Treball Final de Grau

Theoretical study of the enthalpy-entropy compensation effect in chemical kinetics

Estudi teòric de l’efecte de compensació entalpia-entropia en cinètica química

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At the heart of science is an essential balance between two seemingly contradictory attitudes—an openness to new ideas, no matter how bizarre or counterintuitive they may be, and the most ruthless skeptical scrutiny of all ideas, old and new. This is how deep truths are winnowed from deep nonsense.

Carl Sagan

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1. SUMMARY

Many kinetic studies concerning homologous reaction series report the existence of an activation enthalpy-entropy linear correlation (compensation plot), its slope being the temperature at which all the members of the series have the same rate constant (isokinetic temperature). Unfortunately, it has been demonstrated by statistical methods that the experimental errors associated with the activation enthalpy and entropy are mutually interdependent. Therefore, the possibility that some of those correlations might be caused by accidental errors has been explored by numerical simulations. As a result of this study, a computer program has been developed to evaluate the probability that experimental errors might lead to a linear compensation plot parting from an initial randomly scattered set of activation parameters (p-test). Application of this program to kinetic data for 100 homologous reaction series extracted from bibliographic sources has allowed concluding that most of the reported compensation plots can hardly be explained by the accumulation of experimental errors, thus requiring the existence of a previously existing, physically meaningful correlation.

Keywords: activation parameters, compensation effect, experimental errors, isokinetic temperature, numerical simulations.
2. Resum

Nombrosos estudis cinètics sobre sèries de reaccions homologues mostren l’existència d’una correlació lineal entre l’entalpia i l’entropia d’activació (efecte de compensació), sent el pendent de la recta la temperatura en la que tots els membres de la sèrie tenen la mateixa constant de velocitat (temperatura isocinètica). Desafortunadament, s’ha demostrat mitjançant mètodes estadístics que els errors experimentals associats amb l’obtenció de l’entalpia i entropia d’activació són mútuament interdependents. Per aquest motiu, la possibilitat que aquestes correlacions puguin ser causades per errors accidentals ha estat explorada mitjançant simulacions numèriques. Com a resultat d’aquest estudi, s’ha desenvolupat un programa per avaluar la probabilitat que els errors experimentals puguin explicar una correlació lineal entalpia-entropia partint d’una situació inicial en la que els paràmetres d’activació es troben distribuïts a l’atzar ($p$-test). L’aplicació d’aquest programa a dades cinètiques per a 100 sèries de reaccions homologues extretes de la bibliografia ha permès concloure que la majoria de les gràfiques de compensació descrites a la literatura no poden explicar-se per l’acumulació d’errors experimentals en les seves mesures. Per tant, es requereix l’existència d’una correlació prèvia físicament significativa entre aquests paràmetres d’activació.

Paraules clau: efecte de compensació, errors experimentals, paràmetres d’activació, simulacions numèriques, temperatura isocinètica.
3. INTRODUCTION

A common practice in chemical kinetics that provides useful information on the reaction mechanism is to study a series of closely related processes, differing among them either in the nature of an inert substituent in one of the reactant molecules\(^1,2\) or in the solvent employed to perform the experiments.\(^3,4\) An intriguing result often found in this kind of kinetic studies is the observation of a linear correlation between the activation parameters [activation energy \((E_a)\) and logarithm of the pre-exponential factor \((A)\) or, alternatively, enthalpy \((\Delta H^\circ_x)\) and entropy \((\Delta S^\circ_x)\) of activation] corresponding to the members of the homologous series.\(^5\)

The existence of such linear relationship would be important at a theoretical level because it can be easily demonstrated that it would imply that at a certain temperature (called isokinetic temperature) all the members of the reaction series have the same rate constant.\(^6\) Unfortunately, it has been shown by statistical methods that the experimental errors associated with the activation energy and the logarithm of the pre-exponential factor are not mutually independent. In fact, they are linearly related, with a slope that depends on the mean experimental temperature.\(^7-9\) The same can be stated with respect to the errors associated with the enthalpy and entropy of activation. As a consequence, when the divergences between the activation parameters for a series of related reactions are small in comparison with their respective experimental errors, a linear relationship tends to appear both in the \(E_a\) vs. \(\ln A\) and \(\Delta H^\circ_x\) vs. \(\Delta S^\circ_x\) planes.

Because of this, some authors have considered that the so-called enthalpy-entropy compensation effect is a mere artefact derived from experimental errors.\(^10,11\) However, other authors have argued that in certain cases, when the errors are quite small in comparison with the divergences between the activation parameters for the different members of the reaction series, the linear correlation must be considered as physically meaningful and caused by a mechanism other than the experimental errors committed in the determination of the activation parameters. Several theories have been proposed to explain the origin of this statistically meaningful compensation effect. A comprehensive review developing some of them has been published.\(^12\) More recently, other theoretical interpretations of this phenomenon have been
reported, such as the models of selective energy transfer (SET)\textsuperscript{13} or multiexcitation entropy.\textsuperscript{14} Nevertheless, although many different explanations of the kinetic compensation effect have been propounded, a generally accepted theory is still missing.

An interesting point in this context is the fact that this kind of linear relationships tends to appear not only in the field of chemical kinetics, but also in other disciplines working with different processes ruled by mathematical laws of the type:

\[
y = y_\infty e^{-\frac{x}{T}}
\]

where \(y_\infty\) is the value of the magnitude \(y\) at \(T = \infty\) and \(x\) has the units of an absolute temperature. In the experimental studies involving this type of equations it is often found that there exists a correlation between the values of \(x\) and \(y_\infty\), so that when one of them increases the other increases too. For instance, in chemical thermodynamics it has been found an enthalpy-entropy compensation effect for the temperature dependence of the equilibrium constants corresponding to many homologous reaction series (isoequilibrium relationships).\textsuperscript{15} In addition, similar compensation effects have been reported for a wide range of phenomena including those such as heating-induced changes in food chemistry,\textsuperscript{16} protein folding/unfolding and ligand binding/unbinding in biochemistry,\textsuperscript{17} as well as polymer relaxation,\textsuperscript{18} thermal electron emission from semiconductor traps\textsuperscript{19} and electron conduction\textsuperscript{20} in physics. Precisely, this ubiquitous character of the compensation effect makes it important as an objective of research.

4. Objectives

Three different objectives will be considered in this project. Given that it has been predicted by statistical methods that the experimental errors committed in the determination of the kinetic data may lead to linear activation enthalpy-entropy relationships, even when the real activation parameters for the different members of the reaction series are not actually correlated, the first part of the present work will be dedicated to confirm this prediction. Therefore, numerical simulations will be performed in order to clarify if the effect of experimental errors is enough to
explain the existence of a $\Delta H^0_\infty$ vs. $\Delta S^0_\infty$ linear correlation when the real activation parameters for the reaction series are randomly scattered.

Once confirmed this point, and due to the fact that the experimental errors may in that case lead to spurious enthalpy-entropy linear correlations, it would be convenient to develop a test capable to discriminate whether the relationship is caused by the uncertainties associated with the experiments or by the existence of a physically meaningful phenomenon. Although some authors have published partially useful tools for this purpose, the search for a different alternative, potentially providing more useful information, will be the second objective of this theoretical research.

After the test is actually found, it will be used to check its applicability to different experimental enthalpy-entropy linear correlations extracted from the chemical kinetics literature (third objective).

The rationale for this research project can be summarized as follows: to try to extract useful information on the real kinetic behavior of the homologous series of reactions from the pattern observed in the laboratory, since the latter is strongly contaminated by experimental errors.

