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Fukui 函数和局域软度应用于亲电加成反应的区位选择性的研究

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摘要: Fukui函数、局域软度、广义Fukui函数以及广义软度通常被称为反应描述符。使用它们研究和探讨了HCl与不对称烯烃以及溴苯硒与不对称苯乙烯的亲电加成反应的区位选择性。在MP2/6-311++G(d,p)理论水平下, 采用有限差分方法计算这些反应描述符, 同时也使用ABEEM $\sigma\pi$ 方法进行了计算。ABEEM $\sigma\pi$ 模型下的局域软度和广义局域软度, 分别结合局域硬-软酸碱(HSAB)原理, 得出亲电试剂氯化氢与溴苯硒, 更容易进攻不对称乙烯和苯乙烯中的马氏碳原子, 符合马氏规则。而有限差分方法不能完全地解释该系列反应的区位选择性。此外, 主要产物所对应的马氏碳原子的广义局域软度值, 就能够预测出此类反应的活性序列, 所得结果与速率常数有很好的关联。

关键词: Fukui函数; 局域软度; 局域硬-软酸碱原理; 亲电加成反应; 有限差分近似; ABEEM $\sigma\pi$ 模型

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Fukui Function and Local Softness Related to the Regioselectivity of Electrophilic Addition Reactions

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Abstract: Regioselectivities of electrophilic addition reactions of hydrogen chloride to asymmetric alkenes and benzeneselenenyl bromide to substituted styrenes have been investigated by using reactivity descriptors, including Fukui function $f(r)$, local softness $s(r)$, generalized Fukui function $f^G(r)$, and generalized local softness $s^G(r)$. All of them are obtained from the finite difference approximation method calculated by *ab initio* method at MP2/6-311++G(d,p) level of theory and our ABEEM $\sigma\pi$ model, respectively. According to the generalized version of the local hard-soft and acid-base (HSAB) principle, the forecasted regioselectivities of our investigated additions using the ABEEM $\sigma\pi$ model are in fair agreement with the experimental values. In particular, we can also rationalize their reaction rate constants by the generalized local softness, i.e., the softest the site is, the easiest the reaction is. Hence, the generalized reactivity descriptors work quite well.

Key Words: Fukui function; Local softness; Local hard-soft and acids-bases (HSAB) principle; Electrophilic addition reactions; Finite difference approximation; ABEEM $\sigma\pi$ model

1 Introduction

Electrophilic addition of an electrophile to alkenes is one of

the most widely studied electrophilic reactions¹⁻⁹, as shown in Fig.1. The analysis of this sort of reactions has attracted great

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Fig.1 The regioselectivities of electrophilic additions of hydrogen chloride to the substituted ethenes ($\text{R}_3 = \text{H}$) and benzeneselenenyl bromide to substituted styrenes ($\text{R}_1 = \text{R}_2 = \text{H}$), including Markovnikov and anti-Markovnikov products.

concern of both experimental and theoretical studies. Regioselectivity for the electrophilic addition has been shown to follow the empirical Markovnikov's rules¹⁰, the addition of an acidic proton to a double bond of an alkene yields a product where the proton is bound to the carbon atom bearing the largest number of hydrogen atoms when the substituent of alkene is electron-donating group. And when the substituent is electron-accepting group, the proton of acid favors to attack the carbon atom bearing the smallest number of hydrogen atoms, which calls the anti-Markovnikov's rule. Many theoretical^{1-4,8} and experimental^{5-7,9} studies have focused on the regioselectivity of electrophilic addition to alkene all the while, such as, frontier molecular orbital (FMO) theory is sometimes used for explaining the regioselectivity of reaction⁸. Suresh and his coworkers have employed the molecular electrostatic potential to confirm the regioselectivity of Markovnikov reaction². Recently, Yang, Ding and Zhao¹ have performed to use the frontier electron density of initial-state carbon atoms in molecular face theory (MFT) to estimate its regioselectivity: if the frontier electron density encoded on the Markovnikov carbon atom is larger than that of anti-Markovnikov, the reaction may be predicted to proceed on the Markovnikov route, and otherwise it may prefer the anti-Markovnikov route.

The local hard-soft and acids-bases (HSAB) principle is an efficient method in conceptual density functional theory (CDFT) to predict the regio- and stereoselectivities of reactions, especially the corresponding softness matching in a local approach¹¹⁻¹⁷ for two or four or much more reactive points between two reactants. Li-Evans¹⁸ proposed that for a hard reaction the site of minimal Fukui function (FF) is preferred and for a soft reaction the site of maximal Fukui function is preferred. Gazquez and Mendez¹⁹ stated that the reaction between two chemical species will not necessarily occur through their softest atoms, but through those sites whose local softness are close to each other. In this respect, Geerlings, Proft and Langenacker²⁰ suggested that local softness should be used as an intermolecular reactivity descriptor, whereas the FF is as an intramolecular one. Thus, the comparisons of the FF or condensed FF values for different systems are meaningless because they represent only the relative reactivity among

different sites within a molecule. Therefore, in order to rationalize the intermolecular reactivity, we have proposed a series of generalized reactivity descriptors²¹, including generalized Fukui function (GFF) and generalized local softness (GLS)²².

