

Hammett Equation and Generalized Pauling's Electronegativity Equation

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Substituent interaction energy (SIE) was defined as the energy change of the isodesmic reaction $X\text{-spacer-Y} + H\text{-spacer-H} \rightarrow X\text{-spacer-H} + H\text{-spacer-Y}$. It was found that this SIE followed a simple equation, $\text{SIE}(X,Y) = -k\sigma_X\sigma_Y$, where k was a constant dependent on the system and σ was a certain scale of electronic substituent constant. It was demonstrated that the equation was applicable to disubstituted bicyclo[2.2.2]octanes, benzenes, ethylenes, butadienes, and hexatrienes. It was also demonstrated that Hammett's equation was a derivative form of the above equation. Furthermore, it was found that when spacer = nil the above equation was mathematically the same as Pauling's electronegativity equation. Thus it was shown that Hammett's equation was a derivative form of the generalized Pauling's electronegativity equation and that a generalized Pauling's electronegativity equation could be utilized for diverse X-spacer-Y systems. In addition, the total electronic substituent effects were successfully separated into field/inductive and resonance effects in the equation $\text{SIE}(X,Y) = -k_1F_XF_Y - k_2R_XR_Y - k_3(F_XR_Y + R_XF_Y)$. The existence of the cross term (i.e., F_XR_Y and R_XF_Y) suggested that the field/inductive effect was not orthogonal to the resonance effect because the field/inductive effect from one substituent interacted with the resonance effect from the other. Further studies on multi-substituted systems suggested that the electronic substituent effects should be pairwise and additive. Hence, the SIE in a multi-substituted system could be described using the equation $\text{SIE}(X_1, X_2, \dots, X_n) = -\sum_{i=1}^{n-1} \sum_{j=i+1}^n k_{ij}\sigma_{X_i}\sigma_{X_j}$.

1. INTRODUCTION

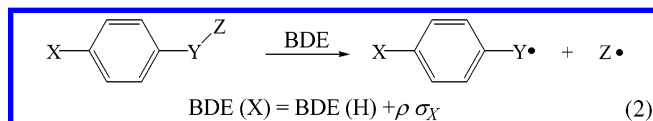
In the 1930s, Hammett noted that there is a linear relationship between the acidities of substituted benzoic acids and the rates of many chemical reactions.¹ For instance, the rates of hydrolysis of substituted ethyl benzoates follow eq 1:

$$\log k_X - \log k_H = \rho(\log K_X - \log K_H) = \rho\sigma_X \quad (1)$$

where K is the acid ionization constant, k is the reaction rate constant, X is the substituent, H is the hydrogen atom, and σ_X is the substituent constant. Regression slope, ρ , is also called the reaction constant.

To date, the Hammett relationship has occupied a central position in theoretical organic chemistry. The validity of eq 1 has been confirmed by countless studies. Considerable efforts have been devoted to the compilation of substituent² and reaction constants.³ Various approaches have also been used to study the mechanistic issues involved in the Hammett relationship.⁴ Despite intensive studies, little has been known about the physical origin of the Hammett relationship.

We recently conducted several systematic studies on the Hammett relationship in radical chemistry.⁵ A central question in those studies was how to predict the ρ values for various Y–Z bond dissociation energies (BDEs) as shown in eq 2.



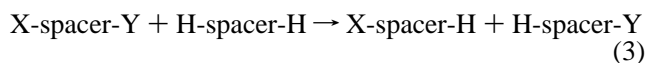
It had been previously proposed that ρ values for BDEs should be dependent on the polarity or electronegativity of the Y–Z moiety.⁶ However, we found that the determining factor for the ρ values is the change of electron demand from Y–Z to Y•. This change of electron demand can be quantitatively reflected by the change of acidity from $\text{HOOC-C}_6\text{H}_4\text{-Y-Z}$ to $\text{HOOC-C}_6\text{H}_4\text{-Y}^\bullet$.⁷

Obviously, the substituent constant (σ) is also quantitatively determined by the change of acidity from $\text{HOOC-C}_6\text{H}_4\text{-X}$ to $\text{HOOC-C}_6\text{H}_4\text{-H}$. Therefore, σ constants for Y–Z and Y• moieties should also reflect their electron demands. As a result, the ρ value for Y–Z BDEs can be predicted from the change of σ constant from Y–Z to Y•.⁷

Surprisingly, the dependence of ρ on σ is a new finding despite innumerable applications of Hammett equation in the past. On the basis of this finding, we attempted to derive an equation more fundamental than eq 1 that can be used to predict or interpret the observed electronic substituent effects in various systems.

