

Chemistry from Telephone Numbers: The False Isokinetic Relationship

George C. McBane

Department of Chemistry

The Ohio State University

September 30, 1998

Abstract

The “isokinetic relationship” is a purported linear relationship among the enthalpies and entropies of activation along a series of reactions. The standard technique for determining whether an isokinetic relationship holds for a particular group of reactions is incorrect, and will “discover” the relationship where it does not exist. The paper describes an amusing example of its failure, shows why the false correlations occur, and gives brief descriptions of correct approaches and references to them.

1 Introduction

Kenneth Connors's textbook *Chemical Kinetics: The Study of Reaction Rates in Solution* (1) contains an interesting homework problem:

From the last four digits of the office telephone numbers of the faculty in your department, systematically construct pairs of "rate constants" as two-digit numbers times 10^{-5} s^{-1} at temperatures 300 K and 315 K (obviously the larger rate constant of each pair to be associated with the higher temperature). Make a two-point Arrhenius plot for each faculty member, evaluating ΔH^\ddagger and ΔS^\ddagger . Examine the plot of ΔH^\ddagger against ΔS^\ddagger for evidence of an isokinetic relationship.

I assigned this problem to the students in my graduate chemical kinetics course. The ΔH^\ddagger vs. ΔS^\ddagger plot from a typical solution set is shown in Figure 1. The students were mostly astonished at the result; the naively calculated correlation coefficient r is 0.9999.

2 The isokinetic relationship

Consider a series of reactions which are sufficiently similar that one might expect the same mechanism to operate along the series. The oxidations of ethanol, n-propanol, n-butanol, etc., to their corresponding acids are an example. Since the alkyl chain is not expected to participate in the reaction in any important way, the properties of the transition state for the rate limiting step of each oxidation should be similar. If that is the case, one might expect the enthalpy and entropy of activation ΔH^\ddagger and ΔS^\ddagger to change in a simple way as the chain length of the substrate is increased. The term *isokinetic relationship* was first defined as a linear dependence of ΔH^\ddagger on ΔS^\ddagger for a series of reactions (labeled by n):

$$\Delta H_n^\ddagger = \beta \Delta S_n^\ddagger + \Delta H_0^\ddagger. \quad (1)$$

If that relationship holds, then at temperature β all the reactions in the series have the same rate coefficient. β is therefore called the isokinetic temperature. In practice β has usually been positive, so that the changes in rate coefficients along a series are less extreme than would be expected purely on the basis of enthalpy changes. That observation has led to the

alternative term *compensation effect* for the isokinetic relationship.

3 History

Correlations between enthalpies and entropies were noted early in chemistry, but were not widely used until Leffler published (2) a long list of $\Delta H^\ddagger - \Delta S^\ddagger$ correlations of apparently high quality and suggested chemical interpretations. More examples and analysis were given in Leffler and Grunwald's influential textbook *Rates and Equilibria of Organic Reactions* (3). Rather quickly, some workers expressed concerns about experimental errors in the measured ΔH^\ddagger and ΔS^\ddagger values and how they might contribute to spurious correlations, and two papers (4, 5) showed that the problem is really caused not by experimental errors but by an inherent correlation between ΔH^\ddagger and ΔS^\ddagger which arises when both are computed from the same data set.

Exner reviewed the problem in 1973, showing that the use of $\Delta H^\ddagger - \Delta S^\ddagger$ plots invariably leads to poor results, and also showing how to use an accurate statistical treatment on the *untransformed* data to ascertain the existence of a linear isokinetic relationship along a reaction series and to evaluate the isokinetic temperature and its uncertainty (6). Exner gave a good review

of the literature up to that point and the reader is referred to his paper for further background.

