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DETERMINATION OF THE EXISTENCE, VALUE AND UNCERTAINTY OF THE COMPENSATION OR ISOKINETIC TEMPERATURE

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The demonstration of the existence of a compensation effect, the linear dependence of the enthalpy on the entropy for a series of chemical reactions, is often complicated by an apparent linear dependence arising solely from experimental errors. A non-linear least squares method has been developed for establishing the existence or non-existence of a compensation effect and for determining the value of the compensation temperature if the effect exists. The uncertainty in the value of the compensation temperature can be determined by means of a Monte Carlo procedure. If a compensation effect does not exist, three cases can be distinguished: (1) the relationship between the enthalpy and entropy is linear, but the compensation temperature is 0 K; (2) the various reactions cannot be distinguished from each other because of experimental errors; and (3) the reactions do differ, but the relationship (if one exists) between the enthalpy and entropy is not linear. The method is illustrated using both hypothetical and experimental examples.

INTRODUCTION

A van't Hoff plot of $R \ln K$ vs $-1/T$, where K is the equilibrium constant for a chemical reaction at temperature T and R is the gas constant, gives rise to a straight line whose slope is ΔH and intercept is ΔS, assuming that both ΔH and ΔS are independent of temperature. Similarly, an Arrhenius plot of $R \ln k$ vs $-1/T$, where k is the rate constant, also results in a straight line. The slope and intercept of this line are the activation energy and the logarithm of the pre-exponential factor, respectively, which are related to the enthalpy and entropy of activation for the reaction. In this treatment we make the customary assumption that the pre-exponential factor is independent of temperature.

If either Arrhenius or van't Hoff plots are generated for a series of related chemical reactions and the (activation) enthalpies are plotted against the (activation) entropies, the result is often a straight line. This linear relationship is called a compensation effect or, in the case of kinetic data, an isokinetic effect. The slope, which has dimensions of temperature, is called the compensation or isokinetic temperature. This effect was first described by Leffler in his seminal 1955 paper.[1]

Compensation effects are widespread in chemistry. In a review, Linert[2] cites a large variety of studies in such areas as catalysis, vaporization, solid-state interdiffusion, thermal dissociation, electron diffusion in organic semiconductors, pharmaceutical and biochemical systems, electrode kinetics, chemical adsorption and the viscosity of liquids.

Although a linear relationship between the enthalpy and entropy in a series of reactions can be due to the underlying chemistry of the reactions, it is often simply an artifact of the experimental uncertainties in measuring the equilibrium or rate constants. To differentiate between these two effects, we shall refer to the linear correlation induced by experimental errors as the pseudo-compensation effect and to a real relationship as simply a compensation effect.

The nature of the pseudo-compensation problem was first elucidated by Exner.[3] The pseudo-compensation effect arises because the slope and intercept for each van't Hoff or Arrhenius plot are correlated. The values of $R \ln K$ ($R \ln k$) and $1/T$, on the other hand, are statistically independent because their values are obtained from separate independent experiments. Exner's key insight into this problem was the realization that if a true compensation effect exists, and if all the van't Hoff or Arrhenius lines are plotted on a single $R \ln K$ ($R \ln k$) vs $1/T$ plane, then these lines will intersect in a single point whose abscissa is the reciprocal of the true compensation temperature. In essence, Exner rec-

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ognized that the linear (compensation) relationship between ΔH and ΔS, whose uncertainties are correlated, can be reformulated as a non-linear relationship between $R \ln K$ ($R \ln k$), whose uncertainties are uncorrelated, and $1/T$, whose values can be assumed to have zero uncertainty.

