

1975

Further refinements in the value of the faraday

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Further refinements in the value of the faraday

by

William Frederick Koch

**A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY**

**Department: Chemistry
Major: Analytical Chemistry**

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For the Graduate College

**Iowa State University
Ames, Iowa**

1975

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I. INTRODUCTION

A. Background

The laws governing the relationship of electric current, time and the amount of chemical change effected by the electric current, discovered by Michael Faraday in 1833 (15), are expressed in modern terminology by the algebraic formula

$$G = \frac{1}{F} It \frac{\text{Mol. Wt.}}{n} \quad (1)$$

G being the weight of chemical undergoing change, in grams;

I being the current, in amperes;

t being the time, in seconds;

Mol. wt./n being the electrochemical equivalent weight, that is

the molecular weight divided by the number of electrons involved in the change (change in valence at the electrode); this term is currently commonly referred to by physicists as a mole (one gram-molecular weight), a useage sharply differing from that of chemists.

The proportionality factor, F, is appropriately called the "faraday".

The work described in the present thesis deals with the measurements leading to a numerical value of this constant.

It is common in physical science that the evaluation of a proportionality constant is involved intimately with the establishment of the units of measurement of the physical quantities involved. In the instance of electricity, the ampere, the unit of measurement of electric current, and the faraday are so interrelated. Given that the Faraday

laws of electrolysis are valid, the ampere could be and was defined in terms of the chemical change effected by the current, specifically (and with what proved to be misleading convenience) in terms of the weight of metallic silver deposited from a solution of silver nitrate. The inevitable improvements which were made subsequent to the original experimental work in measuring the amount of silver undergoing change with a given amount of current, that is, improvements in the design and operation of the so-called "silver coulometer" (coulomb = 1 ampere flowing for one second), made it necessary to change either the ampere or the faraday at intervals. Wisely, because of the ramifications of electricity into numerous other branches of science and technology, the definition of the ampere was held constant and the value of the faraday subjected to correction. Thus, at the turn of the century, the ampere was defined by (21, 40, 54):

The international ampere is defined as that steady or unvarying current which when passed through a solution of silver nitrate in water deposits 1.11800 milligrams of silver per second.

The quantity 1.11800 mg. of silver was obtained using the atomic weight of silver then in use. A history of the evolution of the units of electricity is given in the monograph of Hamer (21).

In practice, current is measured by measuring the potential drop over a known resistance through which the current is passing (Ohm's law: $I = E/R$) and each of the principal countries maintains in a national laboratory standards of potential and resistance. In the United States these standards are maintained at the National Bureau of Standards,

Washington, D. C. Standards of electrical potential (saturated Weston cells) and resistance (coils of a wire having little change in resistance with temperature) are easily constructed and maintained with high reproducibility and accuracy; in contrast the measurement of current by the chemical change effected is time consuming, inconvenient and very difficult to carry out with precision and accuracy. In practice then the "NBS" or "United States legal" ampere is defined by the ratio of the NBS volt to the NBS ohm.

Methods of measuring electrical quantities in centimeter-gram-second electromagnetic units evolved slowly but ultimately reached such a stage of perfection that it became possible, in 1948, to change from the various national ("international mean") units to absolute units. The goal in such work is to define the units in such manner and terms that anyone, anywhere, willing to make the effort can reproduce the unit without comparison with an arbitrary standard. Thus, the unit of length is defined in terms of the wavelength of the orange line of the spectrum of krypton. The factor for converting the NBS ampere to the absolute ampere has undergone several changes since 1948, the latest change resulting from the shift of the standard of electrical potential from the bank of saturated Weston cells at the National Bureau of Standards to the Josephson junction (1, 16). The conversion factor in effect at present, 1975, is $\text{NBS ampere} = A_{\text{BI69}} = 1.000,000,3 \text{ absolute ampere}$ (8, p. 715, Table 32-1, col. 1). For the details of the recent changes in this quantity, the relationships of the present NBS ampere

(now designated A_{BI69}) to the amperes of the other national laboratories, see the work of Cohen and Taylor (8, p. 697 and following pages).

B. The Deposition-of-Silver and the Dissolution-of-Silver Coulometers

The silver coulometer, on which the early definition of the ampere was based and later, after the definition of the ampere had been fixed, the value of the faraday was determined, depends on measuring the weight of silver deposited at a cathode from a water solution of silver nitrate by a measured current flowing for a measured time. The silver coulometer is subject to a serious error caused by the inclusion of solvent within the crystals of silver deposited. Although some fourteen papers were published between 1884 and 1916 on this problem, a satisfactory answer was never obtained and the silver coulometer was abandoned. The subject was reviewed in 1953 by Scott (45) and again in 1968 by Hamer (20). Other coulometers were devised but none proved satisfactory; these have been discussed critically by Hamer (20) and the literature has been reviewed by Hoyle (23, p. 4).

The work on which the current (1975) value of the faraday is based is the anodic dissolution-of-silver experiment of Craig, Hoffman, Law and Hamer (10). In the dissolution-of-silver coulometer, highly purified, metallic silver was fused in a vacuum (in some experiments in hydrogen) and the silver bar subjected to anodic attack in an electrolyte containing perchloric acid and some silver perchlorate. From the loss in weight of the silver, corrected for the impurities present as determined spectrographically, and the coulombs passed was calculated the electrochemical equivalent weight of silver, $1.117,972 \pm 0.000,019$

milligrams per coulomb (a coulomb is equal to one ampere flowing for one second). The question of the possible separation of the isotopes of silver (^{107}Ag and ^{109}Ag) during the purification was settled by a determination of the abundance ratio of the isotopes in silver from various sources and in the silver of Craig, Hoffman, Law and Hamer; the measurements were made by Shields, Craig and Dibeler (46) and Shields, Garner and Dibeler (47).

The value of the faraday calculated from the Craig, Hoffman, Law and Hamer work, which was reported in 1960 (10), became the accepted value and has remained so since, although repeatedly modified slightly by recalculation (Committee of the National Academy of Science-National Research Council, 1963 (2); Hamer, 1968 (20); Taylor, Parker and Langenberg, 1969 (51); Cohen and Taylor, 1973 (8)). The recalculations were made to correct: (a) for the change in the basis of the atomic weight scale to carbon-12, (b) for changes in the atomic weight of silver, (c) for changes in the coulomb resulting from various shifts and adjustments consequent to shifting from the NBS standards to the absolute standards, and (d) for an extensive reassessment and statistical treatment of the random and systematic errors in the experimental work. The current value is that calculated by Cohen and Taylor (8, pp. 679, 718), which reflects the shift during 1972 of the standard of potential to the Josephson junction:

$$F = 96,486.72(0.66)(6.8 \text{ ppm}) \quad \text{NBS coulombs per g.-eq. wt.}$$

In this expression, following the modern practice of physicists, the number in the first set of parentheses is a measure of the uncertainty obtained by combining the random and systematic errors and expressed as

the standard deviation of the mean in coulombs per gram-equivalent weight and the number in the second set is the same quantity expressed as a relative value in parts per million.

This experimental value for the faraday, based on the work of Craig, Hoffman, Law and Hamer (10), was declared suspect by Taylor, Parker and Langenberg (51) and flatly rejected by Cohen and Taylor (8), a matter which is discussed below. Although Taylor, Parker and Langenberg painstakingly reworked the results and applied a more sophisticated statistical treatment to the random and systematic errors in the Craig, Hoffman, Law and Hamer work, and Cohen and Taylor considered it again, it remained for Hoyle (23) to point out the most likely source of error.

In the anodic attack of metallic silver, the silver is not dissolved uniformly; rather, pits develop and undercutting proceeds to the point where particles of silver fall from the electrode. In the Craig, Hoffman, Law and Hamer work, the silver which flaked from the electrode amounted to two to twenty-five per cent of the silver dissolved electrolytically. Craig, Hoffman, Law and Hamer say relatively little about this, but to a chemist trained in gravimetric analysis and experienced with the problems of the recovery, transfer, filtration and drying of solid materials with a loss less than 30 $\mu\text{g.}$, it is a most serious matter. Hoyle (23) has discussed this at some length.

C. The Fundamental Constants and the Value of the Faraday

From the standpoint of the relative errors tolerated, chemical technology is conducted rather crudely; measurements and results to within 1 part in 1000 are almost invariably acceptable. The analytical

chemist is thus seldom called on to exert himself to the 1 in 10,000 level; and in the entire history of chemistry only a handful, possibly fifteen or twenty, analyses have been conducted such that the uncertainty could be considered to be as low as a few parts in 100,000. Putting it bluntly, for a value of the faraday good to 1 in 100,000 the chemist could not care less. It is quite the reverse with the physicist. For him, an accurate value for the faraday and a knowledge of the precision of the measurement and of the error inherent to it is a vital concern.

The faraday is involved not only in all phases of electrochemistry but appears in numerous ways in the thermodynamic expressions of the laws governing the behavior of solutions and in many important laws of physics. Of particular importance are the numerous laws in the area of quantum electrodynamics in which the faraday appears in many surprising places. The square of the velocity of light divided by the faraday is the factor for converting atomic mass units to electron volts, for example. Over the last two generations, improvements in the measurement of the various physical quantities, reflected in the values of some fifty fundamental constants, have resulted in correction and refinement of theory, and this in turn has demanded more accurate measurements. This cyclic interplay, closely tied up, of course, with the conversion from the various arbitrary to absolute standards, goes on with increasing precision, and complexity, and scope. Currently (1975), the faraday is one of the least accurately known of the important fundamental constants.

The particular group of workers interested in the interrelationships of the fundamental constants, precision measurements and theory

are led by B. N. Taylor, W. H. Parker, D. N. Langenberg and E. R. Cohen. Their work has been embodied in various popular publications, in journal articles, and in books reporting the papers presented at the periodic conferences held by the workers in the field. Of the popular accounts, the articles by Langenberg, Scalapino and Taylor (29), Taylor, Langenberg and Parker (50) are of particular interest, both to the layman and to the scientist unaware of the recent developments and the current excitement in the field. The main scientific papers are two exhaustive, least-squares treatments of the fundamental constants: Taylor, Parker and Langenberg (51) in 1969, and Cohen and Taylor (8) in 1973. The papers given at a major conference, held at the National Bureau of Standards in 1970, have been published in book form (37). Papers given at a similar meeting, The Fifth International Conference on Atomic Masses and Fundamental Constants, held in Paris June 2-6, 1975, are due for publication late in 1975 (38).

In the course of their 125-page, definitive, least-squares treatment of the fundamental physical constants, Taylor, Parker and Langenberg (51, pp. 704, 705, 717, 718, 723-725) reviewed in minute detail the experimental work of Craig, Hoffman, Law and Hamer (10), on which the current value of the faraday is based, and examined minutely the theory and the precision and accuracy with which certain other physical measurements were made from which a value for the faraday can be calculated. The difference between the experimental and calculated values was so great that Taylor, Parker and Langenberg issued repeated calls for further experimental work both on the direct measurement of the faraday

and on the physical measurements with particular attention to the resolution of certain inconsistencies among the latter.

By the time the continuation study of the least-squares adjustment of the constants was prepared in 1973, Cohen and Taylor (8, pp. 679, 705, 717), improvements in the physical measurements involved had been made, notably in the measurement of the gyromagnetic ratio of the proton (γ_p) and in the ratio of the magnetic moment of the proton to the nuclear magneton (μ_p/μ_N). The 1973 evaluation of the direct, experimental value for the faraday drew on the 1969 review of the Craig, Hoffman, Law and Hamer work but in addition included two other recent evaluations of the faraday, which had not been considered in the 1969 adjustment. These were the evaluations of the faraday by the high-precision, coulometric titrations of benzoic acid and of oxalic acid dihydrate by Marinenko and (J. K.) Taylor (33). Again the work was subject to critical review, a new assessment of the systematic errors made, and a least-squares weighting of the results made. Based on the 1972 NBS electrical units (by this time brought into identity with the units of the Bureau International des Poids et Mesures and designated by the subscripts BI69 and corrected for the now known steady change of the potential of the bank of saturated Weston cells at the National Bureau of Standards), the values for the faraday, recalculated experimental values and indirect calculated values, are those given in Table 1.

The difference between the experimental and the calculated values, 22 ppm, is ten times the estimated uncertainty in the calculated value. Reluctantly, Cohen and Taylor came to the conclusion that, although the agreement between the Craig and coworkers and Marinenko and Taylor

Table 1. Summary of values for the faraday as calculated by Cohen and Taylor in 1973

Author, Location, Year, Method	Value of the Faraday (Uncertainty) ^a $A_{BI69} \cdot \text{sec} \cdot \text{mole}^{-1}$
Craig, Hoffman, Law and Hamer (10), NBS, 1960. Dissolution of silver.	96,486.72(0.66)(6.8)
Marinenko and Taylor (33), NBS, 1968. Reduction of benzoic acid ^b .	96,487.30(1.12)(12)
Marinenko and Taylor (33), NBS, 1968. Reduction of oxalic acid dihydrate ^b .	96,486.25(1.57)(16)
Average of benzoic acid and oxalic acid values.	96,486.95(0.93)(9.6)
Weighted average of the Craig, et al value and the average of the Marinenko and Taylor value.	96,486.79(0.54)(5.6)
Cohen and Taylor (8), NBS, 1973. Indirect, calculated.	96,484.56(0.27)(2.8)

^aUncertainty includes random and systematic errors and is in terms of the standard deviation of the mean, first in coulombs per mole and then in parts per million.

^bReduction in the sense of titration with hydroxyl ion generated at the cathode.

values was good, the evidence "pointed the finger of suspicion unequivocally at the faraday measurements." In their final, 1973 adjustment of the physical constants, they deleted the experimental value of the faraday from consideration and in their final table of recommended values for the fundamental constants give the calculated value $96,484.57 \text{ A}_{\text{BI69}} \cdot \text{sec} \cdot \text{mole}^{-1}$.

This rejection of the experimental value for the faraday provoked considerable comment and has stimulated further work on a direct measurement, notably at the National Bureau of Standards, where the iodine coulometer has been reexamined and then abandoned and where a repetition of the dissolution-of-silver experiment is now underway (1975), and at the National Physical Laboratory, where work on the same two methods is now underway. In 1969, before the publication of the Taylor, Parker and Langenberg and Cohen and Taylor papers were published, work was underway at Iowa State University to determine the value of the faraday; the approach adopted, the high-precision coulometric titration of the organic base 4-aminopyridine, was quite different from that taken at the other laboratories.

The rejection of the experimental value for the faraday by Cohen and Taylor has not, of course, been accepted by everyone working in the area and already a new value for the Avogadro constant has been published (12) which alters the calculated value for the faraday so as to reduce the discrepancy reported above by about half. Obviously, however, that so fundamental a constant should rest on a single measurement is not desirable and equally obviously, the burden of proof has shifted to the electrochemist.

D. Coulometric Titrations. Background of Work in
High-Precision Coulometry at Iowa State University

By a coulometric titration is meant that method of chemical analysis in which electricity is used to generate a chemical which will react with a second chemical the amount of which is to be determined; from the quantity of electricity (the size of the current in amperes multiplied by the time of flow in seconds) and the gram-equivalent weight of the second chemical, the weight of the latter in grams can be calculated. The method is based on the Faraday laws of electrolysis, equation (1) above, and is based on the assumptions that: (1) the first substance, the titrant, can be generated with 100 per cent current efficiency, (2) that the reaction between the first and second substances is stoichiometric (that is, proceeds in simple whole number ratios of the molecules) and complete, and (3) that an end-point can be located telling exactly when just sufficient titrant has been added to react exactly with the substance titrated.

Such titrations were first carried out by Szabellody and Smogyi (49) in 1938. Many more were devised during the 1940's and 1950's and it became apparent that the technique possessed advantages over ordinary titrimetric methods of analysis using volumetric glassware:

1. The electrochemistry can be carried out at either the cathode or the anode and thus involve as the basic chemistry either reduction or oxidation and, of course, also neutralization because acids and bases can be generated electrically.

2. The electricity can be delivered at any desired potential and thus specificity obtained in the chemistry effected.

3. The titration can be carried out with very small or very large amounts of chemicals because of the ease with which electricity in any range can be measured.

4. The titration can be carried out with exceptional accuracy because electricity can be measured with great accuracy.

5. No increase in volume occurs during the titration.

6. The electron, regarded as a chemical, is pure and provided that one reaction only takes place at the electrode the ultimate in accuracy is possible.

Offsetting these advantages is the relative complexity of the apparatus necessary, in the electrical equipment required and more particularly in the electrolysis cell which must be of the type referred to as a partition cell in which the liquids surrounding the cathode and anode respectively must be separated by a porous membrane.

The merits of coulometric titrations were quickly recognized by analytical chemists and by 1955 it became generally evident that the electron would become the ultimate primary standard in chemical analysis. The actual statement was first made by Tutundzic (53).

Because coulometric titrations are based on Faraday's laws of electrolysis, the proportionality factor (F in equation (1)), the so-called faraday, 96,486.7 coulombs per gram-equivalent weight, assumes peculiar importance. This quantity of electricity is one-gram equivalent weight of electrons and is equal in action to one liter of a one normal solution.

The precision with which coulometric titrations were carried out increased remarkably and by 1959 it became possible to check the purity of the highest grade primary standard materials by the method. This was done first at the National Bureau of Standards by (J. K.) Taylor and Smith (52), who titrated primary standard potassium acid phthalate (NBS 84d), three other primary standard acids, and sodium carbonate with an error estimated to be less than 4 parts in 100,000. This work was followed by four papers in which accuracy of the same order was achieved: Marinenko and Taylor, 1963 (35), on the titration of halides; Marinenko and Taylor, 1963 (36), on the titration of potassium dichromate NBS 136b; Marinenko and Taylor, 1967 (34), on the titration of arsenic oxide, NBS 83c; and Marinenko and Taylor, 1968 (33), on the titration of benzoic acid and of oxalic acid dihydrate.

During 1965 apparatus was put on the market making it possible for the analytical chemist to carry out high-precision coulometric titrations without having to assemble his own electrical equipment and titration cell; the instrument was the "Coulometric Analyzer" of the Leeds & Northrup Company, described by Eckfeldt and Shaffer (14). In addition to incorporating a stable current source and the high-precision electrical measuring equipment of the Leeds & Northrup Company, Eckfeldt and Shaffer designed for the apparatus a new titration cell which was more convenient and in certain respects better than the cell of Taylor and coworkers.

The work at Iowa State University in high-precision coulometry was begun in 1966 with a study by Knoeck and Diehl (26) of the primary standard materials potassium dichromate (NBS 136b), potassium acid

phthalate (NBS 84d) and ammonium hexanitratocerate; a long-standing controversy on the composition of ammonium hexanitratocerate was settled unequivocally. The Leeds & Northrup equipment was used in this work but improvements were made in the titration cell. In another study, Knoeck and Diehl (25) titrated potassium dichromate (NBS 136b) as an acid and for the purpose designed a new cell and procedure by which electro-active materials could be titrated.

The work at Iowa State University was continued with a study of the primary standard bases 4-aminopyridine and tris(hydroxymethyl)-aminopyridine, the objective shifting from a study of the materials as primary standards to a determination of a value for the faraday. 4-Aminopyridine was selected for the final faraday work. A quantity of it was prepared in highly pure form by sublimation in an atmosphere of nitrogen by Mr. William C. Hoyle (23). The purity of this preparation of 4-aminopyridine was established by the freezing-point method by Mr. Hoyle, Mr. Frederick R. Kroeger, a graduate student in physics, and Professor Clayton A. Swenson of the Department of Physics and the Ames Laboratory of the Atomic Energy Commission; the 4-aminopyridine was shown to contain less impurity than could be detected by the method, 10 ppm (23). Attempts to titrate the bases 4-aminopyridine and tris-(hydroxymethyl)aminomethane coulometrically with acid generated at a platinum anode in an electrolyte consisting of 1 M sodium perchlorate failed by two to four per cent and this was shown by Mr. Hoyle to be caused by a side reaction at the anode producing a previously unknown chemical species, peroxyperchlorate. Mr. Hoyle was able to devise a new method for carrying out the coulometric titration of a base,

a procedure given the name "the hydrazine-platinum anode". Preliminary titrations of 4-aminopyridine were carried out by Mr. Hoyle but the Leeds & Northrup equipment was not sufficiently precise for the purpose of determining a value for the faraday and certain units of it were beginning to fail from wear.

The purpose of the work described in this thesis is the high-precision titration of 4-aminopyridine with the objective of establishing a value for the faraday with an uncertainty less than 10 to 20 ppm. The 4-aminopyridine prepared by Hoyle has been used and additional 4-aminopyridine has been prepared. Modifications in the Leeds & Northrup Company coulometric titration equipment have been made, further modifications have been made in the Knoeck and Diehl titration cell, the electrical, mass and time standards have been recalibrated, and precision titrations both of 4-aminopyridine and of tris(hydroxymethyl)-aminomethane have been carried through successfully. An explanation has been found for the unsatisfactory character of tris(hydroxymethyl)-aminomethane as a primary standard. Proof has been secured that the hydrazine-platinum anode functions with 100 per cent current efficiency in the generation of hydrogen ion. A new lot of highly pure 4-aminopyridine has been prepared and it has been titrated with my cell and procedure in the laboratory of the Electricity Division of the Institute for Basic Standards of the National Bureau of Standards, Gaithersburg, Maryland, using the electrical, mass and time standards of the Bureau. The work has been successful and a new value for the faraday has been obtained.

II. HIGH-PRECISION COULOMETRIC TITRATIONS OF 4-AMINOPYRIDINE CONDUCTED AT IOWA STATE UNIVERSITY

4-Aminopyridine, purified by sublimation by Hoyle (23), was titrated coulometrically both at the cathode (back-titration method) and at the anode (hydrazine-platinum anode method). The results of the back-titrations were previously reported, in my M.S. thesis (27), but in the present work were recalculated to reflect the recalibrations of the standards of mass, potential and resistance.

A. Electrical Circuitry and Standards

The basic elements of the circuitry used in these series of titrations are shown in Figure 1.

