

Nucleophilic reactivity analysis: atom-bond electronegativity equalization method

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Received 28 December 1998; accepted 11 May 1999

Abstract

The reactivity of maleic anhydride and β -propiolactone with respect to different nucleophiles is studied using atom-bond electronegativity equalization method. From our study, hardness and softness are found to be relative properties and that the Fukui function is not the only factor to determine the selectivity of a chemical reaction, while the hard and soft acid and base principle, in a local sense, can be used to understand this kind of reactivity. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Atom-bond electronegativity equalization method; Density functional theory; Chemical reactivity; Hard and soft acid and base principle; Hardness; Fukui function; Local softness

1. Introduction

Without resorting to potential energy surfaces, the frontier orbital theory [1,2], the Woodward–Hoffmann rules [3,4] and the hard and soft acid and base (HSAB) principle [5,6] have played a key role in understanding the reactivity of many chemical reactions. However, all these theories are mainly qualitative. Within the framework of density functional theory (DFT) [7,8] where the electron density $\rho(\mathbf{r})$ is basic variable [9,10], several global and local quantities related to chemical reactivity are defined rigorously and quantitatively so that the DFT also becomes a convenient and powerful tool for explaining and predicting chemical reactivity.

The electronegativity [11], hardness [12] and softness [13] are global quantities which characterize a molecule as a whole and are defined respectively as

$$\chi = -\mu = -\left(\frac{\partial E}{\partial N}\right)_V, \quad (1)$$

$$\eta = \frac{1}{2}\left(\frac{\partial \mu}{\partial N}\right)_V = \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right)_V, \quad (2)$$

$$S = \frac{1}{2\eta}\left(\frac{\partial N}{\partial \mu}\right)_V = \left(\frac{\partial^2 N}{\partial E^2}\right)_V, \quad (3)$$

where μ is the chemical potential, E is the total electronic energy, N is the number of electrons and $V(r)$ is the external nuclear potential in the molecule.

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Table 1

Atom and bond valence-state parameters

	A	B	C	D
H–	1.770	5.789	0.602	
C–	2.307	3.529	2.546	
N–	2.620	4.518	1.534	
O–	3.292	4.344	4.991	
S–	2.403	2.369	2.586	
Cl–	3.184	3.739	7.631	
C=	2.172	3.300	1.935	
O=	3.166	3.519	5.678	
N=	2.778	3.691	2.308	
H–C	8.742	57.852	3.193	2.011
H–S	5.160	37.844	2.275	2.127
H–N	4.007	12.829	0.518	2.050
H–O	4.236	21.867	2.831	3.418
C–S	2.476	1.098	2.382	1.625
C–N	3.433	9.728	2.433	2.433
C–O	3.174	8.862	2.350	2.350
C–Cl	3.429	12.153	2.736	3.828
C–C	3.747	12.772	2.196	2.196
C=C	2.934	3.945	2.286	2.286
C=O	3.066	5.441	2.331	2.331
C=N	3.444	6.734	2.517	2.517

The Fukui function [14] and local softness [13] are local quantities that can be used to differentiate the reactive behavior of different sites within a molecule:

$$f(r) = \left[\frac{\delta\mu}{\delta V(r)} \right]_N = \left(\frac{\partial \rho(r)}{\partial N} \right)_V, \quad (4)$$

$$s(r) = \left(\frac{\partial \rho(r)}{\partial \mu} \right)_V = \left(\frac{\partial \rho(r)}{\partial N} \right)_V \left(\frac{\partial N}{\partial \mu} \right)_V = f(r) S. \quad (5)$$

From the DFT and electronegativity equalization principle [15,16] have developed the electronegativity equalization method (EEM) [17,18] and atom-bond electronegativity equalization method (ABEEM) [19,20] with which these quantities mentioned above could be calculated more directly and more rapidly. For example, the Fukui function and hardness can be calculated with no use of the finite difference approximation [12,21,22]. In this paper, the ambident reactivity of maleic anhydride and β -propiolactone with respect to nucleophiles will be rationalized in terms of the results calculated from ABEEM.