5. METHODS AND CALCULATIONS

5.1. STATISTICAL METHODS

Both the $(E_a, \ln A)$ and $(\Delta H^0_\infty, \Delta S^0_\infty)$ couples of simulated data where fitted to linear relationships by means of the following mathematical expressions\textsuperscript{23} derived from the method of least squares:

$$a = \frac{\sum_{i=1}^{N} x_i^2 \sum_{i=1}^{N} y_i - \sum_{i=1}^{N} x_i \sum_{i=1}^{N} x_i y_i}{N \sum_{i=1}^{N} x_i^2 - (\sum_{i=1}^{N} x_i)^2}$$

(2)
where $x_i$ and $y_i$ stand respectively for the abscissa and ordinate of each couple of data, $N$ is the total number of points, $a$ the intercept and $b$ the slope of the straight line, $r$ the correlation coefficient, $E(a)$ the intercept error and $E(b)$ the slope error.

### 5.2. Random-number Generator

Several programs where written in BASIC language in order to simulate the effect of accidental errors on the isokinetic relationships. All of them shared two different generators of
random numbers, both starting with the calculation of the square root of a series of non-integer numbers, one in the increasing \( (J + n) \) and the other in the decreasing \( (L + n) \) directions, where \( J \) took the integer values from 1 to a fixed maximum limit \( (N) \) and \( L \) decreased in the opposite direction, \( \eta \) being a non-integer number (to avoid the occurrence of perfect squares). The random values were taken from the different decimal digits of the corresponding square roots (either \( \sqrt{J + n} \) or \( \sqrt{L + n} \)), and an aleatory positive or negative sign was ascribed depending on the nature of the first digit (even or odd). These ensembles of random numbers were used with two finalities: to obtain a set of scattered couples \( (\Delta H^o, \Delta S^o) \) with no enthalpy-entropy correlation, and to simulate the accidental errors associated with the experimental determination of the rate constants at different temperatures.

5.3. CALCULATIONS AND GRAPHICS

The hardware used in all the numerical simulations and figures was either a Sony Vaio or a Toshiba personal computer, and the software employed for the calculations was the programming language BBC BASIC (version for Windows) and for the graphics the program KaleidaGraph (version 4.03).

6. THEORETICAL BACKGROUND

The dependence of the rate constants on the absolute temperature is given by the Arrhenius equation:

\[
k = A e^{-\frac{E_a}{RT}}
\]

where \( A \) is the pre-exponential factor, \( R \) the gas constant and \( E_a \) the activation energy of the process. According to the chemistry literature, when this equation is applied to the different members of a homologous reaction series it is often found that there exists a linear relationship between the Arrhenius parameters:

\[
E_a = E_{a,o} + RT_{ik} \ln A
\]
where the intercept, \( E_{a,o} \), is the activation energy for a hypothetical member of the series with a pre-exponential factor \( A = 1 \) (usually s\(^{-1}\) or M\(^{-1}\) s\(^{-1}\)), and \( T_{ik} \) is the isokinetic temperature. The reason why the latter parameter receives this name is because it can be easily demonstrated that when \( T = T_{ik} \) all the reactions of the series have the same rate constant. Effectively, by substitution of eq 10 into eq 9 it can be obtained that:

\[
k_{is\,o} = f e^{-\frac{E_{a,o}}{RT_{ik}}}
\]  

(11)

\( f \) being a unit-conversion factor (1 s\(^{-1}\) for first-order reactions and 1 M\(^{-1}\) s\(^{-1}\) for second-order reactions). It follows immediately from eq 11 that all the reactions have the same value of the rate constant \( (k_{is\,o}) \) at that temperature, because both \( E_{a,o} \) and \( T_{ik} \) are constant for the homologous series.

On the other hand, the temperature dependence of the rate constants can be described, as an alternative to the Arrhenius law, by means of the Eyring equation:

\[
k = \frac{k_B T}{h} \left( c^o \right)^{1-n} e^{\frac{\Delta S^o}{R}} e^{-\frac{\Delta H^o}{RT}}
\]  

(12)

\( k_B \) and \( h \) being respectively the Boltzmann and Plank constants, \( c^o \) the standard concentration (1 mol L\(^{-1}\)), \( \Delta S^o \) the activation entropy and \( \Delta H^o \) the activation enthalpy.

Each Eyring parameter is related with one of the Arrhenius parameters. In order to find these relationships, let us start by applying logarithms in both eqs 9 and 12:

\[
\ln k = \ln A - \frac{E_a}{RT}
\]  

(13)

\[
\ln k = \ln \left[ \frac{k_B T (c^o)^{1-n}}{h} \right] + \frac{\Delta S^o}{R} - \frac{\Delta H^o}{RT}
\]  

(14)

Now, taking the corresponding derivatives with respect to temperature:

\[
\frac{d(\ln k)}{dT} = \frac{E_a}{RT^2}
\]  

(15)
Theoretical study of the enthalpy-entropy compensation effect in chemical kinetics

\[
\frac{d(\ln k)}{dT} = \frac{1}{T} + \frac{\Delta H^o}{RT^2}
\]  

(16)

and equaling both temperature dependences of the rate constant:

\[
E_a = \Delta H^o + RT_m
\]  

(17)

In eq 17 the variable temperature \( T \) has been replaced by its mean value \( T_m \). This approximation is only valid for narrow ranges of that variable, and the reason for its requirement comes from the assumption made by both Arrhenius and Eyring that their respective parameters are independent of it. Nevertheless, since the pre-exponential factor in eq 12 is directly proportional to the temperature (unlike that in eq 9), eqs 15 and 16 predict that the difference between the activation energy and enthalpy is temperature dependent. This anomaly is avoided by the use of \( T_m \) instead of \( T \).

From eqs 13, 14 and 17, the following relationship between the Arrhenius pre-exponential factor and the activation entropy can be deduced:

\[
\ln A = \ln \left[ \frac{e^{k_B T_m (c^o)^{1-n}}}{h} \right] + \frac{\Delta S^o}{R}
\]  

(18)

By substitution of eqs 17 and 18 into eq 10, it can be inferred:

\[
\Delta H^o = \Delta H^o_{\neq,0} + T_{ik} \Delta S^o_{\neq}
\]  

(19)

This means that, if there exists a linear relationship in the \( E_a \) vs. \( \ln A \) plane for a particular series of homologous reactions, then there must also exist one in the \( \Delta H^o_{\neq} \) vs. \( \Delta S^o_{\neq} \) plane. The intercept \( \Delta H^o_{\neq,0} \) has to be physically interpreted as the activation enthalpy corresponding to a hypothetical member of the series with \( \Delta S^o_{\neq} = 0 \), and it is correlated with the intercept involved in eq 10 by the following mathematical expression:
\[ E_{a,o} = \Delta H_{x,o} + RT_m + RT_{ik} \ln \left( \frac{h (c^o)^{n-1}}{e k_B T_m} \right) \]  

(20)

Finally, by application of the Eyring equation (eq 12) at the isokinetic temperature \( T = T_{ik} \) and replacement of the activation enthalpy (variable for each member of the reaction series) given by eq 19, it can be obtained that:

\[ k_{iso} = \frac{k_B T_{ik}}{h} \left( c^o \right)^{1-n} e^{-\frac{\Delta H_{x,o}^o}{RT_{ik}}} \]  

(21)

Since both \( \Delta H_{x,o}^o \) and \( T_{ik} \) are constant for the homologous series, eq 21 demonstrates that there exists a certain temperature \( T_{ik} \) at which all the related reactions have the same rate constant \( k_{iso} \), provided that the linear relationship defined by eq 19 holds.

### 7. Effect of Experimental Errors

It has been reported in the bibliography\(^7\)-\(^9\) that, when the temperature-rate-constant data are fitted according to an Arrhenius plot, the experimental errors associated with the pre-exponential factor and the activation energy are mutually interdependent. This result has been qualitatively illustrated in Figure 1.