2. SUBSTITUENT INTERACTION ENERGY

Let us consider the following isodesmic reaction in the gas phase:



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where X and Y are substituents and H is hydrogen atom. The details about the spacer will be discussed in the following sections. The energy change of the above isodesmic reaction is clearly due to the interactions between the substituents X and Y. Therefore, we name this energy change as substituent interaction energy (SIE).⁸

It is worth mentioning that the entropy change of a gas-phase isodesmic reaction is very small,⁹ because the number of bonds of each formal type remains the same on each side of the reaction equation. Therefore, we do not need to consider the entropy contributions in the present study. Also, only the gas-phase energy changes are considered here. We do not include the solvent effects because we wish to focus on the intrinsic electronic substituent effects that are free from the solvent effects.

Certainly the energy change of eq 1 can be calculated using the experimental formation energies (or combustion energies) of compound X-spacer-Y, H-spacer-H, X-spacer-H, and H-spacer-Y. However, not all of these experimental data are available. Therefore, in the present study we use a theoretical method (B3LYP/6-311++G(2df,p)//B3LYP/6-31G(d)¹⁰) to obtain all the energy changes. According to many recent studies,¹¹ this theoretical method should be sufficiently reliable for us to study the energy changes of isodesmic reactions.

3. 1,4-DISUBSTITUTED BICYCLO[2.2.2]OCTANE

1,4-Disubstituted bicyclo[2.2.2]octane is an important system because the bicyclo[2.2.2]octane skeleton eliminates any conjugation or steric interaction between the two substituents.¹² Early studies on the ionization of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids and quinuclidines have provided important insights into the substituent inductive/field effects.¹³ A few scales of inductive/field substituent constants have also been established from these studies.

Herein we focus on the energy changes (SIEs) of the following reactions, whose detailed numerical results are listed in the Supporting Information:



Our finding is that the SIEs fit the following equation

$$\text{SIE}(\text{X}, \text{Y}) = -\phi_X^I \phi_Y^I \quad (5)$$

where ϕ_X^I and ϕ_Y^I are the substituent constants that are defined in eq 6:

$$|\phi_X^I| = \sqrt{\text{SIE}(\text{X}, \text{X})} \quad (6)$$

The sign of each ϕ_X^I can be determined using the following procedure. (1) We assume that the sign for ϕ_F^I is positive. (2) From the equation $\text{SIE}(\text{X}, \text{F}) = -\phi_X^I \phi_F^I$, we can then determine the sign for each ϕ_X^I value. The detailed values for ϕ_X^I are listed in Table 1.

The validity of eq 5 is shown in Figure 1. As seen from Figure 1, the predicted SIEs correlate with the actual SIEs very well for 66 pairs of X and Y. The correlation coefficient is -0.991 . The standard deviation (SD) is 0.17 kcal/mol.

Table 1. Substituent Constants for 1,4-Disubstituted Bicyclo[2.2.2]octanes

X	ϕ_X^I	σ_1 (Grob) ^a	σ_1 (Stock) ^a
H	0.00	0.00	0.00
Li	-2.00		
F	1.15	0.46	
Cl	1.13	0.44	0.47
CH ₃	0.39	-0.01	-0.02
CN	1.45	0.55	0.54
NO ₂	1.64	0.63	0.68
OH	0.79		0.26
OCH ₃	0.62	0.31	0.30
NH ₂	0.42	0.17	0.15
COCH ₃	0.62	0.29	0.26

^a These constants are taken from ref 12.

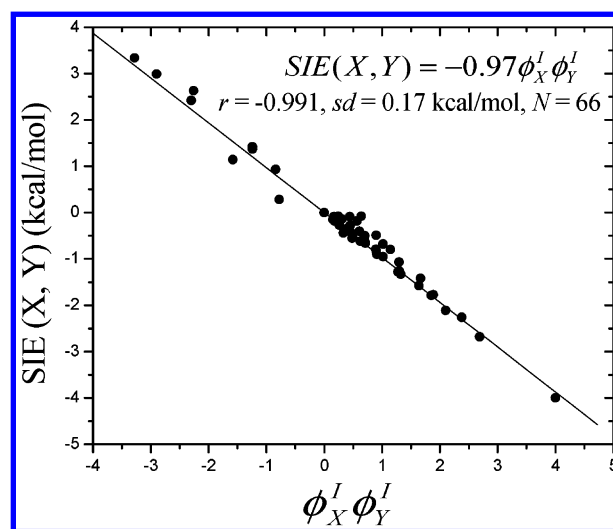


Figure 1. Correlation between SIEs and $\phi_X^I \phi_Y^I$ for 1,4-disubstituted bicyclo[2.2.2]octanes.

