STATISTICS OF THE ENTHALPY–ENTROPY RELATIONSHIP. III.*
PROCESSING OF CALORIMETRIC DATA

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The relationship between reaction enthalpies and reaction entropies within a series of related reactions can be based on a direct calorimetric determination of ΔH^0 and on equilibrium measurement at a single temperature. A correct statistical treatment in this case consists of linear regression (or simple plotting) in the coordinates ΔH^0 *vs* ΔG^0, the latter being usually considered an exact quantity. On the other hand, regressions in the coordinates ΔH^0 *vs* ΔS^0 or ΔS^0 *vs* ΔG^0, frequently employed in the literature, are misleading and yield incorrect values for the slope and/or for the correlation coefficient; the reason is the *a priori* dependence of the two quantities correlated. This can be proved mathematically when the problem is treated as coordinate transformation in the plane. Nevertheless, this type of experimental data is usually more favourable from the statistical point of view than measurement of temperature dependence of equilibrium constants.

The linear relationship between reaction enthalpies ΔH^0 and standard reaction entropies ΔS^0, or between activation enthalpies ΔH^* and activation entropies ΔS^* is of fundamental importance in structure-reactivity correlations and in mechanistic studies[1,2]. Its validity within a series of closely related reactions means that the reactivity sequence does not change with temperature and hence can be discussed in temperature independent terms, as electronic effects of substituents, ring strain etc. When common symbols ΔH abd ΔS are used for activation or reaction parameters the relationship reads

$$\Delta H = h_0 + \beta \, \Delta S \qquad (1a)$$

and is called the isokinetic or isoequilibrium relationship, respectively. Since the intercept h_0 is usually given no physical meaning, the form of the equation may be conveniently expressed

$$\delta \, \Delta H = \beta \cdot \delta \, \Delta S , \qquad (1b)$$

where the operator δ denotes the difference between the given and the reference reaction.

The verification of equation (*1*) and determination of the slope β, the so-called isokinetic temperature, is connected with serious problems of a statistical nature, which demonstrate uniquely the importance of a correct statistical approach even in exact science[3,4]. Its neglect has lead to numerous erroneous statements in the literature and to false correlations which are directly at variance with original experimental findings, see[2-4]. The heart of the problem is the a priori dependence of the two quantities correlated, which are obtained from the same set of primary experimental data.

ΔH and ΔS can be obtained in one of two possible ways. In the first, the rate constants k or equilibrium constants K are measured at different temperatures and their logarithms plotted against T^{-1}; ΔH is obtained from the slope of the relationship and ΔS from its intercept. The statistical treatment is relatively difficult in this case and improper processing, particularly plots of the coordinates ΔH *vs* ΔS, can yield completely wrong results; the smaller the interval of experimental temperatures, the greater the danger. However, unobjectionable statistical methods have been developed in preceding papers[4-6], which allow the validity of equation (*1*) to be judged, the slope β to be estimated and the intercept h_0 to be evaluated with the confidence intervals *etc.* The choice between these methods depends on the character of available data (measurements at two temperatures[4], at several corresponding temperatures[5], at arbitrary temperatures[6]) and upon the technique employed (graphical treatment[4], desk calculator[5], or computer[6]).

The second way is possible only with reaction parameters, it consists in determination of ΔH^0 directly from calorimetry and combination with ΔG^0 obtained from equilibrium constants, measured at a single temperature. The value of ΔS^0 is obtained from the basic equation:

$$\Delta S^0 = (\Delta H^0 - \Delta G^0)/T. \qquad (2)$$

The isoequilibrium relationship is then tested either in terms of the dependence of ΔH^0 upon ΔS^0 according the equation (*1*), or as the dependence of ΔS^0 upon ΔG^0, or of ΔH^0 upon ΔG^0, since from equations (*1*) and (*2*) the relationships may be directly derived*

$$\delta \, \Delta S^0 = \frac{1}{\beta - T} \, \delta \, \Delta G^0 \qquad (3)$$

and

$$\delta \, \Delta H^0 = \frac{\beta}{\beta - T} \, \delta \, \Delta G^0 . \qquad (4)$$