2. Atom-bond electronegativity equalization method

Based on DFT, the molecular electron density is partitioned as

$$\rho(r) = \sum_a \rho_a(r) + \sum_{g-h} \rho_{g-h}(r) \quad (6)$$

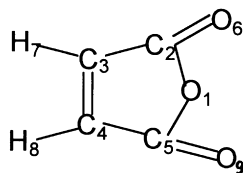
in which $\rho_a(r)$ denotes the electron density located on the atom “a” and $\rho_{g-h}(r)$ denotes the electron density allocated around the g–h bond region between atom “g” and atom “h”. Then we can get the effective electronegativities of an atom and a bond:

$$\chi_a = A_a + B_a q_a + C_a \sum_{a-b} q_{a-b} + k \left(\sum_{b(\neq a)} \frac{q_b}{R_{a,b}} + \sum_{g-h(\neq a-b)} \frac{q_{g-h}}{R_{a,g-h}} \right), \quad (7)$$

$$\chi_{a-b} = A_{a-b} + B_{a-b} q_{a-b} + C_{a-b,b} q_b + k \left(\sum_{g(\neq a,b)} \frac{q_g}{R_{a-b,g}} + \sum_{g-h(\neq a-b)} \frac{q_{g-h}}{R_{a-b,g-h}} \right), \quad (8)$$

Table 2

Charges, Fukui functions and local softnesses of maleic anhydride



	$q(r)$	$f(r)$	$s(r)$
O ₁	– 0.203	0.102	0.069
O ₆	– 0.209	0.223	0.151
C ₂	0.550	– 0.025	– 0.017
C ₃	0.105	0.069	0.047
H ₇	0.169	0.089	0.060
C ₂ –O ₁	– 0.066	0.012	0.008
C ₂ –O ₆	– 0.090	0.042	0.029
C ₃ –C ₂	– 0.175	0.012	0.008
C ₃ –C ₄	– 0.142	0.045	0.030
C ₃ –H ₇	– 0.112	0.003	0.002

where q_a and q_{a-b} are the partial charge of atom “a” and bond a–b, respectively; $R_{a,b}$, $R_{a,g-h}$, and $R_{a-b,g}$ and $q_{a,b,g-h}$ are the distance between atom “a” and “b”, atom “a” and bond g–h, bond a–b and atom “g” and bond a–b and bond g–h, respectively; k is a correction factor; A , B , C and D are the valence-state parameters.

More than 200 molecules were selected as model molecules. The ab initio STO-3G SCF method was used to calculate their charge distributions via Mulliken population analysis. The bond charge q_{g-h} which is placed on the point that partitions the bond length according to the ratio of covalent atomic radii of atoms “g” and “h”, was made equal to the Mulliken interatomic population on the bond g–h multiplied by a correction factor λ . The remainder of the Mulliken interatomic population for bond g–h was equally allotted to the atoms “g” and “h”. The parameters λ and k were optimized to be 0.15 and 0.57, respectively. Then the charge distributions obtained for the model molecules were brought into Eqs. (7) and (8) to determine the coefficients A , B , C and D through a regression and least-square optimization procedure. The outcome was listed in Table 1.

Table 3

Hardnesses reaction sites with maleic anhydride of some nucleophiles

Nucleophile	Hardness	Attacking point	Reference
H ₂ O	1.70	C ₂	[23]
NH ₃	1.32	C ₂	[24]
CH ₃ OH	1.13	C ₂	[25]
CH ₃ NH ₂	1.02	C ₃	[24]
CH ₃	0.95	C ₃	[26]
Pyrrole	0.79	C ₃	[27]

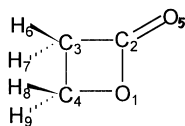
If the configuration of a molecule is known, we can calculate its electronegativity and the charge distribution on each atom and each bond from the following equation which comes from the electronegativity equalization along with the constraint on its net charge (i.e., its total charge is q_{mol}):