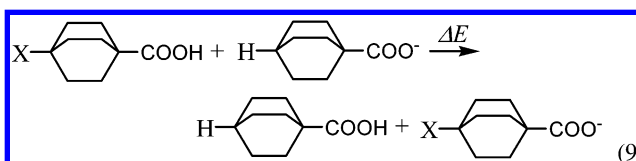
Interestingly, the ϕ_X^I constants correlate very well with the σ_1 substituent constants previously determined from the ionization of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids or quinuclidines (eqs 7 and 8).

$$\sigma_1 (\text{Grob}) = 0.388 \phi_X^I \quad (r = 0.960, \text{SD} = 0.06, N = 9) \quad (7)$$

$$\sigma_1 (\text{Stock}) = 0.390 \phi_X^I \quad (r = 0.961, \text{SD} = 0.07, N = 9) \quad (8)$$

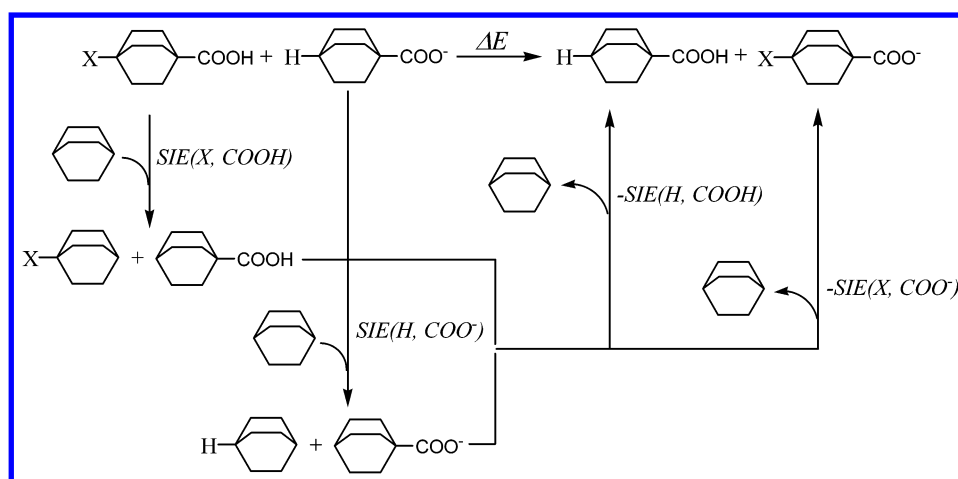
Therefore, the ϕ_X^I constants are consistent with the traditional scales of inductive/field substituent constants.

It is worth noting that from eq 5 we can derive the Hammett equation for 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids. According to Hammett's equation, the energy change of the following reaction (ΔE) should correlate with the substituent constant σ_1 , i.e., $\Delta E = \rho \sigma_1$.¹⁴



On the other hand, on the basis of the thermodynamic cycle shown in Scheme 1, we can also calculate ΔE from SIEs using eq 10:

Scheme 1

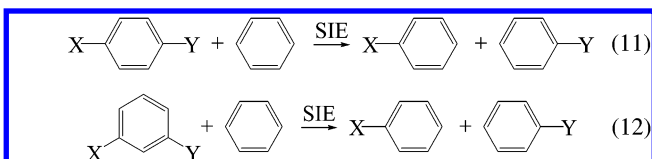


$$\Delta E = \text{SIE}(\text{X}, \text{COOH}) + \text{SIE}(\text{H}, \text{COO}^-) - \text{SIE}(\text{H}, \text{COOH}) - \text{SIE}(\text{X}, \text{COO}^-) = (\phi_{\text{COO}^-}^{\text{I}} - \phi_{\text{COOH}}^{\text{I}})\phi_{\text{X}}^{\text{I}} \quad (10)$$

Because $\phi_{\text{COO}^-}^{\text{I}}$ and $\phi_{\text{COOH}}^{\text{I}}$ are constants and $\sigma_{\text{I}} \propto \phi_{\text{X}}^{\text{I}}$, it is clear that eq 10 is equivalent to Hammett's equation. However, from Hammett's equation ($\Delta E = \rho\sigma_{\text{I}}$), we cannot derive eq 5. Therefore, eq 5 is more fundamental than Hammett's equation.

