

Reactions in Closed Batch Reactors, Operational and Safety Issues: A Model To Predict How Degree of Filling and Rate of Heating Affect Reaction Times and Buildup of Internal Pressure

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Abstract:

The time needed to complete reactions utilizing volatile reactants in closed batch reactors may be very different, according to the degree of filling of the reactor. A model, developed to predict how time varies, is confirmed by experimental tests which allow Henry's constant for the couple reactant/solvent to be determined. A second model is developed to predict how for such processes heating rate and degree of filling of reactor affect buildup of internal pressure.

Introduction

Performing a reaction at a temperature higher than the boiling point of one of the reactants nearly always requires closed reactors to prevent its removal from the system. Even if condensers are placed in the vapour line of the reactor, it is very difficult to avoid at least some of the reactant escaping from the reaction mixture. In closed reactors, the definitions of the batch size and of the degree of filling for the reactor, as well as the rate of heating, have interesting implications dealing with reaction time, buildup of overpressure in the reactors, and ultimately safety.

As a matter of fact, a personal experience of one of us during industrial scaling-up of an alkylation of an amine with ethyl bromide showed that the rate of this reaction, performed at a temperature higher than the boiling point of ethyl bromide, was largely affected by the batch size and, ultimately, by the degree of filling of the reactor. Moreover, the degree of filling of the reactor affected the extent of the pressure buildup during the course of the process, so much so that in some cases the temperature had to be lowered to prevent blasting of burst disks. All these facts prompted us to give a deeper insight into this topic, due to its clear implications pertaining to process management and safety.

Standard chemical engineering textbooks would categorize this issue in the general case of kinetics of heterogeneous systems, namely gas/liquid systems.¹ Treatment of such cases implies the use of Henry's coefficients to define effective reaction rates which is the starting point for the model proposed in this report. While there are reports on the effect of the degree of filling on pressure–temperature phase diagrams for crystallizations of inorganic salts performed in autoclave at high pressure,² for batch processes a clear definition of the effect of the degree of filling on kinetic

parameters is not reported. A possible explanation is that reactions performed under pressure usually utilize a gaseous reactant whose pressure is maintained constant in the reaction vessel by a pressure reducer. On the contrary, the case we describe is characterized by adding a liquid reactant, closing the system, and reaching a reaction temperature where the reactant is partially in the gaseous form.

The need to operate at reduced batch size is a common situation encountered during scaling-up of batch processes. Moreover, in many cases scaling-up implies the use of batch reactors at different degrees of filling. Therefore, a study of the effect of a parameter defined as “degree of filling of the reactor” on a process may be useful. This report analyzes such cases, determining the relationship between the degree of filling of a batch reactor and the reaction time. Experimental results are provided to support the model, and an equation is derived to predict when overpressures are generated.

Partition of a Reactant between Liquid and Gaseous Phase. In a closed reactor containing a volume V_{sol} of solvent reactant A is dissolved. A reaction is performed at a temperature higher than the boiling point of A. Reagent A will cause an overpressure due to the equilibrium between A dissolved in the solvent and A in gaseous phase.

Let us suppose that A reacts only in the liquid phase, i.e., the reaction does not occur in the gaseous phase. From a kinetic point of view, this implies that the reaction rate is only a function of [A], not of the partial pressure P_A .

The volume of the reactor which is not occupied by the solution is V_{gas} .

The actual concentration of A will be less than the concentration calculated as moles A/V_{sol} , since part of A is removed into the gaseous phase.

Determining how [A] varies as a function of V_{sol} and V_{gas} permits prediction of how the degree of filling of the reactor affects the actual concentration of A in solution and, as a consequence, how it affects the time needed to complete the reaction.

Now we assume that the equilibrium between gaseous and dissolved A is attained at a rate much higher than the reaction rate. Efficient stirring of the solution should be enough to warrant this assumption.

(1) Steinbach, J. *Safety Assessment for Chemical Processes*; Wiley-VCH: Weinheim, 1999; p 79.

(2) Liebertz, J. *Chem.-Ing.-Tech.* **1969**, *41*, 12; Laudige, R. A.; Nielsen, J. W. In *Solid State Physics*; Seitz, F., Turnbull, D., Eds.; Academic Press: New York, 1961; Vol. 12, p 149–222. Kennedy, G. C. *Am. J. Sci.* **1950**, *248*, 540.

The increase of the empty volume will result in evaporation of A, thus giving a lower actual concentration of A. With an infinite empty volume, A will completely evaporate, and its actual concentration in the solution will be zero.

In a quantitative treatment the ratio between the partial pressure of A and the concentration of A in solution is a constant at a given temperature:

$$P_{A(\text{gas})}/[A] = H \quad (1)$$

or

$$[A] = P_A/H \quad (2)$$

By using the approximation for ideal gases, the partial pressure P_A is defined as:

$$P_A = (n_{\text{gas}}RT)/V_{\text{gas}} \quad (3)$$

where n_{gas} are the moles of A which instant-by-instant enter the gaseous phase.

