

A Flow Micro Reaction Calorimeter

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A flow micro reaction calorimeter has been designed and tested. The construction is a twin heat conduction calorimeter. Heat evolved in a flow reaction cell is conducted to a surrounding heat sink through a semiconductor thermopile. Electrical calibration experiments indicate the precision at steady state conditions to be 0.1% if the heat effect is $> 100 \mu\text{cal/sec}$. Heat effect sensitivity is approximately $0.1 \mu\text{cal/sec}$. Test experiments involving mixing efficiency in a flow cell and heat of dilution of urea and sucrose solutions are reported and discussed. A comparison is made between the properties for the present flow calorimeter and those for the batch calorimeter on which design it is based.

Flow reaction calorimetry has several advantages over a batch calorimetric method. The operation at a calorimetric experiment can be made exceedingly simple and equilibration time prior to the experiment can be omitted. Mixing of reactants can be achieved without the presence of a gaseous phase which is of great importance when experiments are performed with volatile liquids and in micro-calorimetric experiments where very small condensation-evaporation effects may affect the result. Surface adsorption effects which may cause serious systematic errors in micro calorimetry can be neglected if a steady liquid flow is allowed to continue until possible wall reactions have occurred.

Recently a precise micro reaction calorimeter based on the heat conduction principle was reported.¹ The reactants were contained in a mixing vessel of two compartments and the reaction was started by rotation of the calorimeter block. In this paper is described the design of a liquid flow calorimeter which is based on the same principle as the earlier reported batch calorimeter.

Several liquid flow calorimeters have been reported. They were designed primarily for studies of reaction rates² or enthalpy titration (see, *e.g.*, Refs. 3, 4). Flow reaction calorimeters have also been reported.^{5,6} The calorimeter

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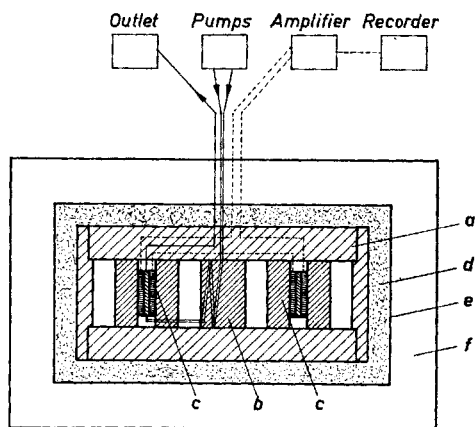


Fig. 1. Principal arrangement of the calorimeter.

described by Stoesser and Gill⁶ is, similar to the present construction, a micro calorimeter designed for precise work.

GENERAL DESCRIPTION OF THE APPARATUS

The arrangement of the apparatus is shown in Fig. 1. A metal block heat sink, *a*, contains a centrally located heat exchange unit, *b*, surrounded by calorimetric units, *c*, in a twin arrangement. The calorimetric units consist of flow reaction cells surrounded by surface thermopiles which are in contact with primary heat sinks. The heat sink is thermally insulated and immersed in a thermostated water bath. The calorimetric liquids are pumped through the heat exchange unit to one of the reaction cells and from there to a receiver outside the calorimetric system.

The voltage signal recorded at an experiment is the differential signal from the two thermopiles and external thermal disturbances are therefore largely expected to cancel. Liquid flows only through one cell during an experiment and a correction is applied for zero effects arising from liquid flow.

CALORIMETRIC PRINCIPLE

Two calorimetric liquids are brought together in a mixing zone of the flow cell. A constant flow rate will give rise to a constant heat effect in the calorimetric cell. If this heat effect is allowed to continue long enough steady state conditions will be established, *i.e.* heat generated in the cell will per unit time be equal to the heat transported out from the cell. Utilization of steady state conditions is the most accurate method of operating the present calorimeter and is the principle which will be discussed here.

A major part of the heat effect generated in the cell (W) will at steady state be transported from the cell by heat conduction through the surrounding thermopile (W_t), and to a minor extent will be lost through the air gap between

parts of the flow cell surface not in contact with the thermopile. A small fraction of the total heat effect generated will also leave the cell by the liquid flow.

