Estimation of Activation Parameters from One Kinetic Experiment (Varytemp Method). Error Analysis and Revised Computer program

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Recently, a new method (the Varytemp method) was published which makes it possible to accurately determine activation parameters ($\Delta H^\pm$, $\Delta S^\pm$, and $\Delta C^\pm$) from only one kinetic experiment in which the temperature is varied in a controlled way. The data resulting from a Varytemp run consist mainly of a number (N) of data triplets $(y_i, T_i, t_i)$, where $y_i$ is the observed substrate concentration dependent variable (e.g. rotation of polarized light or resistance of a conductimetric cell), $T_i$ the temperature (K) and $t_i$ the time after the start of the run. The index $i$ denotes the $i$th observation.

The data analysis, preferably made by a computer, consists in principle of the following steps.

1. Smooth and differentiate the $y$ and $T$ values to obtain $\tilde{y}_i$, $\tilde{T}_i$, $(dy/dT)_i$ and $(dT/dt)_i$.
2. Compute rate constants $k_i$ for each temperature $T_i$, e.g. for a first order reaction

   \[ k_i = \frac{[1 + \beta_1(T_i - T_0)](dy/dT)_i/[\tilde{y}_i - c] - \beta_1(dT/dt)_i(1 + \beta(T_i - T_0))}{(dT/dt)_i} \]

   $T_0$ is the temperature at which the catalyst concentration is measured, $c$ the infinity value of $y$, $\beta_1$ the volume expansion coefficient of the experimental solution and $\beta_2$ the change of $y$ with $T$ without reaction.

3. Fit these computed $(k_i, \tilde{T}_i)$ pairs to an adequate Arrhenius equation \(^,*\) by the method of least squares with proper weights $w_i$ by minimizing the sum of squared residuals ($U$) for the parameters $A, B, \ldots$

   \[ \log k_i = A + B(1/\tilde{T}_i - 1/T_0) + \ldots + \epsilon_i \]

   \[ U = \sum \epsilon_i^2 w_i \]

4. Compute the activation parameters with corresponding standard deviations (SD's) from the parameters $A, B, \ldots$ and their variance-covariance matrix.

In the first version of the computer program, \(^,*\) a standard technique was used for the smoothing and differentiation in step 1. Different third order polynomials were fitted to the data points using 31 consecutive points at a time. The computed value of the polynomial and its derivative at the 16th point were used as smoothed value and derivative for this point. This method has two disadvantages, first, since 31 points are used for each computation the range of values in step 2 - 4 is decreased since derivatives are not computed for the first and last 15 points. Secondly, only a fraction of the total number of points are used in each fitting which means that the accuracy of the smoothed values and the derivatives is lower than necessary.

Recently, a powerful spline function technique suitable for smoothing and differentiation has been developed. \(^,*\) As in earlier methods, the data are represented by third order polynomials, one for each point, but additional restrictions are laid on the polynomials. The spline conditions require that the function and its two first derivatives are continuous in the joints (knots). An extra restraint on the spline function used in this application is that the integral of the squared second derivative from the first to the last point shall be minimal under the specified measurement accuracy. This latter condition is very well suited for the representation of experimental data; it makes the spline function as smooth as possible.

This spline function technique has been tested \(^,*\) and incorporated into the Varytemp computer program (the revised version \(*\) is called Vytemp 2) with good results; the accuracy of the estimation method has increased about 2 times.

The use of spline functions for the computation of the derivatives produces residuals ($\epsilon_i$ defined in step 3 above) which are autocorrelated and thus not randomly distributed. Though the consistency of the parameter estimates is not affected by this autocorrelation, the ordinary least squares techniques for the estimation of SD's are generally no longer valid.\(^,*\)

To investigate the deviations between true and computed SD's and to make sure that the Varytemp method gives

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* Program list and manual are available on request to the author.

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unbiased estimates for the activation parameters, the following Monte Carlo analysis was made.

Synthetic data (181 points) were generated with a certain set of activation parameters and almost linear temperature variation. Normally distributed errors of measurement with specified SD (proportional to $y$) were then added, producing a simulated Varytemp run with known theoretical activation parameters. Estimation of the activation parameters and their SD's from these data then gives information about deviations from the theoretical values. By making many simulations for the same set of theoretical parameters, one can estimate mean values and confidence intervals for the estimated parameters and thus obtain information about eventual systematic deviations from the "true" values.

Three different sets of simulations were performed, the ranges of the generating parameters are seen in Table 1. (a) Individual simulations to investigate whether the estimated SD's could be used to estimate confidence intervals for the activation parameters. (b) Series of five simulations with identical parameters to investigate whether theoretical and estimated SD's agree. (c) Series of 35 simulations with identical parameters to investigate eventual systematic deviations of the estimated activation parameters.

