

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 (ΔH^\ddagger , ΔS^\ddagger , and Δc_p^\ddagger) from only one kinetic experiment in which the temperature is varied in a controlled way.^{1,2} 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 conductrimetric 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,² consists in principle of the following steps.

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

$$k_i = [1 + \beta_1(\bar{T}_i - T_0)] \left[-\frac{(dy/dt)_i}{(\bar{y}_i - c)} - \beta_2 \frac{(dT/dt)_i}{(1 + \beta_2(\bar{T}_i - T_0))} \right]$$

T_0 is the temperature at which the catalyst concentration is measured, c the infinity value of y , β_1 the volume expansion coefficient of the experimental solution and β_2 the change of y with T without reaction.

3. Fit these computed (k_i , \bar{T}_i) pairs to an adequate Arrhenius equation^{3,4} by the method of least squares with proper weights w_i by minimizing the sum of squared residuals (U) for the parameters A, B, \dots

$$\log k_i = A + B(1/\bar{T}_i - 1/T_0) + \dots + \varepsilon_i$$

$$U = \sum_i \varepsilon_i^2 w_i$$

4. Compute the activation parameters with corresponding standard deviations

(SD's) from the parameters A, B, \dots and their variance-covariance matrix.

In the first version of the computer program,² 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 16:th 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.⁵ 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 tested⁶ 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 (ε_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.⁷

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

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

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) Indi-

vidual 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 esti-

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 ΔH^\ddagger and ΔS^\ddagger . Δc_p^\ddagger is somewhat underestimated, however not seriously, and very little in runs giving Δc_p^\ddagger values significantly different from $-R$.

Further, the estimates of ΔH^\ddagger and ΔS^\ddagger are not significantly changed if a Δc_p^\ddagger of $-35 \text{ cal deg}^{-1} \text{ mol}^{-1}$ on a temperature interval of 10°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 Δc_p^\ddagger more serious. The estimated SD's of ΔH^\ddagger and ΔS^\ddagger 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 ΔH^\ddagger as a function of the relative SD of y .

Table 1. Parameter values used in the simulations.

N	181	181
ΔH^\ddagger kcal mol ⁻¹	12.23	7.912
ΔS^\ddagger e.u.	-30.36	-41.70
Δc_p^\ddagger cal deg ⁻¹ mol ⁻¹	-2.0 -35.0	
cat. conc. mol l ⁻¹	0.06815	0.02200
$\sigma(y)/y$	0.0002 -0.005	
$\sigma(T)$ deg.	0.0003 -0.005	

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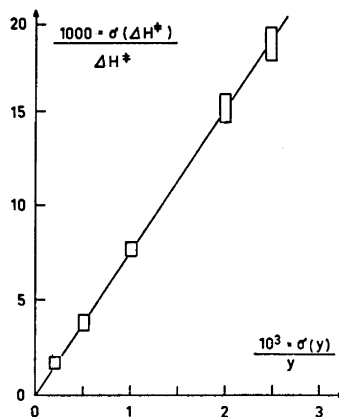


Fig. 1. Estimated SD of ΔH^\ddagger (mean value) as a function of the relative accuracy of measurement ($\sigma(y)/y$). Temperature interval 10°C . Number of points 181.

Table 2. Typical results from Varytemp simulations. Values within paranthesis indicate fixed (not estimated) values due to choice of model. Units the same as in Table 1. All estimated values are mean values.

$\sigma(y)/y$	0.0002	0.0005	0.0005	0.0005	0.001	0.002	0.0005	0.0005	0.0005	0.0005
$\sigma(T)$	0.002	0.002	0.001	0.0003	0.002	0.001	0.0005	0.0005	0.0005	0.0005
Temp. interval	10	10	20	10	20	10	10	10	10	10
No. of simulations	35	35	35	35	35	35	1	1	1	5
True ΔH^\ddagger	12.23	7.912	12.23	12.23	12.23	12.23	12.23	12.23	12.23	12.23
Mean est. ΔH^\ddagger	12.232	7.932	12.217	12.221	12.236	12.229	12.243	12.327	12.200	12.246
True SD(ΔH^\ddagger) $\times 10^3$	1.1	0.7	1.8	2.3	3.3	10	—	—	—	6.2
Est. SD(ΔH^\ddagger) $\times 10^3$	2.0	3.1	2.5	4.9	3.5	20	4.0	2.5	6.4	4.2
True $\Delta S^\ddagger \times (-1)$	30.36	41.70	30.36	30.36	30.36	30.36	30.36	30.36	30.36	30.36
Mean est. $\Delta S^\ddagger \times (-1)$	30.352	41.63	30.402	30.433	30.340	30.356	30.315	30.034	30.460	30.307
True SD(ΔS^\ddagger) $\times 10^3$	4	2	6	8	11	35	—	—	—	2
Est. SD(ΔS^\ddagger) $\times 10^3$	7	10	8	16	11	66	13	8	21	14
True Δc_p^\ddagger	-35	-2	-35	-35	-2	-2	-2	-2	-2	-2
Mean est. Δc_p^\ddagger	-34.5	(-2)	-30	(-2)	(-2)	(-2)	(-2)	(-2)	(-2)	(-2)
True SD(Δc_p^\ddagger)	7	—	11	—	—	—	—	—	—	—
Est. SD(Δc_p^\ddagger)	13	—	8	—	—	—	—	—	—	—