Recently, based on the generalized reactivity descriptors we have been successful to predict and to explain the regio-/stereoselectivities of Diels-Alder reactions²² and the enzymatic catalyzed reactions of biological system²¹ and to correlate their intermolecular reactivities of all reactions in terms of the atom-bond electronegativity equalization method (ABEEM $\sigma\pi$) model with the local HSAB principle at its generalized version. And we have obtained the results in good agreement with the experimentally observed outcomes.

In this paper, we will use the usual reactivity descriptors and the generalized one combined with the local HSAB principle to investigate the regioselectivities of the electrophilic additions of alkene including the hydrogen chloride and benzeneselenenyl with unsymmetrical alkene and to rationalize their order of reaction rate constants by the *ab initio* method at the level of MP2/6-311++G(*d,p*) with the finite difference approximation (FDA) method and the ABEEM $\sigma\pi$ model. It should be noted that the FDA method involves the three systems of N , $N+1$, and $N-1$ electrons, but ABEEM $\sigma\pi$ model only involves one system of N electron.

2 Theory background

2.1 The reactivity descriptors

Fukui function (FF) is one of the important reactivity descriptors in predicting the intramolecular reactivity in CDFT^{23,24}. Parr and Yang defined the FF $f(\vec{r})$ and local softness $s(\vec{r})$ ^{25,26} as:

$$f(\vec{r}) = \left(\frac{\partial \rho(\vec{r})}{\partial N} \right)_{v(\vec{r})} \quad (1)$$

$$s(\vec{r}) = \left(\frac{\partial \rho(\vec{r})}{\partial \mu} \right)_{v(\vec{r})} = \left(\frac{\partial \rho(\vec{r})}{\partial N} \right)_{v(\vec{r})} \left(\frac{\partial N}{\partial \mu} \right)_{v(\vec{r})} = f(\vec{r})S \quad (2)$$

where $\rho(\vec{r})$ is the electron density at $\vec{r}$, N is the number of electrons for a molecular system, μ is the chemical potential, the negative of the electronegativity, $v(\vec{r})$ is the external potential generated by the nuclei, S is the global softness.

2.2 The finite difference approximation (FDA)

In the FDA method, according to the Eq.(1), the condensed FF of nucleophilic attack for systems with electron gain can be written as

$$f_k^+ = q_k(N+1) - q_k(N) \quad (3)$$

and the condensed FF of electrophilic attack for systems with electron donation can be expressed as

$$f_k^- = q_k(N) - q_k(N-1) \quad (4)$$

where $q_k(N+1)$, $q_k(N)$, and $q_k(N-1)$ stand for the partial charges on atom k in a molecule with $N+1$, N , and $N-1$ electrons at the same geometry structure, respectively²⁷.

A local softness descriptor $s(\vec{r})$ is related to the FF via Eq.(2), so the condensed local softness is related to the condensed FF²⁶ through

$$s_k^+ = S f_k^+ = S [q_k(N+1) - q_k(N)] \quad (5)$$

$$s_k^- = S f_k^- = S [q_k(N) - q_k(N-1)] \quad (6)$$

where, s_k^+ and s_k^- imply how global softness is redistributed among various atoms of the molecule by the condensed Fukui function. The global softness, S , can be given as²⁴ $S = 1/I - A$ where I and A are the ionization potential and electron affinity, respectively. The first ionization potential I can be obtained by $I = E_{N-1} - E_N$ and the electron affinity A by $A = E_{N+1} - E_N$ with E_{N-1} , E_N , and E_{N+1} denoting the total energies of the systems with $N-1$, N , and $N+1$ electrons, respectively. The quantities involved can be calculated by an *ab initio* method at high level of theory.

2.3 ABEEM $\sigma\pi$ model

Based on the DFT and electronegativity equalization method (EEM)²⁸⁻³⁴, Yang and his coworkers have developed ABEEM $\sigma\pi$ model³⁵⁻⁴⁵, which explicitly partitions a molecule into atom, chemical bond, and lone pair (*lp*) regions. In this model, the single bond consists of one σ region, where the center of the charge for σ bond is located on the position of the ratio of the covalent atomic radii of two bonded atom; the double bond consists of one σ region and four π regions, where center of the σ bond charge is similar with the σ region of single bond and the π bond partial charges are placed above and below the double-bonded atoms at the covalent radii of the this double-bonded atoms perpendicular to the plane formed by the σ bond; and the center of charge and its orientation for the *lp* region is determined in terms of the chemical surrounding.

