Available online at www.sciencedirect.com

SCIENCE DIRECT®

Thermochimica Acta 402 (2003) 75–80

thermochimica acta

www.elsevier.com/locate/tca

A mathematical approach for the calculation of reaction order for common solution phase reactions

Richard J. Willson [a,*], A.E. Beezer [b]

[a] GlaxoSmithKline, Consumer Healthcare R&D, St. George's Avenue, Weybridge, Surrey KT13 ODE, UK
[b] Medway Sciences, Medway University Campus, NRI University of Greenwich, Chatham Maritime, Kent ME4 4TB, UK

Received 29 August 2002; accepted 30 October 2002

Abstract

This paper describes a mathematical procedure for the direct calculation of reaction orders for typical solution phase reactions. The algorithm described has no dependence on reaction constants that are part of a formal rate expression, for example the rate constant. All that is required is a data set containing a measured reaction rate and a corresponding time interval or a corresponding reaction concentration. From this data set, the reaction order can be directly calculated from a minimum of two data points. By systematic application of the mathematical procedure to a data set, changes in reaction order can be deduced during the course of a reaction, be it integral or non-integral. Such application may be used to characterise complex reaction schemes such as parallel and consecutive reactions or for reactions where there is a change in reaction order. Data simulated from formal rate expressions have been used to illustrate the principles of the analysis and to examine the limitations when used in conjunction with more complex reaction schemes. A procedure of systematic calculation of reaction orders has been developed using a mathematical spreadsheet, MathCad$^{\text{TM}}$ version 2000 [http://www.mathcad.com].

© 2002 Elsevier Science B.V. All rights reserved.

Keywords: Reaction order; Kinetics; Reaction rates; Calculation of reaction order; MathCad

---

1. Introduction

Where there is a desire to determine the chemical kinetics of a reaction, there is a requirement to determine the dependency that the reaction rate has on the quantity of material that is reacting. Zero order reactions are a special case where the rate of reaction has no dependency on the quantity of reactant. For all other reaction schemes the reaction rate has some dependency on reactant quantity. The dependency on reaction quantity is the quantity of reactant raised to a power (the reaction order), which can in principle be any value, integral or non-integral. Literature examples of non-integral orders are not in abundance, maybe as a result of the difficulty in determining non-integral orders. However, there are some examples in the literature [1–4]. There are several approaches that have been successfully used for the calculation of reaction order in the past. The method of integration was first used in 1850 by Wilhelmy [5] and then by Hardcourt and Esson [5]. The principle of this method is to construct a graph of some function of concentration against time using a linearised form of an integrated rate expression. Such method of analysis, although widely used, is often restricted to simple reaction orders where a linearised expression of a rate equation can be determined. There is a certain amount of subjective assessment of such linear plots that may lead to falsely ascribing a reaction

---

[*] Corresponding author.

0040-6031/03/$ – see front matter © 2002 Elsevier Science B.V. All rights reserved.
PII: S0040-6031(02)00534-8

order. For example, a reaction having a reaction order of 1.7 may fit the second order integrated equation and so be miss-ascribed. In addition the data must be tested using each linear form of equation for each reaction order and an assessment of the best fit made. The method of integration can also lead to difficulties for bi-molecular reactions where the reaction orders for each reacting specie is not equal to one, because of the mathematical difficulties of integration of the rate expression. Some of the more complex reaction schemes have been discussed by Capellos and Bieski [6]. A second approach is the differential method that was first suggested by van't Hoff in 1884 [7]. This method requires that rates of reactions are determined from the initial slope of concentration–time graphs at various concentrations of reactant. A double logarithmic plot of ln rate versus ln concentration gives a straight line of slope (n). This method can be adapted so that the rate of reaction, at a given initial reactant concentration, is studied as a function of time. By comparing the reaction order calculated from the initial reaction rates to the reaction order determined as a function of time, changes in reaction order can be deduced. This method, too, has some limitations. The first is that it may be difficult to ascertain the instantaneous rate of a reaction, and the second is that the analysis tends to be time consuming. Miller [8] has made reference to both these methods concluding that the method of integration was one of “guess and try” whereas the method of differentiation he stated as being “the method of systematic exploration”.

The purpose of this paper is to present a general and rapid method for the calculation of reaction order that provides many of the benefits of the methods previously described but offers a reduction in the complexity and uncertainty of the previous methods. The calculation does not rely on knowing any of the reaction parameters for a reaction such as the rate constant. In addition there are no constraints on the value of the reaction order. At present this method has been explored through solution phase reaction schemes of the type,

$$A \to Z, \quad A + B \to Z, \quad A + B + C + \cdots \to Z,$$
$$A \to 2Z, \quad 2A \to Z, \text{ etc.}$$

where there is a single reactant or where two or more reactants are at equal or non-equal concentrations.