Recent developments in calorimetry have made this approach feasible and many correlations according to equations (*1*), (*3*), (*4*) have been reported[7-17]. However,

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* Instead of ΔS^0, $T \Delta S^0$ can be plotted in the graphs. This has the advantage that both variables are expressed in the same units. Further conclusions of this paper are not affected by this modification, only the values of the slope are multiplied or divided by T.

equations (1), (3) and (4), although equivalent algebraically, are not equivalent from the statistical point of view, so that careful experimental work can be invalidated by improper statistical treatment. The object of this paper is to analyse the various possible treatments and to establish the correct procedure. The mathematical approach is similar as used with kinetic data obtained at two temperatures[4]; the relation of equations (1), (3) and (4) is treated as a coordinate transformation in the plane. At the first inspection the problem is somewhat simpler than in the case mentioned[4], since one coordinate always remains unchanged. Nevertheless the results show that correlations according to equations (1) or (3) may be wrong as far as the values of the slope and of the correlation coefficient are concerned.

THEORETICAL

The starting point of the analysis is the statement that correlations according to equation (4) are statistically unobjectionable since the two variables have been obtained directly and quite independently of each other. The plot of ΔH^0 against ΔG^0 thus gives a true picture of the real relationship. When a statistical regression is to be made, the common formulae for linear regression (with ΔG^0 as independent variable) can be usually employed to a good approximation. It is so because the experimental errors in ΔG^0 are commonly smaller, or even much smaller than errors in ΔH^0. *E.g.* in the data on dissociation of carboxylic acids, listed in ref.[8], the standard error in ΔH^0 is 0·05 to 0·10 kcal mol^{-1}. The corresponding pK data are given to 2–4 places of decimals; the upper limit of 0·01 pK units would correspond to 0·013 kcal . . mol^{-1}. Hence in common practice, ΔG^0 is at least 5-times, but often 50-times more accurate than ΔH^0; the range of values being approximately the same for the two quantities or even larger for ΔG^0. The ratio is in principle reversed only when rather bad equilibrium data are combined with extremely good calorimetric values. Such a limiting case in encountered in the dissociation of substituted anilines[13]; the precision here is given to ± 0.03 kcal mol^{-1} for ΔH^0 and ± 0.027 kcal mol^{-1} for ΔG^0 (Example 1). Such sets of data with comparable errors in the two variables would require special statistical methods; if the errors in both were exactly of the same magnitude, the regression procedure could be applied, minimizing the squared deviations normal to the regression line[18].

For the following conclusions it is assumed that values of ΔG^0 are more precise than values of ΔH^0; accordingly only errors in the latter are depicted in the graphs ΔH^0 *vs* ΔG^0 (Figs 2–6). The errors in ΔH^0 are reflected in ΔS^0 according to equation (2). Hence in graphs of ΔS^0 *vs* ΔG^0 only the former quantity is weighted with error, as are both variables in graphs of ΔH^0 *vs* ΔS^0. In this case the errors are mutually dependent so that a point can move only along a given line with a slope equal to the experimental temperature T.

With these presumptions the slope b_{HG} of the regression line in the coordinates ΔH^0 *vs* ΔG^0 is a characteristic quantity of the correlation. According to common regression formulae* this slope is given by

$$b_{HG} = s_H r_{GH}/s_G \,, \tag{5}$$

where s_H and s_G are standard deviations for the variables ΔH^0 and ΔG^0 from their mean values, and r_{GH} is the correlation coefficient. From b_{HG} the isokinetic temperature β can be obtained with respect to *(4)*, thus

$$\beta = T b_{HG}/(b_{HG} - 1) = T s_H r_{GH}/(s_H r_{GH} - s_G) \,. \tag{6}$$

It is now pertinent to explore what happens when the regression is carried out with respect to other coordinates, either according to the equations *(1)* or *(3)*. Following an approach similar to that adopted previously[4] we can treat the transition to these equations in pure geometrical terms as a coordinate transformation, in which the original coordinates $x \equiv \Delta G^0$ and $y \equiv \Delta H^0$ are replaced by new ones, either $x' \equiv \Delta S^0$ and $y' \equiv \Delta H^0$, or $x'' \equiv \Delta G^0$ and $y'' \equiv \Delta S^0$. One coordinate thus remains unchanged in each case, whilst the other is transformed according to equation *(2)*.