In terms of the definition of electronegativity based on DFT, the effective electronegativity of a region a , χ_a , can be expressed as:

$$\chi_a = \chi_a^* + 2\eta_a^* q_a + k \left[\sum_{b \neq a} \frac{q_b}{R_{a,b}} \right] \quad (7)$$

where χ_a^* and $2\eta_a^*$ are valence-state electronegativity and hardness of the region a , respectively. a and b denote two regions, including the atom or single bond σ or double bond σ and π or lone pairs regions. q_a and q_b are the partial charges of regions a and b , $R_{a,b}$ denotes the distance between regions a and b , and k , 0.57, is an overall correction coefficient in this formalism^{22,35-47}. The electronegativity equalization principle demands that the effective electronegativity of every region is equal to the overall electronegativity of the molecule, χ_{mol} :

$$\chi_a = \chi_b = \dots = \chi_m = \dots = \chi_{\text{mol}} \quad (8)$$

For an arbitrary molecule partitioned into m regions, solving the Eq.(8) with the constraint Eq.(9) on its net charge, q_{mol} , if the parameters χ_a^* and $2\eta_a^*$ are known, we can obtain the charge of every region.

$$\sum_a q_a + \sum_b q_b + \dots + \sum_m q_m = q_{\text{mol}} \quad (9)$$

On the basis of the definition of the FF, we can express the FF of region a in our ABEEM $\sigma\pi$ model as:

$$f_a = - \left(\frac{dq_a}{dN} \right)_\mu \quad (10)$$

So, the global hardness $2\eta_{\text{mol}}$ can be expressed as:

$$2\eta_{\text{mol}} = - \left(\frac{\partial \chi_a}{\partial N} \right)_v = 2\eta_a^* f_a + k \left[\sum_{b \neq a} \frac{f_b}{R_{a,b}} \right] \quad (11)$$

Hardness expressions for all the regions in a molecule like Eq.(11), altogether with the normalization condition of the FF, $\int f(r) dr = 1$, can be also solved to directly and quickly give the molecular hardness, $2\eta_{\text{mol}}$, and in particular, the condensed FF f_a of each region in the molecule if all parameters $2\eta^*$ in Eq.(11) have been calibrated.

2.4 The generalized reactivity descriptors

The generalized Fukui function (GFF) $f^G(\vec{r})$ and the generalized local softness (GLS) $s^G(\vec{r})$ have been proposed and their definitions²² are expressed as Eqs.(12) and (13):

$$f^G(\vec{r}) = N_M f(\vec{r}) \quad (12)$$

$$s^G(\vec{r}) = f^G(\vec{r}) S = N_M f(\vec{r}) S = N_M s(\vec{r}) \quad (13)$$

where, the $f(\vec{r})$ and $s(\vec{r})$ are local Fukui function (FF) and local softness, the usual reactivity descriptors, N_M is the number of atoms for a molecular system, and S is the global softness. Obviously, according to Eq.(12), the GFF $f^G(\vec{r})$ is normalized to N_M because $f(\vec{r})$ is normalized to 1 for a molecule. And $s^G(\vec{r})$ is normalized to $N_M S$ rather than S , which means that the global softness is the average of the generalized local softness $s^G(\vec{r})$. Based on the definition of $f^G(\vec{r})$, the reactivity descriptor of the site is not only dependant on its charge and $f(\vec{r})$, but also related to the number of the atoms in the molecule, N_M , where the detailed ratiocination has been represented in Ref. 22.

3 Computational details

We investigated the electrophilic additions of hydrogen chloride to asymmetric alkenes and benzeneselenenyl bromide to substituted styrenes, as shown in Fig.1. The geometries of all reactants were optimized and obtained by the B3LYP/6-311+G(*d,p*) level of theory in Gaussian-03⁴⁸. All optimized reactants were stationary points of potential energy surface after checking the frequencies at the same level of theory.

3.1 Calibration of parameters χ^* and $2\eta^*$ for ABEEM $\sigma\pi$ Model

According to Eq.(7) and Eq.(11), we have calibrated the parameters χ^* and $2\eta^*$, through a regression and least-squares optimization procedure by dealing with some model molecules³⁵. For all model molecules, *ab initio* Hartree-Fock MO calculations were performed with STO-3G basis sets in Gaussian 03⁴⁸ and then the partial charges of all the model molecules were obtained by the Mulliken population analysis. Then the charge distributions obtained for the model molecules were brought into Eqs.(7-9) in order to determine the parameters χ^* and $2\eta^*$ through a regression and least-squares

Table 1 Parameters χ^* and $2\eta^*$ in ABEEM $\sigma\pi$ Model.