The current source was manufactured by the Leeds & Northrup Company, Model Number 7960, and has nominal outputs of 64.3, 6.43 and 0.643 mA (milliamperes). The large current was used during the major portion of the titrations, while the mid-range (6.43 mA) was used in the region of the end-points.

The current-sensing resistor, nominally 20 ohms, was manufactured by the Leeds & Northrup Company, North Wales, Pennsylvania, Catalog Number 4025-B-S, Serial Number 1711765. The calibrations of this resistor and the uncertainty are given in Table 2. The value 19.999,703 ohms at 25.00^o was used in calculating the results of the titrations made in this work, Tables 3 and 4.

The temperature coefficient of resistor 1711765 was stated by the Leeds & Northrup Company to be given by

$$R_t = R_{25} [1 + 0.000,002(t - 25) - 0.000,000,5(t - 25)^2]$$

Figure 1. Circuitry of the coulometric titration apparatus at Iowa State University

- A. "Coulometric Analyzer" of the Leeds & Northrup Company, Constant Current Source
- B. Electronic timer
- C. Standard resistor (20 ohms)
- D. Potentiometer, Leeds & Northrup Company, Type K-5
- E. Weston unsaturated cell
- F. Titration cell

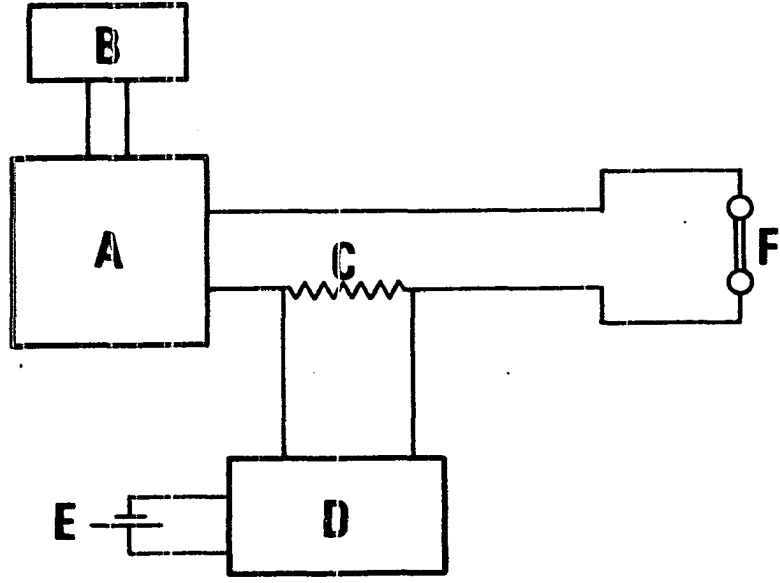


Table 2. Calibration of standard resistor, Leeds & Northrup Company, serial number 1711765

	Resistance ohms at 25.00°	Uncertainty ppm
Leeds & Northrup Company, January 1967 ^a	19.999,79	20
C. A. Swenson ^b , July 1973	19.999,6	10
National Bureau of Standards ^c , October- December 1974	19.999,703	0.2

^aAfter having been stored by the manufacturer for one year. Value traceable to the National Bureau of Standards through NBS Test Number 211.01/189516 and 189517, August 1966.

^bBy comparison with five 10-ohm resistors of similar construction by the Leeds & Northrup Company using an A.C. potentiometer, Automatic Systems Laboratories, Ltd., Leighton Buzzard, England, Model 103, Serial Number 014. Values of the 10-ohm resistors traceable to the National Bureau of Standards.

^cCalibration made under the same loading (64 mA) as used in the coulometric titration made in this work.

During the course of the titrations, the resistor was immersed in an oil bath at 25.0° . A rise in temperature of the resistor of 1.5° occurred owing to the passage of current (about 64 mA). During each titration the temperature of the resistor was measured and the resistance at that temperature used in the calculations.

Two standard cells were used, both unsaturated Weston cells manufactured by the Eppley Laboratory, Inc., Newport, R. I., Catalog Number 100, Serial Numbers 791896 and 806020. The potentials of these cells were determined by Mr. Wayne A. Rhinehart in the Ames Laboratory of the U. S. Atomic Energy Commission during October 1973, during March 1974, during April 1974, and again during October 1974, by comparison with a bank of three saturated Weston cells in a constant temperature box, Eppley Model 121, Serial Number 3955. The potential of these three cells is traceable via an Eppley certificate dated July 1, 1969 to a National Bureau of Standards calibration, Test Number 197281, dated February 20, 1969. The potentials of these cells was thus on the basis of value of the NBS volt adopted January 1, 1969. The potentials of the three cells were redetermined during November 1974 by comparison with the traveling volt standard of the National Bureau of Standards, Enclosure 1900 operating at a nominal temperature of 32.00° ; NBS Test Number 211.01/211655 dated December 19, 1974. The procedure followed in this calibration was that prescribed by the NBS. The values obtained for the three cells in set 3955 were on the average 3.01 ppm higher than those of the 1969 calibration. On the assumption that the cells of set 3955 remained unchanged during the period October 1973 to October 1974, the potentials of the cells of set 3955 and of the unsaturated

cells used in the titration work were recalculated during January 1975 to the NBS values of December 1974; the entries in Tables 3 and 4 carry these recalculations. The calibration of December 1974 places the potentials on the basis of the NBS (U. S. legal) volt, which since July 1, 1972 (16) has been referred to the Josephson junction.

The coulometric titrations were carried out in a constant temperature room held at 23.5 to 24.5^o, average temperature 24.0^o. Cells 791896 and 806020 were placed inside a box with polystyrene walls 5 cm. thick. The temperature of the cells followed changes in the room temperature very slowly and at no time changed sufficiently to vary the potential more than 3 μ V. Intercomparison of the two cells was made at intervals using the Type K-5 potentiometer used in the titration work.

Cell 791896 proved stable throughout the work; cell 806020 underwent changes when moved, all below 10 μ V. Hence, the potentiometer was calibrated with cell 791896, cell 806020 being used only as a cross-check to indicate gross irregularities. By a detailed review of the calibration work, Mr. Wayne A. Rhinehart placed the uncertainty in the potential of cell 791896 at 4 ppm. A complete history of the cells and the resistor, including temperature coefficients, is given in my M.S. thesis (27).

The potential drop over the 20-ohm resistor, Number 1711765, was measured with a Leeds & Northrup Type K-5 potentiometer, Model 7555-1-B, Serial Number 1713729. This potentiometer was calibrated at the standardization laboratory of the Leeds & Northrup Company in February 1967 at a room temperature of 25^o. The calibration data are traceable

to a set of reference standards maintained by the Leeds & Northrup Company and calibrated at regular intervals by the National Bureau of Standards, the immediately previous test had been made in August 1966, NBS Test Numbers 211.01/189516 and 189517. During August 1973, a check of the calibration of the K-5 potentiometer was made in accordance with the operating manual of the instrument, Directions 177362. No adjustments were necessary. At the potentials measured, no corrections to the potential readings were required. The certificate accompanying the instrument places the error on the 1.6 V range at less than ± 0.001 per cent + 2 μV . This error applies to the difference in the potentials measured in the calibration (cell 791896), 1.019,241 V, and that observed at the 63.4 mA current, 1.268 V, or about 0.2498 V; the error is thus 2.5 μV . Since the end correction of + 2 μV in effect cancels, the error in the measurement of potential drop was estimated to be less than 3 μV .

B. Standards of Mass. Weighing.

Correction for the Buoyant Effect of Air

The standards of mass used in this work were: (1) a set of two-piece, rhodium-plated brass weights, Wm. Ainsworth, Inc., Denver, Colorado, Serial Number 9156, NBS Calibration Test Number G-37168, May 1967, and (2) two, one-piece (Class M), stainless steel (Brunton metal) weights (1-g. and 10-g.), Wm. Ainsworth, Inc., NBS Calibration Test Number G-38117, May 1967. In the weighings of 4-aminopyridine only three weights, 1-g., 2-g. and 10-mg. rider, from the two-piece set were used. These three weights were recalibrated by Mr. V. E. Bower and Dr.

R. S. Davis of the Electricity Division of the Institute for Basic Standards of the National Bureau of Standards, during January 1975. The January 1975 values were used in recalculating the results of the titrations of 4-aminopyridine described in this part of this thesis ("ISU titrations").

4-Aminopyridine was weighed on an Ainsworth FDJ equal-arm microbalance to the nearest 3 micrograms; to reduce rounding off errors figures to 0.1 microgram, obtained by averaging swings, were carried through the calculations. All weighings of 4-aminopyridine were made by substitution; the empty glass cup and the weight of appropriate size were weighed together (tared), the weight removed, and the 4-aminopyridine added to the cup until the weight was within 0.002 g. of the tare, and the weighing completed using the calibrated rider. Cup and 4-aminopyridine together subsequently entered the reaction vessel and electrolyte.

Weights of 4-aminopyridine were corrected for the buoyant effect of air using for the density of 4-aminopyridine the value 1.2695 g./ml. (found by Hoyle by the pycnometer method using mineral oil as the transfer medium), for the density of the weights 8.40 g./ml., and for the density of air a value obtained by measuring the barometric pressure, temperature, and humidity prevailing at the time of the weighing. For convenience in making the routine determinations of the density of air, a Baxter's globe was constructed, the exterior volume of the globe determined by hydrostatic weighing, and the calibration checked occasionally under different conditions of barometric pressure, temperature and humidity.

A plastic bottle with closure bearing a tip with a very fine bore was used as a weight buret for delivering perchloric acid in the back-titration method. This bottle was more convenient than the conventional weight buret because the sample could be transferred and weighed in a much shorter time and losses due to evaporation minimized. The time of transfer, that is, from initial weighing to final weighing, was less than three minutes. The loss in weight from the tip was less than 0.1 mg. in twenty minutes and thus the loss in weight during the transfer process was estimated to be less than 0.01 mg.

The weight buret containing the perchloric acid was weighed on an Ainsworth, single-pan balance, Model 28N, from which the last three figures (down to 0.1 mg.) are obtained from an optically projected scale. Weighings were made by the double substitution method. The buret was weighed and removed; then weights from the set of two-piece, rhodium-plated brass weights were placed on the pan, totaling to the nearest 0.1 g. the weight of the buret; the last three significant figures (down to 0.1 mg.) were obtained from the optically projected scale. The optical scale was checked against the 50 mg. and 100 mg. weights of the set at loads of 0, 25 and 50 g. and found to be independent of the load and true to 0.1 mg. The weight of perchloric acid taken was of the order of 25 g. so that the error in the weighing, 0.1 mg., represented a relative error of less than 4 ppm. In making the correction to weight in vacuum, the density of 1.0504 g./ml. for perchloric acid, obtained by direct pycnometric measurement, the density of 8.4 g./ml. for the weights, and the density of air prevailing at the

time of the weighing, calculated from the barometric pressure, temperature and humidity, were used.

C. Measurement of Time

The "Coulometric Analyzer" of the Leeds & Northrup Company has a built-in timing device, a mechanical counter driven by a frequency standard, American Time Products, Model 20005A. The counter became inoperable because of excessive wear early in this work and although great effort was expended on its repair, it was necessary to abandon it. This mechanical counter was replaced by an electronic timer, Computer Measurements Company, Model 225CN, Serial Number 74186, incorporated into the circuitry and tied to the current-control switch by a simple relay. This timer was calibrated using the standard time signals of the National Bureau of Standards Radio Station WWV. The timer was slow by 19.4 ppm, but reproducible to better than 0.2 ppm. The correction of 19.4 ppm was added to all time intervals recorded. A more detailed account of the calibration of this timer is given in my M.S. thesis (27).

D. Measurement of pH

The pH was measured with a combination electrode and an Expanded Range pH Meter manufactured by Hach Chemical Company, Ames, Iowa, Model No. 8596, Serial No. 4, readable to 0.001 pH. The solution surrounding the external, silver-silver chloride reference electrode of the combination electrode, 4 M potassium chloride was replaced with 4 M sodium chloride to prevent the precipitation of potassium perchlorate at the porous ceramic junction. The pH meter was calibrated using the National

Bureau of Standards buffer 0.025 M potassium dihydrogen phosphate-0.025 M disodium hydrogen phosphate, pH 6.865 at 25^o, immediately before each titration. The drift of this unit, as indicated by the change in calibration from day to day, was less than 0.02 pH units per 24 hours.

E. Titration Cell

The titration cell used, shown in Figure 2, was essentially the same as that used by Hoyle (23). An unfired Vycor rod, 25 mm. in length, 14 mm. in diameter, was used in the construction of the shield tube, Figure 3. In the work of Hoyle this rod was sealed inside a glass tube 1.5 mm. larger in diameter with Silicon Seal (General Electric Company). The seal was allowed to cure for a minimum of two weeks. In this work, the Vycor rod was butted against a glass tube of identical outside diameter and the assembly jacketed with 50 mm. of heat-shrinkable Teflon tubing, Figure 3b. The Teflon tubing was obtained from Chemplast, Inc., Wayne, New Jersey. About 2 mm. of the Teflon tubing was left projecting beyond the end of the rod. The assembly was heated in an oven for three hours at 115^o. At higher temperature the Vycor shattered. Both assemblies, 3a and 3b, were soaked in 1.0 M sodium perchlorate for 48 hours and conditioned by running electricity through them for 8 hours in a mock coulometric titration. This conditioning was essential to remove the acid remaining within the Vycor from the manufacture. Considerable trouble was experienced with 3a cracking and 3b proved better in routine use.

In this work also, electrolyte was removed periodically by siphoning through the tube shown in Figure 3b; the level of the electrolyte

Figure 2. Coulometric titration cell

- A. Platinum working electrode**
- B. Platinum counter electrode**
- C. Glass frit on bottom of inner shield tube**
- D. Unfired Vycor on bottom of intermediate chamber**
- E. Nitrogen inlet**
- F. Combination pH electrode**
- G. Sample inlet**
- H. Magnetic stirring bar**
- I. Plexiglass covers**

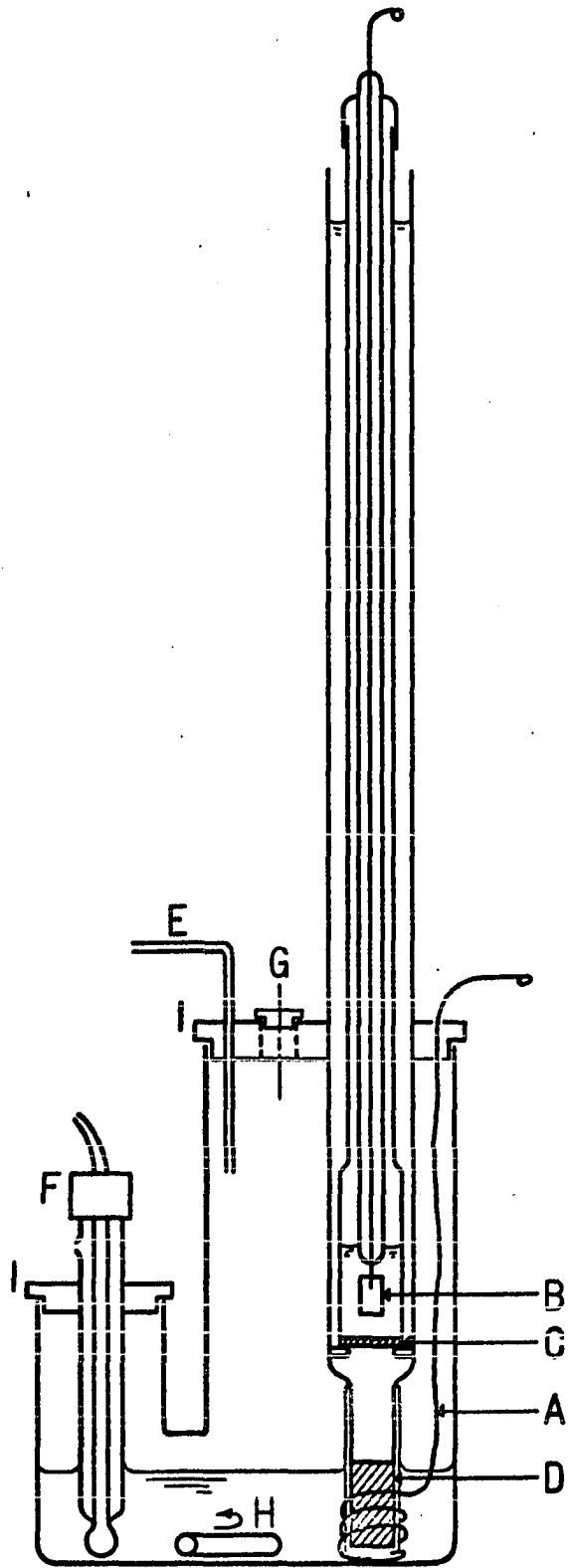
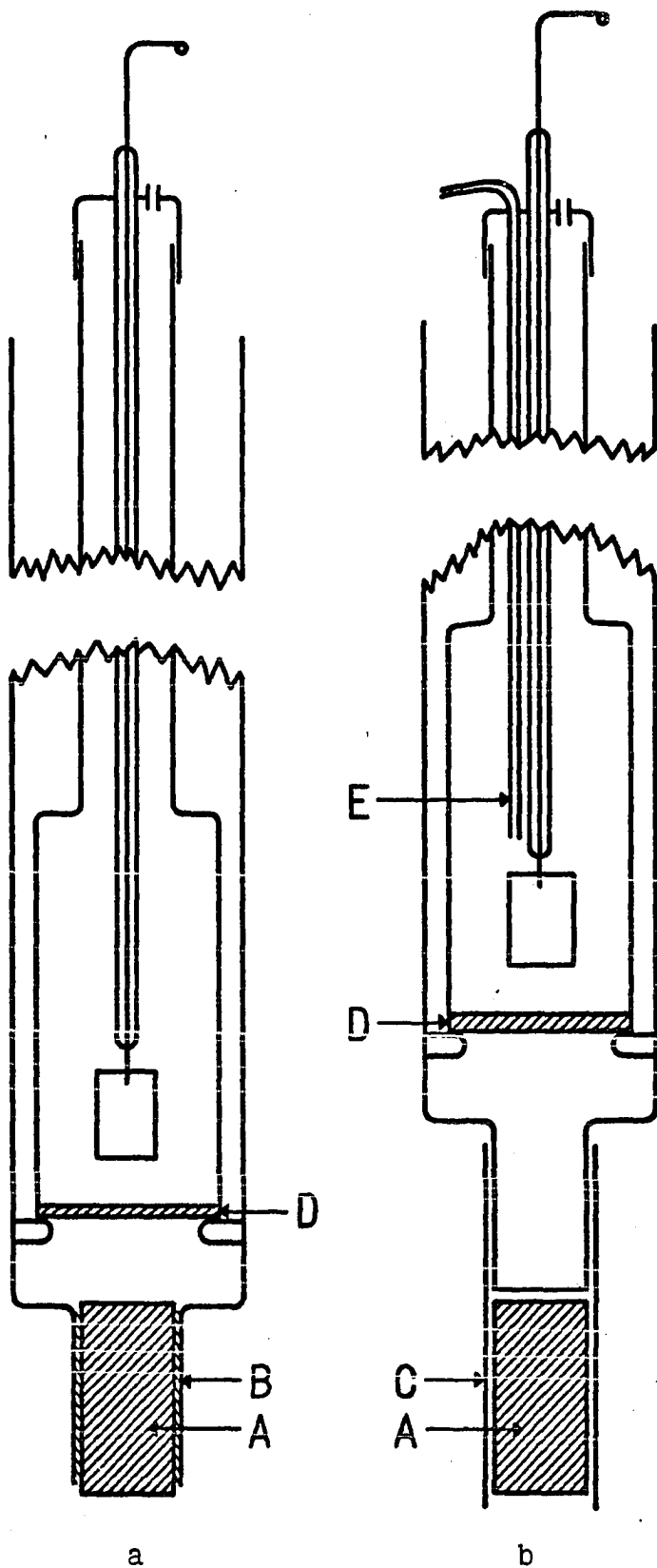


Figure 3. Shield tube using unfired Vycor

- a. Seal made with Silicon Seal
 - b. Seal made with heat-shrinkable Teflon
-
- A. Unfired Vycor
 - B. Silicon seal
 - C. Heat-shrinkable Teflon
 - D. Glass frit
 - E. Siphon tube



around the counter electrode was kept just above the top of the electrode thus insuring continual flow of electrolyte from the intermediate chamber into the counter electrode compartment.

F. Procedure in the Titration of 4-Aminopyridine
by the Back-Titration Method

The outer chamber of the shield tube ("intermediate chamber" of the titration cell) was filled with 7.5 M sodium perchlorate and the inner chamber surrounding the counter electrode (anode in this instance) was filled with 1.0 M sodium perchlorate sufficient to just cover the electrode. In the titration cell, Fig. 2, were placed 80 ml. of 1.0 M sodium perchlorate and a magnetic stirring bar. The pH was brought to 3 by the addition of 1 M perchloric acid (the same acid as used later). Purified nitrogen was bubbled through the solution for two hours to remove carbon dioxide. The flow of nitrogen was maintained over the solution throughout the titration. The electrolyte was then "pre-titrated" to remove any electroactive species present by cathodically generating hydroxide ion in the cell. When the solution reached pH 9, the electrolysis was stopped and the solution was acidified by the addition of 1 M perchloric acid.

This sequence was repeated three times. During the third electrolysis data were taken, pH versus time, at the lower current setting, approximately 6.4 mA. The potential drop across the standard resistor was also recorded. The weighed sample of 4-aminopyridine was introduced by lowering the weighing cup plus the amine into the electrolyte by a platinum wire. A slight excess of standard perchloric acid was added

from the weight buret. The solution was then electrolyzed cathodically, the current being approximately 63.4 mA. At five minute intervals, the potential across the standard resistor, the temperature of the resistor and the pH of the solution were recorded. Analyte was extracted from the inner shield tube and 7.5 M sodium perchlorate added to the outer chamber of the shield tube to maintain a slow flow of electrolyte into the anode chamber. When the main solution reached pH 3.5 the titration was interrupted and the walls of the titration chamber rinsed with triply distilled water. The titration was continued at a current of approximately 6.4 mA delivered in increments of twenty seconds, pH, time, and potential drop across the resistor being measured. Between additions sufficient time was allowed for the solution to equilibrate before the pH was recorded.

