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Batch calorimetry with solids, liquids and gases in less than 1 mL total volume

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Abstract

An add-on batch delivery system for measuring heats of reaction of milligram amounts of solids, liquids and gases with less than 1 mL of liquid in a Calorimetry Sciences Corporation model 4200 calorimeter is described. The system was tested with reactions of dry N_2 gas with H_2O, HCl(aq) with aqueous tris(hydroxymethyl)aminomethane (tris), KCl(s) with H_2O, tris(s) with HCl(aq), Zn(s) with HCl(aq), 2-propanol with H_2O, and CO_2(g) with NaOH(aq). The precision and accuracy of a single heat measurement is 2–3 mJ or 1–2%, whichever is larger.
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1. Introduction

The enthalpy changes for dissolution of solids and gases in liquids, for reactions of suspensions and solutions, and for mixing of liquids are important and useful physical properties that are best measured by direct calorimetry whenever possible [1]. However, obtaining reliable calorimetric data from batch processes when only very small quantities of substances are available is not possible with most calorimeters. To fill this need, a batch delivery system as an add-on option for the Calorimetry Sciences Corporation model 4200 ITC has been designed and tested. The model 4200 ITC has a detection limit of $0.010\,\mu W$ or $0.5\,\mu J$, high gain range of $\pm450\,\mu W$ and low gain range of $\pm15{,}000\,\mu W$ in a 1.3 mL, removable, stirred, reaction vessel usually constructed of Hastelloy-C. [2] With addition of the batch delivery system, this calorimeter has the capability of measuring heats of solution of sub-milligram amounts of solids, heats of dissolution of $100\,\mu L$ of gases, and heats of mixing of up to $50\,\mu L$ of liquids, solutions or suspensions with 300–$750\,\mu L$ of liquid solvent, reactant solution or suspension.

The difficulties of working in this size range are not caused by the size of the heat effect. Heats of reaction of milligram amounts of material typically are hundreds of millijoules, e.g. the heat of solution of KCl in water is about $235\,\mathrm{mJ\,mg^{-1}}$. The difficult issues at these dimensions are sample preparation, mixing of the solution in the reaction vessel, venting of gases, and precision and accuracy of the blank. At milligram and microliter scales, surface and electrostatic forces can completely dominate gravitational forces. Sample preparation involves transferring, weighing and containing the solid, liquid or gas reactant in a sealed container which can then be brought to the same temperature as, and opened into, the stirred liquid in the calorimeter reaction vessel. With larger calorimeter vessels this has most commonly been done with a glass container submerged in a stirred liquid and crushed to mix the reactants, with two compartments separated by a membrane that was punctured, or with a two compartment reaction vessel that was inverted to mix the reactants. None of these methods is reliable or applicable to the small scale of the model 4200 ITC. For batch additions in this calorimeter a plunger was designed to open a $100\,\mu L$ inner vessel into a 1 mL outer vessel. The plunger can be operated manually or automated with the system software. Both the inner and outer vessels are removable for cleaning, drying, and filling with reagents. The inside of the reaction vessel and the injector exposed to liquid were designed to avoid gas bubbles that tend to stick to surfaces at this scale. Thermal equilibration between the injector, sample and reaction vessel liquid is obtained through the metal wall of the reaction vessel.

Fig. 1 is a schematic of a prototype mixing vessel previously designed for the Calorimetry Sciences Corporation model 4100 MC-DSC which also has 1 mL removable vessels and can be operated as an isothermal calorimeter. In this system, which