Since 1973, discussions of the isokinetic relationship and its use in interpreting other correlation parameters such as Hammett's ρ have appeared in many places. Some have fully stated the errors inherent in the $\Delta H^\ddagger - \Delta S^\ddagger$ treatment, some have given some warnings but not expressed the real danger, and others have not seemed to notice that a problem exists. The present paper is intended to slow the proliferation of the problem by calling it to the attention of chemical educators, to present a simple analysis of the problem that makes the origin of the false correlations clear, and to draw general conclusions about the procedures of correlation analysis. The procedure described here also constitutes a simple, qualitative "litmus test" which can be applied to nearly any correlation procedure.

4 Origin of the false correlation

The problem expressed in terms of telephone numbers is simpler than the treatment of real kinetic data, where rate coefficients at more than two temperatures might be measured for each reaction and where the experimental

temperatures for different reactions might not be the same. Exner (6) and Krug et al. (7,8) have described good procedures for treatment of real chemical data. However, the spurious correlations appear for exactly the same reasons in the simpler phone number problem and it affords a clear picture of their origin.

The phone number problem implies specific constraints. The rate coefficients always have values between 0 (practically, 1) and $99 \cdot 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$, and the rate coefficient is always higher at higher temperature. The (k_1, k_2) data pairs are therefore always located in the region of (k_1, k_2) space outlined in the upper panel of Figure 2. A search for correlations in the data must at least be a test of the hypothesis that the distribution of rate pairs inside that region is not uniform. If the correlations are to be sought in a different space than the original one, then the uniform probability distribution should be transformed to the new space and the distribution of transformed data must be shown to be different from the transformed uniform distribution. In fact, a uniform distribution of (k_1, k_2) pairs transforms to a highly correlated distribution of $(\Delta S^\ddagger, \Delta H^\ddagger)$ pairs.

4.1 Formulation of the problem

The necessary transformation of a probability distribution function $P(k_1, k_2)$ over a region R into a new function $P'(\Delta S^\ddagger, \Delta H^\ddagger)$ has two parts. First, the boundary of the region R must be mapped into the corresponding boundary R' in the new space. Second, the Jacobian (or “area element”) J must be evaluated over the region R . If the Jacobian has the same sign throughout R , then the new distribution in the $(\Delta S^\ddagger, \Delta H^\ddagger)$ space is given by

$$P'(\Delta S^\ddagger, \Delta H^\ddagger) = P(k_1(\Delta S^\ddagger, \Delta H^\ddagger), k_2(\Delta S^\ddagger, \Delta H^\ddagger)) |J| \quad (2)$$

where the functions $k_1(\Delta S^\ddagger, \Delta H^\ddagger)$ and $k_2(\Delta S^\ddagger, \Delta H^\ddagger)$ give the original variables in terms of the transformed ones. The transformation is defined by the transition state theory expressions for the rate coefficients (9):

$$k = \frac{k_B T}{h} \exp\left(\frac{\Delta S^\ddagger}{R}\right) \exp\left(-\frac{\Delta H^\ddagger}{RT}\right) (c^\ominus)^{(1-m)}. \quad (3)$$

In eq 3, k_B and h are Boltzmann’s and Planck’s constants respectively, R is the gas constant, c^\ominus is the concentration in the standard state to which the activation parameters ΔS^\ddagger and ΔH^\ddagger are referred, and m is the “molecularity”

(unity for a unimolecular reaction, 2 for a bimolecular reaction, and so on). For compactness of notation I define the rate coefficients k_1 and k_2 to be the coefficients measured at temperatures T_1 and T_2 respectively, divided by the concentration units $(c^\ominus)^{(1-m)}$; this definition forces the coefficients to have units of inverse seconds. The transformation from $(\Delta S^\ddagger, \Delta H^\ddagger)$ space to (k_1, k_2) space is obtained by inserting first k_1 and T_1 and then k_2 and T_2 into eq 3:

$$k_1 = \frac{k_B T_1}{h} \exp\left(\frac{\Delta S^\ddagger}{R}\right) \exp\left(-\frac{\Delta H^\ddagger}{RT_1}\right), \quad (4)$$

$$k_2 = \frac{k_B T_2}{h} \exp\left(\frac{\Delta S^\ddagger}{R}\right) \exp\left(-\frac{\Delta H^\ddagger}{RT_2}\right). \quad (5)$$

