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The high-precision thermometric and coulometric assay of primary standard 4-aminopyridine

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The high-precision thermometric and coulometric assay of primary standard 4-aminopyridine

by

William Charles Hoyle

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

Approved:

In Charge of Major Work

For the Major Department

For the Graduate College

Iowa State University
Ames, Iowa

1973

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QUOTATION

"Mosques fall, palaces crumble into dust but knowledge remains."

Ulug Beg, the great
Uzbet astronomer of the
fifteenth century.

CHAPTER I. THE FARADAY AND HIGH-PRECISION COULOMETERS

Significance and History

The laws governing the relationship between electric current, time and the amount of chemical change effected by the electric current were discovered by Michael Faraday in 1833. Faraday expressed the relations in a series of statements, introducing at the same time a new terminology. The principal of these statements are:[21]

> 783. The chemical power of a current of electricity is in direct proportion to the absolute quantity of electricity which passes.
>
> 824. The numbers representing the proportions in which they (anions, cations) are evolved I propose tc call <u>electro-chemical equivalents</u>.
>
> 835. Electro-chemical equivalents are always consistent; *i.e.*, the same number which represents the equivalent of substance A when it is separated from substance B, will also represent A when separating from a third substance C.
>
> 836. Electro-chemical equivalents coincide, and are the same, with ordinary chemical equivalents.

Curiously, the text books for over a hundred years continued this non-symbolic statement of the laws and it was only about 1950 that the laws appeared in a textbook in the algebraic formulation

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

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 equivalent weight, that is, the molecular weight divided by the number of electrons involved in the change (change in valence at the electrode).

The proportionality factor, F, is appropriately called the "faraday." The work described in the present thesis deals with measurements leading to a numerical value of this constant.

It is common in physical science that the evaluation of a proportionality constant is tied up intimately with the establishment of 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 a 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 faraday or the ampere at intervals. Wisely, because of the ramifications of electricity into numerous other branches of science and technology, the definition of the ampere has been held constant and the values of the faraday subjected to correction. Thus, the ampere is defined by

> The international ampere is defined as that steady or unvarying current which when passed through a solution of silver nitrate in water deposits 1.11880 milligrams of silver per second.

The quantity 1.11800 mg. of silver was arrived at from the value of the faraday and of the atomic weight of silver current at the time the definition was made.

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., and the United States legal or NBS 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 stage of perfection that it became possible in 1948, to change from various national ("international mean") units to absolute units. The factor for converting the NBS ampere to the absolute ampere has undergone further change, the improvements having to do with better measurements of the acceleration of gravity at Washington and efforts to bring all physical units and constants into an internally consistent system. The conversion factor is given by

NBS ampere = 1.000,000,7 absolute ampere

(Taylor, Parker and Langenberg;[73] see also, however, Appendix I for a review of the recent history and uses of this constant.)

The Silver Coulometer

The silver coulometer is subject to a serious error, namely the inclusion of solvent in the crystals of silver deposited electrolytically. Some fourteen papers were published between 1884 and 1916 on this problem but a satisfactory answer was really never obtained. The subject was reviewed in 1953 by Scott[65] and again in 1968 by Hamer.[25] By 1970 other coulometers had been devised, notably the iodine coulometer (Washburn and Bates[83] in 1912, Rosa, Vinal and McDaniel[62] in 1914, Bates and Vinal[6] in 1914), the oxalate oxidation coulometer (Craig and Hoffman[16] in 1953), and the silver dissolution coulometer (Craig, Hoffman, Law and Hamer[17] in 1960); by 1970 also, contributions from the field of high-precision coulometric titrations began to merit consideration.

The work on which the current (1973) value of the Faraday is based is the silver dissolution coulometer of Craig, Hoffman, Law and Hamer.[17] In the silver dissolution method, 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 g.-equivalent weight of silver.

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 in silver from various sources, including the silver of Craig, Hoffman, Law and Hamer, by Shields, Craig and Dibeler[66] and Shields, Garner and Dibeler.[67] Using the Craig, Hoffman, Law and Hamer[17] equivalent weight of silver,

$$E = 1.117{,}92 \pm 0.000{,}019 \text{ mg. per NBS coulomb}$$

the atomic weight of silver on the ^{12}C scale, 107.8685 (Shields and others:[66,67] 107.8685; 1967 Table of the Commission on Atomic Weight: 107.868), and the conversion factor

$$\text{NBS ampere} = 1.000{,}012 \text{ absolute ampere}$$

$$F = 96{,}487.0 \pm 1.6 \text{ absolute coulombs per g.-equiv. wt.}$$

the error being 95 per cent confidence limit (two times the standard deviation). See the 1968 review paper of Hamer[25] for a review of this; the value is identical with that accepted in 1963 by a committee of the National Academy of Science-National Research Council.[13]

In an effort to bring all physical units and constants into a unified and internally consistent system, Taylor, Parker and Langenberg[73] made an extensive and critical review of the experimental work bearing on the problem, including reviews of the work of Craig, Hoffman, Law and Hamer[17] on the equivalent weight of silver, of the work on the abundance ratio of the isotopes of silver of Shields and co-workers,[66,67] of the absolute masses of the silver isotopes of silver by Mattauch, Thiele and Wapstra,[50] and of the very recent work leading to the new values of the acceleration of gravity at Washington, D. C. and the conversion of the NBS electrical units (as maintained units) to absolute units. Their final assessment was based on the experimental values

E(Ag) = 1.117,972,2(72) mg. per NBS coulomb (6.5 p.p.m.)

M(Ag) = 107.8683(23) a.m.u. (2.1 p.p.m.)

NBS ampere = 1.000,000,7 absolute ampere (2.6 p.p.m.)
(after 1 Jan. 1969)

F = 96,485.70(66) NBS coulombs per g.-equiv. (6.8 p.p.m.)

(The number in parentheses represents the uncertainty in the measurement, expressed as one standard deviation, in the last digits of the quoted value; the number appearing in parentheses after the expression of the units is the estimated total error, a combination of the estimates of the possible random and systematic errors.) Worked into the entire system with a least squares treatment of the errors these experimental results gave for the values finally recommended

F = 96,486.70(54) absolute coulombs per g.-equiv. (5.5 p.p.m.)

F = 96,486.62(55) NBS (as maintained) coulomb per g.-equiv. (5.7 p.p.m.)

Taken into account was the change made January 1, 1969 in the relation of the NBS as maintained volt to the absolute volt.

Commenting on the work of Craig, Hoffman, Law and Hamer,[17] Taylor, Parker and Langenberg[73] (page 403, column 1) state:

> In 1960, Craig, Hoffman, Law and Hamer of NBS reported an extremely careful and painstaking determination of E(Ag), the electrochemical equivalent of silver, using a silver-perchloric acid coulometer.

and again further (page 405, column 2):

> . . . , it is rather unfortunate that there is but one modern, high-accuracy measurement of F. This lack is all the more regrettable because of the possible systematic errors inherent in experimental determinations of F. Questions relating to modification of isotopic abundances in the electrolytic process, the presence of inclusions in the starting material, etc., must all be investigated carefully. While Craig et al. carried out what can only be described as a remarkably thorough experiment, additional measurements of F would make everyone feel more comfortable.

About the only criticism that an old-line, atomic weight chemist (of the Richards school) can offer in examining the work of Craig, Hoffman, Law and Hamer is that it involves a transfer of finely divided solid material from suspension in a liquid and collection on a filter. In the anodic attack of metallic silver, the silver in not dissolved uniformly; rather, pits develop and undercutting proceeds to the point where particles of silver fall off the electrode. In the Craig, Hoffman, Law and Hamer work, the silver which flakes from the electrode amounted to two to twenty-five percent of the silver dissolved electrolytically. Craig, Hoffman, Law and Hamer say relatively little about this, simply stating (ref. 17, page 392, column 2):

> As the silver goes into solution some particles (sediment) fall to the bottom of the anode beaker. This sediment was collected in a weighed Pyrex crucible with a fritted bottom, repeatedly washed with conductivity water, dried at 110°C, and weighed. This weight of the sediment was then subtracted from the difference between the initial and final weights of the sheet or rod to give the weight of silver which was electrolytically dissolved.

A parallel blank determination was run as a check on contamination by dust but the electrolyte in the blank was filtered a day later through the same crucible used to collect the sediment. The quantities of silver dissolved were between 2 and 6 g. and the weighings were made to 1 μg. Thus, in a typical run (Table 10, number 8), 3.755131 g. of silver were dissolved, 0.102182 g. of sediment were collected. Accuracy to 1 part in 100,000 thus calls for transfer to be complete to at least 30 μg. Even seeing such small quantities is difficult and the removal of particles adhering to the glass by rubbing with a rubber tipped stirring rod offers possibilities for contamination and loss. Although it is unlikely that any finely divided (colloidal) silver would have passed through the filtering crucible undetected, there remains the troublesome matter of the hygroscopicity of fritted glass and the changes in weight filtering crucibles undergo on exposure to humid air.

It was to meet this very problem of eliminating the transfer of solids that T. W. Richards devised the titration procedures and the solid to solid conversions in gaseous atmospheres that characterized the atomic weight work at Harvard from 1904 on. The titrimetric method, applied particularly to metal halides, was brought to perfection by the invention of the nephelometer and the nephelometric end-point, and the conversion of solid to solid by heating in a gaseous atmosphere was effected in the so-called "bottling apparatus". The solid to solid procedure was used in the several, all important determinations of the atomic weight of silver that marked the highest point to which the chemical determination of atomic weight could be carried. When filtration could not be avoided, complete transfer was proven by chemical recovery of traces of materials left on glass walls; the effectiveness of the filter was checked by repeated filtration of filtrates; and constant checks were made on the stability of filters. And, of course, the elimination of water from materials was a matter of constant preoccupation. A survey of these problems and an introduction to the Harvard work on atomic weights appears in Richards' "Determination of Atomic Weights" Carnegie Institution of Washington, Publication No. 125.[61] Chemical methods for the determination of atomic weight have been long superseded by the more accurate mass spectrographic method but the chemical method lingers on and applies in a very real way in the problem of evaluating the faraday.

Coulometry

Beginning with the work of Szebelledy and Somogyi[72] in 1938, there has grown up an extensive body of literature on a methodology known as "coulometric titration". The technique is a variation on the coulometer just discussed, the objective being to determine some chemical which is made to undergo an electrochemical change by measuring the electricity required. The stream of electrons acts as a titrating agent, that is, replaces the standard solution delivered from a buret in ordinary volumetric (titrimetric) analysis. The field became a popular one for investigation during the 1940's and 1950's and, as was almost inevitable, it ultimately became clear that the electron was the only really pure chemical and that one Avagadro's number of electrons, that is, one faraday of coulombs was equal to one liter of a one normal solution of an oxidizing (or reducing) agent and thus that the ultimate primary standard for all titrimetric work was the coulomb. The formal announcement came from Tutundzic[77] but the advantages had not been lost on a generation of analytical chemists.

The electric current used in such titrations can be held rigidly constant and the time measured accurately; thus "constant current coulometric titration". Or, the current may be progressively decreased during the electrolysis so that one electrochemical reaction may be made to occur to the exclusion of a second; hence "controlled cathode, or controlled anode, potential coulometric titration".

Precision in the business of coulometric titration is a natural, the limits being based on the ability to guarantee one hundred percent current efficiency in the electrochemical change being undergone by the substance being measured, the ability to locate the equivalence-point decisively, the ability to make the weighings and the electrical and time measurements accurately, a knowledge of the atomic weights involved, and finally a knowledge of the value of the faraday. All of these factors can be precisely controlled in many cases.

The extent to which the technique can be pushed was pointed out by Taylor and Smith,[74] who in 1959 titrated primary standard potassium hydrogen 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 in 1963 by three papers in which accuracy of the same order was achieved: Marinenko and Taylor[46] on the titration of halides; Marinenko and Taylor[47] on the titration of potassium dichromate as an oxidizing agent; and Cooper and Quayle[60,14] on the titration of sodium carbonate. In 1965 apparatus was put on the market making it possible for just about anyone seriously interested in the business to do equally well; the instrument is the "Coulometric Analyzer" of the Leeds and Northrup Company, described by Eckfeldt and Shaffer.[20] A catalog of the high-precision (to 5 parts or less in 100,000) coulometric titrations that have now been carried out is given in Table 1.

High-Precision Coulometric Titrations

Of the high-precision coulometric titrations which have been carried out on materials the purity of which have been established by other methods, three have been singled out as competent to provide an evaluation of the Faraday.[49]

The iodide oxidation, coulometric titration of arsenious oxide, Marinenko and Taylor,[48] lead to the value

$$F = 96{,}485.5 \pm 3.2 \text{ NBS coulombs per mole.}$$

The arsenic trioxide titrated was NBS 83c, the purity of which was established by titration with iodine purified by sublimation.

Direct coulometric titration of benzoic acid by Marinenko and Taylor[49] gave

$$F = 96{,}486.7 \pm 2.5 \text{ NBS coulombs per mole.}$$

The benzoic acid used was purified by recrystallization from molten benzoic acid, a procedure which earlier had yielded benzoic acid 99.997 mole per cent pure by the freezing curve method and 99.999 mole per cent pure by the calorimetric procedure. The two lots of benzoic acid were intercompared by titrations of sodium carbonate, yielding for the Marinenko and Taylor material a purity of 99.9955 ± 0.0014 mole per cent.

A direct coulometric titration of oxalic acid dihydrate was also made by Marinenko and Taylor.[49] This gave

$$F = 96{,}485.4 \pm 3.4 \text{ NBS coulombs per mole.}$$

The oxalic acid dihydrate used was from a lot of optically clear crystals selected from crystals grown from acetone-water mixtures by Torgesen and Strassburger.[76] The purity of the material, 99.9871 per cent, was established by calculation from determinations of seven metallic impurities (practically all sodium); nothing is said about occluded solvent.

In the work being reported in this thesis, another attempt has been made to establish a value for the faraday by a coulometric titration. The compound selected for titration, 4-aminopyridine, was chosen because it has several very favorable characteristics:

> It can be purified by sublimation, thus assuring the absence of occluded solvent.
>
> It is a weak base but sufficiently strong to provide an end-point on titration sufficiently distinct to meet the accuracy demanded.
>
> It melts in a convenient temperature range and is stable at the melting point to make possible obtaining a freezing curve to establish purity.
>
> It is made up only of carbon, hydrogen, and nitrogen, elements for which variations in the isotope abundance ratios, natural or a result of processing, is probably negligible, but elements for which, if necessary, the abundance ratios can be determined without too much difficulty. The atomic weights of these elements, and the weights of their isotopes also, being accurately know, calculation of a value for the faraday can be based directly on carbon-twelve.

In the course of the experimental work to be described, the purification of the 4-aminopyridine by sublimation proved straight-forward and successful. The freezing curve determination of impurity, which required most of the time devoted to the investigation, was beset by an unexpected difficulty which I believe, however, was successfully surmounted. The direct titration as I had originally proposed to carry it out proved inexact. The reason for this and for the failure of others to titrate a weak base successfully coulometrically was explained and two ways of circumventing the difficulty were found. Two series of high-precision coulometric titrations of 4-aminopyridine, differing in technique, were finally carried out. The value found for the faraday does not differ greatly from other, recent values, but the value has now been established for the first time by the titration of a base. Or, reversing the argument, weak bases can now be titrated coulometrically with assurance that the process is valid.

Table 1. High-precision coulometric titrations

Substance	Authors	Year	Reference
Acids			
Potassium hydrogen phthalate			
NBS 84d	Taylor and Smith	1959	74
	Eckfeldt and Shaffer	1965	20
	Knoeck and Diehl	1969	34
NBS 84h	Paabo	1971	43
Benzoic acid			
NBS Calorimetric Standard	Taylor and Smith	1959	74
	Marinenko and Taylor	1967	49
Hydrochloric acid, constant boiling	Taylor and Smith	1959	74
	Eckfeldt and Shaffer	1965	20
Adipic acid	Taylor and Smith	1959	74
Potassium dichromate			
NBS 136b	Knoeck and Diehl	1969	34
Oxalic acid dihydrate	Marinenko and Champion	1971	44
Boric acid			
NBS 951	Marinenko and Champion	1971	44
Bases			
Sodium carbonate	Taylor and Smith	1959	74
	Cooper and Quayle	1963	14

Table 1. (Continued)

Substance	Authors	Year	Reference
Trishydroxymethylaminomethane (THAM; tris)			
NBS 723	Marinenko	1970	42
Oxidizing Agents			
Potassium dichromate			
NBS 136b	Marinenko and Taylor	1963	47
	Knoeck and Diehl	1969	33
NBS 136c	Marinenko	1970	42
Ammonium Hexanitratocerate	Knoeck and Diehl	1969	33
Reducing Agents			
Arsenic trioxide			
NBS 83c	Marinenko and Taylor	1967	48
Halides			
Sodium chloride	Marinenko and Taylor	1963	46
Sodium bromide	Marinenko and Taylor	1963	46
Potassium iodine	Marinenko and Taylor	1963	46
Metals			
Zinc	Marinenko and Foley	1971	45

CHAPTER II. PROPERTIES OF 4-AMINOPYRIDINE

Synthesis

The distribution of the isotopes of nitrogen in the 4-aminopyridine titrated in the course of this work is a matter of concern in the final calculations of a value for the faraday. The two nitrogen atoms in the 4-aminopyridine might well be derived from different sources, that in the pyridine ring from coal tar pyridine and thus from coal of ancient age, that in the amino group from ammonia and thus from a recent preparation from nitrogen of the atmosphere. Again, a knowledge of the synthetic route followed in the manufacture would be useful in making judgement as to the nature of the impurities present and of the best method of eliminating them.