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was only tested for measuring heats of solution of very soluble solids in water, the small hole in the inner vessel was sealed with stopcock grease, and since the outer vessel had to be a sealed, constant volume container, mixing was done by increasing or decreasing the pressure in the outer vessel by means of a syringe outside the calorimeter connected to the reaction vessel through a small bore teflon needle. Increasing pressure in the outer vessel broke the grease seal and forced water into the inner vessel. Or, water could be placed in the inner vessel and drawn into the outer vessel by decreasing the gas pressure in the outer vessel. While this system was capable of producing accurate data on sub-milligram amounts of reaction, it had some major limitations. First, mixing was only possible by cycling the syringe. Second, determination of the concentration of the final solution was difficult because transfer was not complete. Third, and most problematic, very careful corrections had to be made for VdP work and vaporization and condensation of water. Neither the work term nor the water term was insignificant. The work term is obvious. When gas is compressed or expands, work is done on or by the system and appears as heat in the calorimetric output. The evaporation/condensation term is not so obvious. When gas is withdrawn with the syringe, part of the water vapor in the reaction vessel is removed, the partial pressure of water in the gas remaining in the reaction vessel is thus decreased, and water evaporates to achieve the equilibrium partial pressure. If gas containing water vapor is injected into the system in Fig. 1, water condenses to achieve the equilibrium water partial pressure. If dry gas is injected, then water neither evaporates nor condenses because the partial pressure of the water remains unchanged. Because of these difficulties, the batch adaptor for the model 4200 ITC was designed to operate at constant pressure instead of constant volume. In this case, gases produced by the reaction or introduced when the injector is opened into the reaction vessel are vented to the atmosphere. This transfer of gas must be taken into account when the blank is determined [3]. The blank must incorporate both the heat of opening of the inner vessel and any vaporization of solvent and solute.

In related work by others [1,4,5], a system for injecting mg amounts of solids into about 20 mL of liquid in a Thermometrics calorimeter was tested with heats of solution of KCl, acetanilide, adenine, and sucrose in water, tris(s) in 0.1 M HCl, and
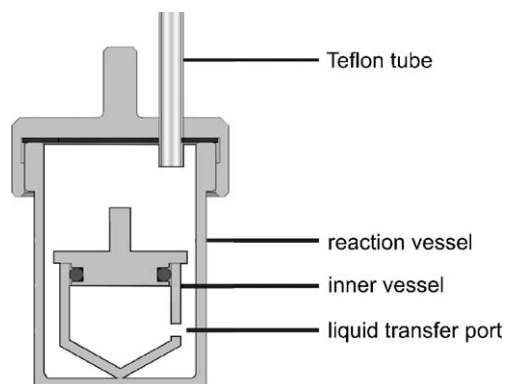
paracetamol and sodium diclofenac in phosphate buffer and in DMSO. The published data [1] suggest a precision of 2–5 mJ or 2–3% (S.D. with $n \approx 8$) on measurements of the heat of solution of KCl. The system is limited to solid pellets in the injector and liquid volumes greater than about 15 mL in the reaction vessel.

2. Materials and methods

Water was deionized with a Barnstead E-pure system, HCl was Aldrich volumetric standard, either 1.004 N or 0.1009 N, trishydroxymethylaminomethane (tris) was Sigma reagent grade, N_2 was pure grade, dry gas from Air Liquide, KCl was NBS standard reference material 1655 purchased from NIST [3], Zn metal was granular, 20 mesh, certified ACS reagent grade from Fisher, and 2-propanol was certified ACS reagent grade (0.04% water) from Fisher. NaOH(aq) was prepared by weight from pellets (Fisher certified ACS grade) and CO_2 was obtained from Air Liquide.

The balance used to weigh samples into the injector was a Mettler M5 SA with a 20 g capacity and readable to 5 μg. Calibration of the μg scale on the balance was checked at 3.5 g total load with class A, milligram weights. The accuracy of sample weights is thus better than 0.02 mg.

The design of the batch delivery system is shown in Fig. 2. All parts in contact with reactants are Hastelloy-C except the O-rings, which were Viton for the experiments described here. Other metals and O-ring materials could be substituted as required to avoid corrosion by the reactants. The space above the solvent in the reaction vessel is vented to the atmosphere by a vent tube sized large enough to provide atmospheric pressure in the vessel and rapid equilibration of the vapor pressure of solvent in the tube, but small enough to allow only a very small heat rate from evaporation. The vent tube may be closed off if required by plugging the vent tube outlet at the top of the insert. Or, the O-ring b in Fig. 2A may be replaced with an O-ring with oversized cross-section so that it closes off the annular space between the injector and the inner wall of the reaction vessel. Fig. 2B–H show the sequence of assembly and operation of the injector and batch delivery system.