The work based on these ideas analyzes the various linear relationships obtained by plotting all the data on a single $\ln k$ vs $1/T$ plane. For example, Linert[4] examined the following sums of squares of deviations: first, the experimental points for each reaction from the straight line 'constrained' by the hypothesis of the existence of a real isokinetic effect to pass through the point of intersection of all the Arrhenius lines; and second, the experimental points for each reaction from the original Arrhenius line unconstrained by this hypothesis. The abscissa of the point that minimizes the first sum of squares is the candidate for the isokinetic temperature. The existence of the isokinetic effect and hence of this temperature is validated by examining whether the ratio of the two sums of squares is small as measured by the Fisher–Pearson *F*-test. Note that this statistical test, a parametric one, is used only to determine the existence of a compensation effect; it does not provide an estimate of the uncertainty in the value of the compensation temperature. Other methods, such as that of Krug,[5] also use parametric statistical methods to analyze linear relationships (in this case a ΔG vs ΔH relationship). Krug's method, unlike Linert's, does provide estimates of confidence intervals for the compensation temperature.

In this paper, we show that the problem of determining the existence of, the value of and the uncertainty in a real compensation temperature is fundamentally a non-linear problem. We present a systematic method for determining a compensation or isokinetic temperature (if it exists) and its error. Because the problem is a non-linear one, parametric methods for estimating the uncertainty in the compensation temperature are not reliable. However, confidence intervals for the compensation temperature can be obtained using Monte Carlo methods. In addition, our method distinguishes among the various circumstances that result in the absence of a compensation effect.

THE PSEUDO-COMPENSATION EFFECT

Before presenting our method, we give a discussion of the origin of the pseudo-compensation effect. The purpose of this discussion is to delineate the circumstances for which the pseudo effect becomes a problem. Our examples, given later in this paper, will be based on these situations.

If a set of N data points (x_i, y_i) is fitted to a straight line by means of a least-squares analysis, the intercept, **a**, and the slope, **b**, are not independent parameters. If σ_i is the uncertainty in y_i (x_i is assumed to be error-free), the covariance σ_{ab}^2 is given by[6]

$$\sigma_{ab}^2 = -S_x/\Delta \tag{1}$$

where

$$\Delta = SS_{xx} - (S_x)^2 \tag{2a}$$

and

$$S = \sum_{i=1}^{N} 1/\sigma_i^2 \tag{2b}$$

$$S_x = \sum_{i=1}^{N} x_i/\sigma_i^2 \tag{2c}$$

$$S_{xx} = \sum_{i=1}^{N} x_i^2/\sigma_i^2 \tag{2d}$$

For the case of a van't Hoff plot for a single chemical reaction, we have $x_i = -1/T_i$, $y_i = R \ln K_i$, $\mathbf{a} = \Delta S$ and $\mathbf{b} = \Delta H$.

The correlation coefficient, r_{ab}, between the uncertainty in **a** and the uncertainty in **b** is given by[6]

$$r_{ab} = \sigma_{ab}^2/\sqrt{\sigma_a^2\sigma_b^2} = -S_x/\sqrt{SS_{xx}} \tag{3}$$

where σ_a^2 and σ_b^2, the variances in the estimates of **a** and **b**, respectively, are equal to

$$\sigma_a^2 = S_{xx}/\Delta \quad \text{and} \quad \sigma_b^2 = S/\Delta \tag{4}$$

The correlation coefficient takes values between -1 and 1. A correlation of 1 or -1 implies a perfect linear relationship between **b** and **a**; a correlation of 0 implies that these two parameters are uncorrelated, i.e. their covariance is zero.

Consider the experiment in which several, say **n**, reactions are analyzed. Assume that the set of temperatures used for generating the van't Hoff plot for each reaction is the same. Now suppose that for each temperature the errors in the measured quantity $R \ln K$ are large, i.e. of the same order of magnitude as the difference among the values of $R \ln K$ for the different reactions. For this situation, the **n** data sets for the **n** reactions can be considered to be replicates of each other. Consequently, the standard deviation of the **n** values of **a** (which we denote by Q_a) obtained from the **n** reactions is approximately equal to σ_a, the uncertainty in **a** obtained from any one of the reactions using equation (4). Similarly, the standard deviation of the **n** values of **b** (Q_b) is approximately equal to σ_b, and the covariance between the **n** values of **a** and the **n** values of **b** (Q_{ab}^2) is approximately equal to σ_{ab}^2, obtained from equation (1).