It can be observed that, when the laboratory uncertainties lead to a linear plot (green line) with a slope more negative than that corresponding to the real reaction, the intercept associated with \( 1/T = 0 \) is higher than the value that would be obtained in the absence of errors (blue line). On the contrary, when the experimental errors lead to a linear plot (red line) with a slope less negative than that corresponding to the real reaction, the intercept is lower than that to be obtained in the absence of errors. This means that a positive error in the activation energy is always associated with a positive error in the pre-exponential factor, whereas a negative error in the activation energy is always associated with a negative error in the pre-exponential factor.
Given the relationships existing between the activation energy and enthalpy (eq 17) on the one hand, as well as between the pre-exponential factor and the activation entropy on the other (eq 18), this result can be easily extrapolated from the $E_a$ vs. $\ln A$ plane to the $\Delta H^o$ vs. $\Delta S^o$ one. Hence, it is clear that the ubiquity of experimental errors in all laboratory measurements should be considered as (at least) one of the possible explanations of the compensation effect: an increase of the activation energy (or the activation enthalpy) is usually associated with an increase of the pre-exponential factor (or the activation entropy), the former causing a decay of the reaction rate and the latter an enhancement, whereas a decrease of the first parameter (positive effect on the reaction rate) is very often associated with a decrease of the second (negative effect on the reaction rate), thus leading to the appearance of a compensation effect.

Hereafter, when the appearance of a compensation straight line is caused by experimental errors the corresponding slope shall be called apparent isokinetic temperature, reserving the name isokinetic temperature only for those cases (if any) in which the phenomenon has a different, physicochemically meaningful origin.
8. NUMERICAL SIMULATIONS

8.1. SIMULATION PROGRAMS

Some parameters had to be introduced at the beginning in order to perform the calculations. The first magnitudes required were the mean value \( T_m \) and the difference between the maximum and minimum values \( \Delta T \) of the experimental temperature. All the programs had in common the same set of 5 simulated kinetics experiments, corresponding to the temperatures \( T_m - (1/2) \Delta T, T_m - (1/4) \Delta T, T_m, T_m + (1/4) \Delta T \) and \( T_m + (1/2) \Delta T \).

In this part of the present research, it has been taken as an initial hypothesis that the real activation parameters corresponding to the different members of the reaction series present no correlation at all, parameter \( F \) measuring the dispersion factor of the enthalpy and entropy of activation with respect to the assumed mean values \( \Delta H_{\text{m},m}^{o} \) and \( \Delta S_{\text{m},m}^{o} \), according to the equations:

\[
\Delta X_{\neq}^{o} = \frac{100}{100 + FA_N} \Delta X_{\neq,m}^{o} \quad (22)
\]

\[
\Delta X_{\neq}^{o} = \left(1 + \frac{FA_N}{100}\right) \Delta X_{\neq,m}^{o} \quad (23)
\]

where \( X = H \) or \( S \), and \( A_N \) is an aleatory number \( (0 \leq A_N \leq 10) \), so that when \( F = 1 \) the maximum relative deviation with respect to the mean activation parameters is \( \pm 10.0\% \). These equations have been used to obtain activation parameters either lower (eq 22) or higher (eq 23) than the mean values, respectively, and were applied in a parity manner, each being responsible for a half of the simulated activation parameters.

An additional parameter necessary to start the simulations was the experimental error coefficient \( (Q) \), involved in the following equations relating the experimental \( (k_{\text{exp}}) \) and theoretical \( (k_{\text{th}}) \) rate constants:

\[
k_{\text{exp}} = \frac{100}{100 + QA_N} k_{\text{th}} \quad (24)
\]

\[
k_{\text{exp}} = \left(1 + \frac{QA_N}{100}\right) k_{\text{th}} \quad (25)
\]
This parameter quantifies the maximum uncertainty allowed to the laboratory determination of the rate constants, so that when \( Q = 1 \) the maximum relative accidental error is \( \pm 10.0 \% \). Again, eqs 24 and 25 were applied in a parity manner, each being responsible for a half of the simulated error-affected rate constants. The theoretical rate constants were obtained from the Eyring equation (eq 12), using the activation parameters given by eqs 22 and 23, whereas their experimental counterparts were either lower (eq 24) or higher (eq 25) than them.

The final parameter required was the number of members of the homologous reaction series \((N)\).

<table>
<thead>
<tr>
<th>Program</th>
<th>( T_m ) [K]</th>
<th>( \Delta T ) [K]</th>
<th>( \Delta H^0 , m ) [kJ mol(^{-1})]</th>
<th>( \Delta S^0 , m ) [J K(^{-1}) mol(^{-1})]</th>
<th>( F )</th>
<th>( Q )</th>
<th>( N )</th>
</tr>
</thead>
<tbody>
<tr>
<td>IKR-1</td>
<td>298.15</td>
<td>20.0</td>
<td>50</td>
<td>100</td>
<td>0</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>IKR-2</td>
<td>298.15</td>
<td>20.0</td>
<td>50</td>
<td>100</td>
<td>0 – 0.75</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>IKR-3</td>
<td>100 – 500</td>
<td>20.0</td>
<td>50</td>
<td>100</td>
<td>0 – 8.65</td>
<td>1</td>
<td>1000</td>
</tr>
<tr>
<td>IKR-4</td>
<td>100 – 500</td>
<td>20.0</td>
<td>50</td>
<td>100</td>
<td>0.25</td>
<td>0.1 – 8.7</td>
<td>1000</td>
</tr>
<tr>
<td>IKR-5</td>
<td>100 – 500</td>
<td>0.02 – 558.2</td>
<td>50</td>
<td>100</td>
<td>0.25</td>
<td>1</td>
<td>1000</td>
</tr>
<tr>
<td>IKR-6</td>
<td>100 – 500</td>
<td>20.0</td>
<td>0 – 1000</td>
<td>100</td>
<td>0.25</td>
<td>1</td>
<td>1000</td>
</tr>
<tr>
<td>IKR-7</td>
<td>100 – 500</td>
<td>20.0</td>
<td>50</td>
<td>0 – 1440</td>
<td>0.25</td>
<td>1</td>
<td>1000</td>
</tr>
</tbody>
</table>

(a) \( T_m \) is the mean experimental temperature and \( \Delta T \) the difference between its maximum and minimum values.

(b) \( \Delta H^0 , m \) and \( \Delta S^0 , m \) are the mean values of the activation parameters.

(c) \( F \) is the dispersion factor of the activation parameters and \( Q \) the experimental error coefficient of the rate constants.

(d) \( N \) is the number of members of the homologous reaction series.

Table 1. Parameters required for the numerical simulations.

The first program (IKR-1) was designed for the calculation of the pre-exponential factors and the activation energies of a simulated family of 100 homologous reactions, using for the linear fit the Arrhenius equation (with \( F = 0 \) and \( T_m = 298.15 \) K). The second (IKR-2) was aimed to obtain the enthalpy and entropy of activation (also for a series of 100 related reactions), employing in this case the Eyring equation (with a fixed value of \( F \) in the range \( 0 – 0.75 \) and \( T_m = 298.15 \) K). The remaining programs applied in this section were modifications of the former, using different values of the mean experimental temperature in the range \( T_m = 100 – 500 \) K and allowing in
each case the systematic change of one of the parameters involved in the calculations: the dispersion factor \( F \) in IKR-3, the experimental error coefficient \( Q \) in IKR-4, the difference between the maximum and minimum values of the experimental temperature \( \Delta T \) in IKR-5, the mean activation enthalpy \( \Delta H^{\circ}_{\neq,m} \) in IKR-6 and, finally, the mean activation entropy \( \Delta S^{\circ}_{\neq,m} \) in IKR-7. The parameters used in the performance of the distinct programs have been compiled in Table 1, whereas the magnitude varied systematically and the results looked for in each case are shown in Table 2.