Electrical calibration was done with the heater embedded in the reaction vessel holder in the calorimeter. The total sample volume of the injector was determined to be 116 μL from the difference in mass of the dry injector and the injector filled with water. All experiments in this study were run with the amplifier on low gain, with no software deconvolution to remove the instrument time constant, and at one data point every 0.5 s.

3. Results

The results are summarized in Table 1. Various blank experiments were done to determine the reproducibility and effects of variables on blanks. Examples of blank data are shown in Fig. 3. The first three types of experiments listed in Table 1 were done with O-rings a, c and d lightly lubricated with silicone stopcock grease. In the remaining experiments the O-rings were not greased, i.e. clean in Table 1. Even if the O-rings are not greased, liquid in the reaction vessel above 465 μL acts as a

Fig. 1. Schematic of mixing vessel for the Calorimetry Sciences Corporation model 4100 MC- DSC.

Table 1
Results of test experiments with batch adaptor in CSC model 4200 ITC at 298.15 K

Injector contents	Ampule contents	Conditions	Heat effect[a]/mJ	Heat of reaction/kJ mol^{-1}	
				Measured	Literature
50 μL H$_2$O	500 μL H$_2$O	no stirring, greased O-rings	20 ± 1, $n = 5$	–	–
116 μL dry N$_2$	500 μL H$_2$O	no stirring, greased O-rings	7 ± 2, $n = 4$	–	–
50 μL H$_2$O	500 μL H$_2$O	400 rpm, greased O-rings	19 ± 2, $n = 6$	–	–
116 μL lab air	350 μL H$_2$O	300 rpm, clean O-rings	24 ± 3, n = 3	–	–
116 μL lab air	750 μL H$_2$O	400 rpm, clean O-rings	17 ± 2, $n = 3$	–	–
50 μL 0.1009 M HCl	750 μL 0.2 M tris	400 rpm, clean O-rings	$242^b \pm 2$, n = 2	$-48.1^c \pm 0.4$ $(0.8\%)^d$	-47.9^c [7]
50 μL 1.004 M HCl	750 μL 0.2 M tris	400 rpm, clean O-rings	$2499^b \pm 29$, $n = 3$	$-49.7^c \pm 0.6$ $(1.2\%)^d$	-48.8^c [7]
mg KCl(s) (3.050, 3.150, 4.095, 2.175)	350 μL H$_2$O	300 rpm, clean O-rings	$(-733, -758, -935, -497)^b$	17.5 ± 0.4 $(2.3\%)^d$	17.58 [3]
mg tris(s) (2.290, 2.585, 1.930)	350 μL 0.28 M HCl	300 rpm, clean O-rings	$(542, 645, 439)^b$	-28.8 ± 1.1 $(3.8\%)^d$	-29.74 [4]
50.43 mg H$_2$O	374 mg (500 μL) 2-propanol	300 rpm, clean O-rings	-1090^b	0.166^f	0.174^f [8]
41.22 mg 2-Propanol	498.6 mg H$_2$O	300 rpm, clean O-rings	8290^b	-0.292^f	–
20.87 mg 2-Propanol	495.2 mg H$_2$O	300 rpm, clean O-rings	4446^b	-0.160^f	–
10.135 mg 2-Propanol	587.9 mg H$_2$O	300 rpm, clean O-rings	2320^b	-0.0707^f	–
7.925 mg 2-Propanol	586.2 mg H$_2$O	300 rpm, clean O-rings	1865^b	-0.0568^f	–
4.975 mg 2-Propanol	586.5 mg H$_2$O	300 rpm, clean O-rings	1184^b	-0.0363^f	–
1.970 mg 2-Propanol	586.4 mg H$_2$O	300 rpm, clean O-rings	438^b	-0.0134^f	–
1.315 mg 2-Propanol	589.6 mg H$_2$O	300 rpm, clean O-rings	295^b	-0.0090^f	–
mg Zn (0.810, 0.820)	500 μL 6M HCl	400 rpm, clean O-rings	$(1699, 1760)^{b,e}$	$-139 \pm 2 (1.6\%)^d$	-139.4 [9]
116 μL CO$_2$ at 0.85 bar	350 μL 0.4M NaOH	300 rpm, clean O-rings	$(418, 428)^b$	$-104 \pm 1 (1.0\%)^d$	-108.5 [9]
116 μL CO$_2$ at 0.85 bar	500 μL 0.4M NaOH	300 rpm, clean O-rings	$(425, 432)^b$	$-105 \pm 0.9 (0.8\%)^d$	-108.5 [9]