Type of ABEEM $\sigma\pi$ parameter		χ^*	$2\eta^*$
Cl ₁₇ -Ph-C ₆₂₆ =C ₆₂	C ₆₆ in -Ph	2.500	6.800
	π_{66}	3.850	94.150
	C ₆₂₆	2.500	7.200
	π_{626}	3.790	94.150
	Cl ₁₇	3.010	20.099
	C ₆₂	2.500	10.200
C ₆₂ =C ₆₄ -R	π_{62}	3.500	80.319
	C ₆₄	2.600	6.200
	π_{64}	3.580	88.150
	Se-	1.800	34.970
Br-		2.880	70.019
σ_{C-Se}		4.900	35.000
σ_{Se-Br}		6.950	75.000
lp_{Cl}		5.536	46.900
lp_{Br}		5.965	70.000
lp_{Be}		3.700	7.164

optimization procedure^{22,35-38,46,47}. The old types of parameters were obtained from our previous work³⁷, and the new added types and parameters of χ^* and $2\eta^*$ are listed in Table 1.

For the calibration, the reason why we use the minimum STO-3G basis set is not due to its time-consuming but more importantly due to its physical significance. *Ab initio* calculation with a higher level of basis set can give more accurate prediction of energy and geometry, but can not give more suitable partial charges than lower level of basis set for practical use. This phenomenon comes from the fact that a diffuse basis function located on an atom may to some extent cover the regions of the other adjacent atoms leading to a somewhat overestimating population of this atom in the Mulliken population analysis. Derouane and coworkers⁴⁹ showed that the formal charges calculated with the 6-21 basis set are higher than those computed with the STO-3G basis set, and thus suggested STO-3G charges may be more reliable. Wilson and Ichikawa⁵⁰ and Torrent-Sucarrat and their coworkers⁵¹ pointed out that the charge transfer between atoms in a molecule is overestimated when the polarization basis sets are used. Huzinaka *et al.*⁵² and Jakalian *et al.*⁵³, as well as our group⁴⁷, had experienced that the use of higher level of basis sets overestimates the overlapping between their respective basis functions belonging to two atoms in a molecule. For example, if the 6-31G* basis set is used, the polarity of a molecule calculated by the partial charges is overestimated by 10%–15% than if the STO-3G basis set is used⁵³. Therefore, in the calibration process of the parameters, STO-3G basis set has been used in the *ab initio* calculations for all the model molecules to obtain the partial charges from Mulliken population analysis.

3.2 Calculation of Fukui function and local softness

Geerlings, Proft and Langenacker²⁰ suggested that local softness should be used as an intermolecular reactivity descriptor, whereas the FF is as an intramolecular one. Under the FDA method, *via* $S = 1/(I - A)$, the global softness were

obtained, where the first ionization potential I and the electron affinity A were calculated by *ab initio* method at MP2/6-311++G(*d,p*) level of theory. In terms of Eqs.(3) and (4), the condensed FFs of center atoms were calculated using the natural population analysis (NPA) at the MP2/6-311++G(*d,p*) level of theory, then obtained their local softness *via* Eqs.(5) and (6).

In the ABEEM $\sigma\pi$ model, the FFs of center atoms were calculated by Eq.(11), then their GFFs were calculated by Eq.(12). Their global softness was obtained by Eq.(11) because of it being the inverse of the hardness, hence the local softness and the GLS were calculated by Eqs.(2) and (13), respectively.

3.3 Expression of the local HSAB principle under the finite difference approach and ABEEM $\sigma\pi$ model

The local HSAB principle claimed¹⁹ that the interaction between two molecules will occur not necessarily through their the softest atoms but rather through those atoms of two systems, and their Fukui functions of which are close. Based on this principle, the softness-matching criteria was proposed by Chande, Nguyen, Geerlings and coworkers for understanding the regioselectivity of cycloaddition reactions^{11-13,15,16}. The softness-matching criterion at a local-local approach in the case of multiple sites of interaction has been cast in the form of the minimization of a quadratic form to articulate. In our investigated reactions, because there are two reaction center atoms in electrophilic additions, we will use the absolute values of differences between the local softness of the reaction center atoms of two reactants to express.

Hence, within the FDA method, the expression of the local HSAB principle is written as Eq.(14), where the i is the site of reactivity on molecule A, and the k is the site of reactivity on molecule B, as seen in Fig.1, and the s_{Ai}^+ is the condensed local softness of the i th atom in A, which represents that the electrophile H atom in HCl or [PhSe] group in PhSeBr acquires a electron sharing from the π -bond of substituted ethene and the s_{Bk}^- is the condensed local softness of the k th atom in B, which represents that the reactant B will be attacked by H atom or [PhSe] group to donate an electron to be shared. And then, based on the proposed generalized reactivity descriptor, the local HSAB principle can be expressed as the Eq.(15). In this kind of the reaction, the superscript + denotes the reactivity descriptor of the electrophilic H atom, while the superscript - represents the reactivity index of double bond C atom in alkene.