No evidence was found in the literature that 4-aminopyridine is found in nature or that it is isolated directly from coal tar. Of the numerous synthetic routes which have been used, three appear to have received most attention:

1. From isonicotinic acid by reaction of the amide with hypobromite (Hofmann degradation), Camps,[10] or by conversion of the azide to the phenylurethane and hydrolysis (Curtius reaction), Camps.[10]
2. By reduction of 4-nitropyridine-N-oxide by iron in glacial acetic acid, Hertog and Overhoff,[27] Ochiai.[56]
3. From 4-pyridylpyridinium dichloride by treatment with ammonia, Koenigs and Greiner,[35] Hauser and Reynolds,[26] Albert,[1] Mosher,[53] Wibaut, Herzberg and Schlatmann.[86]

By any one of the three routes, the amino group is derived from ammonia, hydrazine, or nitric acid of recent origin from nitrogen of the atmospheres; the pyridine is most likely derived from coal of ancient age (however, see next paragraph).

The 4-aminopyridine used in this work was purchased from Reilly Tar and Chemical Corporation, Indianapolis, Indiana. Personnel of the company have informed[31] me that: "Both nitrogen atoms, that of the ring and that of the amino group, enter our operation as liquid ammonia".

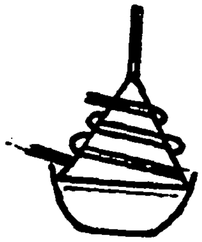
Purification

4-Aminopyridine, Reilly Tar and Chemical Corporation, Indianapolis, Indiana, was powdered and dried at 105°C for ten hours. The dried material was placed in a large evaporating dish resting in an electric heating mantle and covered with an inverted, glass funnel. The material was heated to 100°C for twenty hours. A low melting impurity with appreciable vapor pressure and yellow in color collected on the funnel; this was removed and discarded. A large, perforated filter paper was placed over the material in the dish, the funnel replaced, and a coil of lead tubing was wrapped around the outside of the funnel. A stream of cold water was passed through the tubing and the temperature of the material in the dish was raised to 125°C. Colorless, crystalline sublimate formed above the paper. The sublimate collected during the first twenty-four hours was discarded; that collected subsequently (during several days) was collected and subjected to further sublimation.

During the initial sublimation process just described there formed above the crude material in the evaporating dish a hemispherical shell of sublimed material. This shell consisted of numerous layers of crystalline material of varying colors. From the inside out, that is, from the air pocket above the black residue in the evaporating dish, was, first, a light brown layer, then a very dark brown layer, and then a series of layers varying progressively in color from brown to light brown to tan to colorless. Apparently a zone refining operation was occuring by sublimation. The material collected for further purification had apparently passed through this shell. The material collected was found by titration with standard acid to be 100 percent pure within the limits of titrimetric analysis using volumetric glassware without temperature correction, that is, to within 1.5 parts in 1000.

The final purification of the 4-aminopyridine was carried out by sublimation in an atmosphere of nitrogen in the apparatus shown in Figure 1. The 4-aminopyridine was placed in the 500-ml., round bottom flask, the flask embedded in copper shot (to insure uniform distribution of temperature), the atmosphere in the flask replaced by nitrogen, and flask and material heated to 105°C. The neck of the apparatus was maintained at 95°C and the elbow at 90°C by means of heating tapes, the collecting tube was held at room temperature. The sublimation was carried out at the rate of 1.5 to 2.0 g. per day. The sublimate appeared in successive steps in the neck, elbow, and collecting tube. The material which passed farthest along the collecting tube was rejected as possibly having an impurity of similar but slightly lower volatility than

Figure 1. Sublimation apparatus



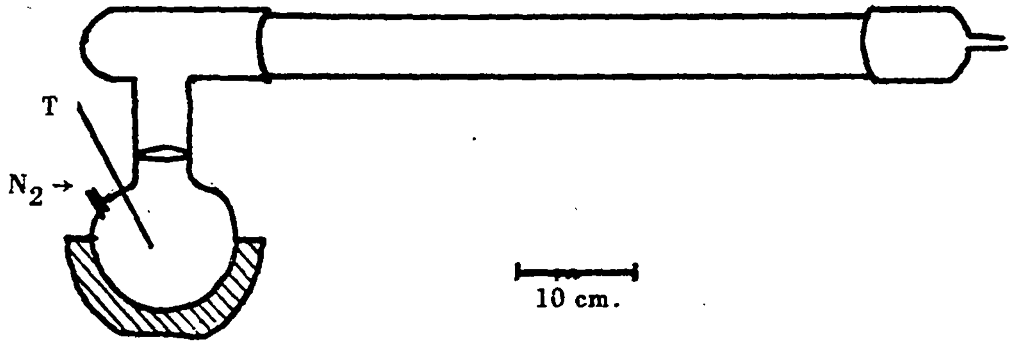

T
N_2 →
10 cm.

Table 2. Dissociation constant of 4-aminopyridine in solutions of sodium perchlorate of various concentrations. 24.4°C

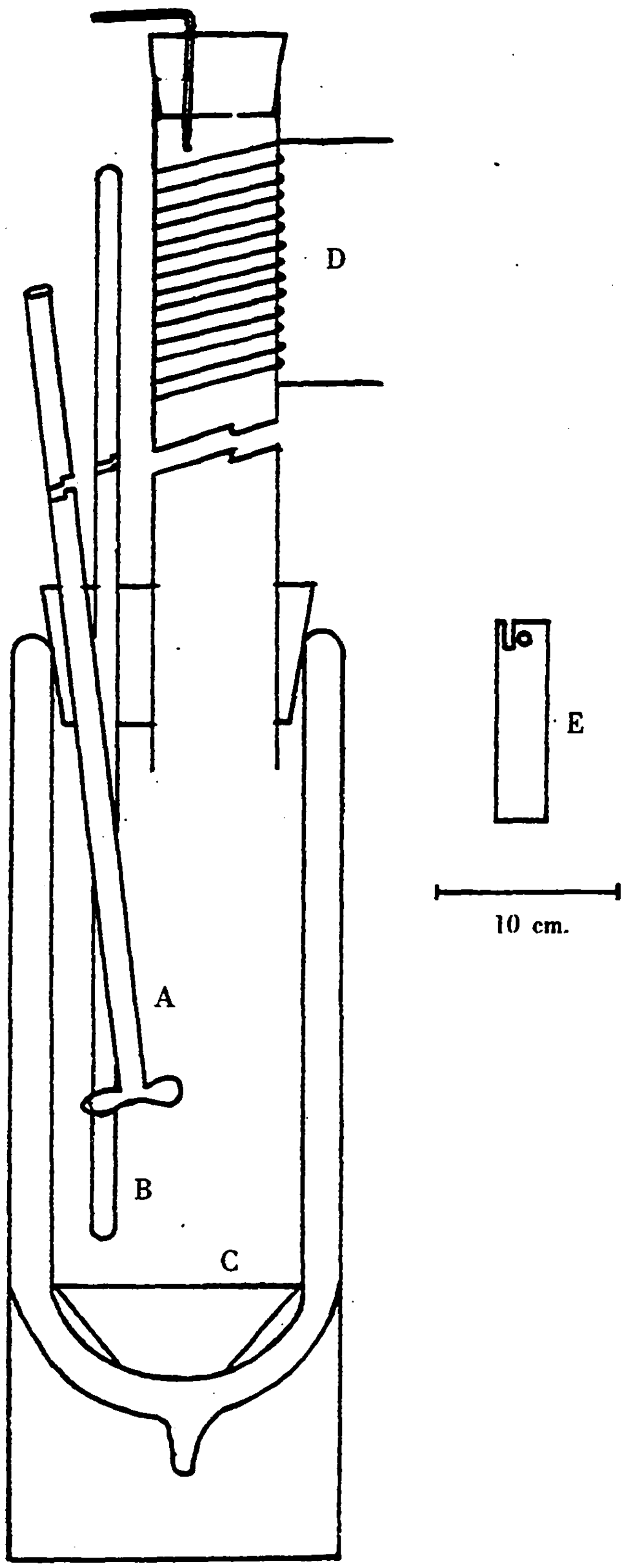
Concentration of sodium perchlorate, M	pK_a $= pH_{mid\text{-}point}$	pK_b $= pK_w - pK_a$
1.15	9.131	4.879
1.00	9.174	4.836
0.65	9.211	4.799
0.40	9.272	4.738
0.15	9.374	4.636

Table 3. Dissociation constant of 4-aminopyridine at various temperatures in 1.00 M sodium perchlorate

Temperature °C	pK_a $= pH_{mid\text{-}point}$	pk_b $= pK_w - pK_a$	pK_w[a]
24.4	9.174	4.836	14.010
30.0	9.096	4.737	13.833
38.0	9.041	4.552	13.593

[a] By interpolation of the data of Bates[5], p. 448.

Figure 2. Calorimeter used in the determination of the latent heat of fusion of 4-aminopyridine.
A. Stirrer; B. Thermometer; C. Brass Screen;
D. Furnace; E. Copper slug.


D
E
10 cm.
A
B
C

4-aminopyridine. The material in the first 15 cm. (from the neck) of the collecting tube was taken for the high-precision titration, the objective of this work; this portion constituted about 90 percent of the total sublimate which appeared in the collecting tube.

Dissociation Constant

The dissociation constant of 4-aminopyridine was measured in solutions of sodium perchlorate of various concentrations. Titrations of the 4-aminopyridine with 0.1 M hydrochloric acid were carried out in the various solutions of sodium perchlorate from which carbon dioxide had been expelled by the passage of nitrogen gas. The titration cell was immersed in a constant temperature bath maintained at 24.4 ± 0.05°C. The titration was followed with a high alkalinity glass electrode and s.c.e. The pH meter was calibrated using two standard buffers of the National Bureau of Standards: 0.01 M borax and 1:3.5 phosphate (Bates[5, p. 73 to 96]). The pH at the mid-point was taken and subtracted from the logarithm of the dissociation constant of water (14.010 at 24.4°C) to obtain pK_b, Table 2, and no correction for activity was made. A plot of pK_b versus the logarithm of the concentration of the sodium perchlorate was linear over the range studied. Values for the dissociation constant were also obtained at two other temperatures, Table 3.

Latent Heat of Fusion

The latent heat of fusion of 4-aminopyridine was determined using the simple calorimeter shown in Figure 2. This calorimeter consisted of a Dewar flask, a brass screen to protect the bottom, a stopper, a motor-driven stirrer, a thermometer, and a tubular furnace for heating materials prior to immersion in water in the calorimeter. The weight of deionized water placed in the Dewar flask in each experiment was 400.00 g. The temperature of the furnace was measured with an iron-constantan thermocouple. The temperature of the water was measured with a glass thermometer (Parr Instrument Company, Calorimeter Thermometer, Cat. No. 1622), always immersed to the same depth and read to 0.002°.

The heat capacity of the calorimeter was obtained by heating a previously weighed bar of copper, National Bureau of Standards 45b, Freezing Point Copper, to a known temperature, dropping the bar into the water, and measuring the temperature of water and bar after thermal equilibrium was attained. The heat capacity (calorimeter plus water) was calculated using the equation

$$C_{cal} = \frac{(c_{Cu})(Wt._{Cu})(T_{Cu,initial} - T_{Cu,final})}{(T_{cal,initial} - T_{cal,final})}$$

in which

C_{cal} = heat capacity of the calorimeter (plus water), in cal/°C

c_{Cu} = specific heat of copper in cal/°C·g.

$Wt._{Cu}$ = weight of copper bar in g.

$T_{Cu,initial}$ and $T_{Cu,final}$ = temperature of copper bar before immersion and after thermal equilibrium has been established

$T_{cal,initial}$ and $T_{cal,final}$ = temperature of calorimeter before immersion and after thermal equilibrium has been established.

The value, $c_{Cu} = 0.09305$ cal./°C·g., was taken from The Handbook of Chemistry and Physics. The values found for the heat capacity of the calorimeter were:

$$C_{cal} = 448.6,\ 444.3,\ 444.6,\ 445.9;\ \text{average } 445.9 \text{ cal./}^{o}\text{C}$$

$$1866 \text{ J/}^{o}\text{C}$$

(using the conversion factor: 1 calorie = 4.1840 joule).

A glass ampule was used to introduce the 4-aminopyridine into the calorimeter. The specific heat of the glass used to make the ampule, c_{glass}, was determined in the same manner, the results being calculated by

$$c_{glass} = \frac{C_{cal}(T_{cal,initial} - T_{cal,final})}{(T_{glass,initial} - T_{glass,final})(Wt._{glass})}.$$

The values found for the specific heat of the glass were

$$c_{glass} = 0.1965,\ 0.1971,\ 0,1971;\ \text{average } 0.1969 \text{ cal./}^{o}\text{C·g.}$$

$$0.8238 \text{ J/}^{o}\text{C·g.}$$

In handling the 4-aminopyridine, the empty ampule was weighed, filled with the 4-aminopyridine, weighed, sealed, ampule plus 4-aminopyridine were then heated to a temperature just below the melting point of 4-aminopyridine, and after suitable time for thermal equilibrium to be established, the ampule was dropped into the calorimeter. The specific heat of 4-aminopyridine, c_{4AP}, was then calculated by

$$Q_1 = (T_{(\text{glass+4AP}),\text{initial}} - T_{(\text{glass+4AP}),\text{final}})(\text{Wt.}_{\text{glass}})(c_{\text{glass}})$$

$$Q_2 = (T_{(\text{glass+4AP}),\text{initial}} - T_{(\text{glass+4AP}),\text{final}})(\text{Wt.}_{4\text{AP}})(c_{4\text{AP}})$$

$$Q_3 = C_{\text{cal}}(T_{\text{cal,initial}} - T_{\text{cal,final}})$$

$$T_{\text{cal,final}} = T_{(\text{glass+4AP}),\text{final}}$$

$$Q_3 = Q_1 + Q_2 .$$

The values found for the specific heat of solid 4-aminopyridine were:

$c_{4\text{AP}} = 0.4391,\ 0.4411,\ 0.4432$; average 0.4411 cal./°C·g.

1.846 J/°C·g.

(using the conversion factor 1 cal = 4.1840 joules).

Finally the latent heat of fusion, l_f, was measured. The filled ampule was heated to 165°. When all of the 4-aminopyridine was melted, the temperature was lowered slowly to within 1° of the freezing point. The ampule was then dropped into the calorimeter.

$$Q_4 = (T_{(\text{glass+4AP}),\text{initial}} - T_{(\text{glass+4AP}),\text{final}})(\text{Wt.}_{\text{glass}})(c_{\text{glass}})$$

$$Q_5 = (T_{(\text{glass+4AP}),\text{initial}} - T_{(\text{glass+4AP}),\text{final}})(\text{Wt.}_{4\text{AP}})(c_{4\text{AP}})$$

$$Q_6 = (\text{Wt.}_{4\text{AP}})(l_f)$$

$$Q_7 = C_{\text{cal}}(T_{\text{cal,initial}} - T_{\text{cal,final}})$$

$$T_{\text{cal,final}} = T_{(\text{glass+4AP}),\text{final}}$$

$$Q_7 = Q_4 + Q_5 + Q_6 .$$

The values obtained for the latent heat of fusion were:

$$l_f = 64.96,\ 66.12,\ 66.51,\ 65.89,\ 66.11;\ \text{average } 65.9 \text{ cal./g.}$$

$$275.8 \text{ J/g.}$$

Using for the molecular weight of 4-aminopyridine the molar heat of fusion is

$$L_f = 6204 \text{ cal./mole}$$

$$= 25{,}960 \text{ J/mole.}$$

The overall error in this measurement is estimated to be less than 15 parts per 1000.

CHAPTER III. PURITY OF 4-AMINOPYRIDINE AS DETERMINED FROM FREEZING CURVES

This chapter done jointly with Mr. Frederick R. Kroeger and Professor Clayton A. Swenson of the Ames Laboratory, United States Atomic Energy Commission and the Department of Physics, Iowa State University.

Freezing Curves and Melting Curves as Criteria of Purity

Of the various methods of establishing the purity of compounds, the freezing point depression procedures have received the most attention as at once providing the most favorable approach experimentally and entailing measurements which can be made with high sensitivity and accuracy. Two approaches are taken: cooling the substance through the freezing range, generally referred to as the "freezing curve method" or sometimes as the "thermometric method", and heating through the melting range, generally referred to as the "calorimetric method." The freezing curve method has been most popular but both methods have been demonstrated to yield reliable figures for total, small impurity, with a precision of 0.005 mole percent or so.

The depression of the freezing point is related to the concentration of the impurity present by the relation

$$x_2 = \frac{L_f(T_m - T_o)}{RT_m^2} \tag{1}$$

in which

x_1 = mole fraction of major component

x_2 = mole fraction of minor component (impurity)

L_f = latent heat of fusion, in cal./mole

T_m = freezing temperature of the pure major compound, in K (K = degrees on Kelvin scale)

T_o = freezing temperature of impure major compound (temperature of initial crystallization), in K

T = temperature during the freezing process, in K

R = gas constant (1.9872 cal./mole • K).

A constant, A, called the cryoscopic constant is defined by

$$A = \frac{L_f}{RT_m^2} . \tag{2}$$

Thus

$$x_2 = A(T_m - T_o) . \tag{3}$$

For a derivation of equation (1), see Washburn,[82] White,[84] Schwab and Wichers,[63] Mair, Glasgow and Rossini,[41] and Pilcher.[58] The assumptions made in the derivation are

1. That thermal equilibrium between liquid and solid exists.
2. The impurity remains entirely in the liquid phase during the freezing process.
3. That the liquid behaves as an ideal solution.

Solutions containing a very small amount of impurity conform to the laws of ideal solutions but solid solution can occur when the molecular size and shape of the impurity is similar to that of the major component or when the heat of fusion of the major component is small.