Results. Some typical results of the simulations are shown in Table 2. First and most important, the results confirm that the method gives unbiased estimates for the activation parameters $\Delta H^\pm$ and $\Delta S^\pm$. $\Delta C_p^\pm$ is somewhat underestimated, however not seriously, and very little in runs giving $\Delta C_p^\pm$ values significantly different from $R$.

Further, the estimates of $\Delta H^\pm$ and $\Delta S^\pm$ are not significantly changed if a $\Delta C_p^\pm$ of $-35$ cal deg$^{-1}$mol$^{-1}$ on a temperature interval of $10^\circ$C is neglected. This is an advantage with the Varytemp method as compared with the classical method, where the use of larger temperature intervals makes neglect of $\Delta C_p^\pm$ more serious.

The estimated SD's of $\Delta H^\pm$ and $\Delta S^\pm$ in general are somewhat too large; this overestimation is, however, not more than about 50%. The estimated SD's can thus safely be used for computation of confidence intervals of the activation parameters in the usual way. Trials were made to adapt the method worked out in Ref. 7 for correction of the SD's for the residual autocorrelation to the present case of non-stationary data; no significant improvement was made.

Fig. 1 shows the estimated SD (which is an upper bound to the "true" SD) of $\Delta H^\pm$ as a function of the relative SD of $y$.

![Fig. 1. Estimated SD of $\Delta H^\pm$ (mean value) as a function of the relative accuracy of measurement ($\sigma(y)/y$). Temperature interval 10°C. Number of points 181.](image-url)
Table 2. Typical results from Varytemp simulations. Values within parenthesis indicate fixed
(not estimated) values due to choice of model. Units the same as in Table 1. All estimated values
are mean values.

<table>
<thead>
<tr>
<th>$\sigma(y)/y$</th>
<th>0.0002</th>
<th>0.0002</th>
<th>0.0005</th>
<th>0.0005</th>
<th>0.0005</th>
<th>0.001</th>
<th>0.002</th>
<th>0.002</th>
<th>0.0005</th>
<th>0.0005</th>
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<tr>
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<td>0.0002</td>
<td>0.0001</td>
<td>0.0003</td>
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<tr>
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<td>20</td>
<td>10</td>
<td>20</td>
<td>10</td>
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<td>10</td>
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<td>1</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

| True $\Delta H^\pm$ | 12.23  | 7.912  | 12.23  | 12.23  | 12.23  | 12.23  | 12.23  | 12.23  | 12.23  | 12.23  | 12.23  | 12.23  |
| True $\text{SD}(\Delta H^\pm) \times 10^6$ | 1.1    | 0.7    | 1.8    | 2.3    | 3.3    | 10     |       |       |       |       | 5.5    | 4.2    |
| Est. $\text{SD}(\Delta H^\pm) \times 10^6$ | 2.0    | 3.1    | 2.5    | 4.9    | 3.5    | 20     | 4.0    | 2.5    | 6.4    | 4.2    | 6.2    | 4.2    |

| True $\Delta S^\pm \times (-1)$ | 30.36  | 41.70  | 30.36  | 30.36  | 30.36  | 30.36  | 30.36  | 30.36  | 30.36  | 30.36  | 30.36  | 30.36  |
| Mean est. $\Delta S^\pm \times (-1)$ | 30.35  | 41.63  | 30.402 | 30.433 | 30.340 | 30.356 | 30.315 | 30.034 | 30.460 | 30.307 |
| True $\text{SD}(\Delta S^\pm) \times 10^6$ | 4      | 2      | 6      | 8      | 11     | 35     |       |       |       |       |       | 2      |
| Est. $\text{SD}(\Delta S^\pm) \times 10^6$ | 7      | 10     | 8      | 16     | 11     | 66     | 13     | 8      | 21     | 14     | 2      | 2      |

| True $\Delta c_p^\pm$ | -35    | -2     | -35    | -35    | -2     | -2     | -2     | -2     | -2     | -2     | -2     | -2     |
| Mean est. $\Delta c_p^\pm$ | -34.5  | -2     | -30    | -2     | -2     | -2     | -2     | -2     | -2     | -2     | -2     | -2     |
| True $\text{SD}(\Delta c_p^\pm)$ | 7      | -11    |       |       |       |       |       |       |       |       |       |       |
| Est. $\text{SD}(\Delta c_p^\pm)$ | 13     | -8     |       |       |       |       |       |       |       |       |       |       |

Fig. 2 shows the corresponding plot for $\Delta c_p^\pm$. The figures show values estimated with temperature intervals of 10°C; these values are to be multiplied by the correction factors $10/\Delta T$ and $(10/\Delta T)^4$, respectively, if a temperature interval of $\Delta T$ is used, since $\Delta H$ is computed from the linear variation of log ($k$) with $T$, $\Delta c_p^\pm$ from the quadratic variation. Modern apparatus in general has an accuracy (SD of $y$) of about 5/10 000. Thus, in order to obtain reasonable accuracy of $\Delta c_p^\pm$ one should use a temperature interval of 20°C.

