Electrophilicity Index

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Abstract: Prompted by a recent paper by Maynard and co-workers (Maynard, A. T.; Huang, M.; Rice, W. G.; Covel, D. G. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 11578), we propose that a specific property of a chemical species, the square of its electronegativity divided by its chemical hardness, be taken as defining its electrophilicity index. We tabulate this quantity for a number of atomic and molecular species, for two different models of the energy−electron number relationships, and we show that it measures the second-order energy change of an electrophile as it is saturated with electrons.

Ligand-binding phenomena are of general interest in catalysis, drug design, and protein and DNA functioning. Although many kinds of interactions are involved in the process, in many cases partial charge transfer through covalent bonding, dative bonding, or hydrogen bonding takes place. The capability of a ligand to accept precisely one electron from a donor is measured by its electron affinity (EA). However, the question we here address is to what extent partial electron transfer contributes to the lowering of the total binding energy by maximal flow of electrons. As yet there has been no direct answer to this question. We here provide validation for the recent qualitative suggestion by Maynard et al.[1] that electronegativity squared divided by hardness measures the electrophilic power of a ligand, its propensity to "soak up" electrons, so to speak.

Consider an electrophilic ligand immersed in an idealized zero-temperature free electron sea of zero chemical potential, which could be an approximation to its binding environment in a protein, a DNA coil, or a surface. It will become saturated with electrons, to the point that its chemical potential increases to zero, becoming equal to the chemical potential of the sea. To second order, the energy change ΔE due to the electron transfer ΔN satisfies the formula[2]

$$\Delta E = \mu\Delta N + 1/_2\eta\Delta N^2 \tag{1}$$

where μ and η are the chemical potential (negative of the electronegativity)[3] and chemical hardness[4] of the ligand, defined by $\mu = (\partial E/\partial N)_v$ and $\eta = (\partial^2 E/\partial N^2)_v$. If the sea provides enough electrons, the ligand becomes saturated with electrons when $\Delta E/\Delta N = 0$. That is,

$$\Delta E = -\frac{\mu^2}{2\eta} \quad \text{and} \quad \Delta N_{\max} = -\frac{\mu}{\eta} \tag{2}$$

Notice that since $\eta > 0$, $\Delta E < 0$, i.e., the charge transfer process is energetically favorable. We propose

$$\omega \equiv \mu^2/2\eta \tag{3}$$

as the measure of electrophilicity of the ligand. In view of the analogy between eq 2 and the equation, power $\equiv W = V^2/R$ in classical electricity, one may think of ω as a sort of "electrophilic power". Various other theoretical and experimental discussions of electrophilicity are available in the literature,[5−11] without there being a consensus as to how it should best be determined or defined. Even if third-order and higher terms are important to add to eq 1, we suggest retaining eq 3 as the definition of electrophilicity index of a species.

To obtain approximate expressions for ω, we consider two models of the total energy E as a function of the electron number N, $E(N)$. The first is the ground-state parabola model, where[2]

$$E(N) = E(N_0) - \frac{I+A}{2}(N-N_0) + \frac{I-A}{2}(N-N_0)^2 + \ldots \tag{4}$$

where I and A denote the ionization potential (IP) and EA, respectively. For this model, one has

$$\Delta N_{\max} = N_{\max} - N_0 = \frac{I+A}{2(I-A)} \tag{5}$$

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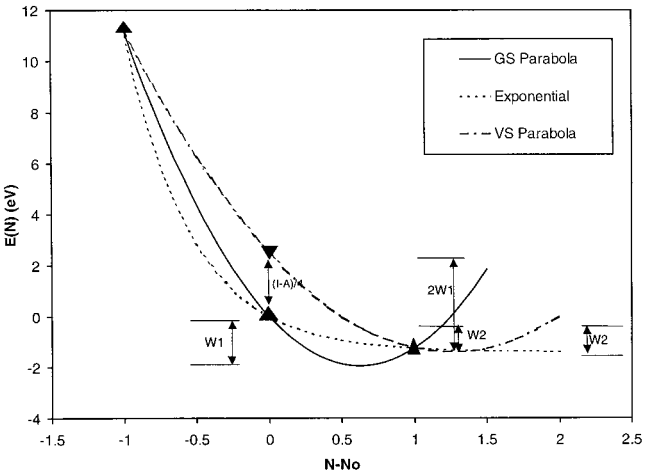

Figure 1. Plots of $E(N)$ for the carbon atom, in the ground-state parabola model, the valence-state parabola model, and the ground-state exponential model. $W1$ is the electrophilicity index of the ground-state parabola model and $W2$ is the energy lowering relative to the ground state in the valence-state parabola model.