The first transformation, into the ΔH^0 *vs* ΔS^0 plane, is a homologous affinity with the affinity axis $y = (T + 1) x$, with affinity direction equal to zero (slope of invariant straight lines) and affinity ratio $-1/T$; parallel lines are transformed into parallel ones and an ellipse into an ellipse. Similarly as in the previous case[4] the correlation coefficient of a set of points changes its value by the transformation and the regression line does not remain after transformation. The correlation coefficient r_{SH} of the variables ΔS^0 and ΔH^0 is given by the known formula*; by substituting from *(2)* we get

$$r_{SH} = (s_H - s_G r_{GH})(s_G^2 - 2 s_G s_H r_{GH} + s_H^2)^{-1/2} \,. \tag{7}$$

The dependence of r_{SH} on r_{GH} is visualized in Fig. 1a for various values of s_H/s_G. It follows from the graph that the false correlation coefficient r_{SH} is higher in absolute terms than the right one, r_{GH}, when the inequality holds

$$r_{GH} < s_H/2 s_G \,. \tag{8}$$

Both correlation coefficients equal in absolute value, either when the inequality *(8)* transforms into an equality, or, when $s_H = 0$, or finally when $r_{GH} = \pm 1$. The last case is evident, it means that statistics has been replaced by simple geometry.

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*   See ref.[19] for all common statistical terms and formulae.

To conclude, the plot of ΔH^0 vs ΔS^0 will overestimate the actual fit when this fit is poor (r_{GH} small) and always when r_{GH} is negative, further when the variance of ΔH^0 is large (always when $s_H/s_G > 2$). *Vice versa* the fit will be underestimated when it is close (with positive r_{GH}) and when the variance of ΔG^0 is larger than that of ΔH^0. The difference between the correct and false correlation coefficients may be striking (see Examples); even for $r_{GH} = 0$, the apparent correlation coefficient r_{SH} may attain a value as high as 0·9.

The regression coefficients are also changed by the coordinate transformation and the transformed regression line of a set of points is not identical with the regression line of the transformed set. The real regression line in the coordinates ΔH^0 vs ΔG^0 with the slope b_{HG} is mapped into the coordinates ΔH^0 vs ΔS^0 with the slope b'_{HG} given by

$$b'_{HG} = Ts_H r_{GH}/(s_H r_{GH} - s_G) \qquad (9)$$

and is different from the two regression lines produced in these coordinates, having the slopes

$$b_{HS} = Ts_H(s_H - s_G r_{GH})/(s_G^2 - 2s_G s_H r_{GH} + s_H^2) \qquad (10a)$$

$$1/b_{SH} = Ts_H(s_H - s_G r_{GH}) . \qquad (10b)$$

Either expression ($10a$) or ($10b$) equals (9) only in the trivial case, already men-
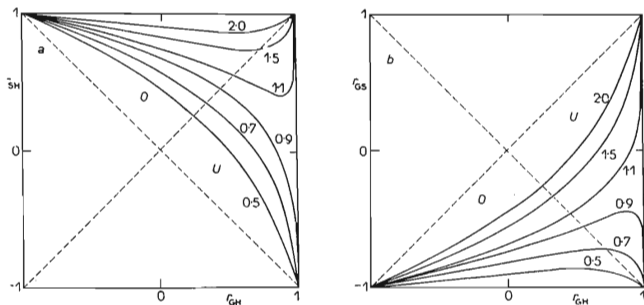

FIG. 1 a, b

Relationships of Correlation Coefficients in Different Coordinates

Apparent correlation coefficients, r_{SH} and r_{GS}, are shown as functions of the real coefficient, r_{GH}; values of $c = s_H/s_G$ indicated with the curves. In area O, the fit is overestimated by the correlation coefficients r_{SH} or r_{GS}, in area U underestimated.

tioned, when $r_{GH} = \pm 1$. (Provided it is assumed that s_G and s_H are non-zero.) When the apparent value β^* of the isokinetic temperature is determined in the improper plot of ΔH^0 vs ΔS^0, it is put equal to b_{HS} (or $1/b_{SH}$) and differs from the right value β given by equation (6) unless r_{GH} equals ± 1. The dependence of β^* on β and possible differences between them will not be derived generally; some typical possibilities are shown in the Examples.

