Equivalent or Alternative Forms of the Evans-Polanyi-Type Relations

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Linear relationships between energies of activation for exoergic free-radical reactions, in which structurally similar substrates are involved, and reaction exothermicities (ΔH^0) or homolytic bond dissociation energies [D(RH)] can be transformed to other equivalent expressions. Similar correlations are shown to hold also for reaction series of structurally similar alkyl free radicals with a given substrate. It is shown that the parameters ΔH^0 and D(RH) are linearly related to each other. The same parameters exhibit linear dependence also on the relevant ionization potentials of free radicals [IP(R)], Taft's alkyl inductive substituent constants [σ_I(R)], and the heterolytic bond dissociation energies for the process $R^+ + H^- \rightarrow RH$ [$D(R^+H^-)$]. Since the parameters ΔH^0, D(RH), σ_I(R), IP(R), and $D(R^+H^-)$ are interrelated, the Evans–Polanyi relationships appear to be alternative and, perhaps, trivial cases of the E_a vs. σ_I(R) correlations. It is pointed out that a given set of kinetic or physical data can be expressed in several alternative self-consistent but, nevertheless, arbitrary ways. In order to demonstrate the arbitrariness of these representations, we used reaction exothermicities for hydrogen abstraction by an iodine atom from a series of hydrocarbons as "additive substituent constants" to represent gas-phase ionization potentials of a series of ketones by the regression equation $\mathrm{IP}(R_1R_2CO) = 3.900(10^{-2}\sum\Delta H^0) + 7.095$ ($r = 0.994$).

The correlation between activation energies and reaction enthalpies for exoergic free-radical reactions was first reported by Polanyi for the reaction of sodium atoms with a series of alkyl halides.[1-3] Similar correlations have also been shown to hold for other free-radical reactions.[4-6] The correlation between activation energy E_a and reaction exothermicity ΔH^0 is of the form of eq 1 where $P = \Delta H^0$.

$$E_a = aP + b \tag{1}$$

A variant of eq 1 has been reported[7] which relates activation energies for hydrogen abstraction by methyl radical from a series of homologous and/or isomeric hydrocarbons with the respective homolytic bond-dissociation energies of the bond that is being *broken*, $P = D$(RH) in eq 1. As it has been pointed out,[6] the Polanyi-type relations hold for series of reactions in which structurally similar *substrates* are involved.

Recently we have correlated activation energies for hydrogen abstraction reactions by free radicals, as well as E_a's for various types of reactions, with the ionization potentials of free radicals [IP(R)],[8] with Taft's alkyl inductive substituent constants [σ_I(R)],[9] and with heterolytic bond-dissociation energies for the process $R^+ + H^- \rightarrow RH$, i.e., $P = D(R^+H^-)$[10] in eq 1.

This paper is intended to (1) point out that Polanyi-type relationships can be put into alternative equivalent forms, (2) report correlations of activation energies for hydrogen abstraction with homolytic bond-dissociation energies of the bond that is being formed, and (3) demonstrate that any two series of parameters used in Polanyi-type relationships are linearly related to each other. It will be shown that representations of physical or kinetic data in terms of substituent parameters may be arbitrary. We will argue that ionization potentials of free radicals should be the parameters of choice for representing these data.

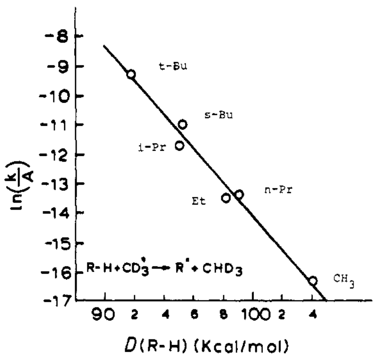

Figure 1. Logarithm of the ratio (rate constant at 164 °C)/(preexponential factor) plotted against D(RH).