$$\begin{bmatrix} q_a \\ q_b \\ \vdots \\ q_n \\ q_{a-b} \\ q_{g-h} \\ \vdots \\ q_{m+n} \\ -\chi \end{bmatrix} \begin{bmatrix} B_a & \frac{k}{R_{a,b}} & \cdots & \frac{k}{R_{a,n}} & C_a \\ \frac{k}{R_{b,a}} & B_b & \cdots & \frac{k}{R_{b,n}} & C_b \\ \vdots & \vdots & & \vdots & \vdots \\ \frac{k}{R_{n,a}} & \frac{k}{R_{n,b}} & \cdots & B_n & \frac{k}{R_{n,a-b}} \\ C_{a-b,a} & D_{a-b,b} & \cdots & \frac{k}{R_{a-b,n}} & B_{a-b} \\ \frac{k}{R_{g-h,a}} & \frac{k}{R_{g-h,b}} & \cdots & \frac{k}{R_{g-h,n}} & \frac{k}{R_{g-h,a-b}} \\ \vdots & \vdots & & \vdots & \vdots \\ \frac{k}{R_{n+m,a}} & \frac{k}{R_{n+m,b}} & \cdots & \frac{k}{R_{n+m,a-b}} & \frac{k}{R_{n+m,g-h}} \\ 1 & 1 & \cdots & 1 & 1 \end{bmatrix} \begin{bmatrix} \frac{k}{R_{a,g-h}} & \cdots & \frac{k}{R_{a,n+m}} \\ \frac{k}{R_{b,g-h}} & \cdots & \frac{k}{R_{b,n+m}} \\ \vdots & & \vdots \\ \frac{k}{R_{n,g-h}} & \cdots & \frac{k}{R_{n,n+m}} \\ \frac{k}{R_{a-b,g-h}} & \cdots & \frac{k}{R_{a-b,n+m}} \\ B_{g-h} & \cdots & \frac{k}{R_{g-h,n+m}} \\ \vdots & & \vdots \\ \frac{k}{R_{n+m,g-h}} & \cdots & B_{n+m} \\ 1 & \cdots & 1 & 0 \end{bmatrix}^{-1} \begin{bmatrix} -A_a \\ -A_b \\ \vdots \\ -A_n \\ -A_{a-b} \\ -A_{g-h} \\ \vdots \\ -A_{n+m} \\ q_{mol} \end{bmatrix} \quad (9)$$

Its hardness and the Fukui function of each atom and each bond can also be calculated:

$$\begin{bmatrix} f_a \\ f_b \\ \vdots \\ f_n \\ f_{a-b} \\ f_{q_{g-h}} \\ \vdots \\ f_{m+n} \\ -2\eta \end{bmatrix} \begin{bmatrix} B_a & \frac{k}{R_{a,b}} & \cdots & \frac{k}{R_{a,n}} & C_a & \frac{k}{R_{a,g-h}} & \cdots & \frac{k}{R_{a,n+m}} & 1 \\ \frac{k}{R_{b,a}} & B_b & \cdots & \frac{k}{R_{b,n}} & C_b & \frac{k}{R_{b,g-h}} & \cdots & \frac{k}{R_{b,n+m}} & 1 \\ \vdots & \vdots & & \vdots & \vdots & \vdots & & \vdots & \vdots \\ \frac{k}{R_{n,a}} & \frac{k}{R_{n,b}} & \cdots & B_n & \frac{k}{R_{n,a-b}} & \frac{k}{R_{n,g-h}} & \cdots & \frac{k}{R_{n,n+m}} & 1 \\ C_{a-b,a} & D_{a-b,b} & \cdots & \frac{k}{R_{a-b,n}} & B_{a-b} & \frac{k}{R_{a-b,g-h}} & \cdots & \frac{k}{R_{a-b,n+m}} & 1 \\ \frac{k}{R_{g-h,a}} & \frac{k}{R_{g-h,b}} & \cdots & \frac{k}{R_{g-h,n}} & \frac{k}{R_{g-h,a-b}} & B_{g-h} & \cdots & \frac{k}{R_{g-h,n+m}} & 1 \\ \vdots & \vdots & & \vdots & \vdots & \vdots & & \vdots & \vdots \\ \frac{k}{R_{n+m,a}} & \frac{k}{R_{n+m,b}} & \cdots & \frac{k}{R_{n+m,a-b}} & \frac{k}{R_{n+m,a-b}} & \frac{k}{R_{n+m,g-h}} & \cdots & B_{n+m} & 1 \\ 1 & 1 & \cdots & 1 & 1 & 1 & \cdots & 1 & 0 \end{bmatrix}^{-1} \begin{bmatrix} 0 \\ 0 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \vdots \\ 0 \\ 1 \end{bmatrix} \quad (10)$$