Also

$$\mu = -\frac{I+A}{2} \quad \text{and} \quad \eta = I - A \tag{6}$$

and the energy produced from the maximal flow of electrons between the donor and acceptor is

$$\omega_{gs} = \frac{(I+A)^2}{8(I-A)} \tag{7}$$

Maynard et al. recently found[1] a good correlation between ω_{gs} and the logarithm of reaction rate of the humans immunodeficiency virus type 1 (HIV-1) nucleocapsid protein p7 (NCp7) zinc finger domains with electrophilic chemotypes.

The second model is the valence state parabola model,[12,13] in which a reference, valence state, is introduced with a promotion energy $(I - A)/4$ included in the neutral state. Here $E(N)$ takes the form

$$E(N) = E(N_0) - \frac{I+A}{2}(N - N_0) + \frac{I-A}{4}(N - N_0)^2 + \frac{I-A}{4} \tag{8}$$

Within this model

$$\Delta N_{max} = N_{max} - N_0 = \frac{I+A}{I-A} \tag{9}$$

$$\mu = -\frac{I+A}{2}, \quad \eta = \frac{I-A}{2} \tag{10}$$

and

$$\omega_{vs} = \frac{(I+A)^2}{4(I-A)} = 2\omega_{gs} \tag{11}$$

The quantity ω_{vs} is the total energy lowering compared with the valence state. Note that $\omega_{vs} = 2\omega_{gs}$, while the energy lowering relative to the ground state is $-\omega_{vs} + I - A/4 = -IA/I - A$. Figure 1 is a sketch of the various quantities.

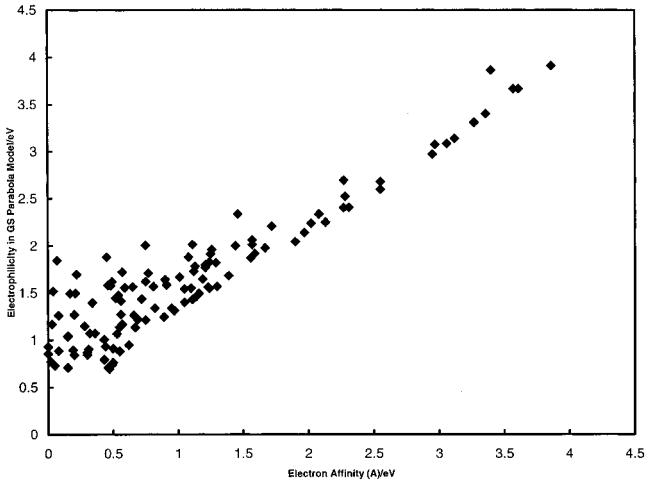

Figure 2. Correlation between electrophilicity index and electron affinity of 54 neutral atoms and 55 simple molecules in the ground-state parabola model.

It is anticipated that ω should be related to EA, because both ω and EA measure the capability of an agent to accept electrons. However, EA reflects the capability of accepting only one electron from the environment, whereas the electrophilicity index ω measures the energy lowering of a ligand due to maximal electron flow between donor and acceptor. The electron flows may be either less or more than one. Meanwhile, in both models, we observe that the electrophilicity index depends not only on EA, but also on IP, and ω differs only by a factor of 2 within the two models, having similar forms within different models. EA and ω are related; yet they are not equal. Figure 2 gives ω_{gs} versus EA for 54 neutral atoms and 55 simple molecules in the ground-state parabola model. Experimental IP and EA values were taken from ref 14. Table 1 gives IP, EA, ω_{gs}, and ΔN_{max} for both the ground-state and valence-state parabola models. One sees that ΔN_{max} from the ground-state model is never larger than one, whereas that of the VS model is always larger than one but smaller than two. In these cases, EA does not correlate well with ω as shown in Figure 2.

In view of the recent interest in stable gaseous dianions,[15,16] one may note that stable dianions are predicted to exist for

$$A \geq {}^3/_5 I \text{ from eq 5} \qquad A \geq {}^1/_3 I \text{ from eq 9} \tag{12}$$

Such extrapolations are dangerous, but in any case we suggest that a dianion is more likely to exist the greater the ratio of A to I.