$$\Delta s = |s_{Ai}^+ - s_{Bk}^-| \quad (14)$$

$$\Delta s^G = |s_{Ai}^{G+} - s_{Bk}^{G-}| \quad (15)$$

In terms of ABEEM $\sigma\pi$ model, the local HSAB principle can be expressed to the Eqs.(16) and (17), where the s_{Ai} , s_{Bk} , and s_{Ai}^G , s_{Bk}^G are the local softness and GLS of i th atom in A and k th atom in B, respectively.

$$\Delta s = |s_{Ai} - s_{Bk}| \quad (16)$$

$$\Delta s^G = |s_{Ai}^G - s_{Bk}^G| \quad (17)$$

According to the local HSAB principle, the smaller the Δs or Δs^G is, the easier the reaction is. In this paper, we only consider the state of single reactant, when $\Delta s_{MA} < \Delta s_{AM}$ or $\Delta s_{MA}^G < \Delta s_{AM}^G$, the Markovnikov product should be the main; and when $\Delta s_{MA} > \Delta s_{AM}$ or $\Delta s_{MA}^G > \Delta s_{AM}^G$, the anti-Markovnikov product should be favored. And the generalized reactivity descriptor can be further used to rationalize the reaction rate constants, i.e., the greater the s_{Bk}^G is, the greater the reactivity is, and the easier the reaction is.

4 Results and discussion

4.1 Regioselectivity of the addition of HCl to alkene

For the addition of HCl to unsymmetrical olefin $CH_2=CR_1R_2$, when the substituent is electron-donating group, such as alkyl, the reactions comply with the Markovnikov's rules to occur. When the substituent is electron-accepting group, such as $-CHO$, $-COOH$, the reactions comply with the anti-Markovnikov's rules. As seen in Fig.1, these substituents belong to the alkyls, so the regioselectivities of these reactions abide by the Markovnikov's rules to produce the Markovnikov's products.

According to Eqs.(14)–(17), the difference values, Δs_{MA} , Δs_{AM} , Δs_{MA}^G and Δs_{AM}^G , for the reactions of HCl with $CH_2=CR_1R_2$ were calculated by using the FDA method and the ABEEM $\sigma\pi$ model, and listed in Table 2. Table 3 presents the detailed values of FF, GFF, local softness, and GLS of reactive center atoms obtained from these two methods.

As shown in Table 2, following the FDA method, the values of Δs_{MA} (0.589), Δs_{AM} (0.589) and Δs_{MA}^G (2.647), Δs_{AM}^G (2.647) for the reaction between HCl with ethene are equal to each

other, respectively, which, of course, indicates that there is no regioselectivity in this reaction. When the olefin is propene, the value of Δs_{MA} (0.533) is smaller than the relevant Δs_{AM} (0.581). According to the local HSAB principle, the H atom of HCl favors to attack the Markovnikov's carbon atom, so this result is in line with the experimental regioselectivity. However, the value of Δs_{MA}^G (6.017) is greater than the Δs_{AM}^G (5.579) by using the generalized local softness, then the regioselectivity of this reaction would be anticipated the anti-Markovnikov's attacking. But, this result is not in agreement with the experimental result. By using the same way to deal with the rest two additions of HCl to 1-butene and 2-methylpropene, we also obtain $\Delta s_{MA} < \Delta s_{AM}$ and $\Delta s_{MA}^G > \Delta s_{AM}^G$. Hence, according to the local HSAB principle, within the FDA method, the predicted results obtained from the usual local softness are better than those from the generalized local softness (GLS).

And then, how about are the results in terms of the ABEEM $\sigma\pi$ model? It is clearly seen from Table 3 that the both values of Δs_{MA} and Δs_{AM} are 0.069×10^{-3} , and both Δs_{MA}^G and Δs_{AM}^G are 5.26 when the olefin is ethene, which indicates that the two double-bonded carbon atoms are identical. When R_1 is H and R_2 is $-CH_3$, Δs_{MA} is 2.099×10^{-3} , Δs_{AM} is 9.250×10^{-3} and Δs_{MA}^G is 73.9, Δs_{AM}^G is 17.60, i.e., $\Delta s_{MA} < \Delta s_{AM}$ and $\Delta s_{MA}^G < \Delta s_{AM}^G$. Therefore, on basis of local HSAB principle, the Markovnikov's product should constitute the main product of this reaction, and this result is in agreement with the Markovnikov's rules. In the same way, when alkenes are 1-butene and 2-methylpropene, both $\Delta s_{MA} < \Delta s_{AM}$ and $\Delta s_{MA}^G < \Delta s_{AM}^G$, so the results are consistent with the Markovnikov's rules. Consequently, both Δs via usual local

Table 2 The difference values, Δs_{MA} , Δs_{AM} , Δs_{MA}^G and Δs_{AM}^G , for HCl with alkene in terms of MP2/6-311++G(d,p) level under the finite difference approximation, and our ABEEM $\sigma\pi$ model.