The perchloric acid was standardized in a similar manner, the current being approximately 6.4 mA during the pre-titration and the final stage of the titration, and approximately 63.4 mA during the major part of the titration. The major part of the titration required about 9 hours; the potential drop over the standard resistor was measured every 30 minutes during this period.

In each analysis, two equivalence-points were determined, that in the pre-titration and that in the actual titration. The equivalence-point in the titrations involving perchloric acid alone, that is, in the pre-titrations and in the standardization of the perchloric acid, was determined using the method of Yan (59), a finite difference method based on four sets of data taken symmetrically about the point of inflection. In the titrations in which 4-aminopyridine was present

(actually back-titrations of excess perchloric acid), the point of inflection was found by fitting the data obtained through the entire equivalence-point region empirically by computer to a cubic equation, setting the second derivative of this equation to zero, and solving for the point of inflection (Chapter VII).

The concentration of the standard solution of perchloric acid, expressed in coulombs per gram, was calculated by

$$C_{\text{HClO}_4} = (A + B + C) / (\text{Mass Solution})$$

in which

A is the number of coulombs delivered during the pre-titration (current approximately 6.4 mA) from the point of inflection to the beginning of the main phase of the titration, as given by $E_1 t_1 / R$.

B is the number of coulombs delivered during the main phase of the titration (current approximately 63.4 mA), as calculated by $E_2 t_2 / R$.

C is the number of coulombs delivered during the concluding phase of the titration (current approximately 6.4 mA), as calculated by $E_3 t_3 / R$.

The quantities E_1 and E_3 were the averages of 4 to 6 readings, E_2 of 15 to 25 readings.

The excess perchloric acid in the back titrations, expressed in coulombs, was calculated by

$$C_{\text{Excess HClO}_4} = -A + B + C$$

in which A, B and C have the same meanings, and the net perchloric acid used, in grams, by

$$C_{\text{Net HClO}_4} = (\text{Wt. HClO}_4)(C_{\text{HClO}_4}) - (C_{\text{Excess HClO}_4})$$

And finally, the value of the faraday was calculated by

$$F = (C_{\text{Net HClO}_4})(\text{Equiv. Wt.}) / (\text{Mass 4-aminopyridine})$$

G. Procedure in the Titration of 4-Aminopyridine

Using the Hydrazine-Platinum Anode

The outer chamber of the shield tube was filled with 7.5 M sodium perchlorate and the inner chamber surrounding the counter electrode was filled with 1.0 M sodium perchlorate sufficient to just cover the electrode. In the titration cell, Figure 2, were placed 100 ml. of a solution consisting of 0.25 M sodium hydrazinium sulfate and 1.0 M sodium perchlorate, and a magnetic stirring bar. Purified nitrogen was bubbled through the solution for two hours to remove carbon dioxide. The flow of nitrogen was maintained over the solution throughout the titration. A pre-titration was then carried out to remove any electro-active species present. The solution was taken forward and backward through the equivalence point region, between pH 3 and 6, three times by electrolyzing with the working electrode alternately anodic and cathodic. During the third anodic electrolysis data were taken, pH versus time, at the lower current setting, approximately 6.4 mA. The potential drop across the standard resistor was also recorded.

The weighed sample of 4-aminopyridine was introduced by lowering the weighing cup plus the amine into the electrolyte by a platinum wire.

The solution was then electrolyzed anodically, the current being approximately 63.4 mA. The major part of the titration required about 10.5 hours for a 3-g. sample. At 30 minute intervals the potential across the standard resistor, the temperature of the resistor, and the pH of the solution were recorded. Catholyte was extracted from the inner shield tube and 7.5 M sodium perchlorate added to the outer chamber of the shield tube to maintain a slow flow of electrolyte into the cathode chamber. When the pH of the main solution reached 5.5 the titration was interrupted and the walls of the titration chamber were rinsed with triply distilled water. The titration was continued at a current of approximately 6.4 mA delivered in increments of twenty seconds, pH, time, and potential drop across the resistor being measured. Between additions sufficient time was allowed for the solution to equilibrate before the pH was recorded.

In each analysis, two equivalence points were determined, that in the pre-titration and that in the actual titration. The point of inflection was found by fitting the data obtained through the entire equivalence point region empirically by computer to a cubic equation, setting the second derivative of the equation to zero, and solving for the point of inflection (Chapter VII), a considerable improvement for this particular problem over location of the point of inflection by visual inspection of a graph or by the finite difference method of Yan (59). The number of coulombs passed was calculated by

$$C_{\text{Total}} = A + B + C$$

in which

A is the number of coulombs delivered during the pre-titration (current approximately 6.4 mA) from the point of inflection to the beginning of the main phase of the titration, as given by $E_1 t_1 / R$.

B is the number of coulombs delivered during the main phase of the titration (current approximately 63.4 mA), as calculated by $E_2 t_2 / R$.

C is the number of coulombs delivered during the concluding phase of the titration (current approximately 6.4 mA), as calculated by $E_3 t_3 / R$.

The quantities E_1 and E_3 were the averages of 4 to 6 readings, E_2 of 15 to 25 readings. The value of the faraday was calculated by

$$F = (C_{\text{Total}})(\text{Equiv. Wt.}) / ((4/5)(\text{Mass 4-aminopyridine}))$$

H. Results and Discussion

From the data obtained in the titrations, the quantity It/G has been calculated for each titration and reported in Tables 3 and 4 under "Electrical Equivalent per Gram". The number of electrons involved per molecule of 4-aminopyridine being one, it remains simply to multiply the electrical equivalent per gram by the best value of the molecular weight to obtain the value of the faraday. Using the new hydrazine-platinum anode five hydrogen ions are generated per four electrons passed; this has been taken into consideration in calculating the electrical equivalents per gram, Table 3.

The values for the faraday obtained by averaging the six titrations by each of the two methods were

Table 3. Coulometric titration of 4-aminopyridine with acid generated at the hydrazine-platinum anode, recalculated on the basis of refined calibrations of potential, resistance and mass

Mass of 4-aminopyridine g.	Mol. wt. 4-aminopyridine = 94.117,02		Value of Faraday 1972 NBS coulombs/mole
	Quantity of electricity 1972 NBS coulombs	Electrical equivalent per gram = (5/4)It/mass 1972 NBS coulombs/g.	
1.007,170,0	826.003,1	1,025.153,4	96,484.38
3.004,428,5	2,464.083,6	1,025.188,1	96,487.65
3.009,783,5	2,468.432,7	1,025.170,3	96,485.97
2.004,910,0	1,644.345,4	1,025.198,9	96,488.66
3.003,387,6	2,463.192,7	1,025.172,6	96,486.19
3.000,431,3	2,460.751,8	1,025.165,8	<u>96,485.55</u>
	Average		96,486.40
	Standard deviation of the individual observation		1.53
	Standard deviation of the mean		0.62

Table 4. Coulometric titration of 4-aminopyridine with perchloric acid (coulometric end-point) and standardization of perchloric acid coulometrically, recalculated on the basis of refined calibrations of potential, resistance, and mass

Mass of perchloric acid g.	Standardization of perchloric acid	
	Quantity of electricity 1972 NBS coulombs	Concentration of perchloric acid 1972 NBS coulombs/g.
25.172,1	2,190.428,0	87.018,087
25.898,5	2,253.676,9	87.019,591
25.842,4	2,248.743,3	87.017,587
30.823,4	2,682.211,2	87.018,667
20.165,9	1,754.802,4	87.018,303
20.163,0	1,754.566,2	<u>87.019,104</u>
	Average	87.018,556
	Standard deviation of the individual observation	0.000,722
	Standard deviation of the mean	0.000,295

Table 4. (Continued)

Titration of 4-aminopyridine						
Heading of columns: A. Mass of 4-aminopyridine; B. Mass of perchloric acid; C. Electricity delivered via perchloric acid; D. Additional electricity to reach end-point; E. Total electricity; F. Electrical equivalent per gram; G. Value of Faraday; C = 1972 NBS coulombs						
Molecular weight of 4-aminopyridine = 94.117,02						
A	B	C	D	E	F	G
g.	g.	C	C	C	C/g.	C/mole
2.183,417,5	27.388,4	2,383.299,0	144.892,6	2,238.406,4	1,025.184,7	96,487.33
2.174,815,3	27.414,6	2,385.578,9	156.007,5	2,229.571,4	1,025.177,3	96,486.63
2.155,223,5	27.149,0	2,362.466,7	152.985,6	2,209.481,1	1,025.174,9	96,486.41
2.083,729,1	25.547,5	2,223.106,5	86.930,6	2,136.175,9	1,025.169,6	96,485.91
2.057,621,6	24.844,7	2,161.949,9	52.515,1	2,109.434,8	1,025.181,0	96,486.98
2.102,142,6	25.885,4	2,252.510,1	97.423,8	2,155.086,3	1,025.185,5	<u>96,487.40</u>
Average						96,486.78
Standard deviation of the individual observation						0.57
Standard deviation of the mean						0.23

By the hydrazine-platinum anode method

$F = 96,486.40$ 1972 NBS coulombs per gram-equivalent weight

$\sigma_1 = 1.53$ (five degrees of freedom)

$\sigma_{\bar{x}} = 0.62$

By the back titration method (platinum cathode)

$F = 96,486.78$ 1972 NBS coulombs per gram-equivalent weight

$\sigma_1 = 0.57$ (five degrees of freedom)

$\sigma_{\bar{x}} = 0.23$

in which σ_1 and $\sigma_{\bar{x}}$ are the standard deviations of the individual observation and of the mean, respectively, random errors only. A weighted average of these values is:

$F = 96,486.69(0.81)(8.40 \text{ ppm})$ 1972 NBS coulombs per gram-equivalent weight

in which the numbers in parentheses are the uncertainty resulting from combining random and systematic errors and expressed as the standard deviation of the mean first in coulombs per gram-equivalent weight and second in parts per million. The systematic errors are discussed individually below, Sections I, J, K, and L.

The weighted average was calculated using the method followed by Taylor, Parker and Langenberg (51, p. 382, equation 10) in which the

$$\bar{x} = \frac{\frac{\bar{x}_h}{\sigma_h^2} + \frac{\bar{x}_b}{\sigma_b^2}}{\frac{1}{\sigma_h^2} + \frac{1}{\sigma_b^2}} \quad (2)$$

$$\frac{1}{\sigma_{h+b}^2} = \frac{1}{\sigma_h^2} + \frac{1}{\sigma_b^2} \quad (3)$$

subscripts h and b refer, respectively, to the hydrazine-platinum anode and back-titration methods, and the standard deviations of the means, σ_h and σ_b , are the combined random error plus those systematic errors not common to the two methods, all being expressed in ppm. The uncertainties were combined by taking the square root of the sum of the squares (root-sum-square, RSS (51, p. 383, equation 11)). Thus

$$\sigma_h = [(\sigma_{\bar{x}',h})^2 + (\sigma_{ep,h})^2]^{\frac{1}{2}} = [(6.40)^2 + (7)^2]^{\frac{1}{2}} = 9.48 \quad (4)$$

$$\begin{aligned} \sigma_b &= [(\sigma_{\bar{x}',b})^2 + (\sigma_{ep,b})^2 + (\sigma_{\bar{x}',stdzn})^2]^{\frac{1}{2}} \\ &= [(2.43)^2 + (3)^2 + (3.39)^2]^{\frac{1}{2}} = 5.14 \end{aligned} \quad (5)$$

in which standard deviations of the mean are expressed as ppm (designated by the prime in the subscript), and the subscripts ep and stdzn designate end-point and standardization. The end-point errors are the best estimates obtained as described in Section J below; for $\sigma_{\bar{x}',stdzn}$ see Table 4. Application of these formulas lead to $F = 96,486.69$ 1972 NBS coulombs per gram-equivalent weight and $\sigma_{h+b} = 4.52$ ppm. To σ_{h+b} was then added, again by the RSS method, the errors common to both methods (in ppm): Weston, unsaturated cell (4 ppm), standard resistor (0.2 ppm), time (0.2 ppm), measurement of potential (3 ppm), mass (4 ppm), purity (3 ppm), molecular weight (0.3 ppm). The total was 8.40 ppm, or 0.81 coulombs per gram-equivalent weight.

The results presented in Tables 3 and 4 are based on a purity of the 4-aminopyridine of 100.000 per cent; introduction of a lower value

for the purity raises the value for the faraday. For the effect of possible impurities in the 4-aminopyridine, see Section L, below. The value used for the molecular weight of 4-aminopyridine was 94.117,02 (0.3 ppm) based on a recalculation of the atomic weight of nitrogen (23).

I. Estimate of Error

In estimating the errors used in the section above, I have attempted to give the best estimate at the one standard deviation (70 per cent confidence) level rather than the maximum possible error. Such estimates, the best guess on the part of the investigator based on his feel for his subject are subjective, of course, but the practice has the sanction, and indeed is the general and preferred operating practice of those engaged in evaluating the fundamental constants; see Taylor, Parker and Langenberg, ref. 51, page 383, and the discussion in the papers of the 1970 symposium (37) at the National Bureau of Standards, in particular the paper of Thomsen (37).

The rationale for the assessment of the errors in the standards of electromotive force, resistance, potential drop, time and mass are given in preceding sections and in my M.S. thesis (27). The larger errors, in the detection of end-point, the measurement and integration of current, and purity, are discussed in the following sections. A summary of the errors is given in Table 5.

J. Precision in Location of End-Point

The time of electrolysis in an individual titration is the difference between the points of inflection in plots of pH versus time during which constant current is flowing made from data at the beginning

Table 5. Error budget for the coulometric titrations of 4-amino-pyridine performed at Iowa State University

	Anodic Titrations	Cathodic Titrations
EMF standard	4. ppm	4. ppm
Resistance standard	0.2	0.2
Time	0.2	0.2
Measurement of potential	3	3
Mass	4	4
Purity	3	3
Molecular weight	0.3	0.3
End-point detection	7	3
Standardization of perchloric acid	0	3.4
Random error	6.4	2.4

of the titration and at the end. Fifteen or so data points enter into the determination of each point of inflection and it is difficult to assess the accumulative effect of the start-stop errors on the time at the point finally selected for the point of inflection. This error was minimized by reducing the current used through the end-point regions to one-tenth that in the main titration. The slope at the point of inflection in the titration using the hydrazine-platinum anode was $0.002\text{pH}/0.0064$ coulombs. Judging from this slope and the rate of change of the slope through the point of inflection, I estimate the error in location of the point of inflection to be 0.013 coulombs. This is about the same variation as obtained for any one set of data by fitting the cubic first as pH as a function of time and then time as a function of pH, and for each, setting the second derivative equal to zero and solving. In terms of the current in the main part of the titration, this is 0.013 coulombs in 2,560 coulombs or 5 ppm. The difference of two end-points is involved and the end-point error is placed at the square root of the sum of the squares, 7 ppm.

Although the slope in the end-point regions in the perchloric acid was much greater, averaging $0.08\text{ pH}/0.0064$ coulombs, the data were not amenable to computer fit to a cubic equation and the Yan method based on four points was used to locate the point of inflection. The uncertainty was placed at 0.004 coulombs, leading to an error of 1.6 ppm. In the back titration of excess perchloric acid in the presence of 4-aminopyridine, the slope was $0.007\text{ pH}/0.0064$ coulombs and the computer method of obtaining the point of inflection could be used; the error was

estimated to be 2.5 ppm. The back-titration procedure involved one each of these end-points and the combined error is thus 3 ppm.

I have identified some five variables affecting the detection of the end-point, control of which must be improved in future work if 1 ppm accuracy is to be achieved. This includes a consideration of the difference between the end-point (point of inflection) and equivalence-point to the extent that such difference is not cancelled as in the present work by using the difference between identical end-points at the beginning and at the end of the titration.

K. Measurement and Integration of Current

Although the error in the measurement of the potential drop over the standard, 20-ohm resistor with the Type K-5 potentiometer was estimated to be 3 ppm, variation in the current supply effected a 5- μ V jiggle on the null-point detector. Slow drifts in the current registering as much as 400 μ V variation in potential drop occurred over the 8-hour runs; these were caused primarily by variations in the 110 V A-C main and were less in runs made at night. The potential measurements were made at intervals not exceeding 30-minutes and the current was obtained by averaging the potential drops recorded. Stepwise integration of current-time with each reading gave almost identical results. It is assumed that a center value was obtained in the readings of the null point detector and that the product of current and time is random and included in the random errors.

L. Effect of Impurities

It is unfortunate that the freezing point study (23) placed only an upper limit, 10 ppm, on the impurity possibly present in the 4-amino-

pyridine. It is the current state of the art that organic impurities at this level in organic compounds (metals having been shown to be absent) cannot be identified and determined. To the extent that the impurities in the 4-aminopyridine are the possible isomeric materials 2-aminopyridine and 3-aminopyridine, the impurities are without effect; the equivalent weights are identical and both isomers are weaker bases and would be titrated together with the 4-aminopyridine in both of the procedures used in this work, that is, by the hydrazine-platinum anode method and by the back titration of excess perchloric acid method. Even the homologous aminomethylpyridines, differing in molecular weight by 14, would be similarly titrated and cause negligible error; thus, 10 ppm of 3-methyl-4-aminopyridine, molecular weight, 108.144,11, $pK_B = 4.55$, would affect the results only by 1.2 ppm. Consideration of the volatility, as reflected in the melting temperature, of the pyridylamines isomeric and homologous to 4-aminopyridine makes the likelihood of any of them being present as an impurity in carefully sublimed 4-aminopyridine remote. The effect of symmetry of the molecule on melting point is about as dramatic among the pyridylamines as in any other class of organic compounds other than the tetraaryl lead compounds, Table 6. Excepting the highly symmetrical 2,6-dimethyl- and 2,3,5,6-tetramethyl- compounds, the low melting and more volatile characteristics of all of these aminopyridines would favor their removal early in the process of subliming 4-aminopyridine. The synthesis of 4-aminopyridine from acetaldehyde and ammonia proceeds through the isolation of 4-methylpyridine from other picolines, the oxidation to pyridine-4-carboxylic acid, conversion to the amide or hydrazide, and degradation to 4-aminopyridine. The quite different properties of the

Table 6. Melting points and pK_B 's of various aminopyridines

Aminopyridine	m.p.	pK_B
4-	159 ^o	4.63
3-Me-4-	108	4.55
3-Et-4-	73	4.51
3-iso-Pr-4-	52	4.41
2,6-Di(Me)-4-	192	
3,5-Di(Me)-4-	83	4.47
2,3,4,5-Tetra(Me)-4-	197	3.43
3-	64	7.97
4-Me-3-	106	
6-Me-3-	96	
2-	56	7.29
3-Me-2-	26	6.76
4-Me-2-	98	6.52
6-Me-2-	41	6.59

hydrocarbon, carboxylic acid, and amide from the aminopyridine make it unlikely that they would be carried through to the final aminopyridine and thus the likely impurities are the isomeric and homologous compounds. There is no gainsaying, however, that the commercial 4-aminopyridine starting product used in this work was oily and that low melting materials were eliminated in the early stages of the sublimation. This puts great reliance on the efficacy of the sublimation and on the proof of purity afforded by the freezing point analysis.

Lacking any definite evidence as to the presence or nature of impurities better than the 10-ppm set by the sensitivity in the freezing point experiment, reliance must be placed on my feel for the chemistry involved. I believe that impurities if present are 2-aminopyridine, 3-aminopyridine and the homologous aminomethylpyridines, the effects of which are either zero or negligible. At the 70 per cent confidence level I place the error at 3 ppm.

III. HIGH-PRECISION COULOMETRIC TITRATIONS OF 4-AMINOPYRIDINE CONDUCTED AT THE NATIONAL BUREAU OF STANDARDS

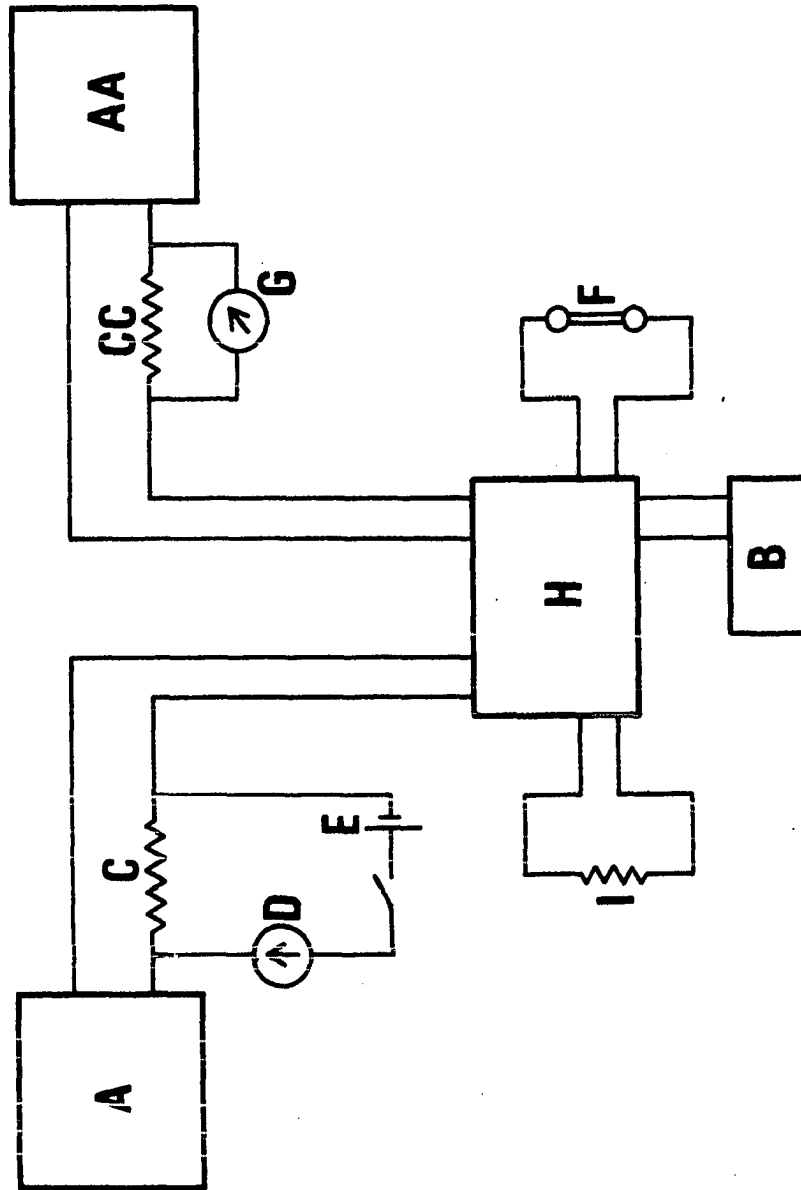
Because of the great interest of physicists in a highly accurate value for the faraday, Dr. B. N. Taylor, Chief of the Electricity Division of the Institute for Basic Standards of the National Bureau of Standards, Gaithersburg, Maryland (mailing address, Washington, D. C. 20234) suggested that the work be repeated at the National Bureau of Standards to take advantage of direct access to the national standards of voltage, mass, time and resistance there. This offer was accepted, a new lot of 4-aminopyridine prepared by sublimation at Iowa State University and the chemicals and titration cell were taken to the laboratory of the Electricity Division of the Bureau. During March, April and May of 1975, the titrations of the new lot of 4-aminopyridine were carried out by both the hydrazine-platinum anode and the back-titration methods.

