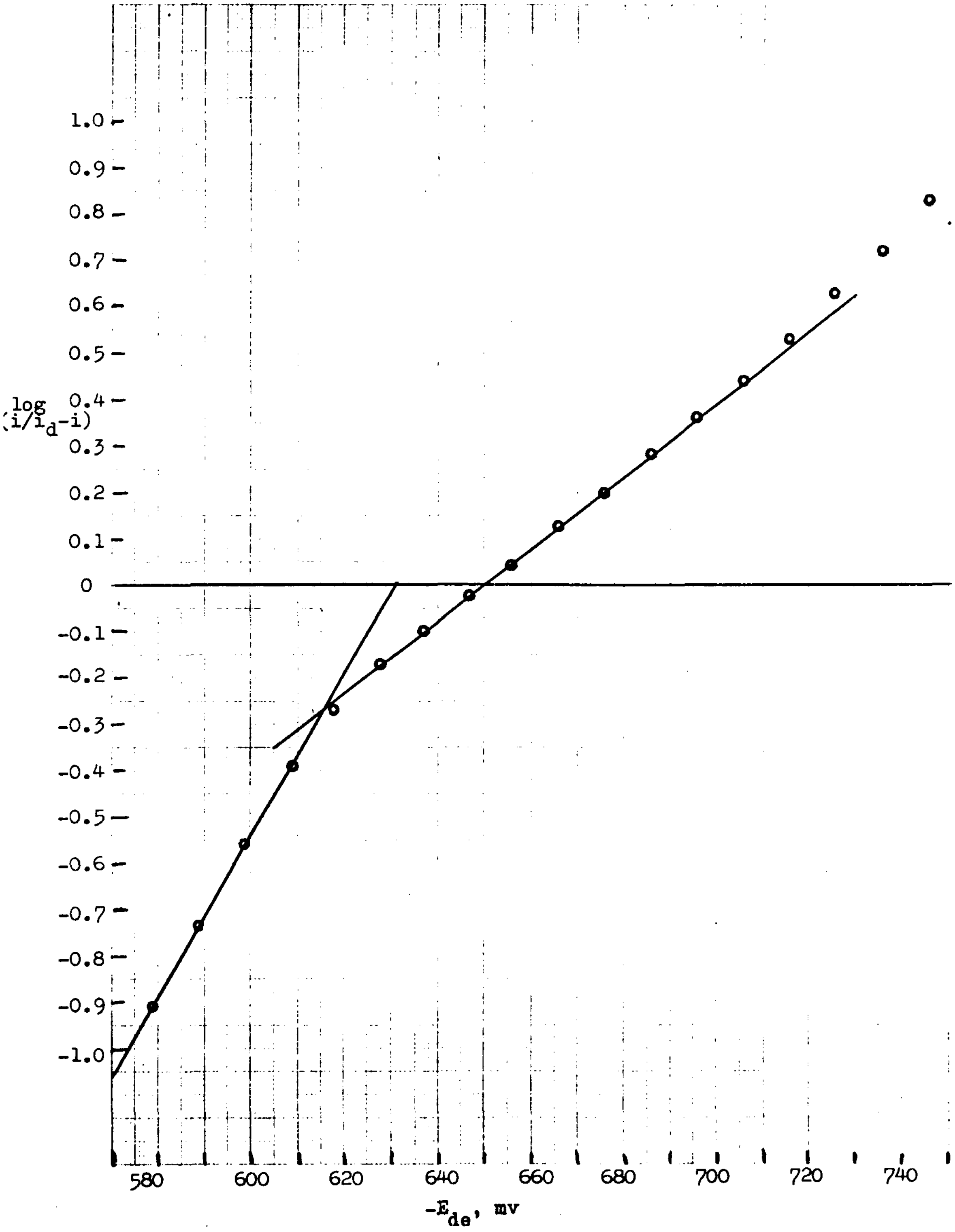
Thus it can safely be assumed that $p = 2$ in this range.

Log plots for wave #1 become more irregular when the pH is higher than 3. At pH 4.80, for example, the log plot obtained in one run consisted of two straight lines of different slopes (see the next page). The first line, from -570 to -615 mv, had a slope which corresponded to a value of $\alpha n = 1.03$. The second line, from -615 mv on, had a slope which corresponded to a value of $\alpha n = 0.47$. Other results were obtained in different runs, and for this reason, no attempt was made to calculate the value of <u>p</u> in this range.

Unlike pyrazinoic acid, the reduction wave #1 of the dicarboxylic acid has a diffusion current which decreases sharply with increasing pH in the vicinity of the polarographic dissociation constant, pK'.

In order to obtain better information concerning the value of pK'. additional polarograms were run with narrower intervals of pH in between runs. These values are shown in the table on page 66 under the heading "Series II"

Log plot: WAVE #1 of pyrazine-2,3-dicarboxylic acid (1×10^{-3} M) in McIlvaine buffer: pH 4.80



and a plot of i_d vs. pH for wave #1 appears on page 67.

From the graph on page 67, the value of pK' can be found directly: it is the pH at which the value of the diffusion current is one-half of its original value.
In the pH range of 1 to 2, $i_d \approx 6.7$ µA; when $i_d = 3.35$ µA, pH = 5.25. Thus pK' = 5.25.

WAVE II

This reduction wave is present throughout the entire pH range; it is well defined (with reproducible $E_{1/2}$ values) in acidic solutions. The reduction appears to be reversible in strongly acidic solutions; a typical log plot of wave #2 in 1 M H_2SO_4 appears on page 68. Here the slope equals -34.25, corresponding to a value of $\alpha n = 2.03$. Immediately the conclusion might be drawn that the reduction wave is reversible with n = 2; however, it must be noted that the diffusion current of wave #2 is approximately twice as much as the diffusion current of wave #1 (see table, p. 61).
If both reduction waves are diffusion-controlled, the Ilkovic equation applies, and the diffusion current is proportional to the number of electrons in the reduction (other things being equal).

It appears that reduction wave #2 is diffusion-controlled in acidic solutions. The diffusion current is

POLAROGRAMS OF PYRAZINE-2,3-DICARBOXYLIC ACID

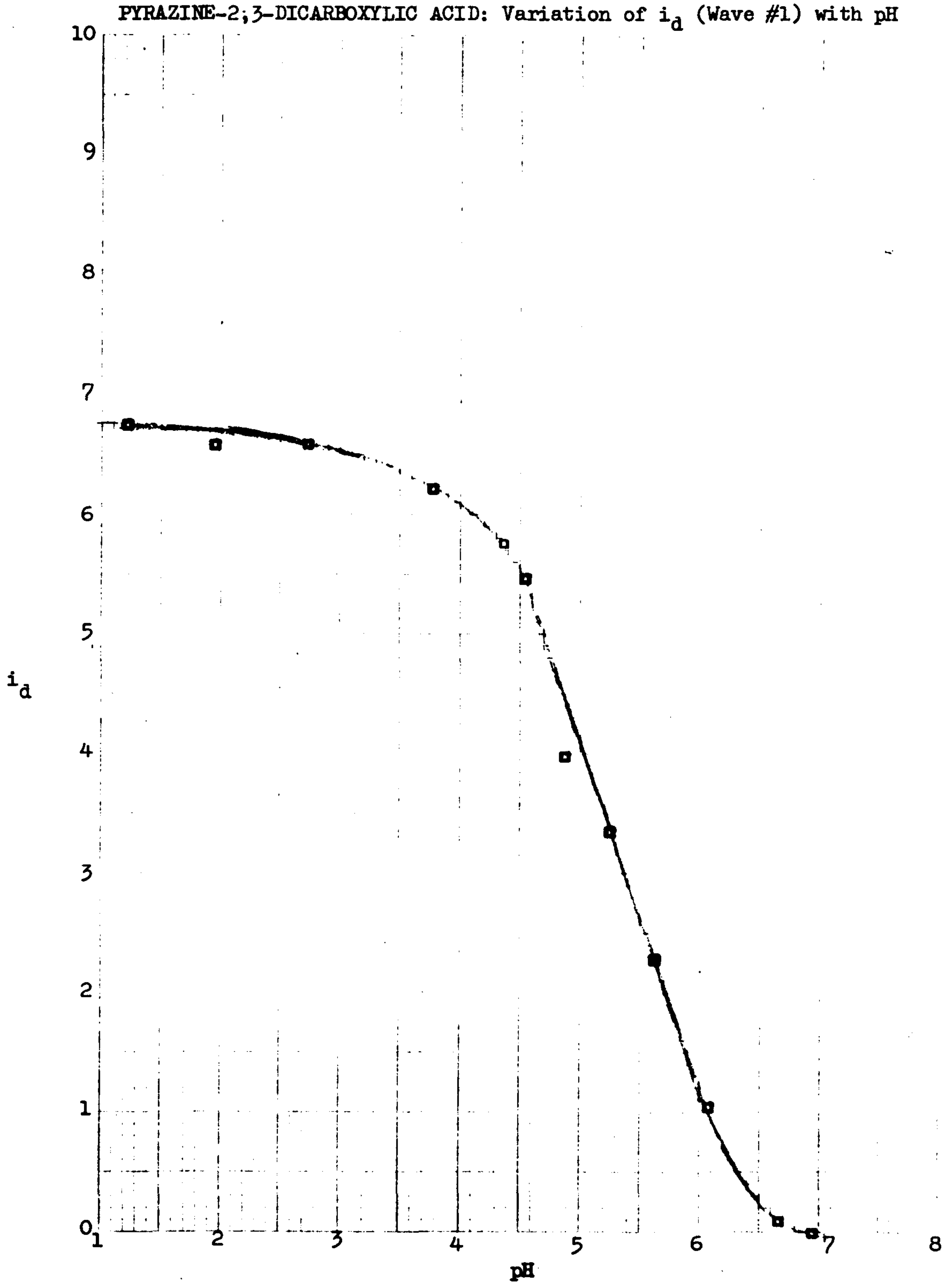
SERIES II

Polarograms in this series were run in order to obtain more information concerning the decrease in the height of wave #1 in the neighborhood of pK'. McIlvaine buffer solutions (no Ca^{++} present) were used throughout this series.

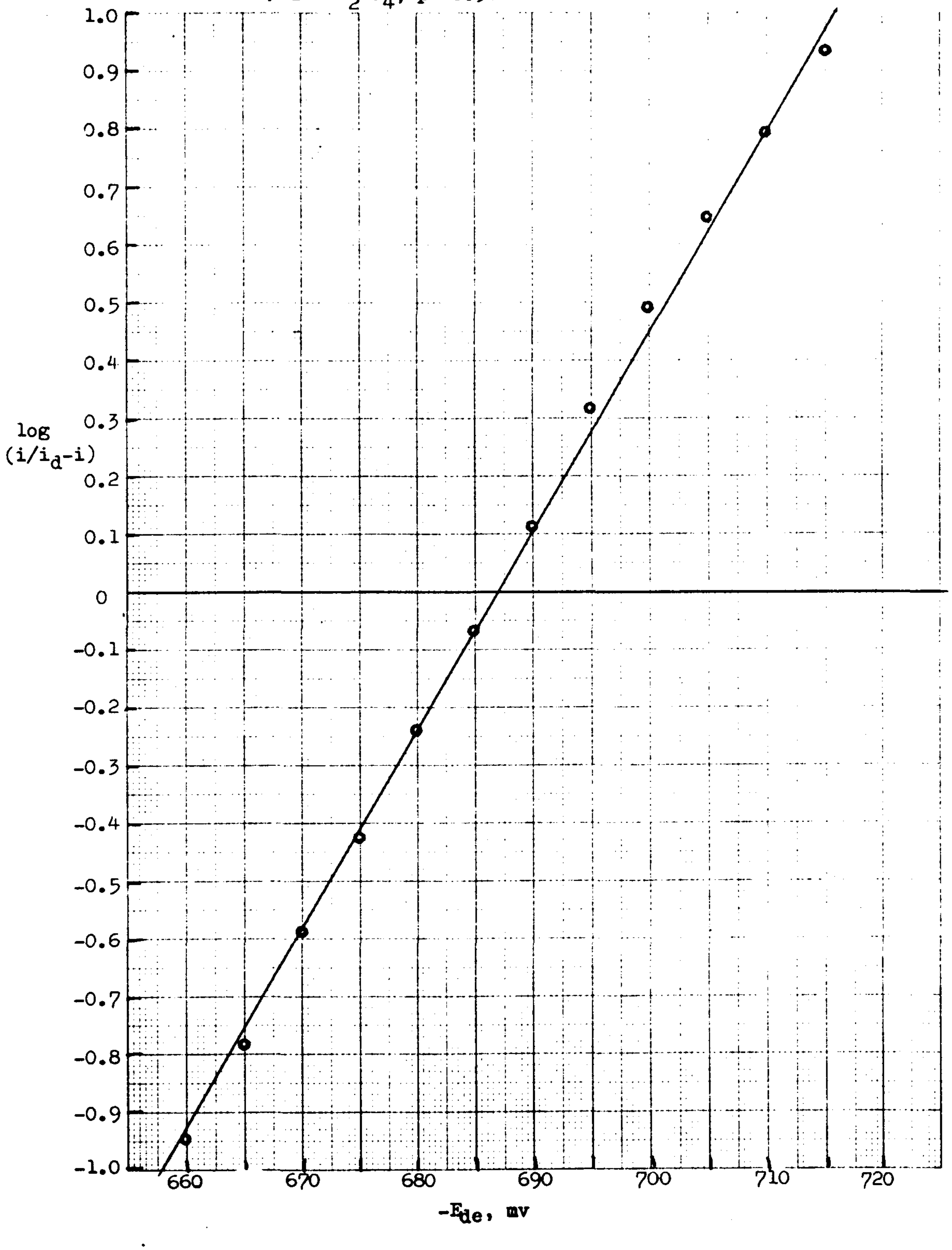
	WAVE #1	
pH	$E_{1/2}$, v	i_d, μA
1.95	-0.341	6.55
2.72	-0.413	6.58
3.77	-0.520	6.20
4.36	-0.618	5.75
4.54	-0.642	5.46
4.87	-0.676	3.97
5.26	-0.753	3.33
5.62	-0.804	2.29
6.08	-0.810	1.02
6.84	absent	absent

Values of $E_{1/2}$ and i_d for wave #2 were not recorded in this series.

PYRAZINE-2,3-DICARBOXYLIC ACID: Variation of i_d (Wave #1) with pH



Log plot: WAVE #2 of pyrazine-2,3-dicarboxylic acid in 1 M H_2SO_4, pH 0.36



proportional to the square root of the mercury height, but it is impossible to determine the temperature coefficient of wave #2. Although this wave is well-defined at 25°C, it is very poorly defined at higher temperatures such as 50°C. However, at 50°C, increasing the mercury height aids considerably in making the wave better defined; the reason for this behavior was not investigated further.

Assuming that wave #2 is diffusion-controlled (at least at room temperature), the fact that the diffusion current of wave #2 is about twice that of wave #1, together with the fact that $n = 2$ for wave #1, would lead one to the conclusion that $n = 4$ for wave #2. If this were so, α would have to be equal to about 0.5 in order for αn to equal 2.03.

Wave #2 becomes quasi-reversible in weakly acidic solutions. In the log plot of wave #2 at pH 2.89 (page 71), αn equals 0.98; at pH = 3.84, $\alpha n = 1.23$. There is no change in the diffusion current in the entire pH range of 0 to 7 pH, so <u>n</u> remains constant throughout this range.

Using the value of $\alpha n = 0.98$ at pH 2.89, the value of <u>p</u> can then be calculated:

$$\frac{\Delta E_{1/2}}{\Delta \text{pH}} = -\frac{0.05915}{\alpha n}\,p = -\frac{0.05915}{0.98}\,p = -0.0604\,p$$

$$-0.115 = -0.0604\,p$$

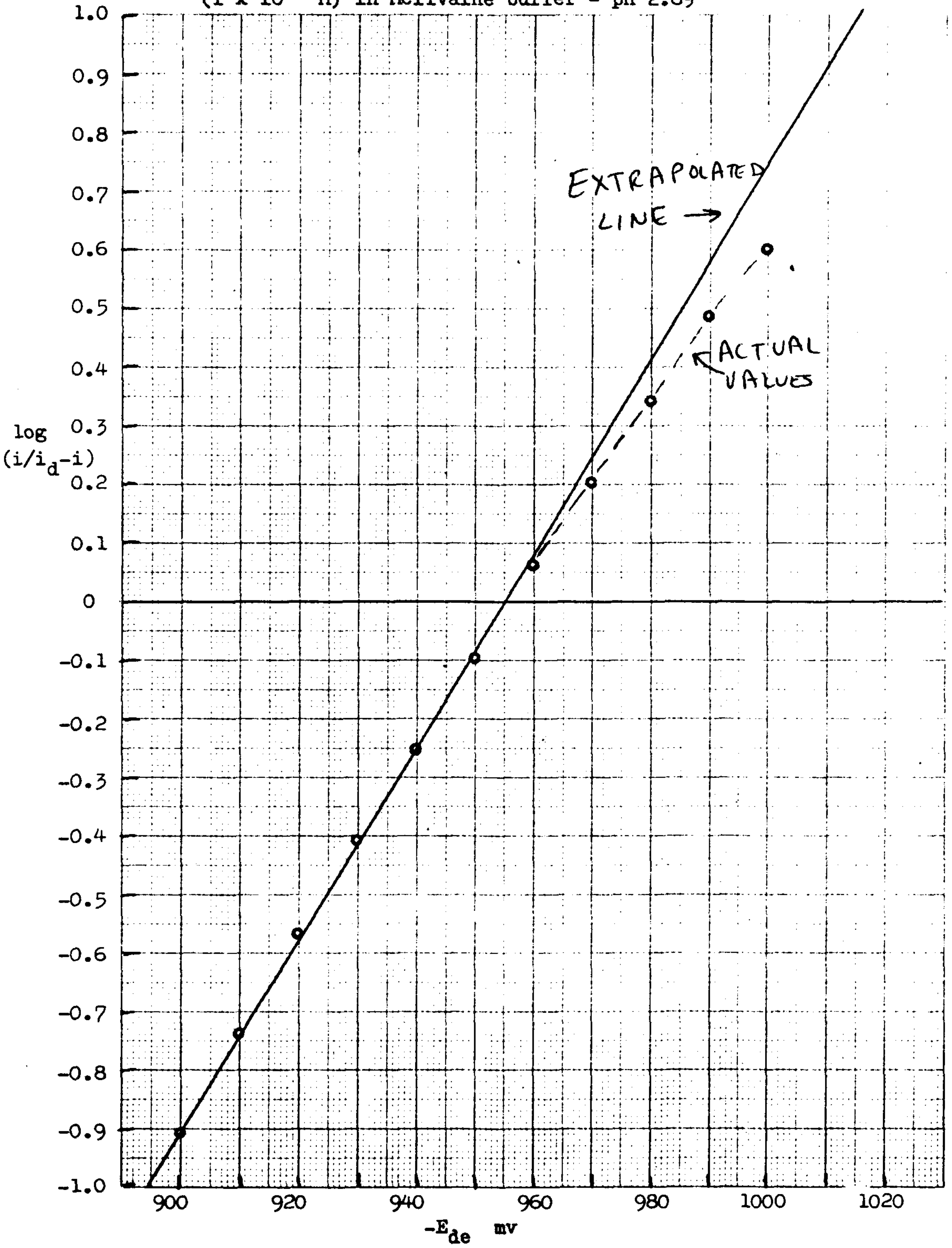
$$p = 1.90$$

If $\alpha n = 1.23$ (pH 3.84), the calculated value of p is 2.39. Thus p = 2 in this range.