The transformation from (k_1, k_2) space to $(\Delta S^\ddagger, \Delta H^\ddagger)$ space is obtained by inverting eqs 4–5:

$$\Delta H^\ddagger = R \left(\frac{T_1 T_2}{T_1 - T_2} \right) \ln \left(\frac{k_1 T_2}{k_2 T_1} \right), \quad (6)$$

$$\Delta S^\ddagger = R \left(\frac{T_1 T_2}{T_1 - T_2} \right) \left[\frac{1}{T_2} \ln \left(\frac{h k_1}{k_B T_1} \right) - \frac{1}{T_1} \ln \left(\frac{h k_2}{k_B T_2} \right) \right]. \quad (7)$$

4.2 Transformation of the boundary

The constraints on measured rate coefficients in the phone number problem are $k_{\min} \leq k_1$, $k_2 \leq k_{\max}$, and $k_1 \leq k_2$. The boundary of the accessible region in (k_1, k_2) space is therefore formed by the three lines $k_1 = k_{\min}$ (boundary (a) in Figure 2), $k_2 = k_{\max}$ (boundary (b)), and $k_1 = k_2$ (boundary (c)). Inserting those relations in turn into eqs 6 and 7 and then eliminating k_1 or k_2 between the two yields the following expressions for the boundary in $(\Delta S^\ddagger, \Delta H^\ddagger)$ space:

$$\Delta H^\ddagger = \begin{cases} T_1 \left(\Delta S^\ddagger - R \ln \left(\frac{hk_{\min}}{k_B T_1} \right) \right) & \text{on boundary (a)} \\ T_2 \left(\Delta S^\ddagger - R \ln \left(\frac{hk_{\max}}{k_B T_2} \right) \right) & \text{(b)} \\ R \left(\frac{T_1 T_2}{T_1 - T_2} \right) \ln \left(\frac{T_2}{T_1} \right) & \text{(c)} \end{cases} \quad (8)$$

A plot of the transformed boundary assuming bimolecular reaction, a standard state of 1 mol L^{-1} and the values of k_{\min} , k_{\max} , T_1 , and T_2 suggested by Connors is shown in the lower panel of Figure 2. One reason for the false correlation is immediately apparent: the boundary of the accessible region in (k_1, k_2) space becomes a sharply acute triangle in $(\Delta S^\ddagger, \Delta H^\ddagger)$ space. All the possible $(\Delta S^\ddagger, \Delta H^\ddagger)$ pairs must fall within the new boundary. If the $(\Delta S^\ddagger, \Delta H^\ddagger)$ pairs cover most of the possible values of ΔS^\ddagger , then a respectable

linear correlation cannot fail to appear.

If experimental errors are associated with the kinetic data, then each point in the (k_1, k_2) space is replaced by a region of finite size, typically an ellipse. Note that those ellipses will all be mapped into the long, narrow triangular region in $(\Delta S^\ddagger, \Delta H^\ddagger)$ space as well, so experimental error will not tend to make the false correlations appear worse. Also note that increasing the value of k_{\max} to allow larger variations in the rate coefficients will tend to extend boundaries (a) and (b) with little effect on the length of boundary (c). The limited range of rate coefficient magnitudes in the phone number problem is therefore not a crucial restriction.