<table>
<thead>
<tr>
<th>Program</th>
<th>Variable parameter</th>
<th>Printed parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>IKR-1</td>
<td>none</td>
<td>( \ln A ) and ( E_a )</td>
</tr>
<tr>
<td>IKR-2</td>
<td>none</td>
<td>( \Delta H^{\circ}<em>{\neq,m} ) and ( \Delta S^{\circ}</em>{\neq,m} )</td>
</tr>
<tr>
<td>IKR-3</td>
<td>( F )</td>
<td>( \Delta H^{\circ}<em>{\neq,0} ), ( E(\Delta H^{\circ}</em>{\neq,0}) ), ( T_{ik} ), ( E(T_{ik}) ) and ( r )</td>
</tr>
<tr>
<td>IKR-4</td>
<td>( Q )</td>
<td>( T_{ik} ) and ( r )</td>
</tr>
<tr>
<td>IKR-5</td>
<td>( \Delta T )</td>
<td>( T_{ik} ) and ( r )</td>
</tr>
<tr>
<td>IKR-6</td>
<td>( \Delta H^{\circ}_{\neq,m} )</td>
<td>( T_{ik} ) and ( r )</td>
</tr>
<tr>
<td>IKR-7</td>
<td>( \Delta S^{\circ}_{\neq,m} )</td>
<td>( T_{ik} ) and ( r )</td>
</tr>
</tbody>
</table>

(a) \( F \) is the dispersion factor of the activation parameters and \( Q \) the experimental error coefficient of the rate constants.
(b) \( \Delta T \) is the difference between the maximum and minimum values of the experimental temperature.
(c) \( \Delta H^{\circ}_{\neq,m} \) and \( \Delta S^{\circ}_{\neq,m} \) are the mean Eyring activation parameters.
(d) \( A \) and \( E_a \) are the Arrhenius parameters.
(e) \( \Delta H^{\circ}_{\neq,0} \) is the intercept in eq 19 and \( E(\Delta H^{\circ}_{\neq,0}) \) its corresponding error.
(f) \( T_{ik} \) is the slope in eq 19 and \( E(T_{ik}) \) its corresponding error.
(g) \( r \) is the correlation coefficient associated with eq 19.

Table 2. Variable and printed parameters for the programs used in the numerical simulations.

### 8.2. RESULTS: EFFECT OF THE DISPERSION FACTOR

The values of the activation energy and the logarithm of the pre-exponential factor obtained by means of program IKR-1 for a homologous series of 100 simulated reactions with a dispersion factor \( F = 0 \) (all the members of the family with identical activation parameters) are shown in Figure 2. It can be seen that the plot approaches very closely to a straight line. Obviously, since it has been assumed as an initial hypothesis the absence of any dispersion among the activation parameters, the linear relationship found in that figure must be attributed
to the experimental errors in the determination of the rate constants. An interesting feature is that the slope is positive ($2.474 \pm 0.006 \text{ kJ mol}^{-1}$) and with a rather high correlation coefficient ($r = 0.99972$). This demonstrates that the ubiquity of experimental errors can explain the observation of linear relationships of the type indicated in eq 10, leading to an apparent isokinetic temperature ($T_{ik} = 297.5 \pm 0.7 \text{ K}$) almost identical to the mean experimental temperature ($T_m = 298.15 \text{ K}$).

Figure 2. Activation energy as a function of the logarithm of the pre-exponential factor for simulations performed with program IKR-1. Parameters: $T_m = 298.15 \text{ K}$, $\Delta T = 20.0 \text{ K}$, $\Delta H^\circ, m = 50 \text{ kJ mol}^{-1}$, $\Delta S^\circ, m = -100 \text{ J K}^{-1} \text{ mol}^{-1}$, $F = 0$, $Q = 1$ and $N = 100$.

Similar calculations have been performed replacing the Arrhenius law (eq 9) by the Eyring equation (eq 12), using to that end program IKR-2 and $F = 0$. The results are shown in Figure 3. The plot is also linear, with a high correlation coefficient, and again with the slope almost identical to the mean experimental temperature. This demonstrates that the experimental errors can lead to linear relationships of the kind indicated in eq 19, causing the appearance of a compensation effect, not only in the $E_a$ vs. $\ln A$ plane (Figure 2), but also in the $\Delta H^\circ$ vs. $\Delta S^\circ$ plane (Figure 3).

By repetition of the calculations with program IKR-2 and using different values of parameter $F$, the effect of the dispersion factor on the activation enthalpy-entropy linear plot can be visualized. The graphs shown on the top of Figures 4 and 5 represent the scattering of the activation parameters for the different members of the homologous reaction series, assuming as
an initial hypothesis the absence of any real correlation between them, whereas those shown on
the bottom represent the linearization caused by the experimental errors.

Figure 3. Activation enthalpy as a function of the activation entropy for simulations performed with
program IKR-2. Parameters: $T_m = 298.15$ K, $\Delta T = 20.0$ K, $\Delta H^0_{m, m} = 50$ kJ mol$^{-1}$, $\Delta S^0_{m, m} = -100$ J K$^{-1}$
mol$^{-1}$, $F = 0$, $Q = 1$ and $N = 100$.

Figure 4. Activation enthalpy as a function of the activation entropy for simulations performed with
program IKR-2 with $T_m = 298.15$ K, $\Delta T = 20.0$ K, $\Delta H^0_{m, m} = 50$ kJ mol$^{-1}$, $\Delta S^0_{m, m} = -100$ J K$^{-1}$
mol$^{-1}$, $F = 0.25$ (left) and 0.50 (right), and $N = 100$. Top: in the absence of experimental errors ($Q = 0$). Bottom: in the
presence of experimental errors ($Q = 1$).
Figure 5. Activation enthalpy as a function of the activation entropy for simulations performed with program IKR-2. Parameters: $T_m = 298.15$ K, $\Delta T = 20.0$ K, $\Delta H^0_{\text{m},m} = 50$ kJ mol$^{-1}$, $\Delta S^0_{\text{m},m} = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0.75$ and $N = 100$. Top: in the absence of experimental errors ($Q = 0$). Bottom: in the presence of experimental errors ($Q = 1$).

The slopes and correlation coefficients corresponding to the straight lines shown in Figures 3-5 have been listed in Table 3. It can be concluded that an increase of parameter $F$ results in a decrease of both the apparent isokinetic temperature and the correlation coefficient.

<table>
<thead>
<tr>
<th>$F$</th>
<th>$T_{\text{ik}}$ [K]</th>
<th>$r$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>$297.5 \pm 0.7$</td>
<td>0.9997</td>
</tr>
<tr>
<td>0.25</td>
<td>$272.2 \pm 9.2$</td>
<td>0.9487</td>
</tr>
<tr>
<td>0.50</td>
<td>$237.6 \pm 16.7$</td>
<td>0.8210</td>
</tr>
<tr>
<td>0.75</td>
<td>$200.4 \pm 22.5$</td>
<td>0.6685</td>
</tr>
</tbody>
</table>

(a) $F$ is the dispersion factor of the activation parameters.
(b) $T_{\text{ik}}$ is the slope in eq 19.
(c) $r$ is the correlation coefficient associated with eq 19.
(d) Calculations performed with program IKR-2.

Table 3. Effect of the dispersion factor on the enthalpy-entropy compensation straight line.
The value of the dispersion factor has been systematically changed from zero to a certain maximum limit by means of program IKR-3, obtaining the parameters associated with each enthalpy-entropy compensation straight line for a family of \( N = 1000 \) simulated homologous reactions and repeating the calculations at five different temperatures in the range 100 – 500 K. The results can be seen in Figures 6-11.

It can be seen that at low temperatures the intercept absolute error decreases monotonously as the value of the intercept corresponding to each straight line increases, whereas at high temperatures the plots show a maximum (Figure 6). The same behavior is observed in relation to the slope absolute error and the slope value (Figure 7).

The apparent isokinetic temperature decreases continuously as the dispersion factor increases at all temperatures (Figure 8). Both the intercept (Figure 9) and the slope (Figure 10) of the enthalpy-entropy compensation straight lines increase as the correlation coefficient associated with the fit increases.