In weakly basic solutions (pH 7 to 10), wave #2 is very poorly defined in ordinary buffer solutions (e.g. veronal) to which no calcium ions have been added. This accounts for the extreme variation in the values of $E_{1/2}$ from -1.3 to -1.6 in this pH range in the graph on page 62.

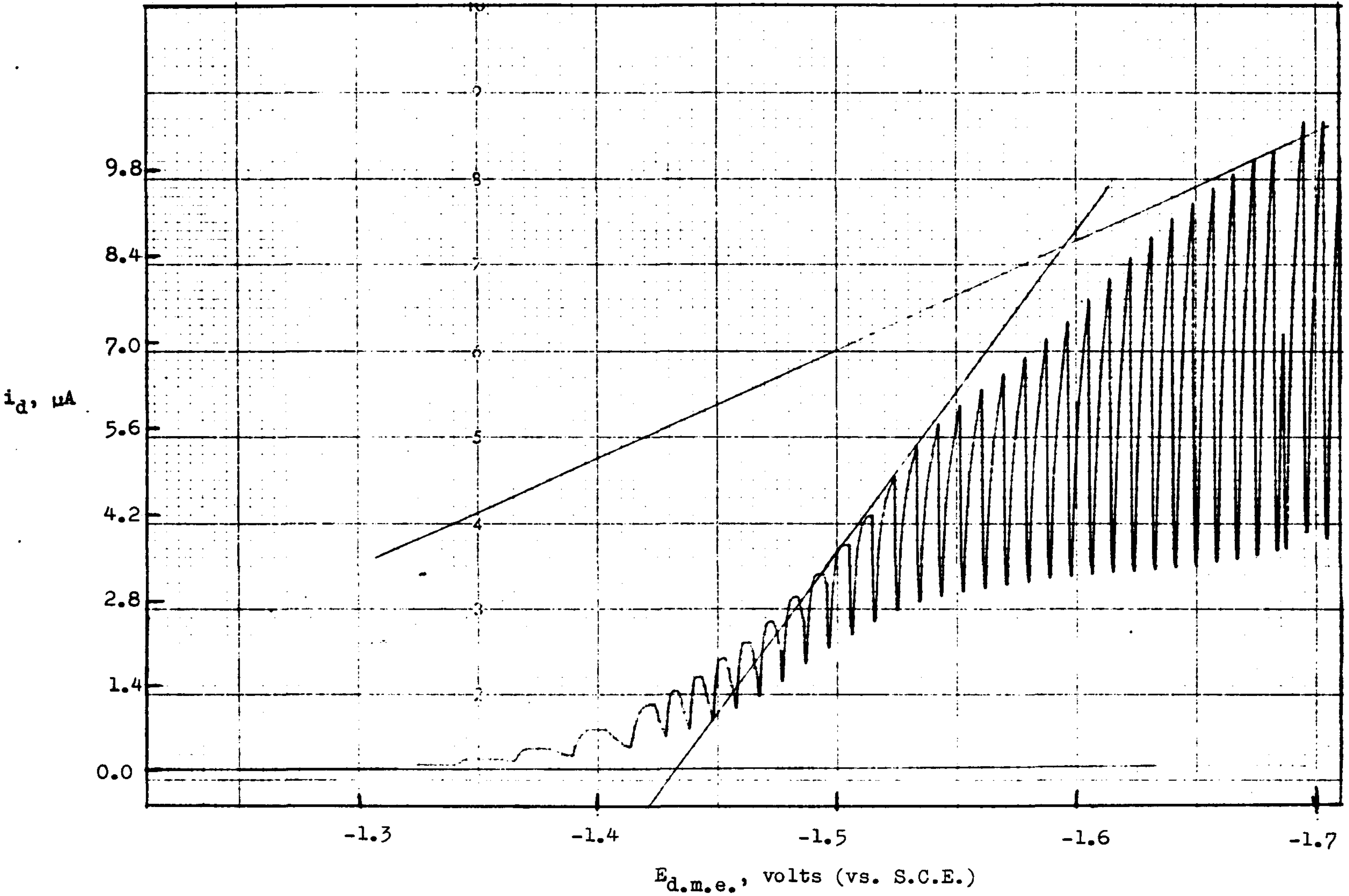
If, however, 0.05 M Ca^{++} is added to solutions in this pH range, a dramatic change occurs and the reduction wave actually splits into two smaller waves designated 2A and 2B in the table on page 61 and the graph on page 62.

The polarogram shown on page 72 was wave #2 of pyrazine-2,3-dicarboxylic acid (1.00×10^{-3} M) in a veronal buffer, pH 9.03. It is very poorly defined and it is impossible to get an accurate value of $E_{1/2}$ from such a polarogram. After 5 ml of 0.05 $\underline{M}$ $CaCl_2$ solution was added to the original solution in the polarographic cell and the solution deaerated a suitable amount of time, the polarogram shown on page 73 was obtained. The sum of the diffusion currents of waves #2A and #2B is approximately equal to the diffusion current of wave #2 before the addition of calcium ions. Very significant is the fact that the half-wave potentials of waves #2A and #2B are reproducible; there is a slight variation of $E_{1/2}$ with pH but this variation is not pronounced.

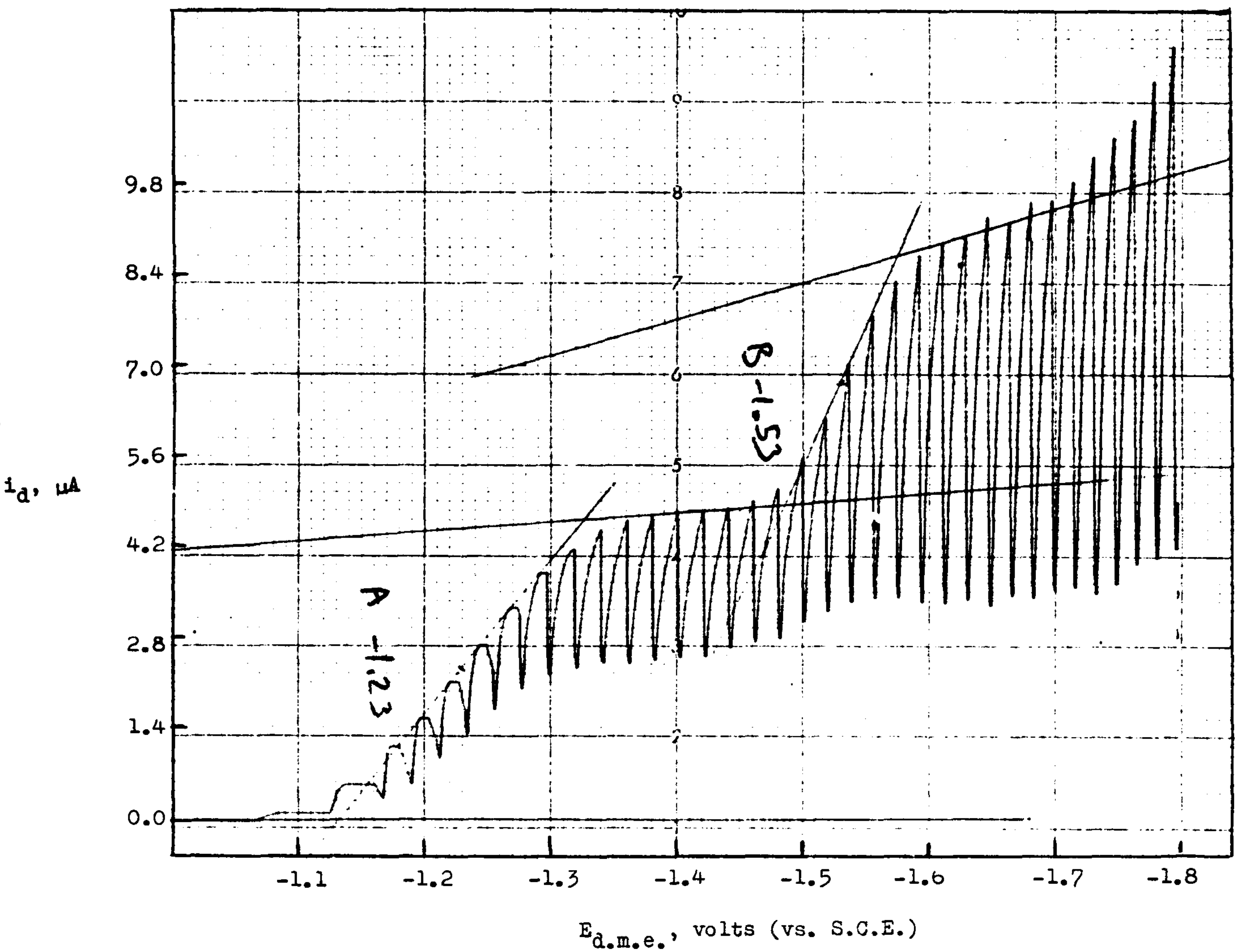


Log plot: WAVE #2 of pyrazine-2,3-dicarboxylic acid
(1×10^{-3} M) in McIlvaine buffer - pH 2.89

WAVE #2 OF PYRAZINE-2,3-DICARBOXYLIC ACID IN VERONAL BUFFER, pH 9.03, BEFORE ADDITION OF CALCIUM IONS



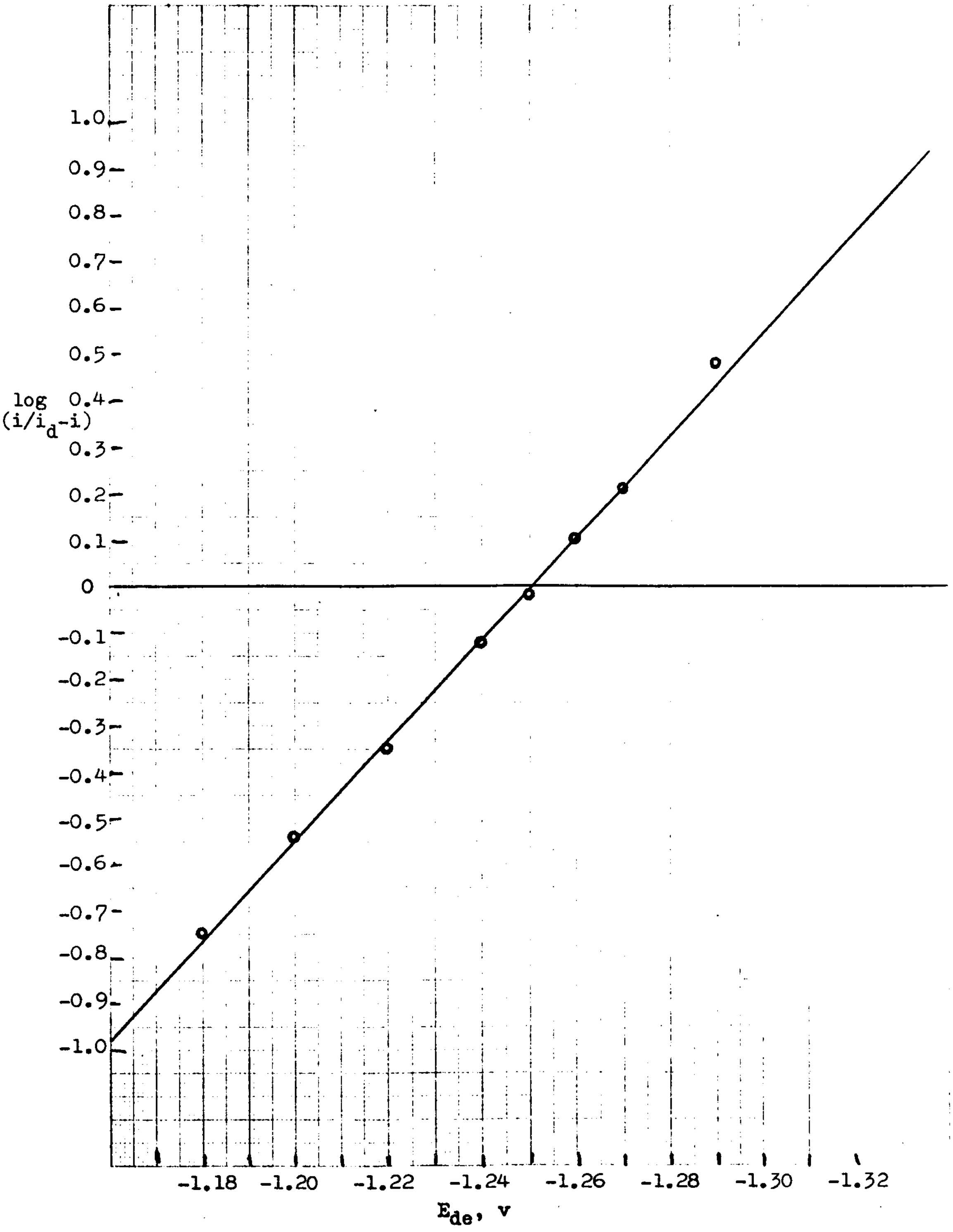
POLAROGRAM OF SAME SOLUTION AFTER ADDITION OF 5 ML 0.5 M $CaCl_2$



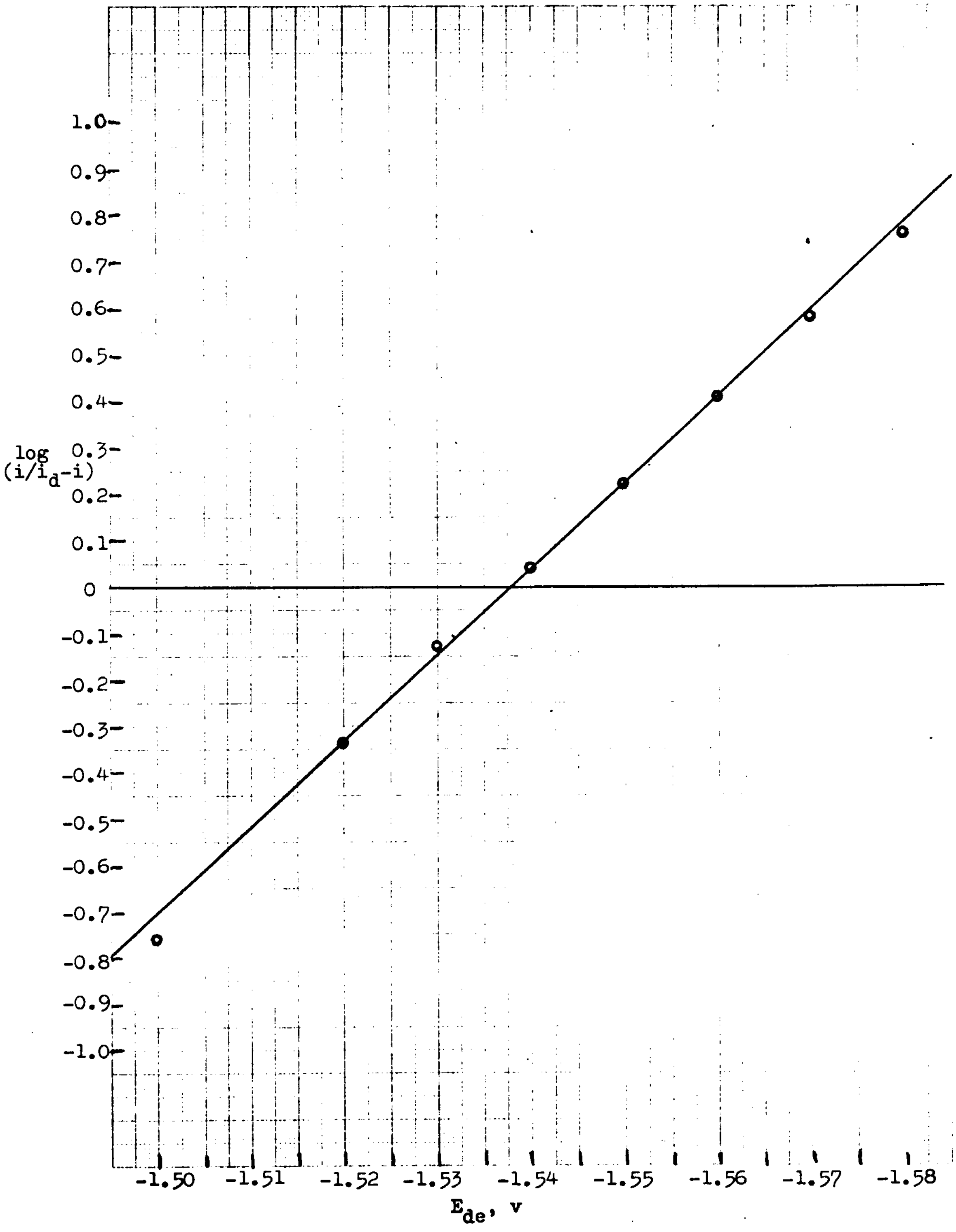
Log plots of waves #2A and #2B (using a veronal buffer with 0.05 M Ca^{++} at pH 8.56) appear on pages 75 and 76, respectively. In wave #2A, the slope is -10.93, which corresponds to $\alpha n = 0.65$. For wave #2B, the slope, -18.69, corresponds to $\alpha n = 1.11$. Thus n is at least equal to 1 in wave #2A and at least 2 in wave #2B; this finding is consistent with the prior finding that for the combined wave #2, n = 4. Since waves #2A and #2B have about the same diffusion current (i.e. one-half of the combined wave #2), it might be assumed that n = 2 for both waves; however, other techniques such as controlled-potential coulometry would be required in order to determine the value of "n" for waves #2A and #2B conclusively.

