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A NEW CALORIMETRIC STANDARD: 4-AMINOPYRIDINE

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ABSTRACT

The need for a new solution calorimetric standard is discussed. The standard proposed is 4-aminopyridine which is shown to be more satisfactory than the previously accepted standards of sodium hydroxide or trishydroxyaminomethane. The reaction is
$HClO_4(aq) + 4\text{-}AP(aq) \rightarrow 4\text{-}APH^+ClO_4^-(aq)$
with $\Delta H_N^\circ(298.15\ K) = 11.164 \pm 0.011$ kcal mol^{-1}.

INTRODUCTION

Although benzoic acid was established long ago as the recognized standard for combustion calorimetry, development of an equivalent standard for solution calorimetry has proved elusive. The only reaction used for many years was the NaOH–HCl neutralization[1]. This was improved substantially when $HClO_4$ was substituted for HCl, thereby reducing greatly corrections for heat of dilution and problems of changing titer of the HCl solution because of volatility. The base in the neutralization remained NaOH with its well-known problems until the work of Irving[2] who suggested that trishydroxyaminomethane (THAM) be used. Subsequent work by Hansen[3] has demonstrated considerable variability in results obtained with THAM. The reason for the variability was not understood until the high precision coulometric work of Koch et al. who reported the presence of occluded mother liquor within the THAM crystals[4]. Our own work on weight titrations of THAM vs. NBS 84f potassium hydrogen phthalate have confirmed that THAM cannot be obtained in a pure form as demonstrated by Koch et al.[5].

The characteristics required of an acceptable primary standard for solution calorimetry include all those given in any good text on quantitative analysis for

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primary standards in titrimetric analysis plus the requirement that the reaction be exothermic with a yield of more than 10 kcal mol^{-1}.

We were led to investigate the possible use of 4-aminopyridine (4-AP) because it is recommended by Diehl[6] as a primary standard for acidimetry in place of THAM. 4-AP is a white crystalline compound, melting[7] at 159.090°C, which is a weak mono-acidic base[8] with $pK_b = 4.882$ at 25°C. The equivalent weight of 4-AP is 94.118 g and it can be readily purified from commercially available stock by recrystallization from toluene solution followed by sublimation at 110°C. Sublimed 4-AP is anhydrous, non-hydroscopic, and does not absorb CO_2 from the air.

EXPERIMENTAL

Anhydrous KCl

Anhydrous KCl used as the standard for heat of solution calorimetry was prepared by dissolving Baker Analyzed Reagent KCl (lot No. 30182, certified 99.7%) in hot distilled water. All water was triply distilled with demineralization after the first distillation and the second distillation from alkaline permanganate. The saturated KCl solution was filtered through a fine porosity fritted glass filter, heated to the boiling temperature, and treated with Cl_2 according to the procedure of Bates[9] for the purpose of oxidizing residual Br^- present as an impurity. The solution was allowed to cool while sparging with prepurified N_2 (certified 99.999%) from Air Products and Chemicals of Allentown, Pa. The heating and cooling cycle was repeated. Large crystals of KCl which formed upon cooling were filtered and recrystallized from distilled water. The recrystallized KCl was ground to 60 mesh or smaller particles using an agate mortar and pestle. The finely ground KCl was heated for a 24-h period at 160°C under a vacuum of 0.5 torr or better. The purity of KCl thus obtained was determined in triplicate by the usual gravimetric procedure[10].

Standard $HClO_4$ (aq)

A saturated solution of Baker Analyzed Reagent NaOH used in the standardization of $HClO_4$(aq) was allowed to settle for one month and, after chilling in an ice bath, was filtered through a fine porosity fritted glass filter under an atmosphere of N_2 in a plastic glove bag. A measured amount of this solution was diluted to prepare a 0.2 m solution of NaOH. The $HClO_4$ solution was prepared by boiling reagent grade acid from G. F. Smith Chemical Co. of Columbus, Ohio, to remove Cl^- and Cl_2 and was sparged with N_2 during cooling. A measured amount of this acid was diluted to prepare a 1.0 m solution. Triply distilled water for these solutions was boiled for 0.5 h before use to eliminate dissolved CO_2 and the water transferred under a N_2 atmosphere.

The reagent solutions were stored in 2-l three-neck Pyrex flasks. The solutions were protected from CO_2 and evaporation losses by bubbler chambers containing NaOH or $HClO_4$ at nearly the same concentration as the primary solutions involved. The $HClO_4$(aq) solution was transferred to the titrant storage bottle used on the thermometric titration calorimeter by a nitrogen flushed polyethylene bottle. The titrant storage bottle was also protected by a bubbler chamber containing $HClO_4$ of the same concentration as used in titrations. Connections were made through Pyrex tubing with Teflon stopcocks.

The NaOH(aq) was standardized by weight titration against National Bureau of Standards primary standard potassium hydrogen phthalate sample 84f. Samples of 1.2–1.4 g of the primary standard to be used for weight titrations were weighed with a precision of ± 0.1 mg. The potassium hydrogen phthalate was dissolved in 100 ml of boiled triply distilled water. The standard NaOH(aq) was placed in a 100-ml polyethylene bottle fitted with a drawn-out Teflon capillary tip and weighed by substitution. The increments of titrant, as small as 6 mg, were added using the plastic bottle as the weight buret. The pH of the solution was measured with a Beckman No. 40495 high alkalinity glass electrode vs. a Beckman asbestos-fiber SCE filled with saturated NaCl(aq). The pH was read with a Corning Digital 119 pH meter to ± 0.001 pH unit. The pH meter was calibrated against two standard buffers originating from the National Bureau of Standards. These buffers were a phosphate buffer of pH 6.685 (25°C) and a borax buffer at pH 9.180 (25°C).

The titration cell was a 300-ml Berzelius beaker fitted with a Teflon top having openings for the monitoring electrodes, a nitrogen dispersion tube and the lead from a Pt-mesh electrode used for solution grounding.

The concentration of $HClO_4$(aq) was determined by titrations in triplicate against the standardized NaOH(aq). Approximately 10 g of $HClO_4$(aq) solution were diluted by 100 ml of boiled triply distilled water prior to titration.