The depression of the freezing point is usually obtained from a freezing curve rather than from a single measurement; the melting point of a 100 percent pure compound usually is not known accurately and the early part of a freezing event is usually distorted by supercooling. Thus, the freezing temperature of the pure compound, T_m, and the temperature of initial crystallization, T_o, are best obtained by an interpretation of the entire freezing curve, a procedure which goes back to White[84] and which was elaborated by Schwab and Wichers[63] and by Glasgow and co-workers.[24] A variation on this interpretation which allows all of the points of the curve to be used was used in the present work and is explained in later paragraphs.

Various apparatus have been devised for application of the freezing curve method at different levels, notably to commercial materials by Witschonke[87,88] (up to 5 mole percent of impurity with precision of 0.1 mole percent), to highly pure, "single crystal" primary standard benzoic acid by Schwab and Wichers[63] (precision 0.001 mole percent), and to highly pure hydrocarbons by Rossini and co-workers,[41,71,75,24] Glasgow, Ross, Horton, Enagonio, Dixon, Saylor, Furukawa, Reilly and Henning[23] (precision 0.001 mole percent). The method has even become "official" for determining the purity of hydrocarbons, ASTM Standards D 1015-70[2] and D 1016-55.[3]

Apparatus have also been perfected for carrying out the calorimetric method (melting curve method) with high precision. The instrumentation is more complex but the method yields in addition to a measure of the purity, the latent heat of fusion. In the freezing curve method the latent heat of fusion, being a component of the cryoscopic constant, must be determined independently. Application of both methods to highly pure benzene was made by Glasgow, Ross, Horton, Enagonio, Dixon, Saylor, Furukawa, Reilly and Henning[23] and thus the opportunity provided for a critical comparison of the two methods. A critical survey of the calorimetric method based on extensive experimental work was reported by McCullough and Waddington.[54] The complications which may affect the calorimetric method owing to complexities which occur in binary systems have also received attention, for alkanes by Mazee,[51] and for long chain fatty acids by Skau, Magne and Mod.[69] A difficulty which disturbs the calorimetric method is the local concentration of impurity during the freezing which follows charging the cell with the molten sample, a process which must precede the melting measurements. The effects of such segregation and other so-called "premelting phenomenon" are discussed in some detail by Ubbelohde,[78] by Glasgow and others,[23] and by McCullough and Waddington.[54]

Values for the cryoscopic constant, A, can be either calculated from a knowledge of the latent heat of fusion and the melting temperature (equation (2)) or determined empirically by the deliberate addition of a measured amount of impurity to a pure compound and obtaining a cooling curve. Because more than two or three significant figures are not needed, cryoscopic constants can be estimated for some materials from compounds of similar nature and about the same melting temperature. Cryoscopic constants for some ninety compounds of commercial importance are listed by Witschonke[88] and the general problem of evaluating cryoscopic constants is discussed at some length by Barnard-Smith and White[4] who also described a simple calorimeter and procedure by which latent heats of fusion can be measured with sufficient accuracy for freezing curve work.

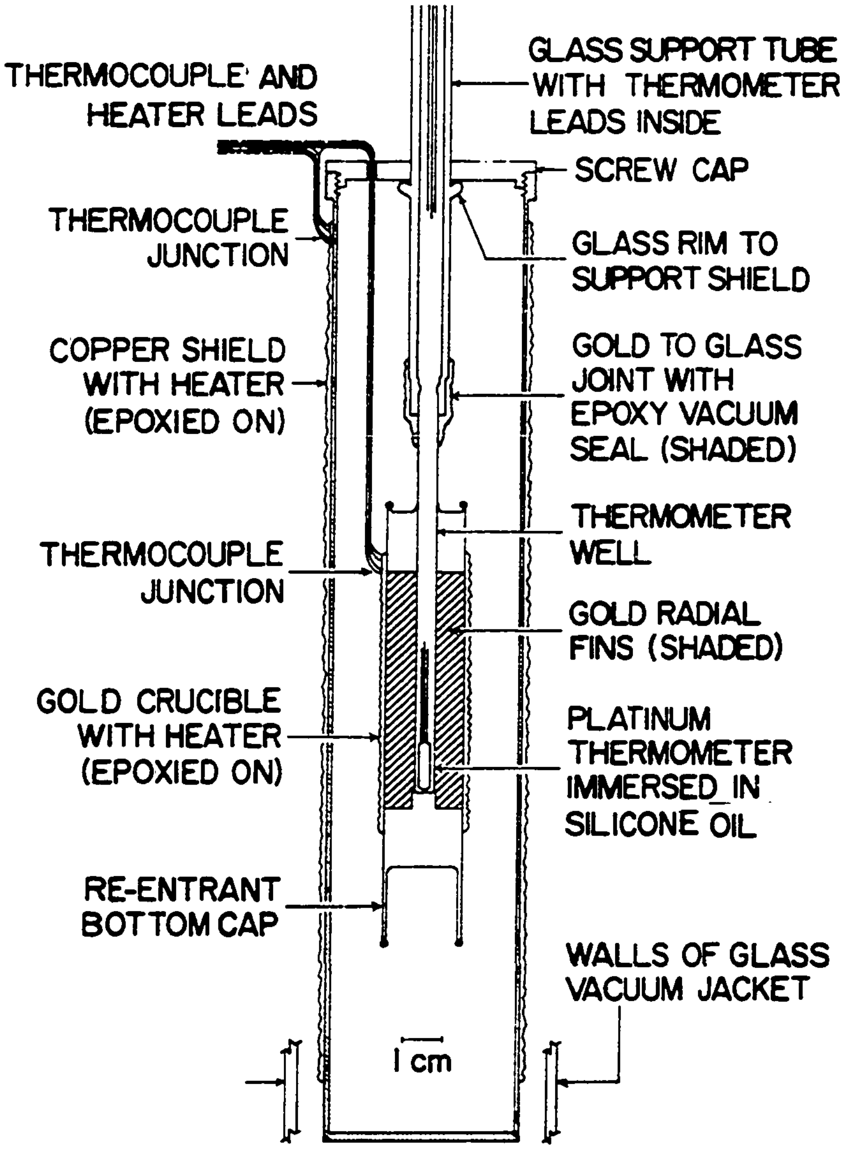
In the early freezing curve apparatus (White,[84] Skau,[68]), temperature was measured by a thermocouple; in all apparatus described since 1940, temperature has been measured using a platinum resistance thermometer. The most precise of the various apparatus described are those of Schwab and Wichers,[63] of Rossini and co-workers,[41,71,75,24] and of Glasgow, Ross, Horton, Enagonio, Dixon, Saylor, Furukawa, Reilly and Henning.[23]

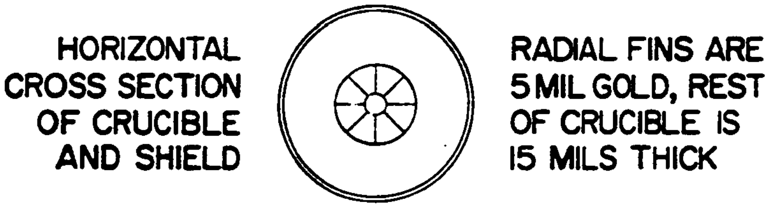
The apparatus used in the present work differs from those of Schwab and Wichers, Rossini, and Glasgow principally in the elimination of mechanical stirring, in the use of a metal rather than a glass container, and in the maintenance, by means of electrical control devices, of an exact and constant temperature difference between the freezing mass and the surroundings as the temperature of the freezing mass drops. Platinum was abandoned after one trial as being too low in thermal conductivity and the final container was made of gold. Gold vanes were placed throughout the melt to promote rapid attainment of thermal equilibrium. Contrary to the results of preliminary trials, my final measurement was disturbed, but I think not fatally, by attack on the gold by the molten 4-aminopyridine.

General Description of the Instrument for Obtaining Melting Curves and Freezing Curves

The present apparatus was designed for the precise measurement of the temperature of the material as a function of time during both melting and freezing. A cross section of the instrument is shown in Figure 3 and a block diagram of the associated electrical equipment is shown in Figure 5. All electrical leads to the crucible were anchored in one sense or another to the shield, so that the heat leak between the shield and the crucible could be varied or controlled very precisely by varying the temperature difference, as measured by a thermocouple, between the shield and the crucible. The assumption was made that if this temperature difference was held constant to better than 1 per cent, the external heat leak to the crucible would be constant to this same factor. In practice, in melting curve experiments, the external heat influx to the crucible was kept very small and the actual heat of melting was given by the amount of electrical energy dissipated in the crucible heater. In a freezing experiment, the temperature of the shield was decreased with respect to the crucible until the rate of freezing was such that the material could be frozen completely over a period of 12 to 20 hours. This temperature difference, which was of the order of $5^{\circ}C$, could be held constant over this time to better than $0.01^{\circ}C$ by manual control of the current passing through the heater on the shield. The magnitude of the cooling could be ascertained by noting the amount of power supplied to the heater on the crucible necessary to keep the crucible temperature constant with this temperature difference.

Figure 3. Instrument for obtaining melting and freezing curves


THERMOCOUPLE AND HEATER LEADS
GLASS SUPPORT TUBE WITH THERMOMETER LEADS INSIDE
SCREW CAP
THERMOCOUPLE JUNCTION
GLASS RIM TO SUPPORT SHIELD
COPPER SHIELD WITH HEATER (EPOXIED ON)
GOLD TO GLASS JOINT WITH EPOXY VACUUM SEAL (SHADED)
THERMOMETER WELL
THERMOCOUPLE JUNCTION
GOLD RADIAL FINS (SHADED)
GOLD CRUCIBLE WITH HEATER (EPOXIED ON)
PLATINUM THERMOMETER IMMERSED IN SILICONE OIL
RE-ENTRANT BOTTOM CAP
WALLS OF GLASS VACUUM JACKET
1 cm


HORIZONTAL CROSS SECTION OF CRUCIBLE AND SHIELD
RADIAL FINS ARE 5 MIL GOLD, REST OF CRUCIBLE IS 15 MILS THICK

Details of Construction

Vertical and horizontal cross sections of the crucible and heat shields are shown in Figure 3. The crucible was made of "five-nines" gold rolled to a thickness of 0.25 mm. A miniature platinum resistance thermometer (MINCO, 25 ohm, Type 51,P/N, S1055-1) was placed in a central well, 6 mm. in diameter, made of gold. The well was filled and the thermometer immersed in silicone diffusion pump oil. Radial vanes made of gold 0.13 mm. in thickness were placed in the crucible; these vanes extended from the thermometer well to the wall of the crucible. The upper end of the thermometer well was sealed into a glass tube with high-temperature epoxy cement (Armstrong 701). The thermometer well and crucible were carried on this glass tube. The crucible was loaded from the bottom, the reentrant cap pressed into position, and the joint sealed by electron beam welding. During the welding, the crucible was placed in a 1200-g. block of copper drilled to accommodate the crucible snugly; the cooper block acted as a heat sink. The reentrant cap was designed to provide a high conductivity heat path to further protect the 4-aminopyridine from becoming too warm. The heater on the crucible was made of No. 32 manganin wire which was wound on and attached to the crucible with high temperature epoxy resin (Armstrong 271). The resistance of this heater was 109 ohms.

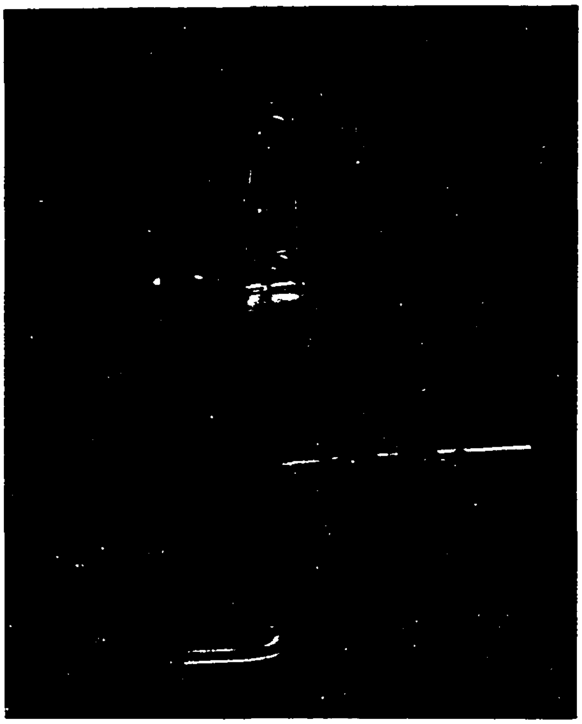
The heat shield surrounding the crucible was made of copper pipe, 1.5 mm. wall thickness, 40 mm. inside diameter. This shield was carried on a screw cap which was in turn supported by a rim on the glass extension of the thermometer well. The copper shield was wrapped with No. 32 manganin resistance wire, the wire being held in place with epoxy cement.

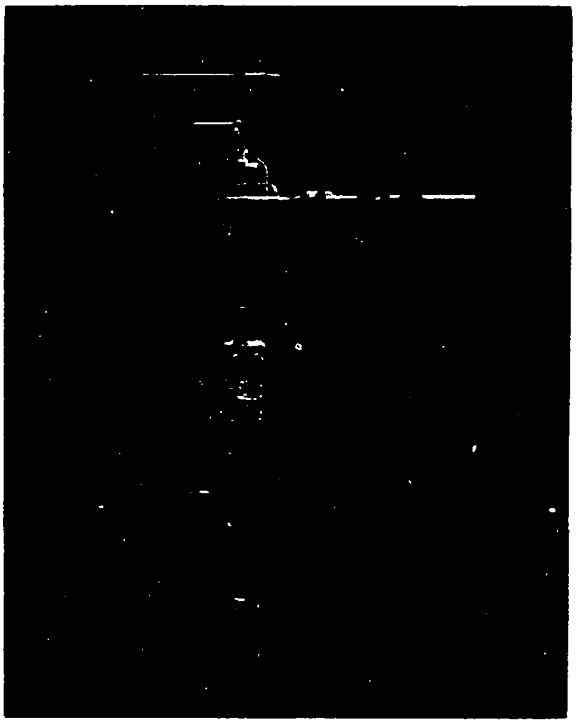
The temperature difference between crucible and the shield was measured with a copper-constantan differential thermocouple attached at the tops of the manganin wire heaters. The heater and thermocouple leads from the crucible were brought out through a hole in the screw cap. The crucible and shield were each wrapped with cleaned aluminum foil to reduce heat transfer by radiation.

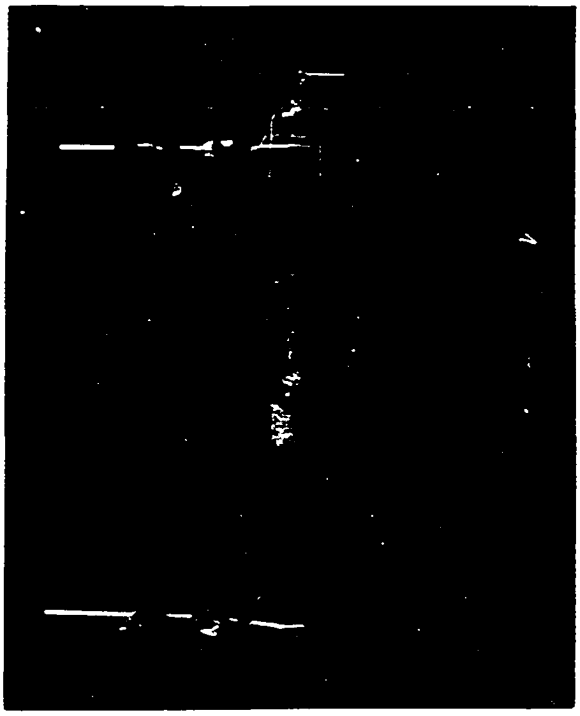
The crucible and shield assembly were enclosed in a glass vacuum jacket, the inside of which was silvered to further reduce heat transfer by radiation. The glass tube supporting the crucible and isothermal shield was an extension of the thermometer well and through it passed the leads from the platinum resistance thermometer. This glass tube was sealed into the top of the glass vacuum jacket; the top and bottom parts of the glass vacuum jacket were sealed with an O-ring. The heater and thermometer leads were passed through a sideport in the bottom portion of the vacuum jacket. The vacuum seal was obtained by passing the leads through a short piece of stainless steel tubing, filling the void with epoxy resin, then placing the tubing in a rubber stopper which filled the port. The vacuum jacket was evacuated only to 0.1 micron, or so, but the major heat loss was caused by radiation rather than by conduction by the residual gas.

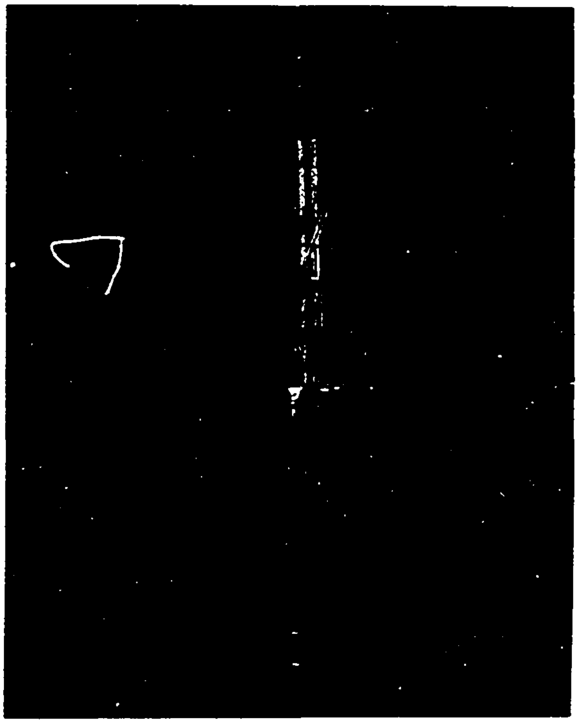
Various stages in the assembly of the instrument are shown in the four photographs in Figure 4.