2. Theoretical

This paper focuses primarily on the relatively more complex reaction schemes of the type $A + B \to Z$, however, the principle of application is the same for all type of reaction schemes.

Kinetic equations that describe solution phase reactions are usually presented in the form of,

$$\frac{\mathrm{d}x}{\mathrm{d}t} = k(A - x)^m (B - x)^n \tag{1}$$

where k is the rate constant, A and B are the initial concentrations of reactants at time $= 0$, x the concentration of reactant that has reacted at any time, $\mathrm{d}x/\mathrm{d}t$ the rate of reaction and m and n are the reaction orders relative to the concentrations A and B. During the course of a reaction, the reaction rate Φ changes as a function of the concentration of material that has reacted x. The remaining parameters in Eq. (1) k, A, B, m and n are unchanging providing there is no change in reaction mechanism. To calculate a reaction order, Eq. (1) can be simplified if the ratio of two reaction rates from the same data set are considered. By selecting two values for the reaction rate Φ_1 and Φ_2 and the corresponding reaction concentration x_1 and x_2 for an observed reaction, the ratio of this data pair can be expressed as,

$$\frac{\Phi_1}{\Phi_2} = \frac{k(A - x_1)^m (B - x_1)^n}{k(A - x_2)^m (B - x_2)^n} \tag{2}$$

This can be simplified to

$$\frac{\Phi_1}{\Phi_2} = (A - x_2)^m \frac{(B - x_1)^n}{(A - x_2)^m (B - x_2)^n} \tag{3}$$

The only unknowns in Eq. (3) are the reaction orders m and n. The values for m and n can be solved by sequentially varying the values of m and n until the product for the right hand part of Eq. (3) is equal to the ratio on the left hand side. This can be conveniently done by varying m from zero, in increments of 0.1, for each 0.1 increment of n. The results can be displayed in a square matrix where rows represent values of m and columns values for n. The co-ordinates of a single value in the matrix that is equal to the ratio of reaction rates Φ_1/Φ_2 gives the values of both m and n. For example the appropriate value of Φ_1/Φ_2 for a reaction of overall order of 2 for which $m = 1.5$ and $n = 0.5$ will be found at the co-ordinates {row 15, column 5} in the matrix. By contrast, a reaction that has an overall order of 2, where $m = 1$ and $n = 1$, the value of Φ_1/Φ_2 will be found at the co-ordinates {row 11, column 11}, etc. This method of order calculation can be extended so that the order is determined for every data point within a data set. This is done using a three dimensional matrix where the third dimension is the number of data pairs in the data set. In this case the x, y co-ordinates gives the values for m and n whereas the z co-ordinates gives the number of data pairs that satisfies the requirements for Eq. (3). The mathematical form of this process can be seen in Eq. (4):

$$\mathrm{sum}_{R,m,n} = \left[\frac{[(A - \vec{x}_1)_R]^{m_i}}{[(A - x_2)_R]^{m_i}}\right]\left[\frac{[(B - x_1)_R]^{n_i}}{[(B - x_2)_R]^{n_i}}\right] \quad (4)$$

where R is a range variable from 1 to the total number of data pairs in the data set, i a range variable that encompasses the values of the reaction orders to be tested, i.e. from 0 to 3 in increments of 0.1. A and B are the start concentrations of the reactants, x_1 and x_2 are the quantities of reaction per unit volume for the corresponding reaction rates and m and n are the reaction orders. The creation of a three-dimensional matrix in this way allows a statistical evaluation of the distribution of the reaction orders m and n over the entire data set, see Fig. 1.

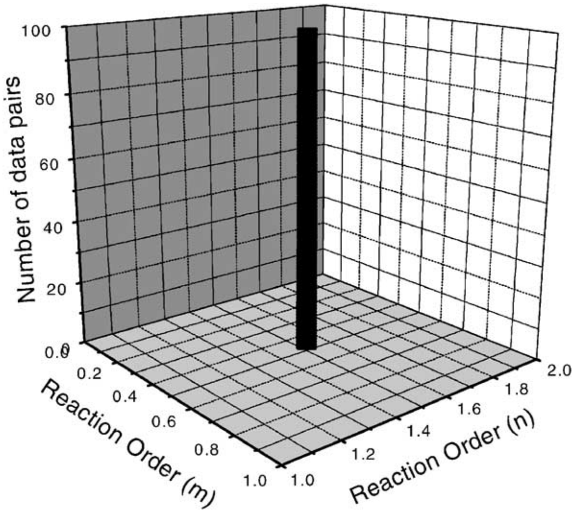


Fig. 1. This graph shows a cubic matrix containing the co-ordinates for values of m and n that satisfy Eq. (3) earlier. The data analysed was a simulated data set of 100 data points and was assigned values of m and n as 0.5 and 1.5, respectively.