Combining eq 3 with eq 2 gives:

$$[A] = \frac{n_{\text{gas}}RT}{HV_{\text{gas}}} \quad (4)$$

A mass balance must be considered:

$$n_{\text{gas}} + n_{\text{sol}} = n_{\text{tot}} \quad \text{or} \quad n_{\text{gas}} = n_{\text{tot}} - n_{\text{sol}} \quad (5)$$

where n_{tot} are the moles of A loaded into the reactor and n_{sol} are the moles of A remaining at any given point in time in the solution.

Since the concentration of A is defined as:

$$[A] = n_{\text{sol}}/V_{\text{sol}} \quad \text{or} \quad n_{\text{sol}} = [A]V_{\text{sol}}$$

eq 5 turns into:

$$n_{\text{gas}} = n_{\text{tot}} - [A]V_{\text{sol}} \quad (6)$$

Combining eq 6 with eq 4 gives:

$$[A] = \frac{(n_{\text{tot}} - [A]V_{\text{sol}})RT}{HV_{\text{gas}}} \quad (7)$$

Rearranging eq 7 gives:

$$[A] = \frac{n_{\text{tot}}RT}{HV_{\text{gas}}} - \frac{[A]V_{\text{sol}}RT}{HV_{\text{gas}}}$$

$$[A] \left\{ 1 + \frac{V_{\text{sol}}RT}{HV_{\text{gas}}} \right\} = \frac{n_{\text{tot}}RT}{HV_{\text{gas}}}$$

$$[A] \frac{HV_{\text{gas}} + V_{\text{sol}}RT}{HV_{\text{gas}}} = \frac{n_{\text{tot}}RT}{HV_{\text{gas}}}$$

and finally:

$$[A] = \frac{n_{\text{tot}}RT}{HV_{\text{gas}} + V_{\text{sol}}RT} \quad (8)$$

This solution defines the actual concentration of A into the solution.

Equation 8 can be modified introducing the following definitions:

$$V_{\text{gas}} = \alpha V_{\text{tot}} \quad (9)$$

$$V_{\text{sol}} = (1 - \alpha)V_{\text{tot}} = \zeta V_{\text{tot}} \quad (10)$$

where V_{tot} is the total available volume of the reactor, i.e., the sum of its filled and empty volumes. ζ is the degree of filling of the reactor.

When definitions 9 and 10 are inserted in eq 8, the following equation is obtained:

$$[A] = \frac{n_{\text{tot}}RT}{H\alpha V_{\text{tot}} + RTV_{\text{tot}} - \alpha RTV_{\text{tot}}}$$

and hence:

$$[A] = \frac{n_{\text{tot}}}{V_{\text{tot}}} \frac{RT}{\alpha(H - RT) + RT} = \frac{n_{\text{tot}}}{V_{\text{tot}}} \frac{RT}{\alpha H + \zeta RT} \quad (11)$$

This equation is verified for two limit cases.

For $\zeta = 1$ ($\alpha = 0$), i.e., when the reactor is completely full, eq 11 is simplified as:

$$[A] = n_{\text{tot}}/V_{\text{tot}}$$

which corresponds to the definition of concentration, since no portion of A can escape from the solvent.

For $H = 0$, i.e., when A is not volatile and, as a consequence, cannot escape into the gaseous phase, eq 11 turns into:

$$[A] = \frac{n_{\text{tot}}RT}{V_{\text{tot}}(1 - \alpha)RT} = \frac{n_{\text{tot}}}{V_{\text{tot}}\zeta} = \frac{n_{\text{tot}}}{V_{\text{tot}}}$$

which is again consistent with the definition of concentration in this particular case.

Finally, eq 11 is split into two factors. In the first factor, all terms dealing with amounts of material actually utilized (moles and volumes) are collected, whereas the second factor collects physicochemical data and the degree of filling of the reactor.

A Kinetic Model Correlating Degree of Filling and Reaction Rate. Equation 11 describes how the degree of filling of the reactor affects the reaction rate at a given temperature. The reaction rate can be presumed to depend on the partition constant H . If H is zero or close to zero, the effect should be negligible. In other words, if reactant A is mainly in the solvent (low volatility) its concentration should be almost the same as the concentration obtained when the reaction mixture has been prepared at a temperature lower than the boiling point of A, whatever the degree of filling of the reactor might be.

As the value of H approaches RT , the effect on reactivity should become sensitive: for instance, if one-third of the reactor is used, $[A]$ should be around one-third of the concentration calculated below the boiling point; use of one-fourth of the reactor should lead to a $[A]$ value which should be one-fourth of the concentration calculated under the boiling point and so on.

As a first attempt to determine how reaction rate is affected by the degree of filling of the reactor, we can assume an ideal case where reaction is performed at temperature T , higher than the boiling point of reagent A, an oversimplification since an industrial operation usually involves mixing of solvent and of reactants at a temperature lower than the boiling point of any of these. The process temperature T is usually reached by subsequent heating of the mixture.