Table 4
Charges, Fukui functions, and local softnesses of β -propiolactone



	$q(r)$	$f(r)$	$s(r)$
O ₁	-0.172	0.128	0.078
C ₂	0.480	-0.015	-0.009
C ₃	0.067	0.054	0.033
C ₄	0.219	0.034	-0.021
O ₅	-0.177	0.257	0.156
H ₆	0.137	0.105	0.064
H ₈	0.120	0.111	0.068
C ₂ -O ₁	-0.066	0.014	0.009
C ₄ -O ₁	-0.072	0.017	0.010
C ₂ =O ₅	-0.130	0.053	0.032
C ₃ -C ₂	-0.103	0.004	0.002
C ₄ -C ₃	-0.107	0.006	0.004
C ₃ -H ₆	-0.114	0.004	0.002
C ₄ -H ₈	-0.113	0.004	0.002

3. Results and discussion

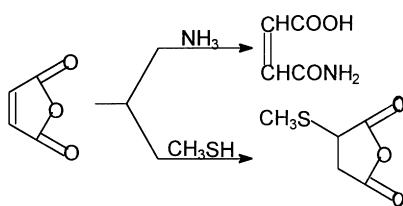
Both maleic anhydride and β -propiolactone have two kinds of active carbons which can react with different nucleophiles. In order to understand their chemical reactivity, we have calculated their charges, Fukui functions and local softnesses (Tables 2 and 4) of different atoms and bonds and the hardnesses of some nucleophiles (Tables 3 and 5).

According to the calculation data in Table 2, the carbonyl carbons (C₂ and C₅) and the carbon atoms

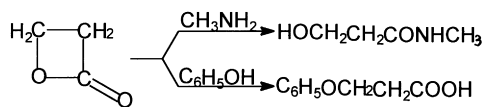
Table 5
Hardnesses and reaction sites with β -propiolactone of some nucleophiles

Nucleophile	Hardness	Attacking point	Reference
CH ₃ NH ₂	1.02	C ₂	[28]
CH ₃ COCl	0.86	C ₂	[29]
Thiourea	0.78	C ₄	[30]
C ₆ H ₅ OH	0.69	C ₄	[31]
C ₆ H ₅ NH ₂	0.66	C ₄	[32]
Indole	0.61	C ₄	[33]

located at the α position to carbonyl carbons (C_3 and C_4) of maleic anhydride have positive net charge, so they are all the sites that can be attacked by nucleophiles. However, the Fukui functions or local softnesses of these two kinds of carbons are different C_2 is the hardest atom of maleic anhydride, i.e., C_3 is softer than C_2 . The $C_3=C_4$ bond is also softer than the C_2-O_1 bond. The experiments [23–27] show that, hard nucleophiles (water, ammonia and methanol) react with the harder sites (C_2 or C_5) and the C_2-O_1 (or C_5-O_1) bond fission occurs; on the other hand, soft nucleophiles (the other three) attack the softer regions (C_3 or C_4) and the $C_3=C_4$ double bond is broken. For example:



The situation is similar for β -propiolactone. The carbonyl carbon (C_2) and the β -carbon atom (C_4) are the active sites which possess positive net charges and can react with nucleophiles (Table 4). C_4 is softer than C_2 and the alkyl-oxygen (C_4-O_1) bond is also softer than the acyl-oxygen (C_2-O_1) bond. The harder nucleophiles (methylamine and acetyl chloride) attack the harder C_2 atom resulting in the ring opening at the C_2-O_1 bond; while the softer nucleophiles (the other four) react with the softer C_4 site and the C_4-O_1 bond is cleaved (Table 5). For example:



If the HSAB principle is accepted in a local version (i.e. given a molecule with different reactive sites, its hard regions prefer to interact with hard species whereas its soft areas prefer soft attacking reagents to react), these results can be explained completely. Because a reagent such as methylamine can behave hard in a reaction while in another reaction it is a soft

reagent, the hardness and softness are relative, system-dependent properties. The nature of chemical reactivity is also relative.

On the basis of the frontier orbital theory, only the site with maximal Fukui function is preferred during a reaction. The only the site with maximal Fukui function is preferred during a reaction. Then only the active C_3 atom of maleic anhydride and the active C_4 atom of β -propiolactone will react with different nucleophiles. Obviously this is not fully correct. Thus the Fukui function is not the only factor to determine the selectivity of a chemical reaction. We can in a sense accept the following viewpoints [34]: for a hard reaction, the site of minimal Fukui function is preferred; for a soft reaction, the site of maximal Fukui function is preferred.

