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Relation between $\Delta C_p^{\ddagger}$ and Pattern in $\Delta G^{\ddagger}$ and $\Delta H^{\ddagger}$ for Organic Solvolyses in H_2O and D_2O

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A multivariate data analysis has been made of the activation parameters $\Delta G^{\ddagger}$ and $\Delta H^{\ddagger}$ for solvolysis reactions in H_2O and D_2O. The results show that it is unnecessary to use the parameter $\Delta C_p^{\ddagger}$ to probe the solvent participation in hydrolysis reactions. Thus the difficulties in determining $\Delta C_p^{\ddagger}$ are avoided.

The temperature dependence of solvolytic reactions in water and mixed aqueous solvents is usually represented by the Arrhenius equation $\ln k = A + B(1/T - 1/T_0)$. The curvature of an Arrhenius plot ($\ln k$ against $1/T$) gives the activation heat capacity ($\Delta C_p^{\ddagger}$). This parameter is often used for mechanistic considerations. For solvolyses it is believed to be related to the degree of solvent order around the transition state.[1] To estimate $\Delta C_p^{\ddagger}$ it is necessary that the rate constants are determined with very high precision (better than 0.5 %).

The determination of $\ln k$ from the raw kinetic data, *i.e.*, plotting $\log C$ against t, is often subject to systematic errors. These systematic errors are masked by the way the data are plotted. Therefore the imprecision of $\Delta C_p^{\ddagger}$ is often grossly underestimated and the utility of $\Delta C_p^{\ddagger}$ for mechanistic studies is somewhat doubtful.[2,3] The present paper investigates the possibility to substitute $\Delta C_p^{\ddagger}$ by parameters derived from a multivariate analysis of kinetic data in H_2O and D_2O.

DATA

The kinetic data (Table 1) were mainly taken from the hydrolysis reactions studied by Robertson and coworkers. Data were collected for reactions run in both H_2O and D_2O. We also included our own hydrolysis data of a secondary methanesulfonate ester. Activation parameters $\Delta G^{\ddagger}$ and $\Delta H^{\ddagger}$ in H_2O and D_2O (Table 1) were calculated at 50 °C by using an extended Arrhenius equation ($\ln k = A + B(1/T - 1/T) + C(1/T - 1/T_0)^2$). The differences between $\Delta G^{\ddagger}$ and $\Delta H^{\ddagger}$ using this equation or the Valentiner equation[15] ($\ln k = A + B/T + C \ln T$) are negligible.[16]

Substrates *2–10* were used as the training set to estimate the principal components model (see below). Substrates *2* (*t*-butyl chloride which often shows an anomalous behaviour) and *11*, *12* (our own data) were used as a test set later fitted to the model. The data were standardized (scaled) by dividing each of the four variables by its standard deviation, resulting in a variance of 1 for each variable when the data analysis starts (see Table 1).

DATA ANALYSIS

The scaled data $y_{1k} = \Delta H^{\ddagger}$ (H_2O), $y_{2k} = \Delta G^{\ddagger}$ (H_2O), $y_{3k} = \Delta H^{\ddagger}$ (D_2O) and $y_{4k} = \Delta G^{\ddagger}$ (D_2O) were fitted to a principal components model using the SIMCA-package.[17] (Index i refers to the variables,

$$y_{ik} = \alpha_i + \sum_{a=1}^{A} \beta_{ia}\theta_{ak} + \varepsilon_{ik}$$

k to the objects and a to the number of product terms in the equation.)

This analysis is closely similar to factor analysis introduced in the analysis of physical chemistry data by Weiner *et al.*[18,19] The analysis corresponds to the least squares fitting of a straight line (for $A = 1$) or an A-dimensional hyperplane to the data points in the 4-dimensional space formed by the

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Table 1. Substrates and activation parameters at 50 °C.