It has already been shown for the case $P = \sigma_I$(R)[9] that eq 1 can be transformed into other equivalent equations by substituting eq 1 into the Arrhenius equation and by incorporating further the appropriate relations from the transition-state theory. Applying the same analysis to the generalized eq 1, one obtains eq 2 and 3. Equation 2

$$\ln k = aP/RT + \ln A + b/RT \tag{2}$$

$$\Delta H^{\ddagger} = aP + b \tag{3}$$

implies that a plot of ln (k/A) vs., e.g., $P = D$(RH) should be linear. An example of such a plot is given in Figure 1 for hydrogen atom abstraction by $CD_3\cdot$ from a series of hydrocarbons.[11] Equation 1 can even be put in the form of a conventional linear free-energy relationship, eq 4. In

$$\log (k/k_0) = a'\Delta H^0 + E \tag{4}$$

$$E = \log (A/A_0) + b' \tag{5}$$

the latter equation a and b are the coefficients of the linear regression equation of $E_a{}^0 - E_a$ vs., e.g., $P = \Delta H^0$, where a' and b' are the respective a and b parameters divided by $2.303RT$, and $E_a{}^0$ is the activation energy of the first member of the series (the reference state). Equation 4 is

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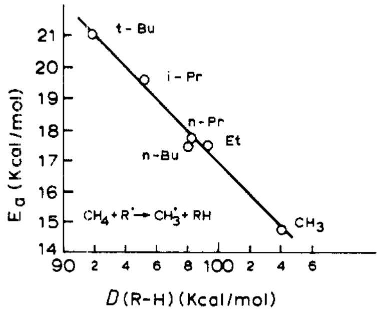

Figure 2. Activation energies for hydrogen abstraction by a series of alkyl radicals from methane plotted against the respective homolytic bond-dissociation energies of the bond that is being formed.

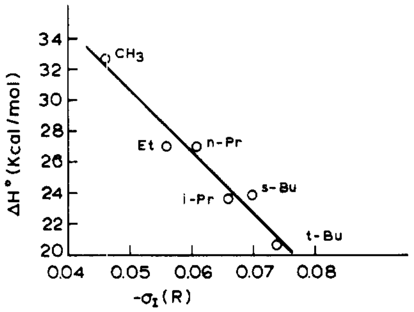

Figure 3. Reaction enthalpies for hydrogen abstraction by an iodine atom from a series of hydrocarbons plotted against Taft's σ_I(R) constants.

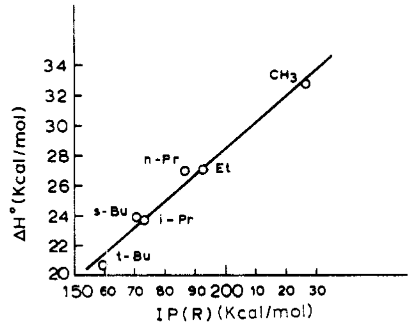

Figure 4. Reaction enthalpies (see caption of Figure 3) plotted against the relevant gas-phase ionization potentials of free radicals.

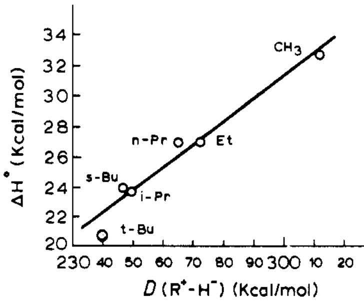

Figure 5. Reaction enthalpies (see caption of Figure 3) plotted against heterolytic bond-dissociation energies for the process $R^+ + H^- \rightarrow RH$.

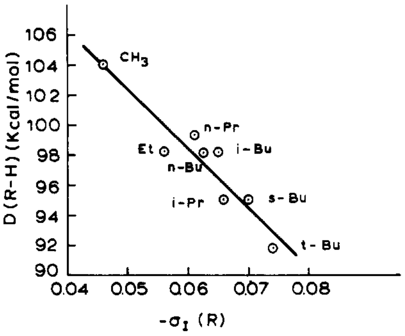

Figure 6. Homolytic bond-dissociation energies plotted as in Figure 3.