Herein we report a model describing the influence on reactivity and internal overpressure of the heating from the mixing temperature up to the prescribed process temperature to outline how reactivity and internal overpressure are affected by heating rate and the degree of filling of the reactor. A simple model is described, which is ideally more similar to a classical kinetic laboratory experiment than to an industrial operation. The model estimates the reaction time as a function of the degree of filling of a batch reactor, and of the partition coefficient of a low-boiling reactant between the liquid and the gaseous phase.

If n_{tot} moles of A are put in solution, a volume V_{sol} is obtained. Moreover, we assume to have an ideal, very rapid heating so that the maintenance temperature T is attained instantaneously with T greater than the boiling point of A.

Finally, we assume samples of the reaction mixture are taken after its successive ideal instantaneous cooling and during each of these operations all of A which was in the gaseous phase is absorbed into the liquid phase. An ideal instantaneous heating back to maintenance temperature T after each sampling is also assumed. These assumptions are made to follow the kinetics of the reaction by expressing reaction rate as a function of the overall concentration of A, including the part of A that is actually removed by evaporation during the reaction.

These assumptions are not necessary if the reaction kinetics are monitored by following the increasing concentration of product Z as a function of time, provided that this is not volatile at temperature T .

Analysis of A, at different sampling times, should show a kinetic behaviour depending on the degree of filling of the reactor.

When V_{sol} corresponds to V_{tot} , a first-order kinetic relationship is obtained:

$$v = -\frac{d[A]}{dt} = \frac{d[Z]}{dt} = k_1[A] \quad (12)$$

where $[A]$, instant-by-instant, is not affected by evaporation of reactant A (eq 11, case $\alpha = 0$, $\zeta = 1$).

However, if the reactor is only partially filled with the liquid phase, the concentration of A in the solvent will be variable instant by instant as eq 11 predicts.

Equation 11 can be modified by taking into account the fact that n_{tot} is changing instant-by-instant due to reaction; therefore, n_{tot} can be defined as

$$n_{\text{tot}} = [A]'V_{\text{sol}} \quad (13)$$

where $[A]'$ is defined as the value that $[A]$ would have after cooling the reaction mixture instantaneously under the boiling point of A. Hence, eq 11 can be written as

$$[A] = [A]'\frac{V_{\text{sol}}}{V_{\text{tot}}}\frac{RT}{\alpha(H - RT) + RT} \quad (14)$$

However, $V_{\text{sol}}/V_{\text{tot}} = (1 - \alpha) = \zeta$, and hence eq 14 is transformed into

$$[A] = [A]'\frac{\zeta RT}{\alpha H + \zeta RT} \quad (15)$$

Since this relationship is continuously valid, the reaction rate with a reactor not completely filled can be described as

$$v = k_1[A] = k[A]'\frac{\zeta RT}{\alpha H + \zeta RT} = k_1f(\alpha)[A]' \quad (16)$$

Since $f(\alpha)$ is constant when filling isothermally, it can be stated that the reaction rate will have an apparent rate constant k_1' , defined as $k_1f(\alpha)$. Hence,

$$v = -\frac{d[A]}{dt} = \frac{d[Z]}{dt} = k_1[A] = k_1'[A]' \quad (17)$$

Internal Overpressures and Reaction Rates as Functions of Degree of Filling and Heating Rates. The model previously described is mainly focused on process time, estimating how it is affected by fractional reaction volumes and assuming that the temperature of the process is attained immediately and is not variable. A second model, based on the first, concerns the overpressure generated when the reaction mixture is heated to a final temperature, a typical situation encountered in batch processes, which usually involve loading reactants and solvents at room temperature then heating the mixture to the final temperature.

First, a kinetic equation shall be derived describing how product Z is produced as a function of time in a system containing no volatile reactant when the system is heated from a starting temperature T_0 at a constant heating rate. This assumption is realistic enough to describe the usual practice with a batch reactor, when the reaction mixture is usually heated at an almost constant rate. It is also assumed that neither endothermic nor exothermic phenomena are associated with heating, so that steady heating implies a linear increase of temperature.

A second step consists of describing what happens when a volatile species A in solution is heated with the same procedure, but assuming that A does not react. A final model will be defined by combining the two equations describing these preliminary partial models.

A First Partial Model: Heating a Reaction Mixture Containing No Volatile Reactant at a Constant Heating Rate. For a first-order reaction

$$v = -\frac{d[A]}{dt} = \frac{d[Z]}{dt} = k_1[A] \quad (18)$$

Arrhenius's law predicts that the rate constant depends on the temperature according to the following equation:

$$k_1 = Q e^{-E/RT} \quad (19)$$

If temperature is raised at a constant rate $r = \Delta T/\Delta t$:

$$k_1 = Q e^{(-E/RT_0 + Rrt)} \quad (20)$$

where T_0 is the starting temperature.