Now plot the **n** values of **b** (i.e. the values of ΔH) versus the corresponding **n** values of **a** (the values of ΔS), assume a linear relationship and calculate the correlation, r, and the slope of the line, β, using standard linear regression techniques:[6]

$$r = Q_{ab}^2/Q_aQ_b \quad \text{and} \quad \beta = rQ_a/Q_b \tag{5}$$

Since the Qs are approximately equal to the corresponding σs, $r = r_{ab}$, and we can make use of equation (3) to find

$$\beta = r_{ab}\sigma_b/\sigma_a = -S_x/S_{xx} \qquad (6)$$

This slope is equal to the pseudo-compensation temperature. From equations (6) and (2), we see that the actual measured values of $R \ln K$ do not appear in the expression for the pseudo-compensation temperature, a result also found by Krug *et al.*[7] The slope depends only on the x_i $(-1/T_i)$ and on the σ_i, the errors in the values of $R \ln K$. Any linear relationship between ΔH and ΔS arises because the errors in the measured values of $R \ln K$ are large enough to allow the **n** data sets from the **n** van't Hoff plots to be considered replicates of each other. As first noted by Exner,[3] the existence of a pseudo-compensation effect and temperature is completely independent of the possibility of the existence or absence of a real chemical relationship between ΔH and ΔS for a series of reactions.

How well do the plotted points (ΔH vs ΔS) fit the regression line whose slope is β? If for the sake of simplicity we choose σ_i to be a constant for all i, equation (6) becomes

$$\beta = \frac{\sum_{i=1}^{N} 1/T_i}{\sum_{i=1}^{N} 1/T_i^2} \qquad (7)$$

This equation shows that as the range of the experimental temperatures decreases, all the temperatures approach some common value, and the value of β, the pseudo-compensation temperature, approaches this common value. Further, from equations 3 and 2, we see that as the range of temperatures decreases, the correlation coefficient increases and reaches its maximum value of 1 in the limit of a single experimental temperature. In this limiting case, all **n** points in the plot of ΔH vs ΔS lie precisely on the line with slope β.

It should now be evident from this discussion and the equations given above why the pseudo-compensation effect is such a problem for equilibrium and kinetic studies. The temperatures are all positive, the range of temperatures is usually small and the errors in the measurement of the equilibrium or rate constants are often large. For example, in a very careful van't Hoff experiment, seven temperatures 283, 293, ..., 343 K might be chosen. If the errors in measuring the equilibrium constants are large, the compensation temperature derived from equation (7) is 310 K and the correlation coefficient is 0·998. Since the fit of the plot of the enthalpies vs the entropies to a straight line is so good in this case, it is extremely difficult to distinguish a 'real' thermodynamic or isokinetic effect from the pseudo-effect.

DETERMINATION OF THE COMPENSATION TEMPERATURE AND ITS UNCERTAINTY

The pseudo-compensation temperature arises because the ΔH and ΔS determined from a van't Hoff or Arrhenius plot are correlated as a result of the experimental errors in measuring $R \ln K$ or $R \ln k$. When ΔH is plotted against ΔS in order to determine a compensation temperature, this pseudo-correlation interferes with the determination of the presence or absence of a correlation arising from a chemical cause. In order to overcome this problem we analyze all the $R \ln K$ vs $-1/T$ data obtained from all the reactions simultaneously.

For each reaction i, where i ranges from 1 to n, and for each temperature T_{ij}, where j ranges from 1 to N_i, the number of data points for the ith reaction, the van't Hoff relationship yields

$$R \ln K_{ij} = (\Delta H_i)(-1/T_{ij}) + \Delta S_i \qquad (8)$$

with a similar relationship for the iskinetic effect. Note that the number of temperatures and their values need not be the same for each reaction.