4. 1,4- AND 1,3-DISUBSTITUTED BENZENES

Disubstituted benzene is another important system in the study of substituent effects. Herein we focus on the SIEs for both 1,4- and 1,3-disubstituted systems. The detailed SIE values are listed in the Supporting Information.



We find that the above SIEs can also be described by equations similar to eq 5 (i.e., $\text{SIE}(\text{X}, \text{Y}) = -\phi_{\text{X}}\phi_{\text{Y}}$). Since from eqs 7 and 8 we know that the ϕ_{X} constants correlate well with the traditional substituent constants, in the following we will use the traditional electronic substituent constants (i.e., σ_{I} , σ_{p} , σ_{m}) instead of defining new scales of

substituent constants. Thus, eq 5 can be written in the following form:

$$\text{SIE}(\text{X}, \text{Y}) = -k\sigma_{\text{X}}\sigma_{\text{Y}} \quad (13)$$

Fifteen classic substituents are considered for the disubstituted benzenes. For 1,4- and 1,3-disubstituted benzenes, we obtain the following equations (also see Figure 2):

$$\text{SIE}_{\text{para}}(\text{X}, \text{Y}) = -6.07\sigma_{\text{p}}(\text{X})\sigma_{\text{p}}(\text{Y}) \quad (r = -0.918, \text{SD} = 0.6 \text{ kcal/mol}, N = 120) \quad (14)$$

$$\text{SIE}_{\text{meta}}(\text{X}, \text{Y}) = -7.29\sigma_{\text{m}}(\text{X})\sigma_{\text{m}}(\text{Y}) \quad (r = -0.966, \text{SD} = 0.3 \text{ kcal/mol}, N = 120) \quad (15)$$

The good correlations indicate that eq 13 is valid for disubstituted benzene systems. It should be mentioned that the correlations in Figure 2 are not perfect because we have not considered the solvation effects in the present study.

Using a similar method as shown in section 3, we can derive the Hammett equations (i.e., $\Delta E = \rho\sigma_{\text{p}}$ and $\Delta E = \rho\sigma_{\text{m}}$) for the para- and meta-substituted benzoic acids from eq 13. However, from the Hammett equations we cannot derive eq 13. Therefore, eq 13 is more fundamental than Hammett equations.

5. FIELD/INDUCTIVE AND RESONANCE EFFECTS

One of the early postulates in the classical English school of organic chemistry was that electronic substituent effects

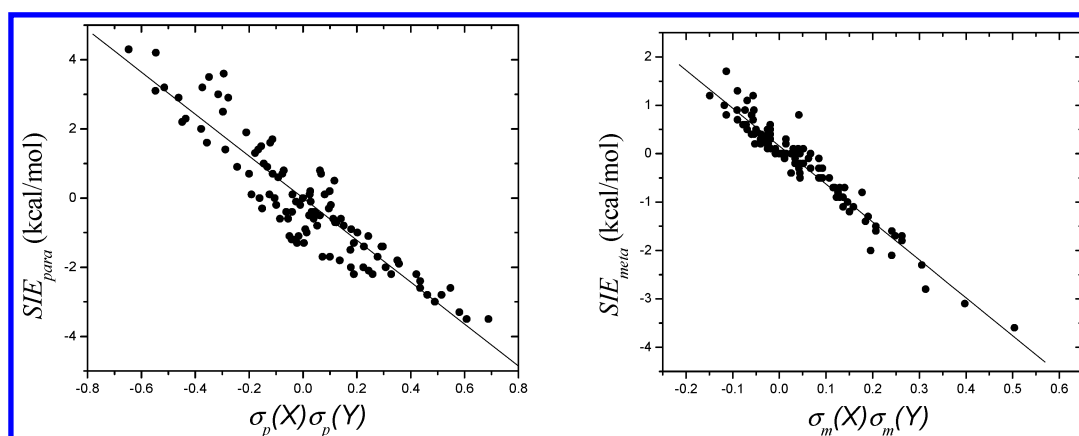


Figure 2. Correlation between SIEs and $\sigma_{\text{p}}(\text{X})\sigma_{\text{p}}(\text{Y})$ or $\sigma_{\text{m}}(\text{X})\sigma_{\text{m}}(\text{Y})$ for para- or meta-disubstituted benzenes.