Inserting eq 20 into eq 18 gives the differential equation:

$$-d[A]/dt = Q e^{(-E/RT_0 + Rrt)} [A] \quad (21)$$

Equation 21 must be integrated to express the concentration of A as a function of time. By separating variables:

$$-\frac{d[A]}{[A]} = Q e^{(-E/RT_0 + Rrt)} dt$$

which gives after integration of the left side term:

$$-\frac{d[A]}{[A]} = Q - \int e^{(-E/RT_0 + Rrt)} dt + \text{const.} \quad (22)$$

$$-\ln A = Q \int e^{(-E/RT_0 + Rrt)} dt + \text{const.} \quad (23)$$

Integration of eq 23 gives eq 24 (details available as Supporting Information), where:

$$q = \frac{E}{RT_0 + Rrt} \quad p = \frac{E}{RT_0}$$

$$\Phi(t) = \left[\frac{e^{-q}}{q} + \ln q - q + \frac{q^2}{2 \times 2!} - \frac{q^3}{3 \times 3!} + \dots - \frac{q^n}{n \times n!} \right]$$

$$\Phi(0) = \left[\frac{e^{-p}}{p} + \ln(p) - p + \frac{p^2}{2 \times 2!} - \frac{p^3}{3 \times 3!} + \dots - \frac{p^n}{n \times n!} \right]$$

$$[A] = [A]_0 e^{(-QE/Rr)(\Phi(t) - \Phi(0))} \quad (24)$$

From a numerical point of view, the series contained in eq 24 converge after some steps and the value depends on the values of parameters Q , E , T_0 , and r . Figure 1 shows a typical plot of $[A]$ against time. Here concentration $[A]$ has been calculated by truncating the series in the integral at $n = 11$. Parameters are reported in the figure, which shows how $[A]$ is changing according to an ordinary first-order kinetic reaction with the rate constant corresponding to the starting and the final temperature, respectively. The final temperature is the value reached after the time reported on the right edge of the figure, namely 299 min.

Figure 1 clearly shows that the values of $[A]$ are almost superimposed on the corresponding values of the slow reaction (at low temperature) at the beginning of the reaction, whereas they gradually diminish to the values of the fast reaction (high temperature) as the reaction goes on.

The importance of having an analytical equation describing the present model rather than a numerical approximation lies in the fact that some useful equations are derived which are no longer expressed in terms of any series.

In a similar way, for a second-order reaction in reactant A, whose integrated kinetic equation at constant temperature is

$$\frac{1}{[A]} - \frac{1}{[A]_0} = k_2 t$$

the integrated expression in a system heated at constant

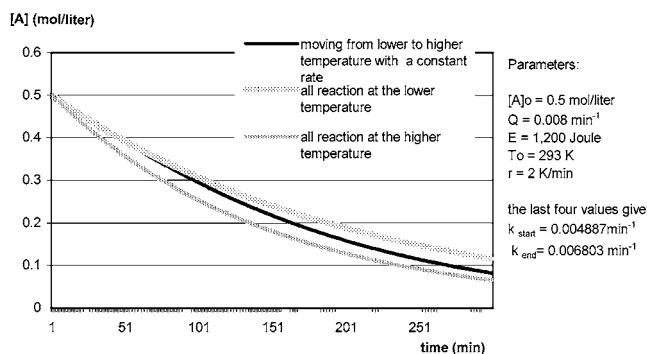


Figure 1. Numerical simulation of the concentration of substrate A in a first-order reaction at two different temperatures and at a steady heating rate from the lower temperature T_0 to the higher temperature T .

heating rate r should be:

$$\frac{1}{[A]} - \frac{1}{[A]^0} = e^{(-QE/Rr)(\Phi(t) - \Phi(0))} \quad (25)$$

A Second Partial Model: Heating a Solution of a Volatile Compound, Which Is Not Reacting, at a Constant Heating Rate. As a second step during development of the final model, let us consider a system containing the volatile species A, but under the assumption that A is not reacting.

Let us assume that the temperature increases from an initial value T_0 (higher than or equal to the boiling point of A) at a constant heating rate r and H is not changing with temperature. This appears to be an oversimplification, since it is known that H increases as T increases³ according to the relationship:

$$\frac{d(\ln H)}{d(1/T)} = \frac{\text{enthalpy of solution}}{R}$$

but as it will be demonstrated in the next headings, this assumption does not affect the conclusions that derive from the model as to the conditions that prevent any pressure buildup, even if the system is oversimplified.