Densities of the standard solutions were determined by the pycnometer using triply distilled water as the reference liquid.

4-Aminopyridine and 4-aminopyride perchlorate

The 4-AP used in this work was part of a sample originating from Reilly Tar and Chemical Corp. of Indianapolis, Ind., and was purified in two stages: recrystallization from dry toluene containing decolorizing carbon followed by sublimation at 110°C. A differential thermal analysis of semi-pure 4-AP revealed that water and solvent were removed at temperatures exceeding 85°C. The purity of the 4-AP was determined by titration with standard $HClO_4$(aq) prepared as described above. The 4-AP and 4-aminopyridine perchlorate (4-APP) were stored in a desiccator over anhydrous $Mg(ClO_4)_2$.

4-APP was prepared according to the procedure of Barnes and Matuszko[11] using recrystallized and sublimed 4-AP and boiled $HClO_4$. Differential thermal analysis and detonation tests were performed to check the thermal and shock stability of 4-APP.

Arc emission spectrographic analysis was performed with an Applied Research Laboratory 26000-1 Spectrographic Analyzer using Kodak 5367 SA-1 film. Duplicate spectral analyses each consumed 15-mg samples in carbon electrodes from Ultra Carbon Corp. of Bay City, Mich. Differential thermal analyses (DTA) were performed on a DuPont 900 thermal analyzer and ADAM-8 constructed at Iowa State University. The heating rates were 2.5°C min^{-1} (ADAM-8) and 10°C min^{-1} (DuPont 900). Thermogravimetric analyses (TG) were performed on a DuPont 950 at a heating rate of 5°C min^{-1}. Nuclear magnetic resonance studies (NMR) were performed in DMSO on a Varian A-60 at ambient temperature with TMS as an internal standard.

Measurements of mass

Measurements of mass required for standardizations of NaOH and $HClO_4$ solutions and purity determinations of KCl were made on an Ainsworth Type 28N single pan balance to ± 0.1 mg. Solid samples ranged in size from 1.1–1.5 g and liquid samples from 10–12 g. Solid samples of 4-AP were approximately 0.2 g and were weighed on an Ainsworth FDJ microbalance to ± 3 μg. All samples were weighed by the difference method and apparent mass was corrected to vacuum using appropriate values for humidity, temperature and barometric pressure.

Calorimetric procedures

(A) *Heat of solution.* The differential isoperibol calorimetric cells were filled with approximately 250 ml of distilled water. The cells were flushed with N_2 prior to filling and watch glasses used as lids were kept in place at all times prior to positioning of the cells in the calorimeter. A N_2 atmosphere was maintained above the solutions in the cells for all calorimetric measurements. The prepurified N_2 was further purified and saturated with water by passage through a purification train. High-vacuum silicone grease was applied to the surface of the Teflon calorimeter lids to insure a vapor-proof seal with the cells.

The temperature of the two calorimetric cells was brought to 25.00 ± 0.05°C during a 30–60 min period for thermal equilibration. During the equilibration period, the trickle heater in the reference cell was used to reduce the temperature difference between the cells to less than 5×10^{-5}°C as determined from a thermometric bridge circuit whose sensitivity[5] was 4005 ± 2 mV°C^{-1}. Approximately one half of the estimated energy absorbed by the endothermic reaction of KCl with water was added to the reaction cell by electrical heating using the 0.05 multiplier setting of a Sargent Model IV Coulometric Current Source, prior to injection of the anhydrous KCl. The calibration heater was shut off when the original bridge output potential ($e_{o,3}$) was approached. Small additional energy increments were added so as to obtain several values of $e_{o,3}$ in the vicinity of the "end point". The blank correction for heat of injection from the solid-sample holder was determined in quadruplicate and applied to all determinations of heat of solution.

(B) *Heat of neutralization.* The motor driven syringes were filled from the titrant reservoir. The drive motor was operated briefly in the forward direction with the three-way stopcock turned to the inject position as a pretitration check of the titrant injection system. The brake was used to stop the titrant syringe pistons at the desired position. The tips of the injection capillaries were wiped clean of acid with a Kimwipe taking care not to withdraw titrant by capillary action. The drive motor was then reversed to bring an air bubble in the capillary tip to prevent pretitration diffusion of the acid into the base.

To reduce contamination by atmospheric $CO_2(g)$ of the triply distilled water added by pipet, the calorimeter cells were flushed before solvent addition with purified nitrogen and covered with watch glasses. These covers were pushed aside only as necessary to add solutions.

Triply distilled water which had been vigorously boiled in a 2-l Pyrex suction flask and cooled to room temperature under purified nitrogen was used for the bulk solution in all determinations of heat of neutralization. The suction flask had been cleaned prior to use with a boiling 1 : 1 mixture of H_2SO_4 and $HClO_4$. The flask was then thoroughly rinsed with triply distilled water.

The initial temperature of the triply distilled water used in heat-of-neutralization calorimetry was adjusted to 24.0 ± 0.1 °C before pipetting by partial immersion of the suction flask into a cold water bath. The lower initial temperature of the triply distilled water for these experiments was necessary since the calorimeter cells were heated twice before a thermometric titration to determine heat capacity ratios.

Throughout temperature adjustment and pipeting, a strong flow of purified N_2 was maintained over the triply distilled water. This was accomplished by connection of the side arm of the suction flask with the flow of N_2.

Purified N_2 was dispersed into the vapor volume of the calorimeter cells through 10-mm medium porosity fritted-glass sparging tubes while the calorimeter assembly was raised in place. The nitrogen sparge was continued approximately 5 min after solution stirring was begun.

After final assembly of the calorimeter, the containers were heated simultaneously to raise their temperatures to approximately 24.6 °C and adjusted to within 0.0001 °C of each other. For these experiments, $e_{o,3}$ was recorded at a sensitivity of 11.15 mV in.$^{-1}$ on a critically damped Heath EU-20W recorder at a chart rate of 0.5 in. min^{-1}. Additionally, $e_{o,4}$ (10 × $e_{o,3}$ displayed on a 4½ digit DVM) was recorded manually on the recorder at 1-min intervals. The time signal of WWV, Fort Collins, Colorado, was used as a time marker in the measurement of $e_{o,4}$.