An algorithm for processing data and calculation of the reaction order was written in MathCad version 2000 (a copy of the algorithm is available from the author [9] and can be used in conjunction with MathCad). The basic structure of the program is to import two columns of data in the form of an ASCII file. The x-column being the concentration of reactant that has reacted and the y-column being the reaction rate. Various combinations of data pairing can then be employed to obtain the correct reaction order.

3. Experimental/discussion

For the determination of a reaction order the kinetic data for a reaction study is collected in the normal way. For example, a reaction rate is followed by recording absorbence, heat flow, quantitative assay, pH, etc. collected over time or as a function of reaction concentration. Where data is in the form of reaction rate as a function of time, this data can be changed to rate versus reaction concentration by direct integration as the area under a plot of dx/dt versus time has the units of moles dm^{-3}, i.e. x. Therefore, dx/dt can be directly converted to dx/dt versus x. Alternatively, for mono-molecular reactions the reaction order can be determined directly from rate versus time data sets [10].

For the analysis, choosing two values of reaction rates can be arbitrary, however, a greater degree of accuracy can be had if the values have maximum separation, see Fig. 2. For the best separation between two values of reaction rates for the entire data set, the first data point in the rate column can be paired with the 51st data point (in a string of 100 data points), etc.

Simulated data sets were constructed to test the analytical algorithm. Such data sets were derived from Eq. (1) where different values of the rate constant, reaction order m and n and initial concentrations A and B were used. Values for the reaction rate were thus derived by varying the reaction quantity x from zero (time = 0) to the initial start concentration A or B, whichever is the smallest. As an example, a data set was simulated using defined reaction parameters. From the analysis of a section of data that made up a 1/5 fraction of the total reaction, it was shown the correct values for m and n could be recovered, see Fig. 3.

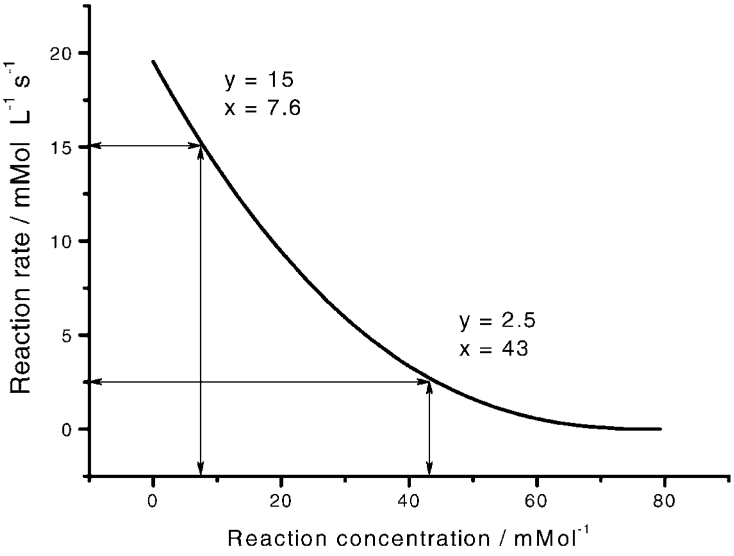


Fig. 2. This shows a graph of a simulated reaction where the rate constant is 3.5×10^{-4}, m and n are 1.5 and 1, respectively and A and B are 80 and 78 mM, respectively. Selection of two values of reaction rate, 15 and 2.5 mM s^{-1} give the corresponding reaction concentrations as 7.6 and 43 mM.

Where the data is a "perfectly" simulated data set, each value of the vector should match exactly with the corresponding value in the matrix. A problem arises when using "real" data where there may be some variability associated with the data set, for example instrument noise. The difficulty faced is how to match the vector with the matrix if the corresponding values are only similar but not necessarily exact. In an attempt to solve this problem each column of the matrix was subtracted from the corresponding rate ratio in the vector.