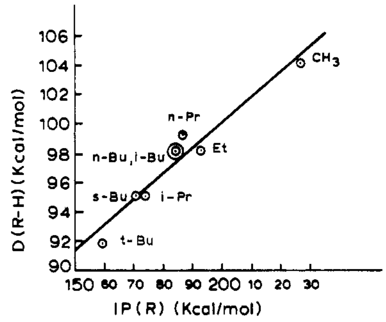

Figure 7. Homolytic bond-dissociation energies plotted as in Figure 4.

formally analogous to the two-parameter equation of Taft.[12]

We have noticed that activation energies for hydrogen abstraction by a series of structurally similar radicals from a given substrate[11] correlate with the respective D(RH)'s of the bond that is being formed, for example, Figure 2 and eq 6, for the reaction $CH_4 + R\cdot \rightarrow CH_3\cdot + RH$. An analogous but less definite correlation appears to hold between activation energies for hydrogen abstraction by an iodine atom from a series of hydrocarbons[6] and the homolytic bond dissociation energies corresponding to the bond R–I, i.e., $D(RI)$[13] (eq 7). Bearing in mind that a correlation such as eq 6 exists between E_a's for H-atom abstraction from a series of substrates by a given radical,[7] one can readily see an analogy between the D(RH)'s and the IP(R)'s, σ_I(R)'s, and $D(R^+H^-)$'s. Indeed, activation energies for free-radical reactions in which either structurally similar substrates or structurally similar radicals are involved do correlate with the IP(R)'s,[8] σ_I(R)'s,[9] and $D(R^+H^-)$'s.[10] It therefore appeared interesting to investigate the possible interrelation of the parameters D(RH), ΔH^0, IP(R), σ_I(R), and $D(R^+H^-)$.

$$E_a = -0.516D(RH) + 68.464 \quad (r = 0.996) \qquad (6)$$

$$E_a = 2.116D(RI) - 84.303 \quad (r = 0.976) \qquad (7)$$

Indeed, as becomes apparent from Figures 3–8 and the respective regression equations (eq 8–13), ΔH^0 and D(RH)

$$\Delta H^0 = -397.033[-\sigma_I(R)] + 50.482 \quad (r = 0.973) \qquad (8)$$

$$\Delta H^0 = 0.174IP(R) - 6.395 \quad (r = 0.988) \qquad (9)$$

$$\Delta H^0 = 0.150D(R^+H^-) - 13.853 \quad (r = 0.988) \qquad (10)$$

$$D(RH) = -339.770[-\sigma_I(R)] + 122.151 \quad (r = 0.937) \qquad (11)$$

$$D(RH) = 0.176IP(R) + 64.901 \quad (r = 0.965) \qquad (12)$$

$$D(RH) = 0.153D(R^+H^-) + 57.169 \quad (r = 0.969) \qquad (13)$$

are linearly related to the relevant Taft alkyl inductive substituent constants, the ionization potentials of free radicals, and the heterolytic bond-dissociation energies for the process $R^+ + H^- \rightarrow RH$.

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[12] Taft, R. W. In "Steric Effects in Organic Chemistry"; Newman, M. S., Ed.; Chapman and Hall: London, 1956; p 556.

[13] Calculated by using data from: Cox, J. D.; Pilcher, G. "Thermochemistry of Organic and Organometallic Compounds"; Academic Press: London, 1970.

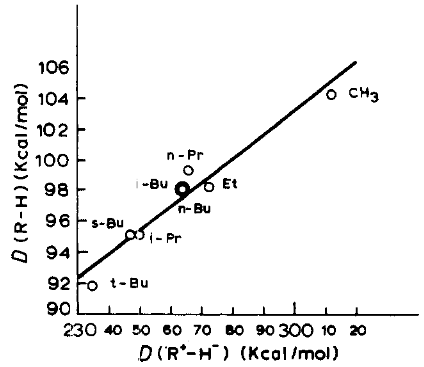

Figure 8. Homolytic bond-dissociation energies plotted as in Figure 5.

