Correlation of Global Electrophilicity with the Activation Energy in Single-Step Concerted Reactions

Priyanka Bagaria and Ram Kinkar Roy*

Department of Chemistry, Birla Institute of Technology and Science (BITS), Pilani-333 031, Rajasthan, India

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The experimental energy of activation (E_a) of the single-step concerted oxidation process of aliphatic primary alcohols by quinolinium bromochromate (QBC) are correlated with the theoretically evaluated global electrophilicity values (w) [as proposed by Parr et al. (*J. Am. Chem. Soc.* **1999**, *121*, 1922)]. Conceptual justification in favor of correlating w of the substrate with E_a involved in a single-step concerted reaction is also discussed. The evaluated w values at HF/cc-pVTZ and MP2/6-31G(d,p) methods are found to be as expected (when we consider structural aspects), although there are some inconsistencies in other methods [e.g., HF/6-31G(d,p), B3LYP/cc-pVTZ, BLYP/dnp, PW91/dnp, PWC/dnp, VWN/dnp]. The reasons for the inconsistencies, even with a superior B3LYP/cc-pVTZ method, are discussed thoroughly. It is observed that the higher the value of w, the more the value of E_a involved in the process of oxidation of primary alcohols by QBC. The present study also reveals that the apparent success of insignificant (i.e., much smaller) local electrophilicity values ($s^+_{O_{OH}}$), evaluated using Hirshfeld population analysis (HPA), in explaining observed trend of experimental E_a values turns out to be ambiguous when more significant (i.e., much larger) local nucleophilicity values ($s^-_{O_{OH}}$) are also compared. This is evident from the corresponding correlation coefficient values.

1. Introduction

Pearson's qualitative "hard and soft acids and bases" concept[1] got its strong foundation when global hardness and global softness were defined analytically by Parr and Pearson.[2] Subsequently, several local reactivity descriptors[3−9] were proposed in last two decades. Together, these are known as "conceptual density functional theory", as the analytical derivation of these reactivity descriptors are based on density functional theory (DFT).[10] A comprehensive overview on the subject is given by Geerlings and co-workers in a recent review.[11]

Maynard et al.,[12] while investigating the reaction of the human immunodeficiency virus type 1 (HIV-1) nucleocapsid protein P7 (NC_p7) with a variety of electrophilic agents, found significant correlation between rates of reaction and the ratio of the square of electronegativity to hardness (i.e., χ^2/η) of the electrophilic species. Parr et al.[13] defined $\chi^2/2\eta$ as "global electrophilicity" of the electrophilic species. Starting from the ground state parabola model of energy vs number of electrons, it was shown that the energy change from maximal flow of electrons between the electrophile and the nucleophile is $-(I + A)^2/8(I - A)$ (i.e., $(-\mu^2/2\eta)$, with $\mu = -(I + A)/2$ and $\eta = I - A$, where I and A are the first vertical ionization potential and the first vertical electron affinity, respectively, of the electrophilic species). Thus, for an electrophile, the higher the value of $\mu^2/2\eta$ the stronger it is. So, while comparing a series of chemical species the order of electrophilicity should follow the order of $\mu^2/2\eta$ values and naturally the order of nucleophilicity should follow the reverse order.

Electrophilicity and nucleophilicity are well-known concepts to organic chemists, which can be used to explain the rapidity or sluggishness of organic reactions (provided steric factors do not play a significant role). But judicious choice of the type of reaction, where these concepts can be applied, is very important. For example, in a multistep process, although the higher electrophilicity of the substrate will favor the first step of the reaction (if the substrate is electron accepting in the reaction), subsequent intermediate steps may be very slow, making the reaction to be sluggish. However, lower electrophilicity of the substrate may not favor the first step of the reaction (for the same type of reaction where the substrate acts as an electron acceptor), so subsequent steps may be faster, making the reaction faster overall. As a whole, we can argue that in multistep reactions electrophilicity of the starting substrate may not provide reliable information on the overall rate of the reaction. But this kind of problem will not arise in the case of single-step concerted reactions, as the stability of the activated complex (which indirectly depends on the electrophilicity of the substrate) affects the rate of product formation (i.e., the rate of the reaction). So, in the case of a single-step concerted reaction comparison of the reaction rate with the electrophilicity of the substrate is less risky. As the rate of the reaction is related to the activation energy (E_a), $\mu^2/2\eta$ values can be correlated with E_a values of such single-step concerted reactions [for details see section 3B(ii)].

In the present study we have chosen nine aliphatic primary alcohols of the general molecular formula RCH_2OH. Experimental activation energies for the oxidation of these alcohols to the corresponding aldehydes by quinolinium bromochromate (QBC) are compared with theoretically evaluated w values. Local electrophilicity or nucleophilicity values of the O_{OH} (O atom of the OH group) of these primary alcohols are also

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* Corresponding author. E-mail: rkroy2@rediffmail.com, rkroy@bits-pilani.ac.in.

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evaluated to demonstrate the superiority of global over local reactivity descriptors in explaining intermolecular reactivity trends.

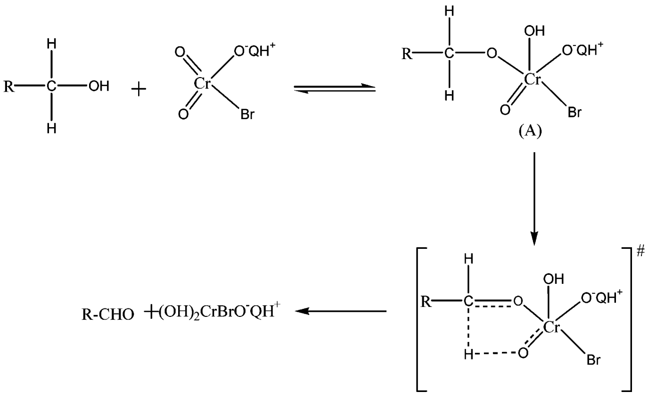
Probable mechanisms of the oxidation of chosen aliphatic primary alcohols by QBC are shown in section 2. The justification of using the global electrophilicity values of the substrates themselves (and not of any intermediates) to be compared with the activation energies (and hence the reaction rates, indirectly) are also discussed. A brief theoretical background of the global electrophilicity (i.e., $w = \mu^2/2\eta$) and local electrophilicity and nucleophilicity (i.e., s_k^+ and s_k^-) descriptors are given in subsections 3A(i) and 3A(ii). The procedure to calculate the activation energy values from experimental rate of reaction is briefly outlined in subsection 3B(ii). Details of adopted computational methods are discussed in section 4. A thorough analysis of global and local descriptor values, as expected from structures of corresponding alcohols, and also their correlation with experimental E_a values are done in different subsections of section 5. Finally, in the concluding section (section 6) we have summarized the whole study.

2. Oxidation of Primary Alcohols by QBC

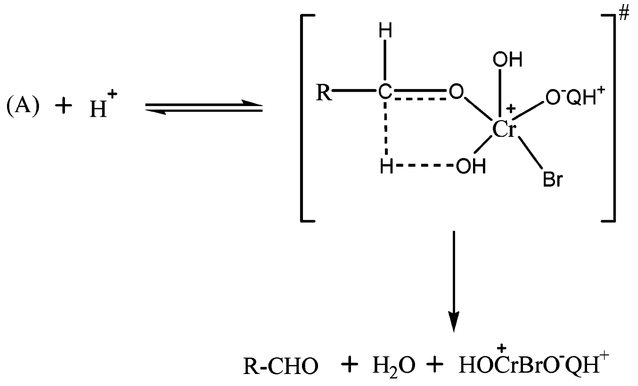
After detailed kinetic analysis, Banerji and co-workers[14−16] proposed two mechanisms for the oxidation of primary aliphatic alcohols by quinolinium bromochromate (QBC) (shown below):

These two mechanisms are

Mechanism I: Acid-Independent Path



Mechanism II: Acid-Dependent Path



Thus, whatever path is followed, the overall mechanism is proposed to involve the formation of a chromate ester in a fast pre-equilibrium step and then a disproportionation of the ester in a subsequent slow step via cyclic concerted symmetrical transition state leading to the product (Mechanism I). Mechanism II explains the observed hydrogen-ion dependence by assuming a rapid reversible protonation of the chromate ester (A), with the protonated ester decomposing at a rate faster than that of (A). So, in either path, the rate depends on the slow step in which the chromate ester (or protonated chromate ester) undergoes a disproportionation reaction leading to the product. As the rate of disproportionation depends on the stability of the activated complex, which indirectly depends on the global electrophilicity of the primary alcohol, w values (of primary alcohols) will have an influence on ΔG (or E_a) of the oxidation reaction [see section 3B(ii)].