In strongly basic solutions, reduction wave #2 is better defined but it still is definitely irreversible. As before, the value of $E_{1/2}$ is not very reproducible (it is -1.35 ± 0.1 v), and the same behavior was obtained with pyrazinoic acid in this pH region.

Log plot: WAVE #2A of pyrazine-2,3-dicarboxylic acid, present in veronal buffer solution (pH 8.56) with 0.05 M Ca^{++}



Log plot: Wave #2B of pyrazine-2,3-dicarboxylic acid, present in veronal buffer solution (pH 8.56) with 0.05 M Ca^{++}



(c) Pyrimidine-4-carboxylic acid

Two reduction waves are obtained for this acid; values of $E_{1/2}$ and i_d obtained in different buffer solutions appear in the table on page 78. This acid is the only acid of the four diazine carboxylic acids in which the theoretical polarographic behavior is, in fact, observed. Wave #1 is present in acidic solutions and the wave height decreases rapidly in the vicinity of pH = 7; by this time, wave #2 has appeared and its height increases rapidly in the vicinity of pH = 7. Thus it is possible to plot the height of both waves as a function of pH (in the vicinity of pH 7) to get an accurate value of the pK'.

WAVE #1

This reduction wave is irreversible throughout the entire pH range of 0 to 9. Values of αn obtained in various trials run from 0.60 to 1.48, with no variation of αn with pH being noted. Using a typical value of αn of 1.0, the number of hydrogen ions involved in the reduction, p, is calculated to be 2:

$$\frac{\Delta E_{1/2}}{\Delta \text{ pH}} = -\frac{0.05915}{\alpha n}\, p = -0.05915\, p$$

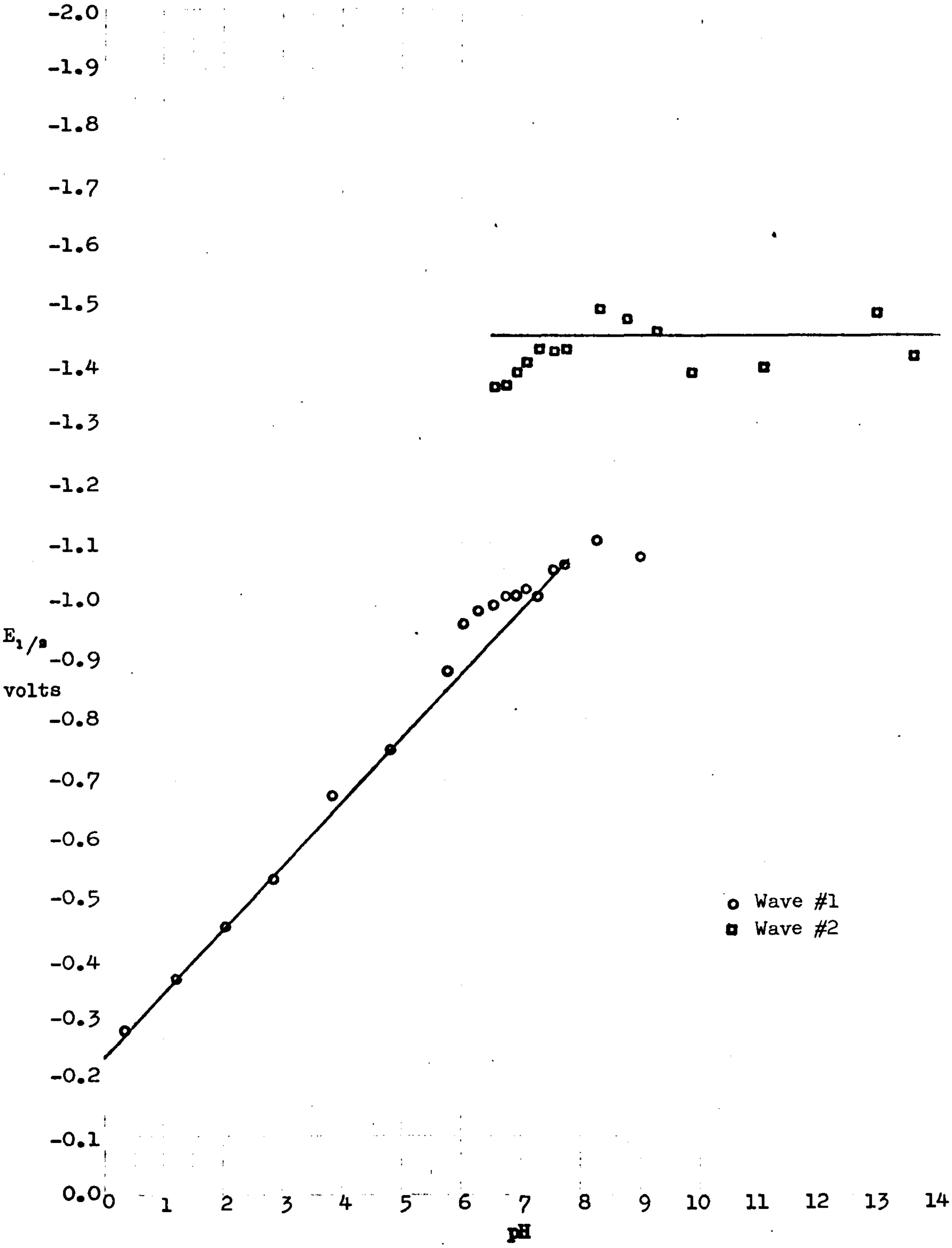
$$-0.108 = -0.05915\, p$$

$$p = 1.83 \approx 2$$

POLAROGRAMS OF PYRIMIDINE-4-CARBOXYLIC ACID

Buffer Solution Used	pH	WAVE #1		WAVE #2	
		$E_{1/2}$, v	i_d, µA	$E_{1/2}$, v	i_d, µA
1 M H_2SO_4	0.35	-0.276	5.35		
0.1 M HCl and 0.9 M KCl	1.22	-0.361	6.59		
McIlvaine buffer solutions:	2.04	-0.455	6.82		
	2.86	-0.534	6.69		
0.2 M Na_2HPO_4	3.85	-0.673	6.87		
and	4.83	-0.751	6.59		
0.1 M citric acid	5.77	-0.886	6.19		
	6.05	-0.961	6.13		
	6.30	-0.989	5.14		
	6.56	-0.999	4.06	-1.360	0.91
	6.78	-1.010	3.46	-1.366	1.67
	6.92	-1.013	3.09	-1.379	2.32
	7.10	-1.021	2.58	-1.403	2.67
	7.30	-1.011	1.50	-1.426	2.41
	7.53	-1.059	1.50	-1.420	3.45
	7.74	-1.062	0.64	-1.424	4.17
Veronal buffer	8.30	-1.105	0.29	-1.492	5.61
solutions	8.79	-1.08	0.06	-1.477	6.18
	9.27	absent	absent	-1.455	6.11
0.5 M $KHCO_3$ and 0.5 M K_2CO_3	9.86			-1.387	5.62
0.25 M Na_2HPO_4 + 0.25 M Na_3PO_4	11.06			-1.394	5.15
0.1 M NaOH	13.0			-1.482	6.89
1.0 M NaOH	13.6			-1.413	6.19

PYRIMIDINE-4-CARBOXYLIC ACID: Variation of $E_{1/2}$ with pH



Here again, in order to determine the value of pK' more accurately, additional polarograms were run using McIlvaine buffer solutions, and values of $E_{1/2}$ and i_d for these polarograms were included in the table on page 78. As expected, as the pH increases in the vicinity of the pK', the diffusion current of wave #1 gradually decreases, and the diffusion current of wave #2 gradually increases.

From the graph on page 81, it can readily be seen that at pH = 7.0, the diffusion current of the free acid equals the diffusion current of the anion. Thus pK' = 7.0, and K' (the polarographic dissociation constant) is equal to 1×10^{-7}. It is then possible to determine the rate constant for the recombination of anions with protons, k_r, using the formula[50]

$$k_r = \frac{1.31}{(K')^2} \cdot \frac{K_a}{t_1}$$

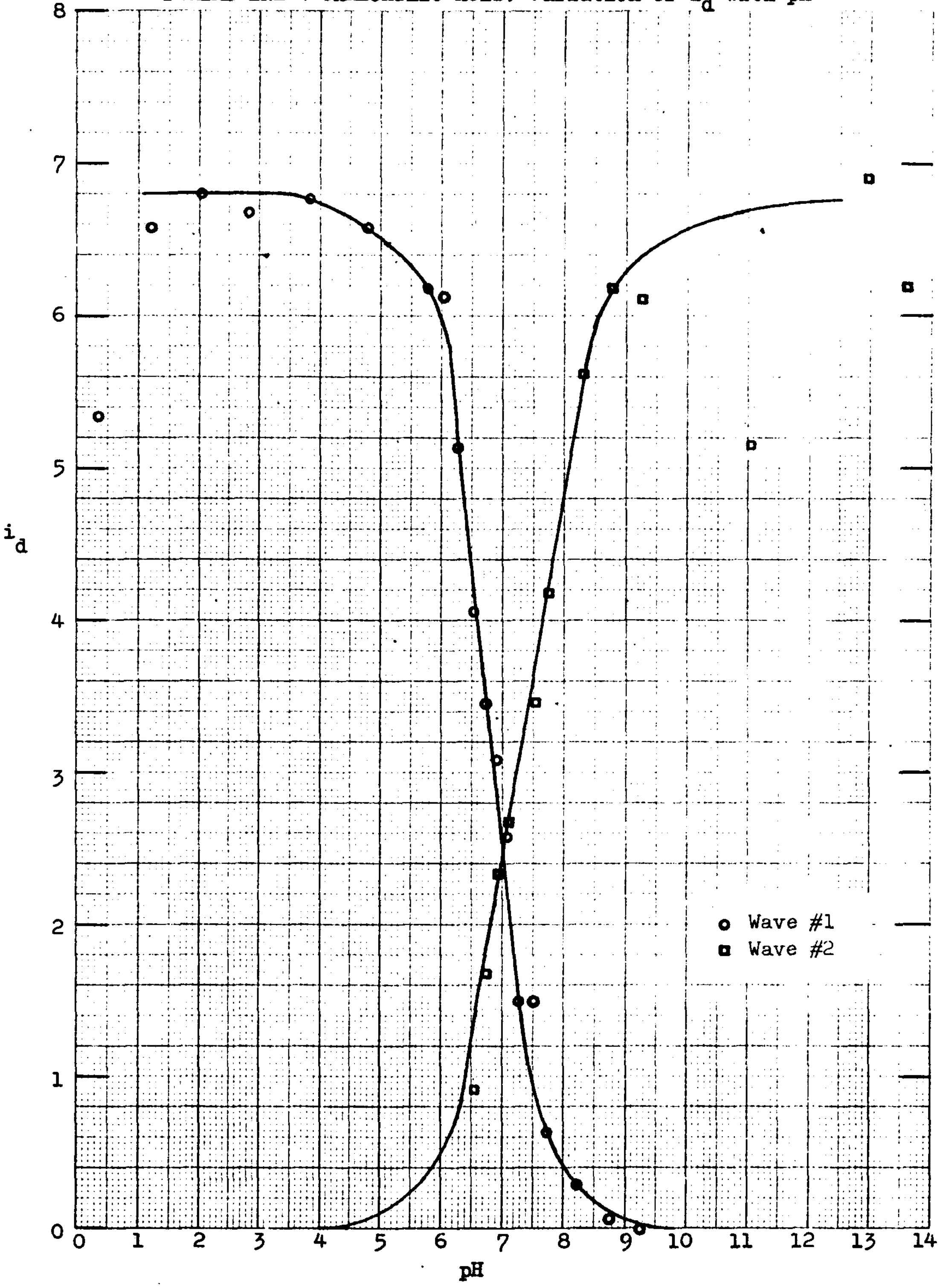
Here $K' = 1 \times 10^{-7}$, $K_a = 1.05 \times 10^{-3}$, and $t_1 = 4.22$ sec. Therefore:

$$k_r = \frac{(1.31)(1.05 \times 10^{-3})}{(1 \times 10^{-7})^2 \ (4.22)} = 3.3 \times 10^{10} \ \frac{\text{liter}}{\text{mole sec}}$$

In addition, since $K_a = k_d/k_r$,

$$k_d = (K_a)(k_r) = (1.05 \times 10^{-3})(3.3 \times 10^{10}) = 3.5 \times 10^{7} \text{ sec}^{-1}.$$

PYRIMIDINE-4-CARBOXYLIC ACID: Variation of i_d with pH



These values of k_r and k_d agree well with those obtained for other carboxylic acids. Heyrovsky and Kůta[71] indicated that the values of k_r for most carboxylic acids are generally between 10^9 and 10^{13}, and the k_r value of picolinic acid was found to be 3.0×10^{11}.

WAVE II

Wave #2, the reduction wave of the anion, has a half-wave potential which is independent of the pH. However, as in the case of pyrazinoic acid, the value of $E_{1/2}$ is not very reproducible; it is (-1.45 ± 0.1) v. Inasmuch as the two waves are clearly defined, there is no problem in distinguishing between the heights and the half-wave potentials of the two waves, as was the case for pyrazinoic acid.

The fact that the half-wave potential is independent of the pH indicates that no hydrogen ions are involved in the reduction.

(d) Pyridazine-3-carboxylic acid

Only one reduction wave is present throughout the entire pH range; in reality, this one wave consists of two waves overlapping each other, as in the case of pyrazinoic acid. A table showing values of $E_{1/2}$ and pH with different buffer solutions appears on the next page, and the plot of of $E_{1/2}$ vs. pH appears on page 85.

For wave #1, the reduction is reversible with $n = 2$ only in strongly acidic solutions (i.e. pH 0 or 1), but at higher pH values the reduction is irreversible with αn varying from 0.63 to 1.66. Using a typical value of αn of 1.1, the number of hydrogen ions is found to be 2:

$$\frac{\Delta E_{1/2}}{\Delta \text{pH}} = -\frac{0.05915}{\alpha n}p = -\frac{0.05915}{1.1}p = -0.0538\ p$$

$$-0.0538\ p = -0.095$$

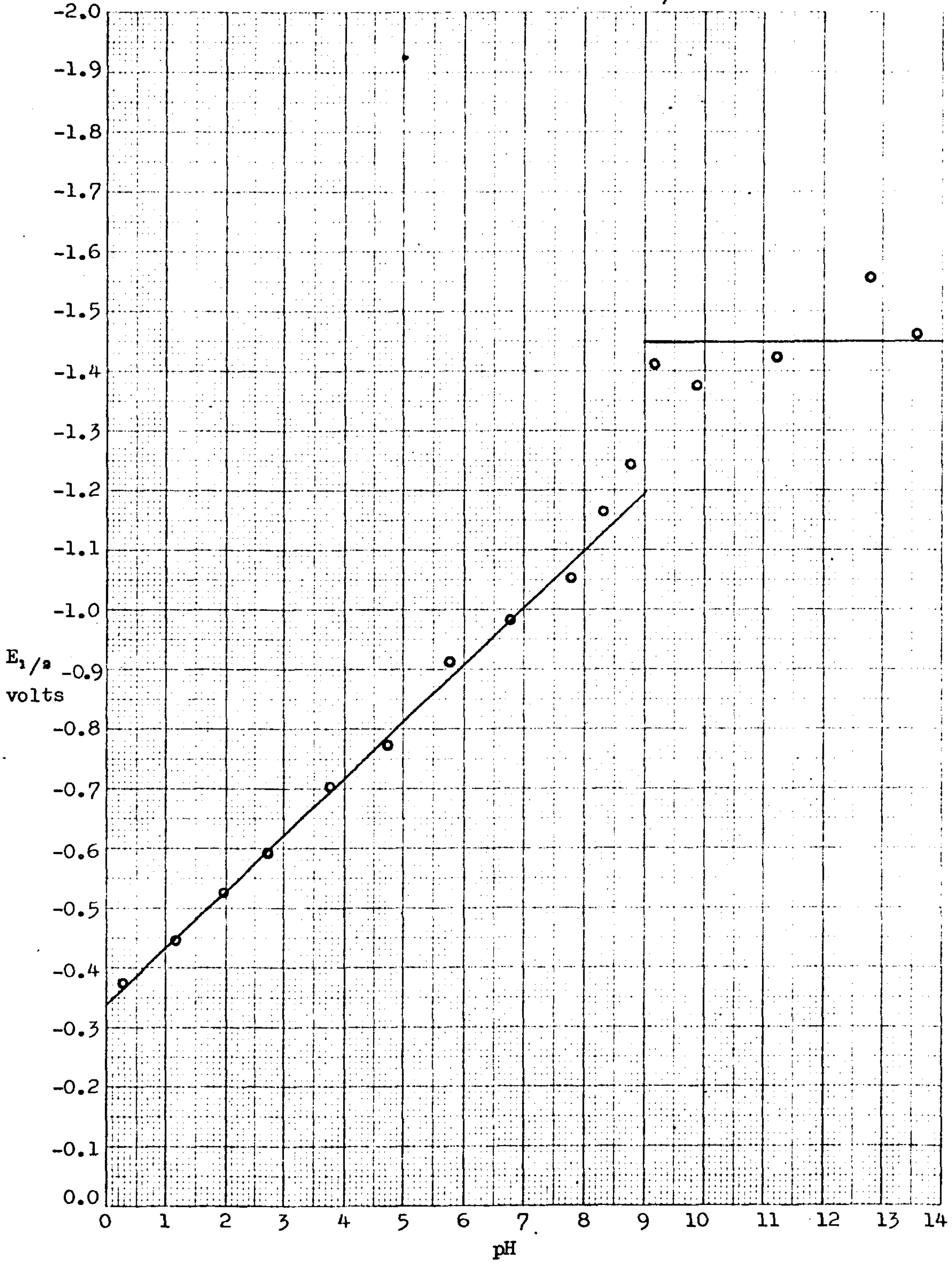
$$p = 1.77 \approx 2$$

Wave #2 is present as with the other acids, and no variation of $E_{1/2}$ with pH is observed. The half-wave potential in all cases is (-1.45 ± 0.1) v.