Since n_{tot} does not change, the concentration of A will change according to modified eq 11:

$$[A] = \frac{n_{\text{tot}}}{V_{\text{tot}}} \frac{R(T_0 + rt)}{\alpha H + \zeta R(T_0 + rt)} \quad (26)$$

It is interesting to know the upper limit of $[A]$, and consequently of P_A , when the temperature is raised very quickly or for very long time (these terms are equivalent, since the terms r and t are interchangeable in the following steps). The value of $[A]$ can never exceed the following limit (it must be recalled that A is not reacting):

$$\lim [A]_{r \rightarrow \infty} = \lim \left[\frac{n_{\text{tot}}}{V_{\text{tot}}} \frac{R(T_0 + rt)}{\alpha H + \zeta R(T_0 + rt)} \right] \quad (27)$$

Limit 27 is calculated according to de l'Hospital's rule as:

(3) Sander, R. Compilation of Henry's Law Constants for Inorganic and Organic Species of Potential Importance in Environmental Chemistry (Version 3); <http://www.mpch-mainz.mpg.de/~sander/res/henry.html>, 1999.

$$\lim [A]_{r \rightarrow \infty} = \lim \frac{n_{\text{tot}}}{V_{\text{tot}}} \frac{1}{\zeta}$$

However, $V_{\text{tot}} \zeta$ is defined as V_{sol} ; therefore,

$$\lim [A]_{r \rightarrow \infty} = \frac{n_{\text{tot}}}{V_{\text{sol}}} \quad (28)$$

Recalling eq 1, pressure P cannot exceed the following value:

$$\lim P_{r \rightarrow \infty} = H \frac{n_{\text{tot}}}{V_{\text{sol}}} \quad (29)$$

The physical meaning of eqs 28 and 29 is that as temperature is raised the vapor pressure of A increases, so that it is increasingly dissolved into the liquid phase. A limit is reached when nearly all of A is in solution as illustrated by eq 28, whereas the pressure generated by residual A remaining in the gaseous phase should approach the limit value given by eq 29.

For each value of t , the value of $[A]$ can be referred to the starting value $[A]_0$ through a function depending on time $\Omega(t)$ defined by the following equation:

$$\Omega(t) = \frac{[A]}{[A]_0} = \frac{R(T_0 + rt)}{\alpha H + \zeta R(T_0 + rt)} \frac{\alpha H + \zeta R T_0}{R T_0} \quad (30)$$

which, rearranged, gives

$$\Omega(t) = \frac{\gamma + \beta t}{\gamma + \delta t} \quad (31)$$

where

$$\beta = \alpha H r + \zeta R r T_0 \quad \gamma = \alpha H T_0 + \zeta R T_0^2 \quad \delta = \zeta R r T_0$$

Combining the Two Partial Models: Heating a Reaction Mixture Containing a Volatile Reactant at a Constant Heating Rate. Finally, the model including the two limiting cases just discussed will be treated in such a manner that the solution containing reactant A is heated at a constant rate from a starting temperature T_0 in a closed reactor. As before to simplify the model, it is assumed that the reactive system is mixed at a temperature at or slightly below the boiling point of A, so that for all intents and purposes t_0 of the reaction can be considered equivalent to temperature T_0 , the boiling point of A.

The concentration of A in the solution will vary according to two opposite phenomena: it will either decrease due to reaction (still assumed as a first-order) or it will increase due to overpressure caused by the portion of A in gaseous phase. The equation describing $[A]$ as a function of time must include the two previously discussed cases.

An equation corresponding to these situations is defined by multiplying the kinetic eq 24 by the coefficient $\Omega(t)$:

$$[A] = [A]_0 \Omega(t) e^{(-QE/Rr)[\Phi(t) - \Phi(0)]} \quad (32)$$

Equation 32 states that the equilibrium between A in solution and A in the gaseous state is attained at a rate much faster than the rate of the chemical reaction consuming A.

The equation can be thus explained: A disappears at a rate that is determined by the kinetic behaviour described for reaction heated at constant heating rate. The instantaneous value of $[A]$ can be calculated by correcting the kinetic value, by use of the coefficient $\Omega(t)$, as previously defined, to account for the change in the distribution of A between the solution and the gaseous phase.

Equation 32 includes the two limit cases. As a matter of fact, if there is no reaction, the term $[\Phi(t) - \Phi(0)]$ is zero, and hence the term $e^{(-QE/Rr)[\Phi(t) - \Phi(0)]}$ is 1. Equation 32 is reduced to

$$[A] = [A]_0 \Omega(t) \quad (33)$$

Equation 33 is the same as eq 30, i.e., the description of change of $[A]$ as a function of time, with no reaction occurring.

When α is zero ($\zeta = 1$), $\Omega(t)$ is 1 (see eq 31). In this case, eq 32 is the same as eq 24, which simply describes changes of $[A]$ due to reaction in a system heated at constant heating rate in a completely full reactor.

By the way, it must be recalled that the gas constant R contained in the $\Omega(t)$ factor of eq 31 is 0.082 (atm L mol⁻¹ K⁻¹), whereas in the $e^{(-QE/Rr)[\Phi(t) - \Phi(0)]}$ term, it assumes the value of 8.23 (J mol⁻¹ K⁻¹).

In industrial practice, buildup of internal pressure is actually observed in some cases, when the reaction mixture is heated. Of course, when the final temperature prescribed for the process is obtained, $[A]$ decreases according to the kinetics typical of this temperature. Understanding conditions that eventually generate overpressure is the topic of next heading.

Conditions That Do Not Generate Any Overpressure.