An interesting result is that the apparent isokinetic temperature \( (T_{ik}) \) is almost coincidental with the mean experimental temperature \( (T_m) \) when either its absolute error approaches zero (Figure 7), the dispersion factor equals zero (Figure 8) or the correlation coefficient is close to unity (Figure 10). As a consequence, both the ratio \( T_{ik} / T_m \) and the correlation coefficient tend to unity simultaneously (Figure 11). This result is coherent with the predictions inferred from statistical studies.\(^{7-9}\)

![Figure 6](image_url)

**Figure 6.** Intercept absolute error as a function of the intercept value corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-3. Parameters: \( T_m = 100 \) (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, \( \Delta T = 20.0 \) K, \( \Delta H_\neq^0, m = 50 \) kJ mol\(^{-1}\), \( \Delta S_\neq^0, m = -100 \) J K\(^{-1}\) mol\(^{-1}\), \( F = 0 – 8.65 \), \( Q = 1 \) and \( N = 1000 \).
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Figure 7. Slope absolute error as a function of the slope value corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-3. Parameters: $T_m = 100$ (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, $\Delta T = 20.0$ K, $\Delta H^0, m = 50$ kJ mol$^{-1}$, $\Delta S^0, m = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0 - 8.65$, $Q = 1$ and $N = 1000$.

Figure 8. Apparent isokinetic temperature as a function of the dispersion factor corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-3. Parameters: $T_m = 100$ (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, $\Delta T = 20.0$ K, $\Delta H^0, m = 50$ kJ mol$^{-1}$, $\Delta S^0, m = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0 - 8.65$, $Q = 1$ and $N = 1000$. 
Figure 9. Intercept as a function of the correlation coefficient corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-3. Parameters: $T_m = 100$ (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, $\Delta T = 20.0$ K, $\Delta H^\circ_{\pm, m} = 50$ kJ mol$^{-1}$, $\Delta S^\circ_{\pm, m} = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0 - 8.65$, $Q = 1$ and $N = 1000$.

Figure 10. Apparent isokinetic temperature as a function of the correlation coefficient corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-3. Parameters: $T_m = 100$ (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, $\Delta T = 20.0$ K, $\Delta H^\circ_{\pm, m} = 50$ kJ mol$^{-1}$, $\Delta S^\circ_{\pm, m} = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0 - 8.65$, $Q = 1$ and $N = 1000$. 
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Figure 1. Ratio between the apparent isokinetic temperature and the mean experimental temperature as a function of the correlation coefficient corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-3. Parameters: $T_m = 100$ (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, $\Delta T = 20.0$ K, $\Delta H^\circ_{\varphi,m} = 50$ kJ mol$^{-1}$, $\Delta S^\circ_{\varphi,m} = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0 - 8.65$, $Q = 1$ and $N = 1000$.

8.3. Results: effect of other parameters

Program IKR-4 has been designed to study the influence of the experimental error coefficient ($Q$) on the properties of the enthalpy-entropy compensation straight lines derived from laboratory uncertainties. The results concerning the slope are shown in Figure 12.

Figure 12. Apparent isokinetic temperature as a function of the logarithm of the experimental error coefficient of the rate constants corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-4. Parameters: $T_m = 100$ (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, $\Delta T = 20.0$ K, $\Delta H^\circ_{\varphi,m} = 50$ kJ mol$^{-1}$, $\Delta S^\circ_{\varphi,m} = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0.25$, $Q = 0.1 - 8.7$ and $N = 1000$. 
It can be seen that an increase of the magnitude of the experimental errors results in an increase of the apparent isokinetic temperature, approaching asymptotically the value corresponding to the mean experimental temperature:

$$\lim_{Q \to \infty} T_{ik} = T_m$$

(26)

The next program, IKR-5, has been used to analyze the effect of the difference between the maximum and minimum temperatures ($\Delta T$) for the experimental interval chosen to perform the determination of the activation parameters on the slope of the enthalpy-entropy straight lines (Figure 13).

Figure 13. Apparent isokinetic temperature as a function of the difference between the maximum and minimum values of the experimental temperature corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-5. Parameters: $T_m = 100$ (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, $\Delta T = 0.2 - 558.2$ K, $\Delta H^0_{m \neq} = 50$ kJ mol$^{-1}$, $\Delta S^0_{m \neq} = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0.25$, $Q = 1$ and $N = 1000$.

In this case, an increase of $\Delta T$ leads to a decrease of the apparent isokinetic temperature, reaching the limit $T_{ik} = T_m$ when $\Delta T = 0$:

$$\lim_{\Delta T \to 0} T_{ik} = T_m$$

(27)
With the aid of programs IKR-6 and IKR-7, it has been possible to study the effects of the values of the mean activation parameters $\Delta H_{\neq, m}^o$ (Figure 14) and $\Delta S_{\neq, m}^o$ (Figure 15), respectively, on the compensation linear relationships.

**Figure 14.** Apparent isokinetic temperature as a function of the mean activation enthalpy corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-6. Parameters: $T_m = 100$ (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, $\Delta T = 20$ K, $\Delta H_{\neq, m}^o = 0 – 1000$ kJ mol$^{-1}$, $\Delta S_{\neq, m}^o = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0.25$, $Q = 1$ and $N = 1000$.

**Figure 15.** Apparent isokinetic temperature as a function of the mean activation entropy corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-7. Parameters: $T_m = 100$ (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, $\Delta T = 20$ K, $\Delta H_{\neq, m}^o = 50$ kJ mol$^{-1}$, $-\Delta S_{\neq, m}^o = 0 – 1000$ J K$^{-1}$ mol$^{-1}$, $F = 0.25$, $Q = 1$ and $N = 1000$. 
The results indicate that, keeping the other parameters constant, the apparent isokinetic temperature increases when either $\Delta H^{0\neq, m}$ decreases or $\Delta S^{0\neq, m}$ increases.

On the other hand, it is interesting to draw attention to how a variation of these four parameters affects the quality of the enthalpy-entropy compensation relationships. According to the results found from the numerical simulations performed, the correlation coefficient increases when $Q$ increases, $\Delta T$ decreases, $\Delta H^{0\neq, m}$ decreases or $\Delta S^{0\neq, m}$ increases. In particular, it should be emphasized that:

$$\lim_{Q \to \infty} r = 1$$  \hspace{1cm} (28)

$$\lim_{\Delta T \to 0} r = 1$$  \hspace{1cm} (29)

Thus, the linearity of the compensation line increases both when the magnitude of the experimental errors increases (eq 28, Figure 16) and when the interval between the maximum and minimum experimental temperatures decreases (eq 29, Figure 17).

![Figure 16. Correlation coefficient as a function of the logarithm of the experimental error coefficient of the rate constants corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-4. Parameters: $T_m = 100$ (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, $\Delta T = 20.0$ K, $\Delta H^{0\neq, m} = 50$ kJ mol$^{-1}$, $\Delta S^{0\neq, m} = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0.25$, $Q = 0.1 - 8.7$ and $N = 1000.$](image-url)
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**Figure 17.** Correlation coefficient as a function of the difference between the maximum and minimum values of the experimental temperature corresponding to the enthalpy-entropy compensation straight lines for simulations performed with program IKR-5. Parameters: \( T_m = 100 \) (red), 200 (blue), 298.15 (violet), 400 (orange) and 500 (green) K, \( \Delta T = 0.2 - 558.2 \) K, \( \Delta H^0, m = 50 \) kJ mol\(^{-1}\), \( \Delta S^0, m = -100 \) J K\(^{-1}\) mol\(^{-1}\), \( F = 0.25\), \( Q = 1 \) and \( N = 1000\).

This is logical indeed, because it has been assumed as an initial hypothesis that there is no real correlation between the activation enthalpies and entropies of the members of the homologous reaction series (in Nature), so that the relationships found in the laboratory must necessarily come from the experimental errors. It can then be concluded that the confidence that is to be attributed to a compensation straight line observed in a certain kinetic research (in the sense that it seems to be caused by a physically meaningful phenomenon) should improve when the experimental errors committed in the determination of the rate constants are as low as possible and when the experimental temperature interval is as wide as possible.