A thermal equilibration period of 30–60 min brought the temperature to approximately 24.7 °C. During the equilibration time, the trickle heater in the reference cell was used to reduce the temperature differential between the calorimeter cells to less than 5×10^{-5} °C as determined by a constant near zero value of $e_{o,3}$. The heat capacity ratio of the calorimeter cells was determined twice both before and after the thermometric titration. Thus, by extrapolation, the heat capacity ratio of the calorimeter cells was determined at the mean temperature of the thermometric titration. Approximately 10 cal were added to each cell simultaneously to determine the heat capacity ratios.

Before titrations were commenced, the baseline was again adjusted to zero and the baseline recorded for a period of time equal to the time anticipated for the subsequent titration.

The temperature of the titrant was monitored versus the temperature of the titrand in the reference cell of the calorimeter. Thermometric titrations were begun when the temperature difference between the titrand and titrant was approximately one-half of the projected temperature rise due to the electrical heating needed to equal the chemical reaction heat in the reaction cell of the calorimeter. Titrant flow-rates ranged from 0.00025–0.005 ml sec^{-1}. The sensitivity of the thermistor bridge used for measuring temperature differences between the titrant and titrand was 68.44 ± 0.08 mV°C^{-1}. This thermistor bridge output was measured with a Corning Digital 112 pH meter in the mV mode. Since the resolution of the pH meter was ± 0.1 mV, the temperature resolution of the second temperature bridge was ± 1.5 m°C.

Approximately one-fourth of the calculated energy was added electrically to the reference cell before simultaneous addition of titrant to both cells was begun. Electrical heating of the reference cell continued during and after the thermometric titration until the recorded output of OA-3 approached the estimated baseline. The estimated baseline position was calculated by extrapolation of the foreslope. Calculations were made with a hand calculator on the $e_{o,4}$ data. Thus, the temperature differential between the calorimeter cells was maintained at the smallest possible amount throughout the titration procedure.

Separate determinations were made of the energy blank of the titrant injection system caused by a slight temperature mismatch of the titrant thermostating reservoirs above each cell of the calorimeters. Energies reported here were calculated on the basis of 4.1840 J cal^{-1}.

RESULTS AND DISCUSSION

Heat of solution of KCl(s)

The energy blank for activation of the solid-sample injector was 1.30 ± 0.90 × 10^{-2} cal on the basis of four determinations. The uncertainty given is the deviation for 95% confidence. The calculated uncertainty in energy based on theoretical considerations of thermometric circuit noise is 0.34 × 10^{-2} cal for a measurement of $e_{o,3}$ over a single time interval and 0.68 × 10^{-2} cal for measurements based on differences of $e_{o,3}$. Hence, the uncertainty of the heat of the sample injection was approximately equal to the theoretical uncertainty.

The purity of KCl(s) after repurification was 99.97 ± 0.20% based on three determinations. Least-squares analysis of the plot of ΔH_S versus $\sqrt{m}$ for five determinations in the concentration range 3.0027 × 10^{-3} – 1.0650 × 10^{-2} m yielded $\Delta H_S = (4115.9 \pm 3.6) + (536.9 \pm 44.8)\sqrt{m}$ cal mol^{-1}. This is in excellent agreement with the value of 4115 ± 10 cal mol^{-1} reported by Parker[12]. The slope of 537 $\sqrt{m}$ is in fair agreement with the reported slope in the range[13] 458–491.

NaOH and $HClO_4$ solutions

The concentration of the solution of NaOH was determined to be 0.21980 m with a relative standard deviation of 0.48 ppt. The concentration of the solution of $HClO_4$ was determined to be 0.96156 m with a relative standard deviation of 0.20 ppt.

The densities of the standard NaOH and $HClO_4$ solutions at 25.02°C were 1.0066 and 1.0535 g cm^{-3}, respectively. At 19.5°C, the respective values were 1.0081 and 1.0557 g cm^{-3}.

Purity and properties of 4-aminopyridine and 4-aminopyridine perchlorate

The purity of 4-AP(s) as determined by triplicate weight titrations with standard $HClO_4$(aq) was 99.983%. The absolute standard deviation calculated according to the procedure of Blaedel and Meloche[14] was 0.034% accounting for the standard deviations for the standardizations of the $HClO_4$ and NaOH solutions.

$$\sigma = (\text{purity of 4-AP})(\delta^2_{NaOH} + \delta^2_{HClO_4} + \delta^2_{4\text{-AP}})^{1/2}$$

No metal impurities were detected by arc emission spectrographic analysis which implies individual metallic contaminants[15] were < 100 ppm. The identity of any impurities present remains unknown; it is suspected that water adsorbed during the brief exposure to the room atmosphere during transfer operations was the largest impurity. These titrations and associated work were performed during periods of time when the relative humidity was approximately 80%. The finely ground material certainly presented a large area for adsorption.

NMR spectra of 4-AP in DMSO showed a AA'XX' spectra with the α-protons absorbing at δ7.92, β-protons at δ6.42 and exocyclic amino(γ-) protons at δ5.86. $J_{\alpha\beta}$ and $J_{\alpha'\beta'}$ were 6 Hz and $J_{\alpha'\beta}$ or $J_{\alpha\beta'}$ were 1 Hz. NMR spectra of 4-APP produced considerable downfield shifts of absorptions: α at δ8.04, β at δ6.76, and $-NH_2$ at δ7.86. The proton of $HClO_4$ bonded to the nitrogen of the pyridine ring gave a very broad absorption at δ12.85 indicating that it is quite acidic. Addition of D_2O removed the absorptions at δ7.86 and δ12.85 confirming the identities of each absorption as due to $-NH_2$ and $-N^+H$, respectively.