No. (k)	Substrate (object)	H_2O $\Delta H^{\neq}$ cal mol^{-1} i=1	H_2O $\Delta G^{\neq}$ i=2	H_2O $\Delta C_p^{\neq}$ cal K^{-1} mol^{-1}	Ref.	D_2O $\Delta H^{\neq}$ cal mol^{-1} i=3	D_2O $\Delta G^{\neq}$ i=4	D_2O $\Delta C_p^{\neq}$ cal K^{-1} mol^{-1}	Ref.
1	*t*-Butyl chloride	20851	21981	−65	4	20530	22158	−90	12
2	2-Chloro-2-methyl-1-propyl methyl ether	22876	25462	−86	5	24089	25559	−73	12
3	2-Bromo-2-chloropropane	23803	25004	−79	6	24190	25179	−89	12
4	2,2-Dibromopropane	24991	25781	−72	6	25155	25946	−102	12
5	1-Chloro-4-hydroxybutane	23172	28180	−45	7	23813	28326	−65	7
6	Isopropyl bromide	24337	27453	−58	8	24642	27619	−68	13
7	2-Bromoisobutyrateion	27150	24994	−65	9	27571	25439	−84	9
8	Methansulfonyl chloride	18584	25427	−44	10	18909	25681	−45	10
9	3-Methyl-2-methane-sulfonyloxybutane	19470	23856	−31	11	19366	23877	−35	11
10	Bensensulfonyl chloride	14979	23947	−55	10	15670	24177	−46	10
11	2-Methanesulfonyloxy-1-propanol[a]	22173	24547	−94	2	22086	24564	−52	14
12	2-Methanesulfonyloxy-1-propanol[b]	22490	24462	−12	2	22571	24550	−11	14

[a] Pure H_2O or D_2O. [b] H_2O or D_2O with 0.2 mol l NaBr.

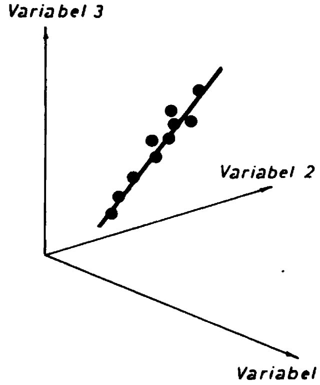

Fig. 1. Principal components model with $A=1$ fitted to points in a three dimensional space.

four variables (Fig. 1). The parameters α_i determine the center of the data set and the parameters β_{ia} are the direction coefficients of the line (plane). For each object (substrate in the present study) the parameters θ_{ak} describe the site of the object point projected down on the model (line or plane). Hence the θ-values in Table 3 can be used to relate the substrates to each other. A physical interpretation of the values is obtained by plotting θ_{1k} against $\Delta C_p^{\ddagger}$ determined by the Arrhenius equation (Fig. 2). We see a correlation for the halides except for t-butyl chloride. A parallel but different correlation is indicated for substrates *8* and *10* (sulfonyl chlorides) and our own data (substrate *12*) measured under the same conditions (salt buffer). Hence, the plot indicates separate models for different kinds of substrates (different types of leaving group). We note that the precision of $\Delta C_p^{\ddagger}$ is about $+/-15$ cal K^{-1} mol^{-1} which explains most of the scatter around the lines in Figs. 2 and 6.[1,2] In the analysis one predominant component is formed which explains about 70 % of the variation in the data. This component is well-illustrated by the linear pattern seen in a plot of variables 1+2 against 3+4 (Fig. 3). The same results are shown quantitatively in Table 3 with the residual standard deviation for each compound shown.

In Fig. 4 a plot of θ_{1k} against θ_{2k} shows a pattern of subgroups. The tertiary substrates (t) lie at the top of the plot, the secondary (s) in the middle and the primary substrate *5* and the two sulfonyl chlorides (p) at the bottom. As can be seen,