**8.4. Comparison between the different effects**

The apparent isokinetic temperatures for the enthalpy-entropy compensation straight lines derived from the numerical simulations performed have been plotted against the corresponding correlation coefficients (Figures 18-20). These curves were done by varying systematically one parameter each time and keeping all the others constant.
Figure 18. Apparent isokinetic temperature as a function of the correlation coefficient corresponding to the enthalpy-entropy compensation straight lines. Parameters: $T_m = 298.15$ K, $\Delta T = 20.0$ K, $\Delta H^0_{\pm, m} = 50$ kJ mol$^{-1}$, $\Delta S^0_{\pm, m} = -100$ J K$^{-1}$ mol$^{-1}$ and $N = 1000$. Red: program IKR-3, $F = 0 - 4.4$, $Q = 1$. Blue: program IKR-4, $F = 0.25$, $Q = 0.06 - 4.00$. The arrows indicate the direction in which the variable parameter increases.

Figure 19. Apparent isokinetic temperature as a function of the correlation coefficient corresponding to the enthalpy-entropy compensation straight lines. Parameters: $T_m = 298.15$ K, $\Delta H^0_{\pm, m} = 50$ kJ mol$^{-1}$, $\Delta S^0_{\pm, m} = -100$ J K$^{-1}$ mol$^{-1}$, $Q = 1$ and $N = 1000$. Red: program IKR-3, $\Delta T = 20$ K, $F = 0 - 4.4$. Blue: program IKR-5, $\Delta T = 0.2 - 198.2$ K, $F = 0.25$. The arrows indicate the direction in which the variable parameter increases.
Figure 20. Apparent isokinetic temperature as a function of the correlation coefficient corresponding to the enthalpy-entropy compensation straight lines. Parameters: $T_m = 298.15$ K, $\Delta T = 20$ K, $Q = 1$ and $N = 1000$. Red: program IKR-3, $\Delta H^{o, m} = 50$ kJ mol$^{-1}$, $\Delta S^{o, m} = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0 - 4.95$. Blue: program IKR-6, $\Delta H^{o, m} = 0 - 100$ kJ mol$^{-1}$, $\Delta S^{o, m} = -100$ J K$^{-1}$ mol$^{-1}$, $F = 0.25$. Green: program IKR-7, $\Delta H^{o, m} = 50$ kJ mol$^{-1}$, $-\Delta S^{o, m} = 0 - 332$ J K$^{-1}$ mol$^{-1}$, $F = 0.25$.

An interesting result is that the same curve is found whether the parameter changed was $F$, $Q$ (Figure 18) or $\Delta T$ (Figure 19). However, the same cannot be stated when the parameter varied was either $\Delta H^{o, m}$ or $\Delta S^{o, m}$, since different plots are obtained in these cases (Figure 20).

9. EXPERIMENTAL ISOKINETIC CORRELATIONS

As it can be remembered, the main objective of the present work is that of developing a test designed to differentiate those isokinetic relationships with an experimental error origin from those caused by a physically meaningful phenomenon. Effectively, it has been observed in Figures 3-5 that an enthalpy-entropy compensation effect is found even when there is no real correlation between the activation parameters, provided that the accidental errors associated with the determination of the rate constants are high enough. Thus, the following goal of this research will be the elaboration of a test capable of discerning whether a certain activation effect
enthalpy-entropy linear relationship found in the laboratory can be explained by the occurrence of experimental errors or not. In the graphical version of the test, three different kinds of information will be represented in the $T_{ik}$ - $r$ plane: i) the curve corresponding to the maximum probability of finding the points when the compensation straight line is caused exclusively by laboratory errors, ii) the points obtained from numerical simulations performed with the same number of reactions in the homologous series than in the real case ($N_{exp}$), and iii) the experimental point.

9.1. Searching for a Test: Maximum Probability Curve

The next step to develop the test will be the calculation of the $T_{ik}$ - $r$ curve corresponding to the maximum probability. For that purpose, it would be required to perform the computer simulations with an infinite ensemble of reactions in the homologous series. However, since this would certainly be impossible, the simulations have been performed with $N = 10^5$ as a good enough approximation.

Different couples of parameters can be used as the basic framework of the desired test, such as the intercept of the compensation straight line and its corresponding absolute error (Figure 6) or the slope and its associated error (Figure 7). However, given the experimental information usually provided in the chemical literature, the parameters selected for this purpose have been the apparent isokinetic temperature (slope) and the correlation coefficient of the enthalpy-entropy compensation linear fit.

Due to the high number (7) of parameters involved in the numerical simulations ($T_m$, $\Delta T$, $\Delta H^\neq$, $m$, $\Delta S^\neq$, $m$, $F$, $Q$ and $N$) and, consequently, of the different combinations to be considered, it is important to establish which of them can be kept constant and which should be varied. Indeed, the number of reactions belonging to the homologous series ($N$) should be specified for each particular case. It has been shown that the $T_{ik}$ - $r$ curve depends on the value of the mean experimental temperature (Figure 10). Although this dependence is clearly weakened by using as ordinate the ratio $T_{ik}/T_m$ instead, the suppression of that dependence is only partial because the resulting curves are still dependent on the value of $T_m$ (Figure 11). The $T_{ik}$ - $r$ plots also depend on the values of the mean activation parameters (Figure 20). Therefore, the mean value of the experimental temperature ($T_m$), as well as those of the activation enthalpy ($\Delta H^\neq$, $m$) and entropy ($\Delta S^\neq$, $m$), have to be also specified for each reaction family.
Parameters $F$ (measuring the dispersion of the real activation parameters) and $Q$ (measuring the maximum limit of the experimental errors) should be employed as variables because, in general, the chemical kinetics bibliography does not contain any information on their values. However, since it has been demonstrated that the $T_{ik} - r$ curve obtained by variation of parameter $Q$ is coincident with that found when $F$ was varied (Figure 18), an increase of the former being equivalent to a decrease of the latter, it will be enough if only one of those parameters is changed. The same happens with $\Delta T$ (Figure 19), its increase being equivalent to an increase of $F$ and to a decrease of $Q$.

The information concerning the different parameters required to initiate the test in order to obtain the maximum probability curve has been summarized in Table 4.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_m$</td>
<td>specified</td>
</tr>
<tr>
<td>$\Delta T$</td>
<td>constant (= 20 K)</td>
</tr>
<tr>
<td>$\Delta H^0_{x,m}$</td>
<td>specified</td>
</tr>
<tr>
<td>$\Delta S^0_{x,m}$</td>
<td>specified</td>
</tr>
<tr>
<td>$F$</td>
<td>variable</td>
</tr>
<tr>
<td>$Q$</td>
<td>constant (= 1)</td>
</tr>
<tr>
<td>$N$</td>
<td>$10^5$</td>
</tr>
</tbody>
</table>

(a) $T_m$ is the mean experimental temperature and $\Delta T$ the difference between its maximum and minimum values.
(b) $\Delta H^0_{x,m}$ and $\Delta S^0_{x,m}$ are the mean values of the activation parameters.
(c) $F$ is the dispersion factor of the activation parameters and $Q$ the experimental error coefficient of the rate constants.
(d) $N$ is the number of members of the simulated homologous reaction series.

Table 4. Parameters used in the test to obtain the maximum probability curve and their respective conditions.

9.2. SEARCHING FOR A TEST: CALCULATION OF THE PROBABILITY PARAMETER

It can be observed that the dispersion of the activation parameters as measured in the laboratory (Figures 4 and 5, bottom) is higher than that associated with the real values as existing in Nature (Figures 4 and 5, top). This is so because of the fact that the experimental
determinations include not only the real dispersion of the activation parameters, but also the scattering caused by the accidental errors. Hence, the maximum limit that can be taken for the variable parameter $F$ should be obtained for a situation of absence of experimental errors ($Q = 0$). Thus, in full coherence with eqs 22 and 23, it can be deduced from the activation enthalpies and entropies determined in the laboratory by means of the following equation:

$$
F_{\text{max}} = 10 \frac{\left( |\Delta X_{\text{g, i}}^o - \Delta X_{\text{g, m}}^o | \right)_{\text{max}}}{\Delta X_{\text{g, m}}^o}
$$

(30)

where $X = H$ or $S$. This limit can be calculated from the highest absolute value of the difference between the individual ($\Delta X_{\text{g, i}}^o$) and mean ($\Delta X_{\text{g, m}}^o$) activation parameters for the reaction homologous series considered.

