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DETERMINATION OF REACTION RATE PARAMETERS USING HEAT CONDUCTION MICROCALORIMETRY

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By using the LKB 2277 thermal activity monitor, it is demonstrated that both ampoule and flow-through modes can be used to monitor the reaction parameters for chemical reactions. Theoretical relationships applicable to first-order reactions are proposed and compared with those reported in the literature. Mathematical relationships applicable to second-order reactions are also proposed. The experimental results confirmed the validity of the theoretical relationships and showed that flow microcalorimetry is a rapid technique in kinetic studies.

The fact that heat is often involved in chemical processes makes microcalorimetry an attractive technique in determining both the thermodynamic and the kinetic parameters of a wide variety of chemical reactions.

In earlier work, a theoretical relationship was reported between the thermal power output of a microcalorimeter and the enthalpy (ΔH), the rate constant (k) and the initial concentration of a reactant under study for zero and first-order reactions in both the flow-through and the mixing mode [1, 2]. Later, Johnson and Biltonen could determine under restricted conditions the second-order rate constant for the basic hydrolysis of ethyl acetate using the mixing mode [2, 3].

In this paper we report on the possibility of using both the ampoule and the flow-through device to monitor reaction parameters (ΔH and k) for reactions of which the half-lives are of the order of minutes. Theoretical relationships applicable to first-order reactions are proposed and compared with those reported in the literature [2].

We also derived theoretical equations for second-order reactions studied in the ampoule and the flow-through device, which could be applied in pharmaceutical research where the determination of reaction rate parameters is routine work which provides valuable information about the stability of pharmaceutical formulations.

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Material and methods

Commercial available acetates, HCl and NaOH of analytical grade were used without any further purification. Solutions were made in CO_2-free distilled water and were used within 24 hours. The LKB 2277 Thermal Activity Monitor (TAM) microcalorimeter [4] was used. The ampoule device, the flow-through device and the titration ampoule v [5] were used in this study. The calibration of the instrument was carried out electrically and all experiments were performed at 298 K. The calorimetric thermal power output was dynamically corrected (cf. e.g. [6]).

Suppose that a reaction proceeds in a solution of volume v inside a heat flow calorimeter. The enthalpy per mol of product X formed is given by ΔH. The total amount of heat Q evolved when x mol of product has been formed is then given by $Q = \Delta H x = \Delta H v\,[X]$, where $[X]$ is the concentration of the product formed in the reacting solution.

The value measured is actually the thermal power:

$$P = \mathrm{d}Q/\mathrm{d}t \text{ or } P = \Delta H\, v\, \mathrm{d}\,[X]/\,\mathrm{d}t \qquad (1)$$

First-order reactions

When a first-order reaction $A \rightarrow X$ is taking place in an ampoule placed inside the microcalorimeter, the change in product concentration is given by:

$$\mathrm{d}\,[X]/\mathrm{d}t = k_1\,[A]_t = k_1 [A]_o \exp(-k_1 t) \qquad (2)$$

where $[A]_o$ and $[A]_t$ are, respectively, the initial concentration and the concentration at time t of component A; k_1 is the first-order rate constant. By substitution of (2) into (1), the thermal power obtained is then:

$$P = \Delta H . v . k_1 [A]_o . \exp(-k_1 t) \qquad (3)$$

From this non-linear relation between the thermal power P and the time, both ΔH and k_1 can be derived from the calorimetric data, provided v and $[A]_o$ are known.

Equation (3) also holds for a reacting solution placed outside the microcalorimeter and continuously pumped through the calorimetric cell: v is then the volume of the solution being measured.

Second-order reactions

In the case $A + B \rightarrow X$, the relation between the change in the concentration of product X with time is:

$$\mathrm{d}[X]/\mathrm{d}t = k_2 [A]_t [B]_t = k_2([A]_o - [X])([B]_o - [X]);$$

$$\text{when } [A]_o = [B]_o, \text{ then } \mathrm{d}[X]/\mathrm{d}t = k_2([A]_o - [X])^2 .$$

The solution of this differential equation is:

$$[X] = \frac{([A]_o)^2 k_2 t}{1 + [A]_o k_2 t}$$

The first derivative of such an equation is given by:

$$\mathrm{d}[X]/\mathrm{d}t = \frac{[A]_o{}^2 k_2}{[1 + [A]_o k_2 t]^2} \tag{4}$$

By substitution of (4) into (1):

$$P = \frac{\Delta H \, v([A]_o)^2 k_2}{[1 + [A]_o k_2 t]^2} \tag{5}$$

k_2 and ΔH can be derived from the calorimetric data. When $[A]_o \neq [B]_o$, the following relation between P and t can be derived:

$$P = \frac{\Delta H \, v \, ([B]_o - [A]_o)^2 k_2 [B]_o/[A]_o \exp \, ([B]_o - [A]_o k_2 t}{[\, [B]_o/[A]_o \exp \, [([B]_o - [A]_o)k_2 t] - 1 \,]^2} \tag{6}$$

Here again, k_2 and ΔH can be obtained providing $[A]_o$ and $[B]_o$ are known. This shows that second-order reactions can be studied using a flow microcalorimeter.