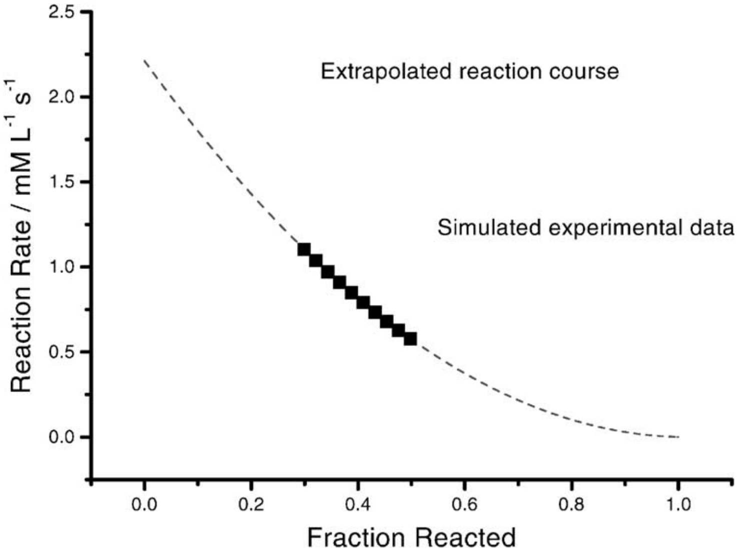


Fig. 3. This shows a graph of a simulated data set that was collected over a 0.2 fraction of the total reaction. The values used to simulate the data were $k = 3.50 \times 10^{-3}$, $A = 800$ mM, $B = 750$ mM, $m = 1.5$ and $n = 0.5$. A total of 10 data points were used.

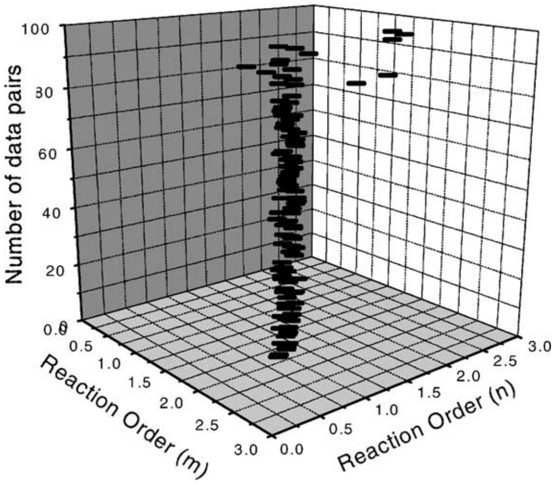
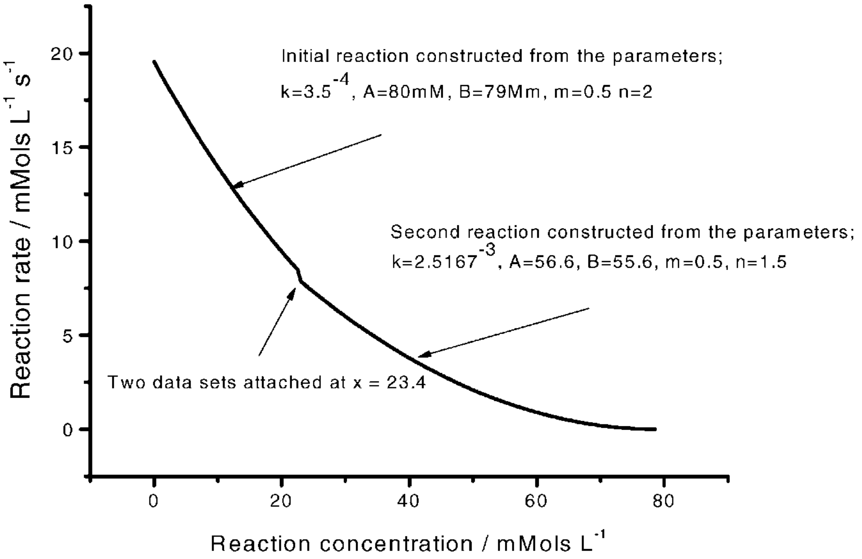


Fig. 4. This shows the distribution of reaction order m and n for a simulated reaction where there is a 5% systematic and random error added to the reaction rate. Values used to construct the simulated data set are $k = 3.5 \times 10^{-4}$, $m = 2$, $n = 1$, $A = 80\,\text{mM}$ and $B = 78\,\text{mM}$. A total of 200 data points were analysed. The distribution of the values for m and n become more broad towards the top of the graph where the relative distance between two reaction rate data pairs becomes less.

Values closest to zero provide the co-ordinates of the values m and n. The distribution of matches can be plotted for each combination of m and n to give a statistical evaluation as to the number of data pairs in the matrix that matched the rate ratios in the vector. The distributions of the calculated values for m and n can thus be shown, see Fig. 4. Note that as a reaction rate tends towards zero, there is an increase in the noise to signal ratio and so there is a greater variability in the calculated reaction orders.