The second possible transformation, into the coordinates ΔS^0 vs ΔG^0 yields only a slightly different picture. The correlation coefficient r_{GS} is given by

$$r_{GS} = (s_H r_{GH} - s_G)(s_G^2 - 2s_G s_H r_{GH} + s_H^2)^{-1/2} . \tag{11}$$

Its dependence on r_{GH} is shown in Fig. 1b, which is essentially a mirror image of Fig. 1a; r_{GS} is higher in absolute terms than r_{GH} when the inequality holds

$$r_{GH} < s_G/2s_H . \tag{12}$$

Both correlation coefficients are equal in absolute value either when (12) transforms into an equality, or, when $s_G = 0$, or, finally, when $r_{GH} = \pm 1$. The plot of ΔS^0 vs ΔG^0 will overestimate the actual fit, either when this fit is poor and always when r_{GH} is negative, or when the variance of ΔG^0 is large compared to that of ΔH^0 (always when $s_H/s_G < 0.5$). In the opposite case the fit is underestimated. It may happen that the two incorrect plots overestimate the fit; according to (8) and (12) this is possible only when $r_{GH} < 0.5$.

The real regression line with the slope b_{HG} is mapped into the coordinates ΔS^0 vs ΔG^0 with the slope b''_{HG} given by

$$b''_{HG} = (b_{HG} - 1)/T = (s_H r_{GH} - s_G)/Ts_G . \tag{13}$$

This time the transformed line is identical with one regression line drawn in the coordinates ΔS^0 vs ΔG^0, namely with that calculated for ΔG^0 as the independent variable (slope b_{SG}). The second regression line has the slope

$$1/b_{GS} = (s_G^2 - 2s_G s_H r_{GH} + s_H^2)^{1/2}/Ts_G(s_H r_{GH} - s_G) . \tag{14}$$

The two expressions (13) and (14) are equal only if $r_{GH} = \pm 1$. Hence the plot ΔS^0 vs ΔG^0 will yield the actual regression line when ΔG^0 is taken as the independent variable. From it the isokinetic temperature β can be obtained according to equations (13) and (6), however, the value of the correlation coefficient r_{GS} in this plot does not give a true picture of the fit (see Examples).

EXAMPLES

The individual examples may give different pictures since they are characterized by two independent parameters: the correlation coefficient r_{GH} expressing the fit in primary independent coordinates, and the ratio $c = s_H/s_G$. It follows from the foregoing analysis (Fig. 1) that good fits are usually underestimated in improper coordinates and bad ones overestimated; in the latter case the slope of the correlation line may also be significantly in error. The following examples show the principal possibilities which may occur.

Example 1. The protonation of aniline and of ten *meta-* and *para-*substituted anilines was followed by calorimetric and emf measurements and values of ΔG^0, ΔH^0 and ΔS^0 have been determined[13]. As already mentioned this set of data lies at the boundaries of the applicability of our approach since the errors in ΔG^0 and ΔH^0 are of comparable magnitude. However, the latter may be somewhat underestimated, as the comparison with other measurements[16,20] suggests. On the other hand this set gives the best correlation known to us and hence cannot be omitted.