Figure 4. Stages in the assembly of the instrument for obtaining melting curves and freezing curves







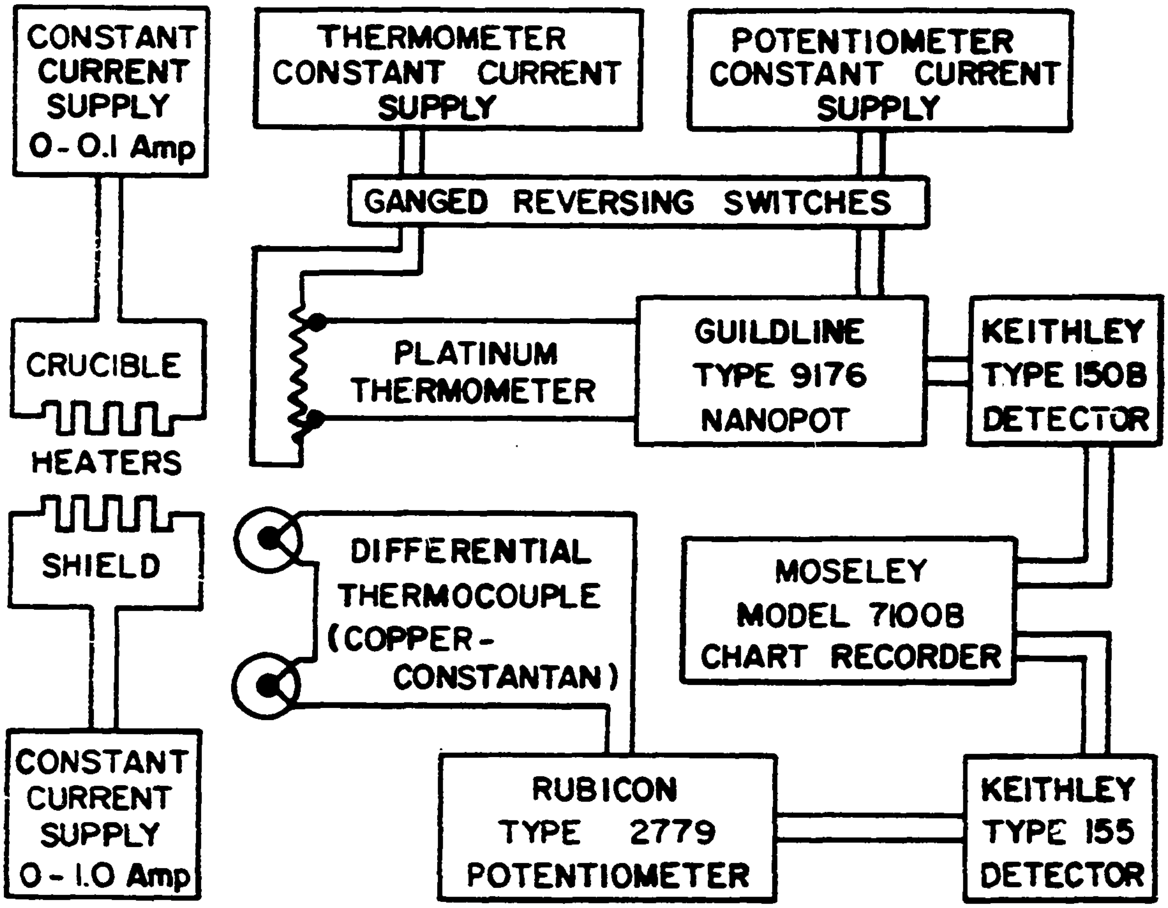


Electrical Components

The various components of the electrical system are shown in Figure 5; each of these components has an obvious relationship to the instrument described immediately above. Sufficiently fine adjustments were provided on the electrical supplies to the two heaters to permit delicate variations in current. The potential of the thermocouple measuring the difference in temperature between the crucible and the shield was opposed by a very stable bucking voltage provided by a Rubicon Type 2779 potentiometer; small variations in the difference of these potentials were displayed on a Keithley 155 microvoltmeter used on the $\pm 10\mu V$ full scale range. The power output of the copper-constantan thermocouple was roughly $40\mu V/^{o}C$ at these temperatures so that temperature variations of $0.003^{o}C$ $(0.10\mu V)$ were observable. These variations were displayed on one pen of a Moseley Model 7100B, dual-pen strip chart recorder.

At the melting temperature of 4-aminopyridine $(159.090^{o}C)$ and the standard current of 2 mA, the potential across the platinum resistance thermometer (25 ohms at $0^{o}C$) was 82.4 mV with a sensitivity of $200\mu V/^{o}C$. Absolute temperature could be determined to $\pm 5m^{o}C$ $(\pm 1\mu V)$ and temperature difference could be determined to $\pm 0.5m^{o}C$ $(\pm 0.1\mu V)$. This thermometer was calibrated by comparison with a Leeds and Northrup Company platinum resistance thermometer which had been calibrated at the National Bureau of Standards. The resistance of the platinum resistance thermometer at any given temperature was obtained by comparing potentiometrically the potential drop across the thermometer and that across a 10-ohm, National Bureau of Standards type, standard resistance manufactured by the Leeds

Figure 5. Components of the electrical measurement system


CONSTANT CURRENT SUPPLY 0-0.1 Amp
THERMOMETER CONSTANT CURRENT SUPPLY
POTENTIOMETER CONSTANT CURRENT SUPPLY
GANGED REVERSING SWITCHES
CRUCIBLE
HEATERS
SHIELD
PLATINUM THERMOMETER
GUILDLINE TYPE 9176 NANOPOT
KEITHLEY TYPE 150B DETECTOR
DIFFERENTIAL THERMOCOUPLE (COPPER-CONSTANTAN)
MOSELEY MODEL 7100B CHART RECORDER
CONSTANT CURRENT SUPPLY 0-1.0 Amp
RUBICON TYPE 2779 POTENTIOMETER
KEITHLEY TYPE 155 DETECTOR

and Northrup Company, Type 4025-B, Serial Number 1765097, using a Guildline, Type 9176 potentiometer. The current supplies to the thermometer and to the potentiometer were of the type described by Kroeger and Rhinehart;[37] these supplies proved stable to better than 10^{-6} over 24-hour periods, twice the time required to obtain a melting curve or a freezing curve. Systematic errors due to thermal emf's were eliminated by using standard current-reversal techniques. The thermometer and potentiometer currents were reversed simultaneously to change the sign of the potentials which were being measured, while the sense of the thermal emf's was not altered. During an experiment, the Guildline potentiometer was kept at a fixed setting, or was reset only occasionally as appropriate, and the variation of the off-balance potential (and hence of the temperature) with time as measured by a Keithley 150B microvoltmeter was recorded on the second pen of the chart recorder using $\pm 1 \mu V$ full scale sensitivity. The chart recorder thus gave both the change in the temperature of the 4-aminopyridine and the difference in temperature of the crucible and shield with time. The MINCO platinum resistance thermometer showed considerable self-heating at the 2 mA current used, $0.014^{\circ}C$, and although this correction was made, it did introduce some uncertainty into the value for the melting temperature of pure 4-aminopyridine. It did not introduce an error into the variations of temperature occurring during the melting-curve and freezing-curve experiments on which estimates of the purity of the 4-aminopyridine are based.

Operation of the Instrument to Obtain a Freezing Curve

The 4-aminopyridine in the gold crucible was melted by heat from the crucible heater. After all of the material was melted, the temperature of the crucible and the temperature of the shield were stabilized by adjusting the power to the heaters so that the temperature of the crucible was 1 to 2°C above the melting temperature. The temperature difference between the crucible and shield was then adjusted and maintained at a value which produced a suitable rate of cooling; this difference in temperature was 5.00 ±0.02°C in most of the experiments. After the temperature difference between the crucible and shield was stabilized, the power to the crucible heater was turned off, and the power to the shield heater was reduced as needed to maintain the temperature difference constant. The temperature of the crucible and the temperature difference between the crucible and the shield were monitored continuously and recorded on the strip chart. The initial portion of the cooling curve represented the cooling of the molten 4-aminopyridine which continued well below the melting temperature; this supercooling amounted usually to about 6°C and lasted approximately 30 minutes. Recovery from the supercooling was rapid and the remaining portion of the cooling curve extended to 10 to 12 hours. After recovery from the supercooling and at intervals of 10 minutes, the sensitivity of the detector for the potential of the platinum thermometer was increased by a factor of 10 for a period of 5 minutes. This was done so that the slope, dT/dt, of the freezing curve could be measured more accurately. The cooling was continued until the slope reflected the heat capacity of the solid. The temperature of the

4-aminopyridine was then held constant about $5^{\circ}C$ below the melting temperature until the next run.

Freezing Curves Obtained on High-Purity 4-Aminopyridine

Exclusive of preliminary, experimental work related to the design of apparatus and establishment of optimum working conditions, freezing curves were obtained on each of two charges ("Charge I" and "Charge II") of the instrument with the 4-aminopyridine purified by vacuum sublimation as described in Chapter II, above. Successive freezing curves were obtained on each of these charges, eight on Charge I (I-1, I-2, and so on), three on Charge II (II-1, II-2, II-3). The mathematical analysis of a typical freezing curve so obtained is given in a following section. Because the impurity in the 4-aminopyridine was found to increase with each successive curve, the total time in which molten 4-aminopyridine was in contact with the gold was computed from the times involved in obtaining each curve. The values of the depression of the freezing point obtained in the various freezing curves are reported in Table 4.

Melting Temperature of Pure 4-Aminopyridine

The melting temperature of pure 4-aminopyridine was obtained by extrapolating the freezing curves back to time equal to $-\tau/2$. (For the nomenclature and symbolism and the procedure for obtaining the total time required for freezing, τ, see the later section of this part of this thesis labeled "General Treatment of Data Obtained from a Freezing Curve.") At a time equal to $\tau/2$, the impurity in the molten 4-aminopyridine is twice that originally present and conversely the impurity at time $t = -\tau/2$ is zero.

In principle this is the same experimentally as determining T_o and $T_m - T_o$. The absolute freezing temperature was calculated from the calibration curve obtained comparing the MINCO platinum resistance thermometer and the Leeds and Northrup platinum resistance thermometer which was calibrated on IPTS-1968 (International Practical Temperature Scale of 1968) at the National Bureau of Standards, thermometer serial number 1676930. The values observed in two runs, after correction for self heating, were T_m = 432.248K, 432.236K; the second of these was from a more satisfactory freezing curve and a weighted mean is used:

$$T_m = 432.240 \pm 0.010\text{K}$$
$$= 159.090 \pm 0.010^{\circ}\text{C}.$$

Melting Curve of 4-Aminopyridine and Latent Heat of Fusion of 4-Aminopyridine Using the Instrument for Obtaining Melting and Freezing Curves

The latent heat of fusion of 4-aminopyridine was calculated from data obtained from a melting curve obtained with the apparatus described on preceding pages. The charge of 4-aminopyridine in the gold crucible of the instrument was melted by passing a current of 50.0 mA through the heater on the crucible while at the same time maintaining the temperature difference between the crucible and the shield at zero. The power necessary to melt the 4-aminopyridine was thus the power required to cause melting less that required to maintain the 4-aminopyridine at the melting temperature:

$$I^2R = (I_1^2 - I_2^2)\ (R_h)$$

in which

I_1 = current to crucible heater to cause melting = 50.0 mA

I_2 = current to crucible heater to maintain constant temperature at the melting point = 14.5 mA

R_h = resistance of crucible heater = 109 ohms

The power required to cause the melting was 0.2507 watts; the time required to melt the 4-aminopyridine with this power input was 260 min. The energy required was thus

$$\begin{aligned} Q_{total} &= (0.2507 \text{ watts})\ (260 \text{ min.})\ (60 \text{ sec./min.}) \\ &= 391{,}100 \text{ watt} \cdot \text{seconds} \\ &= 3911 \text{ joules} \\ &= 934.7 \text{ cal.} \end{aligned}$$

Because a rise in temperature occurred during the melting process, the total energy must be corrected for the energy required to heat the crucible plus addenda (heating wire, cement, part of the glass supporting tube) plus 4-aminopyridine

$$\begin{aligned} Q_{cr} &= (c_{cr})\ (\text{wt.}\ _{cr})\ (\Delta T) \\ Q_{4AP} &= (c_{4AP})\ (\text{wt.}\ _{4AP})\ (\Delta T) \end{aligned}$$

in which

c_{cr} = specific heat of crucible plus addenda = 0.0314 cal./(g.)(°C)

(0.0314 cal./(g.)(°C) = specific heat of gold wt. $_{cr}$ = weight of crucible plus addenda = 115 g.

ΔT = rise in temperature during the melting = 3.32°C

c_{4AP} = specific heat of solid 4-aminopyridine = 0.4432 cal./(g.)(°C)

wt. $_{4AP}$ = weight of 4-aminopyridine = 13.24 g.

from which

$$Q_{cr} = 12.0 \text{ cal.}$$

$$Q_{4AP,\Delta T} = 19.5 \text{ cal.}$$

A better value for $Q_{4AP,\Delta T}$ could be obtained using a weighted average of the specific heats of the liquid and solid 4-aminopyridine, the former being somewhat smaller. The crucible was composed of gold, glass, epoxy cement and manganin wire. Most of the weight was gold and the specific heats of the other materials are not greatly different from that of gold, so that the specific heat of gold was used above. The corrected energy required was thus

$$Q_{4AP,\text{melting}} = Q_{\text{total}} - Q_{cr} - Q_{4AP,\Delta T}$$

$$= 934.7 - 12.0 - 19.5 = 903.2 \text{ cal.}$$

The latent heat of fusion is

$$L_f = (903.2 \text{ cal.})/(13.24 \text{ g.})$$

$$= 68.2 \text{ cal./g.} \quad \text{or } 6420 \text{ cal./mole}$$

$$= 285 \text{ joules/g.} \quad \text{or } 26{,}800 \text{ joules/mole.}$$

Specific Heat of Liquid 4-Aminopyridine

The specific heat of liquid 4-aminopyridine was calculated from data obtained from a freezing curve and the value of the specific heat of solid 4-aminopyridine obtained in the course of the calorimetric measurement of the latent heat of fusion of 4-aminopyridine, Chapter II, above.

Because of the design and mode of operation of the freezing curve instrument described in preceding sections of this part of this thesis, the rate of heat removal from the crucible plus addenda plus 4-aminopyridine was constant. Thus

$$(dQ/dt) = [C_{cr} + (c_{4AP,1})\ (Wt._{4AP})]\ (dT/dt)_1 =$$

$$[C_{cr} + (c_{4AP,s})\ (Wt._{4AP})]\ (dT/dt)_s$$

in which C_{cr} represents the heat capacity of the crucible plus addenda and the subscripts 1 and s refer to liquid and solid, respectively. Thus also

$$(c_{4AP,1})\ (Wt._{4AP}) = [[(c_{4AP,s})\ (Wt._{4AP})]\ [(dT/dt)_s] + C_{cr}\ (dT/dt)_s -$$

$$C_{cr}(dT/dt)_1](\ dT/dt)_1 = c_{4AP,s}\ [(dT/dt)_s/(dT/dt)_1]\ .$$

Data from two freezing curves gave

Curve Number	$(dT/dt)_1$	$(dT/dt)_s$
II-1	8.07 mK/min.	7.18 mK/min.
II-2	7.62	7.04

From Chapter II $c_{4AP,s} = 0.4411$ cal./(g.)(°C) .

Thus,

$$c_{4AP,1} = 0.400 \text{ cal./(g.)(}^{\circ}\text{C)} .$$

The error in this value is estimated to be ±5 per cent. The principal uncertainly was in estimating the time at which the last of the 4-aminopyridine melted. During the terminal portion of the melting curve a series of sudden temperature changes occurred within the crucible, a series of sudden steps being recorded on the strip chart. The time of last melting was taken as the point at which the temperature increase became linear with time for the final time. The "structure" observed toward the close of the melting curve may have resulted from segregation of the impurities in the 4-aminopyridine during the freezing of the 4-aminopyridine after it had been placed in the crucible and melted prior to obtaining the melting curve. The freezing curve method of determining impurities, is, of course, based on the assumption that a concentration of the impurities in the liquid phase occurs and the zone refining process also is based on this; segregation thus probably accounts for the sharp but minor changes observed. This measurement of the latent heat of fusion is in good agreement with the value obtained by the direct calorimetric method (Chapter II) L_f = 25,960 joules/mole; the latter is deemed a more accurate value and has been used in calculating the cryoscopic constant (next section).

Cryoscopic Constant of 4-Aminopyridine

The crysocopic constant of 4-aminopyridine was calculated using data obtained in preceding sections:

L_f = Latent heat of fusion = 2.60×10^4 J/mole

T_m = Melting temperature = 432.24K

R = Gas Constant = 8.314 J/(mole)(K)

and the equation

$$A = \frac{100L_f}{RT_m^{\ 2}} = 1.671 \text{ (mole per cent)/K.}$$

This value for the crysocopic constant is in the range of values for similar compounds[88] for example: 2-nitrodiphenylamine, 1.7; quinoline, 1.95; aniline, 1.4; 4-picoline, 2.0; 2,6-lutidine, 2.2; piperazine, 1.8.

General Treatment of the Data Obtained from a Freezing Curve

As discussed in the first section of this chapter of this thesis, an assumption which is made in the use of freezing curves for the determination of the total small impurity in the material undergoing freezing is that the impurity remains in solution in the liquid phase. The treatment of White,[84] and of all who have followed him, is based on this and on the simple consequence of this that when half of the material has frozen the concentration of the impurity will have doubled. Thus, at the time of half freezing, $T_m - T_o = T_o - T$ and a measure of $T_o - T$ then gives the depression of the freezing point.

In the present work, two modifications of the usual method of handling freezing curve data have been made: (1) The data are handled in differential form; and (2) correction is made for the heat capacity of the instrument.

In addition to the terms defined in the first section of this chapter of this thesis, the following symbols are used, the meaning of which are further clarified by reference to Figure 6.