		Finite difference approximation				ABEEM $\sigma\pi$ model			
		Δs_{MA}	Δs_{AM}	Δs_{MA}^G	Δs_{AM}^G	$10^3\Delta s_{MA}$	$10^3\Delta s_{AM}^G$	$10\Delta s_{MA}^G$	$10\Delta s_{AM}^G$
ethene		0.589	0.589	2.647	2.647	0.069	0.069	0.526	0.526
propene		0.533	0.581	6.017	5.579	2.099	9.250	0.739	1.760
1-butene		0.549	0.556	8.863	8.779	2.867	5.727	0.981	2.012
2-methylpropene		0.604	0.627	8.195	7.924	3.008	6.643	0.964	2.122

Table 3 The values of condensed $f(r)$, $f^G(r)$, $s(r)$, and $s^G(r)$ for the H atom of electrophile HCl and the C_{MA} and C_{AM} of unsymmetrical alkenes at the level of MP2/6-311++G(d,p) and the ABEEM $\sigma\pi$ model.

		Finite difference approximation				ABEEM $\sigma\pi$ model			
		f^+	f^{G+}	s^+	s^{G+}	f	f^G	s	s^G
HCl	H	0.7503	1.5007	1.5446	3.0893	0.2855	0.5709	0.0133	0.0265
		f^-	f^{G-}	s^-	s^{G-}	f	f^G	s	s^G
ethene	C_{MA}	0.4242	2.5451	0.9560	5.736	0.1196	0.7176	0.0132	0.0791
	C_{AM}	0.4242	2.5451	0.9560	5.736	0.1196	0.7176	0.0132	0.0791
propene	C_{MA}	0.4043	3.6388	1.0118	9.106	0.0796	0.7168	0.0112	0.1004
	C_{AM}	0.3849	3.4639	0.9632	8.668	0.1607	1.4464	0.0225	0.2025
1-butene	C_{MA}	0.3952	4.7424	0.9960	11.952	0.0623	0.7481	0.0104	0.1246
	C_{AM}	0.3924	4.7090	0.9890	11.868	0.1139	1.3672	0.0190	0.2277
2-methylpropene	C_{MA}	0.3842	4.6099	0.9404	11.285	0.0632	0.7580	0.0102	0.1229
	C_{AM}	0.3749	4.4989	0.9178	11.013	0.1227	1.4724	0.0199	0.2387

softness and Δs^G via GLS from ABEEM $\sigma\pi$ model can explain and forecast the regioselectivities of these reactions well, and the predicted results are better than those of the FDA method.

It was reported that the rate constants for the addition of HI to ethene, propene, and 2-methylpropene were in the ratio 1:90:700^{5,6}, which indicated that with raising the substituents, the reaction rates gradually became greater and greater. Furthermore, experimental activation energies of the additions of HCl to ethene (166.105 kJ·mol⁻¹), to propene (144.348 kJ·mol⁻¹), and to 2-methylpropene (119.244 kJ·mol⁻¹) were reported^{2,9}, which implied when the substituents gradually become larger and larger, the additions of HCl to CH₂CR₁R₂ are more and more easy to process. The generalized reactivity descriptors, GFF and GLS themselves, can rationalize the intermolecular reactivity, and especially forecast the order of reaction rate constants for a series of reactions. Hence, we applied the GLS, rather than Δs^G to correlate the order of the reaction rate constants for these investigated additions.

The investigated electrophilic additions of HCl to alkenes, we have only considered the reactivity descriptors of reactants, which means that the values of GLS for the H atom of HCl are fixed and just the values of GLS for the C_{MA} of alkenes are taken as variables, where the values of GLS for reaction centers by FDA method and ABEEM $\sigma\pi$ model are listed in Table 3, i.e., we can disregard the GLS of H atom in HCl and only compare the GLS of C_{MA} in alkenes of the main product. It is clear from our calculations that the values of s_{MA}^G obtained from both FDA method and ABEEM $\sigma\pi$ model (in Table 3) for alkenes increase with the substituents rising. Since the higher FF is, the higher reactivity is, i.e., the softest position of the molecule is, the easiest reactive site occurs. Hence, the addition for HCl to 2-methylpropene is the fastest reaction, the addition for HCl to ethene is the slowest one, and the addition of HCl to 1-butene is in the middle. These conclusions are just in agreement with experimental results and the results of usual local softness have not such regularity.