Many other fits of E versus N data are possible. Of course no generally valid E versus N curve exists—circumstances for an atom or group in a molecule certainly vary from case to case. Possible alternatives to the two parabolic fits studied here include, for example, the exponential model of Parr and Bartolotti,[17] the Padé approximation form of Fuentealba and Parr,[18] and the universal ground-state functional proposed by Perdew, Parr, Levy, and Balduz[19] in the grand canonical

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Table 1. Ionization Potential (IP), Electron Affinity (EA), Maximal Charge Acceptance ΔN_{max}, Electrophilicity Index ω_{gs} in the Ground-State Parabola Model, and Electrophilicity Index ω_{VS} in the Valence-State Parabola Model for Atoms and Molecules (eV)

	IP	EA	ΔN_{max}^{gs}	ΔN_{max}^{vs}	$\omega_{gs} = \omega_{vs}/2$		IP	EA	ΔN_{max}^{gs}	ΔN_{max}^{vs}	$\omega_{gs} = \omega_{vs}/2$
H	13.60	0.75	0.56	1.12	2.01	Bi	7.29	0.95	0.65	1.30	1.34
Li	5.39	0.62	0.63	1.26	0.95	Po	8.42	1.90	0.79	1.58	2.04
B	8.30	0.28	0.54	1.08	1.15	Fr	4.07	0.46	0.63	1.26	0.71
C	11.26	1.26	0.63	1.26	1.96	Br_2	10.52	2.55	0.82	1.64	2.68
N	14.53	0.07	0.50	1.00	1.84	BrO	10.46	2.35	0.79	1.58	2.53
O	13.62	1.46	0.62	1.24	2.34	C_2	11.40	3.27	0.90	1.80	3.31
F	17.42	3.40	0.74	1.48	3.86	CH	10.23	1.24	0.63	1.26	1.83
Na	5.14	0.55	0.62	1.24	0.88	CN	13.60	3.86	0.90	1.80	3.91
Al	5.99	0.44	0.58	1.16	0.93	CS	11.33	0.21	0.52	1.04	1.50
Si	8.15	1.39	0.71	1.42	1.68	Cl_2	11.48	3.27	0.90	1.80	3.31
P	10.49	0.75	0.58	1.16	1.62	ClO	10.95	2.28	0.76	1.52	2.52
S	10.36	2.08	0.75	1.50	2.34	FO	12.78	2.27	0.72	1.44	2.69
Cl	12.97	3.61	0.89	1.78	3.67	I_2	9.31	2.55	0.88	1.76	2.60
K	4.34	0.50	0.63	1.26	0.76	NO	9.26	0.03	0.50	1.00	1.17
Ca	6.11	0.02	0.50	1.00	0.77	NS	8.87	1.19	0.65	1.30	1.65
Sc	6.56	0.19	0.53	1.06	0.89	Na_2	4.89	0.43	0.60	1.20	0.79
Ti	6.83	0.08	0.51	1.02	0.88	PbO	9.08	0.72	0.59	1.18	1.44
V	6.75	0.53	0.59	1.18	1.06	SO	10.29	1.13	0.62	1.24	1.78
Cr	6.77	0.67	0.61	1.22	1.13	O_2	13.62	0.45	0.53	1.06	1.88
Mn	7.43	0.00	0.50	1.00	0.93	P_2	10.53	0.59	0.56	1.12	1.56
Fe	7.90	0.15	0.52	1.04	1.05	S_2	9.36	1.67	0.72	1.44	1.98
Co	7.88	0.66	0.59	1.18	1.26	BO_2	13.50	3.57/4.3	0.86/0.97	1.72/1.93	3.67/4.30
Ni	7.64	1.16	0.68	1.36	1.49	CCl_2	9.27	1.59	0.71	1.42	1.92
Cu	7.73	1.24	0.69	1.38	1.55	CF_2	11.44	0.17	0.52	1.04	1.50
Ga	6.00	0.30	0.55	1.10	0.87	CH_2	10.40	0.65	0.57	1.14	1.57
Ge	7.90	1.23	0.68	1.36	1.56	CHCl	9.84	1.21	0.64	1.28	1.77
As	9.82	0.81	0.59	1.18	1.57	CHF	10.06	0.54	0.56	1.12	1.48
Se	9.75	2.02	0.76	1.52	2.24	C_2H	11.61	2.97	0.84	1.68	3.08
Br	11.81	3.36	0.90	1.80	3.40	COS	11.18	0.46	0.54	1.08	1.58
Rb	4.18	0.49	0.63	1.26	0.74	CS_2	10.07	0.90	0.60	1.20	1.64
Sr	5.69	0.05	0.51	1.02	0.73	HNO	10.10	0.34	0.53	1.06	1.40
Y	6.22	0.31	0.55	1.10	0.90	HO_2	11.35	1.08	0.61	1.22	1.88
Zr	6.63	0.43	0.57	1.14	1.00	SO_2	12.35	1.11	0.60	1.20	2.01