3. Theoretical Background

A. Global and Local Reactivity Descriptors. ***(i) Global Electrophilicity.*** Assuming the binding environment of an electrophilic ligand to a protein, a DNA coil or a surface to an idealized zero-temperature free electron sea of zero chemical potential, Parr et al. derived the expression of global electrophilicity (w) indicator to be as[13]

$$w = \frac{\mu^2}{2\eta} \tag{1}$$

Here, w bears the conceptual similarity to power of classical electricity (i.e., power = V^2/R of classical electrophilicity, where V and R represent the potential difference and the resistance, respectively). In eq 1, μ and η are the chemical potential and global chemical hardness defined as

$$\mu = \frac{-(\mathrm{IP} + \mathrm{EA})}{2} \tag{2}$$

$$\eta = (\mathrm{IP} - \mathrm{EA}) \tag{3}$$

where IP and EA are the first vertical ionization potential and first vertical electron affinity, respectively. Earlier efforts to extend the global electrophilicity indices to its local counterpart[17] are credited with limited success [see subsection 3A(iii)]. However, philicity indices are shown to obey the Hammond postulate.[18] Recently, w values could be successfully used to explain the yields of acetalization, thioacetalization, azathioacetalization, and oxathioacetalization products of benzaldehyde and substituted benzaldehydes.[19,20]

(ii) Local Electrophilicity or Nucleophilicity. By local electrophilicity or nucleophilicty we refer to the part of condensed local softness (s_k)[5] [or condensed Fukui function (f_k)[5,6]], which indicates the most preferred site (or an atom in the condensed form) in a molecule to be attacked by an approaching nucleophile (Nu^-) or an electrophile (El^+). Normally, the condensed forms are expressed as

$$s_k^+ = [P_k(N+1) - P_k(N)]S = f_k^+ S \quad \text{for nucleophilic attack} \tag{4}$$

$$s_k^- = [P_k(N) - P_k(N-1)]S = f_k^- S \quad \text{for electrophilic attack} \tag{5}$$

where, $P_k(N+1)$, $P_k(N)$, and $P_k(N-1)$ refer to the electronic population on atom k for $N+1$ (i.e., anionic), N (i.e., neutral), and $N-1$ (i.e., cationic) electron systems, respectively. Here S is known as the global softness and has the relation with global hardness (η) as $S = {}^1/_{2\eta}$.

(iii) Global vs Local Descriptor in Explaining Intermolecular Reactivity Trends. Earlier Roy et al. have shown that (ref 21 and eqs 13−16 of ref 22) for systems having more than one comparatively strong reactive site, the local reactivity descriptor of the strongest site does not always generate a reliable intermolecular reactivity trend. However, for systems having only one distinctly strong reactive site the local reactivity descriptor may generate the global reactivity trend if the system sizes (i.e., number of atoms as well as types of atoms) are comparable.[22] Otherwise, if the number of atoms between two systems varies too much, then for the system having a large size local reactivity values normally decrease (owing to the fact that the Fukui function normalizes to unity), even though the two systems have a comparable band gap. To be more precise, even if two systems have equal global softness values when evaluated using the working equation $S = {}^1/_2\eta = {}^1/_2(\text{LUMO} - \text{HOMO})$, the system in which the number of atoms is more, s_k^α ($\alpha = +, -, 0$) values will, in general, be lower ones (because f_k^α will be summed over to unity).[19]

B. Thermodynamic and Kinetic Aspects of *w*. *(i) Thermodynamic Aspects of w.* The thermodynamic aspect of *w* is established from the fact that it was derived[13] by minimizing the energy change (ΔE) associated with the electron transfer (ΔN) from the free electron sea of zero chemical potential to the electrophile. When $\Delta E/\Delta N = 0$, $\Delta E \approx -\mu^2/2\eta = -w$ (by approximating ΔE, due to the electron transfer ΔN, up to second order). As $\eta > 0$, $\Delta E < 0$; i.e., charge transfer is an energetically favorable process. Thus, given a number of electrophiles to be reacted to a particular nucleophile, that particular reaction will be more favorable, which will lead to more relative stability (with respect to the reactant) of the product. This was the reason why favorable product formation (in terms of percentage of yield) could be explained by comparing the *w* values in our earlier studies.[19,20]

(ii) Kinetic Aspects of w. The expression of *w* can be elaborated in terms of first vertical IP and first vertical EA as follows:[2]

$$w = \frac{\mu^2}{2\eta} = \frac{[-(\text{IP} + \text{EA})/2]^2}{2(\text{IP} - \text{EA})} = \frac{(\text{IP} + \text{EA})^2}{8(\text{IP} - \text{EA})} \qquad (6)$$

We can see from eq 6 that the electrophilicity value depends on the value of EA (also on the value of IP), the higher the EA, the higher the *w* value is. In a chemical reaction (where the substrate acts as an electron acceptor) it is expected that a substrate with a higher EA value will enhance the rate of the reaction more than a substrate with a lower EA provided other factors (i.e., reactant, reaction conditions, etc.) remain same. This establishes the kinetic aspect of global electrophilicity (*w*) values, as defined in eq 1. Because the rate is related to the energy of activation (leading to the activated complex) by the relation, rate $\propto Ae^{-E_a/RT}$, it is also expected that *w* will be correlated with E_a (activation energy) values. Again E_a is related to $\Delta G^{\#}$ (free energy of activation) by the following relation,

$$E_a = \Delta G^{\#} + RT + T\Delta S^{\#} \qquad (7)$$

where $\Delta S^{\#}$ is the entropy of activation. So, $\Delta G^{\#}$ and *w* values can again be correlated. The higher the *w* value of the substrate, the higher should be the $\Delta G^{\#}$ value of the reaction if the substrate has to donate an electron in the reaction involved. If the substrate is an electron acceptor, then the higher *w* value will favor the reaction leading to lower $\Delta G^{\#}$ value.

4. Computational Details

Altogether nine primary alcohols are chosen in the present study, which are oxidized by QBC to the corresponding aldehydes.[16] The rates (or E_a and $\Delta G^{\#}$ values, to say more precisely) are compared with global electrophilicity (*w*) values. The chosen alcohols are of the general form of RCH_2OH, where R stands for H, Me, Et, *n*-Pr, *n*-Bu, *i*-Pr, *t*-Bu, $ClCH_2$, and $MeOCH_2$ groups. Thus, we see that the substituted groups are mainly electron donating (except $ClCH_2$ and $MeOCH_2$) and the variation of the electron donating ability of the substituted groups will have some effect on the *w* values and hence the rates (or E_a and ΔG values). Although $ClCH_2$ is clearly electron withdrawing, the electronic effect of the $MeOCH_2$ group is a little complicated to determine. Normally, the MeO group is electron donating because of the +R effect exerted by the lone pair of electrons on the O atom. But the presence of the intervening CH_2 moiety makes the +R effect ineffective here. Maybe the very weak −I effect will be operative in this system.

Geometries were initially optimized at the semiempirical level using CHEM-3D program system,[23] which were further reoptimized at the HF[24]/6-31G(d,p)[25] level. To enhance the reliability of our comparison, additional calculations are performed by HF/cc-pVTZ,[26] B3LYP[27a−c]/cc-pVTZ, MP2[28]/6-31G(d,p), BLYP[27b,c]/dnp, PW91[29,30]/dnp, PWC[30]/dnp, and VWN[31]/dnp methods. Here "dnp" is a basis set of double-numeric quality (i.e., approximately two atomic orbitals for each one occupied in the free atom) augmented with polarization function. It is approximately of the size as 6-31G(d,p) basis set. To be sure that optimized geometries have reached the global minimum in energy, frequency calculations were performed having no imaginary frequency.