Accurate integration ratios were difficult to obtain because of the broadness of the absorption peak at δ12.85 and the closeness of the absorptions for β-protons and amino protons. The experimental ratio obtained was 64:32:13 for the β + amino proton absorption peaks, proton absorption, and ring nitrogen proton. The values of $J_{\alpha\beta}$ and $J_{\alpha'\beta'}$ were 7 Hz and $J_{\alpha'\beta} = J_{\alpha\beta'}$ were approximately 1.5 Hz for 4-APP, undeuterated.

The conclusions that can be made from these NMR analyses are as follows:

(1) Reactions of 4-AP with strong proton acids produce acidic salts in DMSO.

(2) The proton donated by the acid is bonded to the heterocyclic ring N and not to the exocyclic amino N.

(3) The electron density decreases dramatically at the exocyclic amino nitrogen when the heterocyclic N is protonated as evidenced by the large downfield shift of its absorption.

Although NMR is not accepted as a precise quantitative method for purity determination, the presence of significant amounts (>1% w/w) of decomposition products of 4-AP by $HClO_4$(aq) produced during the synthesis of 4-APP(s) were not found.

DTA of a large sample (~0.15 g) of 4-AP(s) showed a very large depression of the baseline due to thermal lag even with the slow heating rate used, 2.5°C min^{-1}. Integration of the areas of the sublimation endotherm and melting point was used to calculate an approximate value of the heat of sublimation for 4-AP(s). The heat of fusion together with the ratio of areas yielded a value for heat of sublimation of 17 kcal mol^{-1}.

Determination of water adsorbed by 60-mesh and finer particles of 4-AP(s) over a 24-h period was performed with small samples (~1 mg). Only a smoothly decreasing slope and melting point endotherm were observed in DTA of small samples with an observed melting point of 162°C for pure 4-AP(s).

The blank determined with dry 4-AP(s) corresponded to 0.03 mol % impurity which is in excellent agreement with results from weight titrations. DTA showed that 4-AP(s) adsorbed 0.45 mol-% water in an atmosphere of 50% relative humidity and 0.75 mol-% in a water saturated atmosphere. The values reported are corrected for the value of the blank.

TG of dry 4-AP(s) was used to determine an energy of activation for sublimation by slope analysis for weight loss below 150°C. Weight losses were very small for temperatures less than 120°C in agreement with qualitative results found in purification by sublimation of 4-AP(s). Fitting the TG weight loss data to the Arrhenius equation yielded

$$-\frac{1}{w_s}\frac{dw}{dt} = 1.63 \times 10^{9}\ \text{min}^{-1} \exp\left(\frac{-9.97 \times 10^{3}}{T}\right)$$

with a correlation coefficient of 0.992. The pre-exponential frequency factor A is $1.63 \times 10^9\ \text{min}^{-1}$ and the energy of activation equals 19.7 ± 0.8 kcal mol^{-1} for sublimation. The heat of sublimation in this case is nearly equal to the apparent activation energy since the work of transporting the vapor from solid surface to surfaces of the cell enclosure is small in TG. The agreement between values of heat of sublimation determined by DTA and TG is reasonable considering the present lack of agreement as to the validity of using the Arrhenius equation for non-isothermal methods[16].

DTA and TG data for 4-APP(s) are shown in Fig. 1. The melting point of 4-APP(s) determined from DTA is 275°C which is in good agreement with that reported by Barnes and Matuszko[11]. The amount of volatile impurities on 4-APP(s) was 0.04% as determined by TG.

A slight upward swing of the TG trace occurred when the 4-APP(s) detonated at approximately 340°C. This was nearly coincident with the second large exothermic decomposition peak. The cause of detonation is not certain. Aluminum pans were used for TG and perhaps the 4-APP(s) decomposed the usual surface protective coating of Al_2O_3(s) on the pans. Aluminum metal is very reactive with most oxidants once the protective Al_2O_3(s) is removed. Hence, care was exercised in handling 4-APP(s) and in no case should future workers be careless in handling this compound.

The density of 4-APP(s) found corrected to vacuum was 1.5470 g cm^{-3}.

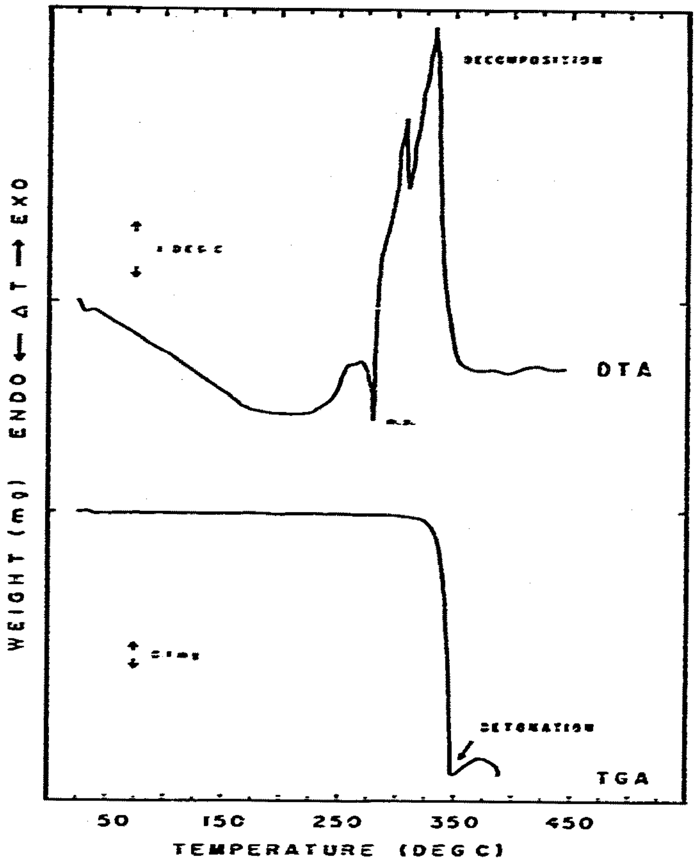

Fig. 1. DTA and TG curves for 4-aminopyridine perchlorate(s). DTA: Size, 4 mm in microtube; reference, glass beads; atmosphere, air; heating rate, 10°C min^{-1}; baseline slope, 0; shift, 0. TG: Size, 10.00 mg; atmosphere, air; heating rate, 10°C min^{-1}; suppression, 9.00 mg; shift, 0; time constant, 1 sec. Note: Temperature scales shown were not corrected for C/A thermocouple non-linearity.