All heats are based on electrical calibration obtained with the built in heater and calibration circuit.

[a] A negative number indicates an endothermic effect.

[b] Corrected for blank.

[c] Corrected for heats of dilution by data in [6].

[d] Relative standard deviation.

[e] Corrected for vaporization of H$_2$O into H$_2$(g) [3].

[f] Per mole of (H$_2$O + IPA).

lubricant on O-ring d (see Fig. 2). If there is liquid in the injector it will act as a lubricant on O-ring a. Lubrication on O-ring a decreases the blank by about 4 mJ. Lubrication on O-ring d decreases the blank by about 7 mJ. Lubrication on O-ring c is probably not significant because the travel distance is very short. Stirring made no difference to the blank. In the case of dry N$_2$ gas or lab air injected into H$_2$O, the blank is decreased by an endothermic effect from evaporation of water. This endothermic effect is reduced by the percent humidity in lab air when lab air is used in the injector; $q_{vap} = (1-RH)\Delta H_{vap} V_s$ where RH is relative humidity, see ref. [3]. For example, since the humidity of our lab air was 17%, the endothermic evaporation effect would be reduced from 6.5 to 5.4 mJ. The reproducibility of the blank is about ± 2 mJ. The results on all of the blanks demonstrate that to obtain data within this accuracy, the blank condition must closely correspond with the experiment condition.
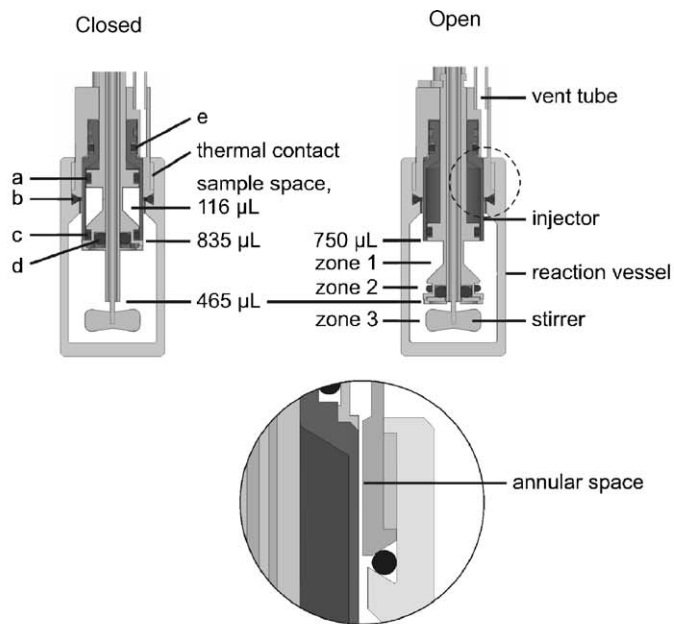
Examples of data from three reference test reactions, tris(s) into excess HCl(aq), KCl(s) into H$_2$O(l), and HCl(aq) into excess tris(aq), are shown in Fig. 4. Samples were loaded into the inner vessel under lab air and weighed by difference. Clean O-rings were used in these experiments, lab air blanks were subtracted from the data for solids, and H$_2$O-into-H$_2$O blanks were subtracted from the HCl(aq) injection data. Heats of dilution were obtained from [6] and used to correct for dilution of the HCl(aq) to the final ionic strength in the tris solution. Numerical results

