SHORT PAPER

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On the correlation between $\Delta H^{\ddagger}$ vs $\Delta S^{\ddagger}$ in the thermal *cis*-to-*trans* isomerization of azobenzenes[†]

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Variable-temperature kinetics allow the determination of $\Delta H^{\ddagger}$ vs $\Delta S^{\ddagger}$ in a single experiment. Multiple variable-temperature data sets for the thermal isomerization of *cis*-azobenzene show an apparent isokinetic relationship, but this is due only to the mathematical correlation between $\Delta H^{\ddagger}$ vs $\Delta S^{\ddagger}$; the magnitude of the effect is almost identical to that observed for the thermal isomerization of a series of *ortho*-alkylated azobenzenes.

Much discussion has surrounded the topic of extrathermodynamic relationships (linear free energy relationships) in physical-organic chemistry since they were first uncovered in the 1920s, notably the existence or non-existence of the entropy-enthalpy relationship[1]. A common strategy is to relate rate or equilibrium constants to a fixed external scale of parameters, such as substituent constants, for analysing a series of mechanistically and structurally related chemical systems. As an approximation, $\Delta H°$ and $\Delta S°$ (or $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for kinetic data) for a given reaction are often taken to be temperature-independent parameters (at least, over moderate temperature intervals). A linear relationship between the enthalpic and entropic contributions implies that the change in enthalpy in proceeding from reaction i to reaction j in a series is accompanied by a parallel change in enthalpy. Under these circumstances a plot of $\Delta H°$ vs $\Delta S°$ (or $\Delta H^{\ddagger}$ vs $\Delta S^{\ddagger}$ for kinetic data) will have slope $\beta = \Delta\Delta H/\Delta\Delta S$, whose units are temperature. Many authors have proceeded to identify the slope β as the so-called isokinetic temperature[1,2], at which all reactions in a series would proceed with the same rate constant, and to draw inferences about its meaning. As Exner[1,3] pointed out, however, the existence of an experimentally accessible isokinetic temperature would be problematic because the reactivity order of a series of compounds would become inverted as one passed over the isokinetic temperature. In other words, the susceptibility of a reaction to substituent effects would be reversed simply by changing the temperature.

Enthalpies and entropies of activation are conventionally obtained from kinetic data from plots of log k vs T^{-1}, affording initially the Arrhenius parameters E_{act} and A, from which $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are obtained from the following relationships.

$\Delta H^{\ddagger} = E_{\mathrm{act}} - RT$;
$\Delta S^{\ddagger} = R\{\ln(A) - \ln(T) - 24.76\}$ for rate constants expressed in s^{-1} or $\mathrm{l\ mol^{-1}\ s^{-1}}$

In principle, enthalpies and entropies are independent parameters that represent temperature-dependent and -independent parameters with respect to K. Experimentally, however, this is not the case, even if the temperature interval is small enough that heat capacity changes can be neglected. One method of gathering equilibrium data is to obtain $\Delta H°$ calorimetrically and $\Delta S°$ from the equilibrium constant: $\Delta S° = \Delta H°/T + R \times \ln(K)$. If $\Delta H°$ is overestimated, it follows that $\Delta S°$ will also be overestimated[4]. When ΔH and ΔS are obtained from the temperature variation of the rate constant or equilibrium constant, they are inevitably statistically correlated. For the variation of the equilibrium constant, one plots ln K vs T^{-1}; the slope is $-\Delta H°/R$ and the intercept $\Delta S°/R$. If the experimental plot has too steep a slope (overestimated $\Delta H°$), the intercept ($\Delta S°$) will also be overestimated. In an Arrhenius plot of ln K vs T^{-1}, the slope is $-E_{\mathrm{act}}/R$ and the intercept is ln(A), and so similar considerations apply to $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$.

In the absence of a detailed statistical analysis[5,6], it is very difficult to know whether some or all of the contribution to β might be caused by this statistical correlation between ΔH and ΔS. We report here an instance where the distinction seems to be fairly clear cut.

Some years ago, we reported an investigation of the thermal *cis*-to-*trans* isomerization of a series of *o*-alkylated azobenzenes[7]. The activation energies for this reaction showed little dependence on the size of the alkyl substituents, a finding that was rationalized in favour of the inversion mechanism of *cis*-to-*trans* isomerization, rather than the alternative of rotation around the N=N bond. We argued that the inversion mechanism would be insensitive to steric hindrance at the *ortho* positions, because the route to the transition state straightens out the molecule, moving the bulky substituents farther apart. In contrast, N=N rotation swings the bulky groups directly past each other. In the present work, we have plotted the values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for the *cis*-to-*trans* isomerization of this series of *ortho*-substituted azobenzenes. The data are reasonably linear (Figure 1), suggesting an enthalpy–entropy relationship with an apparent isokinetic temperature of 338 K, almost in the experimentally accessible range. Exner[1,3] has argued strongly that experimentally accessible isokinetic temperatures are likely to be experimental or computational artifacts, usually caused by the use of a narrow temperature range for making the experimental measurements. We therefore sought to test this question experimentally.