Heat of solution of 4-aminopyridine(s)

Results of the measurement of heat of solution made when 4-AP(s) was added just prior to each thermometric titration are given in Table 1 and are shown in Figure 2. A simple quadratic, $a + bm + cm^2$, gave a reasonable fit of the experimental curve; however, the best fit to the data was obtained for the equation

$$\Delta H_S = a + bm^{1/2} + cm + dm^{3/2} + dm^2$$

The parameters of this equation for ΔH_S (cal mol^{-1}) are

$$\Delta H_S = 3.896 \times 10^3 + 1.4130 \times 10^4\,m^{1/2} - 2.9987 \times 10^5\,m$$
$$+ 3.0683 \times 10^6\,m^{3/2} - 1.1823 \times 10^7\,m^2$$

The average standard deviation between the least squares fit obtained above and the experimental data was 4 cal mol^{-1}. The value of the heat of solution for 4-AP(s) at infinite dilution, ΔH_S°, was calculated to be 3896 cal mol^{-1} with the average standard deviation equal to 4 cal mol^{-1}. Incomplete dissociation of 4-AP(aq) and solvent–base

TABLE I

HEAT OF SOLUTION OF 4-AMINOPYRIDINE(S)

Trial	$n_{4\text{-AP}} \times 10^3$ (mol)	$m_{4\text{-AP}} \times 10^3$ (mol kg^{-1})	$m_{4\text{-AP}}^{1/2} \times 10^2$ (mol kg^{-1})$^{1/2}$	q (cal)	ΔH_S (kcal mol^{-1})	
					Exp.	Calc.
1	1.97610	7.9268	8.9032	8.306	4.203	4.199
2	1.55419	6.2343	7.8957	6.520	4.195	4.193
3	1.11789	4.4844	6.6965	4.668	4.175	4.181
4	0.65132	2.6131	5.1118	2.713	4.166	4.163
5	0.22677	0.90972	3.0162	0.935	4.123	4.123
6	3.14541	12.617	11.233	13.108	4.167	4.165
7	2.62013	10.510	10.252	10.972	4.188	4.193

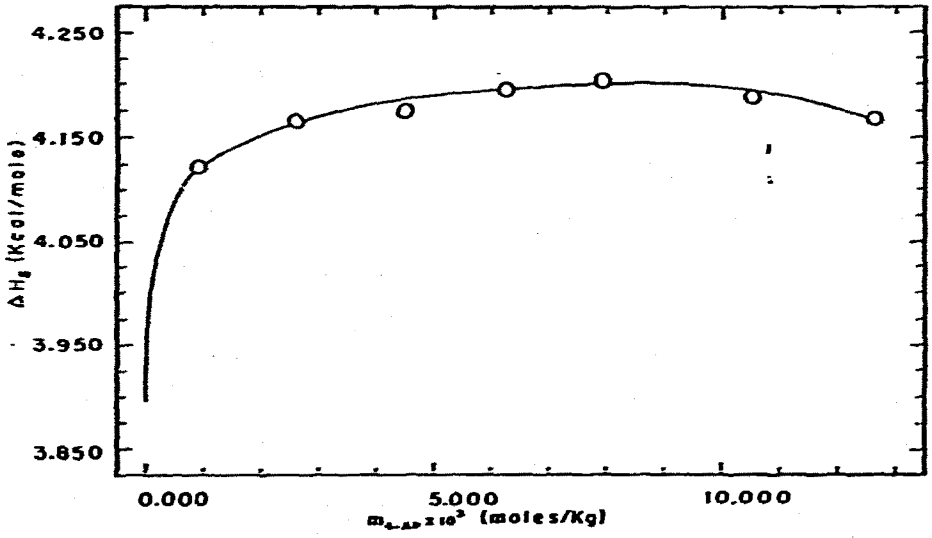

Fig. 2. Heat of solution of 4-aminopyridine(s) as a function of concentration.

reactions are the reasons that the relation of the heat of solution to the solute concentration is more complex than the usual $m^{1/2}$ dependence. The relative error was 1 ppt in these determinations which was the same relative error obtained for the heat of solution of KCl(s).

Titration blank

The energy blank of the titrant injection system as determined from four trials with 2.00 ml of 0.96156 M $HClO_4$(aq) injected into 298.28 g of triply distilled water was, in calories,

$$q_{HClO_4} = (0.0371 \pm 0.0036) + (0.00411 \pm 0.00052)e_{0.5}(\text{mV})$$

The energy blank was exothermic in the reaction cell which implied that the aluminum calorimeter head was warmer above the reaction cell. The friction of a tighter fitting bearing above the reaction cell was probably the source of heat. This conclusion was also in accord with the fact that the trickle heater in the reference cell had to be used continuously to maintain a constant near-zero value of $e_{o,3}$. The temperature difference in the aluminum block as calculated from electrical energy input to the trickle heater and heat transfer coefficients of calorimeter cell probes was approximately 0.0065 °C.

The value of q_{HClO_4} was also corrected for the error due to mismatch of the amount of $HClO_4$(aq) injected into each calorimeter cell. Proportional amounts of q_{HClO_4} were applied to thermometric titrations where the volume of $HClO_4$(aq) titrant added was not equal to 2.000 ml.

Heat of neutralization of 4-aminopyridine(aq) with $HClO_4$(aq)

Thermometric titrations of 4-AP(aq) by $HClO_4$(aq) were performed with the addition of approximately 1.5% excess acid beyond the calculated equivalence point. The excess acid was added on the premise that since the reaction heat was to be calculated from the endpoint value only, suppression of salt hydrolysis was desirable. The excess acid lowered the concentration of free base from approximately 10^{-6} m to 10^{-8} m at a 4-APP(aq) concentration of 10^{-3} m.