4.3 Transformation of the Probability Distribution

A uniform probability distribution

$$P(k_1, k_2) = \frac{2}{(k_{\max} - k_{\min})^2} \quad (9)$$

in the original space will probably not be uniform in the new space. To calculate the new distribution, the Jacobian of the transformation, defined

by

$$J = \begin{vmatrix} \left(\frac{\partial k_1}{\partial \Delta S^\ddagger}\right) & \left(\frac{\partial k_1}{\partial \Delta H^\ddagger}\right) \\ \left(\frac{\partial k_2}{\partial \Delta S^\ddagger}\right) & \left(\frac{\partial k_2}{\partial \Delta H^\ddagger}\right) \end{vmatrix}, \quad (10)$$

where the vertical bars denote the determinant, is required. Evaluation of J is straightforward from eqs 4 and 5; the result is

$$J = \left(\frac{k_B}{Rh}\right)^2 (T_2 - T_1) \exp\left(\frac{2\Delta S^\ddagger}{R}\right) \exp\left(-\frac{\Delta H^\ddagger}{R} \left(\frac{1}{T_1} + \frac{1}{T_2}\right)\right). \quad (11)$$

The Jacobian is positive throughout the region, so the new probability distribution is (from eqs 2, 9, and 11)

$$P'(\Delta S^\ddagger, \Delta H^\ddagger) = \frac{2}{(k_{\max} - k_{\min})^2} \left(\frac{k_B}{Rh}\right)^2 (T_2 - T_1) \exp\left(\frac{2\Delta S^\ddagger}{R}\right) \exp\left(-\frac{\Delta H^\ddagger}{R} \left(\frac{1}{T_1} + \frac{1}{T_2}\right)\right). \quad (12)$$

This new distribution is the product of an exponentially increasing function of ΔS^\ddagger and an exponentially decreasing function of ΔH^\ddagger . For any particular value of ΔH^\ddagger , the corresponding value of ΔS^\ddagger will tend toward high values, meaning that the $(\Delta S^\ddagger, \Delta H^\ddagger)$ pairs will tend to accumulate toward the right-hand side of the region in Figure 2. Similarly, for any value of ΔS^\ddagger , the points will tend toward the lower boundary of the region. The net effect is that points in $(\Delta S^\ddagger, \Delta H^\ddagger)$ space will tend to cluster along boundary (b)

in Figure 2, rather than filling the available region uniformly. The probability distribution strengthens the correlation introduced by the long, narrow shape of the new boundary. Figure 3 was created with the same data used in Figure 1, but using $T_2 = 600$ K instead of 315 K to provide a wider region in $(\Delta S^\ddagger, \Delta H^\ddagger)$ space. The influence of the transformed probability distribution is clear.

Since the slope of the boundary line (b) is T_2 , the “isokinetic temperature” obtained from this analysis will tend to be close to T_2 as well. When a real reaction series is misanalyzed this way, the isokinetic temperature obtained will usually be close to the higher end of the temperature range used for the experimental measurements.

5 Discussion

Is there a real isokinetic relationship with chemical meaning? Yes. One way to find it is to overlay rate constant data for all the reactions in the series of interest on a single Arrhenius plot, and look for a point of common intersection among the best-fit lines. The temperature corresponding to the abscissa of the intersection is the isokinetic temperature β , at which all the

reactions have the same rate coefficient. If no point of common intersection exists within experimental error, then an isokinetic relationship cannot be said to hold for the series of reactions. Often the common intersection point lies well outside the range of experimentally accessible temperatures, and the uncertainty in β will be large. Exner's treatment is essentially a quantitative version of this approach based on least-squares fitting.

Exner suggests another very simple method, applicable when rate constants at two well-separated temperatures are available for each reaction. If plots are made simply of $\log k_1$ vs. $\log k_2$, linear correlation implies a valid isokinetic relationship. However, the method is useful mostly for "quick and dirty" evaluations because it is limited to the two-temperature case.

Krug et al. (7, 8) have suggested another means of searching for isokinetic relationships. They recommend evaluating $\Delta G_{T_{\text{hm}}}^\ddagger$ and ΔH^\ddagger from the kinetic data and searching for correlations in the ΔH^\ddagger - $\Delta G_{T_{\text{hm}}}^\ddagger$ plane, where $\Delta G_{T_{\text{hm}}}^\ddagger$ is the estimated Gibbs energy of activation at the "harmonic mean" experimental temperature, $T_{\text{hm}} = \langle \frac{1}{T_i} \rangle^{-1}$. ΔH^\ddagger and $\Delta G_{T_{\text{hm}}}^\ddagger$ can be evaluated in a way that leaves their values uncorrelated (that is, their covariance near zero).