POLAROGRAMS OF PYRIDAZINE-3-CARBOXYLIC ACID

Buffer Solution Used	pH	$E_{1/2}$, v	i_d, µA
1 M H_2SO_4	0.35	-0.371	6.62
0.1 M HCl and 0.9 M KCl	1.21	-0.445	7.56
McIlvaine buffer solutions: 0.2 M Na_2HPO_4 and 0.1 M citric acid	1.98	-0.528	7.02
	2.75	-0.596	6.72
	3.80	-0.709	6.26
	4.82	-0.776	6.73
	5.81	-0.914	6.25
	6.80	-0.979	3.61
	7.79	-1.058	2.66
Veronal buffer solutions	8.31	-1.165	3.99
	8.79	-1.245	3.03
	9.20	-1.411	5.53
0.5 M $KHCO_3$ and 0.5 M K_2CO_3	9.90	-1.378	4.96
0.25 M Na_2HPO_4 + 0.25 M Na_3PO_4	11.27	-1.427	5.10
0.1 M NaOH	13.0	-1.554	5.81
1.0 M NaOH	13.6	-1.464	5.35

PYRIDAZINE-3-CARBOXYLIC ACID: Variation of $E_{1/2}$ with pH



Footnotes - Chapter IV

65 - J. Volke, *Collect. Czech. Chem. Comm.*, *22*, 1777 (1957).

66 - L. Meites, *op. cit.*, p. 576.

67 - *ibid.*, p. 588.

68 - *ibid.*, pp. 131-132.

69 - *ibid.*, p. 140.

70 - J. Heyrovsky and P. Zuman, *op. cit.*, p. 34.

71 - J. Heyrovsky and J. Kůta, *op. cit.*, p. 368.

CHAPTER V

POLAROGRAPHIC REDUCTION OF THE METAL CHELATES

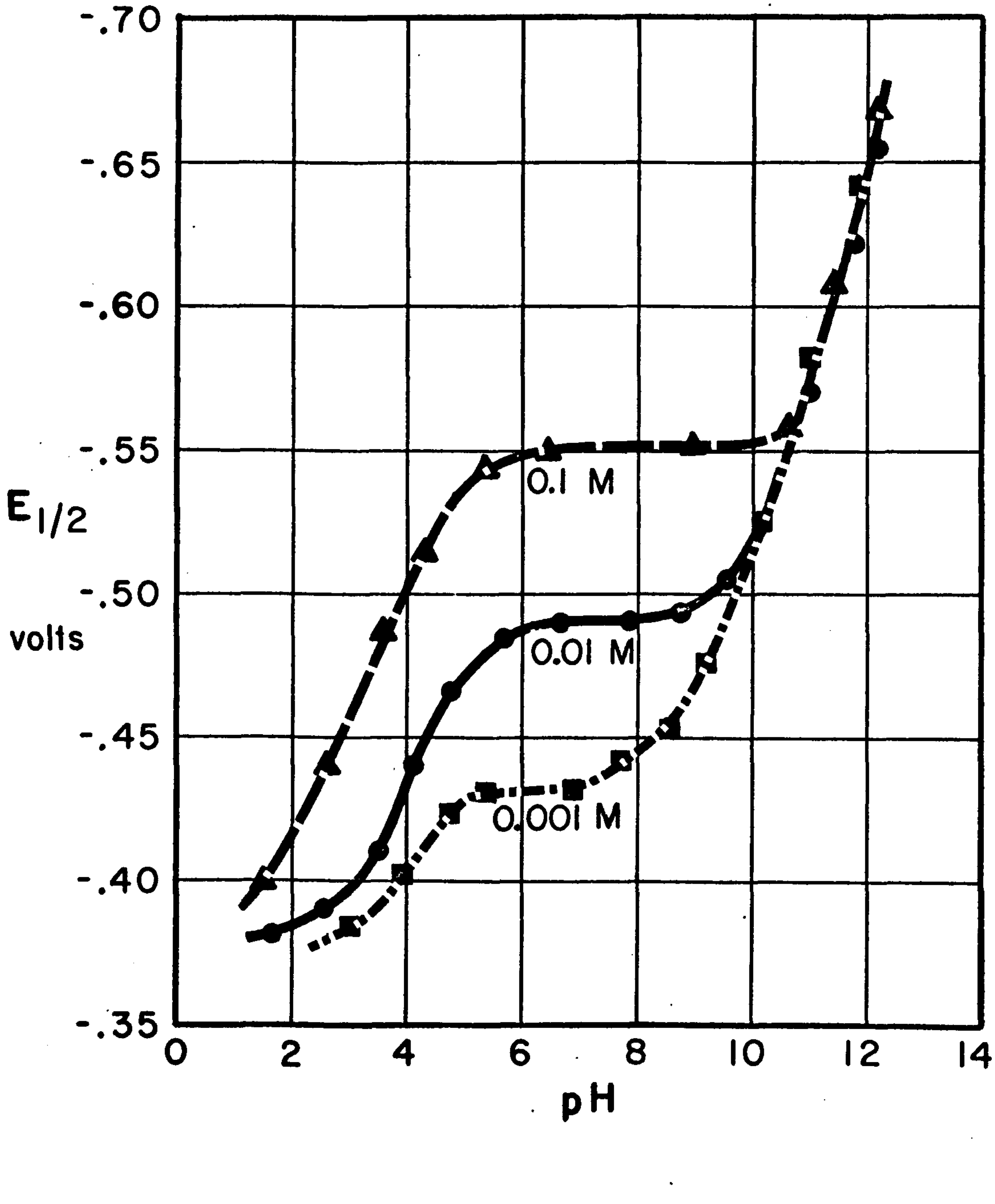
(a) Lead-Picolinic Acid Chelates

1. Reduction wave of the chelate

The polarographic reduction waves for the lead-picolinic acid chelates (and for the free lead ion) are reversible, diffusion-controlled waves; plots of log (i/i_d-i) vs. E were always straight lines in which the values of n (calculated from the slope) were always equal to 2.0. The half-wave potential of the chelate is independent of the concentration of lead ions (provided, of course, that a sufficient excess of chelating agent is present). The diffusion cnrrent is proportional to the square root of the mercury height, and the temperature coefficient is equal to 1.62% / deg., which is normal for a diffusion-controlled wave. The usual methods of calculating the stability constants may therefore be used.

2. Variation of $E_{1/2}$ with pH at different ligand concentrations

In order to determine the pH range at which the polarograms of the chelates should be run, the variation of $E_{1/2}$ with pH at ligand concentrations of 0.00100 M, 0.0100 M, and 0.100 M was first studied. The results are summarized in the graph on the next page. The curve has three regions, LEAD-PICOLINIC ACID CHELATES: Variation of $E_{1/2}$ with pH at total ligand concentrations of 0.00100 M, 0.0100 M, and 0.100 M. (μ = 1.0 M)



as explained on pages 8 and 9. In the first region, using the data at [HPic] = 0.0100 M between the pH values of 3.58 and 4.14,

$$\frac{\Delta\ E_{1/2}}{\Delta\ \text{pH}} = -\ 0.054\ \text{v} = -\ \frac{0.059}{n}\ q$$

Here the number of hydrogen ions involved in the reduction, q, is equal to 2, and a possible equation for the reduction is:

$$[\text{Pb(Pic)}_2]^{\circ} + 2\ \text{H}^{+} + 2\ \text{e}^{-} + \text{Hg} \rightleftarrows \text{Pb(Hg)} + 2\ \text{HPic}$$

The plateau region occurs approximately in the pH region of 6 to 8; here the half-wave potential is independent of the pH and the reaction can be represented as:

$$[\text{Pb(Pic)}_2]^{\circ} + 2\ \text{e}^{-} + \text{Hg} \rightleftarrows \text{Pb(Hg)} + 2\ \text{Pic}^{-} \qquad \text{and}$$

$$[\text{Pb(Pic)}_3]^{-} + 3\ \text{e}^{-} + \text{Hg} \rightleftarrows \text{Pb(Hg)} + 3\ \text{Pic}^{-}$$

All three curves merge into one straight line at pH > 11 due to the formation of Pb(OH)_3^{-} (often written as HPbO_2^{-}). The polarographic reduction of this complex was first studied by Lingane[29], and the equation for the reduction which he gave is:

$$\text{HPbO}_2^{-} + 2\ \text{e}^{-} + \text{H}_2\text{O} + \text{Hg} \rightleftarrows \text{Pb(Hg)} + 3\ \text{OH}^{-}$$

The actual slope of the line which was obtained in this study was -0.082, and it is in good agreement with the theoretical value of -0.089.

A fourth region exists in the curve in which the total ligand concentration is 0.00100 M in the approximate pH range of 7 to 9. It is likely that mixed ligand complexes such as $[Pb(Pic)(OH)_2]^-$ predominate in this region. Since the purpose of this study is to examine the chelates of lead and picolinic acid and not the mixed complexes, all polarograms of the chelates were run in the pH range of 6 to 8.

It was not necessary to adjust the pH of the solutions before running the polarograms by adding small amounts of acid or base since the pH was already in the correct range. In addition, it was neither necessary nor desirable to buffer the solutions at pH $\approx$ 7 since a small change in pH in this region does not change the value of $E_{1/2}$. If buffered solutions were used, the possibility that the components of the buffer might form complexes with the lead always exists, and it is better to run polarograms of unbuffered solutions whenever possible.

3. Variation of $E_{1/2}$ with $[Pic^-]$ at pH ≈ 7

Polarograms were run at a large number of different ligand concentrations; the data and results appear in the table on the following page. For most runs, $[Pb^{++}] = 5 \times 10^{-4}$ M, except in those cases in which $[Pic^-] < 0.007$ M, where the concentration of lead was decreased in order to maintain a sufficiently large ligand to metal ratio. In no case was this ratio smaller than 20:1, and it was usually much larger. The half-wave potential of the simple lead ion, -0.3755 v, was independent of $[Pb^{++}]$.

A plot of $E_{1/2}$ vs. log $[Pic^-]$ at pH ≈ 7 appears on page 93. It contains two straight-line segments: one in which the value of log $[Pic^-]$ is between -3.00 and -1.70, and another in which log $[Pic^-]$ varies from -0.70 to 0.00.

The number of picolinate anions coordinated to the central lead ion was calculated from the slope of plots of $E_{1/2}$ vs. log $[Pic^-]$ according to the equation[29]:

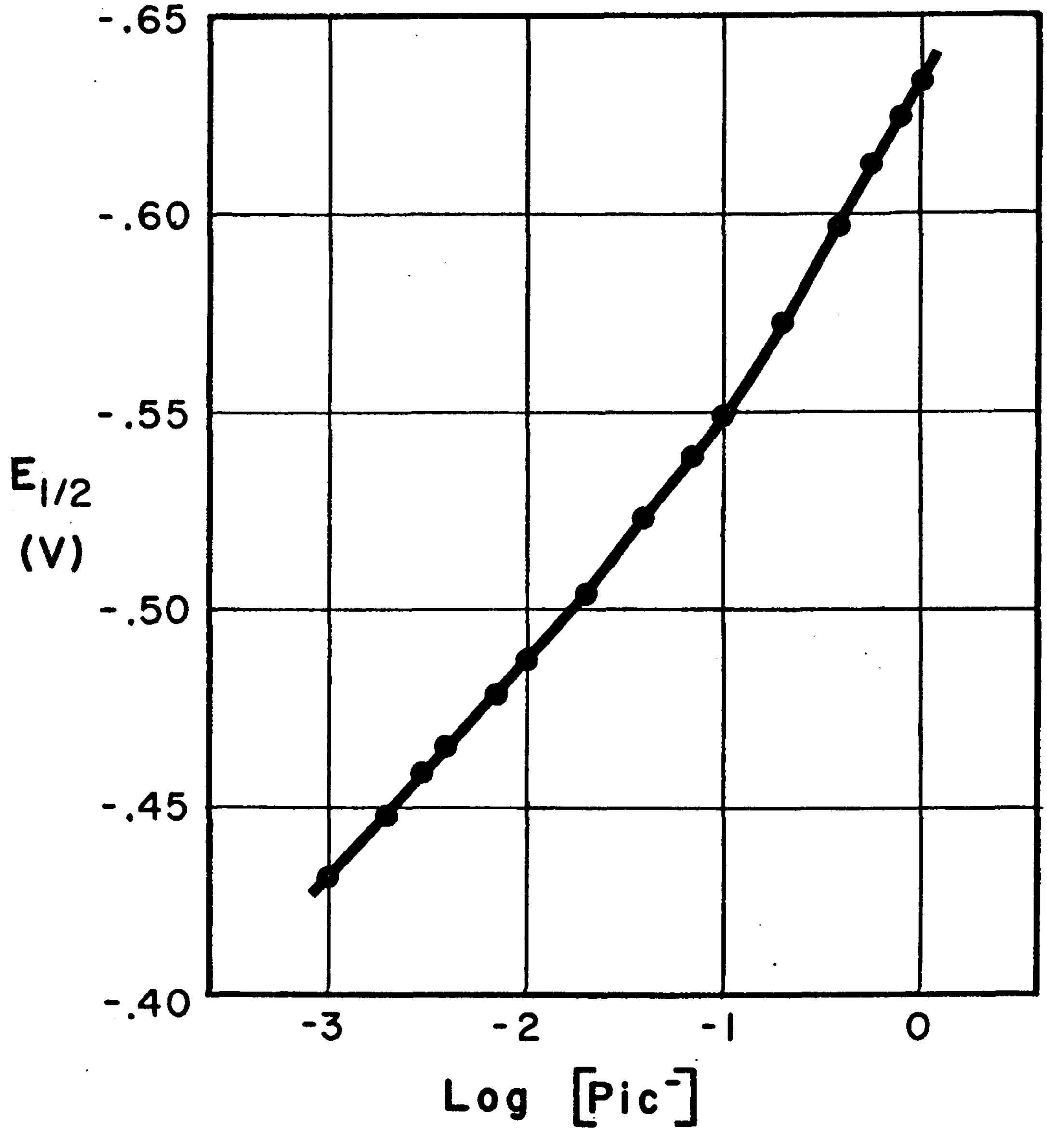
$$\frac{\Delta E_{1/2}}{\Delta \log [Pic^-]} = -0.059 \frac{p}{n} = -0.0295\, p$$

where p is the number of ligands coordinated to the lead ion.

POLAROGRAMS OF LEAD-PICOLINIC ACID CHELATES (pH ≈ 7)

No.	$[Pb^{++}]$	$[Pic^-]$	log $[Pic^-]$	$E_{1/2}$	log I_M/I_C
0	5.000×10^{-4}	0	----	-0.3755	.00
1	5.000×10^{-5}	1.000×10^{-3}	-3.000	-0.4308	.01
2	5.000×10^{-5}	2.000×10^{-3}	-2.699	-0.4479	.01
3	1.000×10^{-4}	3.000×10^{-3}	-2.523	-0.4585	.02
4	1.000×10^{-4}	4.000×10^{-3}	-2.398	-0.4651	.04
5	2.000×10^{-4}	7.000×10^{-3}	-2.155	-0.4785	.05
6	2.000×10^{-4}	1.000×10^{-2}	-2.000	-0.4877	.05
7	5.000×10^{-4}	2.000×10^{-2}	-1.699	-0.5039	.06
8	5.000×10^{-4}	4.000×10^{-2}	-1.398	-0.5232	.10
9	5.000×10^{-4}	7.000×10^{-2}	-1.155	-0.5395	.11
10	5.000×10^{-4}	1.000×10^{-1}	-1.000	-0.5513	.13
11	5.000×10^{-4}	2.000×10^{-1}	-0.699	-0.5722	.14
12	5.000×10^{-4}	4.000×10^{-1}	-0.398	-0.5967	.17
13	5.000×10^{-4}	6.000×10^{-1}	-0.222	-0.6123	.20
14	5.000×10^{-4}	8.000×10^{-1}	-0.097	-0.6238	.22
15	5.000×10^{-4}	1.000×10^{0}	-0.000	-0.6337	.24

LEAD-PICOLINIC ACID CHELATES: Variation of $E_{1/2}$ with log [Pic$^-$] at pH ≈ 7



In the first straight-line segment (log $[Pic^-]$ varies from -3.00 to -1.70), the slope is -0.0569. This corresponds to a value of $p = 2$, indicating that the complex $[Pb(Pic)_2]$ predominates in this region.

In the second segment (log $[Pic^-]$ varies from -0.70 to 0.00), the slope is -0.0875; $p = 3$, and the complex $[Pb(Pic)_3]^-$ predominates here.

When log $[Pic^-]$ is between -1.70 and -0.70, a curved line is obtained, indicating that both complexes are present in significant amounts.

4. Calculated values of chelate stability constants

a. Lingane Method

The value of log β_2 was calculated for polarograms #1 to #7 (i.e. for $[Pic^-]$ varying from 0.001 to 0.02), and log β_3 was calculated for polarograms #11 through #15 (from $[Pic^-] = 0.2$ to 1.0). The results of these calculations appear on the following page.

It is found that log β_2 is 7.86 and log β_3 is 8.92. As a result, $\beta_2 = K_1K_2 = 7.2 \times 10^7$ and $\beta_3 = K_1K_2K_3 = 8.3 \times 10^8$. Thus $\log K_3 = (\log \beta_3 - \log \beta_2) = 1.06$, and $K_3 = 1.2 \times 10^1$.

LEAD-PICOLINIC ACID CHELATES
STABILITY CONSTANTS USING LINGANE METHOD

Polarogram No.	log β_2	Polarogram No.	log β_3
1	7.86	11	8.90
2	7.86	12	8.86
3	7.88	13	8.89
4	7.87	14	8.93
5	7.85	15	8.99
6	7.85		
7	7.81		
AVERAGE	7.86	AVERAGE	8.92

SAMPLE CALCULATIONS

(a) for log β_2 - using data for polarogram #1

$$\log \beta_2 = \frac{(-0.4302)-(-0.3755)}{0.0295} + .01 - (2)(-3.000)$$

$$= 1.854 + .01 + 6.000 = 7.86$$

(b) for log β_3 - using data for polarogram #11

$$\log \beta_3 = \frac{(-0.5513)-(-0.3755)}{0.0295} + .14 - (3)(-0.699)$$

$$= 6.668 + .14 + 2.097 = 8.90$$

b. DeFord-Hume method

Values of $F_0[X]$ and $F_1[X]$ were first calculated; these values appear in the table on the following page. A plot of log $F_1[X]$ vs. $[Pic^-]$ appears on page 98; when this curve is extrapolated to $[Pic^-] = 0$, a value of $\beta_1 = 3 \times 10^4$ is obtained.