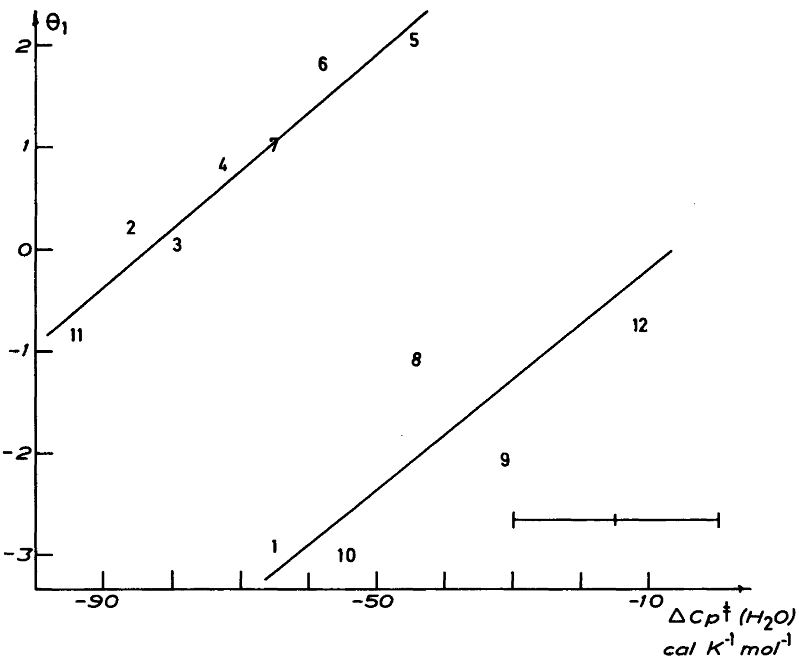

Fig. 2. A plot of the first eigenvector (θ_{1k}) against $\Delta C_p^{\ddagger}$ (H_2O). The numbers are from Table 1. The horizontal bar indicates the approximate precision (standard deviation) according to Refs. 2 and 3.

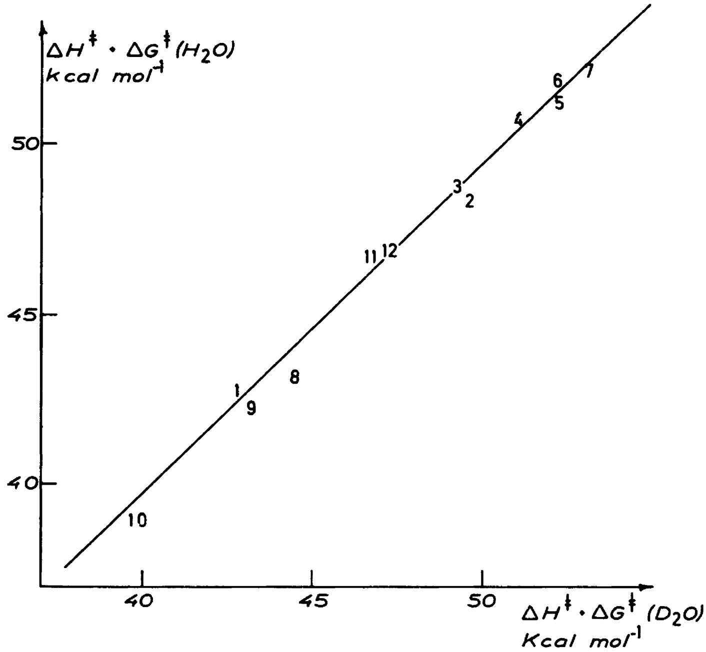

Fig. 3. A plot of $\Delta G^{\neq}+\Delta H^{\neq}$ (H_2O) against $\Delta G^{\neq}+\Delta H^{\neq}$ (D_2O). The numbers are from Table 1.

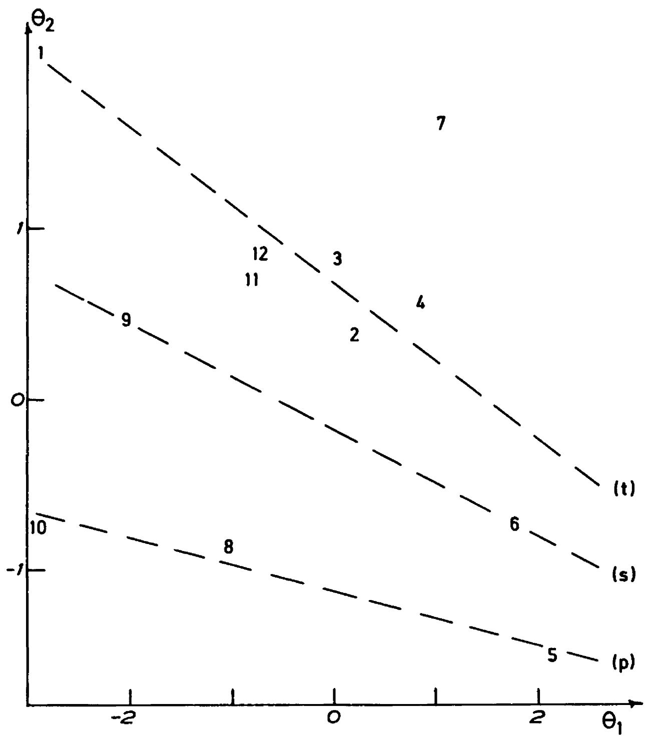

Fig. 4. A plot of the two eigenvectors θ_{1k} and θ_{2k} against each other. Substrate numbers are from Table 1. t, tertiary; s, secondary; p, substrates *5*, *8* and *10*.