Finally it can be seen that with this accuracy $\Delta H^\pm$ is estimated with an accuracy (2-SD) of about 7.5 pro mille, which is consistent with the results of Ahlberg for base-catalyzed indene rearrangements,1 corroborating consistency of the Varytemp method.

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Sulfur Extrusion Reactions

I. On the Decomposition of S-(Alkox thyocarbonyl)thiohydroxylamines

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S-(Alkox thyocarbonyl)thiohydroxylamines have been prepared from O-alkyldithiocarbonates and hydroxylamine-O-sulfonate. They are colourless liquids which are stable at low temperature (e.g. -30°C), whereas they decompose slowly at room temperature. Within 1-2 weeks the decomposition to O-alkyl thiacarbamates and elemental sulfur is complete:

\[
\begin{align*}
\text{S} & \quad \text{S} \\
\text{RO-C-S-NH}_2 & \quad \text{RO-C-NH}_2 \cdot \text{S}
\end{align*}
\]

As part of an investigation of the mechanism of sulfur elimination from this type of compound, exchange experiments have been carried out using \(^{15}\text{N}\) labelled S-(alkox thyocarbonyl)-thiohydroxylamines, which were prepared from Na\(^{15}\text{NO}_3\) (97.4 % \(^{15}\text{N}\)) via the following reaction sequence. \(^{1,2}\) \(^{15}\text{NO}_2\cdot\text{SO}_2\cdot\text{H}_2\text{O} \underset{\text{H}_2\text{O}}{\rightarrow} \text{HO}^{15}\text{N}\text{(SO}_2\text{)}\text{H}^+ \underset{\text{H}_2\text{O}}{\rightarrow} \text{HO}^{15}\text{NH}_3 \cdot \text{SO}_2\text{H}

\[
\begin{align*}
\text{S} & \quad \text{S} \\
\text{NH}_3\text{OSO}_2\text{H} & \quad \text{S}
\end{align*}
\]

Since the mass spectra of O-ethyl thiacarbamate and O-isopropyl thio carbamate do not exhibit peaks above m/e 100, except those of the molecular ions (which, in both cases, are the base peaks), the distribution of \(^{15}\text{N}\) in the reaction mixture is conveniently followed mass spectrometrically.

After completion of the decomposition, the mass spectral data showed that the ratio M\(^+\)(Ia)/M\(^+\)(Ib) within the limits of measurements is equal to the ratio M\(^+\)(IIa)/M\(^+\)(IIb), where M\(^+\) is the relative intensity of the molecular ions, respectively, of i-C\(_3\)H\(_4\)OC(=S)\(^{15}\)NH\(_2\) (Ia), i-C\(_3\)H\(_4\)OC(=S)\(^{14}\)NH\(_2\) (Ib), C\(_6\)H\(_5\)OC(=S)\(^{15}\)NH\(_2\) (IIa), and C\(_6\)H\(_5\)OC(=S)\(^{14}\)NH\(_2\) (IIb). Since the decomposition quantitatively leads to the formation of O-alkyl thiocarbamates, the ratios obtained show that \(^{15}\text{N}\) has been distributed equally between the two amides during the sulfur elimination reaction.

Mass spectra of the reaction mixture were also obtained during the decomposition to observe whether the formation of \(^{15}\text{N}\) labelled O-ethyl thiacarbamate could have been the result of an exchange within the undecomposed S-(alkox thyocarbonyl)-thiohydroxylamines. However, because of the absence of the relevant ions ([C\(_3\)H\(_4\)]\(_2\)-CHOC(=S)S\(^{15}\)NH\(_2\) and C\(_6\)H\(_5\)OC(=S)S\(^{15}\)NH\(_2\)), such an exchange can be excluded with certainty.

Analogous results were obtained from an exchange experiment using \(^{14}\text{N}\) labelled S-(methox thyocarbonyl)thiohydroxylamine and S-(ethox thyocarbonyl)thio hydroxylamine.

Exchange of nitrogen does not take place after decomposition to O-alkyl thiacarbamates as shown by mixing \(^{15}\text{N}\) labelled O-ethyl thiacarbamate (30 % \(^{15}\text{N}\)) with O-isopropyl thiacarbamate. After 4 weeks at room temperature, no nitrogen exchange within the two amides was