Both the simple $\log k_1$ vs. $\log k_2$ plot and the treatment of Krug et al.

remove the main problem of the $\Delta H^\ddagger - \Delta S^\ddagger$ approach, the transformation of the boundary of the data region into a very long, narrow region in the target space. The behavior of their Jacobians for transformation of a uniform distribution into the target space is similar to the $\Delta H^\ddagger - \Delta S^\ddagger$ case, however. The plots in $(\log k_1, \log k_2)$ or $(\Delta H^\ddagger, \Delta G_{T_{\text{hm}}}^\ddagger)$ space will consequently nearly always “look better” than plots in the (k_1, k_2) plane. Careful least-squares treatments are therefore a necessity; the paper of Krug et al. describes a good approach in detail.

6 Conclusion

The isokinetic relationship illustrates a general principle in empirical work. Generally, correlations among directly observed data values will be meaningful. If the search is carried out among functions of the variables, one must be careful to distinguish between correlations which are purely mathematical in nature and ones which have physical meaning. The simple test used here, analysis of a uniform distribution by the chosen technique, might serve as an initial “reality check” in many cases.

Literature Cited

1. Connors, K. A. *Chemical Kinetics: The Study of Reaction Rates in Solution*; VCH: New York, 1990.
2. Leffler, J. E. *J. Org. Chem.* **1955**, *20*, 1202–1231.
3. Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963.
4. Petersen, R. C. *J. Org. Chem.* **1964**, *29*, 3133–3135.
5. Exner, O. *Nature* **1964**, *201*, 488–490.
6. Exner, O. *Prog. Phys. Org. Chem.* **1973**, *10*, 411–482.
7. Krug, R. R.; Hunter, W. G.; Grieger, R. A. *J. Phys. Chem.* **1976**, *80*, 2335–2341.
8. Krug, R. R.; Hunter, W. G.; Grieger, R. A. *J. Phys. Chem.* **1976**, *80*, 2341–2351.
9. Robinson, P. J. *J. Chem. Educ.* **1978**, *55*, 509–510.

7 Figure Captions

Figure 1. Typical solution plot for the phone number problem.

Figure 2. Upper panel: Boundary of accessible (k_1, k_2) values. Lower panel: Corresponding boundary in $(\Delta S^\ddagger, \Delta H^\ddagger)$ space.

Figure 3. Points and boundary assuming $T_2 = 600$ K.