This value of β_1 was then used to calculate the values of $F_2[X]$ at all ligand concentrations, and a plot of log $F_2[X]$ vs. $[Pic^-]$ appears on page 99. Extrapolation to $[Pic^-] = 0$ yields a value of $\beta_2 = 6 \times 10^7$.

Finally, this value of β_2 was used to calculate the values of $F_3[X]$, and a plot of log $F_3[X]$ vs. $[Pic^-]$ appears on page 100. A value of $\beta_3 = 5 \times 10^8$ was obtained when the line was extrapolated to $[Pic^-] = 0$. Values of $[Pic^-] < 0.4$ were not used because of the large scatter of these values.

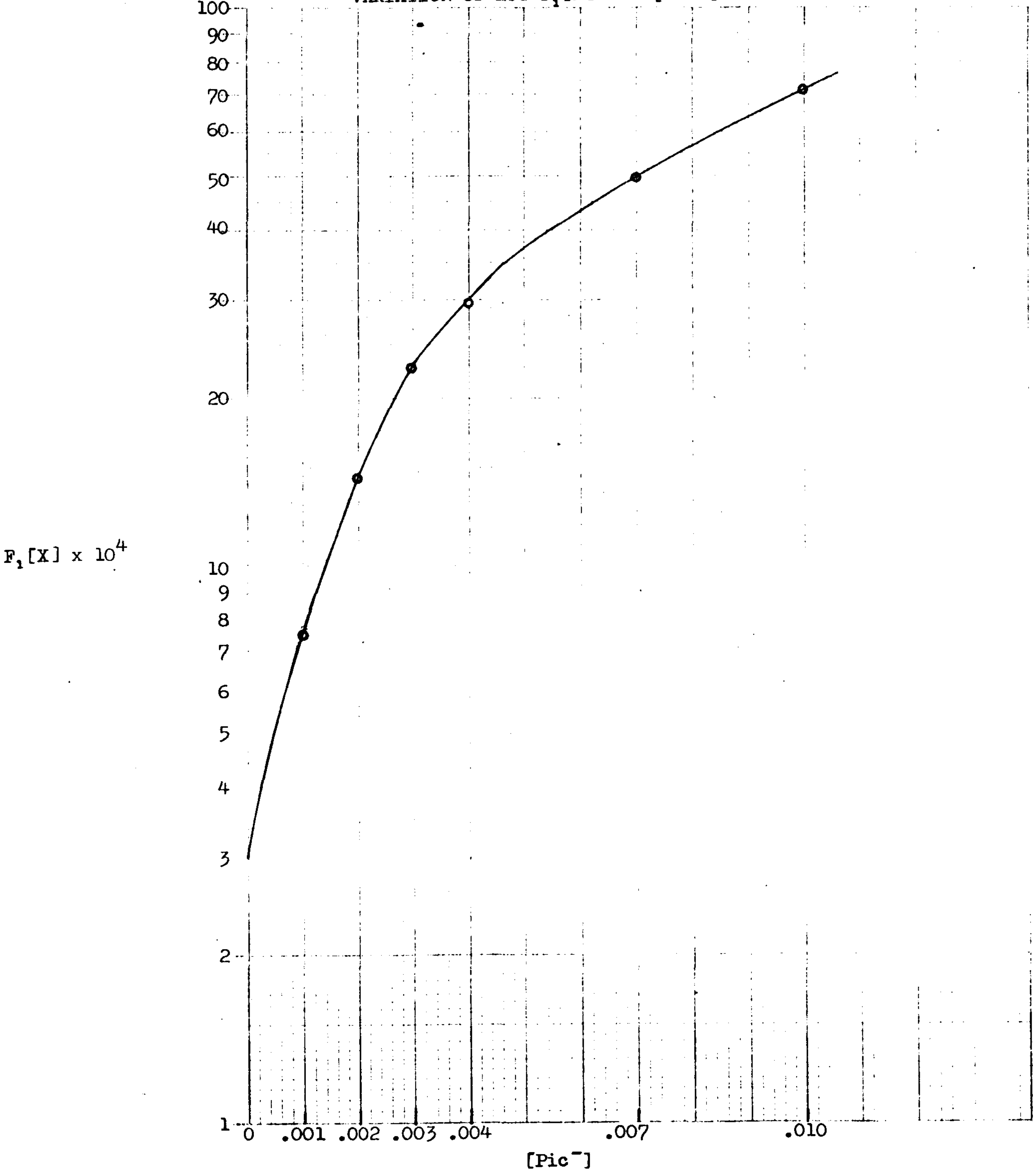
A plot of log $F_0[X]$ vs. log $[X]$ was then prepared; this graph appears on page 101. As explained earlier, the slope at any point equals the value of $\bar{n}$ at that ligand concentration. This graph is similar to the plot of $E_{1/2}$ vs. log $[Pic^-]$ (page 92) in that two straight lines are obtained corresponding to the complexes $Pb(Pic)_2$ and $Pb(Pic)_3^-$ with a small curved region in between these two lines. In no case

DERIVED FUNCTIONS FOR THE LEAD-PICOLINIC ACID SYSTEM

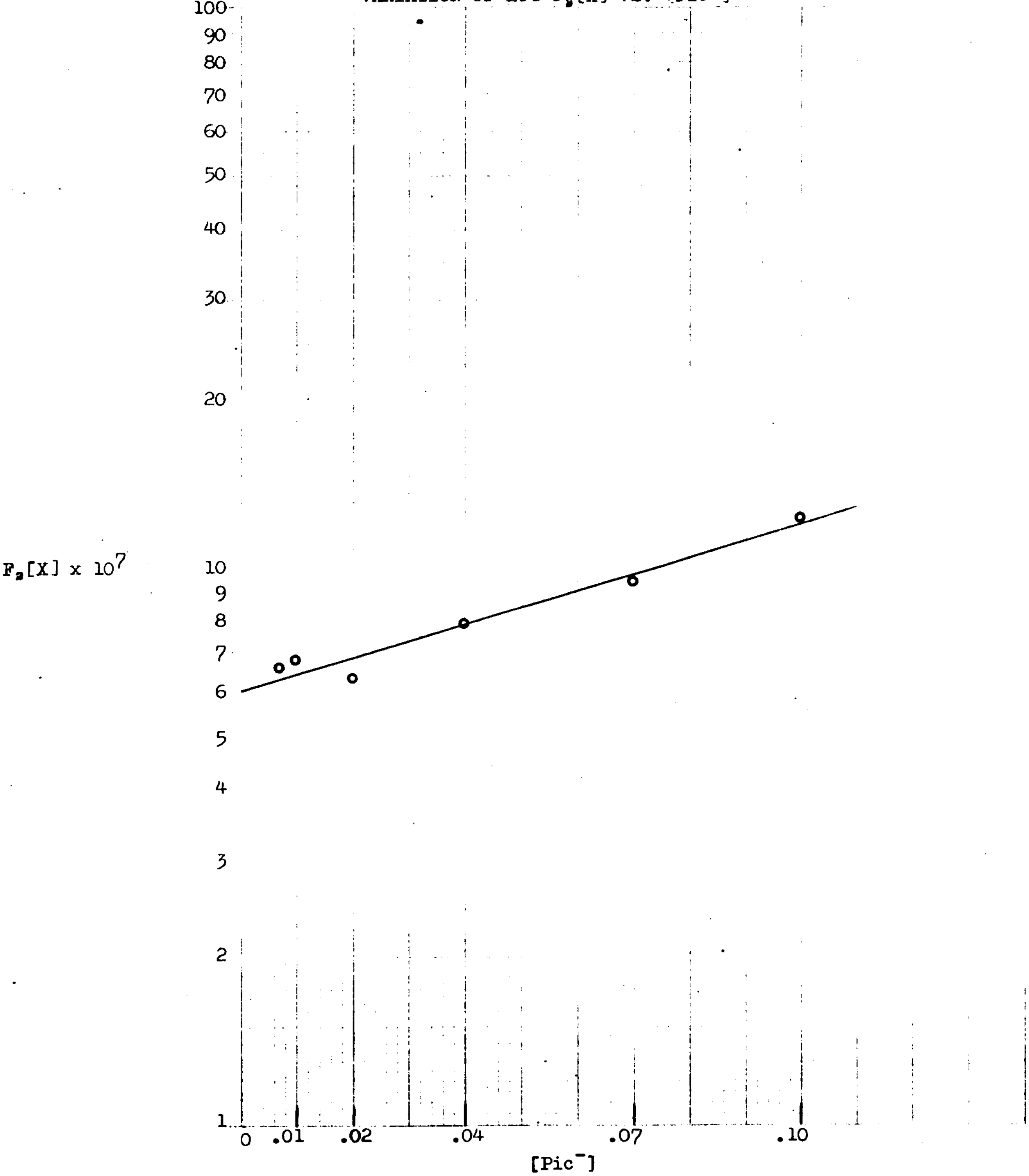
Pol. No.	$F_0[X]$	$F_1[X]$	$F_2[X]$	$F_3[X]$
1	7.678×10^1	7.578×10^4		
2	2.906×10^2	1.448×10^5		
3	6.835×10^2	2.275×10^5	6.584×10^7	
4	1.192×10^3	2.977×10^5	6.692×10^7	
5	3.490×10^3	4.984×10^5	6.692×10^7	9.887×10^8
6	7.130×10^3	7.129×10^5	6.829×10^7	8.286×10^8
7	2.596×10^4	1.298×10^6	6.340×10^7	1.702×10^8
8	1.284×10^5	3.211×10^6	7.953×10^7	4.882×10^8
9	4.663×10^5	6.661×10^6	9.473×10^7	4.962×10^8
10	1.227×10^6	1.227×10^7	1.224×10^8	6.237×10^8
11	6.457×10^6	3.229×10^7	1.613×10^8	5.064×10^8
12	4.663×10^7	1.166×10^8	2.914×10^8	5.784×10^8
13	1.694×10^8	2.824×10^8	4.705×10^8	6.842×10^8
14	4.333×10^8	5.417×10^8	6.770×10^8	7.713×10^8
15	9.866×10^8	9.866×10^8	9.866×10^8	9.627×10^8

$\beta_1 = 3 \times 10^4$; $\beta_2 = 6 \times 10^7$; $\beta_3 = 5 \times 10^8$

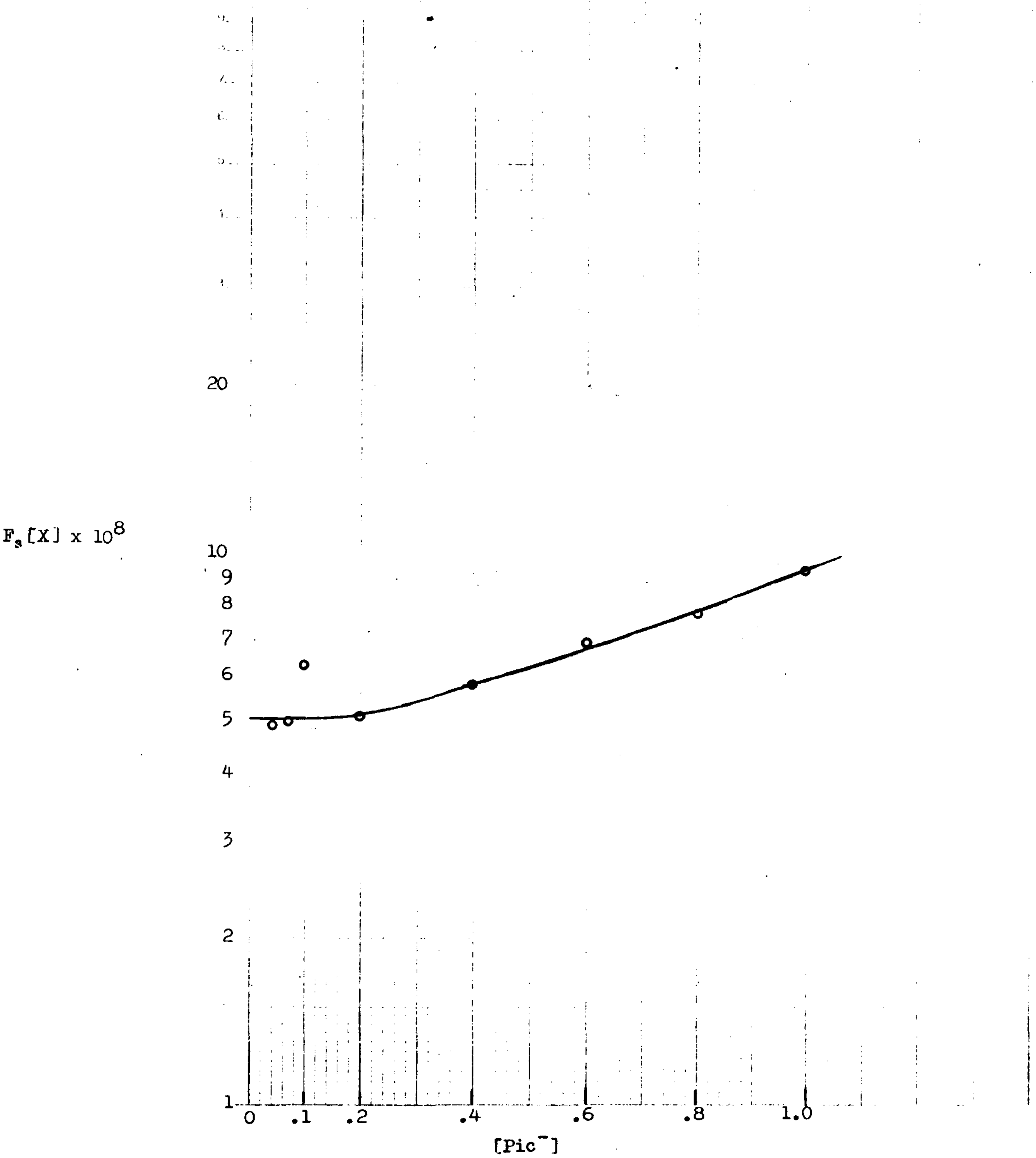
VARIATION OF LOG $F_1[X]$ VS. $[Pic^-]$



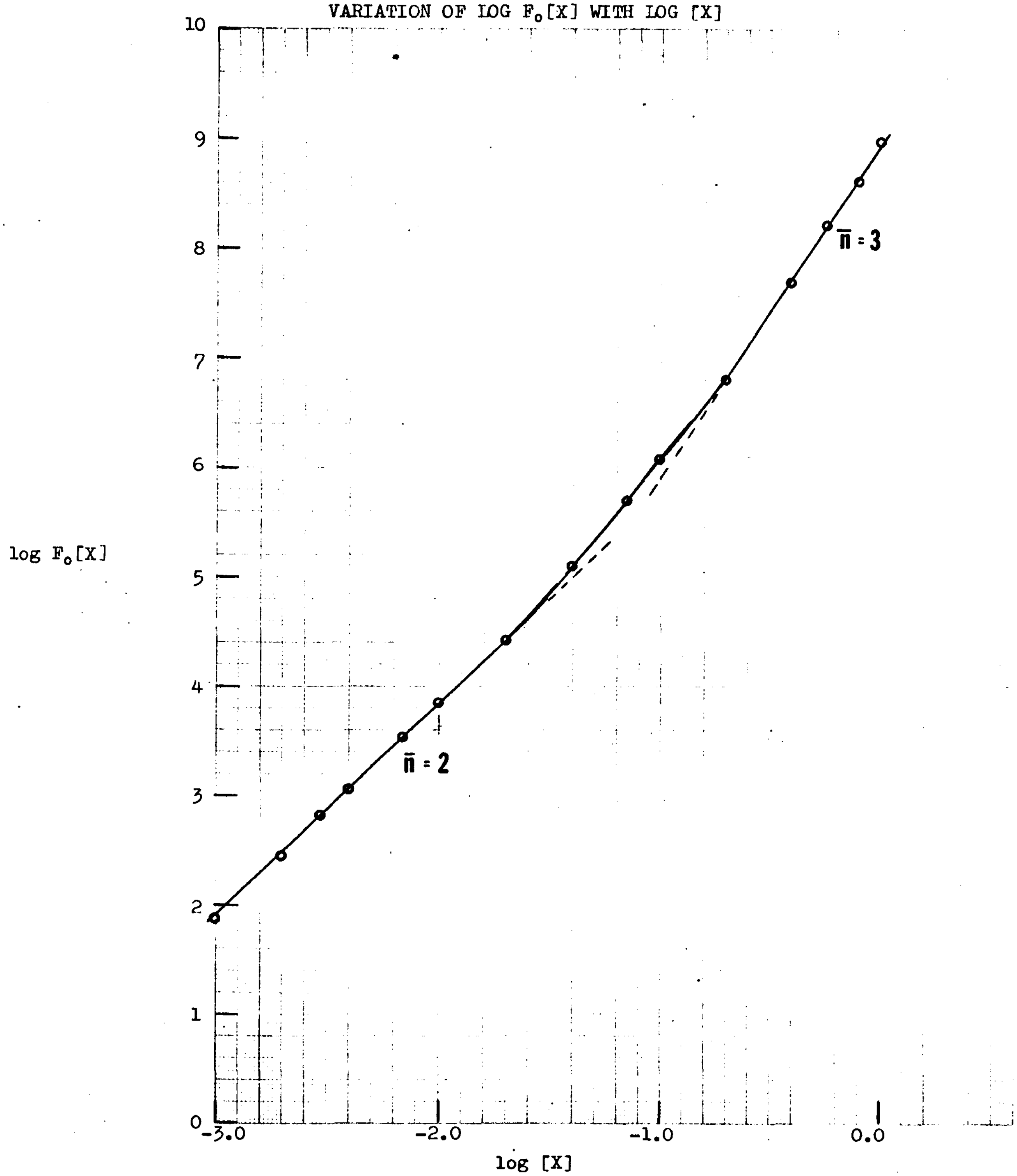
VARIATION OF LOG $F_2[X]$ VS. $[Pic^-]$



VARIATION OF LOG $F_s[X]$ VS. $[Pic^-]$



VARIATION OF LOG $F_o[X]$ WITH LOG [X]



is $\bar{n} < 2$; this indicates that there is no evidence of the presence of the complex $Pb(Pic)^+$ in the range of ligand concentrations studied; similarly, $\bar{n}$ is never greater than 3, showing that the highest-order complex is $Pb(Pic)_3^-$.