A. Electrical Circuitry and Standards

A block diagram of the basic circuitry used at NBS is shown in Figure 4. The 100 mA, constant-current source was used during the major portion of each titration. This current source was designed and built by Mr. Bruce F. Field, an electrical engineer at the National Bureau of Standards. The current from this source was adjusted so that the potential drop across a standard resistor was exactly that of a Weston unsaturated cell. The resistor and cell were arranged in opposition and the difference in potential was measured with a Leeds & Northrup

Figure 4. Circuitry of the coulometric titration apparatus at the National Bureau of Standards

- A. Constant-current source (100 mA)
- AA. Constant-current source (3.35 mA)
- B. Electronic timer
- C. Standard resistor (10 ohm)
- CC. Standard resistor (200 ohm)
- D. Null-point detector
- E. Unsaturated Weston cell
- F. Titration cell
- G. Voltmeter
- H. Relays and switches
- I. Dummy load



Digital Linear Amplifier, Model 9829-D, capable of detecting 0.1 μV . Periodic adjustments were necessary to maintain the balance at zero, but never exceeded 1 ppm per hour.

The standard resistor, nominally 10 ohms, manufactured by the Leeds & Northrup Company, was a wire-wound, spool resistor without a protective canister, and was specifically adapted for coulometric work by Mr. Vincent E. Bower, a research scientist at the National Bureau of Standards. The resistor was immersed in a well-stirred oil bath, regulated to 26.5 $^{\circ}$. The resistance under these conditions was 9.999,757,38(0.2 ppm) ohms, as calibrated against the national working standard of resistance one week prior to the work being reported in this thesis.

The Weston unsaturated cell was placed within an enclosure, the temperature of which was controlled to $\pm 0.01^{\circ}$. The potential of this working cell was compared before each titration to a set of four saturated Weston cells (Guildline Instruments, Standard Cell Enclosure Model 9152T4, Number 2300) which in turn was calibrated weekly against the national working standard of voltage. The value of the cell changed from 1.019,038,59(0.2 ppm) volts at the start of this work to 1.019,038,04(0.2 ppm) volts at the completion, a span of three weeks, the number in parentheses is the standard deviation of the mean. The value obtained on the day of each titration was used in the calculations.

Through the region of the equivalence-point of each titration, a constant-current source designed and built by Dr. Richard S. Davis, a research physicist at the National Bureau of Standards, was used. The output was approximately 3.35 mA, the exact value being obtained

during each titration by measuring the potential drop across a standard resistor. The potential was read directly using a well-calibrated voltmeter, Data Precision Digital Multimeter 2540A1.

Both current sources were allowed to warm-up through a dummy load having a resistance comparable to that of the titration cell, about 150 ohms. A switching system of mercury-wetted relays, built by Dr. Richard S. Davis, was used to switch from the dummy load to the titration cell, simultaneously triggering the timer. No significant switching transients were observed.

B. Standards of Mass. Weighing. Correction

for the Buoyant Effect of Air

The weight buret from which the perchloric acid was delivered in the back-titration method was that used in the corresponding titrations at Iowa State University. It was weighed on a Mettler single-pan, semi-micro balance, Type B6. The internal weights of this balance were calibrated with a set of Ainsworth Class M weights, Serial Number 33074, NBS Calibration Test Number 232.09/307, September 15, 1971. This set had been repeatedly checked by the Mass Section of the National Bureau of Standards since 1971 and the individual weights had not changed in mass.

4-Aminopyridine was weighed on a Mettler, single-pan, microbalance, Type M5/SA, using the double substitution method. Only the 2-g. and the 5-mg. weights of the Class M set were used in these weighings.

All weighings were corrected to true mass using for the density of 4-aminopyridine 1.2633 g./ml. (found by the pycnometer method using

xylylene as the transfer medium), for the density of the perchloric acid solution 1.0504 g./ml. (found by direct pycnometric measurement), for the density of the Class M weights 7.89 g./ml., for the density of the internal weights of the semi-microbalance 7.77 g./ml., and for the density of air, a value obtained by measuring barometric pressure, temperature and relative humidity prevailing at the time of the weighing.

The Baxter's globe used in the determination of the density of air at Iowa State University was recalibrated at the National Bureau of Standards. The exterior volume of the globe, determined by hydrostatic weighing, was found to be 118.464 ml.; its weight in vacuum, as calculated by determining the density of air by equation (7) below and solving for the weight in vacuum in equation (6), was found to be 27.303,77 g. The density of air can then be routinely determined by simply weighing the globe in air and employing equation (6).

$$d_{\text{air}} = \frac{\text{Weight}_{\text{vacuum}} - \text{Weight}_{\text{air}}}{\text{Volume}_{\text{globe}} - \text{Volume}_{\text{weights}}} \quad (6)$$

$$= \frac{27.303,77 - \text{Weight}_{\text{air}}}{114.967}$$

The recalibration of the globe reduced the value for the density of air obtained by this method by 2 parts per thousand. The density of air in the calibration was determined by the formula:

$$d_{\text{air}} = \frac{3.4856 \times 10^{-7} (B - 0.3783h)}{T} \quad (7)$$

in which

B is the barometric pressure (in barye) after making the correction for reduction of the mercury column to standard temperature

using the Smithsonian Meteorological Tables.

h is the aqueous tension (in barye) as determined by psychrometric observations and the use of the Smithsonian Meteorological Tables.

T is the ambient temperature in degrees Kelvin (K).

The value for the density of air obtained by using Baxter's globe tracked the value calculated using equation (7) remarkably well, never varying by more than 1 part per thousand.

The correction to weight in vacuum (true mass) for the weights of 4-aminopyridine and perchloric acid was made using the following equation, using the above stated values for the densities:

$$\text{Weight}_{\text{vacuum}} = \frac{\text{Weight}_{\text{air}}(1 - (d_{\text{air}}/d_{\text{weights}}))}{(1 - (d_{\text{air}}/d_{\text{sample}}))}$$

C. Measurement of Time

The timer was manufactured by General Radio, Counter Model 1192-B. It was tied directly to the 10 KHz standard time signal of the National Bureau of Standards and was accurate to better than 0.001 second.

D. Measurement of pH

The pH was measured with the same equipment as used at Iowa State University, a Hach Expanded Range pH Meter, Model Number 8596, Serial Number 4 and a combination glass electrode.

E. Titration Cell

The titration cell used was the same as that described in Chapter II, Part E. The shield tube assembly was modified slightly; the length

of unfired Vycor was reduced from 25 mm. to 5 mm. to decrease the resistance of the cell from 500 to 150 ohms.

F. Procedures for the Titration of 4-Aminopyridine

The procedures for the titrations were identical to those previously described, Chapter II, Parts F and G, with the following exception. Approximately 1 g. of 4-aminopyridine was dissolved in the electrolyte before the pre-electrolysis and pretitration in all the titrations, including the standardizations of perchloric acid. This was done for two reasons: (1) to make the inflection-points of the pretitration and the final titration more nearly identical, and (2) to make the computer method of locating the inflection-point applicable to all titrations.

G. Results and Assessment of Errors

The results of the titrations are given in Tables 7 and 8 and the estimated values for the systematic errors in Table 9. The errors were combined as outlined in Chapter II, Part H. The values for the faraday thus obtained were:

By the hydrazine-platinum anode method

$$F = 96,486.24 \quad 1972 \text{ NBS coulombs per gram-equivalent weight}$$

$$\sigma_1 = 0.56$$

$$\sigma_x = 0.23 \quad 2.4 \text{ ppm, random error only}$$

By the back-titration method (platinum cathode)

$$F = 96,486.19 \quad 1972 \text{ NBS coulombs per gram-equivalent weight}$$

$$\sigma_1 = 0.67$$

$$\sigma_x = 0.27 \quad 2.8 \text{ ppm, random error only}$$

Table 7. Coulometric titration of 4-aminopyridine with acid generated at the hydrazine-platinum anode, performed at the National Bureau of Standards, Washington, D. C.

Mass of 4-aminopyridine g.	Mol. wt. 4-aminopyridine = 94.117,02		Value of Faraday 1972 NBS coulombs/mole
	Quantity of electricity 1972 NBS coulombs	Electrical equivalent per gram = (5/4)It/mass 1972 NBS coulombs/g.	
2.003,978	1,643.553,92	1,025.182,11	96,487.08
2.003,863	1,643.440,72	1,025.170,33	96,485.98
1.999,284	1,639.689,24	1,025.172,78	96,486.21
1.998,148	1,638.748,54	1,025.167,14	96,485.68
2.002,371	1,642.229,69	1,025.178,20	96,486.72
1.996,423	1,637.334,82	1,025.167,77	<u>96,485.74</u>
	Average		96,486.24
	Standard deviation of the individual observation		0.56
	Standard deviation of the mean		0.23

Table 8. Titration of 4-aminopyridine with perchloric acid (coulometric end-point) and standardization of perchloric acid coulometrically, performed at the National Bureau of Standards, Washington, D. C.

Mass of perchloric acid g.	Standardization of perchloric acid	
	Quantity of electricity 1972 NBS coulombs	Concentration of perchloric acid 1972 NBS coulombs/g.
19.899,32	1,713.152,70	86.091,017
23.351,00	2,010.332,82	86.091,937
21.314,79	1,835.003,90	86.090,639
21.243,80	1,828.925,25	86.092,189
25.358,71	2,183.158,92	86.091,087
25.486,92	2,194.207,08	<u>86.091,496</u>
	Average	86.091,394
	Standard deviation of the individual observation	0.000,591
	Standard deviation of the mean	0.000,241

Table 8. (Continued)

Titration of 4-aminopyridine						
Heading of columns: A. Mass of 4-aminopyridine; B. Mass of perchloric acid; C. Electricity delivered via perchloric acid; D. Additional electricity to reach end-point; E. Total electricity; F. Electrical equivalent per gram; G. Value of Faraday; C = 1972 NBS coulombs						
Molecular weight of 4-aminopyridine = 94.117,02						
A	B	C	D	E	F	G
g.	g.	C	C	C	C/g.	C/mole
1.994,616	26.974,62	2,322.282,64	277.460,64	2,044.822,47	1,025.171,00	96,486.04
2.000,280	28.398,64	2,444,878,50	394.231,91	2,050.646,59	1,025.179,77	96,486.87
2.005,429	26.999,19	2,324.397,90	268.508,52	2,055.889,38	1,025.161,89	96,485.18
2.006,365	31.910,53	2,747.222,01	690.339,41	2,056.882,60	1,025.178,67	96,486.76
2.006,470	27.369,59	2,356.286,16	299.318,70	2,056.967,46	1,025.167,31	96,485.69
2.004,946	25.834,62	2,224.138,45	168.713,83	2,055.424,62	1,025.177,05	<u>96,486.61</u>
Average						96,486.19
Standard deviation of the individual observation						0.67
Standard deviation of the mean						0.27

Table 9. Error budget for the coulometric titrations of 4-aminopyridine performed at NBS

	Anodic Titrations	Cathodic Titrations
EMF standard	0.2 ppm	0.2 ppm
Resistance Standard	0.2	0.2
Time	0.01	0.01
Null point detection	0.1	0.1
Mass	1.0	1.0
Purity	3	3
Molecular Weight	0.3	0.3
End-point detection	7	3
Standardization of perchloric acid	0	2.8
Random error	2.4	2.8

These values were averaged by the weighting method used in Chapter II, Part H, equations (2) through (5); the weighted average is

$$F = 96,486.22(0.50)(5.20 \text{ ppm}) \quad 1972 \text{ NBS coulombs per gram-} \\ \text{equivalent weight}$$

where the values in parentheses, as before, are the standard deviation of the mean expressed in coulombs per gram-equivalent weight and in parts per million, respectively, and include both random and systematic errors.

Most of the systematic errors in the work at the National Bureau of Standards were markedly lower than those in the work at Iowa State University (Chapter II); compare the corresponding values in Tables 5 and 9.

The uncertainty in the electromotive force of the working, unsaturated Weston cell used at the National Bureau of Standards was more than an order of magnitude lower than that of the cell used at Iowa State University. At the Bureau the working cell was calibrated daily against a bank of saturated Weston cells which were in turn calibrated weekly against the working standard of potential of the National Bureau of Standards. At Iowa State University the calibrations made concurrently with the titration work during the winter and spring of 1974 were made with a procedure inherently less accurate, the uncertainty later, in connection with November-December 1974 calibrations of the bank of Weston saturated cells in the Ames Laboratory, being placed by Mr. Wayne A. Rhinehart at 4 ppm. Following the November-December 1974 calibration of the bank of saturated cells in the Ames Laboratory against the traveling standard bank of saturated cells of the National Bureau of Standards,

the method of calibrating cells was greatly improved and cells can now be calibrated at Iowa State University with uncertainty less than 0.5 ppm.

Because the standard resistors in use at Iowa State University and in the laboratory of the Electricity Division of the Bureau were both calibrated at the National Bureau of Standards against the same working standard of resistance of the Bureau, the uncertainties in the corresponding values are identical.

The timing device used at the National Bureau of Standards was tied directly to the national standard time signals. This accounts for the improvement of more than an order of magnitude over the timing device used at Iowa State University.

Because of the method of generating and monitoring the constant current used in the work at the National Bureau of Standards, measurement of potential across the standard resistor was not required, there being no potentiometer in the circuit; however it was necessary to detect a null-point (between the potential of the unsaturated Weston working cell and the potential drop across the standard resistor) and this added an uncertainty of 0.1 ppm.

Improvement in the ability to make mass measurements resulted largely from the use of a more sensitive balance in the weighing of the weight buret in the back-titration method; a semi-micro balance, resolution 0.01 mg., was used rather than an ordinary analytical balance, resolution 0.1 mg. A single-pan microbalance was used at the Bureau for weighing the 4-aminopyridine; this balance was faster and more precise than the double-pan microbalance used at Iowa State University.

Because the 4-aminopyridine titrated in the work at the National Bureau of Standards was prepared in identical fashion to that titrated at Iowa State University, the purity and molecular weight were treated as before. The end-point in each titration at the National Bureau of Standards was located by computer treatment of the data exactly as had been done at Iowa State University; hence the uncertainties remain the same.

The random error in the standardization of the perchloric acid was essentially the same in the work at both institutions, the same being true for the random error in the back-titrations. The reduction in the random error in the anodic titrations by a factor of three was particularly satisfying in that it added support to the validity of the hydrazine-platinum anode method for titrating weak bases. It had been noticed that the current source in the Leeds & Northrup Company "Coulometric Analyzer" used at Iowa State University was beginning to deteriorate during the later stages of the work and finally, after the titrations were completed did require repair (replacement of a capacitor); this could explain the larger scatter reported in the titrations at Iowa State University.

IV. A VALUE FOR THE FARADAY OBTAINED BY COMBINING THE
TITRATIONS MADE AT IOWA STATE UNIVERSITY WITH THOSE
MADE AT THE NATIONAL BUREAU OF STANDARDS

A. Adjustment of Data to the Same Basis

As presented in Chapter II, Part H and in Chapter III, Part G, high-precision coulometric titrations of highly-purified 4-aminopyridine carried out at Iowa State University and at the National Bureau of Standards, at each institution by the same two procedures, have yielded for the faraday the values:

$$F_{\text{ISU}} = 96,486.69(0.81)(8.40 \text{ ppm}) \quad 1972 \text{ NBS coulombs per gram-}$$

$$F_{\text{NBS}} = 96,486.22(0.50)(5.20 \text{ ppm}) \quad 1972 \text{ NBS coulombs per gram-}$$

equivalent weight

equivalent weight

In these expressions, again, the values in parentheses are the standard deviation of the mean expressed in coulombs per gram-equivalent weight and in parts per million, respectively, and include the effects of both random and systematic errors.

Before combining these values it must be noted that these values were calculated using different values for the density of 4-aminopyridine, a value which enters into the calculations through the correction for the buoyant force of air on the 4-aminopyridine during the weighing. The value used at Iowa State University was 1.2695 g./ml., that at the National Bureau of Standards 1.2633 g./ml. Leaving a detailed discussion of these values for Part B, immediately below, it is noted that a recalculation of the data of either series using the other value for the density changes the value for the faraday by 4.3 ppm.

Thus

$$d_{4\text{-aminopyridine}} = 1.2633 \text{ g./ml.}$$

$$F_{\text{ISU}} = 96,486.26 \quad 1972 \text{ NBS coulombs per gram-}$$

$$\text{equivalent weight}$$

$$F_{\text{NBS}} = 96,486.22 \quad 1972 \text{ NBS coulombs per gram-}$$

$$\text{equivalent weight}$$

$$d_{4\text{-aminopyridine}} = 1.2695 \text{ g./ml.}$$

$$F_{\text{ISU}} = 96,486.69 \quad 1972 \text{ NBS coulombs per gram-}$$

$$\text{equivalent weight}$$

$$F_{\text{NBS}} = 96,486.65 \quad 1972 \text{ NBS coulombs per gram-}$$

$$\text{equivalent weight}$$

As of this writing, this problem is unresolved.

Because the standard deviations in these results are not affected by the correction for buoyancy, these values can be averaged by the weighting process given in Chapter II, Part H, equations (2) and (3), in which the averages are combined giving more weight to the measurement having the lowest standard deviation (51, p. 382, equation 10). Applied to the data given above, this weighted average yields for

$$d_{4\text{-aminopyridine}} = 1.2633 \text{ g./ml.}$$

$$F = 96,486.23(0.43)(4.42 \text{ ppm}) \quad 1972 \text{ NBS coulombs per gram-}$$

$$\text{equivalent weight}$$

$$d_{4\text{-aminopyridine}} = 1.2695 \text{ g./ml.}$$

$$F = 96,486.66(0.43)(4.42 \text{ ppm}) \quad 1972 \text{ NBS coulombs per gram-}$$

$$\text{equivalent weight}$$

For comparison, values for the faraday obtained since 1959 are listed in Table 1. The agreement with the value (recalculated to 1972 NBS coulombs) of the dissolution-of-silver experiment of Craig, Hoffman,

Law and Hamer (10) is strikingly good. Nor is the value greatly different from the weighted average of the dissolution-of-silver experiment and the coulometric titrations of benzoic acid and of oxalic acid dihydrate of Marinenko and (J. K.) Taylor as obtained by Cohen and (B. N.) Taylor, Table 1.

The conclusion must be drawn that the work leading to the lower value for the faraday as calculated by Cohen and Taylor (8) from other physical measurements must be reexamined. Alternatively, if the electrochemical value is incorrect, the electrode process in water must be more closely examined for some basic flaw common to such different processes as the anodic dissolution of metallic silver, the anodic generation of hydrogen ions, and the cathodic generation of hydroxyl ions. Establishing a value for the faraday by electrochemistry in a non-aqueous solvent might contribute to the solution to this problem.

B. Density of 4-Aminopyridine

The density of 4-aminopyridine was determined by Hoyle (23) by the pycnometer method using mineral oil as the transfer medium to be 1.2695 g./ml. This value was used in calculating the results of the titrations reported in Chapter II above.

I redetermined the density of 4-aminopyridine while at the National Bureau of Standards. The use of mineral oil proved unsatisfactory; not only does the density of it have a high temperature coefficient, but the material creeps, covers the outside walls of the pycnometer and thus creates problems of cleaning and temperature adjustment. After trials with several other liquids, satisfactory results were obtained

using xylene as the transfer medium. The xylene was first saturated with 4-aminopyridine and filtered through a fine, fritted-glass filter. The interior volume of the pycnometer was determined using distilled water: 10.173,78 ml. (23.3°), standard deviation of the individual observation 0.000,51 ml. (0.05 parts per thousand) (three degrees of freedom). The density of the xylene was determined average, 0.863,30 g./ml. (23.3°), standard deviation of the individual observation 0.000,31 g./ml. (0.36 parts per thousand) (three degrees of freedom). Finally the density of 4-aminopyridine was determined to be 1.2633 g./ml. (23.3°), standard deviation of the individual observation 0.000,6 (0.50 parts per thousand) (fourteen degrees of freedom). The value 1.2633 g./ml. was used in calculating the results of the titrations of 4-aminopyridine made at the National Bureau of Standards, Chapter III above.