It may be expected that for a given calorimeter and for stated values for flow rate, reaction rate and physical properties of the calorimetric liquid the fraction W_t/W will be constant

$$W = \alpha \cdot W_t \quad (1)$$

The transversal temperature gradient at various parts of the thermopile is expected to be proportional both to the heat flow and to the voltage generated. Integration over the total thermopile area will lead to the expression

$$W_t = \beta \cdot V \quad (2)$$

where β is a constant and V is the thermopile voltage.

Combination of (1) and (2) will lead to

$$W = \alpha \cdot \beta V = \varepsilon \cdot V \quad (3)$$

At an experiment a small fraction of the heat effect generated in the cell is a consequence of the flow of liquid through the cell such as heat of friction etc. The contribution to the thermopile signal from this latter heat effect may be determined at separate zero experiments. If this thermopile value is taken as the reference point for the thermopile voltage at the main experiment then

$$W_p = \varepsilon \cdot V_p \quad (4)$$

where W_p is the heat effect connected with the process occurring in the flow cell and V_p is the displacement of the thermopile voltage value from the determined baseline. The constant ε is determined by electrical calibration.

CONSTRUCTION DETAILS

Main heat sink. The main heat sink, *a*, Fig. 1, is similar to that which was described earlier for the batch calorimeter.¹ It is an aluminium cylinder of two parts, diameter 150 mm and length 200 mm. The cylinder has a central 75 mm bore and is fitted with 10 mm end walls. In the bore is contained the heat exchange unit, *b*, and the calorimetric units, *c*.

The aluminium cylinder is covered by a 20 mm layer of polystyrene foam, *d*, and the construction is surrounded by a cylindrical stainless steel jacket, *e*, with a lid fitted with an O-ring gasket. The jacket rests horizontally on a support in a thermostated water bath, *f*, which has a temperature fluctuation of about 0.005°C. Electrical leads and tubings for the calorimetric liquid are taken from the jacket through the bath by a 10 mm steel tube.

Heat exchange unit. The heat exchange unit, *b*, consists of 0.6 mm (*i.d.*) gold tubes which are bedded by tin in a 75 mm brass bolt. In the present construction the gold tubes are about 500 mm long. An established thermopile signal was not affected by a 25°C change in temperature of water pumped into the calorimeter at a rate of 0.17 ml/min.

Calorimetric units. The calorimetric units, *c*, have a similar sandwich type construction as was used in the batch calorimeter.¹ The flow cell which has the external shape of a squared plate is in good thermal contact with the thermocouple plates positioned on either side. These consist of commercially available thermoelectric coolers (Thermoelectric Modulus 3951-1, Cambion, Cambridge, Mass.). Electrical leads from the two thermocouple plates are connected in series. The external surfaces of the thermocouple

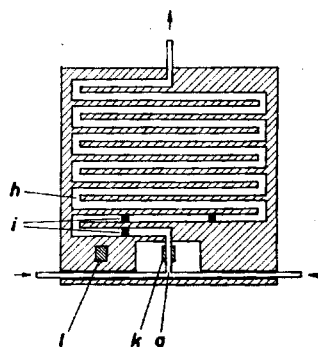


Fig. 2. Section through the flow cell.

plates are in thermal contact with aluminium bolts (75 mm in diameter, 25 mm thickness) acting as primary heat sinks. The calorimetric unit is joined together by three 6 mm screwbolts.

Flow cells. During the course of this work several flow cells of different design were tested. Part of the experience gained will be referred to in a later section of this paper. Here will be described that version which was finally adopted for fast reactions and which was used for the test experiments reported.

A section through the cell is shown in Fig. 2. The cell consists of a flat squared metal plate housing a T-piece, *g*, which leads to a channel system, *h*, milled out from the surface of the plate. The open channel is covered by a lid (a 0.6 mm plate) and the construction is sealed with epoxy resin (Araldite AY103). Between the plate and its channel system and the lid there is positioned a 0.05 mm 24 K gold foil acting as a gasket. The construction material for the plate and the lid is pure silver but all surfaces in contact with the calorimetric liquid are gold plated.

The two incoming streams of liquid are brought together in a gold T-piece positioned in a hole in the cell plate. A gold tube carries the liquid flow to the channel, where, in the mixing zone, three constrictions, *i*, are arranged to ensure complete mixing of the reactants. Each constriction is a plastic plug (Delrin) punctured to form a small hole. The inner dimension of the gold tubes forming the T-piece is 0.6 mm. The channel has a squared section, 1.5×1.5 mm, and the constriction holes are about 0.2 mm.