For the stepwise formation of the lead-picolinic acid chelates:

(1) $Pb^{++} + Pic^- \rightleftarrows Pb(Pic)^+$

$$K_1 = \frac{[Pb(Pic)^+]}{[Pb^{++}][Pic^-]} = \beta_1 = 3 \times 10^4; \quad \log K_1 = 4.5$$

(2) $Pb(Pic)^+ + Pic^- \rightleftarrows Pb(Pic)_2$

$$K_2 = \frac{[Pb(Pic)_2]}{[Pb(Pic)^+][Pic^-]} = \frac{\beta_2}{\beta_1} = \frac{6 \times 10^7}{3 \times 10^4} = 2 \times 10^3$$

$$\log K_2 = 3.3$$

(3) $Pb(Pic)_2 + Pic^- \rightleftarrows Pb(Pic)_3^-$

$$K_3 = \frac{[Pb(Pic)_3^-]}{[Pb(Pic)_2][Pic^-]} = \frac{\beta_3}{\beta_2} = \frac{5 \times 10^8}{6 \times 10^7} = 8$$

$$\log K_3 = 0.9$$

(b) Copper-Pyrazinoic Acid Chelates

As explained earlier, pyrazinoic acid dissociates as follows:

$$HA^{\pm} \rightleftarrows H^{+} + A^{-}; \quad pK_a = 2.92$$

where the symbol $HA^{\pm}$ has been used to represent the zwitterion which is the predominant species in strongly acidic solutions. The anion A^{-} can form two different chelates with copper:

$$Cu^{++} + A^{-} \rightleftarrows CuA^{+} \qquad K_1 = \frac{[CuA^{+}]}{[Cu^{++}][A^{-}]}$$

$$CuA^{+} + A^{-} \rightleftarrows CuA_2 \qquad K_2 = \frac{[CuA_2]}{[CuA^{+}][A^{-}]}$$

and the overall reaction is:

$$Cu^{++} + 2\,A^{-} \rightleftarrows CuA_2 \qquad \beta_2 = \frac{[CuA_2]}{[Cu^{++}][A^{-}]^2}$$

When polarograms of copper-pyrazinoic acid chelates are run, it is found that the reduction is irreversible, with a typical αn value of 1.7. Polarograms were run at a number of ligand concentrations; the data and results for these polarograms appear in the table on the following page.

DATA AND CALCULATIONS OF POLAROGRAMS OF COPPER—PYRAZINOIC ACID CHELATES (pH ≈ 7)

Pol. No.	$[Cu^{++}]$	$[A^-]$	log $[A^-]$	$E_{1/2}$	log I_M/I_C	log β_2 (Lingane method)
0	5.000×10^{-4}	0	----	+0.0367	0.00	
1	5.000×10^{-5}	1.000×10^{-3}	-3.000	-0.0617	0.06	9.39
2	5.000×10^{-5}	2.000×10^{-3}	-2.699	-0.0853	0.06	9.59
3	1.000×10^{-4}	4.000×10^{-3}	-2.398	-0.1069	0.04	9.71
4	2.000×10^{-4}	7.000×10^{-3}	-2.155	-0.1177	0.07	9.61
5	2.000×10^{-4}	1.000×10^{-2}	-2.000	-0.1299	0.08	9.72
6	5.000×10^{-4}	2.000×10^{-2}	-1.699	-0.1464	0.06	9.67
7	5.000×10^{-4}	4.000×10^{-2}	-1.398	-0.1666	0.06	9.75
8	5.000×10^{-4}	7.000×10^{-2}	-1.155	-0.1841	0.09	9.88
9	5.000×10^{-4}	1.000×10^{-1}	-1.000	-0.1906	0.08	9.78
10	5.000×10^{-4}	2.000×10^{-1}	-0.699	-0.2101	0.10	9.86

Average value of log β_2: 9.70

A plot of $E_{1/2}$ vs. log $[A^-]$ appears on the next page. Since this plot is linear, it indicates that a single complex is present in the entire concentration range studied. The formula of the complex can then be determined from the slope of the line:

$$\frac{\Delta E_{1/2}}{\Delta \log [A^-]} = -\frac{0.059}{\alpha n} p = -\frac{0.059}{1.7} p = -0.0347 p$$

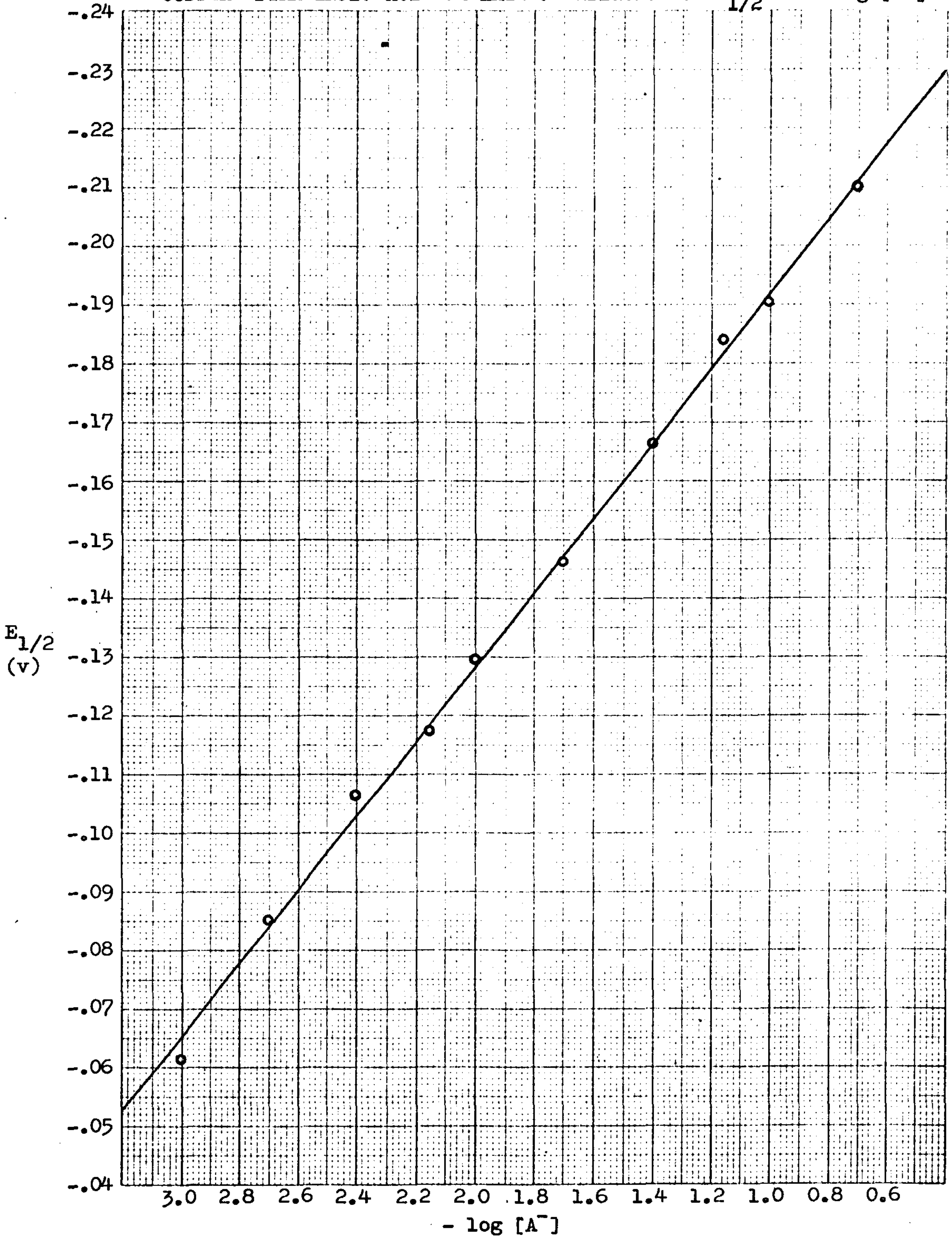
$$-0.063 = -0.0347 p$$

$$p = 1.82 \approx 2$$

Thus the formula of the complex is CuA_2.

It was not possible to use the DeFord-Hume method to obtain stepwise stability constants since only a single complex, CuA_2, was present in all ligand concentrations. Instead, the Lingane method was used to calculate the value of log β_2. The calculated values of log β_2 for each polarogram are shown in the table on page 104. The average value of log β_2 is 9.70, corresponding to $\beta_2 = 5.0 \times 10^9$. A sample calculation (using the data for polarogram #1) appears below.

$$\begin{aligned}\log \beta_2 &= \frac{E_{1/2(s)} - E_{1/2(c)}}{0.0295} + \log \frac{I_M}{I_C} - p \log [A^-] \\ &= \frac{(0.0367)-(-0.0617)}{0.0295} + 0.06 - (2)(-3.00) \\ &= 3.33 + 0.06 + 6.00 = 9.39\end{aligned}$$



COPPER—PYRAZINOIC ACID CHELATES: Variation of $E_{1/2}$ with log $[A^-]$

(c) Copper - Pyrazine-2,3-Dicarboxylic Acid Chelates

This acid dissociates in two steps, as follows:

$$H_2A \rightleftarrows H^+ + HA^- \qquad pK_{a_1} = 0.9$$

$$HA^- \rightleftarrows H^+ + A^= \qquad pK_{a_2} = 2.77$$

The anion $A^=$ then forms two different chelates with copper ions:

$$Cu^{++} + A^= \rightleftarrows CuA \qquad K_1 = \frac{[CuA]}{[Cu^{++}][A^=]}$$

$$CuA + A^= \rightleftarrows CuA_2 \qquad K_2 = \frac{[CuA_2{}^=]}{[CuA][A^=]}$$

and the overall reaction is:

$$Cu^{++} + 2\,A^= \rightleftarrows CuA_2{}^= \qquad \beta_2 = K_1K_2 = \frac{[CuA_2{}^=]}{[Cu^{++}][A^=]^2}$$

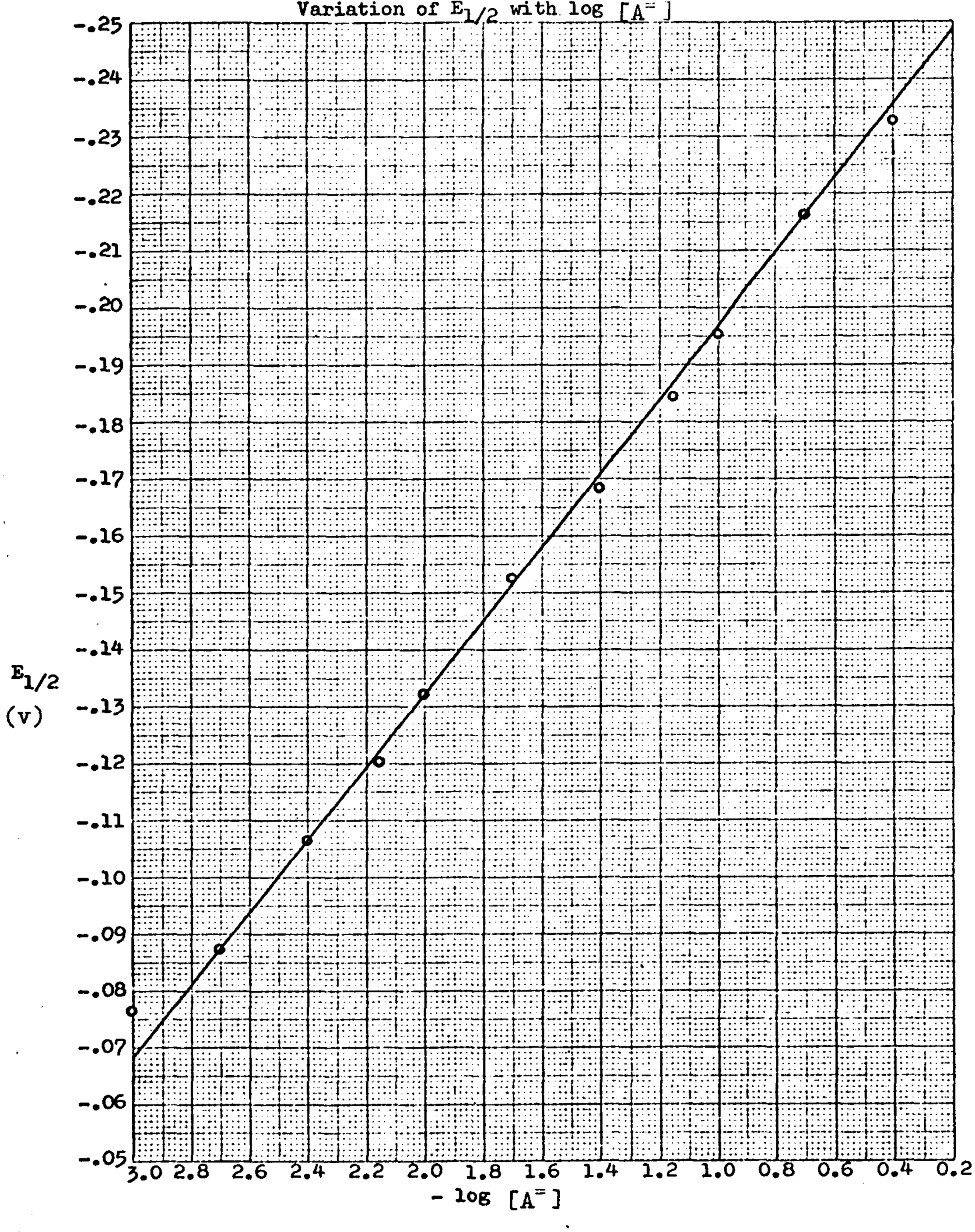
Data and results for polarograms of copper-pyrazine-2,3-dicarboxylic acid chelates appear on the next page, and a plot of $E_{1/2}$ vs. log $[A^=]$ is on page 109. The reduction waves of the chelates are strictly reversible only in the narrow range when the ligand concentration is between 0.004 and 0.01 M. At other concentrations, the reduction is irreversible with values of αn varying from 1.13 to 1.85.

DATA AND CALCULATIONS OF POLAROGRAMS OF COPPER—PYRAZINE-2,3-DICARBOXYLIC ACID CHELATES (pH ≈ 7)

Pol. No.	$[Cu^{++}]$	$[A^{=}]$	log $[A^{=}]$	$E_{1/2}$	log I_M/I_C	log β_2 (Lingane method)
0	5.000×10^{-4}	0	----	+0.0367	0.00	
1	5.000×10^{-5}	1.000×10^{-3}	-3.000	-0.0768	0.02	9.87
2	5.000×10^{-5}	2.000×10^{-3}	-2.699	-0.0876	0.03	9.65
3	1.000×10^{-4}	4.000×10^{-3}	-2.398	-0.1067	0.05	9.71
4	2.000×10^{-4}	7.000×10^{-3}	-2.155	-0.1206	0.05	9.69
5	2.000×10^{-4}	1.000×10^{-2}	-2.000	-0.1323	0.05	9.79
6	5.000×10^{-4}	2.000×10^{-2}	-1.699	-0.1529	0.06	9.88
7	5.000×10^{-4}	4.000×10^{-2}	-1.398	-0.1684	0.07	9.81
8	5.000×10^{-4}	7.000×10^{-2}	-1.155	-0.1849	0.07	9.88
9	5.000×10^{-4}	1.000×10^{-1}	-1.000	-0.1956	0.07	9.95
10	5.000×10^{-4}	2.000×10^{-1}	-0.699	-0.2165	0.10	10.08
11	5.000×10^{-4}	4.000×10^{-1}	-0.398	-0.2270	0.16	9.84

Average value of log β_2: 9.84

COPPER - PYRAZINE-2,3-DICARBOXYLIC ACID CHELATE
Variation of $E_{1/2}$ with log $[A^{=}]$



Using the plot of $E_{1/2}$ vs. log $[A^{=}]$, and a typical value of $\alpha n = 1.8$, the number of anions coordinated to the central copper ion is calculated as follows:

$$\frac{\Delta E_{1/2}}{\Delta \log [A^{=}]} = -\frac{0.059}{\alpha n} p = -\frac{0.059}{1.8} p = -0.0328 p$$

$$-0.065 = -0.0328 p$$

$$p = 1.98 \approx 2$$

Thus the complex $CuA_2^{=}$ predominates in the entire concentration range studied, and the Lingane method was used to obtain the value of log β_2. (See table, p. 108) The average value of log β_2 is 9.87, so that $\beta_2 = 7.4 \times 10^9$.

(d) Copper-Pyrimidine-4-Carboxylic Acid Chelates

The pK_a of this acid is 2.98. Data and results for various polarograms appear on the next page, and the plot of $E_{1/2}$ vs. log $[A^-]$ appears on page 113.

The reduction is reversible in polarograms #1 through #4 with $n = 2.0$; however, the other four polarograms showed varying degrees of irreversibility. In polarogram #6, $\alpha n = 1.50$, and the lowest value of αn (1.03) was obtained in polarogram #8.