Global electrophilicity values (*w*) are calculated using eqs 1−3 whereas the local electrophilicity and nucleophilicity values ($s^+_{O_{OH}}$ and $s^-_{O_{OH}}$) are calculated using eqs 4 and 5. To mimic the experimental solvent condition (i.e., DMSO), self-consistent reaction field (SCRF)[32] based on polarized continuum model (PCM)[33] is used to calculate the *w* values. Calculations at HF/6-31G(d,p), HF/cc-pVTZ, B3LYP/cc-pVTZ and MP2/6-31G(d,p) levels (called set-I methods) are performed using Gaussian program[34] and take care of the solvent effect. Here $s^+_{O_{OH}}$ and $s^-_{O_{OH}}$ values are calculated using Mulliken population analysis (MPA) based atomic charges. Two different schemes are considered to evaluate atomic charges. One is from charges on the individual atoms, and the second one is from atomic charges where charges on H atoms are summed into heavy atoms, to which H is attached. Those at BLYP/dnp, PW91/dnp, PWC/dnp, and VWN/dnp levels (called set-II methods) are performed using DMOL^3 program package[35] and the solvent effect could not be included. Among the DFT methods available in the DMOL^3 program, PWC and VWN are based on the local density approximation (LDA) approach.[30,31] whereas BLYP and PW91 are based on the generalized gradient approximation (GGA) approach.[27b,c,29,30] In LDA, the exchange correlation energy (E_{XC}) functional can be computed from the value of density (ρ) at some position *r* [i.e., the local value of ρ], and GGA depends not only on the local value of the density but also on the extent to which the density is locally changing, i.e., the gradient of the density. Calculations using the DMOL^3 program can provide both HPA and MPA based local descriptors. Thus, at all the four levels, HPA and MPA based $s^+_{O_{OH}}$ and $s^-_{O_{OH}}$ values are evaluated. MPA based $s^+_{O_{OH}}$ values are found to be negative in all the four methods (this is true for some set-I methods also), the interpretation of which is complicated.[36,37] Correlation coefficient (*r*) values are calculated for E_a vs *w*, E_a vs $s^+_{O_{OH}}$, and E_a vs $s^-_{O_{OH}}$ to explain the correlation of theoretically calculated descriptors and experimental energy of activation (E_a) more clearly.

TABLE 1: Global Electrophilicity (i.e., *w*) Values (in au) Generated from Set-I Methods, Experimental Activation Energies E_a (in kJ mol^{-1}), and Experimental Free Energies of Activation $\Delta G^{\#}$ (in kJ mol^{-1}) of the Chosen Primary Alcohols, RCH_2OH (Altogether 9), in the Present Study (Details in the Text)

alcohol (R)	HF/6-31G(d,p)	HF/cc-pVTZ	B3LYPcc-pVTZ	MP2/6-31G(d,p)	E_a	$\Delta G^{\#}$
H	0.017429	0.028485	0.044471	0.014979	83.677	97.5
Me	0.010244	0.020466	0.034573	0.014491	59.377	88.9
Et	0.009762	0.017810	0.032419	0.014337	56.977	88.8
n-Pr	0.003946	0.017174	0.029495	0.014284	52.177	86.6
i-Pr	0.003886	0.014817	0.032674	0.014276	49.377	85.6
n-Bu	0.003882	0.015840	0.033768	0.014252	51.777	86.4
t-Bu	0.004449	0.014356	0.032686	0.010296	33.677	80.8
CH_2Cl	0.016850	0.030700	0.046305	0.023039	73.077	97.1
CH_2OMe	0.009643	0.025266	0.032145	0.015112	64.877	92.7

TABLE 2: Global Electrophilicity (i.e., *w*) Values (in au) Generated from Set-II Methods, Experimental Activation Energies E_a (in kJ mol^{-1}), and Experimental Free Energies of Activation $\Delta G^{\#}$ (in kJ mol^{-1}) of the Chosen Primary Alcohols, RCH_2OH (Altogether 9), in the Present Study (Details in the Text)

alcohol (R)	BLYP/dnp	PW91/dnp	PWC/dnp	VWN/dnp	E_a	$\Delta G^{\#}$
H	0.015520	0.015994	0.017354	0.017370	83.677	97.5
Me	0.015103	0.015058	0.016385	0.016399	59.377	88.9
Et	0.014967	0.015051	0.016575	0.016586	56.977	88.8
n-Pr	0.014396	0.015037	0.016529	0.016540	52.177	86.6
i-Pr	0.015260	0.015623	0.017634	0.017648	49.377	85.6
n-Bu	0.014925	0.015083	0.016647	0.016656	51.777	86.4
t-Bu	0.015621	0.016214	0.018522	0.016853	33.677	80.8
CH_2Cl	0.022195	0.022725	0.023453	0.023466	73.077	97.1
CH_2OMe	0.011893	0.014369	0.016128	0.016142	64.877	92.7

TABLE 3: Hardness (η) and Chemical Potential (μ) Values of Some of the Chosen Alcohols RCH_2OH at the MP2/6-31G(d,p) Level

alcohol (R)	η	μ
(a) When R Is Either H or Any Alkyl Group		
H	0.373604	−0.105793
Me	0.368759	−0.103380
Et	0.368103	−0.102737
n-Pr	0.367828	−0.102508
i-Pr	0.367897	−0.102490
n-Bu	0.367554	−0.102356
t-Bu	0.395050	−0.090195
(b) When R Is Either H or $ClCH_2$ or $MeOCH_2$)		
H	0.373604	−0.105793
CH_2Cl	0.359253	−0.128662
CH_2OMe	0.363586	−0.104828

The experimental energies of activation (E_a) are evaluated from a plot of log *k* vs 1/*T* in the temperature range of 288−318 K. Here *k*, i.e., the rate values, are taken from the experimental paper of Banerji and co-workers.[16] The free energies of activation ($\Delta G^{\#}$) values are as reported in the experimental paper of Banerji and co-workers[16] and can be obtained by using the equation

$$\Delta G^{\#} = -RT \ln \frac{kh}{TK_B} \qquad (8)$$

where *k*, *h*, and K_B represent the experimental rate of reaction, Planck's constant, and Boltzmann's constant, respectively.

5. Results and Discussion

A. Expected Trends of *w* Values. In Tables 1 and 2, we have reported the values of global electrophilicity (*w*) [evaluated by both sets of methods], activation energy (E_a), and free energy of activation ($\Delta G^{\#}$). It is expected that the electrophilicity values of RCH_2OH should decrease with increasing size and branching of the R group (as long as R is an alkyl group). This is because of the increasing +I effect with increasing length and branching of the R group. We observe the expected decreasing trend of *w* values from set-I methods (Table 1) when *R* changes in the sequence H → Me → Et → *n*-Pr → *n*-Bu (except in B3LYP/cc-pVTZ method). Again, when we consider *n*-Pr, *i*-Pr, *n*-Bu, and *t*-Bu systems, normally *i*-Pr and *t*-Bu are expected to be less electronegative and harder than *n*-Pr and *n*-Bu, respectively (because isopropyl and *tert*-butyl groups, which exert higher +I effects, are directly attached to the central C atom in these two systems). So, *w* values of *i*-Pr and *t*-Bu should be lower than those of *n*-Pr and *n*-Bu because of the relation, $w = \mu^2/2\eta = -\chi^2/2\eta$. Interestingly, the expected trend of *w* values within *n*-Pr, *i*-Pr, *n*-Bu, and *t*-Bu systems is observed in the superior HF/cc-pVTZ and MP2/6-31G(d,p) methods (see Table 3a). The irregular trend of *w* values for these systems generated by a comparatively superior (than HF/cc-pVTZ) DFT method (i.e., B3LYP/cc-pVTZ) is discussed in detail in the third paragraph in this section. Also, the highest *w* value for $ClCH_2$ and comparatively higher *w* value for $MeOCH_2$ (but lower for $ClCH_2$), generated by the superior MP2/6-31G(d,p) method (also by HF/cc-pVTZ) can be rationalized when we consider the relative μ (i.e., $-\chi$) and η values of these systems (see Table 3b).

Comparison of *w* values generated by set-II methods (e.g., BLYP/dnp, PW91/dnp, PWC/dnp, and VWN/dnp, which are as implemented in the DMOL^3 package) shows an unexpected trend for *n*-Pr, *i*-Pr, *n*-Bu, and *t*-Bu systems (see Table 2). Although the trend of *w* values in the series H → Me → Et → *n*-Pr is as expected in BLYP/dnp and PW91/dnp methods, the same is not true for PWC/dnp and VWN/dnp methods. However, highest *w* value for $ClCH_2$ and comparatively higher *w* value for the $MeOCH_2$ system is maintained by these DFT based methods also.