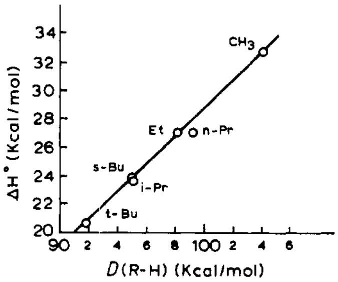

Figure 9. Reaction enthalpies (see caption of Figure 3) plotted against the respective homolytic bond-dissociation energies.

The observed linear correlation of the parameters ΔH^0 and $D(\mathrm{RH})$ with $\mathrm{IP(R)}$,[14] $\sigma_\mathrm{I}(\mathrm{R})$,[15] and $D(\mathrm{R^+H^-})$[10] implies first that ΔH^0 and $D(\mathrm{RH})$ can be linearly dependent on each other. Figure 9 and eq 14 indicate that this is so.

$$\Delta H^0 = 0.967D(\mathrm{RH}) - 68.203 \quad (r = 0.995) \tag{14}$$

$$\Delta H^0 = 1.885D(\mathrm{RI}) - 73.290 \quad (r = 0.999) \tag{15}$$

ΔH^0's are from the reaction $\mathrm{RH} + \mathrm{I} \rightarrow \mathrm{R\cdot} + \mathrm{HI}$.[6] Even ΔH^0 values appear to be linearly related to the homolytic bond-dissociation energies corresponding to the RI series (eq 15). Second, it also implies that ΔH^0 and $D(\mathrm{RH})$ can be linearly related to any IP(RX) or $D(\mathrm{R^+X^-})$ and even to any $D(\mathrm{RX})$ series. This follows from the existing linearity between any two series of IP(RX), including the case when X is an odd electron,[8] and from the linearity between any two of $D(\mathrm{R^+X^-})$[10] or the linearity between any series of IP(RX) and $D(\mathrm{R^+X^-})$.[10] Third, ΔH^0 and $D(\mathrm{RH})$ could behave as additive substituent constants! This is demonstrated in Figure 10, by representing gas-phase ionization potentials of ketones as a $\mathrm{IP(R_1R_2C{=}O)}$[14] vs. $\sum\Delta H^0(\mathrm{R}_i)$ correlation (eq 16). In the correlation, ΔH^0

$$\mathrm{IP(R_1R_2C{=}O)} = 3.900(10^{-2}\textstyle\sum\Delta H^0) + 7.095 \quad (r = 0.994) \tag{16}$$

values are the exothermicities of hydrogen atom abstraction by an iodine atom.[6] Of course, we do not intend to recommend the use of the ΔH^0 parameters as substituent constants for predicting reactivity. This can be done more accurately by using other parameters such as ionization potentials of free radicals [IP(R)[8]] or heterolytic bond dissociation energies [$D(\mathrm{R^+H^-})$] for the process $\mathrm{R^+} + \mathrm{H^-} \rightarrow \mathrm{RH}$.[10] It is felt that IP(R) should be preferred over the parameters ΔH^0 and $D(\mathrm{RH})$ in Polanyi-type relationships for a number of reasons. (1) The range of the structural effect, RSE, in the series of IP(R)'s with R = $\mathrm{CH_3}$, Et, *n*-Pr, *i*-Pr, *n*-Bu, *i*-Bu, *sec*-Bu, and *t*-Bu is 67.08 kcal/mol,[8] by far larger than the corresponding RSE of $D(\mathrm{RH})$ (12.3 kcal/mol[6]) or the ΔH^0 [RH + I; 12.1 kcal/mol[6]]. This means that IP(R)'s are very sensitive to the structural variation of R.[8] (2) IP(R)'s are accessible by direct experimental methods by which they can be measured to within a few tens of calories per mole.[14] As an equally good choice, Taft's $\sigma_\mathrm{I}(\mathrm{R})$ parameters should be used. In the latter case, with eq 2 it is possible in certain instances to separate the steric effect of the substituent.[9] Generally, it can be said that the conventional forms of the Polanyi-type relations, i.e., representing the E_a's for radical reactions in terms of ΔH^0 or $D(\mathrm{RH})$, are not very informative. These paramters fail to suggest any interaction mechanism by which the observed variation of E_a arises. It is the linearity between ΔH^0 and $\sigma_\mathrm{I}(\mathrm{R})$ or $D(\mathrm{RH})$ and $\sigma_\mathrm{I}(\mathrm{R})$ that suggests that one of the possible interaction mechanisms is induction.