The existence of a compensation temperature β implies that

$$\Delta H_i = \alpha + \beta\, \Delta S_i \qquad (9)$$

Substituting equation 9 into equation 8, we obtain

$$R \ln K_{ij} = (\alpha + \beta\, \Delta S_i)(-1/T_{ij}) + \Delta S_i \qquad (10)$$

We now have a set of $\Sigma_i N_i$ equations with $n + 2$ parameters (α, β and the n values of $\Delta\ S_i$). The values of these parameters are to be adjusted in order to best fit the model represented by equation (10). Although these equations are still linear in $-1/T_{ij}$, they are not linear in the parameters. Consequently, a non-linear least-squares procedure must be used to determine the optimized values of the parameters. We used the Levenberg–Marquardt algorithm as implemented by Press *et al.*[6] to solve the non-linear regression problem.

The Levenberg–Marquardt algorithm determines the optimized values of adjustable parameters by minimizing χ^2,

$$\chi^2 = \sum_{i=1}^{n} \sum_{j=1}^{N_i} (y_{ij} - Y_{ij})^2/\sigma_{ij}^2 \qquad (11)$$

the weighted sum of the squares of the deviations of the measured values, $R \ln K_{ij}$ [y_{ij} in equation (11)], from the values calculated using equation 10 [Y_{ij} in equation (11)]. The calculation of Y_{ij} requires initial estimates of ΔS_i, α and β. Initial estimates of ΔS_i are obtained from the van't Hoff plots and those of α and β from the intercept and slope of the plot of ΔH vs ΔS.

When the optimized values of the parameters are substituted into equation (11), χ^2 becomes the goodness-of-fit statistic, providing a measure of the degree to which the data are fitted by the model equations. If the data are well described by the model, the value of χ^2 will be approximately equal to the number of degrees of freedom, $\Sigma_i N_i - (n+2)$; if not, χ^2 would be expected to be significantly larger than this number of degrees of freedom.

In order to apply the Levenberg–Marquardt algorithm, it is necessary to obtain an estimate of σ_{ij}, the uncertainty in each measured value of $R \ln K_{ij}$. If *a priori* estimates of the measurement errors are available then these, of course, would be used. If they are not available, we assume that the uncertainty in each of the measured values in the ith van't Hoff or Arrhenius plot is the same ($\sigma_{ij} = \sigma_i$, for all j). The uncertainty in each measured value used in this ith plot can then be estimated by means of the equation

$$\sigma_i^2 = \frac{1}{N_i - 2} \sum_{j=1}^{N_i} (y_{ij} - Y_{ij})^2 \tag{12}$$

The divisor $N_i - 2$ is used rather than N_i in order to make σ_i^2 unbiased.

Since β is calculated simultaneously with the ΔS_i, the pseudo-correlation between the enthalpy and entropy does not affect the value of β. However, although the Levenberg–Marquardt algorithm provides a value of β, we still must determine whether this value corresponds to a compensation temperature.

The absence of a compensation effect means that there is no correlation between the 'true' values of ΔH and ΔS. Equation (6) shows that $r = 0$ implies $\beta = 0$. Thus, if the Levenberg–Marquardt algorithm returns a value of 0 for β, or if for $\beta \neq 0$ the uncertainty in β is sufficiently large that the appropriate confidence interval about β encompasses 0, then we could conclude that there is no compensation effect. Moreover, if χ^2 were much larger than the number of degrees of freedom, we could conclude that the data do not fit the mathematical model implied by the existence of a compensation effect.

Because the model equation is not linear in its parameters, standard methods using parametric statistics for estimating the uncertainty in β or the other parameters cannot be used. In linear least-squares analyses, the diagonal elements of the covariance matrix give the variances of the adjustable parameters.[6] Confidence intervals for these parameters can then be obtained using the Student t-statistic. For non-linear problems, this is not the case.[6] Although the diagonal elements of the covariance matrix still provides the variances, the t-statistic cannot be used to derive confidence intervals because the distribution of the parameters is not Gaussian (normal). To overcome this difficulty, a Monte Carlo method can be used to obtain accurate estimates of the uncertainties of the parameters.[8] A parametric (Student t) estimate of the confidence intervals often differs from the Monte Carlo estimate by a factor of >2–3[9,10] and in some cases by a factor of 10.[10]

DISCUSSION

We believe that the non-linear regression method for determining compensation temperatures has several advantages over previous methods. First, the method is conceptually obvious; it simply implements the definition of the compensation effect in such a manner as to eliminate spurious correlations between the enthalpy and entropy. Second, and perhaps of greater importance, the method is able to categorize families of reactions more precisely than merely dividing them into those families that exhibit a true compensation effect and those that do not.