$T_m = T_o = \Delta T_o$

$T_m = T = \Delta T$

t = time, measured from the point $T = T_o$

τ = total time required to freeze the material in the absence of heat capacity effects

n = fraction of the material crystallized at time t

The differential treatment of the data was derived in the following manner. When half of the material has crystallized the impurity will have doubled, when seventy-five per cent has crystallized, the concentration will have quadrupled. Letting n be the fraction of the material crystallized, in general

$$T_m - T = \Delta T = \frac{\Delta T_o}{1 - n} \tag{4}$$

If the rate of heat removal and of crystallization is constant

$$n = \frac{t}{\tau} \tag{5}$$

and

$$T = T_m - \frac{\Delta T_o}{1 - (t/\tau)} \, . \tag{6}$$

Equation (6) describes curve C of Figure 6. Differentiation of equation (6) yields

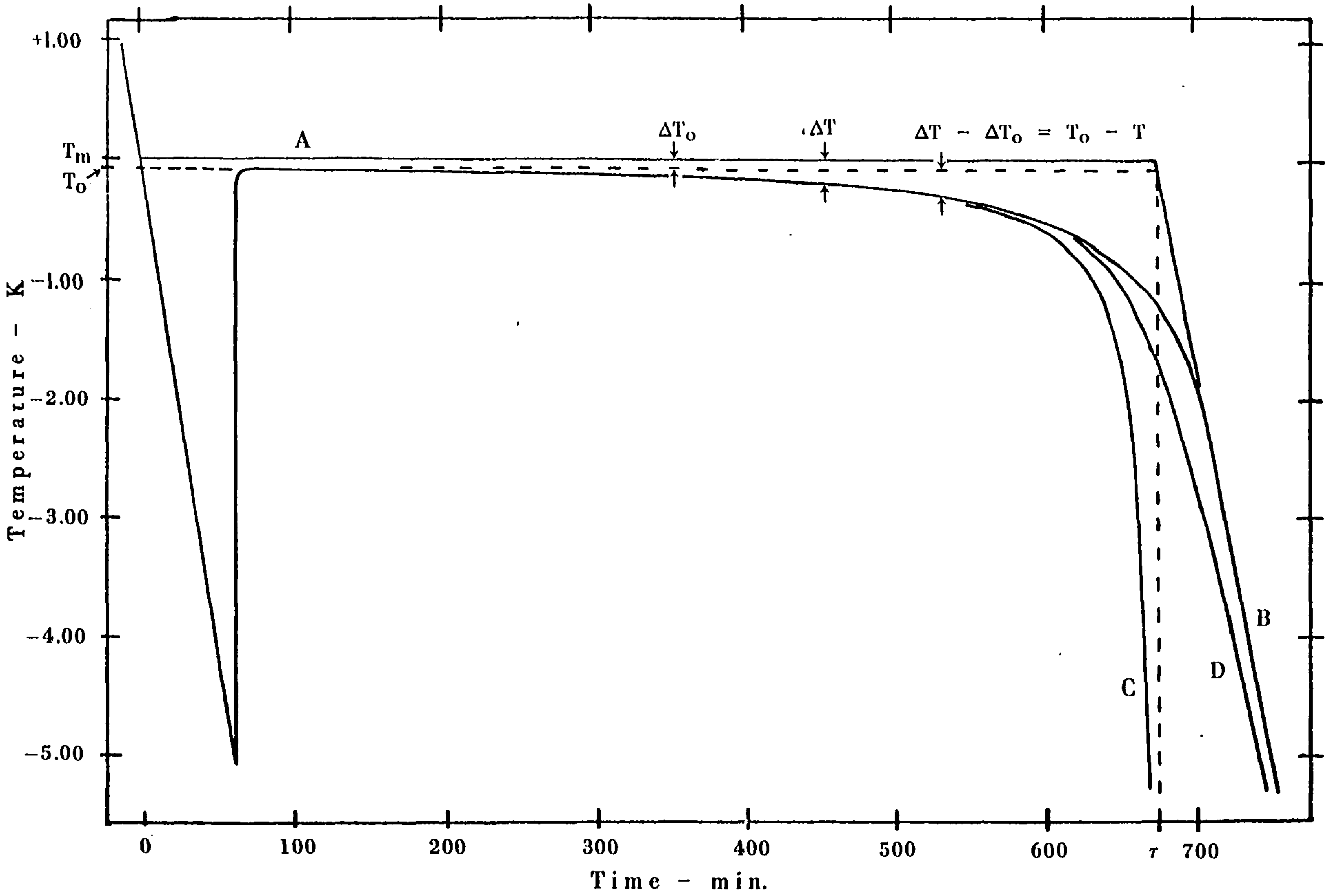
Figure 6. Freezing curves

A. Theoretical curve, pure material, $\Delta T_o = 0$

B. Curve obtained experimentally on 4-aminopyridine

C. Theoretical curve, no heat capacity.
Equation (6). $\Delta T_o = 61$mK. $\tau = 676$ minutes

D. Theoretical curve taking heat capacity of instrument into consideration. $k = 0.00132$. $\Delta T_o = 61$mK.
$\tau = 676$ minutes



+1.00
-1.00
-2.00
-3.00
-4.00
-5.00
Tm
To
Temperature - K
A
ΔTo
ΔT
ΔT - ΔTo = To - T
B
C
D
0
100
200
300
400
500
600
τ
700
Time - min.

$$-\frac{dT}{dt} = \frac{\Delta T_o}{\tau[1 - (t/\tau)]^2} \quad . \tag{7}$$

Thus, by measuring the slope of the cooling curve at a time t the depression of the freezing point, ΔT_o, may be obtained and from it the mole fraction of the impurity, x_2, calculated by equation (3). It is not necessary to know T_m to use equation (7).

Introducing the correction for the heat capacity of the instrument, that is, for the heat liberated during the cooling of the crucible plus addenda (heating wire, cement, and part of the glass support tube), plus 4-aminopyridine, is more involved and is best understood from a more thorough description of what occurs during the process of freezing. It is assumed that the rate of heat removal is constant throughout.

For a completely pure material, 100.000 percent purity or better, the freezing curve would have the form of Curve A of Figure 6, $T_m - T_o$ being zero. The curve begins with a steep, initial negative slope, which is determined by the total heat capacity of the crucible plus addenda plus 4-aminopyridine with the 4-aminopyridine in the liquid state. The temperature, T, falls below T_o owing to supercooling. When nucleation occurs, the temperature rises very rapidly to a temperature close to T_o. The zero of the time scale is taken as the time corresponding to $T = T_o$ on the initial slope, that is, at the onset of supercooling. Recovery from supercooling is accompanied by the freezing of a fraction of the material corresponding to the amount of heat removed during supercooling. After the supercooling period, the temperature remains constant at $T = T_o = T_m$

while the remainder of the material freezes. At time $t = \tau$ freezing is complete and the temperature again begins to fall, the final slope being determined by the total heat capacity of the crucible and addenda and with the material in the solid form.

In an actual freezing curve, as measured by experiment (Figure 6, Curve B), an impurity is present in the material being frozen and heat is given up by the crucible and addenda as the temperature drops through the freezing range. The depression of the freezing temperature, ΔT_o, is real and the temperature following the recovery from supercooling is depressed below the curve of the 100.000 percent pure material (Figure 6, Curve A, $\Delta T_o = 0$), following, however, Curve B rather than Curve C, the one predicted by equation (6). The use of equations (6) and (7) is limited to the first half of the freezing curve, the region in which ΔT is small and the heat released by the crucible plus addenda plus 4-aminopyridine are negligible. The temperature begins to drop rapidly after the 50 percent-frozen point has been passed and a significant part of the total heat removed comes from the crucible plus addenda plus 4-aminopyridine. For a constant rate of withdrawl of heat, the fraction of the material frozen is less than predicted by equation (5) and hence the depression of the temperature and the slope of the curve are less than predicted by equations (6) and (7). Summing the rates of heat removal gives:

$$\frac{dQ_{fr}}{dt} = \frac{dQ_{tot}}{dt} - \frac{dQ_{cr}}{dt} \tag{8}$$

in which the subscripts carry the meanings: fr, freezing; tot, total;

cr, crucible plus addenda plus 4-aminopyridine. The various rates of heat removal are

$$\frac{dQ_{fr}}{dt} = L_f \frac{dM}{dt} \tag{9}$$

M = weight of 4-aminopyridine frozen at time t

$$\frac{dQ_{tot}}{dt} = \frac{L_f G}{\tau} \tag{10}$$

G = total weight of 4-aminopyridine undergoing freezing
(M = G when t = τ)

$$\frac{dQ_{cr}}{dt} = C \frac{dT}{dt} \tag{11}$$

C = heat capacity of crucible plus addenda plus 4-aminopyridine
(in calories per °C per crucible).

From which

$$L_f \frac{dM}{dt} = \frac{L_f G}{\tau} - C \frac{dT}{dt} \tag{12}$$

and

$$\frac{1}{G} \cdot \frac{dM}{dt} = \frac{1}{\tau} - \frac{C}{L_f G} \cdot \frac{dT}{dt} \tag{13}$$

Integration and evaluation of the integration constant (when t = 0, $T = T_o$, and M = 0) gives

$$\frac{M}{G} = \frac{t}{\tau} - \frac{C}{L_f G} (T_o - T) \ . \tag{14}$$

This equation can be rewritten as

$$n' = \frac{t}{\tau} - \frac{k}{\Delta T_o} (\Delta T - \Delta T_o) \qquad (15)$$

by introducing n' as the actual fraction frozen when heat capacities are taken into consideration and k is a new, dimensionless parameter which is defined by

$$k = \frac{C}{L_f G} \Delta T_o \; . \qquad (16)$$

Introducing this expression into equation (4) gives an equation comparable to equation (4) but including consideration of the heat loss by the crucible plus addenda plus 4-aminopyridine:

$$\Delta T = \frac{\Delta T_o}{1 - (t/\tau) + (k/\Delta T_o)(\Delta T - \Delta T_o)} \; . \qquad (17)$$

Solving equation (17) explicitly for ΔT yields

$$\Delta T = (\Delta T_o/2k)\left[\{(1 - (t/\tau) - k)^2 + 4k\}^{1/2} - (1 - (t/\tau) - k)\right] . \qquad (18)$$

As shown below typical values of the constant k are in the range 10^{-3} to 10^{-2}. Equation (18) describes the Curve D of Figure 6. Differentiation of equation (18) yields

$$- \frac{dT}{dt} = (\Delta T_o/2k\tau) \quad 1 - \frac{\{1 - (t/\tau) - k\}}{[\{1 - (t/\tau) - k\}^2 + 4k]^{1/2}} \; . \qquad (19)$$

Because of heat released by the crucible plus addenda plus 4-aminopyridine, the 4-aminopyridine is not completely frozen at $t = \tau$ as is evident from the curves of Figure 6. Theoretically, if the impurities continued to concentrate in the liquid phase, the material would never freeze completely. In reality, the concentration (zone refining) fails at about 90 percent frozen. When the impurities freeze out the depression of the freezing temperature becomes less than that predicted by equation (18). For times such that $\{(t/\tau) - 1\} >> k$, k being positive, equation (19) reduces to

$$- \frac{dT}{dt} = (\Delta T_o/2k\tau)\ 1 - \frac{\{1 - (t/\tau)\}}{[\{1 - (t/\tau)\}^2]^{1/2}}$$

$$= (\Delta T_o/2k\tau)[1 - (-1)]$$

$$= \Delta T_o/k\tau . \qquad (20)$$

For a typical curve obtained experimentally, this value was reached at about $t = 1.1\tau$. This provides a means of obtaining k from the freezing curve.

The evaluation of the depression of the freezing temperature from data obtained from a freezing curve was made using the relations developed above and a curve-fitting or refinement process.

1. The horizontal portion of the freezing curve was extrapolated linearly back across the supercooling region to the initial slope; this established initial values for T_o and $t = 0$, which were then refined in a

series of steps given under 2 through 6.

The initial value for T_o was usually high by 10 percent of ΔT_o. The effect of this error in T_o on t = 0 was negligible owing to the steepness of the initial slope.

Recovery from supercooling was generally accompanied by a small amount of overshoot, 5 to 10 percent of ΔT_o. Theoretically, if the recovery from supercooling were instantaneous, the temperature on recovery would just reach T_o. The overshoot was taken into consideration when performing the above extrapolation.

2. The final part (steep slope) of the freezing curve was extrapolated linearly to the temperature T_o, establishing thereby an initial value for τ.

As with t = 0, the error in the initial value for T_o leads to a negligible error in the initial value for τ because the final slope is also steep.

3. The slope of the freezing curve was measured at several values of time between $t = \tau/3$ and $t = 2\tau/3$, and using the above initial values for t = 0 and τ and equation (7), values for ΔT_o were calculated and the average taken as an initial value for ΔT_o.

4. Using these initial values of t = 0, τ, and ΔT_o and the temperature T from the experimental curve for various times between $t = \tau/3$ and $t = 2\tau/3$, provisional values were calculated for T_m. A horizontal line was drawn through these provisional values of T_m to obtain an initial value for T_m. Then using the initial values for t = 0, τ, ΔT_o and T_m, and equation (6), values of T for various times over the range t = 0 to

$t = \tau/3$ (the supercooling region) were calculated. A smooth curve was then drawn through these points to extend the experimental curve from $t = \tau/3$ back to zero to give a "first corrected" value for T_o and for $t = 0$. Steps 2 and 3 were repeated and first corrected values obtained for τ and ΔT_o. This value for ΔT_o was correct to within a few per cent and the time axis correct to within 0.5 min. or less. From these first corrected values for T_o and ΔT_o, a first corrected value for T_m was then obtained.

5. Correction of the calculated curve to account for the heat capacity of the crucible plus addenda plus 4-aminopyridine was then made. Because most of the temperature drop occurred after the 4-aminopyridine was nearly frozen, the heat capacity of the solid 4-aminopyridine was used. The slope of the final, linear, steep phase of the freezing curve was measured and from it and the values for τ and ΔT_o obtained above, and using equation (20), a value for k was calculated. The value for k was of the order of 0.001 and good to 1 per cent or so.

6. The first corrected values for τ, T_m, and ΔT_o, and the value for k, and equation (18) were then used to calculate values of T over the range $t = 0$ to $t = 1.1$. These values were then plotted on the strip chart carrying the experimental curve. Minor adjustments in the values T_o, T_m and k were made to slightly improve the fit. Equation (19) was also used to check the agreement of the calculated slopes to the experimental slopes throughout the curve. The fit was generally good to $t = 0.90\,\tau$, after which the experimental curve began to deviate from the theoretical curve.

Interpretation of the Data Obtained from Freezing Curves of 4-Aminopyridine

The depression of the freezing temperature, $T_m - T_o (= \Delta T_o)$, was calculated for each of the freezing curves obtained on 4-aminopyridine following the procedure given in the preceding section. The depression of the freezing temperature is directly proportional to the amount of impurity present (see section above entitled "Freezing Curves and Melting Curves as Criteria of Purity," equation (1)). The values of the depression of the freezing temperature increased with each successive curve obtained on each of the two charges, Charge I and Charge II, of the crucible with 4-aminopyridine. The cumulative time in which the molten 4-aminopyridine was in contact with the gold of the crucible was computed according to

$$t_{cum} = (1/2)T_m + t_s + (1/2)\tau$$

in which t_m is the time required to melt the 4-aminopyridine; t_s is the time required to stabilize the 4-aminopyridine prior to cooling, and τ is the time required to freeze the 4-aminopyridine. The values of the depression of the freezing temperature obtained from the successive freezing curves are given in Table 4 as a function of cumulative time.

Of the eight freezing curves obtained on Charge I, the first two (designated I-1 and I-2) were carried out in a relatively short time by using a large temperature difference between the crucible and shield (Table 4). The cumulative time melted for these two curves is correspondingly small. Freezing curves I-3, I-5, I-6, I-7, and I-8 were taken with the same temperature difference, 5°C. The three freezing curves

Table 4. Depression of the freezing temperature, ΔT_o, of 4-aminopyridine as a function of time of contact in the molten state with the gold of the crucible

Freezing curve number	Depression of the freezing point, ΔT_o °C x 1000	Time of contact individual experiment min.	Time of contact cumulative min.	Difference in temperature of shield and crucible °C
Charge I				
I - 1	5	180	180	25
I - 2	30	170	250	12
I - 3	60	400	750	5
I - 4	160	1250	2000	10
I - 5	92	1200	3200	5
I - 6	96	1050	4250	5
I - 7	97	850	5000	5
I - 8	103	1000	6000	5
Charge II				
I - 1	59	500	500	5
I - 2	70	400	900	5
I - 3	80	650	1550	5

obtained on the second charge, curves II - 1, II - 2, and II - 3, were also taken with a temperature difference of 5°C; the values obtained for the depression of the freezing point, ΔT_o, were very close to those obtained on Charge I for the same length of cumulative time in the molten state. It is thus evident that the instrument was functioning properly and giving consistent results from one charge of 4-aminopyridine to the next. It is apparent, however, from freezing curve I - 4 that the depression of the freezing point observed is greatly dependent on the difference in temperature between the crucible and the shield; for a difference of 10°C the depression was close to double that at 5°C (I - 3 and I - 5). This magnification of the depression at larger temperature differences undoubtly also affected freezing curves I - 1 and I - 2, taken at 25°C and 12°C, respectively. The value of the depression found on I - 1, 5m°C, is probably too large and thus represents an upper limit on the impurity. By equation (3) then

$$x_2 = A\Delta T_o = 1.67(0.005) = 0.008 \text{ mole per cent impurity (upper limit).}$$

It is also quite evident that attack on the crucible had been going on from the time of first melting. It appears equally valid therefore to conclude that the depression of the melting point is less than can be detected by this instrument, 1m°C or slightly less. This places a great emphasis on a single freezing curve, I - 1. Although of short duration, this freezing curve was normal, that is, the temperature calculated at times $t = 0.5\,\tau$ and $t = 0.75\,\tau$ using $\Delta T_o = 5$m°C and equation (4) were very close to the temperature observed.