are summarized and compared to literature values in Table 1. For all three reactions the agreement is within the precision of the measurement. This agreement shows that the electrical calibration was accurate for the batch addition system.
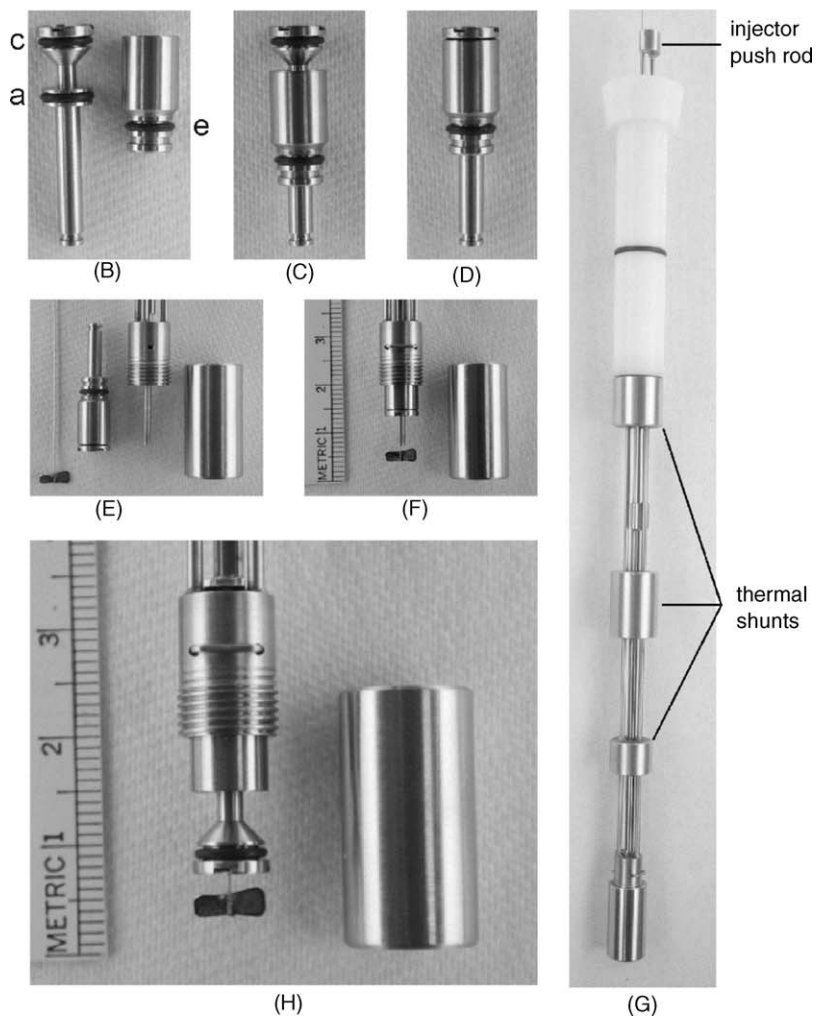
Results of mixing 2-propanol with water are summarized in Table 1. These results show that volatile organic liquids can be used in either the injector or reaction vessel. Fig. 5 compares heats of mixing data in the water-rich region from literature sources and shows that our data agree within expected accuracy of the literature data.

The heat of solution of Zn in 6 M HCl(aq) was measured to verify that the system was capable of measurements on reactions producing large volumes of gas. A sample result is shown in Fig. 6. The raw data must be corrected for the evaporation of water carried out of the system by the exiting gas. The enthalpy change measured for the reaction agrees with literature values [9].