Table 2. α_i and β_{ia} parameters for the component analysis. Weighting factor (w) and standard deviation (SD) for the variables are also presented.

Variable i[a]	α_i	β_{i1}	β_{i2}	$w \times 10^4$	SD
1	5.881	0.497	0.508	2.66	0.056
2	17.72	0.496	−0.511	6.93	0.044
3	5.994	0.503	0.492	2.65	0.056
4	17.87	0.504	−0.489	6.94	0.045

[a] Variable numbers are from Table 1. As can be seen from the SD's the 2-component model describes about 95% of the variation in each variable.

substrate 7 falls outside the tertiary substrates. This substrate is the only ionic species in the data set and one might expect this behaviour. Our data (*11*, *12*) fall into the area of tertiary substrates. It may depend on that they have a cyclic transition state (the hydroxylic group gives assistance).

Analysis of water data. From Table 2 we see that the values of β_{i1} are the same for all four variables and that β_{i2} are pairwise the same for $\Delta H^{\neq}$ (H_2O), $\Delta H^{\neq}$ (D_2O) and $\Delta G^{\neq}$ (H_2O), $\Delta G^{\neq}$ (D_2O), respectively. Therefore $\Delta G^{\neq}$ (H_2O) and $\Delta H^{\neq}$ (H_2O) contain the same information as the full set of four variables albeit with less precision. Hence it should be sufficient to analyze these two water parameters instead of $\Delta C_p^{\neq}$.

Fig. 5 shows a plot of $\Delta G^{\neq}$ (H_2O) against $\Delta H^{\neq}$ (H_2O). It is seen that this plot exhibits the same pattern as Fig. 4. Water data exist for numerous reactions and Fig. 5 also includes most known literature data. It is seen that the patterns indeed are consistent with three groups corresponding to primary, secondary and tertiary substrates, respectively. We note that this plot is actually an isokinetic plot according to Krug and Hunter.[20,21] Isokinetic relationships are expected from groups of similar substrates.[22,23] Hence the present analysis is a corroboration of this expectation and a demon-