A 30 ohm calibration heater, *k*, made from insulated manganine wire is wound on the gold tube between the T-junction and the channel. The heater was insulated by an air gap from the body of the flow cell and most of the heat evolved is therefore taken up by the liquid flow close to a position where heat is evolved in a reaction experiment.

For comparison purposes a second heater is positioned at *l*. This heater was in good thermal contact with the body of the flow cell and its lid.

With this cell design and the combined heat capacity of the thermopile, 15 min was required to reach a steady state and at normal flow rates this represented 1–1.5 ml of each reactant.

Pumps. The liquids were pumped through the flow cells by means of peristaltic pumps (Perpex). These pumps were found to give a very stable long time flow rate which was not affected by a moderate change in back pressure. During a 48 h pumping period the flow rate change was usually $\leq 0.1\%$.

Connecting tubes. In the present work where only aqueous solutions are investigated soft PVC tubings (1 mm i.d.) were used as connections between pumps, heat exchange unit, flow cell and collection vessel.

Detection and recording of thermopile signal. The differential voltage from the thermopile in the two calorimetric units was amplified by a Keithley 150 B Microvolt Ammeter. The amplified signal was recorded with a Sargent SR recorder. At a low signal level the chart readability was increased by use of a ball and disc integrator.

Electrical calibration circuit. A conventional electrical calibration circuit similar to that described in Ref. 1 was used.

ELECTRICAL CALIBRATION EXPERIMENTS

Position of the calibration heater. Heat evolution at a calibration procedure and at a process under investigation must be closely comparable. It is therefore essential that the position of the calibration heater is such that a certain electrical heat effect will give rise to the same thermocouple signal as an identical heat effect from a process in the flow cell. The following series of experiments were undertaken to demonstrate the properties of the present calorimeter in this respect. Electrical calibrations were performed using the regular heater (k in Fig. 2) and the other heater position at l . The position of the regular heater is such that essentially all the heat evolved will be taken up by the liquid at a position where a substantial part of the heat will be evolved in a reaction experiment. Heat evolved in the heater position at l , however, will be directly transferred to the silver body of the flow cell and from there conducted out to various parts of the cell. Electrical heat effects were similar and flow rates were the same for the two series of experiments. The calibration constant, ε , is given in arbitrary units ($\mu\text{cal}/\text{sec}$ -recorder response).

Results of these experiments are summarized in Table 1. It is seen that there is only a small difference (0.4 %) in the calibration constants obtained with the two heaters. It may thus be concluded that for the present calorimeter it is not very critical at what part of the mixing zone the heat is evolved and, therefore, the heater position should be adequate. Further, it may be assumed that the ε -value should not be sensitive to variations in rate of reaction or rate of mixing as long as the process takes place reasonably close to the calibration heater *i.e.* in the mixing zone of the flow cell.

Precision and sensitivity of the calorimeter. From results of repeated calibration experiments it can be concluded that a heat effect measurement under

Table 1. Calibration constants, ε , determined with the regular heater and the heater at l . Total flow rate was 0.182 ml/min.

Heater	Heat effect, $\mu\text{cal}/\text{sec}$	ε
Regular heater	331.0	1.874
	331.2	1.875
	330.8	1.878
	330.9	1.877
	331.0	1.872
	330.6	1.878
		Mean = 1.876 \pm 0.002
Bedded heater	259.6	1.884
	259.6	1.885
	259.4	1.885
	259.5	1.883
	259.6	1.882
	259.3	1.881
	Mean = 1.883 \pm 0.002	

Table 2. Calibration constant, ϵ , at different electrical heat effects. Total flow rate was 0.163 ml/min.

Heat effect, $\mu\text{cal/sec}$	ϵ
88.5	1.879
136.6	1.856
157.4	1.863
241.3	1.870
307.2	1.862
372.9	1.866
	Mean = 1.866 ± 0.003

suitable condition can be made with a precision of 0.1 % at a heat effect of 100 $\mu\text{cal/sec}$ (cf. Table 1) and about 1 % if the heat effect is in the order of 10 $\mu\text{cal/sec}$. A heat effect sensitivity value of 0.1 $\mu\text{cal/sec}$ was evaluated from the stability of the voltage-time curve.