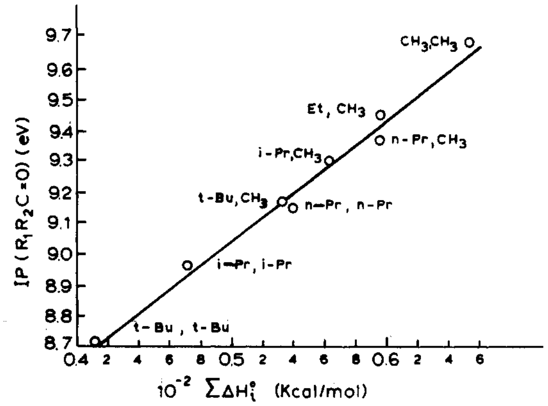

Figure 10. Gas-phase ionization potentials of a series of ketones plotted against the sum of the reaction exothermicities for the process $\mathrm{RH} + \mathrm{I} \rightarrow \mathrm{R\cdot} + \mathrm{HI}$, corresponding to the R's of the ketone.

In the light of the above discussion, the Polanyi-type relations appear to be trivial cases, or at least less useful alternative forms of the E_a vs. $\sigma_\mathrm{I}(\mathrm{R})$ or E_a vs. IP(R) relationships. However, an important question is awaiting an answer: why, apparently, unrelated parameters, such as reaction enthalpies, alkyl inductive substituent constants, homolytic bond-dissociation energies, heterolytic bond-dissociation energies, etc., should be interrelated. Perhaps the assumption that the observed variation in ΔH^0, $D(\mathrm{RH})$, etc. arises by a mainly inductive mechanism could explain the observed interrelation of these parameters. It has been argued[9] that the interrelation of various molecular parameters or substituent constants by which a given set of physical or kinetic data can be alternatively represented points to the conclusion that "a correlation amounts to the division of energy expressed either by E_a or by log (k/k_0) (log k) into two (and possibly more) parts in a more or less arbitrary albeit self-consistant way". It is felt that the findings of this paper appear to strengthen the latter conclusion.

Concluding Remarks

It has been shown that the Evans–Polanyi-type relationships can be expressed by a number of alternative

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[14] The ionization potentials [IP(R), kcal/mol] of free radicals used in the correlations ($\mathrm{CH_3}$, 226.81; Et, 193.16; *n*-Pr, 186.71; *n*-Bu, 184.63; *i*-Bu, 184.63; *i*-Pr, 174.03; *sec*-Bu, 170.80; *t*-Bu, 159.74) are from: Rosenstock, H. M.; Draxl, K.; Steiner, B. W.; Herron, J. T. *J. Phys. Chem. Ref. Data* **1977**, *6*, Suppl. 1.

[15] The new values of $\sigma_\mathrm{I}(\mathrm{R})$ have been used in the correlations. Taft, R. W.; Levitt, L. S. *J. Org. Chem.* **1977**, *42*, 916.

equivalent forms, i.e., eq 2–4. The parameters ΔH^0 and D(RH), in terms of which are represented activation energies for exothermic free radical reactions, are shown to be linearly dependent on each other. The same parameters also exhibit linear dependence on the ionization potentials of alkyl free radicals, on Taft's alkyl inductive substituent constants, and on heterolytic bond-dissociation energies for the process $R^+ + H^- \rightarrow RH$. Since all the abovementioned parameters are linearly interrelated, it appears that the Evans–Polanyi-type relations could be trivial, alternative cases of the E_a vs. σ_I(R) correlations.[9] The conventional forms of the Evans–Polanyi correlations are not very informative because they fail to suggest any interaction mechanism by which the observed variation in the kinetic data arises and because the parameters ΔH^0 and D(RH) exhibit relatively small ranges of structural effect. The latter disadvantage results in less accurate predictions of reactivity when Evans–Polanyi relations are used for such a purpose.