In a word, both the usual reactivity descriptors and the generalized ones from ABEEM $\sigma\pi$ model in combination with the local HSAB principle can successfully interpret and forecast the regioselectivities of the additions of HCl to alkenes, which results are in agreement with the Markovnikov rule, but the results of FDA method are not good. And then, the values of s_{MA}^G for the alkenes calculated by both the FDA method and the ABEEM $\sigma\pi$ model can further correlate the reaction rate constants. When values of s_{MA}^G gradually become big, the studied additions gradually become fast as substituents gradually increasing. But, the usual softness of C_{MA} can not do this result. Therefore, we have chosen the other series of electrophilic additions to further check the validity and practicability of generalized descriptors again, as seen in Fig.1.

4.2 The regioselectivity of addition for benzeneselenenyl bromide with alkene

The additions of benzeneselenenyl bromide to alkenes are

usually considered to be the electrophilic addition reactions⁷. We have chosen four reactions between benzeneselenenyl bromide and substituted styrene (XPhCH=CH₂), where the substituents PhX of alkenes are Ph, 3-ClPh, 4-ClPh and 4-CH₃Ph, respectively. Here, [PhSe] group in electrophile is considered to be the H atom of HCl and it has the positive charge, which attacks one of the double-bonded carbon atoms of alkenes with enriched electron. The Br atomic charges obtained by HF/STO-3G level of theory and ABEEM $\sigma\pi$ model are -0.100 and -0.140 a.u., respectively. Table 4 lists the charges of C_{MA} and C_{AM}, q_{MA} and q_{AM} , calculated by HF/STO-3G level of theory and ABEEM $\sigma\pi$ model, respectively.

These C_{MA} possess much more negative charge and the C_{AM} possess a little charge compared with C_{MA}, hence, the electrophile [PhSe] group will favor to attack the C_{MA}. Here, we could consider the substituents X together with benzene (X-Ph-) as a whole to be the electron-donating groups, i.e. these four reactions should obey the Markovnikov's rules according to the greater attraction between [PhSe] group and C_{MA}, which are just in line with the experimental results⁷. We also can see that the q_{MA} of 3-Cl and 4-Cl are less than that of the others, because the interaction between -Cl, the electron-withdrawing group, and benzene, the electron-donating group, represents the character of the electron-donating group in nonpolar solution, so leading to that result, if the reactions react in polar solution, the result may be the opposite⁷, however, the all calculations about these reactions were calculated at the gas state in vacuum. The charges of ABEEM $\sigma\pi$ and *ab initio* method are in agreement by and large.

Then, we make use of the usual local softness and the generalized one from FDA method and the ABEEM $\sigma\pi$ model combination with local HSAB principle to estimate the regioselectivities of above four additions, the values of Δs_{MA} , Δs_{AM} , Δs_{MA}^G and Δs_{AM}^G from these two methods are listed in Table 5, and the ratio of Markovnikov's product to anti-Markovnikov's from the experiment⁷ are also listed in Table 5.

It can be seen from that Table 5 the four Δs_{MA} and Δs_{MA}^G are all smaller than respective Δs_{AM} and Δs_{AM}^G under the FDA method. And the values of Δs_{MA} and Δs_{MA}^G from ABEEM $\sigma\pi$ model are also smaller than their respective Δs_{AM} and Δs_{AM}^G . Therefore, on basis of local HSAB principle, the

Table 4 The charges of C_{MA}, C_{AM} obtained from HF/STO-3G and ABEEM $\sigma\pi$ Model.

X-PhCH=CH ₂	HF/STO-3G		ABEEM $\sigma\pi$	
	q_{MA}	q_{AM}	q_{MA}	q_{AM}
H	-0.128	-0.057	-0.125	-0.054
3-Cl	-0.122	-0.057	-0.116	-0.042
4-Cl	-0.122	-0.058	-0.116	-0.042
4-CH ₃	-0.129	-0.057	-0.123	-0.051

Table 5 The values of Δs_{MA} , Δs_{AM} , Δs_{MA}^G and Δs_{AM}^G for PhSeBr with substituted styrene ($X\text{-PhCH=CH}_2$) at the level of MP2/6-311++G(*d,p*) with the finite difference approach and ABEEM $\sigma\pi$ model.

$X\text{-PhCH=CH}_2$	finite difference approach				ABEEM $\sigma\pi$ Model				^a MA: AM
	Δs_{MA}	Δs_{AM}	Δs_{MA}^G	Δs_{AM}^G	$10^4\Delta s_{MA}$	$10^4\Delta s_{AM}$	$10^2\Delta s_{MA}^G$	$10^2\Delta s_{AM}^G$	
H	0.841	1.457	8.915	18.780	1.666	1.680	4.683	4.711	78:22
3-Cl	0.854	1.413	9.133	18.066	1.636	1.649	4.600	4.629	59:41
4-Cl	0.857	1.442	9.183	18.534	1.644	1.658	4.625	4.652	76:24
4-CH ₃	0.853	1.517	7.128	19.754	1.579	1.593	6.689	6.721	86:14

^a Those reactions are reacting in benzene at 25 °C.