It has been already observed that $[A]$ and P will never assume values larger than the limits described by eqs 28 and 29. However, it would be of interest to know if the system is tending toward either higher or lower values. $[A]$ and P will not increase after heating starts if the slope of the plot of $[A]$ versus time, calculated at $t = 0$, has either a zero or a negative value.

The condition that the derivative of eq 32 for t is either equal to or less than zero can be expressed by eq 34 (details are available as Supporting Information):

$$\frac{\beta - \delta}{\gamma} \leq Q e^{-E/RT_0} \quad (34)$$

The same equation results by supposing that the rate of consumption of A due to chemical reactivity, $-d[A]/dt = k[A]$ is greater than the absorption of gaseous A into the liquid phase $d[A]/dt = [A]_0 d\Omega(t)/dt$. Recalling how β , γ , and δ have been defined, and considering that the term on the right side of eq 34 is the first-order rate constant measured at the starting temperature $(k_1)'_0$, eq 34 can be modified as:

$$\frac{\alpha H r}{(\alpha H + \zeta R T_0) T_0} \leq (k_1)'_0$$

and since the term $(\alpha H + \zeta R T_0)$ is always positive:

$$r \leq \frac{(k_1)'_0 T_0 (\alpha H + \zeta RT_0) T_0}{\alpha H} \quad (35)$$

It must be pointed out that $(k_1)'_0$ is the value assumed by $(k_1)_0$ after correction through the factor $f(\alpha)$, according to eq 17. To avoid any pressure buildup, the heating rate must be maintained at values depicted by inequality 35.

The same inequality can be expressed as:

$$r \leq (k_1)'_0 T_0 \left(1 + \frac{\zeta RT_0}{\alpha H} \right) \quad (36)$$

According to this inequality, the lower the degree of filling, the lower the rate of heating which must not be exceeded to avoid pressure buildup. The same idea can be expressed by stating that, at a fixed heating rate, the lower the degree of filling, the higher the rate by which overpressure is generated.

Figures 2 and 3 show two numerical simulations of eq 32 with arbitrary parameters. The difference between the two figures is just a different degree of filling ζ . Numerical values of the parameters have been deliberately chosen to magnify differences of $[A]$ as a function of time and H , apart from any reference to an actual physical situation. Partial pressures of A follow a similar trend, due to eq 1.

Verification of Eq 17 as a Model To Correlate Reaction Rate and Degree of Filling. Analysis of Experimental Results. To confirm the model, some reactions were performed at the same temperature with different degrees of filling of the reaction vessel. From each test, k_1' was determined, by measuring the amount of product Z formed in the course of the reaction.

If the model holds, the resulting data can be interpreted by eq 17. This equation gives:

$$k_1' = k_1 f(\alpha) \quad (37)$$

Recalling how $f(\alpha)$ has been defined and defining $g = \alpha/\zeta RT$, the following equations are derived:

$$k_1' = k_1 \frac{\zeta RT}{\alpha H + \zeta RT}$$

which gives

$$\frac{1}{k_1'} = \left(\frac{H}{k_1} \right) g + \frac{1}{k_1} \quad (38)$$

Plotting experimental values of $1/k_1'$ versus g at different degree of filling should result a straight line, whose intercept should give the value $1/k_1$. This value could then be utilized to find the H value from the slope (H/k_1)

The reaction used to verify the model was the alkylation of triethylamine by ethyl bromide (bp 38 °C) to give tetraethylammonium bromide, scarcely soluble in toluene. Solutions of triethylamine and ethyl bromide, both 1.0 M in toluene, were prepared and stored at room temperature. Equal volumes of the two solutions were mixed, and the reaction mixture was poured into a one-necked glass flask. The vessel, containing a magnetic Teflon bar, was sealed with a ground-glass stopper which was secured with a metal clip to avoid the flask's opening under moderate overpressure. The volume

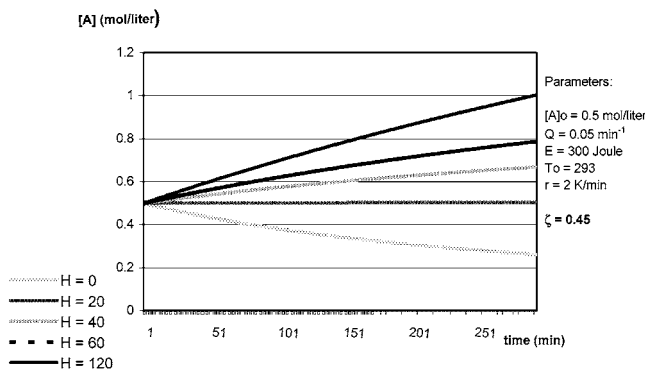


Figure 2. Numerical simulation of eq 32 at $\zeta = 0.45$.