The classification divides families of reactions into two primary categories: first, those for which the goodness-of-fit statistic, χ^2, is approximately equal to the number of degrees of freedom, and second, those for which χ^2 is much larger than the number of degrees of freedom. The first category can, in turn, be separated into three subcategories: (a) if β [defined in equations (9) and (10)] is not equal to 0, a compensation effect exists and the compensation temperature is equal to β; (b) if $\beta = 0$, the data are consistent with a simpler model in which the reactions are isoenthalpic; the apparent differences in the values of ΔH obtained from the van't Hoff or Arrhenius plots are due entirely to experimental error; and (c) if the value of β is not well determined by the data, i.e. any arbitrarily chosen β results in an acceptable χ^2, we cannot distinguish the data from the situation in which all the reactions are replicates of each other. The various values of ΔS and ΔH represent randomly scattered data from a single hypothetical true ΔS, ΔH point. The slope of a line passing through this one point is not determined, and thus any value of the slope will fit the data. This is the case with the pseudo-compensation effect discussed above.

A family of reactions for which the non-linear regression analysis gives a large χ^2 falls into the second primary category. A large χ^2 means that the data do not fit the model. The reactions are indeed different but there is no linear compensation effect. Either reactions with the same ΔS have different values of ΔH or the relationship between ΔH and ΔS is not linear. These various categories and subcategories described in this and the preceding paragraphs are illustrated in the examples in the following sections.

In certain respects, the non-linear regression method is similar to the method described by Linert.[4] Both methods use the $R \ln k$ vs $1/T$ data directly to determine compensation temperatures, thus avoiding the spurious correlations induced by experimental errors. However, unlike the Linert method, the present treatment does not rely on the artificial constraint that the van't Hoff or Arrhenius lines all pass through a single point. In addition, it provides the χ^2 statistic and, further, permits the calculation of confidence intervals for the compensation temperature. The Linert method yields only the probability that an isokinetic effect exists.

Hypothetical examples

In order to illustrate the non-linear least-squares method, we have constructed examples using hypothetical data sets. These examples show that the method can establish the existence or non-existence of a compensation temperature and, if it exists, determine its value and uncertainty.

We generated data for eight hypothetical reactions. We chose eight values for ΔS (-60, -70, -80, -87, -96, -104, -116 and $-125\ \mathrm{J\ mol^{-1}\ K^{-1}}$), chose $\Delta H = -12{\cdot}10\ \mathrm{kJ\ mol^{-1}}$ for the first reaction, assumed a value of the compensation temperature (either 0 or 200 K) and then calculated the value of ΔH corresponding to the remaining seven values of ΔS. For each reaction, we constructed an exact data set of $R \ln K$ vs $-1/T$ using equation (8), where T took the values 283, 293, 303, ..., 343 K for each reaction. Finally, we simulated errors in $R \ln K$ by adding to each value of $R \ln K$ a random number equal to an estimate of the uncertainty in $R \ln K$ times a randomly chosen Gaussian deviate, i.e. a normally distributed random variable with a mean of 0 and a variance of 1. In a given example, we chose a single value for the uncertainty in $R \ln K$ irrespective of the temperature or the reaction. In order to simplify the analysis further while retaining the important features, the data sets in these examples differ only in the choice of compensation temperature and in the choice of the single value of the uncertainty in $R \ln K$.

For each reaction, we used a linear least-squares procedure to generate the van't Hoff plot and obtained values of ΔH and ΔS. Another linear least-squares calculation using the eight sets of enthalpies and entropies provided the slope and intercept and their uncertainties. The calculation of these uncertainties included the contributions from the uncertainties in both ΔH and ΔS and from their covariance. Recall that the slope of this plot is the pseudo-compensation temperature.