In Fig. 2 the three thermodynamic quantities ΔG^0, ΔH^0 and ΔS^0 are plotted against each other in various combinations. The statistically correct plot ΔH^0 *vs* ΔG^0 (Fig. 2a) yields a satisfactory fit ($r_{GH} = 0.9787$); it could be anticipated for a reaction series obeying the Hammett equation at different temperatures[2]. Since the ratio s_H/s_G is close to unity (0.8186) the correlation coefficients in the plots of ΔH^0 *vs* ΔS^0 (Fig. 2b) and ΔS^0 *vs* ΔG^0 (Fig. 2c) are significantly smaller in absolute terms than r_{GH}. The real regression line with the slope $b_{HG} = 0.8012$ has been drawn in Fig. 2a (full line) and mapped into the remaining two (full lines). Its slope in Fig. 2b represents the isokinetic temperature $\beta = -1190$ K; this is a case of so-called anticompensation[2,4]. In Fig. 2c this actual regression line is identical with the regression line drawn in the coordinates em-
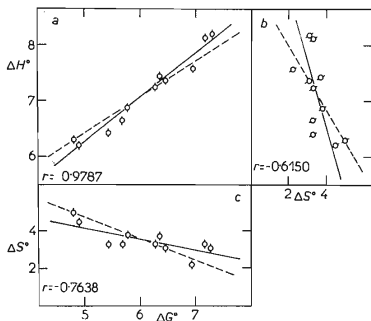

Fig. 2

Isoequilibrium Relationship in Various Coordinates, Protonation of *meta-* and *para-*Substituted Anilines[13] in Water at 25°C

Real and apparent relationships are shown by full and broken lines, respectively. The experimental error shown corresponds approximately to the doubled standard deviation.

ployed and can be determined safely only by computation. In Fig. 2b the real regression line is different from the apparent one, drawn in the coordinates employed (broken line); the latter, corresponding to the apparent isokinetic temperature $\beta^* = -574$ K, has been mapped into the remaining graphs (broken lines). From the mapping into Fig. 2a it is evident that this line bears no relation to original experimental data.

Example 2. From the ample experimental data concerning protonation of amines[10] we selected a reaction series of structurally related compounds, including eleven secondary amines bearing substituents larger than methyl. The data have been processed in the same way as in the foregoing example (Fig. 3). While the ratio s_H/s_G has almost the same value (0·8530) as previously, the main contrast with Example 1 is the lower correlation coefficient $r_{GH} = 0.9317$; the fit can be called only fair. Therefore, the correlation coefficients in Figs. 3b and 3c are so low that no correlation is perceptible at all. In the original literature[10] no correlation was detected between ΔG^0 and ΔS^0 (*i.e.* in the improper coordinates) for the whole set of amines. A further consequence of the low correlation coefficient is a larger divergence between the real ($\beta = -1154$ K) and apparent ($\beta^* = -145$ K) isokinetic temperature.

Example 3. In the foregoing examples a real correlation between experimental quantities ΔG^0 and ΔH^0 exists, so that the validity of the isokinetic relationship could be proven within the limits of a certain accuracy. In the following examples no real correlation exists but an apparent one may appear in one of the possible improper coordinate systems. From the data on ionisation of carboxylic acids[7] we selected those obtained by calorimetry; the set involves 19 aliphatic (with the exception of benzoic acid) monocarboxylic or dicarboxylic acids, mostly without substituents. The second dissociation of racemic 2,3-di-(tert-butyl)-succinic acid has been omitted from the statistical treatment (full points in Fig. 4). Fig 4a reveals no correlation of experimental quantities ($r_{GH} = -0.1883$) but an apparent relationship emerges between ΔG^0 and ΔS^0 with a pretty high correlation coefficient (Fig. 4c). This is due to the low ratio $s_H/s_G = 0.3930$; *i.e.* when the variance of ΔH^0 is negligible, the graph of ΔS^0 *vs* ΔG^0 shows only the dependence
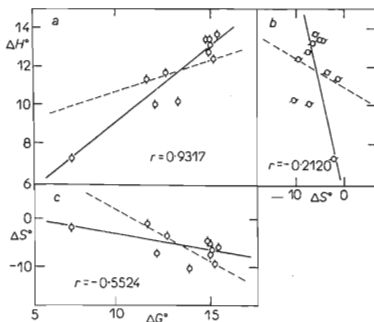

FIG. 3

Isoequilibrium Relationship for the Protonation of Secondary Amines[10]

Notation as in Fig. 2.

of ΔG^0 on itself. Even the graph of ΔH^0 *vs* ΔS^0 overestimates the fit. The apparent isokinetic temperature β^* would be 52 K and the correctly computed one $\beta = 21$ K, even the latter is meaningless since no real isokinetic relationship exists in this case.