are the sum of two components: the field/inductive and the resonance components.¹⁵ On the basis of this postulate, a few scales of field/inductive and resonance constants (e.g., F and R) have been defined.² With these constants, the Hammett equation can be written in a dual-parameter form:

$$\Delta E = \rho_F F + \rho_R R \quad (16)$$

Herein we wish to include the field/inductive and resonance effects into the new equations (eqs 5 or 13). First, it is clear that only the field/inductive effect is present in the 1,4-disubstituted bicyclo[2.2.2]octane systems. Therefore, we must have

$$\text{SIE}_{\text{bicyclooctane}}(\text{X}, \text{Y}) = -kF_X F_Y \quad (17)$$

Correlation analysis indicates that $k = 6.02$ in eq 17. The corresponding correlation coefficient and standard deviation are -0.955 and 0.19 kcal/mol, respectively. Therefore, eq 17 is successful for the disubstituted bicyclooctane system.

For disubstituted benzene systems, both the field/inductive and resonance effects are present. Previous studies suggested that these two effects are orthogonal to each other.^{2,14} If this proposal were correct, one should expect that the substituent interaction between a field/inductive component and a resonance component is zero. This leads to the following equation:

$$\text{SIE}_{\text{benzene}}(\text{X}, \text{Y}) = -k_1 F_X F_Y - k_2 R_X R_Y \quad (18)$$

Applying eq 18 to 1,4- and 1,3-disubstituted benzenes, we obtain

$$\begin{aligned} \text{SIE}_{\text{benzene}}^{\text{para}}(\text{X}, \text{Y}) &= -5.06 F_X F_Y - 3.79 R_X R_Y \\ (r &= 0.796, \text{SD} = 1.2 \text{ kcal/mol}, N = 120) \end{aligned} \quad (19)$$

$$\begin{aligned} \text{SIE}_{\text{benzene}}^{\text{meta}}(\text{X}, \text{Y}) &= -5.14 F_X F_Y - 0.25 R_X R_Y \\ (r &= 0.781, \text{SD} = 0.7 \text{ kcal/mol}, N = 120) \end{aligned} \quad (20)$$

It is clear that the correlations in eqs 19 and 20 are poor. Therefore, the field/inductive and resonance effects are not orthogonal to each other. There must be a cross term (i.e., $F \times R$) that stems from the interaction between the field/inductive component of one substituent and the resonance component of the other. On the basis of this hypothesis, we obtain

$$\begin{aligned} \text{SIE}_{\text{benzene}}(\text{X}, \text{Y}) &= -k_1 F_X F_Y - k_2 R_X R_Y - \\ &\quad k_3 (F_X R_Y + R_X F_Y) \end{aligned} \quad (21)$$

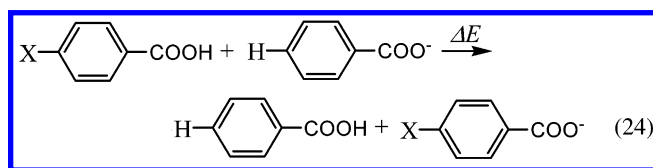
Applying eq 21 to 1,4- and 1,3-disubstituted benzenes, we obtain

$$\begin{aligned} \text{SIE}_{\text{benzene}}^{\text{para}}(\text{X}, \text{Y}) &= -6.54 F_X F_Y - 6.64 R_X R_Y - \\ &\quad 4.61 (F_X R_Y + R_X F_Y) \\ (r &= 0.921, \text{SD} = 0.8 \text{ kcal/mol}, N = 120) \end{aligned} \quad (22)$$

$$\begin{aligned} \text{SIE}_{\text{benzene}}^{\text{meta}}(\text{X}, \text{Y}) &= -7.29 F_X F_Y - 0.89 R_X R_Y - \\ &\quad 3.04 (F_X R_Y + R_X F_Y) \\ (r &= 0.946, \text{SD} = 0.5 \text{ kcal/mol}, N = 120) \end{aligned} \quad (23)$$

The correlations in eqs 22 and 23 are much better than those in eqs 19 and 20, indicating the importance of the cross term.

It is worthy to note that from eq 21 we can derive eq 16. According to eq 16, the energy change of the following equation should obey $\Delta E = \rho_F F_X + \rho_R R_X$.