The probable reason for the failure of some of set-II methods, to generate the expected trend of *w* values, can (probably) be attributed to our inability to take care of solvent effects. However, the irregular trend of *w* values for branched chain systems generated by all DFT based methods (B3LYP/cc-pVTZ, BLYP/dnp, PW91/dnp, PWC/dnp, and VWN/dnp) can be explained from very recent studies. Check and Gilbert[38] showed that the B3LYP model consistently underestimates the reaction energy as the number of C−C single bond increases, even when extremely large basis sets are employed. Some recent other papers discussing the pitfalls and limitations of DFT methods are as follows: Woodcock et al.[39] suggested that the incorrect energy difference between allene and propyne, and energies of other cumulenes as well, stemmed from the unexpected behavior of the Becke exchange term. Bachrach and Gilbert,[40] and Houk and co-workers,[41] have reported cyclizations where B3LYP predictions are inconsistent with those of other higher level wave function based methods. Two papers[42,43] showed that B3LYP performs poorly in predicting C−C bond energies for several short-chain hydrocarbons. Redfern et al.[44] and Curtiss et al.[45]-

showed that the errors in B3LYP-predicted enthalpies of formation for chain and branched hydrocarbons rose rapidly and asymptotically with carbon numbers although values are different. Check and Gilbert also showed that B3LYP methods underestimates energies for both slightly and highly methyl-substituted cyclic and acyclic hydrocarbons, which favors the argument that the errors do not arise from structural issues such as steric repulsion or ring strain energy. Rather, it was observed that the error is associated with the B3LYP approach, to its consistent underestimation of C−C bond energy. As the *w* values are evaluated using eqs 1−3, i.e., based on the energy values of neutral, cationic, and anionic systems, we would expect that B3LYP will cause similar inconsistencies in the evaluated *w* values for systems containing a higher number of C−C bonds. Also, Check and Gilbert[38] observed that other DFT methods show such limitation but to lesser extents whereas the MP2 method avoids the problem of underestimation of reaction energies.

B. Comparison of Experimental E_a (or $\Delta G^{\#}$) Values with Global Electrophilicity (*w*). From Table 1 we see that the trends of E_a values are similar to those of $\Delta G^{\#}$. This normally happens when the values of $\Delta S^{\#}$ follow the same trend of $\Delta G^{\#}$ (from eq 7), which is the situation for the chosen systems in the experimentally studied oxidation reaction [i.e., $(\Delta S^{\#}_{A} - \Delta S^{\#}_{B})$ and $(\Delta G^{\#}_{A} - \Delta G^{\#}_{B})$ have the same sign].

In the oxidation reaction, the primary alcohol donates electron (from O_{OH}, i.e., the O atom of the OH group) to QBC (mechanisms I and II). So, as argued in subsection 3B(ii), the higher the *w* value of the primary alcohol, the higher should be the E_a (or $\Delta G^{\#}$**)** value (i.e., the transition state will be relatively more unstable when compared to the reactants). This is what is observed in the series H > Me > Et > *n*-Pr > *n*-Bu [because MP2/6-31G(d,p) is the most reliable method used in the study, major efforts will be centered on the comparison of *w* values generated by this method with experimental E_a (or ΔG) values]. On the basis of the argument given above we should expect that for the $ClCH_2$ system experimental E_a (or $\Delta G^{\#}$) values should be the highest and for $MeOCH_2$ these values should be the second highest. But experimental E_a (or $\Delta G^{\#}$) values of $ClCH_2$ and $MeOCH_2$ systems are lower than those of the H system. This indicates that only the electronic factor (i.e., *w* value of the initial substrate) may not be sufficient to explain the observed trend of E_a (or $\Delta G^{\#}$) values. Another rational factor, which seems to be operative along with the electronic one, is the “release of the steric crowding” in the transition state. Thus, although the *w* values of $ClCH_2$ and $MeOCH_2$ systems demand that E_a (or $\Delta G^{\#}$) values of these two systems should be higher than those of the H system, release of the steric crowding (which will be higher in the former two systems) causes significant stabilization of the transition state, making E_a values lower for $ClCH_2$ and $MeOCH_2$ systems. Release of steric crowding will be higher for $ClCH_2$ and $MeOCH_2$ systems (than H system, for example) because these two groups are bulkier and abstraction of a H atom in the transition state (from the CH_2 moiety of CH_2OH group, see mechanism I and II) will leave more space to accommodate these bulkier groups. When we move in the series H → Me → Et → *n*-Pr → *i*-Pr → *n*-Bu → *t*-Bu, both the electronic and steric factors (in the transition state) operate in conjugation (unlike the just described series H → $ClCH_2$ → $MeOCH_2$, in which case these two factors act in opposition). That may be the reason for similar trends of *w* and E_a values in this alkyl group containing primary alcohol series.

C. Comparison of Experimental E_a (or $\Delta G^{\#}$) Values with Local Electrophilicity and Nucleophilicity ($s^{+}_{O_{OH}}$ and $s^{-}_{O_{OH}}$). Because O_{OH} (the O atom of the OH group) is directly involved in the oxidation of RCH_2OH by QBC, the local electrohilicity value of O_{OH} (i.e., $s^{+}_{O_{OH}}$) should be compared directly with the corresponding E_a (or $\Delta G^{\#}$) value. Similarly, the local nucleophilicty value (i.e., $s^{-}_{O_{OH}}$) should maintain some reverse trend when compared with E_a (or $\Delta G^{\#}$) values [i.e., E_a (or $\Delta G^{\#}$) values should decrease with increasing $s^{-}_{O_{OH}}$ values]. From Table 4 (i.e., the one that reports $s^{+}_{O_{OH}}$ and $s^{-}_{O_{OH}}$ values calculated using set-I methods), it is clear that the trends generated by $s^{+}_{O_{OH}}$ and $s^{-}_{O_{OH}}$ values are not in conformity with those generated by E_a (or $\Delta G^{\#}$) values. Also, the trend generated by $s^{+}_{O_{OH}}$ and $s^{-}_{O_{OH}}$ values calculated by different methods of set-I (i.e., Table 4) vary from one another. Also, the scheme used to evaluate MPA based atomic charges has a noticeable effect on the values and trends of $s^{+}_{O_{OH}}$ and $s^{-}_{O_{OH}}$. For example, when $s^{+}_{O_{OH}}$ and $s^{-}_{O_{OH}}$ are evaluated on the basis of MPA in which the H_{OH} charge (H atom of the OH group) is summed into O_{OH} charge (rows denoted by I and II of Table 4), the highest $s^{+}_{O_{OH}}$ or the lowest $s^{-}_{O_{OH}}$ value should be for the $ClCH_2$ system (because this system is the most electrophilic one due to the presence of the Cl atom). But the highest $s^{+}_{O_{OH}}$ or the lowest $s^{-}_{O_{OH}}$ values vary with levels of calculation, e.g., highest $s^{+}_{O_{OH}}$ for the Me system and lowest $s^{-}_{O_{OH}}$, for the $MeOCH_2$ system at the HF/6-31G(d,p) level, highest $s^{+}_{O_{OH}}$ and lowest $s^{-}_{O_{OH}}$ for the $MeOCH_2$ system at the HF/cc-pVTZ level, and highest $s^{+}_{O_{OH}}$ and lowest $s^{-}_{O_{OH}}$ for CH_2Cl at the B3LYP/cc-pVTZ level (which seems to be acceptable). But at the B3LYP/cc-pVTZ level the difference between $s^{+}_{O_{OH}}$ values of H and $ClCH_2$ systems is noticeable. In the MP2/6-31G(d,p) level, the highest $s^{+}_{O_{OH}}$ is for $MeOCH_2$ and the lowest $s^{-}_{O_{OH}}$ is for the CH_2Cl system. Also, too low $s^{+}_{O_{OH}}$ values for $ClCH_2$ at HF/6-31G(d,p) and MP2/6-31G(d,p) levels are not acceptable at all (although they are much higher at the HF/cc-pVTZ and B3LYP/cc-pVTZ levels as mentioned above). Similarly, $s^{+}_{O_{OH}}$ values of Me and Et systems higher than that for the H system at the HF/6-31G(d,p) level, a high $s^{+}_{O_{OH}}$ value for *t*-Bu at the HF/cc-pVTZ level (higher than those of H, Me, Et, *n*-Pr, *n*-Bu, *i*-Pr systems), a higher $s^{+}_{O_{OH}}$ for *t*-Bu than for *n*-Bu at the HF/6-31G(d,p) level, etc. cannot explain the observed trend of E_a (or $\Delta G^{\#}$) values.