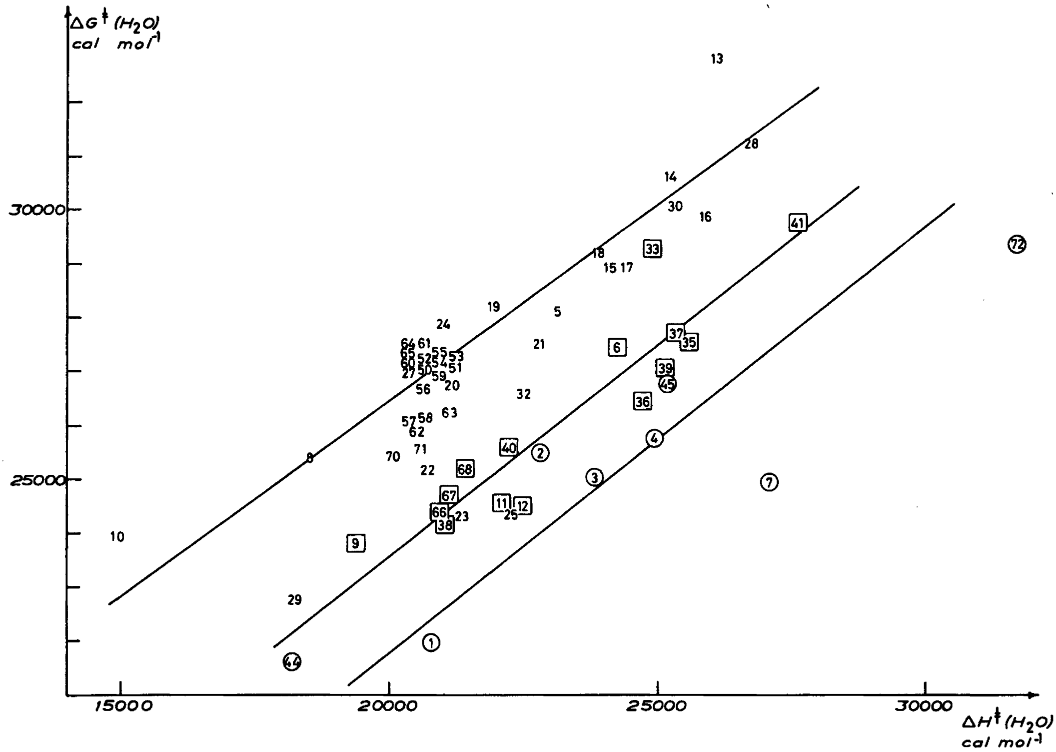

Fig. 5. A plot of $\Delta G^{\neq}$ (H_2O) against $\Delta H^{\neq}$ (H_2O). Numbers *1*–*12* are from Table 1. The other substrate numbers refer to the sequencial number (starting with *13*) in Tables I and II of Ref. 26 *e.g.* methyl fluoride (*13*), isopropyl chloride (*33*), ethyl methanesulfonate (*63*). The tertiary substrates are indicated by ○ and the secondary by □. The unmarked numbers are the primary substrates.