Two different straight lines may be drawn in the plot of $E_{1/2}$ vs. log $[A^-]$ on page 113. Using only the first four polarograms in which reversible reduction waves with $n = 2$ were obtained, the slope equals -0.059. Thus:

$$\frac{\Delta E_{1/2}}{\Delta \log [A^-]} = -\frac{0.059}{n} p = -0.0295 p$$

$$-0.059 = -0.0295 p$$

$$p = 2.0$$

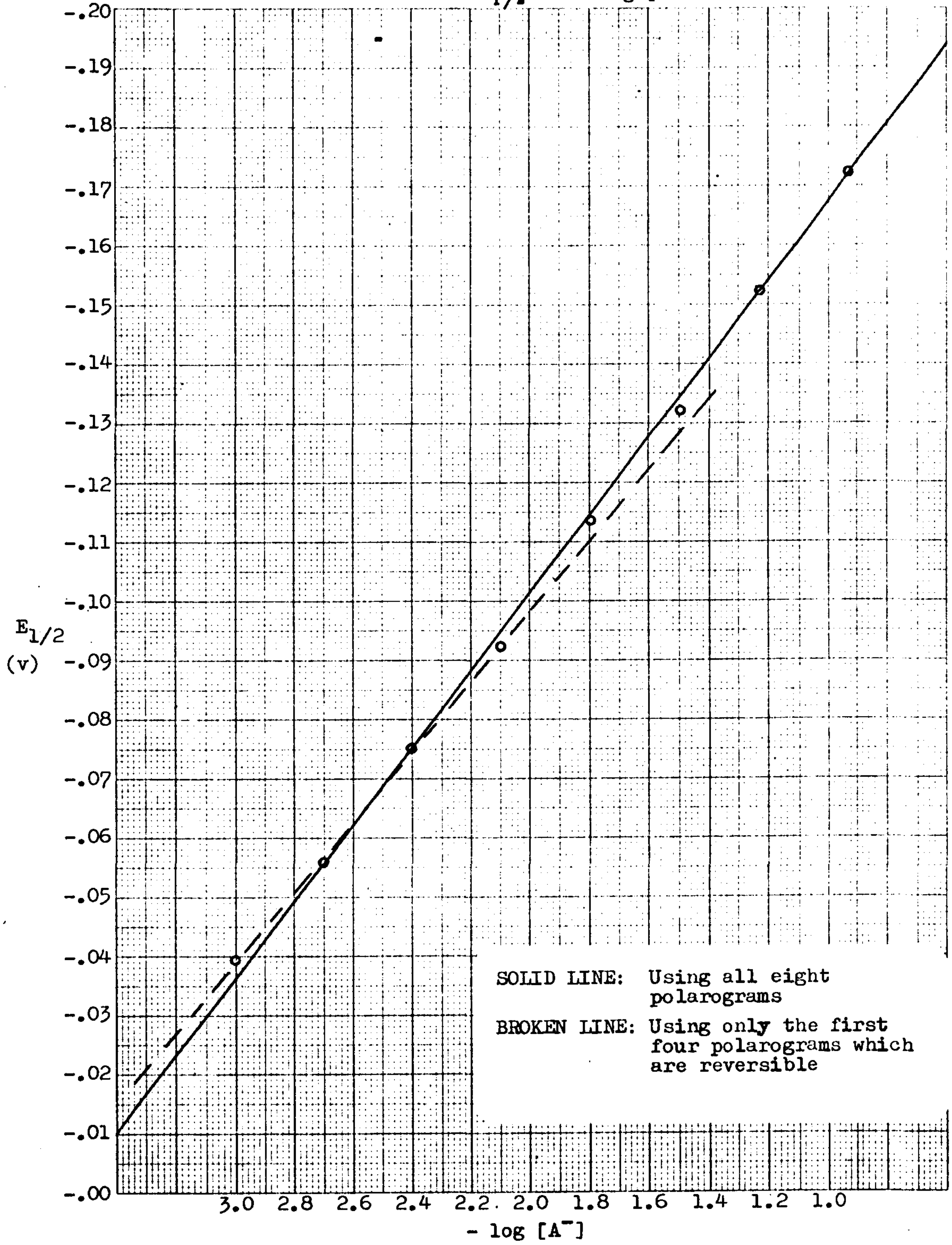
Using the other straight line (the solid line on page 113) which is the best straight line through all eight points, the same value of $p = 2$ is still obtained:

DATA AND CALCULATIONS OF POLAROGRAMS OF COPPER—PYRIMIDINE-4-CARBOXYLIC ACID CHELATES (pH ≈ 7)

Pol. No.	[Cu^{++}]	[A$^-$]	log [A$^-$]	$E_{1/2}$	log I_M/I_C	log β_2 (Lingane method)
0	5.000×10^{-4}	0	----	+0.0367	0.00	
1	5.000×10^{-5}	1.000×10^{-3}	-3.000	-0.0397	0.04	8.63
2	5.000×10^{-5}	2.000×10^{-3}	-2.699	-0.0560	0.08	8.62
3	1.000×10^{-4}	4.000×10^{-3}	-2.398	-0.0753	0.04	8.63
4	2.000×10^{-4}	8.000×10^{-3}	-2.097	-0.0923	0.04	8.61
5	2.000×10^{-4}	1.600×10^{-2}	-1.796	-0.1137	0.03	8.72
6	5.000×10^{-4}	3.200×10^{-2}	-1.495	-0.1322	0.04	8.75
7	5.000×10^{-4}	6.000×10^{-2}	-1.222	-0.1526	0.05	8.91
8	5.000×10^{-4}	1.200×10^{-1}	-0.921	-0.1726	0.04	8.98

Average value of log β_2: 8.73

COPPER—PYRIMIDINE-4-CARBOXYLIC ACID CHELATES
Variation of $E_{1/2}$ with log $[A^-]$



$$\frac{\Delta E_{1/2}}{\Delta \log [A^-]} = -\frac{0.059}{\alpha n} p = -\frac{0.059}{1.8} p = -0.0328 p$$

$$-0.065 = -0.0328 p$$

$$p = 1.98 \approx 2$$

The calculated values of log β_2 (Lingane method) appear in the table on page 112. The average value of log β_2 is 8.73, and β_2 equals 5.4×10^8.

(e) Copper—Pyridazine-3-Carboxylic Acid Chelates

The pK_a of pyridazine-3-carboxylic acid, 3.0, is essentially the same as that of other acids in this study. The table giving data and results for polarograms run at different ligand concentrations is on the next page, and the plot of $E_{1/2}$ vs. log $[A^-]$ appears on page 117.

All polarograms in this series exhibit irreversible behavior, with αn varying from 1.12 to 1.65. As in the case of pyrimidine-4-carboxylic acid, two different straight lines can be drawn in the $E_{1/2}$ vs. log $[A^-]$ plot. Using the broken line (and an approximate value of αn of 1.6), it is calculated that p equals 1.7, which is close to 2. Here again, the formula of the complex is CuA_2.

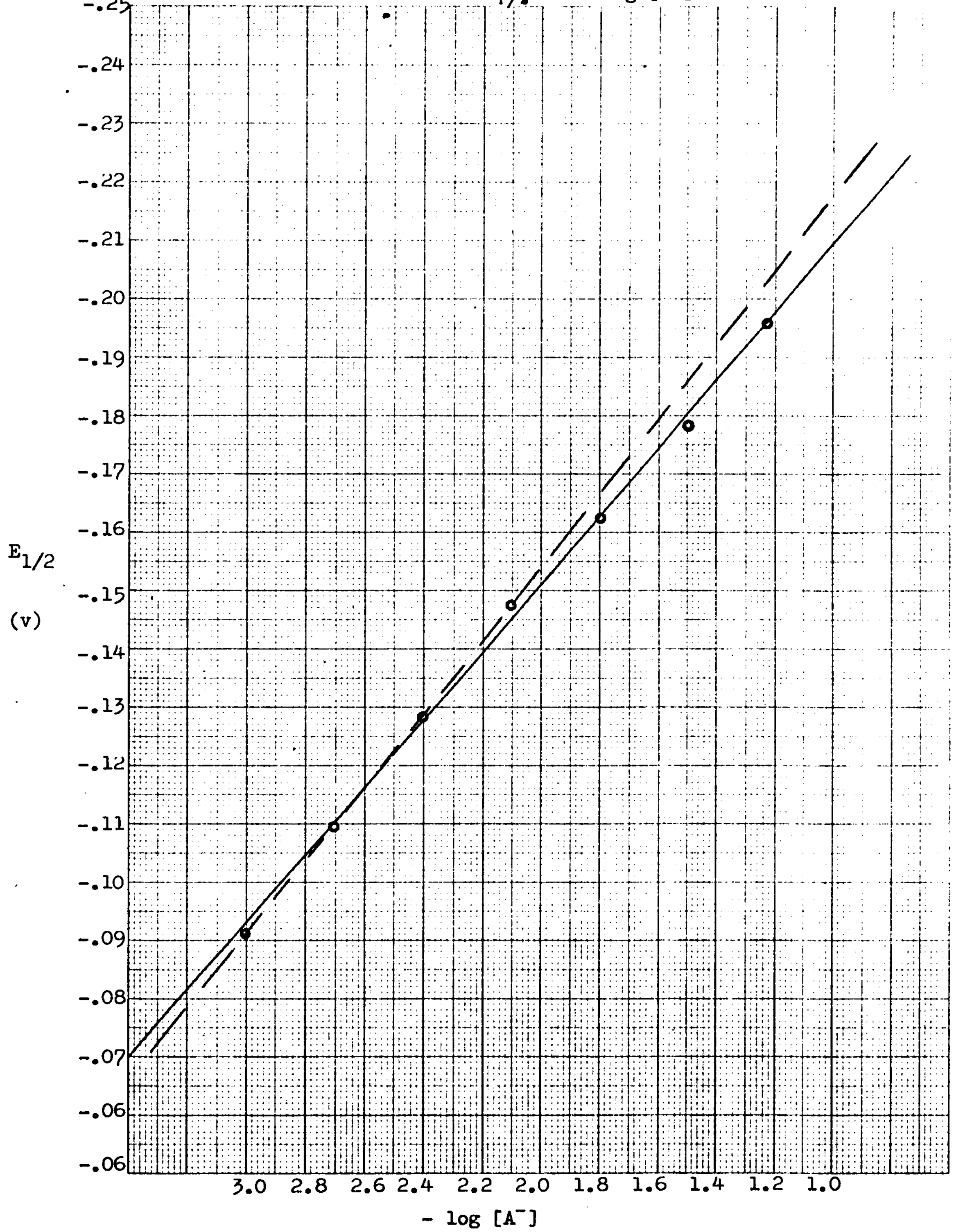
The values of log β_2 which are shown on the next page are significantly higher than the same values obtained with the other acids. The average value of log β_2 is 10.59, and $\beta_2 = 3.9 \times 10^{10}$.

DATA AND CALCULATIONS OF POLAROGRAMS OF COPPER—PYRIDAZINE-3-CARBOXYLIC ACID CHELATES (pH ≈ 7)

Pol. No.	$[Cu^{++}]$	$[A^-]$	log $[A^-]$	$E_{1/2}$	log I_M/I_C	log β_2 (Lingane method)
0	5.000×10^{-4}	0	----	+0.0367	0.00	
1	5.000×10^{-5}	1.000×10^{-3}	-3.000	-0.0911	0.12	10.45
2	5.000×10^{-5}	2.000×10^{-3}	-2.699	-0.1099	0.16	10.53
3	1.000×10^{-4}	4.000×10^{-3}	-2.398	-0.1285	0.17	10.58
4	2.000×10^{-4}	8.000×10^{-3}	-2.097	-0.1478	0.18	10.62
5	2.000×10^{-4}	1.600×10^{-2}	-1.796	-0.1626	0.41	10.76
6	5.000×10^{-4}	3.200×10^{-2}	-1.495	-0.1785	0.32	10.60
7	5.000×10^{-4}	6.000×10^{-2}	-1.222	-0.1960	0.24	10.57

Average value of log β_2: 10.59

COPPER-PYRIDAZINE-3-CARBOXYLIC ACID CHELATES
Variation of $E_{1/2}$ with log [A^-]



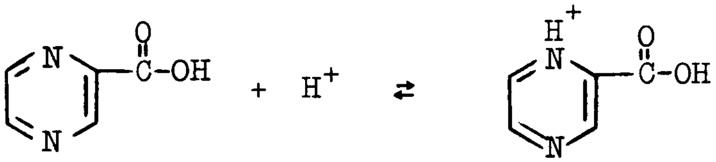
CHAPTER VI

DISCUSSION OF RESULTS

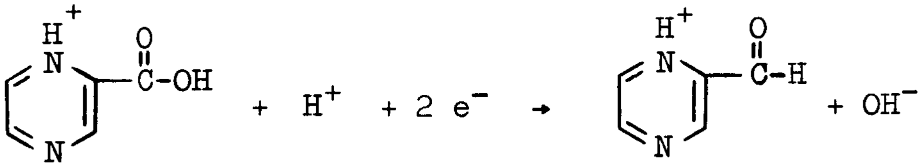
(a) Polarographic Reduction of the Chelating Agents

For all of the monocarboxylic acids, the reduction is usually either irreversible or quasi-reversible. Wave #1, the reduction wave of the free acid, has a half-wave potential which varies with the pH. In all cases, two electrons are involved in the reduction. The value of p, the number of hydrogen ions, is found to be equal to 2. This reduction can be explained as follows:

(1) Protonation of the ring nitrogen atom



(2) Reduction of this intermediate



This mechanism has been proposed for isonicotinic acid[72] and it is essentially the same as that given by Allen[73]. In order to prove this mechanism conclusively, it would be necessary to perform controlled potential electrolysis and identify the products using some method - but such a study was outside the scope of this present investigation.

Wave #2, the reduction wave of the anion, has a half-wave potential which is independent of the pH. This indicates that no hydrogen ions are involved in the reduction. When the reduction of pyrazinoic acid was studied, it was not clear whether wave #2 was a separate wave or whether it was merely a continuation of wave #1. This was due to the poor separation of the two waves; the same behavior was seen in the case of pyridazine-3-carboxylic acid. However, when the polarographic reduction of pyrimidine-4-carboxylic acid was studied, the two reduction waves were very clearly separated, making it possible to determine the value of pK' for this acid.

Since there is no special reason to believe that the reduction of pyrimidine-4-carboxylic acid is different from the reduction of the other two acids, it can be concluded that there are, in fact, two reduction waves for pyrazinoic acid and pyridazine-3-carboxylic acid, but that they overlap so that it is difficult to separate the two waves and determine their individual half-wave potentials and diffusion currents.

In the case of pyrazine-2,3-dicarboxylic acid, the value of p is uncertain due to the irregular values of αn which were obtained; however, it is fairly certain that n = 4 for wave #1. No attempt will be made to speculate on the reaction mechanism since the number of hydrogen ions involved in the reduction is not known.

(b) Polarographic Reduction of the Metal Chelates

(1) Lead-Picolinic Acid Chelates

This research was undertaken because Thomas was unable to prove the existence of the complex $Pb(Pic)_3^-$ using polarographic methods[31,33] while using potentiometric methods he was able to determine the stability constant of this complex[31,32]. This research by Thomas, together with a similar study of copper complexes, was published in 1955 and 1956.

In 1971, another article appeared which duplicated the work of Thomas. This article (by Movchan et. al.[74]) also discussed the polarographic reduction of copper and lead complexes of picolinic acid, and Movchan similarly was unable to prove the existence of $Pb(Pic)_3^-$ using the polarographic method. Moreover, he obtained the same value which Thomas did for log β_2.

At first, it was thought that it was merely a coincidence that Movchan repeated the work of Thomas; however, upon closer examination, it was found that Movchan did not do any original research in his article. All he did was copy tables #27, 28, 30, and 31 appearing in Thomas' Ph.D. Thesis[31], pages 60, 61, and 63, using a very slightly different format. Thus the "research" by Movchan, Savich, and Kudryavtsev can be dismissed without further comment.

It was found that Thomas was unable to obtain a value of β_3 using the polarographic method for the simple reason that his concentration range of $[Pic^-]$ was too small: no polarograms were run in which $[Pic^-] > 0.1$ M. Since the complex $Pb(Pic)_3^-$ predominates only after $[Pic^-] > 0.2$ M, it would not be expected for Thomas to obtain a value of β_3 using only low ligand concentrations.

Moreover, Thomas obtained erroneous values of K_2 and β_2 because of the fact that the wrong supporting electrolyte (1 M KNO_3) was used in determining the half-wave potential of the "simple" (uncomplexed) lead ion.

In order to use either the Lingane or DeFord-Hume methods, it is necessary to determine the value of $E_{1/2(s)}$ very accurately. It is essential that the supporting electrolyte contain no ions which are capable of forming complexes with the metal ion, since complex formation would cause the half-wave potential of the metal ion to be shifted to more negative potentials.

Thomas determined the value of the half-wave potential of the simple lead ion using 1 M $NaNO_3$, and he obtained a value of -0.407 v (vs. S.C.E.); apparently he was unaware of previous research on lead-nitrate complexes.

Hershenson, Smith, and Hume[64] studied these complexes using the DeFord-Hume method and they found that the half-wave potential of lead ions in 1 M $NaNO_3$ was -0.393 v, 21 mv more negative than the half-wave potential in 1 M $NaClO_4$ or $HClO_4$ (-0.372 v).

It was found in this investigation that the half-wave potential of lead ions in 1 M $NaNO_3$ using the modified calomel electrode was -0.3988 v, 23.3 mv more negative than the half-wave potential of lead ions in 1 M $NaClO_4$ (-0.3755 v).

In order to determine what values of stability constants Thomas would have obtained had he accounted for the complex formation of lead and nitrate ions, 0.022 v was added to the half-wave potential he obtained for the simple lead ion (-0.407 v), to give the corrected value of -0.385 v. This value for the half-wave potential was then used to calculate the stability constants using both the Lingane and DeFord-Hume methods.

Thomas' values for the stability constants (both original and recalculated) and the values obtained by others are given in the table on the following page.

STABILITY CONSTANTS OF LEAD-PICOLINIC ACID CHELATES

Reference	Method	Temp.	Medium	log K_1	log K_2	log β_2	log K_3	
Thomas[31,33] Movchan et. al.[74] (using data of Thomas)	Polarograpic	20°	1 M KNO_3	ORIGINAL VALUES:				
				----	----	7.30	----	(L)
				4.5	2.8	7.3	----	(D)
				RECALCULATED VALUES:				
				----	----	7.98	----	(L)
				4.5	3.45	7.95	----	(D)
Thomas[31,32]	Potentiometric	19±2°	μ = 0.008	4.97	3.82	8.79	2.81	
Suzuki[75]	Potentiometric	25°	μ = 0.1 (KNO_3)	4.82	3.06	7.88	----	
Anderegg[76]	Potentiometric	20°	μ = 0.1 ($NaNO_3$)	4.58	3.34	7.92	----	
Lumme[77]	Potentiometric	25°	$\mu \approx 0$	5.07	3.50	8.57	----	
This study	Polarographic	25°	μ=1.0 ($NaClO_4$)	----	----	7.86	1.06	(L)
				4.5	3.3	7.8	0.9	(D)

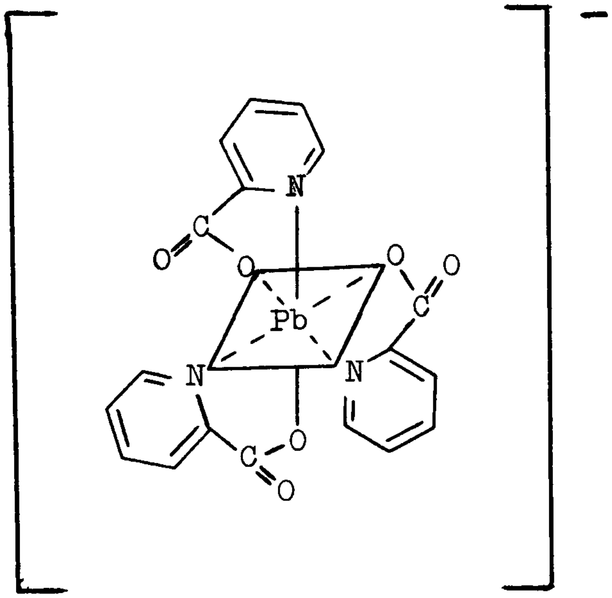
Note: (L) = Lingane method (D) = DeFord-Hume method

The values of K_1 and K_2 obtained in this study agree very well with the recalculated Thomas values and with the values other workers obtained using potentiometry. Thomas, in his potentiometric work, obtained a value of log K_3 (2.81) which none of the other investigators have been able to get using this method. In this study, it was found that log K_3 = 1.06 (Lingane method) and log K_3 = 0.9 (DeFord-Hume method). Both values are significantly less than Thomas' value of 2.8, and the reason for this difference is not clear.