The values of K_b and K_{bh} for 4-AP(aq) were determined very precisely by Bates and Hetzer[8]. From Table 2, the final pH of each thermometric titration was approximately 4 and using the expression for K_{bh}, the concentration of free base was calculated. The maximum error in reaction heats by exclusion of heat of hydrolysis due to free base was then calculated. The error was in the order of 0.1 ppt and was therefore considered negligible. The concentration of 4-APP(aq) was then essentially that calculated on the basis of total 4-AP(s) added to the calorimeter corrected for dilution by the titrant.

Before multiplication by the heat capacity ratio c_2/c_1 at the endpoint, heats of neutralization were corrected for the blank error of the $HClO_4$(aq) titrant discussed previously. The ratio of c_2/c_1 used to calculate the corrected reaction energy was obtained at the mean reaction temperature by a graphical fit of c_2/c_1 versus temperature. The results of seven differential thermometric titrations of 4-AP(aq) with

TABLE 2

PARAMETERS OF THE THERMOMETRIC TITRATIONS OF 4-AMINOPYRIDINE (aq)

Trial	*$m_{1,2}$ (g)*	*$T_{b,1}$ (°C) (mean reaction temp.)*	*Moles excess $HClO_4 \times 10^5$*	*Final solution pH*	*c_2/c_1*	
					Exp.	*Calc.*
1	249.2955	25.029	2.760		1.0105	1.0108
2	249.2988	25.032	0.479	3.948	1.0100	1.0099
3	249.2952	25.007	0.416	3.998	1.0089	1.0089
4	249.2543	24.945	0.758	4.010	1.0080	1.0080
5	249.2790	24.986	0.074	4.057	1.0073	1.0073
6	249.3018	25.025	0.126	3.673	1.0134	1.0136
7	249.2986	24.987	0.906	3.562	1.0128	1.0124

TABLE 3

HEAT OF NEUTRALIZATION OF 4-AMINOPYRIDINE (aq)

Trial	$n_{4\text{-AP}} \times 10^3$ *(mol)*	$m_{4\text{-AP}} \times 10^3$ *(mol kg^{-1})*	$m_{4\text{-APH}}{}^{1/2} \times 10^2$ *(mol kg^{-1})$^{1/2}$*	n_a/n_b
1	1.97610	7.8673	8.8698	1.0149
2	1.55419	6.1978	7.8726	1.0039
3	1.11789	4.4655	6.6824	1.0047
4	0.65132	2.6067	5.1055	1.0033
5	0.22577	0.90892	3.0148	1.0041
6	3.14541	12.468	11.166	1.0049
7	2.62013	10.407	10.201	1.0044

Trial	q_{HClO_4} *(cal)*	q *(cal)*	$-\Delta H_N$ *(kcal mol^{-1})* Exp.	Calc.
1	0.0505	22.217	11.243	11.250
2	0.0349	17.483	11.249	11.238
3	0.0220	12.560	11.236	11.225
4	0.0112	7.290	11.192	11.208
5	0.0032	2.538	11.192	11.189
6	0.0656	35.492	11.284	11.279
7	0.0401	29.495	11.257	11.266

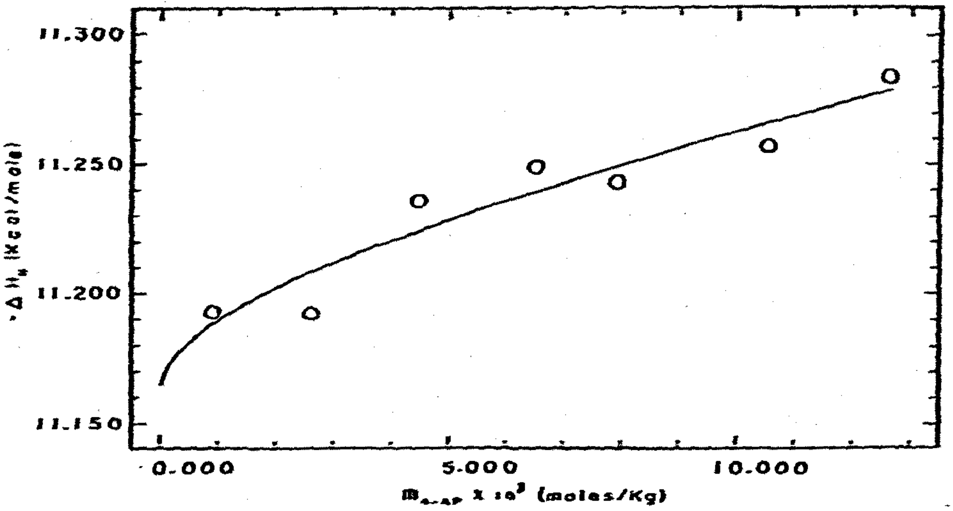

Fig. 3. Heat of neutralization of 4-aminopyridine(aq) as a function of concentration.

$HClO_4$(aq) are given in Table 3 and produced in Fig. 3. The calculated fit to a quadratic equation of the form

$$y = a + bm^{1/2} + cm$$

corresponded best to the experimental results.

The calculated equation for ΔH_N (cal mol^{-1}) was

$$-\Delta H_N = 1.1164 \times 10^4 + 7.37740 \times 10^2 \mathrm{m}^{1/2} + 2.58834 \times 10^3 \mathrm{m}$$

with an average standard deviation of 11 cal mol^{-1}. The standard deviation in experimental results is in excellent agreement with the standard deviation predicted for this equipment. The heat of neutralization at infinite dilution, ΔH_N° was -11164 cal mol^{-1} with an average standard deviation of 11 cal mol^{-1}.