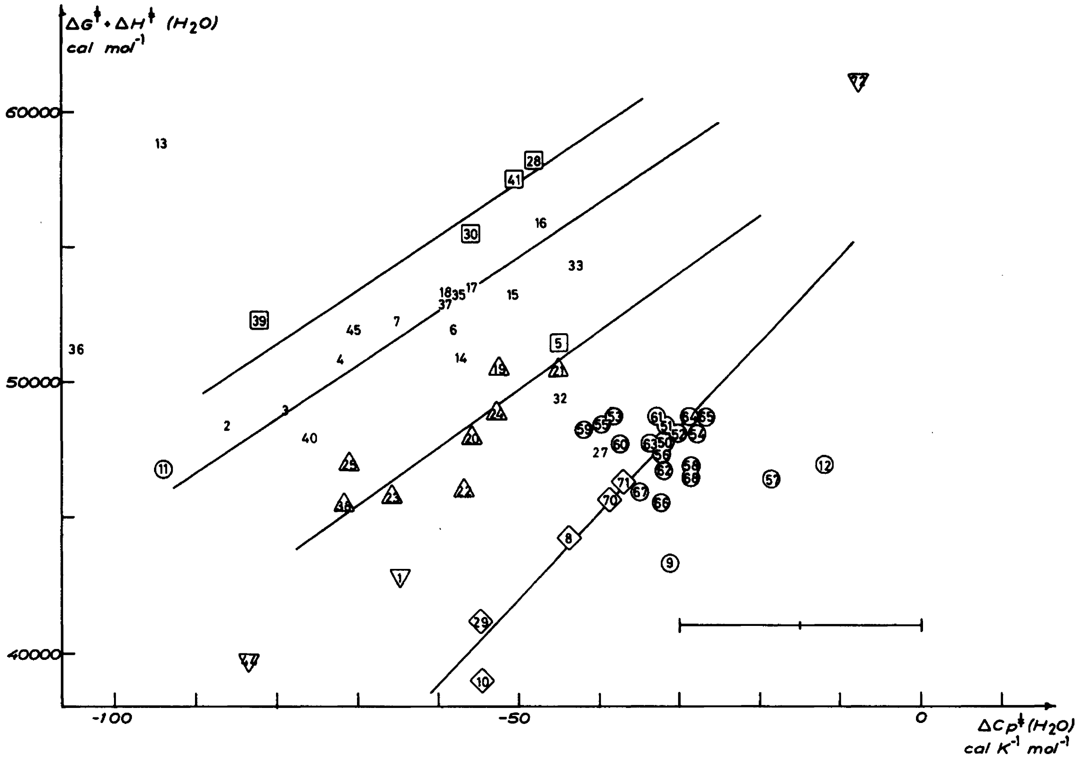

Fig. 6. A plot of $\Delta G^{\neq}+\Delta H^{\neq}$ (H_2O) against $\Delta C_p^{\neq}$ (H_2O). The numbering is explained in Fig. 5. The horizontal bar indicates the approximate precision (standard deviation) according to Refs. 2 and 3. Substrates with a hydroxyl group are indicated by □, unsaturated substrates by △, tertiary substrates by ▽, sulfonate esters by ○, substrates containing sulfur except the sulfonate esters by ◇. Substrates not indicated by a symbol are primary alkyl halides. The plot can be interpreted as a $\Delta S^{\neq}$ *versus* $\Delta C_p^{\neq}$ plot because $\Delta H^{\neq}$ is involved in both axis and $\Delta H^{\neq}+\Delta G^{\neq}=2\Delta H^{\neq}-T\Delta S^{\neq}$. However, the advantage of the plot presented is that $\Delta H^{\neq}$ and $\Delta G^{\neq}$ can be determined independently with good precision. Therefore the sum $\Delta G^{\neq}+\Delta H^{\neq}$ is considerably more precise than $\Delta S^{\neq}$.[23]

stration of the usefulness of such simple plots in physical organic chemistry.

Furthermore, $\Delta G^{\neq}$ (H_2O)+$\Delta H^{\neq}$ (H_2O) is correlated to $\Delta C_p^{\neq}$ as seen in Fig. 6. This plot parallels that of Fig. 2 where θ_{1k} is plotted against $\Delta C_p^{\neq}$ (H_2O). The correlation of substrates 2–7 has been expanded with more halides. In addition the following linear patterns can be seen.

(a) The aliphatic unsaturated substrates (*19–25*, *38*). Substrates *5* and *32* fall in these area, which indicates that they might undergo elimination before substitution.

(b) Substrates which contain a hydroxylic group (*28*, *30*, *39*, *41*) except for substrate *5* which falls into category (a).

(c) The tertiary substrates *1*, *44* and *72*.

(d) Substrates containing sulfur except the sulfonate esters (*8*, *10*, *29*, *70*, *71*).

The sulfonate esters (*9*, *12*, *50–68*) lie in the same region as (d) but form a cluster instead of a linear structure. Some substrates do not fall into the logic patterns described above. Substrate *27* (benzyl chloride) lies in the area of the sulfonate esters (containing benzylic substrates). The position of substrate *36* (cyclobutyl chloride) and of substrate *13* (methyl fluoride) is hard to explain.

CONCLUSION

We have previously shown that the activation heat capacity is hard to determine free of objec-

Table 3. θ_{ak}-values from the component analysis. The residual standard deviation (S_k) is also presented.

Object k[a]	θ_{1k}	θ_{2k}	S_k
1	−2.936	2.046	0.087
2	0.193	0.398	0.125
3	0.038	0.828	0.021
4	0.860	0.579	0.059
5	2.098	−1.498	0.005
6	1.865	−0.736	0.048
7	1.019	1.636	0.082
8	−1.034	−0.886	0.056
9	−2.027	0.461	0.110
10	−2.977	−0.762	0.056
11	−0.830	0.703	0.096
12	−0.757	0.844	0.063

[a] The numbers are from Table 1.

tions.[2] To avoid these difficulties one can instead make a multivariate analysis with the precise and more easily determined parameters $\Delta G^{\neq}$ and $\Delta H^{\neq}$. These variables determined from runs in both H_2O and D_2O seem to give information about the solvent participation in the reactions in a way similar to $\Delta C_p^{\neq}$. Finally it is shown that it is sufficient to use only $\Delta G^{\neq}$ and $\Delta H^{\neq}$ from runs in water to get the same information. Thus $\Delta C_p^{\neq}$ is redundant and the demanding experiments for its determination are not necessary.

From the chemical viewpoint the grouping in Figs. 4 and 5 is an interesting indication of dissimilarities in mechanism between primary, secondary and tertiary substrates. According to the hypothesis of Sneen[24,25] a single mechanistic scheme explains all solvolytic reactions. The results presented here contradict this hypothesis, indicating instead discrete differences between different types of substrates (Fig. 5) and different types of leaving groups. This also indicates that the linear free energy relationships for solvolytic reactivity such as the Winstein-Grunwald relationship are limited to similar substrates in a way analogous to the limitations of other linear free energy relationships.[26]

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