Still another value for the density of 4-aminopyridine was obtained by Professor Jon C. Clardy, Department of Chemistry, Iowa State University, from a determination of the crystal structure of 4-aminopyridine by the X-ray diffraction method. The value found, 1.2710 g./ml. is higher than those by the pycnometric method. Professor Clardy estimates the error in his measurement to be less than 0.001 g./ml.

Experiments were made to determine the density of 4-aminopyridine by the flotation method using concentrated solutions of sodium perchlorate. Not only was the procedure tiresome to carry out with the accuracy needed, but it yielded indeterminate results. In the final experiment with a solution having a density of 1.2636 g./ml., the crystals of 4-aminopyridine, after gentle grinding, dissolved slowly and both rose

and fell in the sodium perchlorate solution. Nor was the temperature of the solution sufficiently well controlled.

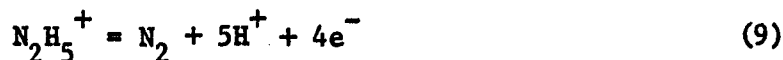
Examination of the crystals of 4-aminopyridine under the polarizing microscope revealed no cavities but the crystals showed gradual extinction over several degrees upon rotating the stage between crossed nicols. This phenomenon is interpreted by Professor Donald L. Biggs, Department of Earth Sciences, Iowa State University, as resulting from strains developed in the long, needle-like crystals, as they grew by sublimation under the force of gravity. Such strains could mean a disordered arrangement of large crystalline aggregates and imply that the effective density of 4-aminopyridine is lower than the X-ray value. On the other hand, the pycnometer methods may be disturbed by microscopic bubbles of air retained on the crystals of 4-aminopyridine, which are lath-like and tend to adhere in bundles.

The problem is an unexpectedly vexing one and in the work of this thesis, no solution to it has been found.

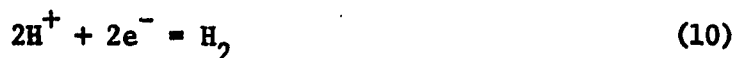
V. THE HYDRAZINE-PLATINUM ANODE

The anodic generation of hydrogen ion in 1.0 M sodium perchlorate on bright platinum is not quantitative. The consequences of this fact with regards to the high-precision, coulometric titrations of bases is discussed at length in the Ph.D. dissertation of W. C. Hoyle (23). Hoyle proposed the use of a "hydrazine-platinum anode" to directly titrate bases coulometrically, the reactions being

at the anode



and at the cathode



I have now shown that the bright platinum anode in sodium hydrazinium sulfate ($\text{Na}(\text{N}_2\text{H}_5)\text{SO}_4$) solution is 100 per cent efficient in the generation of five hydrogen ions per four electrons (equation (9)). Moreover, hydrazine is more readily oxidized than is either THAM or 4-aminopyridine so that the titration of these bases may be carried out directly, that is, with the base dissolved in the solution of sodium hydrazinium sulfate.

As experimental proof of the efficiency of this "hydrazine-platinum anode" for the generation of hydrogen ion I offer the direct, high-precision coulometric titration of THAM and a supplementary analysis of this same material by weight buret titration with perchloric acid, the titration being completed coulometrically and perchloric acid being standardized coulometrically. These titrations were carried out

with the same apparatus and essentially concurrently with titrations of 4-aminopyridine which are reported in Chapter II.

A. Experimental Work

Tris(hydroxymethyl)aminomethane, obtained from a commercial source in the form of large crystals, was ground, dried in a vacuum, again ground, passed through a 100-mesh sieve, and dried in a vacuum over anhydrous magnesium perchlorate. This material was stored over anhydrous magnesium perchlorate; after two weeks there was no further loss in weight. Microscopic examination showed the presence of voids, some containing liquid, in this material (Chapter VI).

Sodium Hydrazinium Sulfate ($\text{Na}(\text{N}_2\text{H}_5)\text{SO}_4$), 0.25 M. Commercial hydrazine sulfate ($\text{N}_2\text{H}_6\text{SO}_4$) was recrystallized from 3 M sulfuric acid. This material was dissolved in 1.0 M sodium perchlorate and the pH brought to 4.5 by the addition of carbonate-free sodium hydroxide. The solution was made 0.25 M in sodium hydrazinium sulfate by diluting with 1.0 M sodium perchlorate.

The high-precision coulometric titrations of THAM were carried out with the apparatus used for the high-precision titrations of 4-aminopyridine (Chapter II); the calibrations of the standards of mass, potential, resistance, and time were the ones used in that work.

Titration of THAM. High-precision titrations of the lot of THAM prepared as described above were carried out two ways: (1) using the new hydrazine-platinum anode, and (2) by the addition of a weighed amount of perchloric acid in slight excess and back-titration at a platinum cathode and coulometric standardization of the perchloric acid. The

procedures followed were identical with those used in titrations of high-purity 4-aminopyridine, described in Chapter II of this work, and indeed the titrations were carried out as part of a sequence involving the repeated calibration of the standard of potential and the titrations of the two bases. Weighings were corrected to weight in vacuum using for the density of THAM 1.32 (found by the pycnometer method using benzene, 1.3184). In calculating the purity of the THAM, the value used for the molecular weight, $C_4H_{11}O_3N = 121.137,2$, was calculated from the atomic weights involved as selected by Hoyle (23). The value for the faraday used, $F = 96,486.23$ 1972 NBS coulombs/mole is the value calculated in Chapter IV.

The results of the titrations of THAM are given in Tables 10 and 11.

The great attention paid to calibrations and techniques in this work is not necessary for work in which allowable error is 1 in 10^3 or 10^4 and the following recommended procedure is written for the more general user of the hydrazine-platinum anode.

B. Recommended Procedure

Use a constant current source, current measuring device, and timing device such as those in the "Coulometric Analyzer" of the Leeds & Northrup Company (14). Use a partition cell such as the one described by Taylor and Smith (52) or the more convenient one of Eckfeldt and Shaffer (14) and Knoeck and Diehl (25, 26). In the titration cell place 100 ml. of a solution 0.25 M in sodium hydrazinium sulfate and 1 M in sodium perchlorate, and a magnetic stirring bar. Charge the

Table 10. Coulometric titration of tris(hydroxymethyl)aminomethane (THAM) with acid generated at the hydrazine-platinum anode

Mass of THAM g.	Mol. Wt. THAM: 121.137,2 Quantity of electricity 1972 NBS coulombs	Faraday: 96,486.23 Electrical equivalent per gram = (5/4)It/mass 1972 NBS coulombs/g.	Purity of THAM Per Cent
2.999,967,3	1,910.022,8	795.851,50	99.918,09
2.999,586,0	1,909.587,8	795.771,38	99.908,03
3.001,108,3	1,910.845,2	795.891,47	99.923,11
3.000,811,1	1,910.670,5	795.897,51	99.923,86
3.004,788,2	1,912.963,9	795.798,11	99.911,38
3.002,499,5	1,911.610,3	795.841,19	<u>99.916,79</u>
	Average		99.916,88
	Standard deviation of the individual observation		0.006,29
	Standard deviation of the mean		0.002,57

Table 11. Titration of tris(hydroxymethyl)aminomethane (THAM) with perchloric acid (coulometric end-point) and standardization of perchloric acid coulometrically

Mass of perchloric acid g.	Standardization of perchloric acid	
	Quantity of electricity 1972 NBS coulombs	Concentration of perchloric acid 1972 NBS coulombs/g.
25.172,1	2,190.428,0	87.018,087
25.898,5	2,253.676,9	87.019,591
25.842,4	2,248.743,3	87.017,587
30.823,4	2,682.211,2	87.018,667
20.165,9	1,754.802,4	87.018,303
20.163,0	1,754.566,2	<u>87.019,104</u>
	Average	87.018,556
	Standard deviation of the individual observation	0.000,722
	Standard deviation of the mean	0.000,295

Table 11. (Continued)

Titration of Tris(hydroxymethyl)aminomethane						
Heading of columns: A. Mass of THAM; B. Mass of perchloric acid; C. Electricity delivered via perchloric acid; D. Additional electricity to reach end-point; E. Total electricity; F. Electrical equivalent per gram; G. Purity of THAM; C = 1972 NBS coulombs						
Mol. Wt. THAM: 121.137,2 Faraday: 96,486.23 C/mole						
A	B	C	D	E	F	G
g.	g.	C	C	C	C/g.	Per Cent
2.756,567,9	28.361,1	2,467.941,9	274.006,0	2,193.935,9	795.894,01	99.923,42
3.195,546,9	30.213,7	2,629.152,5	86.128,5	2,543,024,0	795.802,43	99.911,93
2.953,802,6	28.373,3	2,469.003,5	118.233,9	2,350.769,6	795.845,19	99.917,30
2.783,249,8	27.123,5	2,360.247,8	145.074,5	2,215.173,3	795.894,53	99.923,49
2.706,079,7	26.787,7	2,331.026,9	177.478,6	2,153.548,3	795.818,50	99.913,94
2.768,352,2	25.858,0	2,250.125,8	47.179,8	2,202.946,0	795.760,74	99.906,69
3.054,526,9	29.991,0	2,609.773,5	178.938,8	2,430.834,7	795.813,81	<u>99.913,36</u>
Average						99.915,73
Standard deviation of the individual observation						0.006,15
Standard deviation of the mean						0.002,32

intermediate chamber with 7.5 M sodium perchlorate and the counter electrode chamber with 1 M sodium perchlorate. Pass nitrogen through the liquid and the cell to remove carbon dioxide and oxygen. Electrolyze this solution making the working electrode anodic or cathodic as required to bring the pH to 4.5. Add the weighed sample of the base to be titrated to the solution. Electrolyze anodically, recording the current and time. (Many commercial coulometers have direct read-out in number of microequivalents passed, making current-time integration unnecessary. However, for high-precision work a current-sensing resistor, potentiometer and an accurate time-interval counter are essential.) When the pH of the solution reaches 5.5, interrupt the titration and rinse the walls of the titration chamber with distilled water. Continue the titration, preferably with a smaller current delivered in increments of 1 or 2 microequivalents. After each increment of current, allow sufficient time for the solution to equilibrate before reading the pH meter. The end-point will fall close to pH 4.5. Plot pH versus microequivalents to determine the end-point.

C. Results and Discussion

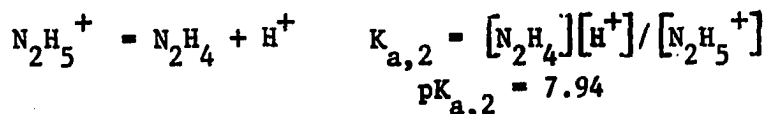
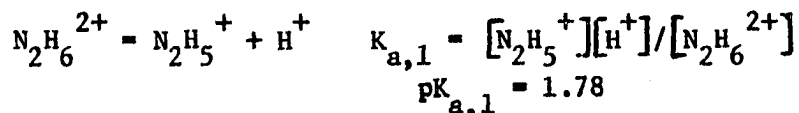
That the hydrazine-platinum anode is completely efficient for the generation of five hydrogen ions for each four electrons passed is borne out by the results obtained in the titration of THAM, Table 10, the purity of the particular lot of THAM analyzed having been established by titration with perchloric acid in turn standardized coulometrically, Table 11.

The standard reduction potential for the hydrazine-nitrogen couple (Equation (9)) was calculated by Latimer (30) from thermodynamic data to be -0.23 V. Even allowing for variation in the single electrode potential of the anode as the acidity increases starting from pH 5, during the generation of hydrogen ion this potential is over a volt negative to the region of oxygen overvoltage on bright platinum dipping into sulfate or perchlorate electrolytes; thus, it is highly unlikely that either oxygen or peroxydisulfate will be formed at bright platinum dipping in hydrazine sulfate. A direct measurement of the potential of a bright, platinum, working electrode dipping into 0.25 M sodium hydrazinium sulfate was made (23), current density 2.6 mA per cm^2 . The platinum anode was slightly positive to the s.c.e.:

pH	3.75	4.00	4.25	4.50	4.75	4.88	5.00	5.25	5.50	6.60
E, mV	15.6	13.1	11.1	10.8	9.0	8.8	8.0	4.8	1.0	-25.0

These values are in rough agreement with somewhat similar measurements made by Lingane and Jones (31) who used hydrazine as an anodic depolarizer in the controlled cathode potential deposition of copper from a tartrate solution. The ease with which bases are attacked anodically varies and each candidate for titration must be considered individually. In general the formation of amine oxides and oxidative degradation requires a high potential and probably it will be found that most amines can be titrated successfully with the hydrazine-platinum anode.

To obviate the confusion which appears in the literature on the dissociation constants of hydrazine I adopt the designations



The value for $K_{a,1}$ was obtained from a potentiometric titration of hydrazine sulfate ($\text{N}_2\text{H}_6\text{SO}_4$) with sodium hydroxide; found at mid-point, $\text{pH} = 1.75, 1.81$, average 1.78 (concentration of salt and acid at this point each about 0.10 M). This is in poor agreement with the value of Gilbert (19), expressed as dissociation as a base, of 8.9×10^{-6} but in fair agreement with that of Kolthoff and Stenger (28) of 3×10^{-13} . The value for $K_{a,2}$ is the average of the three best values reported by Bjerrum, Schwarzenbach and Sillen (6) (8.7×10^{-7} expressed as dissociation as a base ($pK_{b,2} = 6.06$)). Using these values and the usual method of calculating the pH at the equivalence-point in the titration of the first replaceable hydrogen ion of a dibasic acid, the potential at the first equivalence-point should be $(1/2)(pK_{a,1} + pK_{a,2}) = 4.86$. Found in precise coulometric titrations, 4.48. The discrepancy is probably due to the high ionic strength of the electrolyte in the coulometric titrations.

The dissociation constant of THAM as an acid is $K_{a,\text{THAM}} = 8.08$, close to the second ionization constant of hydrazine, $K_{a,2} = 7.94$. The two bases should be neutralized together on titration. In practice only one end-point was found, at $\text{pH} 4.31$. The hydrazine was present as N_2H_5^+ before and after the titration and the hydrogen ion was used to neutralize the THAM. Similarly the dissociation constant as an acid of 4-amino-

pyridine is 9.37; as with THAM only one point of inflection was found, falling in various titrations between 4.44 and 4.66. In general then, it should be possible to titrate coulometrically with the hydrazine-platinum anode any base having a dissociation constant as a base greater than 10^{-6} or perhaps 10^{-7} .

VI. TRIS (HYDROXYMETHYL)AMINOMETHANE, A PRIMARY STANDARD?

In light of the number of times that tris(hydroxymethyl)aminomethane ("THAM", "tris", etc.) has been proposed or used as a primary standard base (18, 22, 32, 42, 44, 55, 56, 57); to express even a bit of doubt would seem to be the science equivalent of attacking motherhood or extolling the virtues of sin. Values for the purity of "reagent grade" and "primary standard" THAM obtained at Iowa State University during recent years, however, have been so uniformly low and variable that all careful workers should exercise wariness if not downright cynicism toward statements on bottles of the material. The reason is not hard to find. Crystals of THAM invariably contain large inclusions of mother liquor. Cavities in crystals of THAM are readily seen under the microscope and, in many meniscuses can be observed, Figures 5-8. I have found the amount of mother liquor so enclosed to be as much as 0.7 per cent, surely almost a record for any chemical; potassium dichromate, SRM 136b of the National Bureau of Standards, has been shown to contain about 250 ppm of water (Knoeck and Diehl (25, 26), Svec and Conzemius (48)). The only way to beat this game is to grind the THAM, pass it through a 100-mesh sieve and dry it in a vacuum desiccator over anhydrous magnesium perchlorate. If this is done, in this sequence, material of quite satisfactory purity can be obtained. Usually, to prevent the formation of a gum, the first grinding must be light and the material dried in vacuum before proceeding.

A. Examination and Reworking of One Lot of THAM

Tris(hydroxymethyl)aminomethane obtained from Fisher Scientific Company, Lot Number 731756, was titrated with standard acid by the usual volumetric technique using methyl red as indicator; found 99.3 per cent purity.

The material was ground, dried in a vacuum, then again ground. It was then sifted through a 100-mesh sieve and dried in a vacuum at room temperature over anhydrous magnesium perchlorate. The loss in weight in the final drying operation (48 hours) was 0.11 per cent. This material was subjected to a high-precision coulometric analysis, the details of which are given in Chapters II and V. Found by titration with perchloric acid (coulometric titration of excess acid and coulometric standardization of the acid): 99.9234, 99.9119, 99.9173, 99.9235, 99.9139, 99.9067, 99.9134, average 99.9157 per cent THAM, standard deviation 0.0062.

B. Microscopic Examination

The cavities in the crystals of THAM formed from water-methanol mixtures are readily seen under the microscope to be numerous, elongated with rough irregular sides, and frequently partially filled with mother liquor, Figures 5 through 8. The meniscus of the mother liquor is concave down (resembling that of mercury in a glass tube). When crystals on the microscope slide are covered with a drop of water, the crystals dissolve at an observable rate and when the end of one of the cavities is exposed water shoots into the cavity with speed. It had been earlier reported by Rose and Van Camp (43) that the crystals of THAM lose birefringence at 135° ; I confirmed this but on the electrically heated

- Figure 5. Two cavities in a single crystal of THAM. Plane of focus is below the surface of the crystal. The tips of the cavities, at left, are in focus; the cavities are inclined down to the right. 100X. Polarized-analyzed light
- Figure 6. Same as Fig. 5 but plane of focus lower to bring the meniscus in the upper cavity into focus. Note the inverted meniscus. 100X. Polarized-analyzed light
- Figure 7. Large cavities in a single crystal of THAM. Liquid partially filling the cavities shows darker than the crystalline material. 100X Polarized-analyzed light
- Figure 8. Single large crystal of THAM showing typical distribution of size of cavities

Photomicrographs were taken by Professor Donald L. Biggs,
Department of Earth Science, Iowa State University

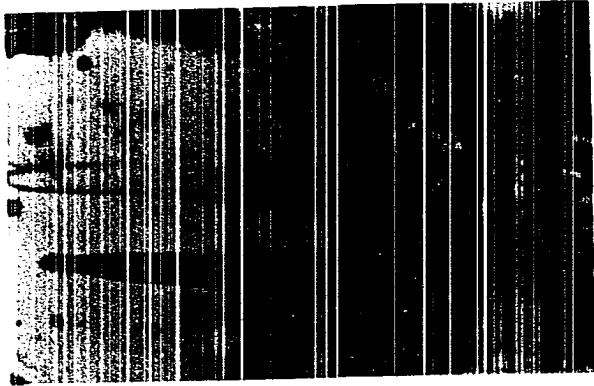


Figure 5

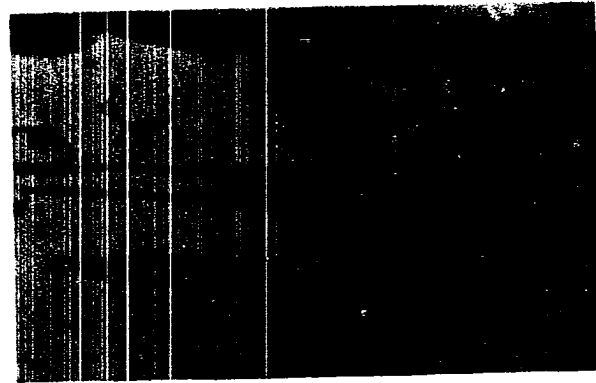


Figure 6

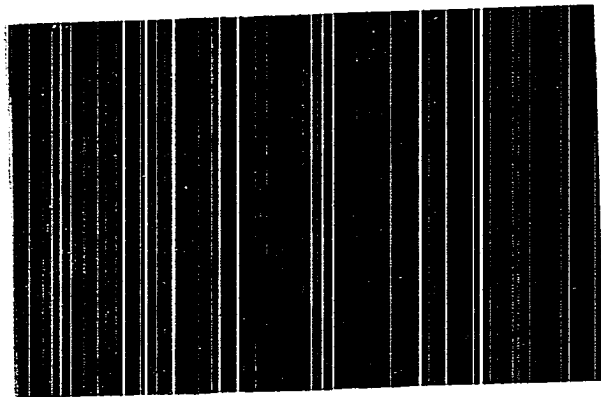


Figure 7

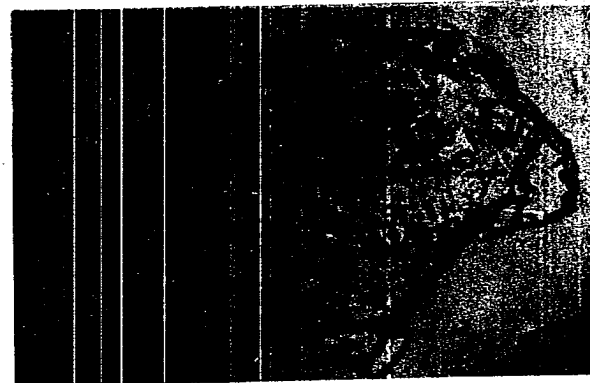


Figure 8

stage the change took place at 149° and reversion at 124° . The crystals were not shattered at these temperatures by the vapor pressure of the trapped mother liquor. Even the crystals of THAM which had passed a 100-mesh screen were observed to hold cavities.

THAM heated on the microscope stage underwent decomposition but also sublimation, forming dendritic growths on the cover glass. The dendritic growths consisted of very small crystals packed closely about a central trunk. Each tiny crystal was birefringent but at different positions of the stage and the whole gave a pretty, Christmas tree effect. The sublimed material was proved by infrared spectroscopy and by X-ray powder diffraction pattern to be THAM and this led directly to the large scale sublimation experiments described below.

C. Behavior on Drying

Large crystals of THAM and material ground and sifted through a 100-mesh sieve were heated in an oven to successively higher temperatures. The ground material turned yellow at 100° , and at 140° obviously had undergone far more extensive deterioration than the coarse crystals. The deterioration was obviously oxidation by air and this proceeded more rapidly with fine than with coarse material.