The values allowed for the dispersion factor will be in the range $0 \leq F \leq F_{\text{max}}$. The lower limit ($F = 0$) corresponds to a situation in which the activation parameters are identical for all the members of the homologous reaction series and the experimental dispersion is thus completely due to accidental errors ($Q = F_{\text{max}}$), whereas the upper limit ($F = F_{\text{max}}$) corresponds to a situation in which the real dispersion of the activation parameters is identical to the one experimentally observed due to the absence of errors ($Q = 0$). Therefore, the values of parameter $Q$ will obey the following equation:

$$
Q = F_{\text{max}} - F
$$

(31)

so that, as parameter $F$ increases from 0 to $F_{\text{max}}$, parameter $Q$ decreases from $F_{\text{max}}$ to 0. The values of the other parameters will be taken as in Table 4 except the number of reactions involved in the simulated homologous series, being now equal to that of the experimental case ($N = N_{\text{exp}}$).

Given that in the experimental cases the number of reactions studied in each homologous family is indeed much lower than that required to obtain the maximum probability curve ($N = 10^5$), when the numerical simulations are done with $N = N_{\text{exp}}$ and represented in a graphic the points will appear scattered above and below that curve. The objective of the test will be, precisely, to determine the probability of finding one of these simulation points in a region of the $T_{ik} - r$ plane near the experimental point.
Although none of the simulations will be exactly coincident with the empirical situation, some of them will potentially lead to points placed close enough: the higher the distance between the experimental point and the maximum probability curve, the lower the probability of finding a simulation point in its vicinity. At this moment, there are two different ways to continue with the calculations. The simpler would be to accept as valid those simulations leading to results contained in certain ranges around \((T_{ik})_{\text{exp}}\) and \(r_{\text{exp}}\). However, the limitation inherent to this procedure would be the choice of the range widths, since an increase of the region area would automatically result in an increase of the corresponding probability. In order to outline the second alternative, one must wonder why the experimental point is not exactly placed on the maximum probability curve. Only two alternative explanations are possible: i) the number of members in the reaction series is too low \((N_{\text{exp}} \ll \infty)\) and ii) the hypothesis based on which the numerical simulations were performed (no real correlation between the family activation parameters) is wrong.

Therefore, the chance of the compensation linear plot being originated by accidental errors will be lower when the experimental point is placed far from the maximum probability curve, either above or below it. However, as mentioned before, it is impossible to find a simulation exactly matching the empirical information obtained from the bibliography:

\[
(T_{ik})_{\text{sim}} \neq (T_{ik})_{\text{exp}} \tag{32}
\]
\[
r_{\text{sim}} \neq r_{\text{exp}} \tag{33}
\]

Once assumed this, it is important to define which simulations will be taken as valid (capable of explaining the experimental isokinetic correlation) and which ones will not:

All the simulations leading to points located farther from the maximum probability curve (as concerning the apparent isokinetic temperature) than the experimental point should be considered as valid, provided that the associated correlation coefficient is high enough.

This condition derives from the fact that the probability of finding a particular \((T_{ik}, r)\) couple of values is inversely proportional to its distance with respect to the curve of maximum probability,
obtained the latter from simulations performed with a value of parameter $N$ (the number of members belonging to the homologous reaction series) as high as possible. It is thus clear that all the simulations, performed with a number of members of the homologous reaction series $N = N_{\text{exp}}$, leading to apparent isokinetic temperatures with at least the same difference (in absolute value) from the slope predicted by the maximum probability curve than that corresponding to the experimental enthalpy-entropy compensation straight line are, in principle, capable of explaining the information found in the laboratory. Only those simulations leading to correlation coefficients too low in comparison with the experimental one should be excluded.

Hence, the test will count the number of simulation points in the $T_{\text{ik}} - r$ plane fulfilling the following criteria:

$$
|T_{\text{ik}}^{\text{sim}} - T_{\text{ik}}^{\text{cmp}}| \geq |T_{\text{ik}}^{\text{exp}} - T_{\text{ik}}^{\text{cmp}}| \quad (34)
$$

$$
r_{\text{sim}} \geq r_{\text{exp}} \quad (35)
$$

where the subscripts indicate whether the slope and the correlation coefficient of the enthalpy-entropy compensation linear plots correspond to the numerical simulation with $N = N_{\text{exp}}$ (sim), the curve of maximum probability with $N = 10^5$ (cmp) or the experimental homologous series (exp). The value of $(T_{\text{ik}})^{\text{cmp}}$ is calculated as that belonging to the curve with the abscissa $r = r_{\text{exp}}$.

Because of the use of absolute values in eq 34, the only simulations regarded as capable of explaining the laboratory kinetic data will be those leading to isokinetic temperatures higher than or equal to the experimental value $[(T_{\text{ik}})^{\text{sim}} \geq (T_{\text{ik}})^{\text{exp}}]$ when the point is placed above the maximum probability curve $[(T_{\text{ik}})^{\text{exp}} > (T_{\text{ik}})^{\text{cmp}}]$, and to isokinetic temperatures lower than or equal to the experimental value $[(T_{\text{ik}})^{\text{exp}} \leq (T_{\text{ik}})^{\text{sim}}]$ when the point is placed below the maximum probability curve $[(T_{\text{ik}})^{\text{exp}} < (T_{\text{ik}})^{\text{cmp}}]$. Moreover, in order for the numerical simulations to be considered as valid, it will be required that the corresponding correlation coefficient be higher than or equal to the experimental one (eq 35).

The final output of the test consists in calculating the probability of the enthalpy-entropy compensation straight line being explainable by accidental errors as:
where the numerators are the numbers of simulations fulfilling the conditions imposed by eqs 34 and 35, whereas the symbol appearing in the denominators stands for the total number of simulations performed with $N = N_{\text{exp}}$. It should be noticed that eq 36 is used when $(T_{ik})_{\text{exp}} > (T_{ik})_{\text{cmp}}$ and eq 37 when $(T_{ik})_{\text{exp}} < (T_{ik})_{\text{cmp}}$. The BASIC-language program written to calculate parameter $p$ for the kinetic data corresponding to each homologous reaction series extracted from the chemical literature was designated as IKR-8.

9.3. Application to bibliographic data

The occurrence of activation enthalpy-entropy compensation plots for different homologous reaction series is rather ubiquitous in the chemical kinetics literature.

![Figure 21](image_url)  
Figure 21. Experimental isokinetic plots for the permanganate oxidation of two homologous series of alkenes containing a functionalized terminal group. Filled circles: oxidant, permanganate ion; reductants (from left to right) (E)-3-phenyl-2-propenoate ion (cinnamate ion), (E)-2-butenoate ion (crotonate ion), propenoate ion (acylate ion), 3-butenoate ion, 4-pentenoate ion and 2-propenol (allyl alcohol); solvent: water (ref. 24). Empty circles: oxidant, tributylmethylammonium permanganate; reductants (E)-3-phenyl-2-propenoic acid (cinnamic acid) derivatives containing the substituents (from left to right) $m$-NO$_2$, $m$-CF$_3$, $m$-Cl, $m$-Br, 3-D, $m$-OCH$_3$, 2-D, none, 2-CH$_3$, p-CH$_3$, o-OCH$_3$, p-OCH$_3$ and 2-C$_6$H$_5$; solvent: dichloromethane (ref. 1). The dashed line corresponds to a linear correlation with slope = $T_m = 286$ K.
Two interesting examples are shown in Figure 21, corresponding to the oxidations of substituted alkenes by permanganate ion in water\textsuperscript{24} and by quaternary ammonium permanganate in dichloromethane.\textsuperscript{1}

Figure 22. Isokinetic temperature as a function of the correlation coefficient for the application of the \( p \)-test to three homologous reactions series. Red lines: maximum probability curves. Blue points: simulation data. Green points: experimental data from ref. 1 (top), 25 (middle) and 26 (bottom). The dashed lines show the limits of the quadrants corresponding to potentially valid simulations.