Without going into details of the trend generated by MPA based $s^{+}_{O_{OH}}$ and $s^{-}_{O_{OH}}$ values (where, unlike the previous one, MPA charges on the individual atoms are only considered), our general observation is that $s^{+}_{O_{OH}}$ values are much smaller than those of $s^{-}_{O_{OH}}$ values and sometimes even become negative (rows denoted by III and IV of Table 4). However, this is expected because O_{OH} in primary alcohols acts predominantly as a nucleophilic center (in the present study), making interpretation of negative $s^{+}_{O_{OH}}$ values complicated.

The trends of $s^{+}_{O_{OH}}$ values obtained from set-II calculations (Table 5) and based on HPA are as expected in most cases (apart from some minor exceptions for branched systems and those are also in the third or fourth decimal points) for the series H → Me → Et → *n*-Pr → *i*-Pr → *n*-Bu → *t*-Bu (rows denoted by I in Table 5). However, the trends are not as expected for the series H → $ClCH_2$ → $MeOCH_2$ [see subsection 5(i)]. This is because the $s^{+}_{O_{OH}}$ value for $ClCH_2$ is lower than those of the H system in all the methods, which is unexpected. However, the apparent success of $s^{+}_{O_{OH}}$ in explaining the experimental trend of E_a values (for the long series, i.e., for alkyl substituted primary alcohols) turns out to be ambiguous when we consider the

TABLE 4: MPA Based $s^{+}_{O_{OH}}$ (Rows Denoted by I and III) and $s^{-}_{O_{OH}}$ (Rows Denoted by II and IV) Values (in au), Where for Each System the First Two Rows (I and II) Are Based on the Atomic Charges with Hydrogen Summed into Heavy Atoms to Which It Is Attached and the Last Two Rows (III and IV) Are Based Only on the Atomic Charges, Experimental Activation Energies E_a (in kJ mol^{-1}), and Free Energy of Activation $\Delta G^{\#}$ (in kJ mol^{-1}) of the Chosen Primary Alcohols, RCH_2OH (Altogether 9), in the Present Study (Details in the Text)

alcohol (R)		HF/6-31G(d,p)	HF/cc-pVTZ	B3LYP/cc-pVTZ	MP2/6-31G(d,p)	E_a	$\Delta G^{\#}$
H	I	1.05787	0.08556	0.04214	1.16411	83.677	97.5
	II	0.84171	0.95925	0.67421	1.00398		
	III	−0.22352	0.04061	0.01526	−0.23009		
	IV	0.64792	0.76592	0.50658	0.82252		
Me	I	1.25864	0.02395	0.16847	1.17767	59.377	88.9
	II	1.03359	1.19018	0.84498	1.00915		
	III	−0.25548	0.02632	0.02235	−0.22423		
	IV	0.85015	1.04629	0.70869	0.82260		
Et	I	1.19642	0.03464	0.14401	1.19467	56.977	88.8
	II	0.99941	1.14277	0.81101	1.00767		
	III	−0.24611	0.03853	0.03878	−0.22483		
	IV	0.82237	1.00143	0.67869	0.82329		
n-Pr	I	0.06301	0.00745	0.03096	1.19515	52.177	86.6
	II	0.89100	1.13619	0.74857	1.00760		
	III	0.02837	0.00755	0.01575	−0.22518		
	IV	0.73291	0.99396	0.63056	0.82316		
i-Pr	I	0.06856	0.09172	0.15598	1.19306	49.377	85.6
	II	0.88185	1.07939	0.71746	1.00044		
	III	0.02508	0.00911	0.03717	−0.22778		
	IV	0.72374	0.93805	0.59704	0.81420		
n-Bu	I	0.03546	0.00748	0.01249	1.19585	51.777	86.4
	II	0.88957	1.11118	0.24751	1.00780		
	III	0.02057	0.01557	0.01686	−0.22521		
	IV	0.73172	0.97181	0.17421	0.82364		
t-Bu	I	0.10543	0.62104	0.56885	0.18561	33.677	80.8
	II	0.89048	1.06382	0.66139	0.92867		
	III	0.01173	−0.05116	−0.05716	−0.00750		
	IV	0.72999	0.91924	0.55570	0.75480		
CH_2Cl	I	0.07197	1.62996	1.37504	0.05989	73.077	97.1
	II	0.05831	0.07309	0.14953	0.04142		
	III	0.01986	−0.21176	−0.16459	−0.00147		
	IV	0.03461	0.04937	0.10429	0.01862		
CH_2OMe	I	1.24727	2.11005	0.03746	1.19655	64.877	92.7
	II	0.05814	0.07214	0.72322	0.04762		
	III	−0.26321	−0.23861	0.01281	−0.23134		
	IV	0.03297	0.02867	0.60941	0.02073		

corresponding $s^{-}_{O_{OH}}$ values also. In fact, comparison of $s^{-}_{O_{OH}}$ values with those of E_a (or $\Delta G^{\#}$) for alkyl-substituted primary alcohols will be more justified as O_{OH} acts as a nucleophilic center in the oxidation reaction, which is also evident from much higher $s^{-}_{O_{OH}}$ values when compared to much smaller and so insignificant $s^{+}_{O_{OH}}$ values. The trend of $s^{-}_{O_{OH}}$ values should be H < Me < Et < *n*-Pr < *i*-Pr < *n*-Bu < *t*-Bu. But this is true neither for MPA nor for HPA generated $s^{-}_{O_{OH}}$ values (rows denoted by II and IV, respectively, of Table 5). On the contrary, the trends of $s^{-}_{O_{OH}}$ values are the same as those of $s^{+}_{O_{OH}}$ values [MPA based $s^{+}_{O_{OH}}$ values (rows denoted by III of Table 5) are not considered here, as all the values are negative and so difficult to compare] in all four methods (except some minor variations for branched systems), which is unrealistic and does not have physical interpretation.

The fact that local electrophilicity or nucleophilicity values (in the present case $s^{+}_{O_{OH}}$ or $s^{-}_{O_{OH}}$) cannot explain the observed intermolecular reactivity trend is not new and theoretical justification as well as analytical reasoning is elaborated in section 3A(iii).[19,21,22] Arguments against the use of frontier orbital-based local reactivity descriptors (e.g., local softness, Fukui function, etc.) for comparing intermolecular reactivities originated from the seminal work of Klopmann.[46] Using polyelectronic perturbation theory, Klopmann showed that soft−soft interaction is orbital-controlled, whereas a hard−hard interaction is mainly charge-controlled. As frontier orbital based reactivity descriptors (e.g., local softness, Fukui function) can take care of the reactivities only when the reactants and the substrates are in closer approach (i.e., intramolecular reactivity or site selectivity), these are not suitable for comparing intermolecular reactivities. Charge-controlled local reactivity descriptors (e.g., local hardness) may be more reliable for this purpose because these are effective from long distance.[47,48]

D. Correlation of E_a with w, $s^{+}_{O_{OH}}$, and $s^{-}_{O_{OH}}$ Values. To represent the calculated data in a more obvious and transparent way, regression analysis is done in terms of coefficient of correlation (r). The r values for the correlation of E_a vs w, E_a vs $s^{+}_{O_{OH}}$, and E_a vs $s^{-}_{O_{OH}}$ are shown in Table 6 (based on data of Table 1 and 4, i.e., generated by set-I methods) and Table 7 (based on data of Tables 2 and 5, i.e., generated by set-II methods). In Table 6, the rows represented by I contain the r values when all nine primary alcohols are used as test systems. The rows represented by II are those in which $ClCH_2$ and $MeOCH_2$ are excluded. The reason for evaluating separate r values after excluding $ClCH_2$ and $MeOCH_2$ systems is that for these two systems [in the superior MP2/6-31G(d,p) method] the w value alone cannot explain the trend of experimental E_a. We have to invoke the concept of “release of steric-crowding” in the transition state to explain the observed trend of E_a values (see section 5B for details). However, from second column of Table 6, we could easily see that r values (for E_a vs w) improves (except in HF/6-31G(d,p) method) after excluding $ClCH_2$ and $MeOCH_2$ systems. Also, it is interesting to note that r value in the B3LYP/cc-pVTZ method is higher than that of MP2/6-31G-