The results for reaction of CO$_2$(g) with NaOH were obtained using two different procedures. In the first, 350 μL of NaOH solution was used and the injector was fully opened. This procedure may allow escape of a small amount of CO$_2$(g) through the unsealed stirrer guide tube. In the second procedure this problem was avoided by increasing the volume of liquid in the reaction vessel to 500 μL, which covers the end of the stirrer guide tube. The injector was then only partially opened to prevent pushing
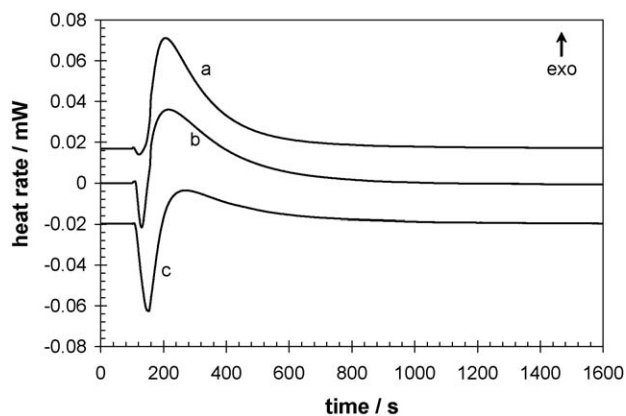
Closed   Open

vent tube
e
thermal contact
a
sample space,
b
116 µL
c
835 µL
d
750 µL
zone 1
465 µL
zone 2
zone 3
injector
reaction vessel
stirrer

annular space

(A)

c
a
e

(B)   (C)   (D)

(E)   (F)

METRIC

injector
push rod

thermal
shunts

(H)   (G)

Fig. 3. Examples of blank data: (a) 50 μL H₂O into 500 μL H₂O; (b) lab air into 750 μL H₂O; (c) dry N₂ into 500 μL H₂O.
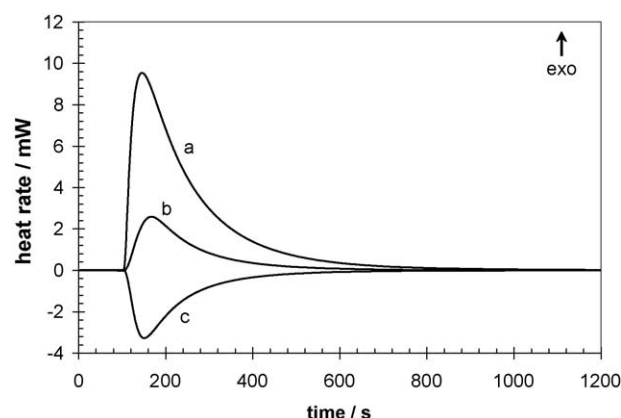

Fig. 5. Comparison of enthalpy changes for mixing of 2-propanol with H_2O determined with the batch addition system and literature data [8] in the water-rich region. The equation is a quadratic fit to the data from this study.

Fig. 4. Examples of data from reaction of (a) 1 M HCl with excess tris(aq), (b) tris(s) with excess 0.28 M HCl, and (c) KCl(s) with H_2O.

Fig. 6. Data for the reaction of Zn metal with 6 M HCl.

liquid up the stirrer guide tube. Results of both procedures are given in Table 1. The measured enthalpy change was about 3–4% low compared with the value calculated from data in ref. [9], but the values agree within the expected accuracy.

4. Discussion

To achieve a high degree of accuracy in the results, blanks must be carefully matched to the experiment. Variables that must be controlled are the composition of the gas in the injector and the condition of the O-rings, e.g. lubricated or not. Lubricated O-rings perform slightly better than unlubricated, but lubrication is not always compatible with the experiment.