On the other hand, the above energy change can be calculated using SIEs:

$$\begin{aligned} \Delta E &= \text{SIE}(\text{X}, \text{COOH}) + \text{SIE}(\text{H}, \text{COO}^-) - \\ &\quad \text{SIE}(\text{H}, \text{COOH}) - \text{SIE}(\text{X}, \text{COO}^-) = \\ &\quad [k_1 (F_{\text{COO}^-} - F_{\text{COOH}}) + k_3 (R_{\text{COO}^-} - R_{\text{COOH}})] F_X + \\ &\quad [k_2 (R_{\text{COO}^-} - R_{\text{COOH}}) + k_3 (F_{\text{COO}^-} - F_{\text{COOH}})] R_X \end{aligned} \quad (25)$$

Clearly eq 25 is in the same form as eq 16. Therefore, the dual-parameter Hammett equation is a derivative form of eq 21.

6. MORE DISUBSTITUTED SYSTEMS

Equations 13 and 21 are the new equations proposed in the present study. Equation 13 is applicable to the systems where the substituent constants are available. In comparison, eq 21 can be applied to the systems where the substituent constants are unknown. Herein we test the applicability of eq 21 to three more systems: *trans*-disubstituted-ethylene ($\text{X}-\text{CH}=\text{CH}-\text{Y}$), *trans*-1,4-disubstituted-butadiene ($\text{X}-\text{CH}=\text{CH}-\text{CH}=\text{CH}-\text{Y}$), and *trans*-1,6-disubstituted-hexatriene ($\text{X}-\text{CH}=\text{CH}-\text{CH}=\text{CH}-\text{CH}=\text{CH}-\text{Y}$). The detailed SIEs are listed in the Supporting Information. The correlation equations are as follows:

$$\begin{aligned} \text{SIE}_{\text{ethylene}}(\text{X}, \text{Y}) &= -15.41 F_X F_Y - 20.36 R_X R_Y - \\ &\quad 3.80 (F_X R_Y + R_X F_Y) \\ (r &= 0.926, \text{SD} = 1.5 \text{ kcal/mol}, N = 105) \end{aligned} \quad (26)$$

$$\begin{aligned} \text{SIE}_{\text{butadiene}}(\text{X}, \text{Y}) &= -6.64 F_X F_Y - 9.63 R_X R_Y - \\ &\quad 6.96 (F_X R_Y + R_X F_Y) \\ (r &= 0.928, \text{SD} = 0.7 \text{ kcal/mol}, N = 105) \end{aligned} \quad (27)$$

$$\begin{aligned} \text{SIE}_{\text{hexatriene}}(\text{X}, \text{Y}) &= -4.70 F_X F_Y - 6.42 R_X R_Y - \\ &\quad 5.47 (F_X R_Y + R_X F_Y) \\ (r &= 0.948, \text{SD} = 0.4 \text{ kcal/mol}, N = 105) \end{aligned} \quad (28)$$

The good correlations indicate that eq 21 is applicable to all these disubstituted systems in addition to disubstituted bicyclooctanes and benzenes.

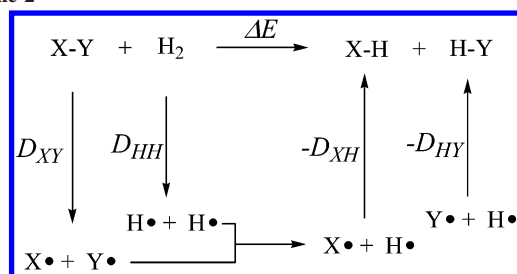
7. PAULING'S ELECTRONEGATIVITY EQUATION

If spacer = nil, then $\text{X-spacer-Y} = \text{X-Y}$. Therefore, X-Y is also a disubstituted system. According to Pauling's electronegativity equation,¹⁶ the bond energy (D) of X-Y should follow eq 29:

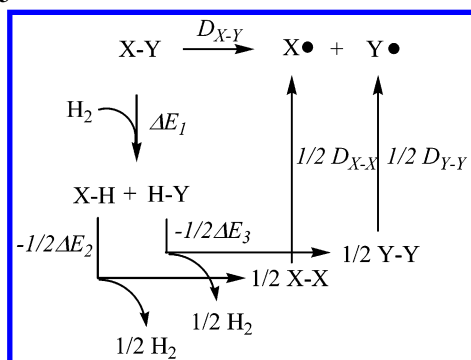
$$D_{\text{X-Y}} = \frac{1}{2} D_{\text{X-X}} + \frac{1}{2} D_{\text{Y-Y}} + 23(\chi_X - \chi_Y)^2 \quad (29)$$

where χ_X and χ_Y are electronegativities of X and Y.