TABLE 5: HPA Based $s^{+}_{O_{OH}}$ (Rows Denoted by I) and $s^{-}_{O_{OH}}$ (Rows Denoted by II) Values and MPA Based $s^{+}_{O_{OH}}$ (Rows Denoted by III) and $s^{-}_{O_{OH}}$ (Rows Denoted by IV) Values (in au), Experimental Activation Energies E_a (in kJ mol^{-1}), and Free Energy of Activation $\Delta G^{\#}$ (in kJ mol^{-1}) of the Chosen Primary Alcohols, RCH_2OH (Altogether 9), in the Present Study (Details in the Text)

alcohol (R)		BLYP/dnp	PW91/dnp	PWC/dnp	VWN/dnp	E_a	$\Delta G^{\#}$
H	I	0.1597	0.1634	0.1513	0.1513	83.677	97.5
	II	0.3888	0.3815	0.3624	0.3625		
	III	−0.1206	−0.1301	−0.1353	−0.1353		
	IV	0.4268	0.4216	0.3992	0.3992		
Me	I	0.1365	0.1373	0.1245	0.1245	59.377	88.9
	II	0.3439	0.3128	0.2899	0.2899		
	III	−0.0927	−0.1199	−0.1202	−0.1202		
	IV	0.3848	0.3518	0.3252	0.3252		
Et	I	0.1212	0.1274	0.1148	0.1148	56.977	88.8
	II	0.3038	0.2747	0.2533	0.2533		
	III	−0.0783	−0.1100	−0.1092	−0.1091		
	IV	0.3392	0.3064	0.2813	0.2813		
n-Pr	I	0.1116	0.1176	0.1054	0.1055	52.177	86.6
	II	0.2481	0.2573	0.2386	0.2386		
	III	−0.1019	−0.1044	−0.1036	−0.1036		
	IV	0.2721	0.2844	0.2618	0.2629		
i-Pr	I	0.1101	0.1129	0.1006	0.1007	49.377	85.6
	II	0.2747	0.2672	0.2496	0.2497		
	III	−0.0755	−0.0841	−0.0791	−0.0802		
	IV	0.3084	0.3012	0.2785	0.2785		
n-Bu	I	0.1126	0.1128	0.1009	0.1010	51.777	86.4
	II	0.2526	0.2436	0.2266	0.2266		
	III	−0.0948	−0.1002	−0.1016	−0.1016		
	IV	0.2777	0.2686	0.2495	0.2495		
t-Bu	I	0.0985	0.0995	0.0877	0.0878	33.677	80.8
	II	0.2611	0.2563	0.2449	0.2448		
	III	−0.0577	−0.0625	−0.0547	−0.0547		
	IV	0.2929	0.2895	0.2745	0.2745		
CH_2Cl	I	0.1250	0.1383	0.1337	0.1338	73.077	97.1
	II	0.2576	0.2504	0.2358	0.2358		
	III	−0.0909	−0.0788	−0.0991	−0.0990		
	IV	0.2810	0.2788	0.2600	0.2599		
CH_2OMe	I	0.1031	0.13820	0.1240	0.1240	64.877	92.7
	II	0.2281	0.2113	0.2040	0.2040		
	III	−0.0505	−0.1097	−0.1078	−0.1078		
	IV	0.2570	0.2340	0.2248	0.2248		

TABLE 6: Correlation Coefficient (*r*) Values for E_a vs *w*, E_a vs $s^{-}_{O_{OH}}$, and E_a vs $s^{+}_{O_{OH}}$ Generated from the Set-I Methods[a]

methods		*r* (E_a vs *w*)	*r* (E_a vs $s^{-}_{O_{OH}}$)		*r* (E_a vs $s^{+}_{O_{OH}}$)	
			A[b]	*B*[c]	*A*	*B*
HF/6-31G(d,p)	I	0.890	0.425	0.455	0.464	0.478
	II	0.880	0.089	0.103	0.641	0.660
HF/cc-pVTZ	I	0.904	0.466	0.497	0.256	0.211
	II	0.943	0.421	0.518	0.573	0.824
B3LYP/cc-pVTZ	I	0.755	0.180	0.234	0.114	0.147
	II	0.813	0.124	0.017	0.652	0.548
MP2/6-31G(d,p)	I	0.650	0.383	0.379	0.135	0.194
	II	0.750	0.624	0.659	0.613	0.618

[a] For each method two rows are presented, rows denoted by I contain all the nine primary alcohols and rows represented by II contain seven alcohols, i.e., after excluding CH_2Cl and CH_2OMe (for details see the text). [b] Local softness values are based on atomic charges (MPA) with hydrogens summed into heavy atoms to which it is attached. [c] Local softness values are based only on atomic charges (MPA).

(d,p), in spite of the fact that in the former method the trend of *w* values for *i*-Pr and *t*-Bu systems are not as expectation. Better correlation of *w* values for other systems make the *r* value higher. Correlation coefficient values for E_a vs $s^{+}_{O_{OH}}$ (shown in two subcolumns of the fourth column in Table 6) are too low to have any significance. Although the values improve after excluding $ClCH_2$ and $MeOCH_2$, interpretation becomes ambiguous when we see the corresponding *r* values correlating E_a vs $s^{-}_{O_{OH}}$. Because local nucleophilicity is totally an opposite property to local electrophilicity, *r* values in this case should show negative correlation (i.e., should have values between −1 and 0). However *r* values in this case (shown in two subcolumns of the third column in Table 6) exhibit positive correlation (i.e., *r* values between 0 and 1) and even are found to be comparable to the *r* values of E_a vs $s^{+}_{O_{OH}}$ [particularly in the superior MP2/6-31G(d,p) method, after excluding $ClCH_2$ and $MeOCH_2$]. This shows unreliability of local reactivity values in explaining the intermolecular reactivity trend [also see Table 4 and relevant discussion in section 5C].

The corresponding correlation coefficient values (*r*) obtained from data generated by set-II methods are shown in Table 7. From the second column we can see that *w* correlates very poorly with E_a in all four methods (rows represented by I), and this is true even when $ClCH_2$ and $MeOCH_2$ systems are excluded from the series (rows represented by II). Interestingly, $s^{+}_{O_{OH}}$ values generated by HPA show very good correlation with E_a values (fourth column in Table 7), thus apparently giving an impression that it is a reliable intermolecular reactivity descriptor. However, we have already argued in section 5C, and it is evident from the data of Tables 4 and 5, that O_{OH} acts as a nucleophilic center in the oxidation reaction. Thus, correlation of E_a with larger $s^{-}_{O_{OH}}$ values will be more justified than that with smaller (and so insignificant) $s^{+}_{O_{OH}}$ values. Also, the correlation coefficient (*r*) values for E_a vs $s^{+}_{O_{OH}}$ and E_a vs $s^{-}_{O_{OH}}$ should be of opposite sign. Because E_a should decrease with increasing nucleophilicity of O_{OH}, the *r* value should be negative here. On the other hand because E_a decreases with the decrease

TABLE 7: Correlation Coefficient (*r*) Values for E_a vs *w*, E_a vs $s_{O_{OH}}^{-}$ (Based on HPA), E_a vs $s_{O_{OH}}^{+}$ (Based on HPA), E_a vs $s_{O_{OH}}^{-}$ (Based on MPA), and E_a vs $s_{O_{OH}}^{+}$ (Based on MPA) Generated from the Set-II Methods[a]

			r (HPA)		*r* (MPA)	
methods		*r* (E_a vs *w*)	E_a vs $s_{O_{OH}}^{-}$	E_a vs $s_{O_{OH}}^{+}$	E_a vs $s_{O_{OH}}^{-}$	E_a vs $s_{O_{OH}}^{+}$
BLYP/dnp	I	0.271	0.500	0.790	0.468	0.542
	II	0.062	0.845	0.961	0.816	0.868
PW91/dnp	I	0.336	0.496	0.961	0.467	0.633
	II	0.040	0.879	0.973	0.854	0.906
PWC/dnp	I	0.228	0.513	0.978	0.486	0.825
	II	0.385	0.856	0.974	0.836	0.914
VWN/dnp	I	0.386	0.513	0.978	0.485	0.826
	II	0.222	0.856	0.975	0.837	0.916

[a] For each method two rows are presented, rows denoted by I contain all the nine primary alcohols and rows represented by II contain seven alcohols, i.e., after excluding CH_2Cl and CH_2OMe (for details see the text).