Obtaining good results with solids in the injector requires consideration of both the amount of liquid in the reaction vessel
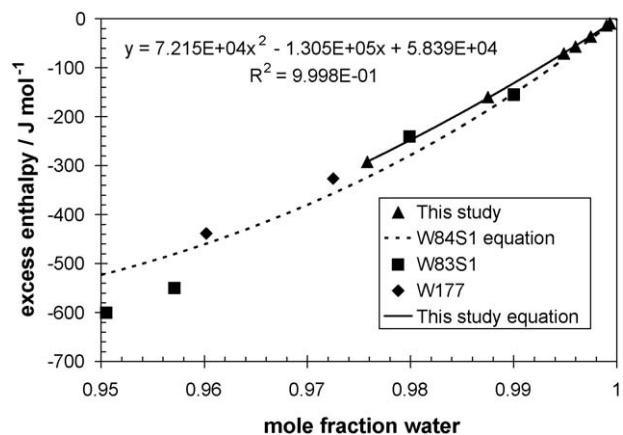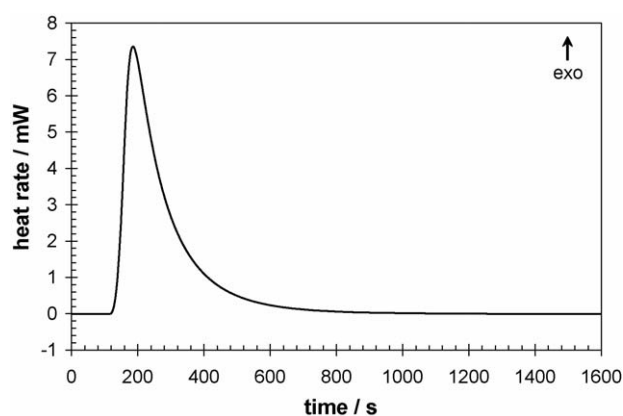
and the nature of the solid, i.e. solubility, rate of dissolution and physical properties of the particles. If the solid will drop cleanly into the liquid, minimal volumes of liquid, i.e. between 350 and 450 μL (zone 3 in Fig. 2A), give the best results. Under these conditions the only effect of the rate of dissolution is to increase the uncertainty of the integrated heat with increasing time. If the solid cannot be pressed into a pellet or is sticky, liquid volumes between 500 and 700 μL must be used to ensure that liquid reaches zone 1 in Fig. 2A. At these larger volumes of liquid in the reaction vessel, zone 2 is a potential barrier that may cause poor mixing between zones 1 and 3. For example, attempts to measure the heat of dissolution of KCl into volumes of water between 500 and 750 μL resulted in large apparent baseline shifts because of incomplete reaction. Under this condition the KCl saturated the

Fig. 2. (A) Schematic of the batch addition system for the Calorimetry Sciences Corporation model 4200 Isothermal Titration Calorimeter. O-rings referred to in the text are indicated by a, b, c and d. The liquid level is indicated at two volumes, 465 μL at the end of the stirrer guide tube and 835 μL at the end of the sample chamber with the injector in the closed position and 750 μL with the injector in the open position. The injector displaces 85 μL when it is opened. The annular space between the injector and reaction vessel connects the vent tube to the vapor space in the reaction vessel. ((B)–(H)) Sequence of pictures showing assembly steps for batch delivery system. (B) Disassembled injector. (C) The 2.8 gram injector, assembled, open and inverted for loading liquid or solid samples. (D) Injector closed after sample loading. (E) Stirrer, injector, lower end of batch delivery system and reaction vessel ready for assembly. O-ring b is inside the reaction vessel. (F) Assembled lower end of the batch delivery system, loaded and closed with injector and stirrer in place, ready to have reaction vessel with liquid screwed on. (G) Fully assembled batch delivery system, ready to be inserted into the calorimeter. (H) Batch delivery system with injector in open position after experiment.
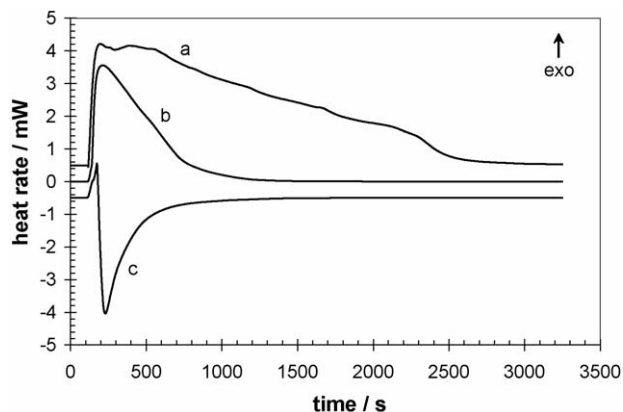
Fig. 7. Data for mixing of (a) 50 µL 2-propanol into 500 µL H$_2$O, (b) 8 µL 2-propanol into 600 µL H$_2$O, and (c) 50 µL H$_2$O into 500 µL 2-propanol.

liquid in zone 1, and the saturated solution very slowly mixed into zone 3. Dissolution of tris(s) into similar volumes of HCl(aq) gave similar results.