References

- [1] K. Fukui, T. Yonezawa, H. Shingu, *J. Chem. Phys.* 20 (1952) 722.
- [2] K. Fukui, *Theory of Orientation and Stereoselection*, Springer, Berlin, 1975.
- [3] R.B. Woodward, R. Hoffmann, *J. Am. Chem. Soc.* 87 (1965) 395.
- [4] R.B. Woodward, R. Hoffmann, *The Conservation of Orbital Symmetry*, Academic Press, New York, 1970.
- [5] R.G. Pearson, *J. Am. Chem. Soc.* 85 (1963) 3533.
- [6] R.G. Pearson, *Hard and Soft Acids and Bases*, Dowden, Hutchinson and Ross, Stroudsburg, 1973.
- [7] R.G. Parr, W. Yang, *Density-Functional Theory of Atoms and Molecules*, Oxford University Press, New York, 1989.
- [8] R.M. Dreilzer, E.K.U. Gross, *Density Functional Theory*, Springer, Berlin, 1990.
- [9] P. Hohenberg, W. Kohn, *Phys. Rev.* 136 (1964) B864.
- [10] W. Kohn, L.J. Sham, *Phys. Rev.* 140 (1965) A1133.
- [11] R.G. Parr, R.A. Donnelly, M. Levy, W.E. Palke, *J. Chem. Phys.* 68 (1978) 3801.
- [12] R.F. Parr, R.G. Pearson, *J. Am. Chem. Soc.* 105 (1983) 7512.
- [13] W. Yang, R.G. Parr, *Proc. Natl. Acad. Sci., USA* 71 (1985) 6723.
- [14] R.G. Parr, W. Yang, *J. Am. Chem. Soc.* 106 (1984) 4049.
- [15] R.T. Sanderson, *Science* 114 (1951) 670.
- [16] R.T. Sanderson, *Polar Covalence*, Academic Press, New York, 1983.
- [17] W.J. Mortier, K.V. Genechten, J. Gasteiger, *J. Am. Chem. Soc.* 107 (1985) 829.
- [18] W.J. Mortier, S.K. Ghosh, S. Shankar, *J. Am. Soc.* 108 (1986) 4315.
- [19] Z.Z. Yang, C.S. Wang, *J. Phys. Chem.* A101 (1997) 6315.
- [20] C.S. Wang, S.M. Li, Z.Z. Yang, *J. Mol. Struct. (Theochem)* 430 (1998) 191.
- [21] W. Yang, W.J. Mortier, *J. Am. Chem. Soc.* 108 (1986) 5708.

- [22] C. Lee, W. Yang, R.G. Parr, *J. Mol. Struct. (Theochem)* 163 (1988) 305.
- [23] O.H. Wheeler, E.F.G. Rodriguez, *J. Org. Chem.* 26 (1961) 4763.
- [24] L.H. Flett, W.H. Gardner, *Maleic Anhydride Derivatives*, Wiley, New York, 1952.
- [25] E.F. Siegel, M.K. Moran, *J. Am. Chem. Soc.* 69 (1947) 1457.
- [26] F.B. Zienty, B.D. Vineyard, A.A. Schleppnik, *J. Org. Chem.* 27 (1962) 3140.
- [27] D.W. Young, *Heterocyclic Chemistry*, Longman, London, 1975.
- [28] T.L. Gresham, J.E. Jansen, F.W. Shaver, R.A. Bankert, F.T. Fiedorek, *J. Am. Chem. Soc.* 73 (1951) 3168.
- [29] T.L. Gresham, J.E. Jansen, F.W. Shaver, *J. Am. Chem. Soc.* 72 (1950) 72.
- [30] T.L. Gresham, J.E. Jansen, F.W. Shaver, *J. Am. Chem. Soc.* 70 (1948) 1001.
- [31] T.L. Gresham, J.E. Jansen, F.W. Shaver, R.A. Bankert, W.L. Beeers, M.G. Prendergast, *J. Am. Chem. Soc.* 71 (1949) 661.
- [32] H.T. Liang, P.D. Bartlett, *J. Am. Chem. Soc.* 77 (1955) 530.
- [33] J. Harley-Mason, *Chem. Ind.* (1951) 886.
- [34] Y. Li, J.N.S. Evans, *J. Am. Chem. Soc.* 117 (1995) 7756.