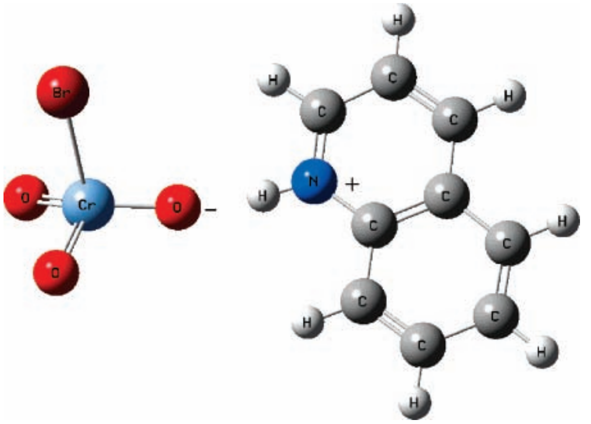


Figure 1. Structure of quinolinium bromochromate [$CrO_2BrO^-C_9H_7NH^+$].

of electrophilicity of O_{OH} (i.e., $s_{O_{OH}}^{+}$), the *r* value should be positive here. But from the third and fourth column of Table 7 (i.e., from HPA-based $s_{O_{OH}}^{+}$ and $s_{O_{OH}}^{-}$ values) we can see that the *r* values for both types of correlation are positive, the physical interpretation of which is that the reactivity increases (i.e., E_a decreases) when both electrophilicity and nucleophilicity of O_{OH} increases. This is ambigious and cannot be accepted from our conventional knowledge of physical chemistry. The fifth and sixth columns of Table 7 present the correlation coefficient for linear regression of E_a vs $s_{O_{OH}}^{-}$ and E_a vs $s_{O_{OH}}^{+}$ evaluated by MPA based charges. Here also we can find that the *r* value increases a lot when $ClCH_2$ and $MeOCH_2$ are excluded from the series. However, *r* values for E_a vs $s_{O_{OH}}^{+}$ (MPA based) do not provide much information because the $s_{O_{OH}}^{+}$ values are so small that they turn out to be negative in all cases and difficult to interpret. Anyway, here also a positive *r* value for E_a vs $s_{O_{OH}}^{-}$ (fifth column of Table 7) is unphysical and cannot be accepted.

6. Conclusion

The kinetic aspect of global electrophilicity descriptor (*w*) is emphasized in the present study. It is argued that the overall rate (and so E_a or $\Delta G^{\#}$) cannot be correlated to the *w* value of the substrate for all types of reactions. Only for single-step reactions (i.e., the concerted ones) is it safe to correlate the *w* value with the reaction rate or E_a (or $\Delta G^{\#}$). For multistep reactions the overall rate depends mainly on the rate-determining step in which the substrate (*w* values for which is being considered) may not be directly involved. Rather, a different activated complex may be involved in that rate-determining step. So, for comparison of intermolecular reactivity even within a homologous series, depending upon the variation of substituted groups, first step may be faster for a particular system although the overall rate may be slower. It should be mentioned in this context that Campodonico et al.[49] also found some linear relationship between the global electrophilicity index (*w*) and experimental rate coefficients for the aminolysis of thiocarbonates and dithiocarbonates. The mechanism of that reaction also clearly shows that the substrate is directly involved in the rate-determining step.

Our argument is justified when we observe a reasonable correlation [supported by corresponding correlation coefficients (*r*)] between experimental values of oxidation [by quinolinium bromochromate (QBC)] rates (or E_a and $\Delta G^{\#}$ values, to say more precisely) of nine primary alcohols to the theoretically generated *w* values at different ab initio wave function based methods. Although the trend of global electrophilicity values (*w*) generated by the superior MP2/6-31G(d,p) method is the best (i.e., as expected from chemical structure) among those generated by all other methods, the corresponding correlation of E_a vs *w* is comparatively poorer. This is because global electrophilicity (*w*) is solely an electronic property of the substrates involved (i.e., of the primary alcohols) but experimental E_a values depend not only on the electron donating power of the primary alcohols (i.e., on *w*) but also on “the release of the steric-crowding” in the transition state. For the series H → Me → Et → *n*-Pr → *i*-Pr → *n*-Bu → *t*-Bu these two factors act in conjugation and we could see the same trend of *w* and E_a values. For the series H → $ClCH_2$ → $MeOCH_2$ these two factors act in opposition, which might be the reason for irregular trends of *w* and E_a values. A convincing proof in favor of the above conjecture would have been to calculate the numerical value of “release of the steric crowding” in the transition state, which requires some kind of transition state optimization. Although there are some routine prescriptions of transition state optimization in the commercial packages (e.g., the Gaussian used in this study), the system used in the present study is complicated. The oxidizing agent quinolinium bromochromate (QBC) exists as a salt, i.e., $CrO_2BrO^-C_9H_7NH^+$ [Figure 1]. Here, the protonated N atom in the quinolinium moiety is already tetravalent and, because a quinquevalent N atom does not exist, the modeling of the geometry for this system in different steps of transition state calculation (i.e., as reactant, as activated complex and as product) is really an arduous task (as there is no covalent bonding between CrO_2BrO^- and $C_9H_7NH^+$ moieties) and no known prescription is available to the authors. Any kind of approximation in the geometry may cause a major change in the E_a values and the trend may be altered.

The local electrophilicity values ($s_{O_{OH}}^{+}$) of O_{OH} (i.e., O atom of the OH group in primary alcohols), generated by wave function based methods and using MPA, show very poor correlation with experimental E_a values. Although MPA based $s^{+}_{\mathrm{O_{OH}}}$ values generated by HF/cc-pVTZ show better correlation (Table 6, sixth column, row-II) and HPA based $s^{+}_{\mathrm{O_{OH}}}$ values obtained from different DFT methods (Table 7) show high positive correlation with experimental E_a values, these $s^{+}_{\mathrm{O_{OH}}}$ values are not recommended to be used as a reliable descriptor of the intermolecular reactivity sequence. The first reason in favor of the above claim is that in the oxidation reaction (mechanisms I and II) the $\mathrm{O_{OH}}$ acts as an electron donor and so local nucleophilicity of $\mathrm{O_{OH}}$ (i.e., $s^{-}_{\mathrm{O_{OH}}}$) would be a better descriptor of reactivity than local electrophilicity ($s^{+}_{\mathrm{O_{OH}}}$). This is also evident from values of $s^{+}_{\mathrm{O_{OH}}}$ (rows denoted by III in Table 4 and by rows I and III in Table 5) much smaller than those of $s^{-}_{\mathrm{O_{OH}}}$. Second, $s^{-}_{\mathrm{O_{OH}}}$ should have a negative correlation with E_a values, because activation energy should decrease with increasing $s^{-}_{\mathrm{O_{OH}}}$ values of $\mathrm{O_{OH}}$. But both $s^{+}_{\mathrm{O_{OH}}}$ and $s^{-}_{\mathrm{O_{OH}}}$ values show a positive correlation with experimental E_a values, which does not have any physical interpretation. Actually, failure of local softness based reactivity descriptors in explaining intermolecular reactivity trends is well-known and the reasons are also thoroughly discussed in the literature.[7a,21,22,47,50]

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References and Notes

(1) Pearson, R. G. *J. Am. Chem. Soc.* **1963**, *83*, 3533.

(2) Parr, R. G.; Pearson, R. G. *J. Am. Chem. Soc.* **1983**, *105*, 7512.

(3) Ghosh, S. K.; Berkowitz, M. *J. Chem. Phys*. **1985**, *83*, 2976.

(4) Yang, W.; Parr, R. G. *Proc. Natl. Acad. Sci. U.S.A.* **1985**, *82*, 6723.

(5) Parr, R. G.; Yang, W. *J. Am. Chem. Soc*. **1984**, *106*, 4049.

(6) Yang, W.; Mortier, W. J. *J. Am. Chem. Soc*. **1986**, *108*, 5708.

(7) (a) Roy, R. K.; Krishnamurti, S.; Geerlings, P.; Pal, S. *J. Phys. Chem. A* **1998**, *102*, 3746. (b) Roy, R. K.; De Proft, F.; Geerlings, P. *J. Phys. Chem. A* **1998**, *102*, 7035.