We analysed the $R \ln K$ vs $-1/T$ data for the eight reactions using the non-linear least-squares method. We note at this point that if we were analysing a real experiment, the uncertainty in each of the measured values of $R \ln K_{ij}$ could be used in equation (11). If these uncertainties were not available, a single uncertainty for each of the values of $R \ln K$ obtained for a given reaction could be derived from the deviations of the experimental points from the van't Hoff line for that reaction. In each of the hypothetical examples described below, we used a single value of σ_{ij} to obtain values of the compensation temperature. Confidence intervals for the compensation temperature were obtained using a Monte Carlo simulation procedure described elsewhere.[8,9] In order to ensure accurate confidence intervals, 400 simulations were performed for each of the examples described below.

Compensation effect is present

As discussed above, in the limit in which the experimental errors are so large that the data for the different reactions are simply replicates, the pseudo-compensation temperature will equal 310 K. In order to distinguish this temperature from a real compensation temperature, we chose a compensation temperature of 200 K. We performed calculations using two values of the uncertainty in $R \ln K$, namely $0{\cdot}1R$ and $0{\cdot}5R$. The smaller absolute uncertainty corresponds to relative uncertainties of approximately 5% for the smallest values of $R \ln K$ and 1.6% for the largest values. More important, the uncertainty of $0{\cdot}1R$ in $R \ln K$ represents 1.3% of the range of the values of ΔS. The relative uncertainties and percentage of the range of ΔS corresponding to the absolute uncertainty of $0{\cdot}5R$ are of course five times larger. The results of the calculations of the compensation and pseudo-compensation temperatures and their uncertainties are given in Table 1.

When the experimental error is small ($0{\cdot}1R$), the regression of enthalpy vs entropy gives a slope of 205 ± 9 K. The uncertainty is the standard error. The non-linear regression calculation of the compensation temperature gave a value of 203 ± 9 K. This uncertainty corresponds to the Monte Carlo 68.3% con-

Table 1. Analysis of the hypothetical equilibrium data

	Compensation temperature[a,b]			
	200	200	0	0
Error in $\ln K$[a]	0·1	0·5	0·1	0·5
Calculated pseudo-compensation temperature	205	274	−8	200
Standard error in calculated pseudo-compensation temperature	9	12	28	36
χ^2 from non-linear regression analysis	43	43	39	37
Degrees of freedom	46	46	46	46
Calculated compensation temperature	203	206	−20	−7
Half-width of 68·3% confidence interval	9	30	29	20
Half-width of 90% confidence interval	15	62	43	70

[a] Values used in constructing the example.

[b] All temperatures are in K.

fidence interval. The values of the compensation and pseudo-compensation temperatures agree with each other and with the value of 200 K used to generate the data set. Finally, $\chi^2 = 43$, a value in good agreement with the number of degrees of freedom, namely $(8 \times 7) - (8 + 2) = 46$.

When the experimental error is five times larger, corresponding to 6.4% of the range of ΔS, the apparent compensation temperature is 274 ± 12 K, a spurious value which approaches the pseudo-compensation temperature of 310 K calculated using equation (7). The non-linear regression calculation gives an essentially correct value of 206 ± 30 K. The difference between these two temperatures is statistically significant with 99% confidence. As was the case for the previous example, the value of χ^2 found by the non-linear regression, in this case 43, is in agreement with the number of degrees of freedom.

Compensation effect is absent

We now examine the results using data sets with the same temperatures and the same values of entropies, but with the compensation temperature set at 0 K. Recall that a compensation temperature of 0 K means that the enthalpies and entropies are not correlated. As in the examples of non-zero compensation temperatures, we perform calculations first with a small $(0 \cdot 1R)$ and then with a larger $(0 \cdot 5R)$ estimate of the uncertainty in $R \ln K$. The results of these calculations are also given in Table 1. The results are totally analogous to those for the case where the compensation temperature was 200 K.