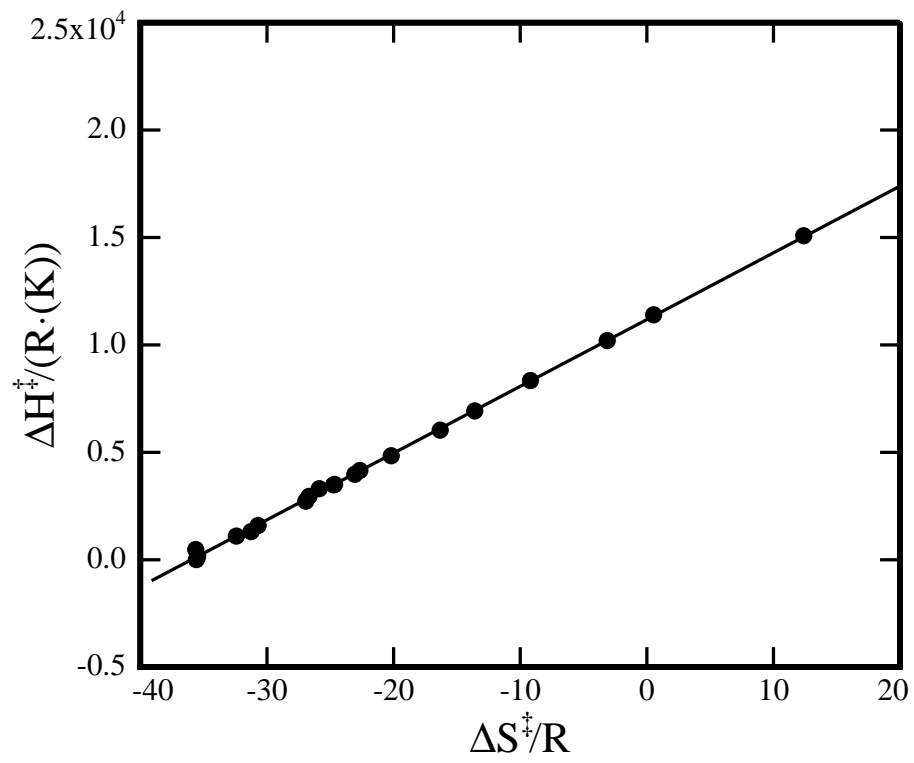


Figure 1: Typical solution for the phone number problem.

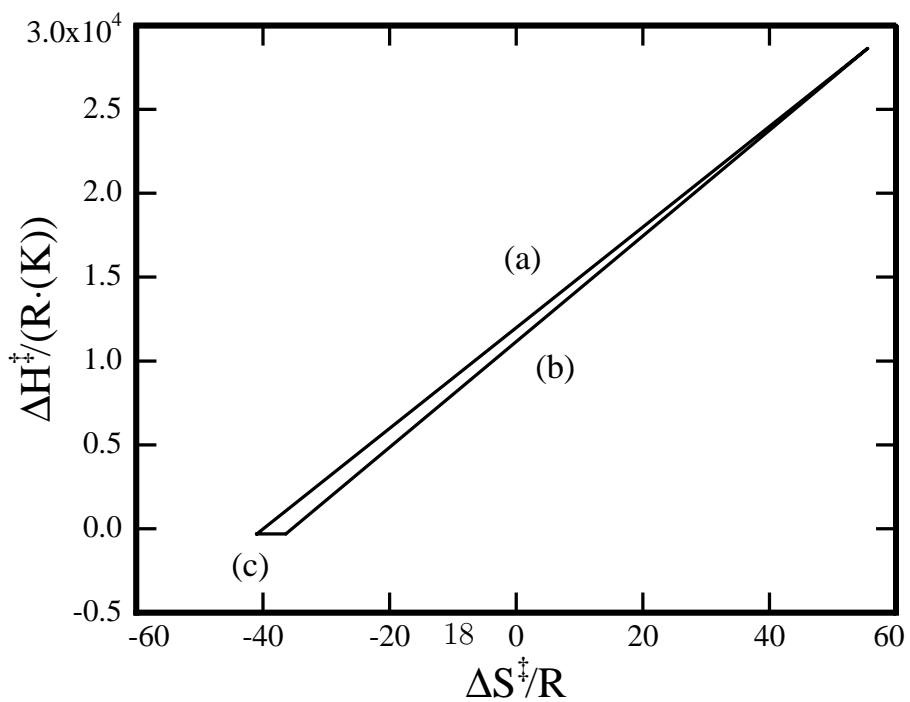
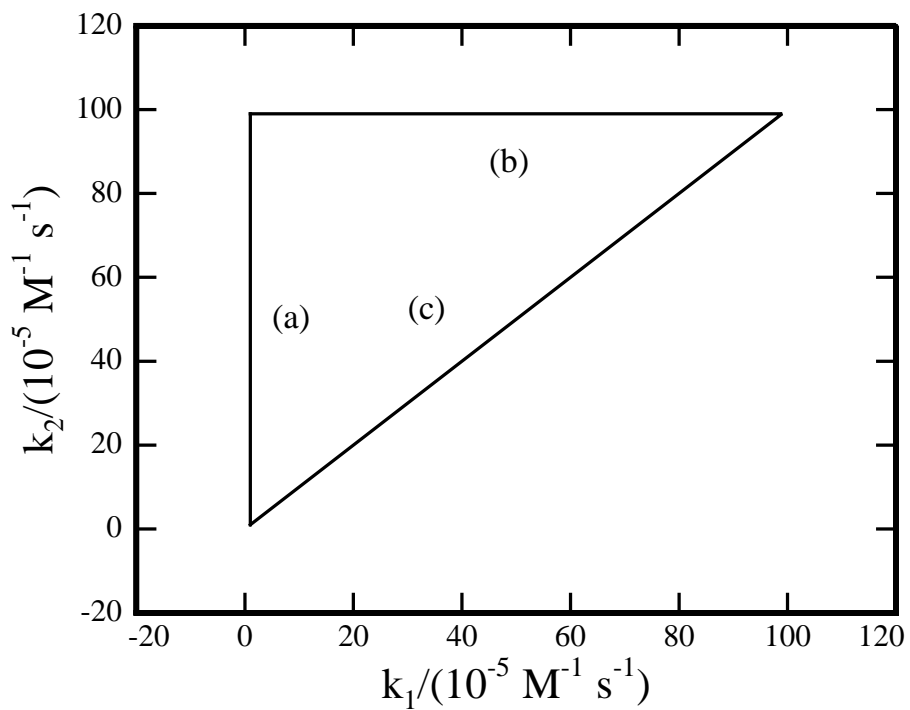