Analyses Made on 4-Aminopyridine Recovered Following Freezing Curve Experiments

Following the experimental work on Charge I and II, the 4-aminopyridine was removed carefully from the crucible in the following manner. The crucible was inverted and electric current passed through the heating wire to melt the 4-aminopyridine and cause it to collect in the bottom (normally the top) end. After cooling the crucible was held horizontally and the welding bead holding the reentrant cap in place was cut off with a jeweler's saw. Gold chips were wiped away and the cap removed. The inner wall of the crucible so exposed was wiped clean, and with a spatula, crystalline 4-aminopyridine to a depth of 5 mm. was removed and discarded. The crucible was then held vertically and current passed through the heater to melt the 4-aminopyridine and cause it to flow into a weighing bottle. The 4-aminopyridine so recovered from Charge I was analyzed directly, that from Charge 2 was first crushed in an agate mortar.

The initial, highly-purified 4-aminopyridine and the materials removed from the crucible of the instrument following the experimental work on Charges I and II were subjected to plasma and spark emission spectrographic analysis by Dr. Richard Kniseley,[32] Ames Laboratory, United States Atomic Energy Commission.

No detectable impurities were present in the initial 4-aminopyridine, the material being as free in this respect as the best grades of spectrographic carbon.

A trace of silicon (possibly 10 p.p.m.) and faint trace of copper, and 10 to 100 p.p.m. of gold were found in the residual material from Charge I.

Neither silicon nor copper were found in the residual material from Charge II. Quantitive analyses for gold indicated that the material was highly inhomogeneous, three results being: less than 50 p.p.m., 65 p.p.m., and 150 p.p.m.

Gold in the residual material from Charge II was also determined by activation analysis by Mr. Richard Clark,[12] Ames Laboratory, United States Atomic Energy Commission; the results on samples approximately 4 mg. in size ranged from 3 to 1200 p.p.m., again indicating great inhomogeneity.

An examination of the residual materials from the freezing curve experiment under the polarizing microscope was made by Professor Donald Biggs, Department of Earth Science, Iowa State University. A very few pieces of metallic gold, diameter less than 20μ were found; the ragged edges indicated that these particles were probably produced by metal fabrication. Many of the crystals of the residual 4-aminopyridine contained within the crystal spots of obviously different material, some brown and some of metallic luster and transparent. Direct visual evidence was thus obtained that an impurity had been introduced and that it was distributed inhomogeneously.

The presence of silicon in the material remaining after the eight freezing curves taken on Charge I and the absence of it in the starting material and in the residual material from Charge II is puzzling. The silicon may well have been derived from a ceramic crucible in which the gold was melted prior to rolling. The fuming perchloric acid leach used to clean the gold crucible before use would be expected to leave any silicon as dehydrated silica and probably on the surface of the gold. This would then be removed during the process of obtaining the freezing curves made on Charge I.

Two mechanisms are suggested for the introduction of the gold into the molten 4-aminopyridine. The first is the dissolution of gold by the action of the molten 4-aminopyridine. As observed, however, that action stops after a limited period. Also in a preliminary experiment, massive gold was immersed in molten 4-aminopyridine for 48 hours and no measureable loss in weight was observed. It would appear, therefore, that the action must be confined to a surface layer and probably to the dissolution of gold oxide. The second mechanism suggested is simply a decomposition of gold oxide. It is known that gold oxide forms on the surface of reduced gold when even briefly exposed to air[40] and to be thermally decomposed[38] about 160°C, the melting temperature of 4-aminopyridine.

CHAPTER IV. HIGH-PRECISION COULOMETRIC TITRATION OF 4-AMINOPYRIDINE

Titration Cell, Electrodes, and Electrolytes

The cell used for the titration of 4-aminopyridine was essentially that described by Eckfeldt and Shaffer[20] as modified somewhat by Knoeck and Diehl[33] and with the addition of the external, "drip" electrode of Knoeck and Diehl.[34] Three major modifications were made:

1. The ultra-fine, glass frit used in the construction of the shield tube was replaced by a length of unfired Vycor, a use of this material proposed by R. A. Durst;[19] the final design is shown in Figure 7. The length of unfired Vycor 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 and the assembly was then soaked in a buffer solution of approximately pH 7 to leach out any remaining acetic acid. It was finally immersed in water for a few days.

2. A side arm of short length and large diameter was added to accommodate more conveniently the glass and saturated calomel electrodes.

3. The external, "drip" electrode used to complete a titration was redesigned, Figure 8. Two sections of unfired Vycor were introduced making a three-compartment device. The level of the electrolyte in the central compartment was maintained above those in the other two compartments so that flow of electrolyte was always outward and diffusion of acid or base from one electrode chamber to the other prevented. The titrant was generated at a platinum wire imbedded in glass and the electrolyte was delivered to this platinum wire by means of a wick of glass fiber which passed through

Figure 7. Shield tube

A. Counter electrode

B. Glass frit

C. Unfired Vycor

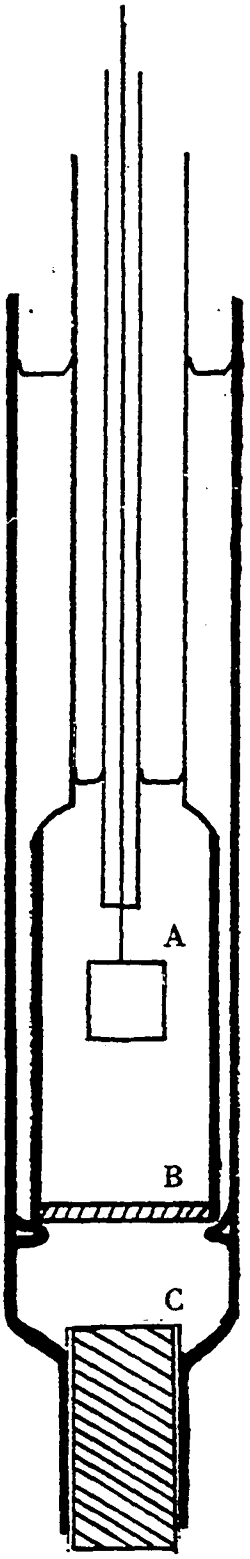

A
B
C

Figure 8. External, "drip" electrode

A. Platinum counter electrode

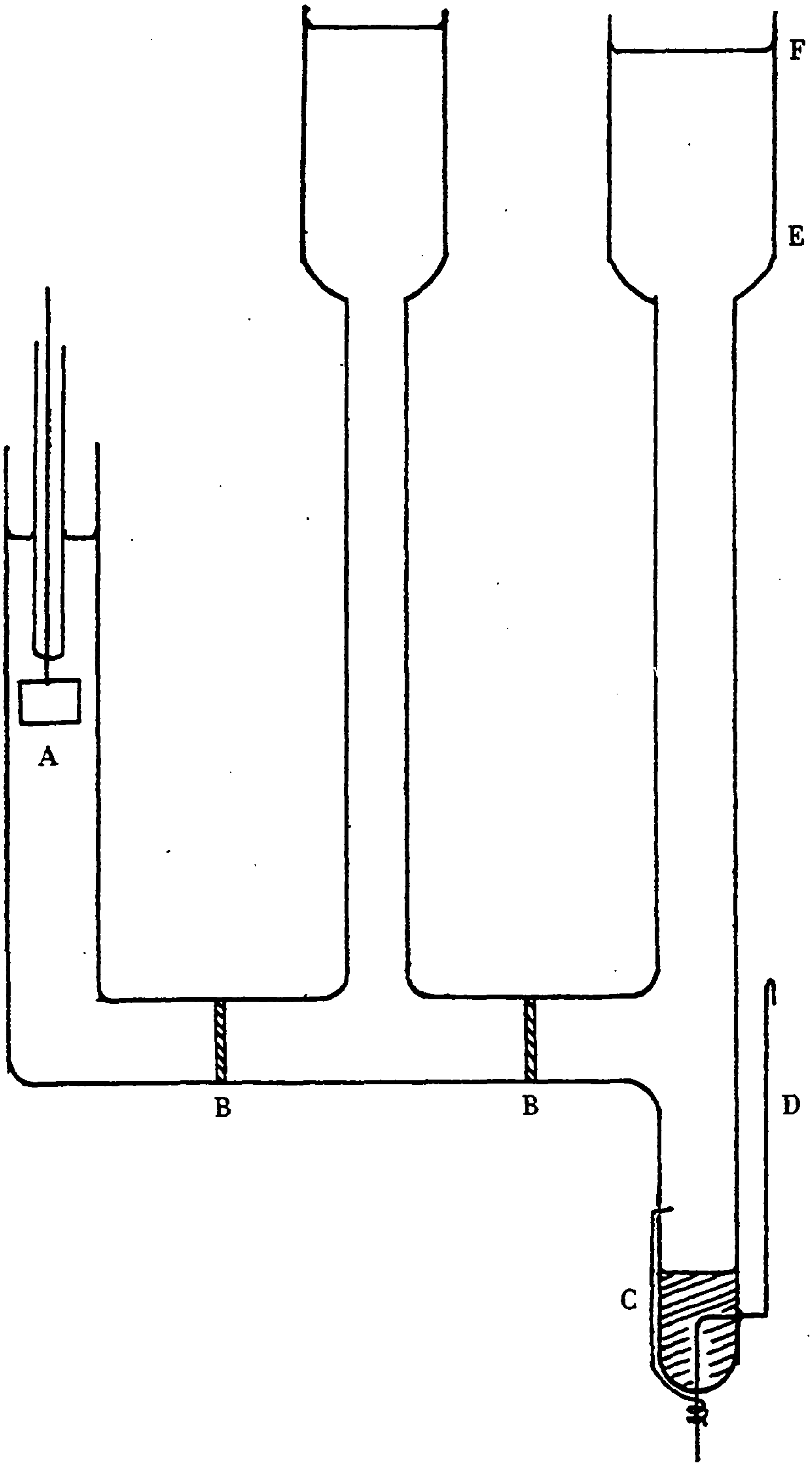
B. Glass frit

C. Fiber glass wick

D. Platinum generating electrode

E. Lower level of electrolyte

F. Upper level of electroylte


F
E
A
B
B
D
C

a small port in the reservoir and down the outside of the chamber to the platinum wire. Electrolyte flowed slowly down this wick and dripped from the platinum wire carrying acid (or base) generated on the platinum wire. pH was measured with a Hach Expanded Range pH Meter, Hach Chemical Company, Ames, Iowa, Model No. 8596-00.

Commercial "prepurified" cylinder nitrogen was passed through a tube containing ascarite then successively through scrubbers containing: 1) distilled water; 2) vanadium (II) sulfate in 1 M sulfuric acid over amalgamated zinc;[52] 3) alkaline permanganate (to insure the absence of hydrogen sulfide which can be generated in the oxygen scrubber); and 4) a solution of 1.0 M sodium perchlorate.

The sodium perchlorate solution used for the catholyte and anolyte was prepared by titrating a solution of approximately 2 M perchloric acid with sodium hydroxide solution to a pH of 7.00 ±0.05, then diluting to 1 M. The 2 M perchloric acid was prepared from 72 per cent perchloric acid which was boiled and then cooled to room temperature with nitrogen bubbling through the solution to remove any chlorine. The carbonate free sodium hydroxide was prepared by filtering a solution of 50 percent sodium hydroxide. All dilutions were made with deionized and triply distilled water.

The anolyte of hydrazinium sulfate was prepared from pure hydrazine sulfate, $N_2H_6SO_4$, by titrating the acid with carbonate free sodium hydroxide to a pH of 4.80 ± 0.10. The purity of the hydrazine sulfate was determined to be better than 99.9 ± 0.15 per cent by titration with hydrochloric acid standardized against potassium acid phthalate. The hydrazinium sulfate solution was diluted to 0.2 M with deionized and triply distilled water for subsequent use as the anolyte.

Measurement of Current, Potential, Weight and Time

A Leeds and Northrup Company "Coulometric Analyzer" (L and N Cat. No. 7960) was used as the source of the constant current. The L and N 7960 has three output currents, of approximately 64.3, 6.43, and 0.643 mA, respectively. Current was determined by measuring the voltage drop across a resistance of 19.99979 ohms, this resistance having been specially constructed and calibrated by the Leeds and Northrup Company (L and N Cat. No. 4025-B-S). The potential was measured with a Leeds and Northrup "potentiometer Facility" (L and N Cat. No. 7555) consisting of a type K-5 potentiometer, a null detector (L and N Cat. No. 9834-1 D. C.), constant voltage supply (L and N Cat. No. 9878), and a Weston standard cell. Voltage regulators were used to eliminate fluctuations in the line voltage. Deviations of 0.002 percent in the IR drop at maximum current flow could be detected with this arrangement. The manufacturer states that the 7960 current source produces an appreciable alternating current ripple but that it falls within the integrating capabilities of the null detector[20].

The 4025-B-S resistor was immersed in a constant temperature bath of mineral oil but even with the bath providing a heat sink, the temperature of the resistor rose with the passage of current. A temperature increase of about one degree occurred in the first few minutes of current passage with the current output of the constant current source at its maximum, 64.3 mamps. After the first few minutes, the temperature increase slowed somewhat and after about 15 minutes, the temperature reached a steady 1.5° above the temperature of the bath. Most of the temperature rise took place during the pretitration, so that the change in resistor temperature during an actual titration never amounted to more than a few tenths of one degree. Nevertheless, each time the IR drop was measured, the temperature of the resistor was recorded and the actual resistance calculated using the temperature coefficients supplied by the manufacturer:

$$R_t = 19.99979\,[\,1 + 0.000002\ (T\text{-}25) - 0.0000005\ (T\text{-}25)^2]$$

Two Weston cells were used alternately; each cell was calibrated every three months against a third resident cell in the Iowa State University Instrument Shop. The third cell was periodically calibrated against a fourth cell which was sent to the National Bureau of Standards for calibration at intervals of six months.

The Type K-5 potentiometer was calibrated at the standardizing laboratory of the Leeds and Northrup Company. At the potentials measured no corrections were required.

The Leeds and Northrup coulometric analyzer is equipped with a synchronous timing motor and a counter reading directly in microequivalents. To eliminate the consequences of possible variations in the frequency of the alternating current, the counter was driven by a frequency standard, model 2005A, manufactured by American Time Products. The frequency standard was calibrated using the time signals of Radio Station WWV of the National Bureau of Standards. Calibration runs were made over elapsed times ranging from 36 to 120 hours. The number of counts never varied more than three parts per million.

A set of rhodium plated weights manufactured by Wm. Ainsworth, Inc., Denver, Colorado, and calibrated at the National Bureau of Standards was used. Weighings were made on an Ainsworth FDJ equal-arm microbalance to the nearest microgram. All weighings of samples of 4-aminopyridine were made by substitution; the empty sample boat and the weight of appropriate size were weighed together (tared), the weight removed, and the sample added to the boat until the weight was within 0.002 g. of the tare, and the weighing completed using a calibrated rider. Only three weights (1-g., 2-g., rider) were involved in the entire set of weighings.

Weighings were corrected to weigh in vacuum using for the density of 4-aminopyridine 1.27 (found by the pycnometer method using mineral oil, 1.2695), for the density of tris(hydroxymethyl)aminopyridine 1.32 (found by the pycnometer method using benzene, 1.3184).

The weights of 4-aminopyridine taken for the individual titrations fell in the range: 1. For direct titration in hydrazinium sulfate electrolyte (anodic generation of hydrogen ion), 1.000,927,2 to 1.006,613,5 g. 2. For the back titration (addition of standard perchloric acid and back titration of the excess perchloric acid by cathodic generation of hydroxyl ion), Series 2. 3.001,923,3 to 3.006,079,4 g.; Series 3. 2.0022522 to 2.0070741 g.

The standard perchloric acid solution was weighed by substitution using an Ainsworth single pan balance (Model 28N, Wm. Ainsworth and Sons, Denver Colorado). The solution was contained in a plastic bottle during the weighings; the bottle had an extremely fine bore tip and was used as a weight buret. This plastic weight buret was used in place of the conventional weight buret because the sample could be transferred and weighed in a much shorter time, thus minimizing losses due to evaporation; the time of transfer, that is, from initial weighing to final weighing, was less than three minutes. The loss in weight from the plastic bottle weight buret was less than one-tenth of a milligram in twenty minutes, thus the loss in weight during the transfer process was estimated to be less than 0.01 mg.

Failure of Anodic Generation of Hydrogen Ion in Sodium Perchlorate Electrolyte

Although a number of high-precision, coulometeric titrations of acids have now been carried out (see review in Chapter I and Table 1), a high-precision, coulometric titration of only one base, sodium carbonate, has been reported.[74,14] A high-precision titration of tris(hydroxymethyl)-aminomethane ("THAM", "tris") was recently carried out by Marinenko[42] by the addition of sulfuric acid and coulometric standardization of the latter. Marinenko reported that direct coulometric titration of tris(hydroxymethyl)aminomethane yielded results consistently low by several percent. He reported also that the literature from 1947 on showed no studies of the electrochemistry of tris(hydroxymethyl)aminomethane and that the evidence in the literature seemed to indicate that attempts to titrate aromatic amines coulometrically failed owing to oxidation of the amines themselves.