The stability of a steady state value during a 12 h period was usually better than 1 $\mu\text{cal/sec}$.

Calibration constant at different electrical heat effects. Eqn. 4 requires that the calibration constant ϵ is a constant which is not affected by a variation in W_p . In a series of calibration experiments the electrical heat effect was varied whereas other experimental parameters were kept constant. Results are summarized in Table 2 from where it is seen that there is no systematic variation in the ϵ -value with the heat effect. The standard deviation of the mean (± 0.2 %) is well within the expected amplification and recording errors.

Variation in calibration constant with flow rate. In Fig. 3 results are summarized from electrical calibration experiments performed with a constant electrical heat effect but with different flow rates. It is seen that the difference in calibration constant from zero flow rate to a normal total flow rate (about 0.17 ml/min) is less than 3 %. At zero flow rate no heat is transported out

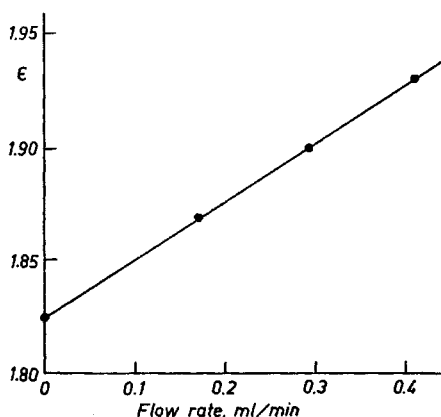


Fig. 3. Variation in calibration constant (ϵ) with flow rate.

from the cell by the liquid flow and $W=W_1$. From the present results it may be concluded that under normal operational conditions 97 % of heat evolved in the flow cell will pass through the thermopile.

ZERO EFFECTS

Heat effect generated by a process under steady state conditions is calculated through eqn. (4), $W_p = \epsilon \cdot V_p$. Here V_p is the displacement of the thermopile signal from a certain voltage base line to the recorded steady state value. The base line value will vary slightly with the experimental conditions and the following experiments were made to get these variations somewhat explored. The zero effect may be expressed in terms of a heat effect, W'

$$W' = \epsilon(V' - V_0) \quad (5)$$

where V_0 is the thermopile voltage under apparent equilibrium conditions for the calorimeter and when the flow rate was zero. V' is the thermopile voltage (the "base line value") at the specified liquid flow. V_0 is usually not zero even after a very long equilibration time for the calorimeter. In the present case V_0 was about 1 μ volt.

In eqn. (5) ϵ is assumed to be identical with that determined at electrical calibration experiments although the correct ϵ -value for this case might be slightly different.

Zero effect at different flow rates. In Fig. 4 W' is given as a function of total flow rate. The flow was equal in both arms and the liquid was pure water. It is notable that the zero effect is increasingly negative at flow rates up to 0.15 ml/min after which the curve will turn in a positive direction and the W' value will be quite sensitive to variations in the flow rate.

Variation in zero effect with the viscosity of the calorimetric liquid. Fig. 5 shows the variation in the zero effect when at a constant flow rate the calorimet-

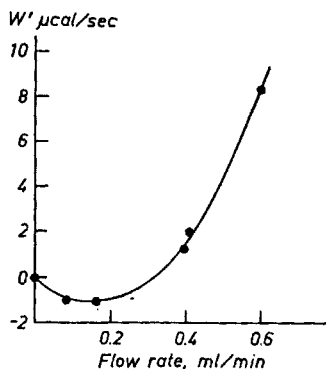


Fig. 4. Zero effect (W') as a function of flow rate.

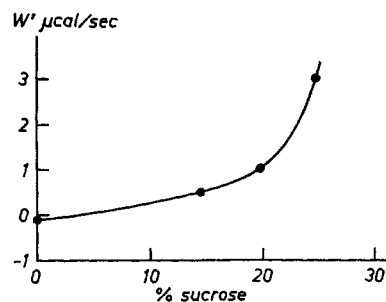


Fig. 5. Zero effect (W') as a function of increasing viscosity of the calorimetric liquid. Solutions of sucrose were pumped through both arms with a total flow rate of 0.165 ml/min.

ric liquid changes viscosity.* Pure water and solutions containing different amounts of sucrose, respectively, were pumped through both of the arms with a total flow rate of 0.165 ml/min. The figure shows that for this particular flow rate the base line value becomes less negative and then positive as the viscosity increases but that the change is small.