(8) Krishnamurty, S.; Pal, S. *J. Phys. Chem. A* **2000**, *104*, 7639.

(9) (a) Pal, S.; Chandrakumar, K. R. S. *J. Am. Chem. Soc*. **2000**, *122*, 4145. (b) Chandrakumar, K. R. S.; Pal, S. *J. Phys. Chem. A* **2002**, *106*, 5737. (c) Tanwar, A.; Bagchi, B.; Pal, S. *J. Chem. Phys.* **2006**, *125*, 214304. (d) De Luca, G.; Sicilia, E.; Russo, N.; Mineva, T. *J. Am. Chem. Soc.* **2002**, *124*, 1494. (e) Mineva, T.; Sicilia, E.; Russo, N. *J. Am. Chem. Soc.* **1998**, *120*, 9053. (f) Mineva, T.; Parvanov, V.; Petrov, I.; Neshev, N.; Russo, N. *J. Phys. Chem. A* **2001**, *105*, 1959.

(10) (a) Hohenberg, P.; Kohn, W. *Phys. Rev. B* **1964**, *136*, 864. (b) Kohn, W.; Sham, L. *J. Phys. Rev. A* **1965**, *140*, 1133.

(11) Geerlings, P.; De Proft, F.; Langenaeker, W. *Chem. Rev*. **2003**, *103*, 1793.

(12) Maynard, A. T.; Huang, M.; Rice, W. G.; Covel, D. G. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 11578.

(13) Parr, R. G.; Von Szentpály, L.; Liu, S. *J. Am. Chem. Soc*. **1999**, *121*, 1922.

(14) Choudhary, K.; Sharma, P. K.; Banerji, K. K. *Int. J. Chem. Kinet.* **1999**, *31*, 469.

(15) Banerji, K. K. *J. Chem. Soc., Perkin Trans.* **1988**, *2*, 547.

(16) Saraswat, S.; Sharma, V.; Banerji, K. K. *Proc. Indian Acad. Sci.* **2003**, *115*, 75.

(17) Chattaraj, P. K.; Maiti, B.; Sarkar, U. *J. Phys. Chem. A* **2003**, *107*, 4973.

(18) Chattaraj, P. K.; Roy, D. R. *J. Phys. Chem. A* **2006**, *110*, 11401.

(19) Roy, R. K.; Usha, V.; Patel, B. K.; Hirao, K. *J. Comp. Chem*. **2006**, *27*, 773.

(20) Roy, R. K.; Bagaria, P.; Naik, S.; Kavala, V.; Patel, B. K. *J. Phys. Chem. A* **2006**, *110*, 2181.

(21) Roy, R. K. *J Phys. Chem. A* **2004**, *108*, 4934.

(22) Roy, R. K.; Usha, V.; Paulovic, J.; Hirao, K *J. Phys. Chem. A* **2005**, *109*, 4601.

(23) **1986−1999** Cambridge Soft Corporation.

(24) Roothan, C. C. J. *Rev. Mod. Phys*. **1951**, *23*, 69.

(25) (a) Gordon, M. S. *Chem. Phys. Lett*. **1980**, *76*, 163. (b) Hariharan, P. C.; Pople, J. A. *Theo. Chim. Acta*. **1973**, *28*, 213. (c) Peterson, G. A.; Al-Laham, M. A. *J. Chem. Phys*. **1991**, *94*, 6081. (d) Peterson, G. A.; Bennett, A.; Tensfeldt, T. G.; Al-Laham, M. A.; Shirley, W. A.; Mantzaris, J. *J. Chem. Phys*. **1988**, *89*, 2193.

(26) Kendall, R. A.; Dunning, T. H.; Harrison, R. J. *J. Chem. Phys*. **1992**, *96*, 6796.

(27) (a) Becke, A. D. *J. Chem. Phys*. **1993**, *98*, 5648. (b) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098. (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(28) Møller, C.; Plesset, M. S. *Phys. Rev*. **1934**, *46*, 618.

(29) Perdew, J. P.; Chevary, J. A.; Vosko, S. H.; Jackson, K. A.; Pederson, M. R.; Singh, D. J.; Fiolhais, C. *Phys. Rev. B* **1992**, *46*, 6671.

(30) Perdew, J. P.; Wang, Y. *Phys. Rev. B* **1992**, *45*, 13244.

(31) Vosko, S. J.; Wilk, L.; Nusair, M. *Can. J. Phys*. **1980**, *58*, 1200.

(32) (a) Miertus, S.; Scrocco, E.; Tomasi, J. *Chem. Phys*. **1981**, *55*, 117. (b) Tapia, O. J. *Math. Chem*. **1992**, *10*, 139. (c) Tomasi, J.; Persico, M. *Chem. Rev*. **1994**, *94*, 2027. (c) Simkin, B.Y.; Sheikhet, I. *Quantum Chemical and Statistical Theory of Solutions-A Computational Approach*; Ellis Horwood: London 1995.

(33) (a) Miertus, S.; Tomasi, J.; *Chem. Phys*. **1982**, *65*, 239. (b) Cances, M. T.; Mennunci, V.; Tomasi, J. *J. Chem. Phys.* **1997**, *107*, 3032. (c) Cossi, M.; Barone, V.; Cammi, R.; Tomasi, J. *Chem. Phys. Lett*. **1996**, *255*, 327. (d) Barone, V.; Cossi, M.; Tomasi, J. *J. Comp. Chem*. **1998**, *19*, 404.

(34) Frisch, M. J.; Trucks, G. W.; Schlegel Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochtersk, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen,W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.9; Gaussian, Inc.: Pittsburgh, PA, 1998.

(35) DMOL3, Version 970818, Accelrys, San Diego, CA.

(36) (a) Roy, R. K.; Pal, S.; Hirao, K. *J. Chem. Phys*. **1999**, *110*, 8236. (b) Roy, R. K.; Hirao, K.; Pal, S. *J. Chem. Phys. A* **2000**, *113*, 1372. (c) Roy, R. K.; Krishnamurty, K.; Hirao, K.; Pal, S. *J. Chem. Phys. A* **2001**, *115*, 2901.

(37) (a) Ayers, P. W.; Morrison, R. C.; Roy, R. K. *J. Chem. Phys.* **2002**, *116*, 8731. (b) Bultnick, P.; Carbo-Dorca, R.; Langenaeker, W. *J. Chem. Phys.* **2003**, *118*, 4349. (c) Ayers, P. W. *Phys. Chem. Chem. Phys.* **2006**, *29*, 3387.

(38) Check, C. E., Gilbert, T. M. *J. Org. Chem.* **2005**, *70*, 9828.

(39) Woodcock, H. L.; Schaefer, H. F., III; Schreiner, P. R. *J. Phys. Chem. A* **2002**, *106*, 11923.

(40) Bachrach, S. M.; Gilbert, J. C. *J. Org. Chem*. **2004**, *69*, 6357.

(41) Leach, A. G.; Goldstein, E.; Houk, K. N. *J. Am. Chem. Soc*. **2003**, *125*, 8330.

(42) Feng, T.; Liu, L.; Wang, J. T.; Huang, H.; Guo, Q. X. *J. Chem. Inf. Comput. Sci*. **2003**, *43*, 2005.

(43) Yao, X. Q.; Hou, X. J.; Jiao, H.; Xiang, H. W.; Li, Y. W. *J. Phys. Chem. A* **2003**, *107*, 9991.

(44) Redfern, P. C.; Zapol, P.; Curtiss, L. A.; Raghavachari, K. *J. Phys. Chem. A* **2000**, *104*, 5850.

(45) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Pople, J. A. *J. Chem. Phys*. **2000**, *112*, 7374.

(46) Klopman, G. *J. Am. Chem. Soc.* **1964**, *86*, 1463. Klopman, G. *J. Am. Chem. Soc.* **1968**, *90*, 223.

(47) Langenaeker, W.; De Proft, F.; Geerlings, P *J. Phys. Chem*. **1995**, *99*, 6424.

(48) Saha, S.; Roy, R. K. *J. Phys. Chem. B* **2007**, *111*, 9664.

(49) Campodónico, P. R.; Fuentealba, P.; Castro, E. A.; Santos, J. G.; Contreras, R. *J. Org. Chem.* **2005**, *70*, 1754.

(50) Roy, R. K.; Tajima, N.; Hirao, K. *J. Phys. Chem. A* **2001**, *105*, 2117.