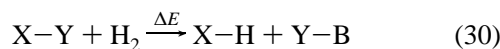
Scheme 2



Scheme 3



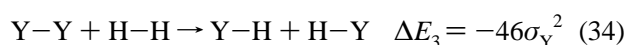
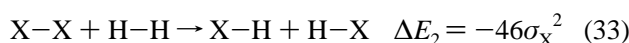
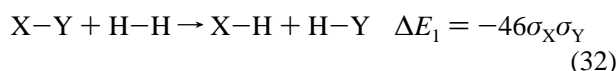
Using the thermodynamic cycle shown in Scheme 2, we can calculate the energy change of the following isodesmic reaction from D_{X-X} , D_{X-Y} , and D_{Y-Y} (see eq 31).



$$\begin{aligned} \Delta E = & 23(\chi_X - \chi_Y)^2 + 23(\chi_H - \chi_H)^2 - \\ & 23(\chi_X - \chi_H)^2 - 23(\chi_Y - \chi_H)^2 = \\ & -46(\chi_X - \chi_H)(\chi_Y - \chi_H) \quad (31) \end{aligned}$$

If we define $\chi_X - \chi_H = \sigma_X$,¹⁷ $\sigma_H = 0$, and $SIE = \Delta E$, we will obtain $SIE(X,Y) = -46\sigma_X\sigma_Y$. This suggests that Pauling's electronegativity equation actually is an alternative form of eq 13 applicable to a specific case, i.e., spacer = nil.

It is worth mentioning that from the equation $SIE(X,Y) = -46\sigma_X\sigma_Y$ we can also derive Pauling's electronegativity equation. The details are as follows. First, according to $SIE(X,Y) = -46\sigma_X\sigma_Y$, we can calculate the energy changes of the following three isodesmic reactions:



Second, using the thermodynamic cycle shown in Scheme 3 and the above three energy changes, we can calculate the bond energy (D) of $X-Y$ from the bond energies of $X-X$ and $Y-Y$ (eq 35):

$$D(X-Y) = \frac{1}{2}D(X-X) + \frac{1}{2}D(Y-Y) + 23(\sigma_X - \sigma_Y)^2 \quad (35)$$

Equation 35 is exactly the same as Pauling's electronegativity equation. Therefore, the newly derived equation (i.e., eq 13)

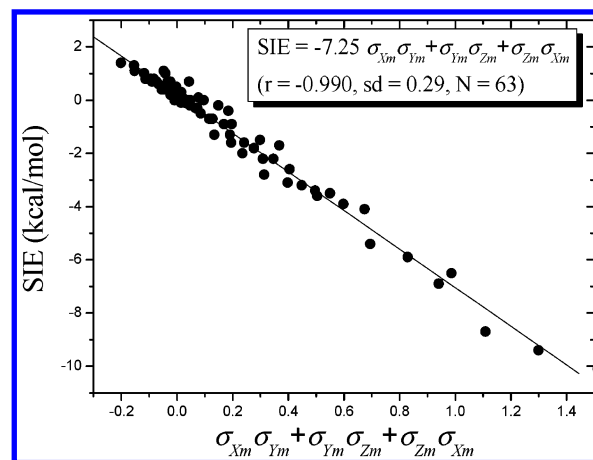
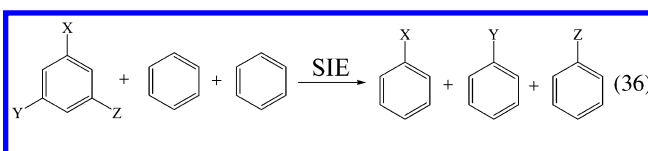


Figure 3. Correlation between SIEs and $(\sigma_{Xm}\sigma_{Ym} + \sigma_{Ym}\sigma_{Zm} + \sigma_{Zm}\sigma_{Xm})$ for 1,3,5-trisubstituted benzenes.

in the present study is mathematically the same as Pauling's electronegativity equation.¹⁸ Pauling proposed that Pauling's electronegativity equation is applicable to various $X-Y$ systems, whereas we find that eq 13 can be utilized in many more systems in a general form, X -spacer- Y .

8. TRISUBSTITUTED BENZENES AND MULTI-SUBSTITUTED SYSTEMS

In the above discussions, we have focused on disubstituted systems. In the present section, we will derive an equation that is applicable to multi-substituted systems. First of all, let us study the electronic substituent effects in 1,3,5-trisubstituted benzenes.