The only reported determination of ΔH_N° for 4-AP by a calorimetric technique was also obtained by thermometric titrimetry. Christensen et al.[17] used a single cell calorimeter, correcting for mechanical and extraneous chemical heats from data obtained in separate experiments. Christensen and co-workers assumed on the basis of previous work[18] with weakly dissociated compounds titrated in the concentration range of 0.005–0.015 M that their experimental value of $\Delta H_N = -11.31$ kcal mol^{-1} for 4-AP(aq) determined at an unspecified concentration within this concentration range was equal to ΔH_N°. That is, they found essentially no systematic variation in values of ΔH_N determined within this concentration range for other compounds and assumed therefore that 4-AP(aq) behaved in like manner. Indeed, with their calculated uncertainty for 4-AP(aq), 0.04 kcal mol^{-1}, such a conclusion is very reasonable. The results given in Table 3 show only a small change of ΔH_N in the concentration range of 0.005–0.013 m and deviations greater than ± 0.02 kcal mol^{-1} would probably obscure any trend in the data.

The non-linear relationship of ΔH_N to the concentration of 4-APP(aq) found in this work presents a dilemma. The fact that ΔH_N decreases with decreasing concentration was expected on the basis of heats of neutralization of NaOH(aq)[5]. However, the lack of agreement with conventional thermometric results indicated that probably either the heat of dilution of $HClO_4$(aq) was not fully compensated for in the differential titrations or the presence of a change in ΔH_N vs. m was masked in previous thermometric titrimetry by an error in the heat of dilution of $HClO_4$(aq). Accurate measurements of heats of dilution are difficult particularly at the low concentrations used in modern thermometric titrimetry. Cabani and Gianni[19] discussed at length the changes in calculated values of ΔH_D for HSO_4^-(aq) as determined by thermometric titrations of Na_2SO_4(aq) with $HClO_4$(aq) when slightly different heat of dilution vs. m relations were assumed.

The value of ΔH_N° determined by Bates and Hetzer[8] from electromotive force measurements was -11.255 ± 0.025 kcal mol^{-1}. There is now a considerable divergence of available values for ΔH_N° for 4-AP(aq) as was the case for NaOH(aq) for many years as discussed by Hale et al.[20]. Hence, an unequivocal recommendation of the correct value for ΔH_N° for 4-AP(aq) could not be given from the results of past and present work.

Taking into account the previous thermometric titration results and the present work, a value for ΔH_N of -11.28 ± 0.04 kcal mol^{-1} is recommended for use when 4-AP(aq) is used as a calorimetric standard in the concentration range of 0.008–0.012 m.

The ratio of the calorimeter cell heat capacities was fitted to an equation of the same form as used to fit ΔH_N 4-AP(aq). The experimental and calculated least squares fit from the following equation are given in Table 2:

$$c_2/c_1 = 1.0074 - 2.6489 \times 10^{-2}\,m^{1/2} + 7.3274 \times 10^{-1}\,m$$

The closeness of the experimental and calculated values bears out the validity of the original assumptions used in derivations of heat capacity ratio determinations[5].

Heat of solution of 4-aminopyridine perchlorate(s)

Determinations of heat of solution of 4-APP(s) in water uncorrected for hydrolysis are given in Table 4 along with the equation used for a least squares fit of the data. Reaction (1) defines the apparent heat of solution as measured experimentally.

$$\text{4-APP(s)} + H_2O(l) \rightarrow \text{4-APP(aq)}(m_1),\ \Delta H_{S,a} \qquad (1)$$

Since 4-APP(aq) is the product of the neutralization reaction of a weak base and a

TABLE 4

HEAT OF SOLUTION OF 4-AMINOPYRIDINE PERCHLORATE(S)

$\Delta H_{S,\pm} = 9.543 \times 10^3 - 1.2112 \times 10^4\,m^{1/2} + 4.4085 \times 10^4\,m.$

Trial	$n_{4\text{-APH}} \times 10^3$ *(mol)*	$m_{4\text{-APH}} \times 10^3$ *(mol kg⁻¹)*	$m_{4\text{-APH}}^{1/2} \times 10^2$ *(mol kg⁻¹)¹ᐟ²*	*q* *(cal)*	$\Delta H_{S,\pm}$ *(kcal mol⁻¹)*	
					Exp.	*Calc.*
1	1.41972	5.6952	7.5467	12.608	8880	8880
2	0.27037	1.0846	3.2933	2.485	9192	9192
3	0.83468	3.3484	5.7865	7.504	8990	8990
4	2.26780	9.0973	9.5380	19.932	8789	8789

TABLE 5

HEAT OF SOLUTION OF 4-AMINOPYRIDINE PERCHLORATE(S) CORRECTED FOR HYDROLYSIS

Trial	$m_{4\text{-APH}} \times 10^3$ *(mol)*	$m_{4\text{-APH}}^{1/2} \times 10^2$ $(mol\ kg^{-1})^{1/2}$	$m_{4\text{-AP}} \times 10^6$ $(mol\ kg^{-1})$	$q_h \times 10^3$ *(cal)*
1	5.6931	7.5453	2.092	5.86
2	1.0837	3.2920	0.913	2.55
3	3.3468	5.7852	1.605	4.49
4	9.0947	9.5366	2.644	7.43

Trial	*q* *(cal)*	$\Delta H_{S,\pm}$ *(kcal mol⁻¹)*	
		Exp.	*Calc.*
1	12.602	8877	8877
2	2.482	9182	9182
3	7.500	8985	8985
4	19.925	8785	8785

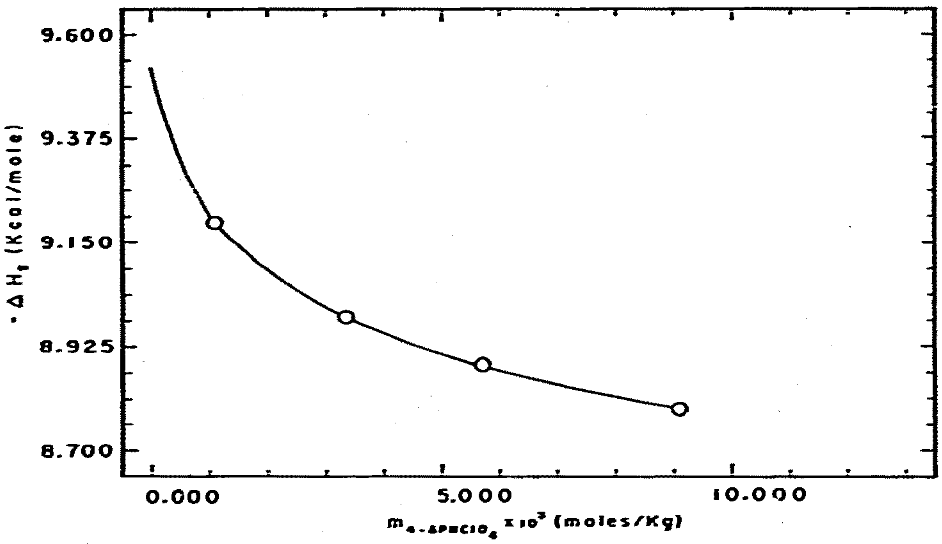

Fig. 4. Heat of solution of 4-aminopyridine perchlorate(s) as a function of concentration.