Good results with liquids in the injector were obtained with volumes of liquid in the reaction vessel between 500 and 750 µL. These volumes ensure contact between the two liquids. The only consideration is that when liquid in the injector is less dense than that in the reaction vessel, mixing may be very slow. For example, mixing 2-propanol into 500 µL of water required about 1 h to complete, Fig. 7 curve a. Mixing was improved by increasing the volume of water in the reaction vessel to 600 µL, Fig. 7 curve b. Because water is more dense than 2-propanol, mixing water into 500 µL of 2-propanol occurred faster, Fig. 7 curve c. However, mixing was still not rapid as shown by the initial exotherm in curve c. When the injector is initially opened, the water mixes with the small amount of 2-propanol in zone 2 (see Fig. 2A) causing an exothermic effect. As mixing continues into zone 3 the mole fraction of water decreases to the 2-propanol-rich region where the heat of mixing is endothermic.

Heats of mixing at very large and very small mole fractions are very difficult to obtain by flow mixing calorimetry because mixing is often very difficult to achieve when the two liquids are flowing at very different rates. Although the batch injector system described here is not well suited for the midrange of mole fractions, it is particularly well suited for accurately defining the heat of mixing curve below about 0.05 and above about 0.95 mole fraction.

Mixing of suspensions of finely divided solids into liquids, liquids into liquids, and gases into liquids can be done either by titration or by batch injection. The batch addition system described here is capable of handling all of these materials, but the batch injection system described in [1] is only capable of handling solids. Batch addition is advantageous over titration when only one data point is required, when the amount of material is limited, when the accuracy depends on knowing the exact amount of reagent injected, when injecting volatile liquids, when injecting gases, and when injecting suspensions. Batch injection requires less material because all of the material is reacted and none is wasted by being left in a syringe, injection needle, equilibration tubing, etc. Batch injection allows weighing the sample before injection and does not have the uncertainty present in the first injection of an incremental titration. The high vapor pressure of volatile liquids may create bubbles or expansion and leakage into the reaction vessel, suspensions may settle in a buret, and gases require elaborate equipment to quantify the amount of gas injected. For gases, the batch addition system described here only requires knowing the gas pressure and temperature when the injector is filled.

Data for heat conduction calorimeters is often deconvoluted to remove instrument time response and thus speed the apparent return to baseline for multiple injections so injections can be done closer together in time. Deconvolution with an algorithm incorporating the instrument time constant does not cause significant error for reactions with a time constant shorter than the instrument time constant. However, when the reaction time constant is longer than the instrument time constant, correct deconvolution would have to be based on the reaction kinetics. Deconvolution based on the instrument time constant apparently caused disagreement between integrated raw data and integrated dynamically-corrected data observed by Ramos et al. [4]. Deconvolution of batch addition data should not be done because it assumes characteristic time constants and a peak shape that are not necessarily applicable (see Fig. 7). Further, there is no advantage to deconvolution of a single batch injection because in any case data collection must continue until the reaction is complete and all heat has been measured. Raw data should be taken at a rate of at least one data point per second so that integration can be done accurately.

The batch addition system described here can be used for measuring heats of dissolution and reaction of solids into liquids, heats of reactions of liquid reagents, heats of mixing of liquids, heats of dissolution and reaction of gases, heats of wetting of solids, heats of vaporization, and heats of reactions of suspensions. Reactions that rapidly produce gas can be measured in this constant pressure system. The precision of a heat measurement is 2–3 mJ or 1–2%, whichever is larger.

Acknowledgements

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