Program IKR-8 has been used to calculate the value of the probability (\( p \)) of finding a numerical simulation able to explain the observation of a particular enthalpy-entropy compensation relationship just as a consequence of experimental errors. Therefore, parameter
p measures the probability that a certain isokinetic plot might accept an accidental-error explanation (error-driven isokinetic plot). The application of the p-test to three bibliography cases,1,25,26 two with the experimental points above the maximum probability curve \((T_{ik})_{\text{exp}} > (T_{ik})_{\text{cmp}}\) and the other below \((T_{ik})_{\text{exp}} < (T_{ik})_{\text{cmp}}\) is illustrated in Figure 22. It can be observed that in the first case there is no simulation that could be considered as valid, whereas in the other two cases some simulations actually fulfilled the conditions imposed by eqs 36 and 37.

The results concerning the application of the p-test to 100 different homologous reaction series taken from the chemical literature1,4,24-89 are shown in Table 5. A very high number \((10^6)\) of numerical simulations were done in each case in order to obtain an accurate value of parameter p.

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Theoretical study of the enthalpy-entropy compensation effect in chemical kinetics

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(a) $N_{exp}$ is the number of members of the homologous reaction series.
(b) $T_m$ is the mean experimental temperature.
(c) $\Delta H_{\neq m}$ and $\Delta S_{\neq m}$ are the mean values of the activation parameters.
(d) $F_{max}$ is the maximum value of the dispersion factor of the activation parameters.
(e) $T_k$ is the experimental isokinetic temperature
(f) $r$ is the correlation coefficient of the experimental isokinetic plot.
(g) $p$ is the probability of the isokinetic plot being explainable by accidental errors.
(h) Calculations performed with program IKR-8.

Table 5. Parameters involved in the application of the $p$-test to different experimental isokinetic plots extracted from the bibliography.
In four series the probability could not be obtained because of its extremely low value \((p < 10^{-6})\). Moreover, the condition of statistical significance (usually accepted as \(p < 0.05\)) was fulfilled for 61 homologous series, not being reached that level of significance in the other 39 cases. It can then be concluded that many of the isokinetic plots found in the bibliography (probably, more than 50%) are difficult to be explained just as a consequence of accidental errors, so that a real activation enthalpy-entropy correlation has to be necessarily postulated for those reaction families.

Although parameter \(p\) is a function of several variables \((N_{exp}, F_{max}, T_{ik}/T_m\) and \(r\)), the only one capable of predicting with some accuracy its value is the correlation coefficient of the experimental isokinetic plot, thus denoting a stronger influence than those of the other three variables. As shown in Figure 23, an increase of the correlation coefficient results in a net decrease of the probability parameter. This means that the higher the linearity of the activation enthalpy-entropy compensation plot the lower the probability that it could be explained by accidental errors.

![Figure 23](image)

**Figure 23.** Probability parameter as a function of the correlation coefficient for the results obtained by application of the \(p\)-test to 100 homologous reaction series taken from bibliographic sources.

An attempt has been made to elucidate the combined effect of the four independent factors on the probability parameter. A reasonably linear relationship (Figure 24) was found when representing \(\log (1 - p)\) against the following variable:
\[ \log z = a \log N_{\text{exp}} + b \log F_{\text{max}} + c \log \left( \frac{T_{ik}}{T_m} \right) + \log r \]  (38)

where \( a = 0.0508 \), \( b = 0.0204 \) and \( c = 0.0738 \) quantify the statistical weight of each factor with respect to that of the correlation coefficient (arbitrarily taken as 1). These parameters were obtained using a computer program (IKR-9), by systematically changing their values in order to minimize the sum of the absolute errors of the individual points with respect to the linear relationship considered as the best fit. The fact that \( a, b, c \ll 1 \) confirms the outstanding influence of \( r \) in comparison with those of \( N_{\text{exp}}, F_{\text{max}}, T_{ik}/T_m \), although the four of them have a positive effect on the value of \( 1 - p \). This indicates that a certain isokinetic plot should be regarded as more physically meaningful (with a lower chance to be an artefact resulting from experimental errors) when the values of these four magnitudes are as high as possible.

Figure 24. Dependence of the probability parameter on the statistically-weighted combination of \( N_{\text{exp}}, F_{\text{max}}, T_{ik}/T_m \) and \( r \) for the results obtained by application of the \( p \)-test to 100 homologous reaction series taken from bibliographic sources.

The present work can be considered as a \textit{reductio ad absurdum} argument: starting as an initial hypothesis that the activation enthalpy-entropy parameters for all the homologous series are randomly scattered in Nature, the final conclusion is that (at least for some reaction families) it cannot be true, since a pre-existing correlation must actually be postulated to explain the experimental data.
10. CONCLUSIONS

(i) The experimental errors associated with the activation enthalpy and entropy (or, alternatively, the activation energy and pre-exponential factor) are mutually interdependent, both in sign and amplitude.

(ii) According to the numerical simulations performed, parting from a set of randomly scattered activation parameters, the occurrence of accidental experimental errors is capable of linearizing the activation enthalpy-entropy plots provided that the magnitude of the errors is high enough in comparison with the dispersion of the activation parameters.

(iii) When both the amplitude of the experimental errors \( Q \) and the experimental temperature range \( \Delta T \) are kept constant, an increase of the dispersion associated with the real activation parameters \( F \) results in a decrease of all the intercept, slope (apparent isokinetic temperature) and correlation coefficient of the enthalpy-entropy compensation plots.

(iv) When both \( F \) and \( \Delta T \) are kept constant, an increase of \( Q \) results in an increase of all the intercept, slope and correlation coefficient of the enthalpy-entropy compensation plots.

(v) When both \( F \) and \( Q \) are kept constant, an increase of \( \Delta T \) results in a decrease of all the intercept, slope and correlation coefficient of the enthalpy-entropy compensation plots.

(vi) The apparent isokinetic temperature approaches the mean experimental temperature as either \( F \) tends to zero, \( Q \) tends to infinity or \( \Delta T \) tends to zero.

(vii) The correlation coefficient values of the activation enthalpy-entropy linear plots approach unity as either \( F \) tends to zero, \( Q \) tends to infinity or \( \Delta T \) tends to zero.

(viii) The maximum probability curve in the \( T_{\text{Ik}} - r \) plane derived from accidental experimental errors can be obtained by indistinctly changing \( F, Q \) or \( \Delta T \), whereas the values of the mean activation enthalpy and entropy have a specific effect on its shape.

(ix) The probability of a particular isokinetic plot being physically meaningful increases with the values of the number of reactions belonging to the homologous series, the maximum
dispersion of the activation parameters, the ratio between the isokinetic and mean experimental temperatures, and the linear correlation coefficient, the latter being the parameter with the highest influence.

(x) A sampling of 100 homologous reaction series extracted from the chemical bibliography suggests that the linear activation enthalpy-entropy compensation plots are physically meaningful at least in more than one-half of the reported cases.
11. REFERENCES


Theoretical study of the enthalpy-entropy compensation effect in chemical kinetics


74. Heidt, L. J.; Purves, C. B. The Unimolecular Rates of Hydrolysis of 0.01 Molar Methyl- and Benzylfructofuranosides and –Pyanosides and of Sucrose in 0.00965 Molar Hydrochloric Acid at 20 to 60° *J. Am. Chem. Soc.* **1938**, *60*, 1206-1210.