strong acid, extensive hydrolysis will occur at low concentrations of 4-APP(aq) and consequent changes in concentration of 4-APP(aq).

$$\text{4-APP(aq)} + H_2O(l) \rightarrow \text{4-AP(aq)}(m_3) + H_3O^+(aq)(m_3) + ClO_4(aq)(m_3) + \text{4-APP(aq)}(m_2) \quad (2)$$

The true concentration of 4-APP(aq) then is m_2 rather than m_1. The heat of hydrolysis was endothermic since the heat of neutralization was exothermic and accordingly $\Delta H_{S,a}$ the apparent heat of solution would be more endothermic than the true heat of solution $\Delta H_{S,a}$. The concentration of free 4-AP(aq) was calculated from the expression for K_{bb} by the method of successive approximations which in turn was used to calculate $n_{4\text{—AP}}$ and the energy correction for hydrolysis (q_h). The corrected concentration for 4-APP(aq) (m_2), 4-AP(aq)(m_3), and q_h along with the corrected reaction heats are given in Table 5. The corrected heats of solution are produced in Fig. 4. These measurements when fitted to a quadratic equation yielded

$$\Delta H_{S,2} = 9.520 \times 10^3 - 1.1620 \times 10^4\, m^{1/2} + 4.1028 \times 10^4\, m$$

with the calculated results being identical to the experimental results in each case. This type of agreement can only be considered fortuitous. The value of $\Delta H_{S,2}^{\circ}$ then is

$$\Delta H_{S,2}^{\circ}(H_2O, 298.15\ K) = 9520 \pm 10\ \text{cal mol}^{-1}$$

Although the corrected and apparent results agreed exactly, the error sum was assigned on the basis of other determinations of heats of solution made in this work.

The results from the work presented allowed the calculation of several other thermodynamic parameters. The reactions involved in heats of solution and neutralization

$$\text{4-AP(s)} + \text{H}_2\text{O(l)} \rightarrow \text{4-AP(aq)(m}_4\text{)}; \Delta H_{\text{S},3} \qquad (3)$$

$$\text{4-AP(aq)(m}_4\text{)} + \text{HClO}_4\text{(aq)(m}_5\text{)} \rightleftarrows \text{4-APP(aq)(m}_6\text{)}; \Delta H_{\text{N}} \qquad (4)$$

when added together yield the reaction of 4-AP(s) with $HClO_4$(aq)(m_5). Such a reaction would then seem to be the compliment of reaction (1). That is,

$$\text{4-AP(s)} + \text{HClO}_4\text{(aq)(m}_5\text{)} \rightarrow \text{4-APP(aq)(m}_6\text{)}; \Delta H_{\text{N},1}$$

$$\text{4-APP(s)} + \text{H}_2\text{O(l)} \rightleftarrows \qquad (5)$$

and $\Delta H_{\text{S},3} + \Delta H_{\text{N}} = \Delta H_{\text{N},1} = -\Delta H_{\text{S},2}$

whence

$$\Delta H_{\text{S},3}^{\circ} + \Delta H_{\text{N}}^{\circ} = \Delta H_{1}^{\circ}$$

Substitution of numerical data yields

$$\Delta H_{\text{N},1}^{\circ}(\text{H}_2\text{O}, 298.15\ \text{K}) = -7269 \pm 15\ \text{cal mol}^{-1}$$

The error sum for $\Delta H_{\text{N},1}^{\circ}$ was taken as the sum of the assigned standard deviations calculated for $\Delta H_{\text{S},3}$ of 4-AP(s) and $\Delta H_{\text{N}}^{\circ}$. Hence, it is evident that $\Delta H_{\text{N},1} \neq -\Delta H_{\text{S},2}$ and there must be another reaction that was ignored in reaction (5). This reaction sequence did not consider the equilibria

$$\text{4-AP(aq)(m}_4\text{)} + \text{H}_2\text{O(l)} \rightleftarrows \text{4-APH}^+\text{(aq)(m}_7\text{)} + \text{OH}^-\text{(aq)(m}_7\text{)}$$
$$+ \text{4-AP(aq)(m}_8\text{)}; \Delta H_{\text{i}}$$

which is the heat of ionization or dissociation of the free base. It should be readily apparent from Hess's Law of Heat Additivities that the true heat of solution for 4-AP(s) is given by

$$\Delta H_{\text{S},1} = \Delta H_{\text{S},3} + \Delta H_{\text{i}}$$

and

$$\Delta H_{\text{S},3} + \Delta H_{\text{i}} + \Delta H_{\text{N}} = -\Delta H_{\text{S},2}$$

whence

$$\Delta H_{\text{i}}^{\circ} = -\Delta H_{\text{S},3}^{\circ} - \Delta H_{\text{S},2}^{\circ}$$

and $\Delta H_{\text{i}}^{\circ}(\text{H}_2\text{O}, 298.15\ \text{K}) = -2252 \pm 24$ cal mol^{-1}. The error sum for $\Delta H_{\text{i}}^{\circ}$ was taken as the sum of the assigned standard deviations of each molar heat of reaction. The value obtained for $\Delta H_{\text{i}}^{\circ}$ is in good agreement with the value of $\Delta H_{\text{i}}^{\circ} = -2268$ cal mol^{-1} calculated by Bates and Hetzer[15] at 25 °C from electromotive force measurements.

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