4. Complex reaction schemes

A data set was simulated where the overall reaction order was initially 2.5, 0.5 with respect to A and 2 with respect to B. Half way through the reaction the order with respect to B changed to 1.5, see Fig. 5. This data set was constructed by attaching two data sets together. The first data set was constructed using $m = 0.5$ and $n = 2$, and the second data set used $m = 0.5$ and $n = 1.5$. The rate constant for the second data set was adjusted so that the reaction rate at the start of the second data set corresponded with the reaction rate at the end of the first data set. The whole data set was analysed by taking consecutive data pairs, i.e. the first data point of the rate column was paired with the second data point in the column. Fig. 6 shows the resulting analysis of such a reaction scheme, where for the first half of the data set the reaction order conformed with the reaction order $m = 0.5$ and $n = 2$. There is then an area where the reaction order is somewhat



Initial reaction constructed from the parameters; k=3.5^{-4}, A=80mM, B=79Mm, m=0.5 n=2

Second reaction constructed from the parameters; k=2.5167^{-3}, A=56.6, B=55.6, m=0.5, n=1.5

Two data sets attached at x = 23.4

Fig. 5. A graph showing a simulated data set where the reaction order changes from 2.5 to 2 over the course of the reaction.

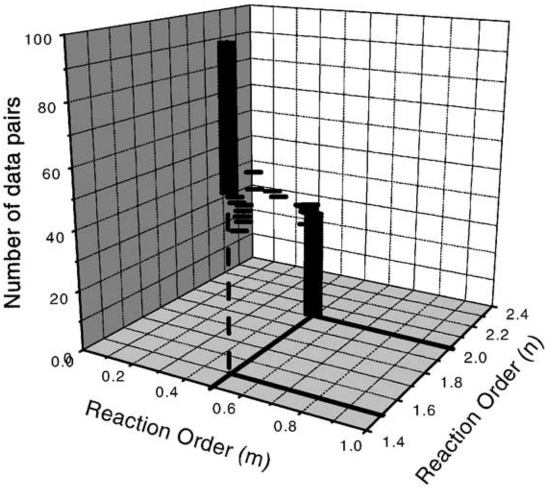


Fig. 6. The graph shows the results of analysis for a simulated reaction where the reaction order changed from $m = 0.5$ and $n = 2$ to $m = 0.5$ and $n = 1.5$. The distribution of the reaction orders calculated for each data pair in the data set can be seen to change at about halfway through the data set.

random, followed by the second half of the data set where $m = 0.5$ and $n = 1.5$.

5. Conclusion

This method for deriving reaction orders, although relatively straightforward, may be a significant contribution to the kinetic analysis of reactions. The method of analysis, described, can provide a direct and rapid method for the calculation of reaction orders. Where a process of sequential application to a complete data set is applied, information about the distribution of reaction orders for each data pair can be found. If the data is “good”, i.e. free of significant noise, information about changes in reaction order can be determined by comparing a section of data at the beginning of a data set with that at the middle and at the end.

The application of this method has been successfully applied to general forms of solution phase reactions of relative simple soichiometries. It may be possible, however, to extend this method to more complex type reactions, for example where a reaction tends towards an equilibrium or for solid state type reactions. The application of this method to such reaction types will be detailed in a future publication.

References

[1] M. Letort, J. Chim. Phys. 34 (1937) 206.
[2] W. Muangsiri, L.E. Kirsch, J. Pharm. Sci. 90 (8) (2001) 1066–1075.
[3] A.A. Frost, R.G. Pearson, Kinetics and Mechanism, 2nd ed., Wiley, New York, 1961 (Chapters 2 and 8).
[4] R.J. Willson, A.E. Beezer, J.C. Mitchell, Int. J. Pharm. 132 (1996) 45.
[5] K.J. Laidler, Chemical Kinetics, 3rd ed., Harper and Row, New York, 1987 (Chapter 2).
[6] C. Capellos, B.H.J. Bieski, Kinetic Systems, Wiley/Interscience, New York, 1972.
[7] J.H. van’t Hoff, Etudes de Dynamic Chimique, Muller, Amsterdam, 1884, p. 84.
[8] Lash Miller, Trans. R. Soc. Can. 11 (Ser. 3: Sec. 3) (1908) 245.
[9] Richard_Willson@gsk.com.
[10] R.J. Willson, Isothermal Microcalorimetry, Ph.D. Thesis, University of Kent, 1995.