We define the SIEs associated with 1,3,5-trisubstituted benzenes in eq 36. Comparing eqs 36 and 13, one may wonder whether we should have $SIE(X,Y,Z) = -k\sigma_X\sigma_Y\sigma_Z$ or $SIE(X,Y,Z) = -k(\sigma_X\sigma_Y + \sigma_Y\sigma_Z + \sigma_Z\sigma_X)$. Using the SIEs calculated by the B3LYP/6-311++G(2df,p)/B3LYP/6-31G* method for 63 different 1,3,5-trisubstituted benzenes, we find that the second equation is correct (also see Figure 3), i.e.

$$\begin{aligned} SIE(X,Y,Z) = & -7.25(\sigma_{X,m}\sigma_{Y,m} + \sigma_{Y,m}\sigma_{Z,m} + \sigma_{Z,m}\sigma_{X,m}) \\ (r = & -0.990, SD = 0.3 \text{ kcal/mol}, N = 63) \quad (37) \end{aligned}$$

The slope in eq 37 is very close to the slope in eq 15 (-7.29) for 1,3-disubstituted benzenes. This observation has the following implications. (1) The electronic substituent effects in 1,3-disubstituted systems are mechanistically the same as those in 1,3,5-trisubstituted benzenes. (2) The electronic substituent effects in a trisubstituted system can be divided into a group of electronic substituent effects of disubstituted systems.

On the basis of the above finding, we hypothesize that the electronic substituent effect in a multi-substituted system, which is depicted by the SIE in eq 38, should follow eq 39.

System(X_1, X_2, \dots, X_n) +

$$(n-1)\text{System}(\text{H}, \text{H}, \dots, \text{H}) \xrightarrow{\text{SIE}} \text{System}(\text{X}_1, \text{H}, \dots, \text{H}) + \dots + \text{System}(\text{H}, \text{H}, \dots, \text{X}_n) \quad (38)$$

$$\text{SIE}(X_1, X_2, \dots, X_n) = -\sum_{i=1}^{n-1} \sum_{j=i+1}^n k_{ij} \sigma_{X_i} \sigma_{X_j} \quad (39)$$

9. SUMMARY

(1) For disubstituted systems, SIE is defined as the energy change of the isodesmic reaction $\text{X-spacer-Y} + \text{H-spacer-H} \rightarrow \text{X-spacer-H} + \text{H-spacer-Y}$. This SIE fits a simple equation, $\text{SIE}(\text{X}, \text{Y}) = -k\sigma_X\sigma_Y$, where k is a constant dependent on the system and σ is a certain scale of electronic substituent constant. The equation is applicable to disubstituted bicyclo[2.2.2]octanes, benzenes, ethylenes, butadienes, and hexatrienes.

(2) From the equation $\text{SIE}(\text{X}, \text{Y}) = -k\sigma_X\sigma_Y$, we can derive Hammett's equation. However, from Hammett's equation we cannot derive the equation $\text{SIE}(\text{X}, \text{Y}) = -k\sigma_X\sigma_Y$. Thus the equation $\text{SIE}(\text{X}, \text{Y}) = -k\sigma_X\sigma_Y$ is more fundamental than the Hammett equation.

(3) When spacer = nil, the equation $\text{SIE}(\text{X}, \text{Y}) = -k\sigma_X\sigma_Y$ is mathematically the same as Pauling's electronegativity equation. Thus, Hammett's equation was a derivative form of the generalized Pauling's electronegativity equation, and a generalized Pauling's electronegativity equation can be utilized for diverse X-spacer-Y systems.¹⁹

(4) We can divide the total electronic substituent effects into field/inductive (depicted by F constants) and resonance effects (depicted by R constants) using the equation $\text{SIE}(\text{X}, \text{Y}) = -k_1F_XF_Y - k_2R_XR_Y - k_3(F_XR_Y + R_XF_Y)$. The existence of cross terms (i.e., F_XR_Y and R_XF_Y) suggests that the field/inductive effect is not orthogonal to the resonance effect.

(5) The electronic substituent effects are pairwise and additive. Therefore, SIE in a multi-substituted system follows the equation $\text{SIE}(X_1, X_2, \dots, X_n) = -\sum_{i=1}^{n-1} \sum_{j=i+1}^n k_{ij} \sigma_{X_i} \sigma_{X_j}$.

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Supporting Information Available: Detailed substituent interaction energies. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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