Comparison of equation (3) with equations reported earlier

In earlier work [2], the relation between the thermal power and time for first-order reactions studied in the flow-through device was derived from the equation obtained using the flow mix mode [1]. This relation was reported to be:

$$P_t = R[A]_o\ \Delta H(1\text{-}\exp k_1 \tau)\exp\text{-}k_1 t \qquad (7)$$

where R is the flow-rate of the reacting solution and τ is the residence time of the reacting solution in the measuring cell.

In the same report, Eq. (3) (with a negative sign) was derived from Eq. (7) as its approximation valid only when $k\tau$ was very small.

Rather high flow rates (about 5.5 μl/s) were used with a view to decreasing the residence time τ and making possible the study of reactions with rate constants of about $10^{-4}\mathrm{s}^{-1}$.

According to the mentioned report, Eq. (7) should be used for fast reactions. However, the presence of the factor R, which can not influence the thermal power when the flow-through device is used, made this equation doubtful. As demonstrated above, Eq. (3) is not an approximation. The deviation in the value of ΔH can be very high when Eq. (7) is used. For a flow rate of 3 ml/s, this deviation reaches 9% for a reaction with $k_1 = 10^{-3}\mathrm{s}^{-1}$, and more than 50% for a reaction with $k_1 = 10^{-2}\mathrm{s}^{-1}$.

Results and discussion

The acid hydrolysis of methyl acetate in hydrochloric acid has been carried out in the ampoule and the flow-through device.

One mmol of methyl acetate was added to 2 ml hydrochloric acid solution in a glass ampoule placed in the measuring position in the TAM. The thermal power curve shifted to a maximum value and decreased exponentially with time to its initial position.

In the flow-through mode, the base line was obtained by flowing the hydrochloric acid solution into the flow-through cell at a constant flow rate R. When a stable base line was obtained, the ester was added to reach a concentration of 0.05 M in the reaction vessel. In order to get the reacting solution into the cell before completion of the reaction, the flow rate was increased up to 8 μl/s, so that the reacting solution reached and filled the measuring cell within about 60 s. The flow was then lowered down again to R. The thermal power curve shifted to a maximum and decreased exponentially with time to its initial value.

These experiments were carried out in 1 N and 4 N HCl; R ranged form 0.1 to 9 μl/s.

Least squares analysis of P against t assuming first-order kinetics (Eq. 3) yielded $\Delta H = 1.98$ kJ/mol ester formed and $k = 0.116 \times 10^{-3} s^{-1}$ and $0.764 \times 10^{-3} s^{-1}$, respectively, in 1 N and 4 N HCl, with an accuracy better than 1%.

As Eq. (3) predicts, no changes in value of either ΔH or k has been observed in the range of flow rates applied. This same technique has been used successfully to study the influence of surfactants on the hydrolysis of a series of esters [7].

In order to test Eq. (5), the hydrolysis of ethyl acetate in NaOH under second-order conditions was carried out in the titration vessel as follows: 3 ml of 6 mM NaOH solution was placed in the titration vessel (under nitrogen). After thermal equilibration, the vessel was lowered down to the measuring position and, when a stable base line was obtained, 50 μl of 0.36 M ethyl acetate solution was added. Under such conditions, [ethyl acetate] = [NaOH] = 6mM. The calorimetric signal was recorded, and least squares analysis of P against t assuming second-order kinetics (Eq. (5)) yielded $\Delta H = 53.97 \pm 1.25$ kJ and $k_2 = 0.112 \pm 0.002$ 1/mol.s.

All the data obtained are in agreement with those reported in the literature [2, 3].

Conclusion

The experiments show that both first and second-order reactions can be studied by means of microcalorimetry. It has been demonstrated that the flow rate has no effect on the calculation of ΔH and k for first-order reactions, and that the relation between the thermal power and the time is given by Eq. (3). Any type of first-order reaction can then be studied by means of flow calorimetry as long as it is accompanied by a flow of heat and provided that the reacting solution reaches the calorimetric flow through the cell before completion.

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Zusammenfassung – Es wird gezeigt, dass mit dem kalorimetrischen Messgerät LKB 2277 Untersuchungen zur Bestimmung der Parameter chemischer Reaktionen sowohl in Ampullen wie auch im Durchflussbetrieb möglich sind. Theoretische Beziehungen für Reaktionen 1. Ordnung werden abgeleitet und mit solchen aus der Literatur verglichen. Vorgeschlagen werden ferner mathematische Beziehungen, die sich auf Reaktionen 2. Ordnung anwenden lassen. Die experimentellen Ergebnisse bestätigen die Gültigkeit der theoretischen Beziehungen und zeigen, dass die Durchfluss-Mikrokalorimetrie eine Schnellmethode für kinetische Untersuchungen ist.

РЕЗЮМЕ — Используя ЛКБ 2277 термомонитор, было показано, что оба метода, как ампул, так и проточный, могут быть использованы для регулирования реакционных параметров химических реакций. Предложены теоретические соотношения, применимые к реакциям первого порядка и которые сопоставлены с приведенными в литературе. Предложены также математические соотношения, применимые к реакциям второго порядка. Экспериментальные результаты подтвердили справедливость теоретических соотношений и показали, что калориметрия в потоке является быстрым метором кинетических исследований.