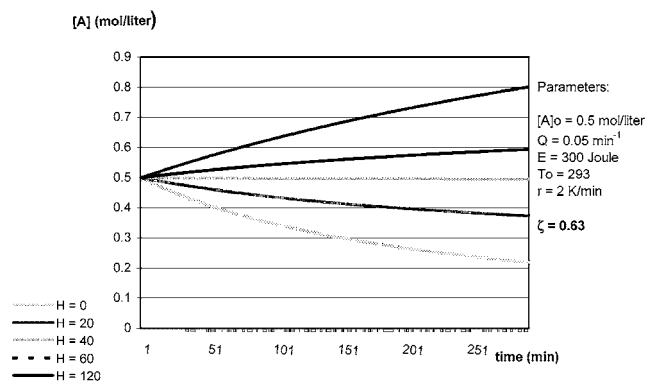


Figure 3. Numerical simulation of eq 32 at $\zeta = 0.63$.

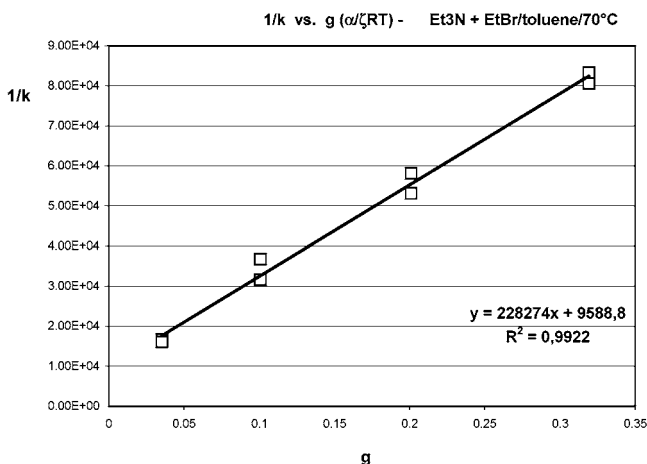
of the flask up to the stopper was 300 mL. Several tests were made at different degrees of filling. The flask was placed in an oil bath held at 70 °C (well below the boiling point of triethylamine and toluene, 89 °C and 101 °C respectively) with a magnetic stirrer and maintained for 3, 6, 12, and 24 h. After each end point the vessel was cooled at 0 °C for half an hour, and its content was filtered under reduced pressure on a Buchner filter. The crystals of tetraethylammonium bromide were dried under reduced pressure to constant weight. The amount of tetraethylammonium bromide was used to calculate the reaction rate of product formed, expressed as $\text{mol L}^{-1} \text{min}^{-1}$. The alkylation reaction was slow, with the largest observed conversion ca. 15%. Hence, reaction rates thus calculated appeared as almost linearly correlated to reaction time, even if the reaction is second order. An initial rate v_0 could then be easily determined. Apparent rate constants k' were calculated by dividing v_0 by 0.25 ($= [\text{triethylamine}]_0 [\text{ethylbromide}]_0$). The results are collected in Table 1.

The experimental values shown in Table 1 were inserted in Figure 4, plotting $1/k'$ vs g values, according to eq 50. A good correlation coefficient was obtained, showing that the model can account for differences in reactivity. From the intercept value, a rate constant at $\zeta = 1$ (completely full reactor) of $0.000104 \text{ min}^{-1}$ can be calculated. By using this value and the slope obtained, a H value of 23.8 is found.

It is noteworthy that when the same experiments were repeated in closed test tubes, such as those typically used for laboratory kinetic experiments and without any stirring, no significant differences in reactivity could be observed for different degrees of filling of the tubes. Kinetic constants

Table 1. Experimental values used in Figure 4

α	ζ	$g = \alpha/(\zeta RT)$	V_0 (mol L ⁻¹ min ⁻¹) $\times 10^6$	k' $\times 10^5$	$1/k'$ $\times 10^{-4}$
0.9	0.1	0.32	3.1	1.2	8.1
0.9	0.1	0.32	3.0	1.2	8.3
0.85	0.15	0.20	4.7	1.9	5.3
0.85	0.15	0.20	4.3	1.7	5.8
0.74	0.26	0.10	7.9	3.2	3.2
0.74	0.26	0.10	6.8	2.7	3.7
0.5	0.5	0.04	15.0	6.0	1.7
0.5	0.5	0.04	15.5	6.2	1.6

**Figure 4.** Verification of eq 17 as a model to correlate reaction rates and degree of filling from experimental rate constants. $T = 70$ °C.**Table 2.** Experimental values used in Figure 5