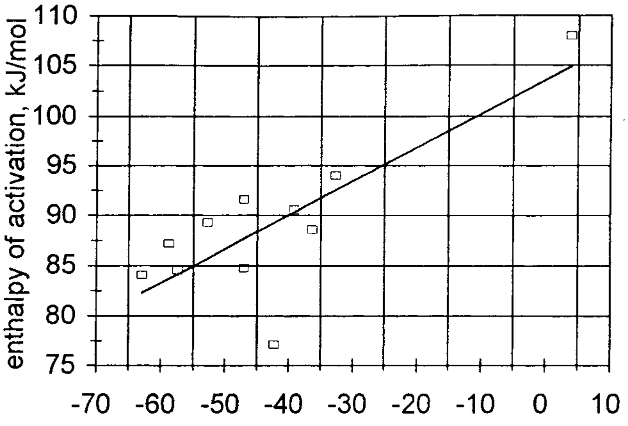

Fig. 1 Isokinetic plot for the thermal isomerization of a series of *o*-alkyl azobenzenes

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

At about the same time as we were studying *o*-alkylated azobenzenes, our laboratory was also investigating the use of variable temperature kinetics to estimate activation energies[8]. This technique involves beginning a kinetic run at a low temperature at which the reaction is very slow, then progressively increasing the temperature. A sigmoid curve of "reactant remaining" vs time is obtained, because the reaction rate initially increases with temperature, but then slows down as the reactant is consumed. The elaboration of the data for variable-temperature kinetics involves the integrated form of the rate equation.

$$[\text{reactant}]_t = [\text{reactant}]_0 \exp[-A \int \exp(E_{act}/RT)\, dt]$$

Multiple linear regression is used to fit the observed values of [reactant], temperature, and time, affording E_{act} and A as the fitted parameters, from which $\Delta H^\ddagger$ and $\Delta S^\ddagger$ are then calculated.

Although we concluded[8] that the variable-temperature method is no less labour-intensive than conventional, constant-temperature kinetics with respect to obtaining activation energies of reasonable precision, a unique feature of the method is that each kinetic run affords its own value of $\Delta H^\ddagger$ and $\Delta S^\ddagger$. In constant-temperature kinetics a single value of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ is obtained from the aggregated data. Variable-temperature kinetics made it possible to examine apparent trends between $\Delta H^\ddagger$ and $\Delta S^\ddagger$ for the case of a single substrate reacting under the same experimental conditions, in our case, the *cis*-to-*trans* thermal isomerization of azobenzene, which was followed spectrophotometrically at 437 nm.

Five completely independent variable temperatures experiments, with replicated data points, were the basis for estimating $\Delta H^\ddagger$ and $\Delta S^\ddagger$. The data were worked up as follows: the five independent experiments; 10 calculations in which two combined data sets were subjected to multiple linear regression; 10 calculations in which three data sets were combined; five calculations using four data sets; and one calculation utilizing all the data. The last calculation gave a grand mean of $\Delta H^\ddagger = 86.0 \pm 4.5$ kJ mol^{-1} and $\Delta S^\ddagger = -63.3$ J mol^{-1} K^{-1}. Figure 2 shows the correlation obtained between $\Delta H^\ddagger$ and $\Delta S^\ddagger$ for the five independent data sets (squares) and the 10 pair-wise data sets (circles). An excellent apparent enthalpy–entropy relationship is seen, with slope $\beta = 331$ *K*, almost identical to the value obtained from Figure 1. In this case, there can be no possibility of a true linear relationship between enthalpy and entropy, since all the data sets represent the same reaction; variations between $\Delta H^\ddagger$ and $\Delta S^\ddagger$ can reflect only statistical correlations in the experimental data. The use of variable temperature kinetics thus enabled us to show that the isokinetic relationship of Figure 1 is almost certainly an artifact.

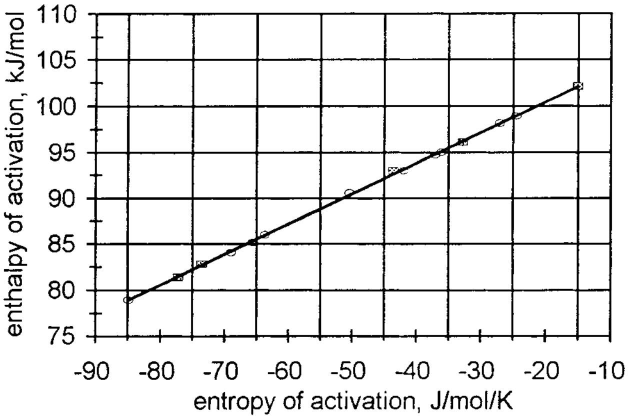

Fig. 2 Isokinetic plot for the thermal isomerization of *cis*-azobenzene: for symbols, see text

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