The present analysis accounts for the statement[7], inconceivable at the first sight, that there is no correlation between the quantities ΔG^0 and ΔH^0 but a good correlation between ΔG^0 and ΔS^0. For the dissociation of carboxylic acids there is quite generally little correlation between ΔG^0 and ΔH^0, and low values of s_H/s_G are typical. This means that ΔH^0 values change little from one compound to another and the entropy term is decisive. Even a selected series of structurally more similar acids[9] yielded qualitatively the same picture.

Example 4. The extent of protonation of methyl-substituted anilines was measured for three mono-, six bis-derivatives and for the parent compound[12]. The graphical treatment (Fig. 5) does not reveal any significant correlation between the experimental quantities ($r_{GH} = 0.0973$). A striking difference compared with the previous example is the high ratio $s_H/s_G = 3.461$, which means that ΔH^0 values extend over a large range and the comparison with later calorimetric[13,16] as well as with temperature-dependence[20] measurements suggests that a major part of this spread is due to gross experimental errors. The high s_H/s_G ratio brings about an apparent correlation in the graph of ΔH^0 *vs* ΔS^0 which is in fact due to the dependence of ΔH^0 (or, say, of errors in ΔH^0) on itself. The apparent isokinetic temperature is $\beta^* = 282$ K, the formally correctly computed one $\beta = -151$ K. The discussion based upon the ΔH^0 *vs* ΔS^0 correlation[12] is clearly in error.

Example 5. The last example is not concerned with simple thermodynamic quantities but with differences of the corresponding values in dilute ethanol (0.9 mol fraction of water) and in pure water, since it was believed that these values should exhibit isokinetic behaviour more precisely[13]. The plot of direct experimental quantities (Fig. 6a) shows actually only small differences in ΔG^0 between individual compounds; even the differences in ΔH^0 exceed only slightly experimental
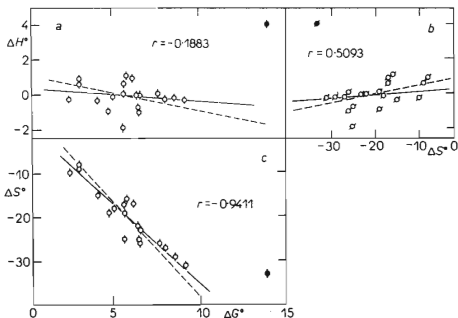

FIG. 4

Isoequilibrium Relationship for the Ionisation of Aliphatic Carboxylic Acids[7]
    Full point omitted from calculations.

errors[13]. The correlation coefficient $r_{GH} = -0.0974$ does not differ significantly from zero and the ratio $s_H/s_G = 5.317$ is still higher than in the foregoing example. Hence in the coordinates of ΔH^0 vs ΔS^0 an apparent correlation emerges with an apparent isokinetic temperature $\beta^* = 283$ K; the formally correct value would be $\beta = 119$ K. The whole picture resembles the foregoing example and even the numerical characteristics are close. The correlation is clearly fictious and cannot support the theoretical concept[15] of internal and external enthalpies and entropies.

DISCUSSION

The main purpose of this analysis is to distinguish correct and incorrect correlation procedures. The theoretical arguments as well as the practical examples cited may suffice to demonstrate that both plots of ΔH^0 vs ΔS^0 (ref.[11-13]) and of ΔS^0 vs ΔG^0 (ref.[7-10,16]) are misleading and yield false ideas regarding the fit; the former gives in addition an incorrect value of the slope. Usually, the situation is somewhat more favourable than for kinetic data[4-6] (or temperature dependence of equilibrium constants) and completely fictious correlations are encountered less frequently (they are possible only with very low or very high values of $c = s_H/s_G$, see Fig. 1a,b). A correct mathematic treatment is also much easier than is the case for kinetic data and nothing more is required than to choose proper coordinates. The only assumption is, as stated at the beginning of this paper, that the error in ΔG^0 is negligible
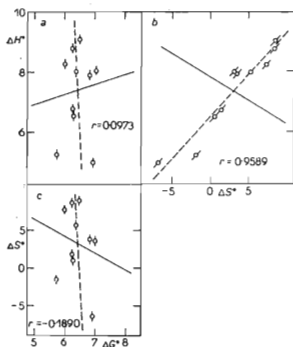