From Figs. 4 and 5 it is evident that variation in zero effect with liquid flow rate and liquid viscosity should be considered when small heat effects are measured. The variation expressed as a heat effect, however, is very small and no significant systematic error will arise if the base line value is determined under conditions (flow rate, viscosity *etc.*) reasonably similar to those in the main experiment.

MIXING EFFICIENCY IN THE FLOW CELL

The mixing efficiency is of critical importance at a reaction or dilution experiment in flow calorimetry. During the course of this work several designs of mixing cells were tested and found to be inadequate at experiments where a complete mixing was required.

As a sensitive test for the mixing efficiency "titration curves" for HCl—NaOH solutions were determined. Through one of the arms in the flow cell NaOH solutions of different concentrations were pumped whereas the concentration of the HCl solution through the other arm was kept constant (0.005 or 0.01 M). Changes in heat effect from dilution and mixing of ionic species can be neglected in the investigated concentration ranges. Ideally one would expect a constant heat effect value as long as NaOH is in excess and from the equivalence point the heat effect should decrease linearly to zero as the NaOH concentration approaches zero. Within limits of error the ideal "titration curve" was obtained with the final cell construction.

The first cell investigated had a gold T-piece and a heater applied as in the final design, Fig. 2. The combined flow was taken through a straight gold tube (0.6 mm i.d.) bedded by Woods metal in a copper plate which formed the body of the cell. Mixing in this cell was very poor. In a titration experiment the heat effect did not approach a constant value until the calculated equivalence point had been exceeded by more than a ten fold excess of NaOH.

In another construction a 0.08 ml mixing reservoir was inserted between the T-junction and the gold tube bedded in the copper plate. The mixing efficiency was increased but not sufficiently as shown by the fact that there was required a two fold excess of NaOH to reach the horizontal part of the titration curve. The design of this cell was modified in different ways, *e.g.* inserting constrictions in the mixing reservoir (cell C). These changes resulted in an improved performance which, however, was not very dependable. It was shown that air bubbles entering the flow system were easily trapped in the reservoir and caused a large decrease in the mixing efficiency.

* Constrictions in the flow cell were not identical with those described in the preceding paragraphs.

Model studies which led to the final design of the flow cell showed that for water at room temperature cross section of tubes or channels used in the present type of cell construction should be ≤ 1.5 mm if air bubbles should not be trapped.

HEATS OF DILUTION OF UREA AND SUCROSE

The neutralization experiments referred to above are not suitable as accurate tests for the absolute value of the heat effect measured with the calorimeter. For that purpose it would be necessary to take rigorous and experimentally difficult precautions to avoid CO_2 interference.

More convenient test reactions for a check of the absolute value are provided by dilution experiments involving, *e.g.*, urea and sucrose. One may note, however, that a successive heat of dilution of a compound usually will result in smaller and smaller heat effects. One can therefore expect to obtain an essentially correct heat of dilution value even if the mixing has not been quite perfect. For one of the earlier flow cells tested during this work (cell C) good heat of dilution values were obtained for urea although it was shown by acid base titration experiments that mixing was not adequate.

Urea solutions suitable for dilution experiments with the present calorimeter can be rather dilute and have a low viscosity. They are therefore comparatively easily mixed with water in a flow cell. Sucrose forms a nearly perfect aqueous solution and heats of dilution are therefore very small. In order to get a reasonable heat effect in a dilution experiment it is necessary to use rather concentrated solutions. Such solutions are quite viscous and are not very easily mixed with water in a flow cell without the use of a mechanical stirrer or a similar device. Experiments with flow cell C resulted in very low values for dilution of a 1 molal sugar solution with an equal volume of water (55 % of the calculated value).

In Tables 3 and 4 results are summarized from dilution experiments with urea and sucrose solutions using the final design of flow cell.

In the experiments Mallinckrodt A.R. urea was used without further purification. Sucrose used was a standard sample (≥ 99.95 % purity) kindly supplied by Dr. Tjebbes at Swedish Sugar Corporation, Arlööv. Solutions were freshly prepared before the experiments. Changes in model concentration

Table 3. Heat of dilution of aqueous urea solutions at 25.00°C.