Fig. 2 shows the corresponding plot for Δc_p^\ddagger . The figures show values estimated with temperature intervals of 10°C; these

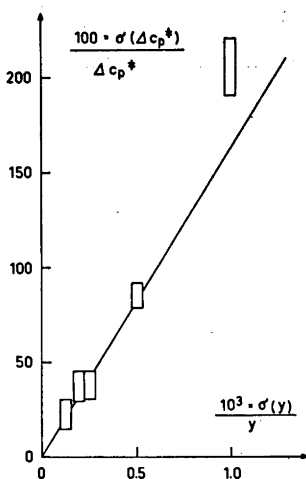


Fig. 2. Estimated SD of Δc_p^\ddagger (mean value) as a function of the relative accuracy of measurement ($\sigma(y)/y$). Temperature interval 10°C. Number of points 181.

values are to be multiplied by the correction factors $10/\Delta T$ and $(10/\Delta T)^2$, respectively, if a temperature interval of ΔT is used, since ΔH is computed from the linear variation of $\log(k)$ with T , Δc_p^\ddagger 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 Δc_p^\ddagger one should use a temperature interval of 20°C.

Finally it can be seen that with this accuracy ΔH^\ddagger 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.

Acknowledgements. The author is greatly indebted to professor Göran Bergson, professor Herman Wold and fil.lic. Per Ahlberg for valuable discussions.

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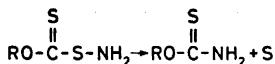
Sulfur Extrusion Reactions

I. On the Decomposition of *S*-(Alkoxythiocarbonyl)thiohydroxylamines

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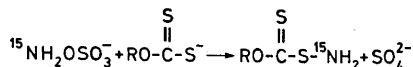
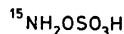
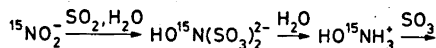
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S-(Alkoxythiocarbonyl)thiohydroxylamines have been prepared from *O*-alkyldithiocarbonates and hydroxylamine-*O*-sulfonate.¹ They are colourless liquids which are stable at low temperature (*e.g.* -30°C), whereas they decompose slowly at room temperature.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



As part of an investigation of the mechanism of sulfur elimination from this type of compound, exchange experiments have been carried out using ¹⁵N labelled *S*-(alkoxythiocarbonyl)-thiohydroxylamines, which were prepared from Na¹⁵NO₂ (97.4% ¹⁵N) *via* the following reaction sequence.^{2,3}

¹⁵N labelled *S*-(isopropoxythiocarbonyl)-thiohydroxylamine was mixed with unlabelled *S*-(ethoxythiocarbonyl)-thiohydroxylamine, and allowed to decompose at room temperature over a period of 4 weeks.



Since the mass spectra of *O*-ethyl thiocarbamate and *O*-isopropyl thiocarbamate 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 ¹⁵N 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*-C₃H₇OC(=S)¹⁵NH₂ (Ia), *i*-C₃H₇OC(=S)¹⁴NH₂ (Ib), C₂H₅OC(=S)-¹⁵NH₂ (IIa), and C₂H₅OC(=S)¹⁴NH₂ (IIb). Since the decomposition quantitatively leads to the formation of *O*-alkyl thiocarbamates, the ratios obtained show that ¹⁵N 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 ¹⁵N labelled *O*-ethyl thiocarbamate could have been the result of an exchange within the undecomposed *S*-(alkoxythiocarbonyl)-thiohydroxylamines. However, because of the absence of the relevant ions ((CH₃)₂-CHOC(=S)S¹⁴NH₂ and C₂H₅OC(=S)S-¹⁵NH₂), such an exchange can be excluded with certainty.

Analogous results were obtained from an exchange experiment using ¹⁵N labelled *S*-(methoxythiocarbonyl)-thiohydroxylamine and *S*-(ethoxythiocarbonyl)-thiohydroxylamine.

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