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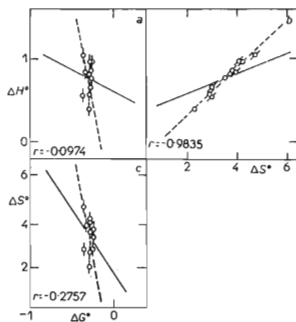Isoequilibrium Relationship for the Protonation of Methyl- and Dimethylanilines[12]

Fɪɢ. 6

Isoequilibrium Relationship of Differential Thermodynamic Quantities for the Protonation of *meta*- and *para*-Substituted Anilines in Dilute Ethanol and Pure Water[13]

compared to the error in ΔH^0; this requirement is generally fulfilled. When computing the Examples all measurements were assumed to equal weight, *i.e.* the same precision, however, different weights can be incorporated easily into the simple regression. We proposed[2,5,6] that this should be done only if there is very good evidence of differing precision, confirmed by statistical tests.

When the correct statistical procedure is applied to available sets of data (essentially those referring to ionisation), very few significant proofs of the isokinetic behaviour are obtained (Examples 1, 2) fewer in fact than one would have expected according the relation to extrathermodynamic relationships. A valid isokinetic relationship is a necessary presumption of these relationships (Hammett, Taft equations *etc.*) to hold at different temperatures[2,21]. Many reaction series, investigated by calorimetry, such as ionisation of substituted carboxylic acids, phenols or anilines, have been of fundamental importance to the discovery and testing of extrathermodynamic relationships, for defining of constants *etc.* Hence one would expect isokinetic behaviour particularly in these series. We suspect that many apparent discrepancies are in fact due to experimental errors, which are, in spite of recent progress in calorimetry, still larger than the correlation would require, and in some cases much larger than the experimenters suppose (see the disagreement in ref.[12,13,16,20]). In our opinion the isokinetic relationship should hold quite commonly in reaction series obeying the Hammett equation and in many others, *i.e.* it should be fulfilled with an accuracy common in extrathermodynamic relationships and in the range of several tens of degrees at least.

Considering the experimental errors we wish to stress that their existence is not essential for the main conclusions of this paper, which would not loose its validity by improving the experimental technique. When a regression line is drawn through a set of points, it is implicitly supposed that there are some factors controlling the linear dependence and in addition other factors causing the scatter. The latter may be
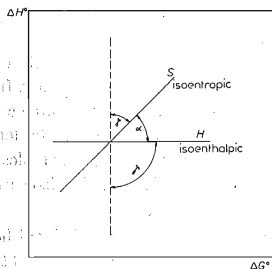

FIG. 7

Schematic Representation of Possible Slopes in the ΔH^0 *vs* ΔG^0 Plot

The ranges denoted α and γ correspond to anticompensation and compensation, respectively.

experimental errors as well as any other factors with zero mean value. The mathematical formulae are the same when one considers relationships between approximate quantities or approximate relationships between exact quantities. (Note also that the overall picture in Fig. 2—6 is not dependent upon the relatively small experimental errors.) In the literature the problem of the isokinetic relationship has been sometimes reduced to a problem of experimental errors[22].