When the experimental error is small $(0 \cdot 1R)$, the plot of enthalpy vs entropy shows a pseudo-compensation temperature of −8 ± 28 K, whereas the non-linear regression analysis gives a value of −20 ± 29 K. When the error is larger $(0 \cdot 5R)$, the pseudo-compensation temperature found from the enthalpy–entropy plot is significantly different from the true compensation temperature. The pseudo-compensation temperature was found to be 200 ± 36 K. The non-linear regression gave a compensation temperature −7 ± 20 K, a value consistent with the hypothesis that no compensation effect is present, i.e. that ΔH does not depend on ΔS.

In order to illustrate the case in which all the reactions are replicates of each other, we fixed ΔS at $-60\ \mathrm{J\ mol^{-1}\ K^{-1}}$ and ΔH at $-12 \cdot 10\ \mathrm{kJ\ mol^{-1}}$ for each of the eight reactions. The values of $R \ln K$ were scattered using an uncertainty of $0 \cdot 1R$. Even though the uncertainty in $R \ln K$ is small, the plot of ΔH vs ΔS gave a pseudo-compensation temperature of 315 ± 9 K. To show that any value of a compensation temperature would fit the data in the non-linear regression, we performed six different non-linear regressions. In each regression β was fixed at one of the values 0, 100, 200, ..., 500 K. The six different values of χ^2 all lay between 42·4 and 44·1, indicating that any one of these compensation temperatures fits the data. In view of our earlier discussion, these results are entirely expected. The $R \ln K$ vs $-1/T$ data do not determine a unique value of β and the different reactions share common values of ΔS and ΔH.

Real examples

Three calculations were performed with real data sets involving the dependence of the rate constant on temperature for a series of reactions: (1) the hydrolysis of ethyl benzoate in various solvents,[11] (2) the oximation of thymyl ketones[12] and (3) the thermal rearrangement of triarylmethyl azides.[13] Since no experimental uncertainties were given for the data in the first two studies, the errors in the rate constants were derived from the scatter of the data about each Arrhenius plot using equation (12). The results of the calculations are given in Table 2.

The ethyl benzoate study showed clear evidence of a compensation effect. Rates for twelve reactions at four temperatures were measured. The slope of the enthalpy–entropy plot was 438 ± 8 K, whereas the non-linear regression gave a value of 444 K. The half-widths of the 68·3% and 95% Monte Carlo confidence intervals were 9 and 18 K, respectively. The value of χ^2 for the non-linear regression was 36, in agreement with the number of degrees of freedom, $(12 \times 4) - 14 = 34$.

The oximation study, on the other hand, showed the absence of a compensation effect. In this study, rates for seven reactions at only three temperatures were measured. The slope of the enthalpy–entropy plot was 316 ± 4 K whereas the non-linear regression value was −16 ± 9 K. The 95% Monte Carlo confidence interval is −16 ± 27 K and includes 0 K. Recall that a slope of 0 K implies that there is no correlation between enthalpy and entropy, and thus no compensation effect. The value of χ^2 and the number of degrees of freedom, 14 and 12, respectively, were again in appropriate agreement. The near-zero value for the compensation temperature and the goodness-of-fit imply that a simpler model in which the activation energies for the various reactions are equal to a constant would fit the data. In this model [see equation (9)], $\beta = 0$. Fixing the value of β at zero in the non-linear regression, the value of χ^2 was 14, in agreement with the 13 degrees of freedom in the system.

The set of azide rearrangement reactions provides an example of the case where the data do not fit the model of a compensation effect. Rates for three temperatures were measured for eight different reactions. Experimental uncertainties associated with these measured rate constants are given in Ref. 13. However, these uncertainties appear to underestimate severely the size of the errors; using them resulted in values of χ^2 in the Arrhenius plots that were orders of magnitude too