D. Sublimation of THAM in Nitrogen

The sublimation apparatus used by Hoyle (23) for purifying 4-aminopyridine was used. The flask was imbedded in copper shot in an electric heating mantle. At a temperature of 140° the THAM was present as a clear, colorless liquid and a few large crystals formed in the upper

portion of the flask, the gooseneck, and the air condenser. The sublimation was very slow, only a very small amount of crystalline sublimate was obtained, decomposition set in after twenty to thirty hours, and this approach was given up.

E. Loss in Weight on Melting in an Atmosphere of Nitrogen

A sample of THAM as received (large crystals, Fisher Lot 73156, 99.3 per cent pure) in a weighing bottle was placed in the flask of the sublimation apparatus mentioned above, the air in the flask replaced by nitrogen, and the flask heated. The material melted at about 140° (reported and confirmed by my experience on a heated microscope stage, 172°). The material was immediately cooled and weighed. The loss in weight was 0.67 per cent. Traces of THAM appeared as sublimate on the gooseneck and air condenser of the apparatus during this experiment; this was recovered by washing with water. From the pH, 9.4, the volume of the wash water, and the dissociation constant of THAM, the amount of THAM so sublimed was calculated to be 4.2 mg or 0.02 per cent of the original weight of 22.11 g. Thus, of the loss in weight 0.65 per cent can be attributed to liquid trapped in the crystals.

F. Comment

Although the THAM ground and sifted through a 100-mesh sieve, 99.915,7 per cent pure in this lot, would be satisfactory as a primary standard for most work, it could hardly be considered a primary standard in a class with potassium acid phthalate and 4-aminopyridine. The 843 ppm of impurity is probably mostly mother liquor and the variability

in the results reported above, standard deviation 62 ppm, is further evidence of this (compare the standard deviation of 5.9 ppm for similar, concurrent work with 4-aminopyridine).

It would indeed be curious if a disparity between reality and reputation of the size reported here should have escaped notice completely; even with the limitation of 1 part in 1000 imposed by the use of volumetric burets by previous workers the discrepancy should have been observed. Actually it had, but it is necessary to read the fine print to find a report of it. In the very first paper on the use of THAM as a primary standard, Fossum, Markunas and Riddick (18), in describing the purification of THAM, direct that the material be ground to pass a 50-mesh screen and be dried in a vacuum of lower than 10 to 15 mm pressure for 12 hours at 60°. The consequences of not grinding the material are nowhere pointed out and the unqualified sentence in the abstract accompanying the paper states that the material can be dried by heating at 100° to 103°. Without prior grinding this simply is not true. Pressure of the vaporizing mother liquor trapped in the crystals of THAM is not sufficient to shatter the crystals even at the melting point; before that temperature, decomposition sets in, a fact reported by Fossum, Markunas and Riddick (18) (at 110°) and a finding I confirm. Decomposition begins at even lower temperature for 100-mesh material.

One of the original authors, Riddick (42), ten years after the publication of the first paper, in a review of the virtues of THAM as a primary standard lists ten merits of the material but singularly

fails to issue prominently the warning that it must be ground, sifted, and dried. Riddick analyzed four commercial preparations of "purified" THAM. Preparations I and II were finely ground materials for which purities of 99.98 and 99.96 per cent were found. Preparations III and IV gave low results until ground. Riddick reported in a footnote that sixteen analyses of preparation IV as received gave results for the purity ranging from 99.32 to 99.79 per cent. In the text Riddick added briefly that in the original study it had been observed that "large crystals analyzed low", and "it is believed that solvent is trapped in the large crystals".

While Fossum, Markunas and Riddick may be criticized for not pointing out prominently the need for grinding, others have said nothing about grinding, being unaware of the problem, ignoring it, or possibly doing what was necessary without comment and reporting their own work on the assumption that others would do the same. There are at least seven of these: Whitehead (55) who simply called attention to the existence of the material and compared the titration curves of THAM and sodium carbonate; Williams and Harley (56) who proposed THAM as a primary standard for non-aqueous titrimetry and compared the titration curves of THAM, potassium acid phthalate, and diphenylguanidine with 0.1 N perchloric acid in acetic acid; Ruch and Critchfield (44) who used it as primary standard for standardizing perchloric acid in Methyl Cellosolve used for the titration of amines; Holler (22) who used it as a standard and titrant in the combustion-acidimetric determination for thermometric titration calorimetry. Even Bates and Hetzler

(4), who laid to rest the false notion that solutions of THAM do not absorb carbon dioxide from the atmosphere, appear to have bought the idea that THAM need only be dried at 100° to 103°.

Analyses of the five lots of THAM which became SRM 723 were made by Marinenko (32) at the National Bureau of Standards by the addition of a weighed amount of sulfuric acid, coulometric titration of the excess sulfuric acid, and coulometric standardization of the sulfuric acid. The average of 30 determinations of the purity was 99.9690 per cent with a standard deviation of the individual results of 8.1 parts per 100,000. In neither Marinenko's report nor the certificate which accompanies SRM 723 is anything said about grinding the material. Marinenko states that the material taken for analysis was dried at 70° in a vacuum oven, weighed, corrected to weight in vacuum, and titrated; no mention is made of grinding prior to drying although this was probably done by the manufacturer (Sigma Chemical Company, St. Louis, Missouri). Presumably the same concern extends to SRM 724a, recommended as a calorimetric standard (7, 39), inasmuch as SRM 724a came from the same lot of material as SRM 723, the basimetric standard.

My own examination of SRM 723 indicated that although the crystals are small, cavities are present. SRM 723, dried in a vacuum over magnesium perchlorate for two weeks but otherwise analyzed as received, was titrated coulometrically using the hydrazine-platinum anode; the titrations were made as a part of the sequence of titrations made to prove the efficiency of the hydrazine-platinum anode. The average of the three titrations (Table 12) was 99.967,8; the range, 37 ppm, and

Table 12. Coulometric titration of SRM 723 tris(hydroxymethyl)aminomethane. Hydrazine-platinum anode method

Mass of THAM g.	Mol. Wt. THAM: 121.137,2 Quantity of electricity 1972 NBS coulombs	Faraday: 96,486.23 1972 NBS coulombs/mole Electrical equivalent per gram = (5/4)It/mass 1972 NBS coulombs/g.	Purity of THAM Per Cent
3.000,002,1	1,911.023,9	796.259,37	99.969,30
3.005,708,8	1,914.646,0	796.253,94	99.968,61
3.004,905,5	1,914.075,9	796.229,63	<u>99.965,56</u>
		Average	99.967,82
		Range	0.003,74

the difference between this value and the Marinenko value, 12 ppm are both less than the standard deviation reported by Marinenko or that reported above for a different lot of THAM.

Still another use of THAM as a calorimetric standard was made by Irving and Wadso (24) who went to considerable trouble to purify their material by the usual water-methanol recrystallization but then used the crystalline material which passed through a 50-mesh sieve but was retained on 100-mesh and was then dried at 80° and finally in a vacuum; no analyses are reported.

About the only workers who have not bought the primary standard myth are Datta, Grzybowski and Weston (11) who found their material by titration to be 99.594 and 99.830, average 99.71 per cent pure (after recrystallization from water-methanol: 99.870, 99.656, average 99.76 per cent) and took this into consideration in their measurement of the dissociation constant.

In the extensive use of THAM and its hydrochloride as a biological buffer (see for example the various papers published in the Annals of the New York Academy of Science (9) following a conference) it is probably immaterial whether occluded water and methanol are taken into account. Such neglect, however, may not be excusable in the careful calibration of buffers in water and water-methanol mixtures such as those carried out by Bates and co-workers (3, 5, 58).

VII. LOCATION OF END-POINTS IN HIGH-PRECISION COULOMETRY

A. Background

Location of the end-point is currently the least accurately known of the variables in high-precision coulometry, the other quantities, weight, potential, resistance, time and molecular weight, being measurable or known to two or three parts per million. The constant current used in such titrations is cut back to a low value, 0.5 to 10 mA, in the region of the end-point and the problem of detecting the end-point is that commonly experienced in titrating with very dilute standard solutions, albeit under the favorable circumstance that no increase in volume occurs. In the titration of weak acids or weak bases, the titration curve under such conditions becomes almost linear in the neighborhood of the end-point and the location of the point of inflection by eye assumes the subjective features of a betting game. Although the "placing of equal bets" has received some sanction in the realistic assessment of the error of measurement in work involving the determination of values of the fundamental physical constants (37), the end-point location problem is obviously one in which application of theoretical and mathematical tools might well prove useful.

Yan (59) in a recent paper refers to Fortuin (17) and the latter in turn supplies a good bibliography to the earlier papers on the subject, principally to works of Kolthoff and of Hahn. The approach of these workers is essentially that of making plots of the first derivative and of obtaining data directly in difference form.

Yan, in the paper just cited, by an elegant finite difference approach based on the assumption that the curve of pH versus moles of titrant could be approximated by a third order polynomial (cubic equation), developed a neat and rapid numerical method utilizing four sets of data chosen symmetrically about the end-point. The selection of a cubic by Yan was made simply because the cubic is the simplest equation having an inflection point, but it has no theoretical basis. It should be noted that although a cubic equation is symmetric about its point of inflection, titration curves are not symmetric, except in a very narrow region. This is made evident by examination of titration curves and a few simple manipulations with tracing paper; work for example with the various curves in Diehl, Quantitative Analysis (13, Chapter 10, pp. 131-154); the data points are not shown but each curve is a careful tracing through actual experimental data. Yan's method is a neat procedure and my own feeling, after applying it to the drawn out end-point data in various, high-precision titrations, is that it is considerably better than eyeballing. However, only four data points per titration are used and there is some dependence on the selection of these. The questions naturally arise: Can one do better using all of the data points? Is the cubic equation the best to use? How well does a cubic fit the experimental data?

The IBM 360/65 computer and the subroutine OPLSPA, developed by the Computer Services Group of the United States Atomic Energy Commission, Ames Laboratory, Ames, Iowa, which fits polynomials up to tenth order to experimental data, makes the above questions easy to test.

The programs were tested on five different coulometric titrations: titrations of tris(hydroxymethyl)aminomethane (THAM) and of 4-aminopyridine by addition of excess perchloric acid and back titration with alkali generated at the cathode; titrations of tris(hydroxymethyl)-aminomethane and of 4-aminopyridine with acid generated at the newly devised hydrazine-platinum anode, and titrations of perchloric acid alone with alkali generated at the cathode. The data were entered into two different programs, each given below (Figures 9 and 10), in which the independent and dependent variables were reversed. The fit was excellent for the titrations involving tris(hydroxymethyl)-aminomethane and 4-aminopyridine. The agreement between Programs A and B (reversal of the independent and dependent variables) was excellent. Agreement with Yan's method was only fairly good, Table 13. However, the method failed for the titrations of perchloric acid, the calculated equations simply not being even a reasonably good fit. Fifth order equations proved no better.

It must be pointed out again that the data being handled was within 30 microequivalents of the end-point and in the titration of perchloric acid within 3.5 pH units of the end-point, a region in which it was difficult to secure many data points. Again also, departure of an experimental titration curve from a cubic was most marked for strong acids and bases.

B. Computer Programs

In Program A, pH is obtained as a cubic function of time:

$$\text{pH} = Q_1 + Q_2(\text{time}) + Q_3(\text{time})^2 + Q_4(\text{time})^3.$$

Table 13. Comparison of end-points obtained by computer programs A and B and method of Yan. Data from various titrations

Titration	pH = f(time) sec.	Time = f(pH) sec.	Yan sec.
4-Aminopyridine, cathodic ^a	236.69	236.61	230.18
4-Aminopyridine, anodic ^b	206.90	206.21	208.47
Tris(hydroxymethyl)amino- methane, cathodic ^a	218.58	218.18	213.91
Tris(hydroxymethyl)amino- methane, anodic ^b	572.49	573.08	579.09
Perchloric acid, cathodic ^c	296.54	862.16	854.53

^aBack titration of excess standard perchloric acid with alkali generated at a platinum cathode.

^bTitration with acid generated at the hydrazine-platinum anode.

^cDirect titration with alkali generated at a platinum cathode.


```

//FORT.SYSIN DD *
C      PROGRAM A
C      THIS PROGRAM FITS TITRATION DATA TO A CUBIC EQUATION,
C      USING A SUBROUTINE DEVISED BY THE AMES LABORATORY
C      COMPUTER SERVICE. THE ENDPOINT IS DETERMINED BY SETTING
C      THE SECOND DERIVATIVE OF THE COMPUTED CUBIC EQUATION
C      EQUAL TO ZERO AND SOLVING FOR THE INDEPENDENT VARIABLE.
C      THE PRINT-OUT INCLUDES: (1) THE COEFFICIENTS OF THE
C      CUBIC, (2) A LISTING OF THE INPUTTED VALUES, (3) A
C      LISTING OF THE CALCULATED VALUES OF THE DEPENDENT
C      VARIABLE FOR EACH DATA POINT, (4) THE TIME AT THE
C      ENDPOINT, (5) THE PH AT THE ENDPOINT, AND (6) THE SLOPE
C      AT THE ENDPOINT.
C      THE FORM OF THE CUBIC EQUATION IS:
C      PH = Q(1) + Q(2)*TIME + Q(3)*TIME**2 + Q(4)*TIME**3
C
      DIMENSION X(50),Y(50),W(50),YCALC(50),NAME(20)
      DOUBLE PRECISION Q(10)
      DATA W/50*1.0/
      READ(5,120) NSETS
120  FORMAT(I2)
      DO 500 K=1,NSETS
      READ(5,100)(NAME(I),I=1,20)
100  FORMAT(20A4)
      WRITE(6,110)(NAME(I),I=1,20)
110  FORMAT('1',20A4)
      WRITE(6,115)
115  FORMAT(1X,'PH = Q(1) + Q(2)*T + Q(3)*T**2 + Q(4)*T**3')
      NDEG=3
      NQ=NDEG+1
      TUWYLO=0.0
      J=0
125  J=J+1
      READ(5,130) X(J),Y(J)
130  FORMAT(F7.2,F6.3)
      IF(X(J).LT.0.0) GO TO 140
      GO TO 125

```

Figure 9. Computer program A

```

140 NPTS=J-1
    CALL OPLSPA(NDEG,NPTS,X,Y,W,Q,TUWYLO)
C
C   OPLSPA SUBROUTINE
C   NDEG = DEGREE OF POLYNOMIAL (1.LT.NDEG.LT.10)
C   NPTS = NUMBER OF DATA POINTS
C   X = TIME IN SECONDS (INDEPENDENT VARIABLE)
C   Y = PH (DEPENDENT VARIABLE)
C   W = WEIGHTING FACTOR
C   Q = THE OUTPUT, A DOUBLE PRECISION ARRAY OF COEFFICIENTS
C   TUWYLO = 0.0 UNLESS LOOP THROUGH DIFFERENT NDEG'S
C   Y = Q(1) + Q(2)X + Q(3)X**2 + Q(4)X**3
C
    WRITE(6,200)(I,Q(I),I=1,NQ)
200 FORMAT(1X,' Q(',I1,') = ',E15.8)
    DO 210 I=1,NPTS
        YCALC(I)=Q(1)+Q(2)*X(I)+Q(3)*X(I)**2+Q(4)*X(I)**3
210 CONTINUE
    WRITE(6,230) (I,X(I),Y(I),YCALC(I),I=1,NPTS)
230 FORMAT(1X,' I = ',I2.4X,' TIME = ',F7.2,3X,' PH = ',F6.3,
&4X,' PHCALC = ',F6.3)
        ENDPT=-Q(3)/(3.0*Q(4))
        ENDPH=Q(1)+Q(2)*ENDPT+Q(3)*ENDPT**2+Q(4)*ENDPT**3
        SLOPE=Q(2)+2.0*Q(3)*ENDPT+3.0*Q(4)*ENDPT**2
        WRITE(6,240)ENDPT,ENDPH,SLOPE
240 FORMAT(1X,' TIME AT ENDPOINT = ',F7.2,6X,' PH AT ENDPOINT'
&,' = ',F6.3, '// ' SLOPE AT ENDPOINT = ',E13.6,' PH/SEC')
        CALL GRAPH(NPTS, X,Y,3,7,7.0,5.0,0.0,0.0,0.0,0.0,
&'TIME;', 'PH;', NAME, ' PH = F(TIME);')
        CALL GRAPHS(NPTS,X,YCALC,0,2,' ;')
        CALL GRAPHS(1,ENDPT,ENDPH,1,7,' ;')
500 CONTINUE
    STOP
    END
//GO.SYSIN DD *
1
N2H5+/PT 4-AP K2: 81

```

Figure 9. (Continued)

0.00	5.072
20.00	5.040
40.02	5.000
60.01	4.962
80.03	4.922
100.07	4.880
120.00	4.830
139.83	4.780
160.01	4.722
180.02	4.668
199.95	4.610
219.99	4.549
240.01	4.491
260.07	4.438
280.14	4.384
300.16	4.331
320.14	4.285
340.21	4.240
360.27	4.201
380.13	4.164
400.10	4.130
420.02	4.098
-1.0	

Figure 9. (Continued)

```

//FORT.SYSIN DD *
C      PROGRAM B
C      THIS PROGRAM FITS TITRATION DATA TO A CUBIC EQUATION,
C      USING A SUBROUTINE DEvised BY THE AMES LABORATORY
C      COMPUTER SERVICE. THE ENDPOINT IS DETERMINED BY SETTING
C      THE SECOND DERIVATIVE OF THE COMPUTED CUBIC EQUATION
C      EQUAL TO ZERO AND SOLVING FOR THE INDEPENDENT VARIABLE.
C      THE PRINT-OUT INCLUDES: (1) THE COEFFICIENTS OF THE
C      CUBIC, (2) A LISTING OF THE INPUTTED VALUES, (3) A
C      LISTING OF THE CALCULATED VALUES OF THE DEPENDENT
C      VARIABLE FOR EACH DATA POINT, (4) THE TIME AT THE
C      ENDPOINT, (5) THE PH AT THE ENDPOINT, AND (6) THE SLOPE
C      AT THE ENDPOINT.
C      THE FORM OF THE CUBIC EQUATION IS:
C      TIME = Q(1) + Q(2)*PH + Q(3)*PH**2 + Q(4)*PH**3
C
      DIMENSION X(50),Y(50),W(50),YCALC(50),NAME(20)
      DOUBLE PRECISION Q(10)
      DATA W/50*1.0/
      READ(5,120) NSETS
120  FORMAT(I2)
      DO 500 K=1,NSETS
      READ(5,100)(NAME(I),I=1,20)
100  FORMAT(20A4)
      WRITE(6,110)(NAME(I),I=1,20)
110  FORMAT('1',20A4)
      WRITE(6,115)
115  FORMAT(1X,'T = Q(1) + Q(2)*PH + Q(3)*PH**2 + Q(4)*PH**3')
      NDEG=3
      NQ=NDEG+1
      TUWYLO=0.0
      J=0
125  J=J+1
      READ(5,130) Y(J),X(J)
130  FORMAT(F7.2,F6.3)
      IF(Y(J).LT.0.0) GO TO 140
      GO TO 125

```

Figure 10. Computer program B

```

140 NPTS=J-1
    CALL OPLSPA(NDEG,NPTS,X,Y,W,Q,TUWYLO)
C
C   OPLSPA SUBROUTINE
C   NDEG = DEGREE OF POLYNOMIAL (1.LT.NDEG.LT.10)
C   NPTS = NUMBER OF DATA POINTS
C   X = PH (INDEPENDENT VARIABLE)
C   Y = TIME IN SECONDS (DEPENDENT VARIABLE)
C   W = WEIGHTING FACTOR
C   Q = THE OUTPUT, A DOUBLE PRECISION ARRAY OF COEFFICIENTS
C   TUWYLO = 0.0 UNLESS LOOP THROUGH DIFFERENT NDEG'S
C   Y = Q(1) + Q(2)X + Q(3)X**2 + Q(4)X**3
C
    WRITE(6,200) (I,Q(I),I=1,NQ)
200 FORMAT(1X,' Q(',I1,') = ',E15.8)
    DO 210 I=1,NPTS
        YCALC(I)=Q(1)+Q(2)*X(I)+Q(3)*X(I)**2+Q(4)*X(I)**3
210 CONTINUE
    WRITE(6,230) (I,X(I),Y(I),YCALC(I),I=1,NPTS)
230 FORMAT(1X,' I = ',I2,4X,' PH = ',F6.3,4X,' TIME = ',F7.2,
&3X,' YCALC = ',F7.2)
    ENDPH=-Q(3)/(3.0*Q(4))
    ENDPT=Q(1)+Q(2)*ENDPH+Q(3)*ENDPH**2+Q(4)*ENDPH**3
    SLOPE=Q(2)+2.0*Q(3)*ENDPH+3.0*Q(4)*ENDPH**2
    SLOPE=1./SLOPE
    WRITE(6,240)ENDPT,ENDPH,SLOPE
240 FORMAT(1X,' TIME AT ENDPOINT = ',F7.2,6X,' PH AT ENDPOINT'
&,' = ',F6.3, //' SLOPE AT ENDPOINT = ',E13.6,' PH/SEC')
    CALL GRAPH(NPTS, Y,X,3,7,7.0,5.0,0.0,0.0,0.0,0.0)
&' TIME;', 'PH;', 'NAME,' TIME = F(PH);')
    CALL GRAPHS(NPTS,YCALC,X,0,2,' ;')
    CALL GRAPHS(1,ENDPT,ENDPH,1,7,' ;')
500 CONTINUE
    STOP
    END
//GO.SYSIN DD *
i

```

Figure 10. (Continued)

B.T. THAM WFK 2 25

0.0	3.710
99.94	3.902
129.77	3.975
149.74	4.027
169.69	4.082
189.67	4.140
209.53	4.199
229.59	4.258
249.62	4.316
269.60	4.373
289.64	4.429
309.72	4.480
329.76	4.528
349.79	4.572
399.85	4.674
450.03	4.760
-1.0	

Figure 10. (Continued)

In Program B time is obtained as a cubic function of pH:

$$\text{time} = Q_1 + Q_2(\text{pH}) + Q_3(\text{pH})^2 + Q_4(\text{pH})^3.$$

In both programs the best values of the coefficients Q_1 through Q_4 are determined, the second derivative of the resulting cubic equation is set equal to zero, and the equation solved for the independent variable (point of inflection). If the calculated cubic equation fits the titration data exactly, then the point of inflection will indeed be the end-point of the titration (and the equivalence-point to the extent that the two may be identical). In the computer output are listed: (1) the computed coefficients, (2) the experimental data, (3) the calculated values of the dependent variable for each data, (4) the computed time at the end-point, (5) the computed pH at the end-point, and (6) the slope of the titration curve at the end-point. A high-level plotting system, SIMPLOTTER, was used to plot automatically pH versus time, superimposing the calculated cubic equation on the experimental data. Representative outputs are shown in Tables 14 - 19 and the corresponding Figures 11 - 16.