TABLE I

Classification of Reaction Series and Slopes in Various Coordinates

No	Characterisation	Isokinetic temperature β	Slope in the coordinates		
			$\Delta H^0 \, vs \, \Delta G^0$ b_{HG}	$\Delta H^0 \, vs \, \Delta S^0$ b'_{HG}	$\Delta S^0 \, vs \, \Delta G^0$ b''_{HG}
1	isoentropic	∞	1	∞	0
2	isoenthalpic	0	0	0	$-T_{exp}^{-1}$
3a		$> T_{exp}$	> 1	$> T_{exp}$	> 0
3b	compensation	$0 < \beta < T_{exp}$	< 0	$0 < b' < T_{exp}$	$< -T_{exp}^{-1}$
3c		T_{exp}	∞	T_{exp}	∞
4	anticompensation	< 0	$0 < b < 1$	< 0	$-T_{exp}^{-1} < b'' < 0$

The slope β of the isokinetic relationship has been used for classification of reaction series[2,4,23] into isoenthalpic, isoentropic, and those with compensation and with anticompensation. The slopes in the graphs of $\Delta S^0 \, vs \, \Delta G^0$ and of $\Delta H^0 \, vs \, \Delta G^0$ depend upon β according to equations (3) and (4); the possible values for individual classes are given in Table I. Particularly the plot $\Delta H^0 \, vs \, \Delta G^0$, statistically correct for calorimetric measurements, is convenient, since the various classes can be distinguished even more easily than from temperature dependence, *i.e.* from the graph of log K (or log k) $vs \, T^{-1}$. The reaction series is isoenthalpic when the variance in ΔH^0 is not significant, it is isoentropic when the slope is not significantly different from unity (Fig. 7), in the remaining cases either compensation or, less frequently, anticompensation takes place. According to experience in measurements of temperature dependence, a positive value of β, higher than the experimental temperature should be most frequent (case 3a, Table I), however, both Examples 1 and 2 belong to case 4. In contradistinction to kinetics the case 3c could be also easily realized, when only the differences in ΔG^0 would be insignificant.

Since isoenthalpic and isoentropic reaction series often cannot be distinguished in practice and even the theoretical meaning is not unambiguous, we suggested that the only meaningful classification is one based upon series with increasing (cases 1, 3a

and 4 in Table I) and decreasing (case 3*b*) selectivity[4]. The arguments given do not retain their full validity for calorimetric data, especially since the isoenthalpic and isoentropic reactions series can usually be discerned with relative confidence. In addition the term selectivity must be somewhat redefined; when it denotes simply larger differences in reactivity between individual reactions (compounds), it can be applied to kinetics as well as to equilibria. In Fig. 7 lines with positive slopes correspond to decreasing selectivity (common feature) those with negative slopes to increasing selectivity (not observed as yet with calorimetric data). The proper meaning of the whole classification is not yet understood and requires a new theoretical approach.

With the present paper we consider statistical problems connected with the isokinetic relationship to be essentially solved in as much as the parameters ΔH^0, ΔS^0 or ΔH^*, ΔS^* are treated as temperature independent. Their variability with temperature makes a statistical treatment much more difficult; some problems connected with this will be dealt with in a subsequent communication[24].

LIST OF SYMBOLS

b_{HG}, b_{HS}, b_{SH}	slopes of regression lines (the first subscript indicates the independent, the second
b_{GS}, b_{SG}	the dependent variable)
b'_{HG}	slope of the regression line in coordinates ΔH^0 vs ΔG^0 mapped into coordinates ΔH^0 vs ΔS^0
b''_{HG}	slope of the regression line in coordinates ΔH^0 vs ΔG^0 mapped into coordinates ΔS^0 vs ΔG^0
c	ratio s_H/s_G
ΔG^0	free enthalpy of reaction
h_0	intercept in equation (*1a*)
ΔH	common symbol for reaction or activation enthalpy
ΔH^0	enthalpy of reaction
r_{GH}, r_{GS}, r_{SH}	correlation coefficients (subscripts indicate the variables)
s_G, s_H	standard deviations (from the averages) of the quantities indicated by subscripts
ΔS	common symbol for reaction or activation entropy
ΔS^0	standard entropy of reaction
β, β^*	isokinetic temperature (actual and apparent)
δ	operator indicating the difference when comparison is made to a reference reaction
Δ	operator indicating the difference of the final (transition) and ground stages

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