Initial	Molality		Heat effect $\mu\text{cal/sec}$	ΔH cal/mole		$\frac{\Delta H_{\text{exp}}}{\Delta H_{\text{calc}}} \times 100$
	Final			Experimental	Calculated	
0.916	0.447		40.38	36.54	36.34	100.6
1.053	0.512		52.16	41.31	41.28	100.1
1.279	0.619		74.68	49.16	49.10	100.1
1.456	0.700		94.29	55.28	55.15	100.2
1.659	0.806		119.49	61.60	60.78	101.3
1.957	0.933		158.70	70.25	70.64	99.4

Table 4. Heat of dilution of aqueous sucrose solutions at 25.00°C.

Initial	Molality		Heat effect $\mu\text{cal}/\text{sec}$	$-\Delta H$ cal/mole		$\frac{\Delta H_{\text{exp}}}{\Delta H_{\text{calc}}} \times 100$
	Final			Experimental	Calculated	
0.516	0.250		22.45	34.49	34.37	100.3
0.731	0.347		43.22	48.81	48.77	100.1
0.752	0.375		41.45	47.40	47.75	99.3
1.252	0.598		106.42	79.70	79.50	100.3

were calculated from measured volume/time flow rates and known densities for solutions of urea,⁷ and sucrose,⁸ respectively.

The obtained heat of dilution values are compared with data calculated from the expressions given by Gucker *et al.* for the apparent heat content of urea⁹ and sucrose¹⁰ in aqueous solution. All experiments were made at 25.00°C.

From the tables it is seen that in all cases there is a good agreement between determined and calculated values. The differences, usually less than 1 %, are judged to be well within the combined limits of uncertainty. Recently¹ the heat of dilution of a 0.2 molal sucrose solution with twice the amount of water was determined with the aforementioned batch micro calorimeter and found to be 1.4 % higher than the calculated values. With the same batch calorimeter the heat of dilution of a 1.05 molal urea solution with twice the amount of water has been determined and was found to agree within 0.2 % with the calculated value. Stoesser and Gill recently reported⁶ a value 3 % lower than the calculated value* for the dilution of a 1 molal urea solution with an equal volume of water.

COMPARISON BETWEEN THE BATCH AND THE FLOW MICRO CALORIMETER

The present flow calorimeter is based upon the design of the earlier reported batch micro calorimeter. Some concluding remarks where the two calorimeters are compared will be given here.

Operational procedure. The experimental procedure with the batch calorimeter is very simple. The present flow method, however, is by principle completely automatic and does not require any equilibration time. The flow method will therefore offer distinct advantages in particular if the calorimeter is used for extensive series of measurements or if it is used as an analytical tool.¹¹

Sensitivity and accuracy. The sensitivity in terms of thermopile voltage at a given heat effect is essentially the same for the two constructions. The batch calorimeter will in practice be a more sensitive instrument as heat from the combination of about 5 ml of calorimetric liquids is evolved as a

* A calculation error appears in Ref. 6. The value calculated from the data by Gucker *et al.*⁹ for the process referred to in Ref. 6 should be 3.74 mcal.

pulse (for a fast process). In the flow version corresponding heat is continuously evolved during about half an hour.

It is judged that the present flow method can be developed to give a considerably higher sensitivity whereas for the batch version possible systematic errors¹ might make an increased sensitivity of little practical value.

Reaction time. The batch calorimeter is suitable for reactions ranging from instantaneous processes to reactions with a duration of several hours. For the flow calorimeter it is for a normal operational procedure required that heat should be evolved in the mixing zone, *i.e.* the reaction time should be short compared to the retention time for the liquid in the flow cell. For the present flow cell and with a normal flow rate the retention time is about 5 min. It is considered that any reaction shorter than 1 min is suitable for precise measurements. For slow reactions it is possible to perform "stopped flow" experiments where a pulse of the calorimetric liquids is pumped into the flow cell in which the reaction mixture is kept until all the heat is given off. However, the batch calorimeter will give considerably more precise results than a stopped flow experiment.

The flow method will offer great advantages compared to the batch procedure when steady state reactions, like enzymatic processes with substrate saturated enzyme, are studied. This is in particular apparent when the calorimeter is used as an analytical instrument.¹¹

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