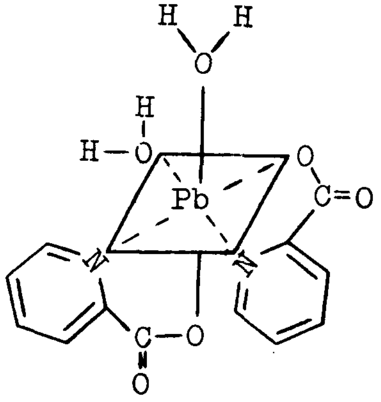
It is possible that in the DeFord-Hume method that a poor extrapolation in the plot of log $F_1[X]$ vs. $[X]$ might cause an inaccurate value of K_2 and K_3 to be obtained, but the magnitude of this possible error is much less than the actual difference in the log K_3 values obtained here (see the appendix). Furthermore, if an error was made in the DeFord-Hume method in obtaining the value of log K_3, the Lingane method should still yield the correct result. Here both methods yielded almost the same value of log K_3, indicating that no significant error was made in the DeFord-Hume method.

It is equally possible that the values of log K_3 obtained in this study are more accurate than the value obtained by Thomas in his potentiometric work. Inasmuch as all of the other workers who used potentiometry were unable to obtain a value of log K_3, it is possible that the difficulties inherent in this method preclude an accurate value of log K_3 from being obtained. Consequently it is an open question which of the two values is more accurate.

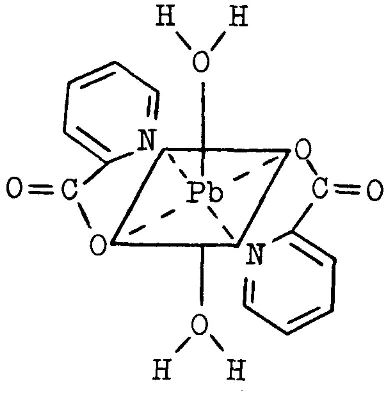
Inasmuch as the coordination number of lead is 6, and since picolinic acid is a bidentate ligand, the complex $Pb(Pic)_3^-$ would have the following structure:



The complex $Pb(Pic)_2$, which predominates if the ligand concentration is less than about 0.1 M, is more accurately written as $Pb(Pic)_2(H_2O)_2$. Here the two picolinate anions may be either <u>cis</u> or <u>trans</u> to each other:



CIS



TRANS

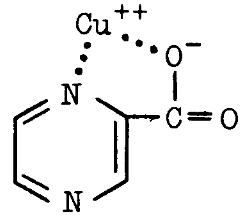
It has thus been shown that use of the polarographic method does, in fact, prove the existence of the three complexes $Pb(Pic)^+$, $Pb(Pic)_2$, and $Pb(Pic)_3^-$ in neutral solutions, and the results generally agree quite well with the values obtained using other methods.

If desired, the mixed ligand complexes present in mildly alkaline solutions at low ligand concentrations, such as $Pb(Pic)(OH)_2^-$, can be studied using the method of Schaap and McMasters[78] in order to determine the types of complexes which are present and to calculate their stability constants. Such calculations, however, are quite involved and this is outside the scope of the present study.

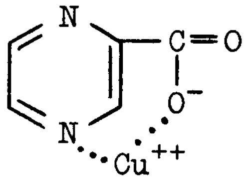
2. Copper-Pyrazinoic Acid Chelates

In the case of pyrazinoic acid, four different types of complexes may be formed:

(a) chelates using the oxygen of the carboxyl group and the adjacant ring nitrogen atom. Here the chelates would be formed exactly the same way as in the case of picolinic acid which was previously considered.



(b) chelates using the oxygen of the carboxyl group and the opposite ring nitrogen atom. Such six-member chelate rings cannot form due to steric factors.[23] For exactly the same reasons, nicotinic acid (pyridine-3-carboxylic acid) does not forr any chelates, and only simple complexes - i.e. (c) or (d) below - are formed.

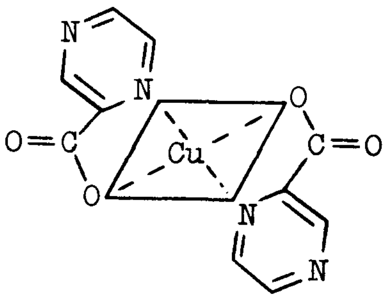


(c) simple complexes using only the oxygen atom of the carboxyl group; here four anions would be coordinated to each copper ion.

(d) simple complexes using only one of the ring nitrogen atoms. Here again four anions would be coordinated to each copper ion.

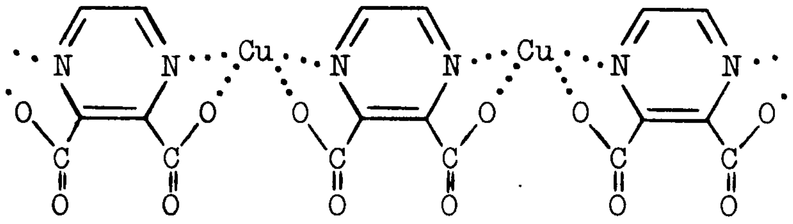
As a result, if the ligand to metal ratio is found to equal 2, this would indicate that type (a) complexes are formed, since type (b) is impossible in this case. However, if the ligand to metal ratio equals 4, this could mean that the complexes are either type (c) or type (d), and further research would be required to determine the actual structure.

Cu^{++}, a d^9 ion, normally has a coordination number of 4 and forms square planar complexes. In the case of copper—pyrazinoic acid chelates, the ligand to metal ratio is always equal to 2, indicating that type (a) chelates are formed, and that the structure is square planar:



3. Copper—Pyrazine-2,3-Dicarboxylic Acid Chelates

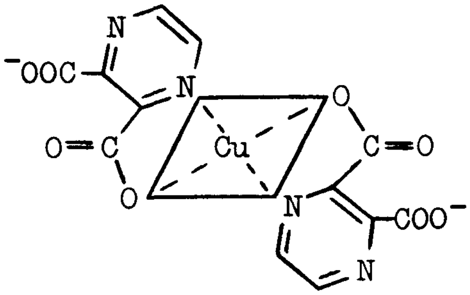
In the case of this dicarboxylic acid, in addition to the usual types of complexes - types (a) through (d) - a fifth type of structure, a polymer, is possible:



Such polymers with ligand to metal ratios of 1:1 have been found by various researchers.[15-21] Thus if the ligand to metal ratio obtained here is 1:1, it can be concluded that a polymeric structure is formed.

However, the ligand to metal ratio here clearly was 2:1, as had been the case with pyrazinoic acid. This might have been due to the fact that a large excess of ligand was present; had the ligand and metal been present in approximately the same concentrations (which would have made it impossible to determine the stability constants), it is possible that a polymer might have formed under such circumstances.

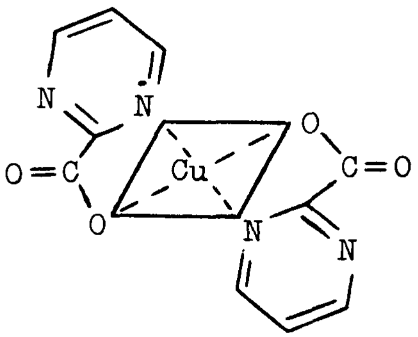
The structure of the chelate is therefore square planar:



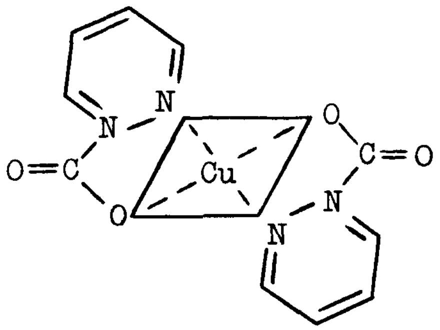
The value of log β_2 obtained here, 9.84, is only slightly larger than the value of log β_2 obtained for pyrazinoic acid (9.70). The fact that the two stability constants are almost the same is added proof that the structure of the chelates is the same in both cases.

4. Copper Chelates of Pyrimidine-4-Carboxylic Acid and Pyridazine-3-Carboxylic Acid

For both of these chelates, only five-membered rings - type (a) - can be formed. As expected, the ligand to metal ratio for both of these chelates equals 2, confirming the square planar structure:



Copper chelate of pyrimidine-4-carboxylic acid



Copper chelate of pyridazine-3-carboxylic acid

(c) Correlation between the structure of the chelating agents and the stability constants of the chelates

It is interesting to note the trend in the stability constants for the monocarboxylic acids. These values are summarized in the following table:

		COPPER CHELATE	
Chelating agent	pK_a	$\log \beta_2$	β_2
Picolinic acid*	5.32	15.37	2.3×10^{16}
Pyrazine-2-carboxylic acid	2.92	9.70	5.0×10^{9}
Pyrimidine-4-carboxylic acid ...	2.98	8.73	5.4×10^{8}
Pyridazine-3-carboxylic acid ...	3.0	10.59	3.9×10^{10}

* - For comparison purposes. Thomas' data for $\log \beta_2$ was used here.

Thus the values of pK_a of the three diazine carboxylic acids are essentially the same, but in spite of this, there is a significant variation in the resulting stability constants.

Considerable research has been performed in order to correlate trends in stability constants with a number of variables. It is frequently found that the chelate stability constants are a function of the pK_a of the chelating agents. For example, for a series of monodentate heterocyclic amines which coordinate with Ag^+, equations of the form

$$pK_{AgAm_2} = A \cdot pK_{H^+} + B$$

can be written, where A and B are constants, pK_{AgAm_2} is the logarithm of the stability constant of the silver amine chelate, and pK_{H^+} is the pK_a value of the amine.[79]

In comparing the copper-picolinic acid chelate with the copper-pyrazinoic acid chelate, it would be reasonable to state that the decreased stability of the latter chelate is due to the fact that pyrazinoic acid is a much stronger acid, in accordance with the general rule given above.

However, it is impossible to use this reason to account for the trend in the stability constants for the pyrazine, pyrimidine, and pyridazine carboxylic acid chelates since all of the chelating agents have essentially the same value of pK_a.

A study was made to determine what factors affect the stability constants of a series of heterocyclic carboxylic acids, all of which were capable of forming a 5-member chelate ring; one of the acids studied was pyrazine-2,3-dicarboxylic acid.[80] In this case, it was found that there was no actual correlation between the tendency of complex formation and the dissociation constants of the chelating agents. It was concluded that the aromatic character of the heterocyclic ring system had the greatest influence on the chelate stability, rather than the basicity of the chelating agent.

A similar conclusion was reached in two studies involving silver complexes with aromatic and heterocyclic nitrogen bases.[81,82] It was found that the stability of the chelate is directly related to the π electron density of the nitrogen atom.

Such a conclusion would be reasonable in this study also, in view of the fact that the dissociation constants of the three acids are essentially the same. While various people have determined electron densities for pyrazine, pyrimidine, and pyridine, no such work has been done for the carboxylic acids so far. This type of research must be done first before any attempt is made to correlate stability constants with electron densities. In any event, since the pK_a values of the three monocarboxylic acids are almost the same, it is clear that the variation in the chelate stability constants is primarily due to differences in the heterocyclic ring system, as had been the case with other complexes.

(d) Possible further areas of investigation

One technique which would be helpful to obtain information on electron densities is photoelectron spectroscopy. Although it was not possible to run photoelectron spectra of the chelating agents or the metal chelates as part of this work, this information would be very valuable in determining whether or not there is a good correlation between the eletron density of the ring nitrogen atom and the chelate stability constant.

The polarographic method of determining chelate stability constants is best applied to metal ions which are reduced reversibly at the D.M.E., and since it is essential that the reduction wave of the chelating agent and the metal chelate not overlap each other, the number of possible metal ions which can be studied is quite small. For example, an attempt was made to run polarograms of lead chelates of pyrazinoic acid but it was found that the reduction wave of the complex overlapped with the reduction wave of the pyrazinoic acid, making the experiment impossible. It is possible, however, to use copper as an indicator metal ion to study lead complexes of pyrazinoic acid using the technique developed by Ringbom and Eriksson.[83] Similarly, chelates of other metal ions with pyrazinoic acid could be studied using the indicator ion method, and the other diazine carboxylic acids could be studied at the same time.

Other techniques, in addition to polarography, can be used to study chelates of pyrazine, pyrimidine, and pyridazine carboxylic acids. For example, potentiometric methods could be used to obtain information on the structure and stability constants of the chelates, and those results could be compared with those obtained using polarographic methods. In addition, spectrophotometric techniques could be used to study certain of the chelates - such as the red-brown ferrous chelates of pyrazinoic acid.

Turquoise blue crystals of the copper chelate of pyrazinoic acid precipitate out of solution when concentrated solutions of pyrazinoic acid (as the sodium salt) and copper ions are mixed. Information on the crystal structure of the chelates could be obtained using various methods.

Additional information on the polarographic reduction of the chelating agents could be obtained by the use of such methods as a.c. polarography and controlled potential coulometry. It may be possible to isolate reaction intermediates using such techniques.

Finally, mixed ligand complexes such as $Pb(Pic)_2(OH)^-$ could be studied using the polarographic techniques developed by Schaap and McMasters.[78]

Footnotes - Chapter VI

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APPENDIX

ERROR ANALYSIS - DETERMINATION OF THE STABILITY CONSTANTS

(1) Lingane Method

Since the basic equation in this method is:

$$\log \beta_n = \frac{E_{1/2(s)} - E_{1/2(c)}}{0.0295} + \log \frac{I_M}{I_C} - p \log [X]$$

it follows that the possible error in log β_n is equal to the sum of the possible errors in each of the three terms. In the first term, an estimate of the error in $E_{1/2(s)}$ is ± 0.5 mv, and for $E_{1/2(c)}$ it is ± 1.5 mv. The maximum possible error when the difference is taken is therefore ± 2 mv, resulting in an error of $\pm (0.002 / 0.0295)$ or ± 0.07 in the first term.

For the second term, the maximum error of $\log (I_M/I_C)$ is about ± 0.03, and there is no error associated with the third term since both p and log [X] are known quantities. Thus the maximum error in log β_n is equal to $\pm (0.07 + 0.03)$, or ± 0.10. If $\log \beta_n = 8$, this 0.1 error in log β_n corresponds roughly to a 20% error in β_n itself, so that β_n would then be equal to $(1.0 \pm 0.2) \times 10^8$.

As indicated on page 124, Thomas obtained a value of 2.8 for log β_3, while the values obtained here were 1.06

(Lingane method) and 0.9 (DeFord-Hume method). The results of this error analysis show that the discrepancy between Thomas' value (obtained using potentiometry) and the values obtained here cannot arise due to such factors as poor extrapolations or random errors in $E_{1/2}$. The difference must be due to other factors - such as difficulties inherent in the potentiometric method which may make it impossible to obtain an accurate value of log β_3.

(2) DeFord-Hume Method

The same errors discussed earlier - i.e. those involving the determination of $E_{1/2(s)}$, $E_{1/2(c)}$, and log (I_M/I_C) - will also cause the calculated values of β_1, β_2, etc. in the DeFord-Hume method to differ from the actual values. In addition, there is a special problem in the DeFord-Hume method which makes it very difficult to get accurate values of some of the stability constants; this results from the necessity of extrapolating various curves to $[X] = 0$ in order to get the values of the stability constants.

This problem can clearly be seen in the plot of $F_1[X]$ vs. $[X]$ for the lead-picolinic acid chelates which appears on page 98. In this plot, the value of β_1 obtained from the extrapolation could be anywhere from (1×10^4) to (4×10^4); the value actually used in this study was

3×10^4. Since the value of β_1 obtained here is used in the calculation of $F_2[X]$, it becomes necessary to see whether or not a poor extrapolation in the plot of $F_1[X]$ vs. $[X]$ will cause an error in the other stability constants.

Seven values of $F_1[X]$ were used: 1.0×10^4, 1.5×10^4, 2.0×10^4, 2.5×10^4, 3.0×10^4, 3.5×10^4, and 4.0×10^4. In each case, values of $F_2[X]$ were calculated for polarograms #1 through #10 - i.e. $[X]$ varying from 0.001 to 0.100 - and individual plots of $F_2[X]$ vs. $[X]$ were made for each of the seven cases. It was found that the exact same value of $F_2[X]$ (6×10^7) was obtained in all seven trials. As a result, an error in the extrapolation of the plots of $F_1[X]$ vs. $[X]$ will affect only the value of β_1 and will not cause any errors in β_2 or β_3.

Similarly, an error in the extrapolation in the plot of $F_2[X]$ vs. $[X]$ (causing an inaccurate value of β_2 to be obtained) may, or may not, affect the resulting values of β_3. In the plot of $F_2[X]$ vs. $[X]$ for the lead-picolinic acid chelates (which appears on page 99), the range of possible values of β_2 is 5×10^7 to 7×10^7.

Five values of $F_2[X]$ were used: 5.0×10^7, 5.5×10^7, 6.0×10^7, 6.5×10^7, and 7.0×10^7. In each case, values of $F_3[X]$ were calculated for polarograms #8 through #15 - i.e. $[X]$ varying from 0.040 to 1.000 - and individual plots of $F_3[X]$ vs. $[X]$ were made for each of the five cases. The results were as follows:

Value of $F_2[X]$ used	Value of β_3 obtained
5.0×10^7	$(4.5 \text{ to } 6) \times 10^8$
5.5×10^7	$(4.6 \text{ to } 5.5) \times 10^8$
6.0×10^7	$(4.4 \times 5) \times 10^8$
6.5×10^7	4×10^8
7.0×10^7	4×10^8

In this case, the value of $F_2[X]$ used had a slight effect on the value of β_3 obtained from the graph. Taking into account this source of error and the other errors discussed previously, the value of β_3 could best be expressed as $(5 \pm 2) \times 10^8$. This represents a 40% error in the value of β_3.