Table 14. Computer print-out of cathodic titration of 4-aminopyridine, pH as a function of time

Titration of 4-aminopyridine by back titration of excess standard perchloric acid with alkali generated at the cathode. pH as a function of time

CATHODIC TITRATION OF 4-AMINOPYRIDINE

$$PH = Q(1) + Q(2)*T + Q(3)*T**2 + Q(4)*T**3$$

$$Q(1) = 0.406836270 \ 01$$

$$Q(2) = -0.489721410-02$$

$$Q(3) = 0.499390380-04$$

$$Q(4) = -0.703305120-07$$

I = 1	TIME = 100.00	PH = 4.010	PHCALC = 4.008
I = 2	TIME = 139.98	PH = 4.170	PHCALC = 4.168
I = 3	TIME = 160.13	PH = 4.271	PHCALC = 4.276
I = 4	TIME = 180.02	PH = 4.390	PHCALC = 4.395
I = 5	TIME = 199.91	PH = 4.520	PHCALC = 4.523
I = 6	TIME = 219.82	PH = 4.660	PHCALC = 4.658
I = 7	TIME = 239.71	PH = 4.801	PHCALC = 4.795
I = 8	TIME = 259.60	PH = 4.940	PHCALC = 4.932
I = 9	TIME = 279.55	PH = 5.067	PHCALC = 5.066
I = 10	TIME = 299.52	PH = 5.192	PHCALC = 5.192
I = 11	TIME = 319.42	PH = 5.303	PHCALC = 5.307
I = 12	TIME = 339.40	PH = 5.403	PHCALC = 5.409
I = 13	TIME = 359.40	PH = 5.488	PHCALC = 5.494
I = 14	TIME = 379.38	PH = 5.566	PHCALC = 5.558
TIME AT ENDPPOINT = 236.69		PH AT ENDPPOINT = 4.774	

$$\text{SLOPE AT ENDPPOINT} = 0.692273\text{E}-02\text{PH/SEC}$$

Figure 11. Titration curve of cathodic titration of 4-aminopyridine, pH as a function of time

Titration of 4-aminopyridine by titration of excess standard perchloric acid with alkali generated at cathode. pH as a function of time. x, Experimental data. Solid line, cubic equation fitted by computer. See Table 14 for data

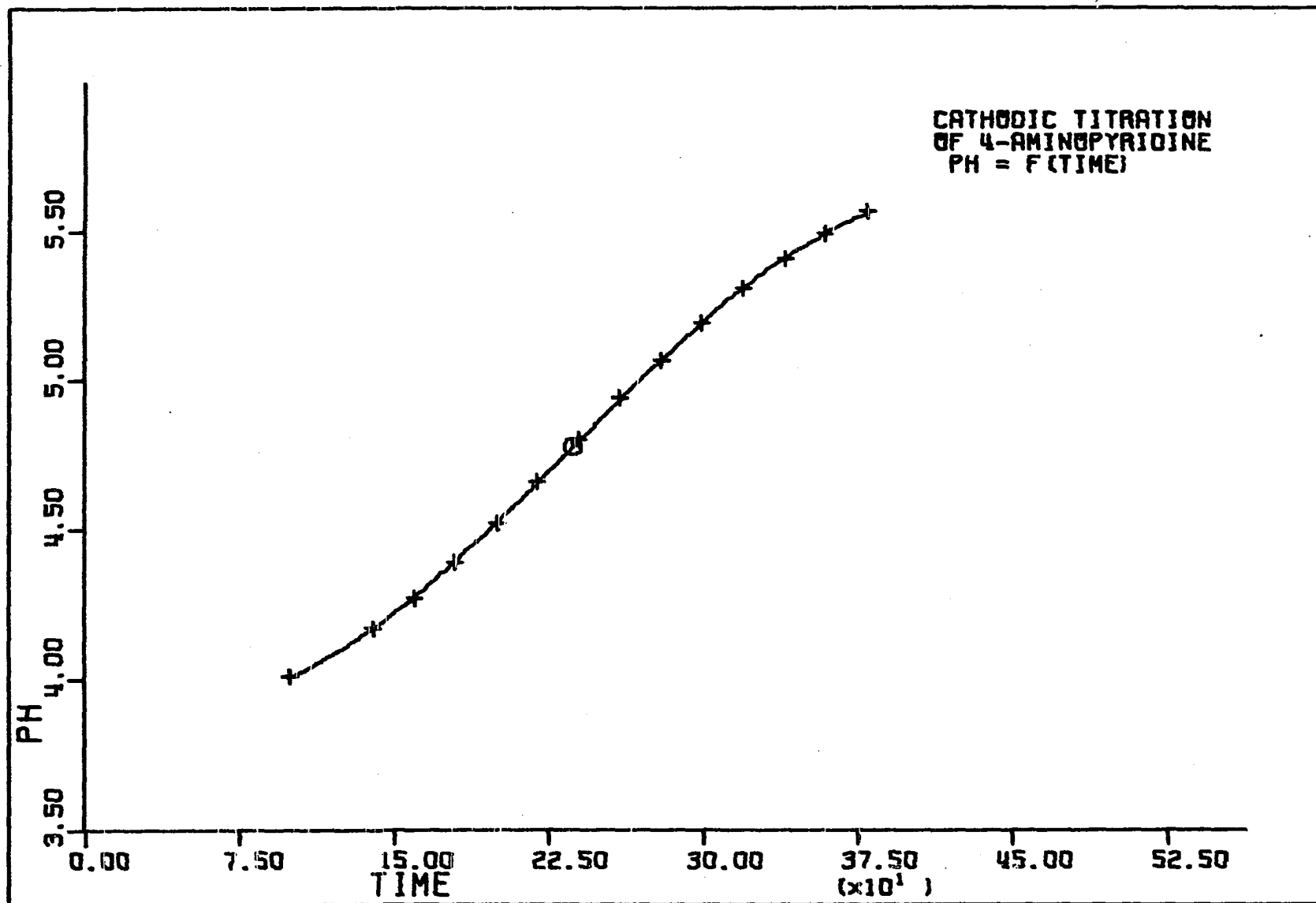


Table 15. Computer print-out of cathodic titration of 4-aminopyridine, time as a function of pH

Titration of 4-aminopyridine by back titration of excess standard perchloric acid with alkali generated at the cathode. Time as a function of pH

CATHODIC TITRATION OF 4-AMINOPYRIDINE

$$T = Q(1) + Q(2)*PH + Q(3)*PH**2 + Q(4)*PH**3$$

$$Q(1) = -0.79248911D 04$$

$$Q(2) = 0.48546860D 04$$

$$Q(3) = -0.98819748D 03$$

$$Q(4) = 0.68998059D 02$$

I = 1	PH = 4.010	TIME = 100.00	TCALC = 101.16
I = 2	PH = 4.170	TIME = 139.98	TCALC = 138.65
I = 3	PH = 4.271	TIME = 160.13	TCALC = 158.91
I = 4	PH = 4.390	TIME = 180.02	TCALC = 180.10
I = 5	PH = 4.520	TIME = 199.91	TCALC = 200.68
I = 6	PH = 4.660	TIME = 219.82	TCALC = 220.89
I = 7	PH = 4.801	TIME = 239.71	TCALC = 240.31
I = 8	PH = 4.940	TIME = 259.60	TCALC = 259.66
I = 9	PH = 5.067	TIME = 279.55	TCALC = 278.49
I = 10	PH = 5.192	TIME = 299.52	TCALC = 298.91
I = 11	PH = 5.303	TIME = 319.42	TCALC = 319.29
I = 12	PH = 5.403	TIME = 339.40	TCALC = 339.95
I = 13	PH = 5.488	TIME = 359.40	TCALC = 359.53
I = 14	PH = 5.566	TIME = 379.38	TCALC = 379.38

TIME AT ENDPOINT = 236.61 PH AT ENDPOINT = 4.774

SLOPE AT ENDPOINT = 0.729955E-02PH/SEC

Figure 12. Titration curve of cathodic titration of 4-aminopyridine, time as a function of pH

Titration of 4-aminopyridine by titration of excess standard perchloric acid with alkali generated at the cathode. Time as a function of pH. x, Experimental data. Solid line, cubic equation fitted by computer. See Table 15 for data

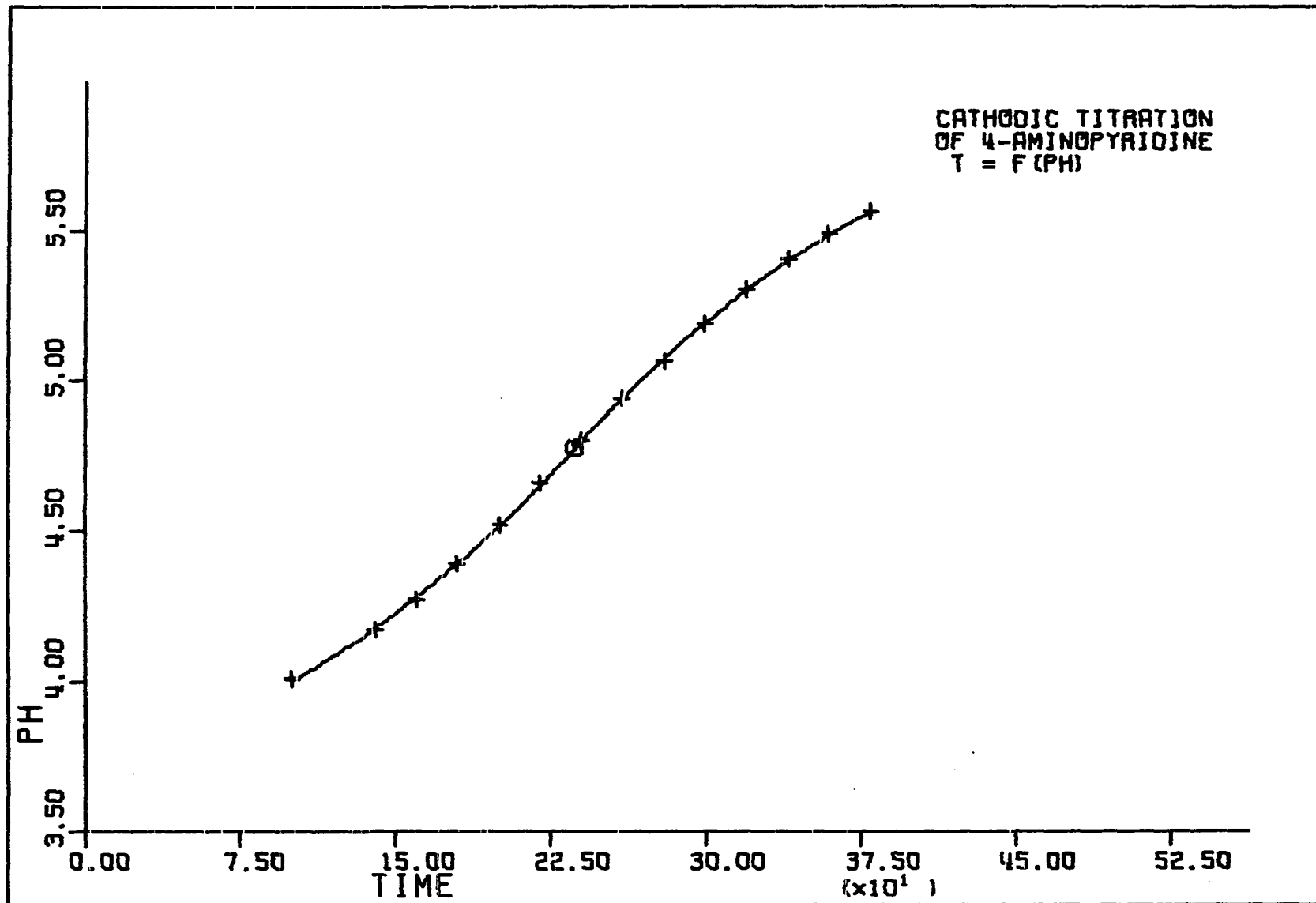


Table 16. Computer print-out of anodic titration of THAM, pH as a function of time

Titration of tris(hydroxymethyl)aminomethane with acid generated at the hydrazine-platinum anode. pH as a function of time

ANODIC TITRATION OF THAM

$$PH = Q(1) + Q(2)*T + Q(3)*T**2 + Q(4)*T**3$$

$$Q(1) = 0.46360363D 01$$

$$Q(2) = 0.18681322D-02$$

$$Q(3) = -0.65447312D-05$$

$$Q(4) = 0.38106563D-08$$

I = 1	TIME = 300.16	PH = 4.710	PHCALC = 4.710
I = 2	TIME = 400.19	PH = 4.578	PHCALC = 4.580
I = 3	TIME = 440.22	PH = 4.516	PHCALC = 4.515
I = 4	TIME = 460.22	PH = 4.481	PHCALC = 4.481
I = 5	TIME = 480.21	PH = 4.448	PHCALC = 4.446
I = 6	TIME = 500.23	PH = 4.410	PHCALC = 4.410
I = 7	TIME = 520.24	PH = 4.375	PHCALC = 4.373
I = 8	TIME = 540.31	PH = 4.339	PHCALC = 4.336
I = 9	TIME = 560.27	PH = 4.297	PHCALC = 4.298
I = 10	TIME = 580.25	PH = 4.260	PHCALC = 4.261
I = 11	TIME = 600.21	PH = 4.220	PHCALC = 4.224
I = 12	TIME = 620.22	PH = 4.185	PHCALC = 4.186
I = 13	TIME = 640.20	PH = 4.148	PHCALC = 4.149
I = 14	TIME = 660.32	PH = 4.112	PHCALC = 4.113
I = 15	TIME = 680.07	PH = 4.078	PHCALC = 4.078
I = 16	TIME = 700.17	PH = 4.044	PHCALC = 4.044
I = 17	TIME = 720.05	PH = 4.011	PHCALC = 4.011
I = 18	TIME = 740.03	PH = 3.980	PHCALC = 3.979
I = 19	TIME = 800.07	PH = 3.898	PHCALC = 3.893
I = 20	TIME = 850.06	PH = 3.832	PHCALC = 3.836

TIME AT ENDPOINT = 572.49

PH AT ENDPOINT = 4.276

SLOPE AT ENDPOINT = -0.187869E-02PH/SEC

Figure 13. Titration curve of anodic titration of tris(hydroxymethyl)aminomethane, pH as a function of time

Titration of tris(hydroxymethyl)aminomethane with acid generated at the hydrazine-platinum anode. pH as a function of time. x, Experimental data. Solid line, cubic equation fitted by computer. See Table 16 for data

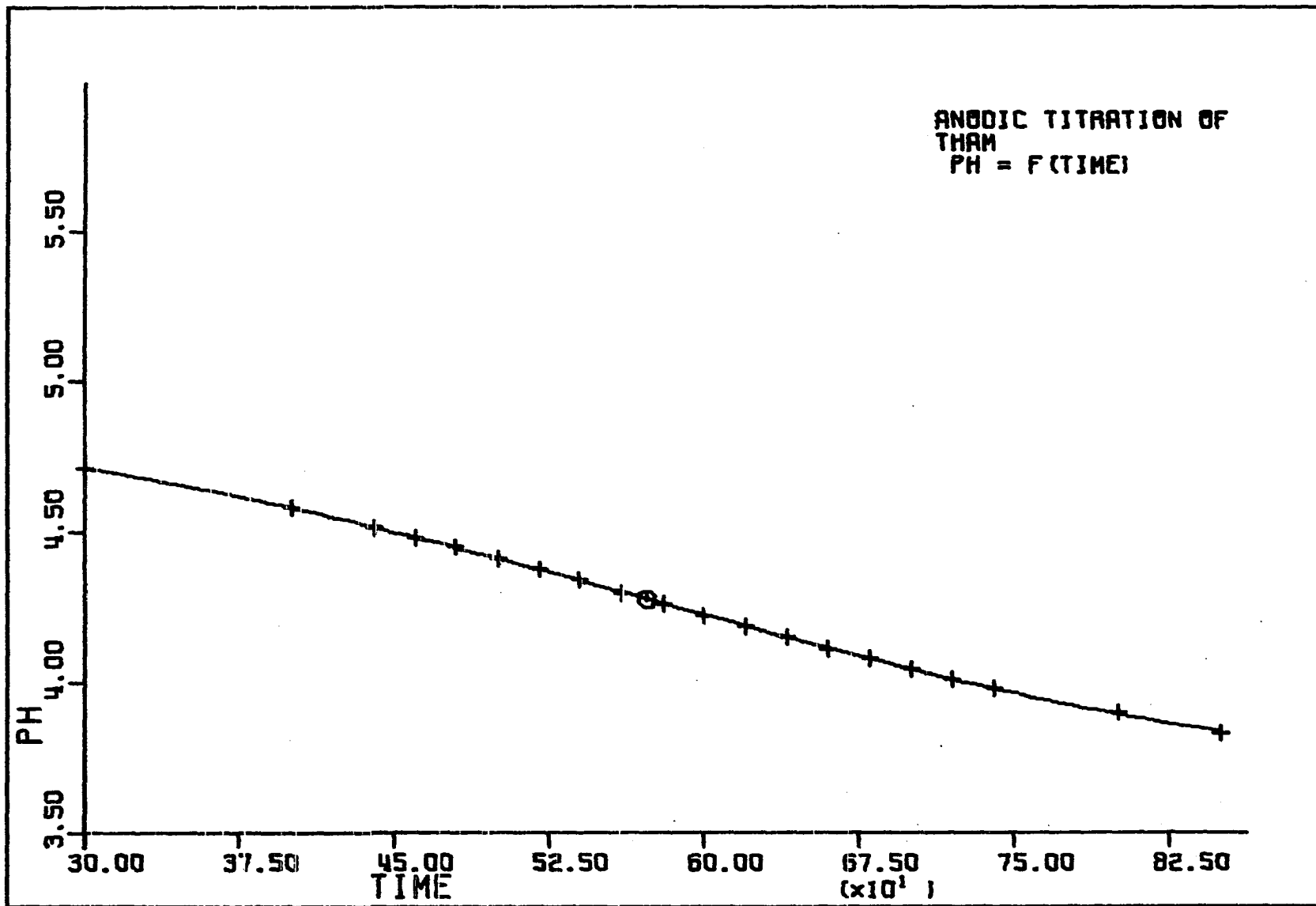


Table 17. Computer print-out of anodic titration of THAM, time as a function of pH

Titration of tris(hydroxymethyl)aminomethane with acid generated at the hydrazine-platinum anode. Time as a function of pH

ANODIC TITRATION OF THAM

$$T = Q(1) + Q(2)*PH + Q(3)*PH**2 + Q(4)*PH**3$$

$$Q(1) = 0.45755989D 05$$

$$Q(2) = -0.30670315D 05$$

$$Q(3) = 0.70535759D 04$$

$$Q(4) = -0.55007135D 03$$

I = 1	PH = 4.710	TIME = 300.16	TCALC = 300.63
I = 2	PH = 4.578	TIME = 400.19	TCALC = 399.49
I = 3	PH = 4.516	TIME = 440.22	TCALC = 439.40
I = 4	PH = 4.481	TIME = 460.22	TCALC = 460.53
I = 5	PH = 4.448	TIME = 480.21	TCALC = 479.74
I = 6	PH = 4.410	TIME = 500.23	TCALC = 501.02
I = 7	PH = 4.375	TIME = 520.24	TCALC = 520.11
I = 8	PH = 4.339	TIME = 540.31	TCALC = 539.21
I = 9	PH = 4.297	TIME = 560.27	TCALC = 561.27
I = 10	PH = 4.260	TIME = 580.25	TCALC = 580.53
I = 11	PH = 4.220	TIME = 600.21	TCALC = 601.44
I = 12	PH = 4.185	TIME = 620.22	TCALC = 619.97
I = 13	PH = 4.148	TIME = 640.20	TCALC = 639.96
I = 14	PH = 4.112	TIME = 660.32	TCALC = 660.03
I = 15	PH = 4.078	TIME = 680.07	TCALC = 679.50
I = 16	PH = 4.044	TIME = 700.17	TCALC = 699.80
I = 17	PH = 4.011	TIME = 720.05	TCALC = 720.27
I = 18	PH = 3.980	TIME = 740.03	TCALC = 740.47
I = 19	PH = 3.898	TIME = 800.07	TCALC = 798.48
I = 20	PH = 3.832	TIME = 850.06	TCALC = 851.15
TIME AT ENDPOINT = 573.08		PH AT ENDPOINT = 4.274	

SLOPE AT ENDPOINT = -0.191967E-02PH/SEC

Table 14. Titration curve of anodic titration of tris(hydroxymethyl)aminomethane, time as a function of pH

Titration of tris(hydroxymethyl)aminomethane with acid generated at the hydrazine-platinum anode. Time as a function of pH. \times , Experimental data. Solid line, cubic equation fitted by computer. See Table 17 for data