In the course of the work of this thesis, I titrated 4-aminopyridine coulometrically and obtained high results, presumably because the amine was altered at the anode. To circumvent this, I added the amine after the coulometric generation of the base. The amine was placed in a boat suspended above the electrolyte (1 M sodium perchlorate), the three steps in the pretitration carried out (see next paragraph), and then 99.95 percent of the required acid was generated anodically, the reaction being

$$2H_2O = O_2 + 4H^+ + 4e^- .$$

The 4-aminopyridine was then added to the solution and the titration finished coulometrically with acid generated at an external (dripping) electrode. The apparatus used is described above, the working electrodes (main and dripping) being anodes. The results were consistently high, by four to six percent: 104.00, 106.02, 105.12 per cent 4-aminopyridine. Thus it became apparent that the primary difficulty in the coulometric titration of bases is in the anodic generation of hydrogen ion. The textbooks and treatises are silent on this matter.

Before each titration, a pretitration of the electrolyte was made coulometrically to remove carbon dioxide and any electroactive species present and to adjust the pH. The carbon dioxide was removed by purging the solution for at least two hours with purified nitrogen treated as described above. Electroactive material was eliminated by titrating the electrolyte, alternately anodically and then cathodically, well past the equivalence-point and using the high current output of the constant current source. The procedure was repeated three times in each direction and the final titration was carried out at the lowest current to bring the pH of the electrolyte to 7.00 ± 0.05. The final titration to the equivalence-point was always made in the same direction as in the subsequent titration of the 4-aminopyridine.

Experiments on the solution remaining after anodic generation of hydrogen ion and oxygen on bright platinum in 1 M sodium perchlorate threw some light on the side reaction which was consuming the extra four percent or so of electricity. Tests for hydrogen peroxide failed. A new oxidizing agent was present, however, one that reacted only slowly with ferrous sulfate at room temperature but with speed on the addition of a little silver ion. This oxidizing agent underwent spontaneous decomposition as was shown by iodometric titration of aliquots taken at intervals; some five hours were required for complete decomposition. The Riesenfeld-Liebhafsky[64] test indicated that a true peroxy acid was present. The phenomena observed resemble with respect to formation by anodic oxidation and behavior toward reducing agents and catalysts those of peroxydisulfuric acid (see for example Yost and Russell[89]). No hydrogen ion is involved in the anodic formation of peroxydisulfate anion, $2SO_2{}^{2-} = S_2O_8{}^{2-} + 2e^-$. Tentatively, the new oxidizing agent is identified as a peroxydiperchlorate, Cl_2O_8.

That the hydrogen-oxygen gas coulometer (sulfuric acid electrolyte) yields low results owing to a shortage of oxygen was observed by Faraday[21] who confirmed the finding of still earlier workers that a compound "oxy-water", with bleaching power is formed at the anode even though chlorine and similar bodies were rigidly excluded. Page and Lingane[57] also reported the hydrogen-oxygen gas coulometer to give low results and attributed the extra current required to the formation of hydrogen peroxide and the subsequent reduction of the hydrogen peroxide at the cathode. The nature of the reactions on a platinum electrode in sulfate and perchlorate electrolytes has been studied by several workers, and particular by Johnson, Napp and Bruckenstein,[29] who reported that a soluble compound is formed at the anode in addition to oxygen and that the compound was definitely not hydrogen peroxide. This is in agreement with my finding and an interesting problem, the isolation and characterization of the peroxyperchlorate formed, is offered for future work.

Attempts to Make an Anode 100 Percent Efficient for the Generation of Hydrogen Ion

It was pointed out by Knoeck and Diehl[34] in their paper on the high-precision titration of potassium dichromate as an acid, that the generation of hydroxyl ion by the reduction of water at the cathode

$$2H_2O + 2e^- = H_2 + 2OH^-$$

that if the reduction of the perchlorate of the electrolyte occurred as a side reaction

$$ClO_4^- + 2e^- + 2H^+ = ClO_3^- + H_2O$$

$$(\text{alternatively: } ClO_4^- + 2e^- + H_2O = ClO_3^- + 2OH^-)$$

that no error would result inasmuch as two hydrogen ions are used up.

For the current problem it appeared that chlorate in the 1 M sodium perchlorate might prove beneficial in that the oxidation of it might occur in preference to the formation of peroxydiperchlorate as discussed above and would release two hydrogen ions per mole. By trial I found that it did not, either admixed with sodium perchlorate or alone:

Electrolyte	Purity of 4-Aminopyridine
1 M sodium perchlorate also 0.5 M in sodium chlorate	103.18 percent
1 M sodium chlorate	105.55 percent

Sodium chlorate is not readily oxidized to sodium perchlorate. Commercially the reaction is carried out on bright platinum at a very high anode potential. The interesting question now arises as to whether a peroxydichlorate may be formed concurrently with perchlorate and the peroxydiperchlorate postulated above. Commercially the oxidation of sodium chlorate is never carried above 95 to 97 per cent completion to avoid the deterioration of the platium anode which accompanies further oxidation. It seems odd that the large scale production of sodium perchlorate should have gone on now for a half-century without the peroxydiperchlorate having come to attention. Sodium perchlorate is isolated following electrolytic oxidation by boiling to evaporate and concentrate, the peroxydiperchlorate would be decomposed in the process, and thus it has never caused any problem.

One more attempt was made to improve the efficiency of the perchlorate-platinum anode for the generation of hydrogen ion, this by using a platinum anode covered with platinum black. Platinum black, of course, greatly reduces hydrogen overvoltage; apparently it has no effect on oxygen overvoltage. Result: 106.01 per cent 4-aminopyridine.

An anode 100 percent efficient for the production of hydrogen ions was found, one using hydrazine sulfate as electrolyte; this is discussed in the next section.

A Hydrazinium Sulfate-Platinum Anode as a Generator of Hydrogen Ion

After learning of the deficiency of the hydrogen-oxygen gas coulometer and still needing a coulometer to integrate current varying with time, Page and Lingane[57] devised another gas coulometer, the hydrogen-nitrogen coulometer. In this coulometer, hydrazine sulfate is used as the electrolyte, the reactions at the anode and cathode, respectively, being:

$$N_2H_5^+ = N_2 + 5H^+ + 4e^- \tag{1}$$

and

$$2H^+ + 2e^- = H_2 \, . \tag{2}$$

Page and Lingane reported the results to be somewhat low, presumably because of the loss of gas by solubility in the electrolyte.

I have shown that the bright platinum anode in hydrazinium sulfate

($(N_2H_5)_2SO_4$) solution is 100 per cent efficient in the generation of five hydrogen ions per four electrons (above equation (1)). Moreover, hydrazine is more readily oxidized than is 4-aminopyridine so that the titration of the latter may be carried out directly, that is, with the 4-aminopyridine dissolved in the solution of hydrazinium sulfate.

The standard reduction potential for oxidation of the hydrazinium ion to nitrogen (equation (1)) was calculated by Latimer[39] 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 hydrazinium sulfate.

As experimental proof of the efficiency of the hydrazinium sulfate-platinum anode for the generation of hydrogen ion, three experiments were performed: (1) The direct, coulometric titration of highly purified 4-aminopyridine; (2) Titration of the same 4-aminopyridine with standard perchloric acid by the weight buret technique, the perchloric acid in turn being standardized by coulometric titration; and (3) Titration of a sample of tris(hydroxymethyl)aminomethane analyzed by Marinenko[42] at the National Bureau of Standards by titration with sulfuric acid, the latter being standardized by coulometric titration.

End-point Detection Using the Hydrazinium Sulfate-Platinum Anode for the Titration of a Base

Hydrazine, N_2H_4, is a diacidic base, presumably, like ammonia, hydrated at least in part in water solution to the hydroxide, $N_2H_6(OH)_2$. The first replaceable hydroxyl group is an exceptionally weak base ($K_{b,1} = 3 \times 10^{-13}$ according to Kolthoff and Stenger,[36] $= 8.9 \times 10^{-16}$ according to Gilbert).[22] The second replaceable hydroxyl group is a weak base ($K_{b,2} = 8.7 \times 10^{-7}$ ($pK_{b,2} = 6.06$), average of three best values reported by Bjerrum, Schwarzenbach and Sillen).[8] There is some confusion in the literature as to the designations given these quantities and for the purpose of this thesis, the constants are best treated as dissociation constants as acids, the relation between the dissociation constant as an acid and the dissociation constant as a base for any one ionization step being $K_b \cdot K_a = K_w$.

Hydrazine sulfate, $N_2H_6SO_4$, can only be obtained from aquesou solutions if a high concentration of sulfuric acid is present, 2 to 3 M. Aqueous solutions of hydrazine sulfate react strongly and when titrated potentiometrically with strong base yield two inflection points, corresponding to the reactions:

$$N_2H_6^{2+} + OH^- = N_2H_5^+ + H_2O$$

or alternatively: $2N_2H_6SO_4 + 2NaOH = (N_2H_5)_2SO_4 + Na_2SO_4 + 2H_2O$

and

$$N_2H_5^+ + OH^- = N_2H_4 + H_2O$$

or alternatively: $(N_2H_5)_2SO_4 + 2NaOH = 2N_2H_5OH + Na_2SO_4$.

The ionizations and dissociation constants involved are:

$$N_2H_6^{2+} = N_2H_5^+ + H^+ \qquad K_{a,1} = \frac{[N_2H_5^+][H^+]}{[N_2H_6^{2+}]}$$

$$N_2H_5^+ = N_2H_4 + H^+ \qquad K_{a,2} = \frac{[N_2H_4][H^+]}{[N_2H_5^+]}$$

$$= 1.15 \times 10^{-8} \ (pK_{a,2} = 7.94)$$

$$(\text{from } pK_w - pK_{b,2}) \ .$$

A value for $K_{a,1}$ was obtained from a potentiometric titration of hydrazine sulfate with sodium hydroxide; found at mid-point, pH = 1.75, 1.81, average 1.78 (concentration of salt and acid at this point each about 0.10 M). Using the values $pK_{a,1} = 1.78$ and $pK_{a,2} = 7.94$, the potential at the first equivalence-point should be $= (1/2)(pK_{a,1} + pK_{a,2}) = 4.86$; found in precise coulometric titrations, 4.88.

The dissociation constant of 4-aminopyridine in solutions of various concentrations of sodium perchlorate was reported in Chapter II. Titrations of 4-aminopyridine dissolved in water alone with sodium hydroxide, gave for the dissociation constant (pH at mid-point) pK = 4.82. The corresponding dissociation constant as an acid is $pK_{a,4AP} = pK_w - pK_{b,4AP} = 9.18$. 4-Aminopyridine is thus a weaker acid than the hydrazinium ion, $N_2H_5^+$, $pK_{b,2} = 7.94$.

In practice, using the hydrazinium sulfate-platinum anode for the coulometric titration the pretitration was carried to pH 4.88 (platinum anode in final step), the 4-aminopyridine added, and the 4-aminopyridine titrated coulometrically (platinum anode). Only one point of inflection was observed, between 4.70 and 4.85. The hydrazine was present as $N_2H_5^+$ before and after the titration and the hydrogen ion was used to neutralize only the 4-aminopyridine.

In general if the base being titrated is a stronger base than the hydrazinium ion, $pK_b < K_{b,2} = 6.06$, the titration should be successful and the pH at the end-point that of dihydrazine sulfate, that is, of the $N_2H_5^+$ ion, 4.88. The dissociation constant of tris(hydroxymethyl)-aminomethane (THAM) is $K_{b,THAM} = 1.202 \times 10^{-6}$ ($pK_{b,THAM} = 5.92$) and $pK_{a,THAM} = 8.08$; as with 4-aminopyridine, one point of inflection was found in the titration of tris(hydroxymethyl)aminomethane.

Working Potential of the Hydrazine Sulfate-Platinum Anode

The working potential of the platinum anode in a solution of 0.25 M hydrazine sulfate was measured vs. a saturated calomel electrode; the potential was measured over the pH range 3.75 to 6.00 while passing 64.3 mA. The platinum working anode was 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	6.00
E, mV	15.6	13.1	11.1	10.8	9.0	8.8	8.0	4.8	1.0	-25.0

The working anode was a helix of platinum wire with a surface area of 25 cm^2, the current density was thus 2.6 mA per cm^2.

Combination Hydrazinium Sulfate-Platinum Anode and Cathode as a Generator of Hydrogen Ion

An intriguing feature of the hydrazinium sulfate-platinum electrode is the possibility of operating the cell without a partition, and thus, providing the cathode reaction be 100 percent efficient in the utilization of hydrogen ion (equation (2), above), of generating only one hydrogen ion per four electrons passed. Conceivably it could work, although the standard reduction potential for the reduction of hydrazinium ion to the ammonium ion at the cathode

$$N_2H_5^+ + 3H^+ + 2e^- = 2NH_4^+$$

is reported by Latimer[39] to be +1.275 V. In practice the scheme failed by several per cent, presumably because this reduction went on concurrently with the reduction of the hydrogen ion (equation (2)).

Titration of 4-Aminopyridine Using the Hydrazinium Sulfate-Platinum Anode

Six titrations of the 4-aminopyridine purified as described in Chapter II were made using the hydrazinium sulfate-platinum anode. All of the titrations were successful and the results are given in Chapter V and Table 5. In the first five of the titrations, the 4-aminopyridine was added immediately to the 0.2 M hydrazinium sulfate and was present throughout the generation of the hydrogen ion; in the sixth titration the 4-aminopyridine was added after 99.9 per cent of the hydrogen ion had been generated. The results were the same and it is not necessary to use the external drip anode to complete the titration.

In each titration, a pretitration was made coulometrically through the equivalence-point of the hydrazinium sulfate electrolyte; three passes were made anodically and three passes cathodically, with the final pass made anodically to bring the final pH to 4.880 ± 0.010. At the end of the titration, data was taken through the end-point region, the data plotted to locate the point of inflection. The end-point in each case occurred within the pH range 4.70 to 4.88.

Titration of 4-Aminopyridine Using Perchloric Acid Standardized Coulometrically

Inasmuch as the titrations of 4-aminopyridine are used (Chapter V) to establish a new value for the faraday and it is assumed in this calculation that the current efficiency of the hydrazinium sulfate-platinum anode is 100 percent, the results of the titrations reported in Table 5 can hardly be accepted as proof of 100 per cent current efficiency. For this reason a second series of titrations were carried out in which the 4-aminopyridine was titrated with standard perchloric acid using the weight buret technique, completing the titration coulometrically, and standardizing the perchloric acid coulometrically. Two sets of such titrations were made, designated, respectively, as Series 2 and Series 3.

The titration of Series 3 were made with larger quantities of a less concentrated perchloric acid and the relative error in the weighings is smaller. Somewhat closer attention was paid also to the final rinsing of the upper walls of the titration cell.

Titration of Tris(hydroxymethyl)aminomethane Using the Hydrazinium Sulfate-Platinum Anode

As a second check on the validity of the hydrazinium sulfate-platinum anode as a coulometric generator of hydrogen ions, titrations were made of tris(hydroxymethyl)aminomethane.

In exploratory work in connection with this thesis, I examined several lots of tris(hydroxymethyl)aminomethane but was unable to find material of purity above 99.6 per cent. Nor was I able to devise a method for purifying and drying the material. The purity decreased on each recrystallization from acetone and subsequent drying in a vacuum at 50°C. The compound was found also to decompose slowly on drying at 105°C, the loss in weight being appreciable in one hour.

Marinenko at the National Bureau of Standards did obtain a lot of highly pure tris(hydroxymethyl)aminomethane and titrated it with sulfuric acid by the weight buret technique and coulometric standardization of the sulfuric acid; the results of some thirty titrations were reported[42] in 1970, the purity being 99.9690 ± 0.0030. This same material is marketed by the National Bureau of Standards as SRM 723. Funds were not available for obtaining this material, which is highly priced, but we obtained as a gift from Dr. Marinenko sufficient material for six titrations. Three of the titrations were lost as a result of interruptions of the electrical power line by a storm and subsequent repair work. The three results obtained were: 99.781, 99.786, 99.778, average 99.782. The precision is good but the results differ by an order of magnitude from the Marinenko value. Either the titration with the hydrazinium sulfate-platinum anode fails with tris(hydroxymethyl)aminomethane or some mixup occurred in the identification of the material. Insufficient material was left for a weight buret titration with perchloric acid and the problem was left unsolved. In making these calculations, the values used for the molecular weight of tris(hydroxymethyl)aminomethane was $C_4H_{11}O_3N$ = 121.1372 and the value of the faraday[73] F = 96,486.62(55) NBS coulombs/mole.

CHAPTER V. CALCULATION OF A VALUE FOR THE FARADAY

Molecular Weight of 4-Aminopyridine

For calculating the molecular weight of 4-aminopyridine, the following values for the atomic weights of carbon, hydrogen and nitrogen were used:

$$C = 12.011,15 \pm 0.000,05$$

$$H = 1.007,97 \pm 0.000,01$$

$$N = 14.006,72 \pm 0.000,01 \ .$$

The values for carbon and hydrogen are those given in the 1961 Table of Atomic Weights[9] and were used rather than those of the 1971 Table[28] in which the 1961 numbers have been rounded off for general chemical use. A value for the atomic weight of nitrogen was calculated using for the abundance ratio $r = {}^{14}N/{}^{15}N = 272 \pm 0.3$ and the recent values for the absolute masses of the isotopes of nitrogen of Wapstra and Gove[81]

$${}^{14}N = 14.003,074,40 \pm 0.000,000,13$$

$${}^{15}N = 15.000,109,3 \pm 0.000,000,5$$

which, using the usual formula

$$N = {}^{14}N + ({}^{15}N - {}^{14}N)(1 + r)$$

yields

$$N = 14.006,726 \pm 0.000,000,5.$$

The value $r = {}^{14}N/{}^{15}N = 272.0$ is that of Junk and Svec[30], based on the mass spectrographic analysis of air of different but recent geographical origin. An earlier value of Nier[55], ${}^{14}N/{}^{15}N = 273$ is an unweighted mean of two sets of measurements, made on different instruments; much better precision was obtained on one instrument and the average of the measurements on it give a higher value, leading to $^{14}N/^{15}N = 273$, in agreement with Junk and Svec. A more recent work on the abundance of the isotopes of nitrogen by Pilot[59] is devoted to a study of nitrogen from rock and mine gases and appears less relevant to the present work than the Junk and Svec work. The value for the atomic weight of nitrogen reported by De Bievre, Gallet and Debus[18] is based on the unweighted abundance ratios of all three of the works just mentioned and was rejected here in favor of the value calculated above. For the present work, the calculated value was rounded down to

$$N = 14.006{,}72$$

giving some weight to the results of the second set of measurements of Nier.