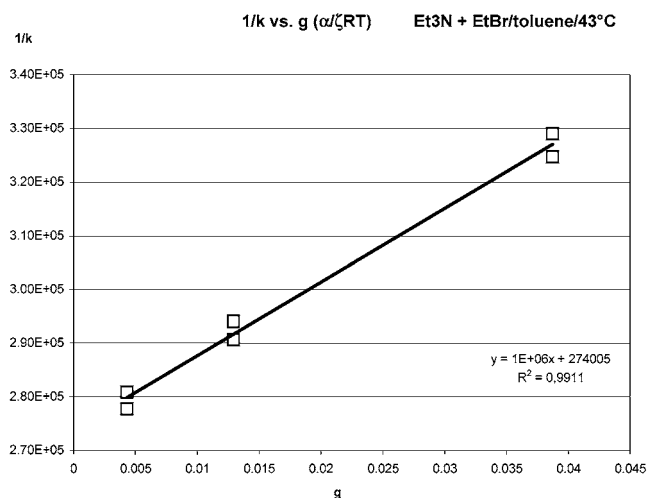
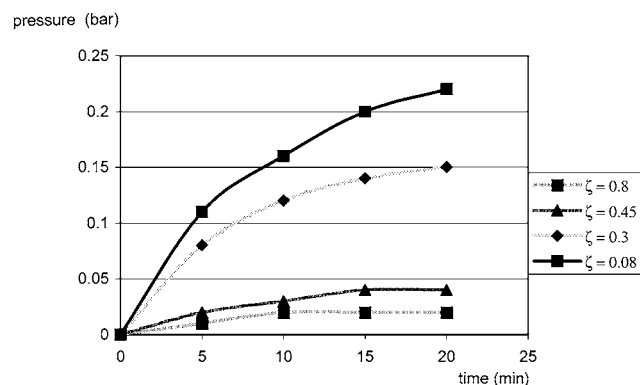
α	ζ	$g = \alpha/(\zeta RT)$	V_0 (mol L ⁻¹ min ⁻¹) $\times 10^7$	k' $\times 10^6$	$1/k'$ $\times 10^{-5}$
0.5	0.5	0.32	7.7	3.1	3.2
0.5	0.5	0.32	7.6	3.0	3.3
0.25	0.75	0.20	8.6	3.4	2.9
0.25	0.75	0.20	8.5	3.4	2.9
0.1	0.9	0.10	9.0	3.6	2.8
0.1	0.9	0.10	9.0	3.6	2.8

thus determined are more erratic, but still approximately in line with the values found in the tests with stirring for $\zeta \approx 0.8$. These results agree with the assumption previously made that efficient mixing should permit the equilibrium between the liquid and the gaseous phase to be attained at a rate greater than the reaction rate.

From a standpoint of industrial practice and unless the reaction is heterogeneous, it could be inferred that the best practice should be not to stir to attain a vigorous reaction. As a drawback, an unstirred system could result in a sudden internal evolution of gas due to a variety of reasons (vibration, occasional stirring, crystal formation, etc.), and this should be avoided for safety reasons.

Tests were repeated at 43 °C, just over the boiling point of ethyl bromide. Results are shown in Table 2 and Figure 5. Equation 50 is again verified.

From the data reported, a H_0 value of 3.6 is found by using the same calculation applied for the previous set of

**Figure 5.** Verification of eq 17 as a model to correlate reaction rates and degree of filling from experimental rate constants. $T = 43$ °C.**Figure 6.** Buildup of internal pressure vs time for different degrees of filling. Reaction as in Figures 4 and 5.

tests. It is noteworthy to consider that such a value, when compared to the value of 23.8 determined at 70 °C is consistent with the relationship between Henry's constants and temperature.

Experimental Verification of the Conditions To Prevent Buildup of Internal Pressure. Tests were made on a stainless steel cylinder (volume = 30 mL), secured with a screw cap of the same material, and equipped with a manometer through a sidearm just below the cap and a magnetic stir bar. The cylinder was filled at room temperature with the same reaction mixture used in the previous test, at four different degrees of filling, and was placed into a water bath previously heated to 70 °C, simulating a rapid constant heating during the early stages of this operation. Pressure buildup was recorded at different times. Parallel tests were made without ethyl bromide in the reaction mixture. Overpressures generated during these blank trials, due to air expansion and partial vaporization of other components of the mixture, were subtracted from the values obtained with ethyl bromide. The values thus obtained were plotted against time in Figure 6. Since the heating rate can be considered as constant for the four tests, Figure 6 verifies the statement that at a fixed heating rate, the lower the degree of filling, the higher the rate by which overpressure is generated.

Conclusions

The model developed allows for a prediction of different reaction rates as a function of the degree of filling and is confirmed by experimental results. This is in line with empirical observations observed during scaling-up of some processes. Moreover, the model appears to be useful as a tool to define experimentally, at different temperatures, the Henry's law constants for volatile organic reactants and solvents. This can be useful considering that several compilations of Henry's constant have been prepared for aqueous systems, due to implications for environmental chemistry, while values for organic solvent systems are rare.

The model proposed relies on several assumptions which seem to be acceptable, even if they oversimplify the system described. Recent reports show that longer processing times represent one of the most important reasons for failure during scaling-up processes from laboratory- to pilot scale, with 20 out of 70 cases of such failures reported by pharmaceutical

and fine chemical companies attributed to longer processing times.⁴ It would be interesting to know how many failures of scaling-up processes could be attributed to any decrease in reactivity due to the partition of one or more reactants into the gaseous phase.

Supporting Information Available

Integration of eq 23 to give eq 24 and derivative of eq 36 leading to eq 34. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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