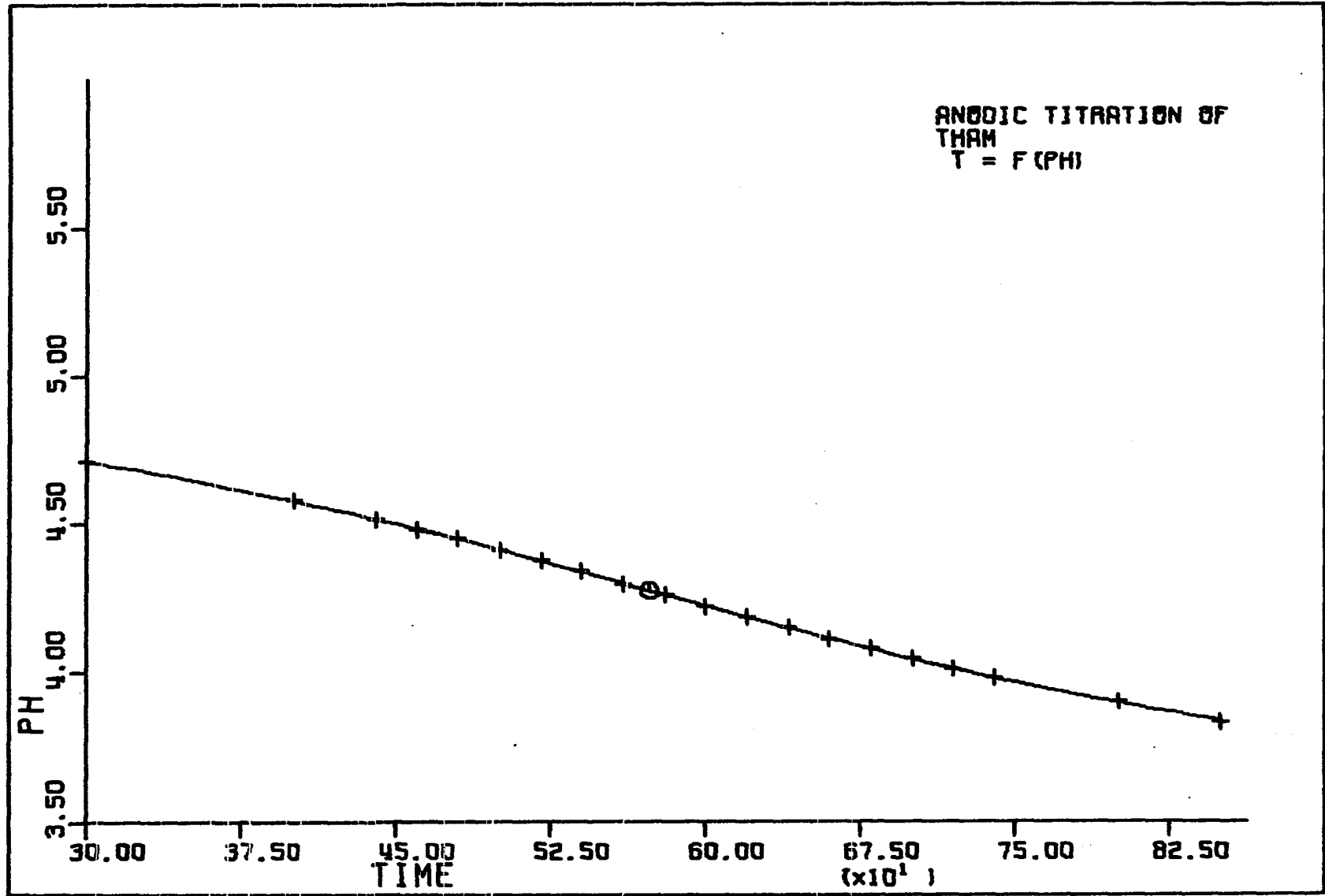


Table 18. Computer print-out of cathodic titration of perchloric acid, pH as a function of time

Titration of perchloric acid with alkali generated at cathode. pH as a function of time

CATHODIC TITRATION OF PERCHLORIC ACID

$$PH = Q(1) + Q(2)*T + Q(3)*T**2 + Q(4)*T**3$$

$$Q(1) = 0.28765780D 01$$

$$Q(2) = 0.48614234D-02$$

$$Q(3) = -0.21576863D-04$$

$$Q(4) = 0.24254057D-07$$

I = 1	TIME = 0.0	PH = 2.891	PHCALC = 2.877
I = 2	TIME = 199.89	PH = 3.031	PHCALC = 3.180
I = 3	TIME = 399.86	PH = 3.212	PHCALC = 2.921
I = 4	TIME = 599.87	PH = 3.520	PHCALC = 3.264
I = 5	TIME = 699.80	PH = 3.805	PHCALC = 4.024
I = 6	TIME = 799.73	PH = 4.536	PHCALC = 5.370
I = 7	TIME = 819.66	PH = 4.860	PHCALC = 5.721
I = 8	TIME = 829.68	PH = 5.119	PHCALC = 5.909
I = 9	TIME = 839.62	PH = 5.451	PHCALC = 6.103
I = 10	TIME = 849.77	PH = 6.025	PHCALC = 6.310
I = 11	TIME = 859.75	PH = 7.307	PHCALC = 6.521
I = 12	TIME = 869.79	PH = 7.792	PHCALC = 6.741
I = 13	TIME = 879.80	PH = 8.065	PHCALC = 6.969
I = 14	TIME = 889.73	PH = 8.242	PHCALC = 7.204
I = 15	TIME = 939.72	PH = 8.763	PHCALC = 8.518
I = 16	TIME = 989.72	PH = 9.080	PHCALC = 10.066
TIME AT ENDPOINT = 296.54		PH AT ENDPOINT = 3.053	

$$SLOPE AT ENDPOINT = -0.153697E-02PH/SEC$$

Figure 15. Titration curve of cathodic titration of perchloric acid, pH as a function of time

Titration of perchloric acid with alkali generated at cathode. pH as a function of time. x , experimental data. Solid line, cubic equation fitted by computer. See Table 18 for data

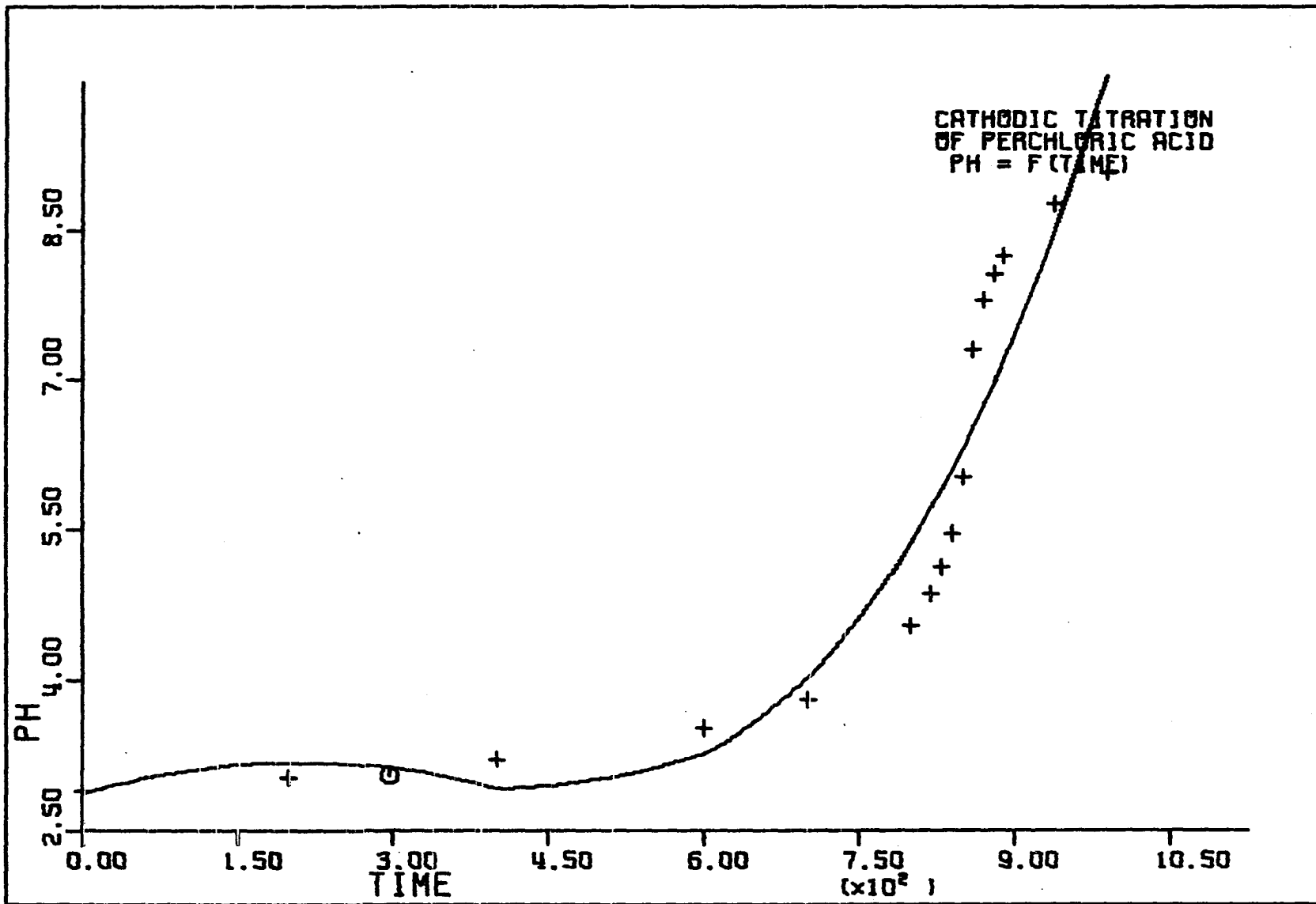


Table 19. Computer print-out of cathodic titration of perchloric acid, time as a function of pH

Titration of perchloric acid with alkali generated at cathode. Time as a function of pH

CATHODIC TITRATION OF PERCHLORIC ACID

$$T = Q(1) + Q(2)*PH + Q(3)*PH**2 + Q(4)*PH**3$$

$$Q(1) = -0.40907860 \text{ 04}$$

$$Q(2) = 0.232181700 \text{ 04}$$

$$Q(3) = -0.360824020 \text{ 03}$$

$$Q(4) = 0.183072660 \text{ 02}$$

I = 1	PH = 2.891	TIME = 0.0	TCALC = 129.92
I = 2	PH = 3.031	TIME = 199.89	TCALC = 223.25
I = 3	PH = 3.212	TIME = 399.86	TCALC = 332.66
I = 4	PH = 3.520	TIME = 599.87	TCALC = 491.42
I = 5	PH = 3.805	TIME = 699.80	TCALC = 609.94
I = 6	PH = 4.536	TIME = 799.73	TCALC = 807.23
I = 7	PH = 4.860	TIME = 819.66	TCALC = 853.95
I = 8	PH = 5.119	TIME = 829.68	TCALC = 876.93
I = 9	PH = 5.451	TIME = 839.62	TCALC = 891.03
I = 10	PH = 6.025	TIME = 849.77	TCALC = 885.74
I = 11	PH = 7.307	TIME = 859.75	TCALC = 833.58
I = 12	PH = 7.792	TIME = 869.79	TCALC = 836.04
I = 13	PH = 8.065	TIME = 879.80	TCALC = 850.51
I = 14	PH = 8.242	TIME = 889.73	TCALC = 866.30
I = 15	PH = 8.763	TIME = 939.72	TCALC = 948.45
I = 16	PH = 9.080	TIME = 989.72	TCALC = 1029.44

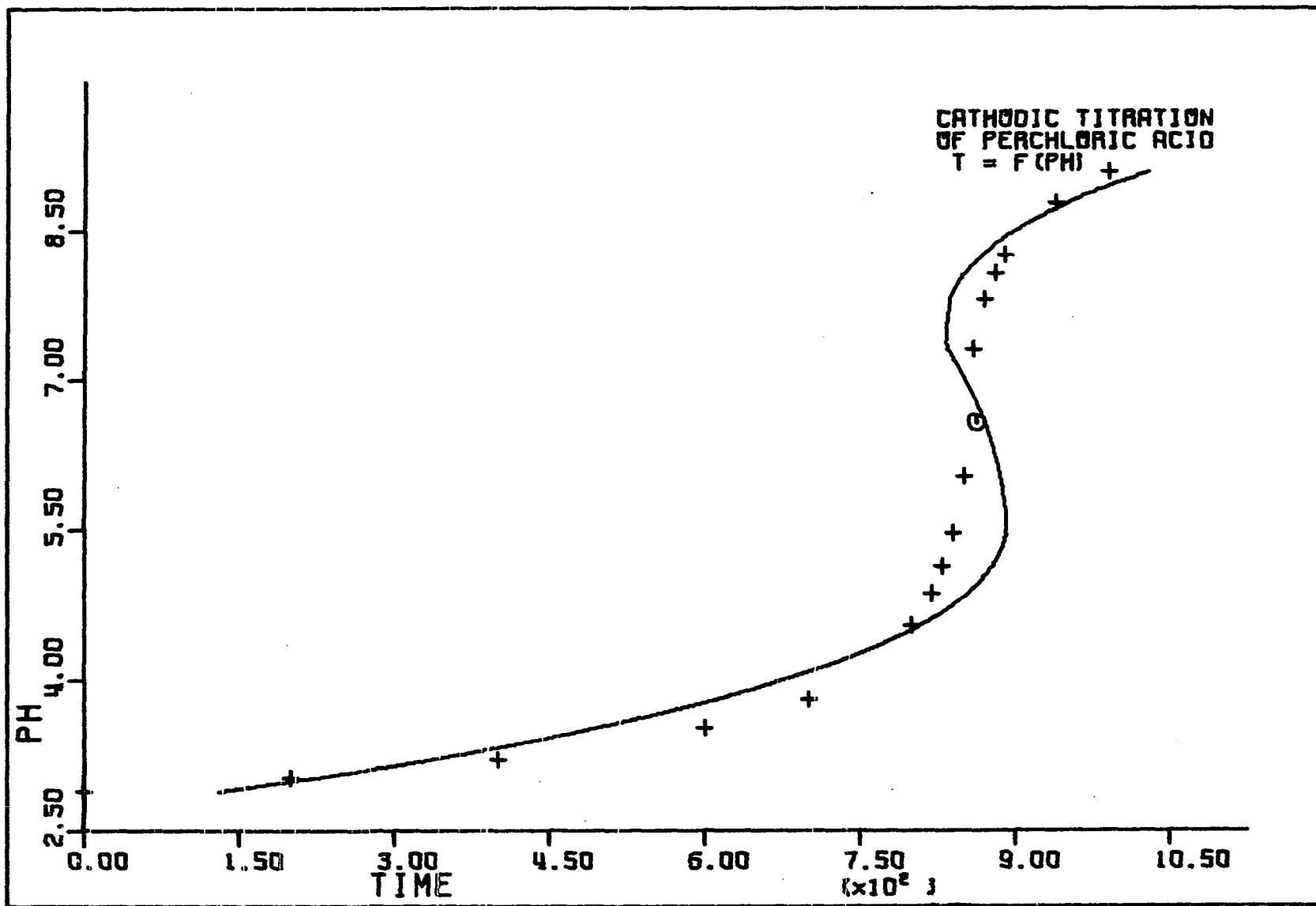
TIME AT ENDPOINT = 862.16

PH AT ENDPOINT = 6.570

SLOPE AT ENDPOINT = -0.205268E-01PH/SEC

Figure 16. Titration curve of cathodic titration of perchloric acid, time as a function of pH

Titration of perchloric acid with alkali generated at cathode. Time as a function of pH. \times , experimental data. Solid line, cubic equation fitted by computer. See Table 19 for data



VIII. SUMMARY

A review has been made of the nature of the fundamental constant interrelating chemistry and electricity, the faraday, and of the historical relationship of it to the ampere. It has been emphasized that the faraday now plays an important role not only in electrochemistry but also in many areas of quantum electrodynamics.

Reference has been made to recent developments in the area of the interrelationships among the fundamental constants. It has been noted that the faraday is currently the least precisely known of the fundamental constants. Further, it has been noted that the currently accepted value for the faraday, 96,486.72 coulombs per gram-equivalent weight, based on electrochemical work, is held suspect by physicists, and that an indirect value, 96,484.56 coulombs per gram-equivalent weight, obtained by calculations involving more precisely known fundamental constants, has been held to be more accurate.

The history of coulometric titrations has been traced and emphasis has been placed on the use of coulometry in the certification of primary standard materials. A review of the coulometric work performed at Iowa State University since 1966 has been presented.

The advantages of the coulometric titration method over ordinary titrimetric methods have been discussed in some detail with reference to their versatility, specificity, selectivity, sensitivity, precision, and accuracy. The disadvantage of the complexity of the apparatus required has been noted.

The standards of mass, time, resistance and potential in use at Iowa State University for high-precision coulometric work have been recalibrated. These calibrations have referred the standards directly in a single step, to the standards of the National Bureau of Standards. These calibrations were made either at the National Bureau of Standards (resistance and mass) or in the Ames Laboratory of ERDA at Iowa State University (potential).

The value for the faraday obtained by the high-precision coulometric titration of high-purity 4-aminopyridine by the addition of excess perchloric acid, titration of the excess perchloric acid by cathodic generation of base, and coulometric standardization of the perchloric acid in identical fashion, reported earlier (my M.S. thesis) has been recalculated in light of the new calibrations. The final value, 96,486.78 coulombs per gram-equivalent weight, is based on a density of 4-aminopyridine of 1.2695 g./ml. as determined by Hoyle.

Another series of high-precision coulometric titrations of the high-purity 4-aminopyridine has been conducted using the hydrazine-platinum anode and a second value of the faraday obtained: 96,486.40 coulombs per gram-equivalent weight, for the density of 4-aminopyridine the value 1.2695 g./ml. again being used.

The weighted average of the two series of titrations, back-titration (generating electrode functioning as cathode) and hydrazine-platinum anode, has been calculated to be 96,486.69(0.81)(8.40) 1972 NBS coulombs per gram-equivalent weight, in which the numbers in parentheses are the uncertainty expressed as the standard deviation of the mean in

coulombs per gram-equivalent weight and in ppm, respectively. This standard deviation reflects both systematic and random errors assessed and combined by procedures developed at the National Bureau of Standards and followed by the principal workers in the field of precision measurement of the fundamental constants.

A new lot of high-purity 4-aminopyridine has been prepared by repeated sublimation. This lot of 4-aminopyridine has been subjected to two series of high-precision coulometric titrations, identical in nature to those reported above but carried out at the National Bureau of Standards, Gaithersburg, Maryland. These titrations were performed utilizing a current source more stable than that at Iowa State University and the working standards of mass, resistance, potential and time which were frequently checked against the principal standards of the Bureau.

The density of 4-aminopyridine has been redetermined by the pycnometer method using xylene as the transfer medium; a value of 1.2633 g./ml. has been obtained.

Values for the faraday have been calculated from the titrations of 4-aminopyridine conducted at the National Bureau of Standards: 96,486.19 coulombs per gram-equivalent weight using the back-titration method, and 96,486.24 coulombs per gram-equivalent weight using the hydrazine-platinum anode method. The weighted average of these titrations has been calculated: 96,486.22(0.50)(5.2 ppm) 1972 NBS coulombs per gram-equivalent weight, in which the numbers in parentheses are the standard deviation of the mean expressed in coulombs per gram-equivalent weight and in parts per million respectively, and reflect

the combined random and systematic errors. The value 1.2633 g./ml. for the density of 4-aminopyridine (entering in correcting the weight of 4-aminopyridine for the buoyant effect of air) was used in making these calculations.

The value for the faraday obtained from the titrations of 4-aminopyridine conducted at Iowa State University has been recalculated based on the density of 4-aminopyridine, 1.2633 g./ml., the value is 96,486.26(0.81)(8.40 ppm) 1972 NBS coulombs per gram-equivalent weight.

The values for the faraday obtained at the two laboratories have been combined and a new value for the faraday has been advanced:

$$F = 96,486.23(0.43)(4.42 \text{ ppm}) \text{ 1972 coulombs per gram-equivalent weight,}$$

in which the numbers in parentheses are the standard deviation of the mean expressed in coulombs per gram-equivalent weight and in parts per million respectively, and include the effects of both random and systematic errors.

The hydrazine-platinum anode has been proven to function with 100 per cent current efficiency in the generation of hydrogen ion by two series of high-precision coulometric titrations of commercial, primary standard tris(hydroxymethyl)aminomethane, (THAM). In the first series, THAM has been assayed coulometrically by the back-titration method (addition of excess perchloric acid and return to the equivalence point by electrogeneration of base at the cathode and coulometric standardization of the perchloric acid by an identical procedure). The purity found was 99.9157 per cent. In the second series, THAM has been assayed using the hydrazine-platinum anode (electrolyte,

0.25 M sodium hydrazinium sulfate/1.0 M sodium perchlorate); found 99.9169 per cent pure. Further proof of the efficiency of the electrode has been shown by the coulometric assay of primary standard tris(hydroxymethyl)aminomethane, SRM 723 of the National Bureau of Standards using the hydrazine-platinum anode; found 99.9678 per cent pure (NBS value: 99.9690 per cent).

A simplified procedure for routine use of the hydrazine-platinum anode for the direct coulometric titration of bases has been developed.

Commercial tris(hydroxymethyl)aminomethane has been shown to contain large amounts of solvent and to be poor as a primary standard. The solvent is trapped in cavities in the crystal and has been found in one lot of material to amount to 0.7 per cent. It has been shown that material of higher purity can be obtained by a programmed procedure of repeated grinding, sifting and drying in vacuum over anhydrous magnesium perchlorate. At best, the material so prepared was a poor primary standard.

It has been found that tris(hydroxymethyl)aminomethane, SRM 723 also contains inclusions.

A computer method for locating the end-point in a high-precision coulometric titration has been devised. A cubic equation is fitted to the experimental data of pH and time at constant current, the point of inflection found by setting the second derivative equal to zero. It has been found that it is immaterial if the data is handled with either time or pH as the independent variable. The method has been found superior to location of the point of inflection visually on a plot of

the data and also superior to the earlier finite difference method of Yan which is based on only four, carefully selected points. The method has been applied successfully to the titrations of 4-aminopyridine and tris(hydroxymethyl)aminomethane, but has been shown to fail in the titration of perchloric acid.

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