The numbers following the ± sign in the above values represent the maximum variation reported in various studies resulting from natural variation in isotopic composition. This is specifically so stated in the 1961 Report of the International Commission on Atomic Weights.[9] In the De Bievre, Gallet and Debus[18] values these numbers are given as a standard deviation "as it reflects the variation in isotopic composition of the samples used by the different authors, as well as many differences in the preparation and measurement technique of the sample". In calculating the molecular weight of 4-aminopyridine these numbers were handled by summing the squares (variance) thus

					Variance
5C	5(12.011,15)	=	60.055,75	$5(5 \times 10^{-5})^2$	125×10^{-10}
6H	6(1.007,97)	=	6.047,82	$6(1 \times 10^{-5})^2$	6×10^{-10}
2N	2(14.006,72)	=	28.013,45	$2(1 \times 10^{-5})^2$	2×10^{-10}
			94.117,02	Σ(Variance) =	133×10^{-10} .

The standard deviation was calculated by the formula[85]

$$\sigma = \left[(1/(n_C + n_H + n_N))(\Sigma V_C + \Sigma V_H + \Sigma V_N) \right]^{1/2}$$

(V = variance, in carbon, hydrogen and nitrogen, respectively)

$$= \left[(1/13)(133 \times 10^{-10}) \right]^{1/2} = 3.1 \times 10^{-5}.$$

The molecular weight of 4-aminopyridine is

$$C_5H_6N_2 = 94.117,02 \pm 0.000,03 \ .$$

Thus the natural variation in the abundance of the isotopes of carbon, hydrogen and nitrogen which have been reported when transferred to 4-aminopyridine is 3 parts in 10,000,000 and thus almost two orders of magnitude smaller than the error (standard deviation) in the coulometric titrations being reported in this work.

Possible Effect on Molecular Weight of Chemical Processing

The question of the separation of the various species of 4-aminopyridine resulting from the existence of isotopes of each of the three elements making up the compound is not readily answered. 4-Aminopyridine was chosen so that if judged necessary the actual abundance ratios could be determined. It is now judged such determinations are unnecessary. As shown above the maximum natural variation which could be present is 3 parts per 10,000,000, well below the error inherent to the coulometric titration process. Separation must occur during the chemical processing and in this work principally in the purification step. Chemicals differing in isotopic composition have been separated (water from deuterium oxide, ^{14}N from ^{15}N by ion exchange chromatography of ammonia on a sulfonated cation exchange resin,[70] etc.) but an extremely large number of repetitive steps are involved. In the repeated sublimation steps by which the 4-aminopyridine of this work was purified probably not more than 20 successive sublimations were made but the number is uncertain owing to the complexity of what happened in the formation of the layered, hemispherical shell of 4-aminopyridine which formed above the crude mass during the preliminary sublimation. It seems unlikely, however, that the successive steps were any where near sufficient in number to disturb the abundance ratios greater than the 2 parts per 100,000 aimed for in this work.

Calculation Using Data Obtained in the Various Coulometric Titrations

The basic calculations for obtaining a value of the faraday are made on the basis of the Faraday laws of electrolysis, expressed by the mathematical formula

$$G = \frac{1}{F} I t \frac{\text{Mol. Wt.}}{n} .$$

(See Chapter I, paragraph 1). From the experimental data, obtained as reported in Chapter IV, above, the quantity It/G has been calculated for each titration and reported in Tables 5, 6 and 7 under "Electrical Equivalent per Gram". The number of electrons involved per molecule of 4-aminopyridine being one, it remains simply to multiply the electrical equivalents per gram by the best value of the molecular weight to obtain the value of the faraday. Using the new hydrazinium sulfate-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 5). The calculations presented in Tables 5, 6 and 7 are based on the assumption that the purity of the 4-aminopyridine is 100.000 percent; introduction of a value for the purity of 4-aminopyridine less than 100,000 reduces the weight taken, G, a term which appears in the denominator, and raises the value of the faraday.

Averaging the final values obtained in Series 1, Series 2, and Series 3 gives

$$F = 96{,}485.48 \qquad \sigma = 2.20 \qquad \text{NBS coulombs per mole}$$

the standard deviation of the mean being computed by

$$\sigma = \left[(1/(6 + 6 + 6)) (V_1 + V_2 + V_3) \right]^{1/2}$$

that is, the square root of 1/18 the sum of the variances of the three sets.

Series 3 is a repetition of Series 2 with certain experimental conditions under better control (larger weight of perchloric acid, extra

Table 5. Coulometric titration of 4-aminopyridine with acid generated at the hydrazinium sulfate-platinum anode. Series I

(Mol. wt. 4-aminopyridine: 94.117,02)

Weight of 4-aminopyridine g.	Quantity of electricity NBS coulombs	Electrical equivalent per gram = (5/4)It/wt. NBS coulombs/g.	Value of Faraday NBS coulombs/mole
1.006,613,5	825.581	1,025.196	96,488.39
1.000,927,2	820.891	1,025.163	96,485.29
1.003,587,8	823.062	1,025.149	96,483.97
1.003,283,4	822.824	1,025.164	96,485.38
1.002,060,0	821.814	1,025.155	96,484.53
1.004,573,5	823.867	1,025.145	96,483.59
		Average	96,485.19
		Standard deviation	1.72

Table 6. Coulometric titration of 4-aminopyridine with perchloric acid (coulometric end-point) and standardization of perchloric acid coulometrically. Series 2

Standardization of perchloric acid

Weight of perchloric acid g.	Quantity of electricity NBS coulombs		Concentration of perchloric acid NBS coulombs/g.
5.034,9	1,572.518		312.324
5.508,8	1,720.476		312.314
5.693,7	1,778.142		312.300
7.507,6	2,344.618		312.299
5.708,7	1,782.892		312.311
9.068,3	2,832.354		312.336
4.987,4	1,557.665		312.320
		Average	312.315
		Standard deviation	0.013
		Relative standard deviation	4.2 parts per 100,000

Table 6. (Continued)

Titration of 4-aminopyridine

Heading of columns: A. Weight of 4-aminopyridine; B. Weight or 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. = NBS coulomb. Molecular weight of 4-aminopyridine = 94.117,02.

A	B	C	D	E	F	G
g.	g.	C.	C.	C.	C./g.	C./mole
3.003,456,3	10,181,0	3179.679	100.500	3,079.179	1,025.212	96,489.88
3.006,079,4	11,062,9	3455.110	373.247	3,081.863	1,025.210	96,489.72
3.003,389,4	10.776,6	3365.694	286.824	3,078.870	1,025.132	96,482.35
3.004,572,4	10.062,1	3142.545	62.290	3,080.255	1,025.189	96,487.74
3.004,411,9	10.437,8	3259.882	179.982	3,079.900	1,025.126	96,481.78
3.001,923,3	10.045,5	3137.360	59.899	3,077.461	1,025.163	96,485.30
					Average	96,486.13
					Standard deviation	3.56

Table 7. Coulometric titration of 4-aminopyridine with perchloric acid (coulometric end-point) and standardization of perchloric acid coulometrically. Series 3

Standardization of perchloric acid

Weight of perchloric acid g.	Quantity of electricity NBS coulombs	Concentration of perchloric acid NBS coulombs/g.
26.491,5	2,145.568	80,990,8
32.159,3	2,604.655	80.992,3
21.046,5	1,704.572	80.990,8
25.805,8	2,090.046	80.991,3
25.853,6	2,093.898	80.990,6
21.306,9	1,725.669	80.991,1
	Average	80.991,1
	Standard deviation	0.000,62
	Relative standard deviation	0.76 parts per 100,000

Table 7. (Continued)

Titration of 4-aminopyridine

Heading of columns: A. Weight of 4-aminopyridine; B. Weight or 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. = NBS coulomb. Molecular weight of 4-aminopyridine = 94.117,02.

A g.	B g.	C C.	D C.	E C.	F C./g.	G C./mole
2.002,392,4	26.2368	2,124.947	72.182	2,052.765	1,025.156	96,484.63
2.002,252,2	26.0501	2,109.826	57.229	2,052.597	1,025.144	96,483.50
2.004,845,0	26.7703	2,168.156	112.892	2,055.264	1,025.148	96,483.87
2.007,074,1	26.0267	2,107.931	50.344	2,057.587	1,025.167	96,485.66
2.002,324,0	26.1041	2,114.200	61.458	2,052.742	1,025.180	96,486.89
2.002,598,5	27.9442	2,263.231	210.221	2,053.010	1,025.173	96,486.23
					Average	96,485.13
					Standard deviation	1.35

final rinse of cell). The average of the final values of Series 1 and Series 3 gives

$$F = 96,485.16 \qquad \sigma = 1.41 \qquad \text{NBS coulombs per mole}$$

the standard deviation of the mean being computed as the square root of 1/12 the sum of the variances of the two sets.

For comparison, values of the faraday obtained since 1960 are tabulated in Table 8.

Table 8. Summary of recent values for the Faraday

	NBS coulombs per mole	
Silver oxidation	96,485.8(1.6)	Craig, Hoffman, Law and Hamer;[17] see also Hamer.[25]
	96,486.62(0.55)	Craig, Hoffman, Law and Hamer[17] as recalculated by Taylor, Parker and Langenberg.[73]
Iodide oxidation	96,485.5(3.2)	Marinenko and Taylor.[48]
Benzoic acid reduction[a]	96,486.7(2.5)	Marinenko and Taylor.[49]
Oxalic acid dihydrate reduction[a]	96,485.4(3.4)	Marinenko and Taylor.[49]
4-Aminopyridine oxidation[a]	96,485.16(1.41)	This work

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[a] Reduction in the sense of titration with base generated at the cathode; oxidation in the sense of titration with acid generated at the anode.

CHAPTER VI. SUMMARY

A review has been made of the high-precision coulometers which have been used in evaluating the faraday, together with the related topics: the interrelation and changes which have been made in the National Bureau of Standards ("as maintained" and "U.S. legal") electrical units and absolute electrical units; the ratio of the abundances of the isotopes of silver and the atomic weight of silver as these factors affect the silver coulometer; possible error in the silver coulometer; and the field of high-precision coulometric titrations and the use of such titrations in establishing the value of the faraday.

A high-precision coulometric titration of 4-aminopyridine has been proposed as a new method of evaluating the faraday. The favorable characteristics of 4-amimopyridine have been pointed out: ease of purification by sublimation; favorable melting and crystallizing characteristics which permit an independent determination of total impurity; favorable characteristics as a base which yield an end-point detectable with sufficient accuracy for a high-precision titration; and composition limited to three elements, carbon, hydrogen and nitrogen, the isotopes of which do not vary significantly in abundance and for which the abundance ratio can be determined fairly readily if judged necessary.

A lot of 4-aminopyridine has been rendered highly pure by repeated, fractional sublimation. The dissociation constant of 4-aminopyridine as a base has been measured in solutions of sodium perchlorate of concentrations 0.1 to 1.15 M at 24.4°C and in 1.00 M sodium perchlorate at

24.4°C, 30.0°C and 38.0°C.

> *The work reported in the following paragraphs designated by → was carried out jointly with Mr. Frederick R. Kroeger and Professor Clayton A. Swenson of the Ames Laboratory, United States Atomic Energy Commission and the Department of Physics, Iowa State University.*

→ A highly sensitive freezing curve apparatus has been constructed consisting of a gold crucible, interior heat transmitting vanes of gold, a platinum resistance thermometer enclosed in a gold tube within the crucible, electric heating element and thermocouple on the exterior of the gold crucible, copper heat shield carrying an electric heating element, thermocouple for measuring the temperature difference between crucible and shield, and elaborate electrical control devices for measuring the resistance of the platinum thermometer and the differential thermocouple potential and for maintaining a constant difference in temperature between crucible and heat shield.

→ Two sequences of cooling curves of the highly-purified 4-aminopyridine have been made, the 4-aminopyridine having been placed in the gold crucible, the crucible closed by electron beam welding, and the cooling curves obtained with temperatures measured to 0.0002°C.

→ A modification of the conventional method of obtaining and handling freezing curve data has been devised; this improvement is based on a direct measurement at regular intervals of the slope of the freezing curve and a mathematical treatment of values of the slope so obtained.

→ A further improvement in the method of working up the data of a freezing curve has been devised in which the heat released by the crucible plus addenda plus 4-aminopyridine as the temperature drops through the freezing range is taken into consideration. This treatment involves the depression of the freezing point and five other parameters and provides a rigorous theoretical basis and a handy sequence of approximations and curve fitting so that all points on the freezing curve obtained experimentally are used and the final value found for the depression of the freezing point is good to 1 per cent.

The latent heat of fusion of 4-aminopyridine has been measured by a direct calorimetric experiment which gave the value 25,960 joules per mole (6,240 calories per mole), the error being estimated to be 1.5 per cent.

→ The latent heat of fusion of 4-aminopyridine has also been measured by an analysis of the heat required for melting in the freezing curve apparatus described above, a method which has yielded the value 26,800 joules per mole (6,420 calories per mole), the error being estimated to be 5 per cent.

The specific heat of solid 4-aminopyridine has been found to be 1.846 joules per degree per gram (0.4411 calories per degree per gram); that of liquid 4-aminopyridine has been found to be 1.6736 joules per degree per gram (0.400 calories per degree per gram.)

The cryoscopic constant of 4-aminopyridine, $A = L_f/RT^2$, has been calculated from the latent heat of fusion and the melting temperature ($T_m = 159.090 \pm 0.010^\circ C$) to be: $A = 1.67$ (mole per cent) per degree.

→ It has been found from the successive freezing curves obtained on two charges of the instrument with the high-purity 4-aminopyridine that gold is taken from the instrument into the molten 4-aminopyridine. Considerations of the depression of the freezing point obtained in the various freezing curves has led to the conclusion that the depression of the freezing point of the highly-purified 4-aminopyridine is less than can be detected by this instrument, that is less than 0.001°C corresponding to less than 0.0016 mole per cent.

It has been found that high-precision coulometric titrations of 4-aminopyridine by the anodic generation of hydrogen ion in 1.0 M sodium perchlorate electrolyte failed by several per cent. This failure has been traced to the production at the platinum anode of a soluble chemical species with oxidizing power, this species and the consequent deficiency in the yield of hydrogen ion being produced also in solutions of sodium perchlorate alone. This oxidizing species has been found definitely not to be hydrogen peroxide and has been tentatively identified as a peroxyperchlorate, previously unknown.

It has been found that in solutions of sodium chlorate and of sodium chlorate plus sodium perchlorate the anodic generation of hydrogen ion is also incomplete, both at bright platinum and platinum black electrodes.

A new coulometric generator of hydrogen ion has been devised and shown to operate with 100 per cent current efficiency. The generator consists of a platinum anode operating in a solution 0.2 M in hydrazinium sulfate brought to a pH of 4.88 (hydrazine present as the $N_2H_5^+$ ion). Five hydrogen ions are generated for each four electrons passed. The chemistry of hydrazine has been discussed as it relates to the detection of end-points in the titration of weak bases with this hydrazinium sulfate-platinum anode.

Certain modifications have been made in the design of the cell used for the coulometric titrations to increase convenience and further insure against mixing of catholyte and anolyte.

A new external, "drip" electrode has been devised.

The high-purity 4-aminopyridine has been titrated with the new hydrazinium sulfate-platinum anode, the titrations being designated Series 1.

The high-purity 4-aminopyridine has also been titrated with perchloric acid, the titration being completed coulometrically and the perchloric acid being standardized coulometrically by cathodic generation of hydroxyl ion. These titrations have been designated Series 2 and Series 3.

A specimen of tris(hydroxymethyl)aminomethane has also been titrated with the hydrazinium sulfate-platinum anode; the purity found, 99.782 percent, failed to agree with that found by Marinenko of the National Bureau of Standards, 99.969 ± 0.0030 per cent, by titration with sulfuric acid, the latter having been standardized coulometrically. This disagreement has been left unresolved.

As a result of titrations of high-purity 4-aminopyridine new values for the faraday have been found:

Series 1. 96,485.19(1.72) NBS coulombs per mole

Series 2. 96,486.13(3.56) NBS coulombs per mole

Series 3. 96,485.13(1.35) NBS coulombs per mole.

The standard deviation (six measurements in each series) is given in parentheses in parts per 100,000. Series 3 is a repetition of Series 2 with certain experimental conditions under better control. Averaging the results of Series 1 and Series 3 yields

$$F = 96{,}485.16(1.41) \quad \text{NBS coulombs per mole.}$$

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APPENDIX

Note on the Conversion of the NBS Ampere to the Absolute Ampere. In the course of an evaluation of all physical units and constants, Taylor, Parker and Langenberg[73] surveyed in detail each of the five measurements of the ratio of the NBS ampere to the absolute ampere made between 1942 and 1948 (see pages 383 to 385 and their Table XII, page 403 for listing of the individual results) and concluded the best values to be

Prior to 1 Jan. 1969

NBS ampere = 1.000,009 absolute ampere error: 2.6 p.p.m.

After 1 Jan. 1969

NBS ampere = 1.000,007 absolute ampere error: 2.6 p.p.m.

In his review of 1968 of the values of the faraday, Hamer[25] reported calculations based on each of the two conversion factors

NBS ampere = 1.000,011 absolute ampere

NBS ampere = 1.000,012 absolute ampere

pointing out, however, that further work on the subject was underway at the National Bureau of Standards.

These relations, along with the atomic weights, current at any one time are needed in recalculating the results of early work.