Nb	6.76	0.89	0.65	1.30	1.25	BH_3	12.03	0.04	0.50	1.00	1.52
Mo	7.09	0.75	0.62	1.24	1.21	HNO_3	11.95	0.57	0.55	1.10	1.72
Tc	7.28	0.55	0.58	1.16	1.14	NO_2	9.59	2.27	0.81	1.62	2.40
Ru	7.36	1.05	0.67	1.34	1.40	N_2O	12.89	0.22	0.52	1.04	1.70
Rh	7.46	1.14	0.68	1.36	1.46	SiF_3	9.99	2.95	0.92	1.84	2.97
Pd	8.34	0.56	0.57	1.14	1.27	NH_2	11.14	0.77	0.57	1.14	1.71
Ag	7.58	1.30	0.71	1.42	1.57	CF_3I	10.23	1.57	0.68	1.36	2.01
In	5.79	0.30	0.55	1.10	0.84	CH_3	9.84	0.08	0.51	1.02	1.26
Sn	7.34	1.11	0.68	1.36	1.43	CH_3I	9.54	0.20	0.52	1.04	1.27
Sb	8.61	1.05	0.64	1.28	1.54	CH_3NO_2	11.08	0.48	0.55	1.10	1.58
Te	9.01	1.97	0.78	1.56	2.14	CH_3O	10.72	1.57	0.67	1.34	2.06
I	10.45	3.06	0.91	1.82	3.09	C_2HF	11.26	1.72	0.68	1.36	2.21
Cs	3.89	0.47	0.64	1.28	0.69	C_2H_2	11.40	0.49	0.54	1.08	1.62
Ba	5.21	0.15	0.53	1.06	0.71	C_2H_5N	9.50	0.56	0.56	1.12	1.42
La	5.58	0.50	0.60	1.20	0.91	C_3H_3N	10.91	1.25	0.63	1.26	1.91
Hf	6.83	0.00	0.50	1.00	0.85	$C_4H_2O_3$	10.80	1.44	0.65	1.30	2.00
Ta	7.55	0.32	0.54	1.08	1.07	C_4H_4	9.58	0.91	0.60	1.20	1.59
W	7.86	0.82	0.62	1.24	1.34	C_6F_6	9.89	0.52	0.56	1.12	1.45
Re	7.83	0.15	0.52	1.04	1.04	$C_6H_4ClNO_2$	9.94	1.29	0.65	1.30	1.82
Os	8.44	1.10	0.65	1.30	1.55	$C_6H_4FNO_2$	9.90	1.12	0.63	1.26	1.73
Ir	8.97	1.56	0.71	1.42	1.87	$C_6H_5NO_2$	9.86	1.01	0.61	1.22	1.67
Pt	8.96	2.13	0.81	1.62	2.25	$C_8H_4O_3$	10.10	1.21	0.64	1.28	1.80
Au	9.23	2.31	0.83	1.66	2.41	Azulene	7.38	0.69	0.60	1.20	1.22
Tl	6.11	0.20	0.53	1.06	0.84	Anthracene	7.44	0.57	0.58	1.16	1.17
Pb	7.42	0.36	0.55	1.10	1.07	Perylene	6.96	0.97	0.66	1.32	1.31

ensemble at zero temperature, where fractional occupations are taken into account.

One might imagine taking the total energy gain upon saturation with electrons as the electrophilicity index, but our definition, $^1/_2(\mu^2/\eta)$, has the advantage that it is an expression in terms of the basic quantities governing only small changes away from an initial state, the first-order μ and second-order η. The precise situation in a given case demands its own detailed examination—valence state and its changes, etc.—but the quantity of the first significance in most cases should be the quantity $\mu^2/2\eta$ that we propose be called the electrophilicity index.

In actual chemical systems, many relatively independent atoms or a group of atoms often concertedly interact with a substrate, collectively contributing to the stability of the whole system. Strictly speaking, solvent effects are significant in electrophile/nucleophile interactions.[10] However, in a close encounter between the reacting species in a biological system, water (solvent) molecules have already been pushed out,[20] and hence gas-phase properties, such as ω can determine the reactivity. The circumstances can be dealt with in the present manner.

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