Markovnikov's products should constitute the main products of these four reactions by means of FDA method and ABEEM $\sigma\pi$ model, which results are in line with the experimental regioselectivities.

We can obtain two sequences: $\Delta s_{MA}^G(4\text{-CH}_3) < \Delta s_{MA}^G(\text{H}) < \Delta s_{MA}^G(3\text{-Cl}) < \Delta s_{MA}^G(4\text{-Cl})$ via FDA method and $\Delta s_{MA}^G(3\text{-Cl}) < \Delta s_{MA}^G(4\text{-Cl}) < \Delta s_{MA}^G(\text{H}) < \Delta s_{MA}^G(4\text{-CH}_3)$ via ABEEM $\sigma\pi$ model. According to the local HSAB principle, the smaller Δs^G is, the easier reaction is. Luk and his coworkers⁷ gave second-order rate constants, k , its unit being $\text{dm}^3\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$ of these reactions which are in order $k^{\text{H}}(2.58 \pm 0.15) \times 10^{-2}$, $k^{3\text{-Cl}}(1.57 \pm 0.07) \times 10^{-2}$, $k^{4\text{-Cl}}(2.20 \pm 0.1) \times 10^{-2}$, and $k^{4\text{-CH}_3}(2.77 \pm 0.1) \times 10^{-2}$, as shown in Fig.2 (upper). The order of the experimental reaction rates is $k^{3\text{-Cl}} < k^{4\text{-Cl}} < k^{\text{H}} < k^{4\text{-CH}_3}$. Therefore, the intermolecular reactivity predicted by ABEEM $\sigma\pi$ model is just in a reverse order compared with the experimental rate constants.

Fig.2 (middle) displays the line chart of the s^G obtained from the ABEEM $\sigma\pi$ model. And Fig.2 (lower) represents the line charts of the s^{G^-} of the C_{MA} atoms calculated by FDA method. It can be found from the Fig.2 that the order of $s_{MA}^{G^-}$ is $s_{MA}^{G^-}(4\text{-Cl}) < s_{MA}^{G^-}(3\text{-Cl}) < s_{MA}^{G^-}(\text{H}) < s_{MA}^{G^-}(4\text{-CH}_3)$ (FDA method) and that of s_{MA}^G is $s_{MA}^G(3\text{-Cl}) < s_{MA}^G(4\text{-Cl}) < s_{MA}^G(\text{H}) < s_{MA}^G(4\text{-CH}_3)$

Fig.2 The line charts of the reaction rates (upper), the s^G (middle) and s^{G^-} (lower) of C_{MA} atoms in the four additions of benzeneselenenyl bromide to the substituted styrenes.

(ABEEM $\sigma\pi$ model). The sequence via ABEEM $\sigma\pi$ model is just in accord with that of the experimental reaction rates, but that of FDA method is not for the $-\text{Cl}$ substituted additions.

Therefore, the applications of the generalized reactivity descriptor combined with the local HSAB principle on this series of electrophilic additions demonstrate that both the values of Δs and Δs^G from ABEEM $\sigma\pi$ model can forecast their regioselectivities and only the values of center atoms' generalized local softness of substituted ethenes calculated by ABEEM $\sigma\pi$ model can rationalize the reaction rate constants rather than the difference of center atoms' generalized local softness of the two reactants. However, the results of the finite difference approximation are not well related to the experimental results.

5 Conclusions

For the addition reactions of HCl to the substituted ethenes and benzeneselenenyl bromide to the substituted styrenes, according to the local HSAB principle, the values of the softness differences, Δs , in terms of *ab initio* method at the level of MP2/6-311++G(*d,p*) with the finite difference approximation (FDA) method and the ABEEM $\sigma\pi$ model have been used to relate to their regioselectivities.

As the performance of the generalized reactivity descriptor, it is shown that the C_{MA} atoms of all reactions prefer to be attacked in terms of ABEEM $\sigma\pi$ model, which is in agreement with the experimental results. But, the results of FDA method can not obtain such good indication. However, it is shown that there are two inverse orders, compared with the orders of experimental rate constants for these two series of electrophilic additions by using the Δs^G from FDA and ABEEM $\sigma\pi$ model. In fact, only generalized local softness (GLS) of center atoms can be related to the orders of the experimental reaction rate constants by both the FDA method and the ABEEM $\sigma\pi$ model except the results of the FDA method for 3-Cl substituted addition with a little flaw.

Up to now, we have applied the generalized reactivity descriptors to study on several kinds of reactions, such as to predict the regio- and stereoselectivity of Diels-Alder reactions and to correlate their reaction rate constants, to rationalize the intermolecular reactivities and regioselectivities of enzymatic

catalyzed nucleophilic reactions, etc. Moreover, we will continue to apply the generalized Fukui function and the generalized local softness to investigate other systems and to further check their rationality and validity.

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