Table 2. Analysis of the experimental kinetic data

	Hydrolysis of ethyl benzoate[a]	Oximation of thymyl ketones[b]	Rearrangement of triarylmethyl azides[c]
Calculated pseudo-compensation temperature[d,e]	438	316	486
Error in calculated pseudo-compensation temperature[e]	8	4	9
χ^2 from non-linear regression analysis[e]	36	14	65
Degrees of freedom[e]	34	12	14
Calculated compensation temperature[e]	444	−16	481
Half-width of 68.3% confidence interval[e]	9	9	5
Half-width of 95% confidence interval[e]	18	27	11
Krug *et al.*'s value of compensation temperature[f]	422		476
Krug *et al.*'s 95% confidence interval for the compensation temperature[f]	401–431		471–486

[a] Data from Ref. 11.
[b] Data from Ref. 12.
[c] Data from Ref. 13.
[d] All temperatures are in K.
[e] This work.
[f] Ref. 14. No compensation effect found for oximations. See text.

large. We therefore used the scatter of $R \ln k$ about the Arrhenius lines as described earlier to estimate the uncertainties of $R \ln k$ for each of the eight reactions.

Although the best value of the compensation temperature given by the non-linear regression is 481 K, in good agreement with the value of 477 K found by plotting ΔH vs ΔS, the value of χ^2 is 65, considerably larger than the number of degrees of freedom, 14. A table of the distribution of χ^2 indicates that the probability that χ^2 is this large simply due to chance is much less than 0·001. The unacceptably large value of χ^2 might be due to chemical effects or to the presence of one or two outlier values of ΔS. We compared the Arrhenius ΔS estimates with those obtained from the non-linear regression. The differences appear to be randomly distributed, that is, the large value of χ^2 is not due to one or two severe outliers. Instead, the set of differences $y_{ij} - Y_{ij}$ appear to be characterized by a normal distribution. We thus conclude that the family of azide reactions are not characterized by a compensation temperature; there is no linear relationship between ΔH and ΔS. Moreover, the deviations of the $R \ln k$ vs $-1/T$ data from the model represent systematic deviations which are not explained by the random experimental uncertainties. These systematic deviations may be due to either chemical phenomena or to systematic measurement errors.

The interpretation of the χ^2 statistic in terms of probabilities relies on the assumption that the values of $R \ln k$ are normally distributed. Even though this assumption may appear to be reasonable, we require only that the value of χ^2 be accurate as an order-of-magnitude estimate. For example, we interpret the result that the probability of χ^2 being equal to 65 for a system with 14 degrees of freedom is much less than 0·001 to mean that it is unlikely that the observed value of χ^2 is a result arising from random error alone. Even if the actual value of χ^2 were such that the probability were ten times larger, we would still conclude that it is legitimate to reject the hypothesis that a compensation effect exists.

Our results for the first two studies are consistent with the corresponding analyses of Krug *et al.*,[7,14] who found a compensation effect in the first but not in the second study. However, they were not able to determine that the absence of a compensation effect was due to a compensation temperature of 0 K, i.e. that the oximation reactions are isoenthalpic, as was readily apparent from the non-linear regression analysis.

Krug *et al.*[14] did find a compensation temperature for the azide rearrangement reactions in the range 470·7–485·6 K, where this range represents the 95% confidence interval. Although the non-linear regression algorithm found a best fit of the data at a temperature of 481 K, lying well within that interval, we believe that the goodness-of-fit as characterized by χ^2 is too poor to enable us to accept the hypothesis that a compensation temperature exists.

CONCLUSIONS

The non-linear least squares method for determining compensation temperatures together with the Monte Carlo method for estimating confidence intervals for these temperatures provide a systematic means of establishing the existence, value and uncertainty of a compensation temperature. Once the uncertainty in the measured values of $R \ln K$ or $R \ln k$ has been determined, either from an *a priori* estimate or from the deviations of the experimental points from the appropriate van't Hoff or Arrhenius lines, the value of χ^2, the magnitude of the calculated compensation temperature and its associated confidence interval provide an indication of whether a true compensation effect exists. If no compensation effect exists, the analysis provides a means of determining whether the various reactions are (1) isoenthalpic or (2) replicates of each other with common values of ΔS and of ΔH (χ^2 is approximately equal to the number of degrees of freedom) or (3) whether the reactions are intrinsically different but that any possible relationship between the enthalpy and entropy is not linear (χ^2 is large).

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