Figure 2: Upper panel: Boundary of accessible (k_1, k_2) values. Lower panel: Corresponding boundary in $(\Delta S^\ddagger, \Delta H^\ddagger)$ space.

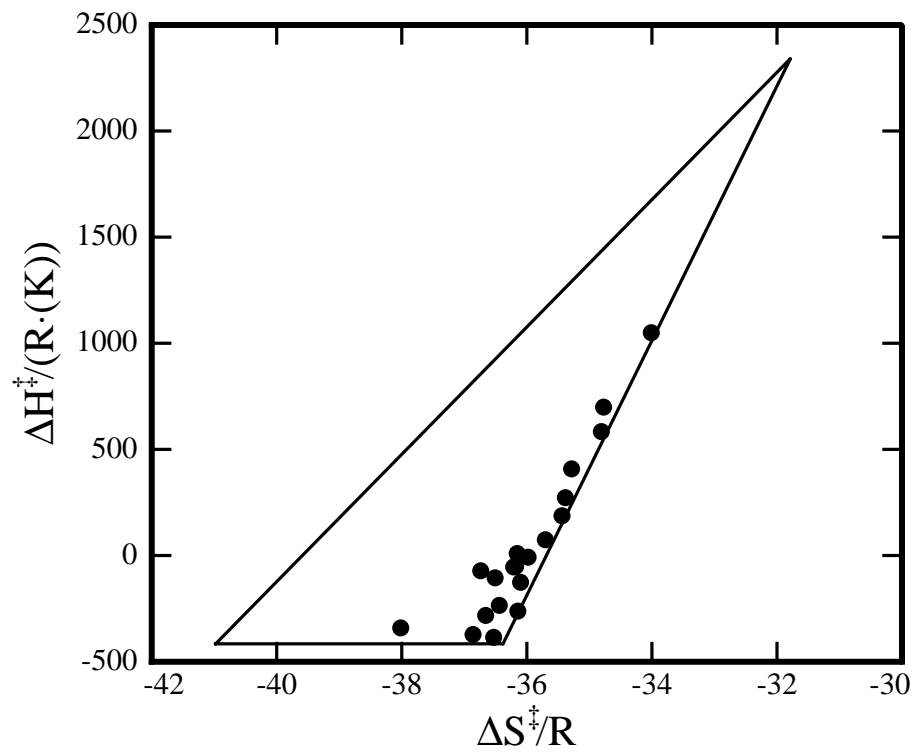


Figure 3: Points and boundary assuming $T_2 = 600$ K