A considerable number of molecular and/or substituent parameters have been shown in this paper and in previous ones[8-10] to be interrelated, i.e., IP(R), σ_I(R), υ_R, υ_{OR}, υ_{SR}, $\upsilon_{NR_1R_2}$, $E_s{}^c$(R), E_s(R), IP(RX), D(RH), D(R^+H^-), and ΔH^0. This points to the conclusion that a given set of kinetic or physical data can be represented by several alternative self-consistent but, nevertheless, arbitrary ways. Equation 16 provides rather convincing evidence that representation of physical (or kinetic) data in terms of substituent parameters may be arbitrary. It becomes, therefore, evident that instead of proliferating "new" substituent constants, we should examine which of the existing parameters serve the purpose of linear free-energy relationships best. It is the feeling of this author that the parameter of choice for representing kinetic or physical data and for predicting reactivity should be the ionization potentials of free radicals. The reason for this is that IP(R) values have a very large range of structural effects, i.e., are very sensitive to structural variation in R, and they are accessible by direct experimental methods.

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Enantioselective Ester Hydrolysis by Hydroxamic Acids of *N*-Benzyloxycarbonyl-L-amino Acids or Optically Active Amines in Cetyltrimethylammonium Bromide Micelles

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Hydrolysis of *p*-nitrophenyl esters of amino acids by hydroxamic acids of *N*-benzyloxycarbonyl-L-amino acids or optically active amines of L-amino acids in the presence of CTABr micelles showed effective enantioselectivities (D/L = 2.51 and 2.65, respectively) as well as enhanced rate constants (k_{obsd} = 0.8 s^{-1} for hydroxamic acid), demonstrating the propriety of synthetic design for enzyme models that we previously reported. In the case of the aminolysis reaction, no enantioselectivity was observed with an optically active amine which has an amino group far from the asymmetric carbon atom. On the other hand, optically active amines with amino groups at positions α to the asymmetric carbon atoms showed effective enantioselectivities. Furthermore, the reaction products of optically active amines and D substrates gave highly optically active substances.

In our previous reports cetyltrimethylammonium bromide (CTABr) micelles have proved to provide effective incorporation sites for enantioselectively catalyzed hydrolysis by *N*-lauroyl-L-histidine.[1,2] In addition, the enantioselectivity depended on the steric factors of the compounds.[3,4]

This work deals with the catalyzed hydrolysis of optically active esters by hydroxamic acids of L-amino acids and optically active amines that demonstrates potent enantioselectivity in a micellar system. A great many hydroxamic acid derivatives showing distinguished catalytic actions on the hydrolysis of esters in the mixed micellar system[5,6] have been synthesized. However, few papers have been published on their applications to enantioselective catalysis. There have been no reports on enantioselective aminolysis in the micellar system either.

The optically active hydroxamic acids were prepared from *N*-benzyloxycarbonyl-L-phenylalanine[7] and N^α,N^ϵ-bis(benzyloxycarbonyl)-L-lysine[8] by converting them into mixed anhydrides with ethyl chloroformate at −15 °C followed by treatment with hydroxylamine or methylhydroxylamine. *N*-Benzyloxycarbonyl-L-phenylalanine hydroxamic acid (**1a**), mp 99.0–99.5 °C, *N*-benzyloxycarbonyl-L-phenylalanine *N'*-methylhydroxamic acid (**1b**), oil, N^α,N^ϵ-bis(benzyloxycarbonyl)-L-lysine hydroxamic acid

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