Nucleophilic Substitution Reaction of Alkyl Halides: A Case Study on Density Functional Theory (DFT) Based Local Reactivity Descriptors

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Received: July 18, 2002; In Final Form: October 9, 2002

Density functional theory (DFT) based local reactivity descriptors, e.g., condensed Fukui function (FF) indices (or condensed local softness) have been tested on the nucleophilic substitution reaction of alkyl halides. As the carbon atom of the C−X (X = Cl, Br, and I) bond (hereafter denoted as C_{C-X}) is the center for nucleophilic substitution, it should emerge as the most preferable site for an attack by a nucleophile (hereafter denoted as Nu^-). It was found out when local reactivity descriptors are evaluated from the atomic charges derived from Mulliken population analysis (MPA), the C_{C-X} did not emerge out to be the strongest electrophilic center in majority of cases. However, when these local reactivity descriptors were evaluated by a newly proposed way in which the Mulliken charges on the H-atoms are summed up to those of the heavy atoms to which they are bonded, the results improved significantly. When the reactivity descriptors are evaluated employing the later method and at elongated C−X distances (thus mimicking the situation of the nucleophilic substitution of alkyl halides, in which case the C−X bond is gradually broken), the results show significant improvement. In addition, the present study demonstrates that as the C−X bonds are elongated the global softness values of the systems increase in nearly all cases, thus confirming the validity of maximum hardness principle (PMH).

1. Introduction

In the last 2 decades, several global and local reactivity descriptors based on density functional theory (DFT) (ref 1) have been proposed. The global reactivity descriptors, e.g., the global hardness η and the global softness S (ref 2a) have been useful tools to extend our understanding of the most stable state of chemical species,[2b−d] the correlation of hardness (or softness) with other chemical parameters,[2e] and also the profile of a reaction path.[2f] The local reactivity descriptors allowed us to explain the intra- and intermolecular reactivities. Reactivity descriptors, e.g., the hardness and softness kernels,[3a,b] the local hardness,[3a,4] the local softness,[4] and Fukui functions (FF) (ref 5), have become popular in understanding the details of different classes of chemical reactions. Theoretical studies of nucleophilic reactions become complicated when molecular electrostatic potential (MESP) (ref 6) is used as the reactivity descriptors (because the potential always shows the maximum over a nuclei and thus masking the real active site), although some alternative methods have been suggested to avoid it.[7] But studies have shown that no such problem appears when local softness or FFs are used as the local reactivity descriptors.

Recently Parr et al.[8] have proposed a new global electrophilicity index of any chemical species, which is the square of its electronegativity divided by its chemical hardness. A successful application of this newly defined global reactivity index was made by Domingo et al.,[9] who could characterize quantitatively the global electrophilicity power of common diene/dienophile pairs used in Diels−Alder reactions. In a separate interesting study,[10] the same group has extended the concept of global electrophilicity index to define local electrophilicity index and successfully explained the regioselectivity in Diels−Alder reactions.

The nucleophilic substitution reactions (both bimolecular, i.e., S_N2 and unimolecular, i.e., S_N1) at the C_{C-X} of alkyl halides are among the most intensely studied of all chemical reactions and nowadays a textbook subject.[11] These two types of reactions are schematically represented in Figure 1. For S_N1 or S_N2, whatever way the substitution reaction proceeds, the most preferable center for nucleophilic attack should be C_{C-X}. The present study concerns only on this particular aspect, in which it has been investigated whether the condensed FF indices or local softness values of the atomic centers in the alkyl halides can really predict the C_{C-X} to be the strongest electrophilic center to initiate a nucleophilic attack on it.

In addition, it has been investigated whether the PMH[2b,c] holds true when the C−X bond is elongated (to mimic the progress of the substitution reaction).

The article is organized as follows: In section 2, the theoretical backgrounds of the local reactivity descriptors have been discussed briefly. A very simple and novel way of evaluating these reactivity descriptors is proposed with its physical justification. The methodology adopted in the present study and the computational techniques have been elaborated in section 3. Section 4 contains the discussion on the results obtained in the study. Finally in the summary (section 5) the final outcome of the study is summarized and the areas in which improvements are sought for is discussed in brief.

2. Theoretical Background

A. Local Reactivity Descriptors Based on Softness and Fukui Function Indices. The local softness parameter $s(\bar{r})$ is increasingly used in recent days as a local reactivity descriptor and is defined analytically as follows:[4]

$$s(\bar{r}) = \left(\frac{\partial \rho(\bar{r})}{\partial \mu}\right)_{\upsilon(\bar{r})} \tag{1}$$

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10.1021/jp021664t CCC: $25.00

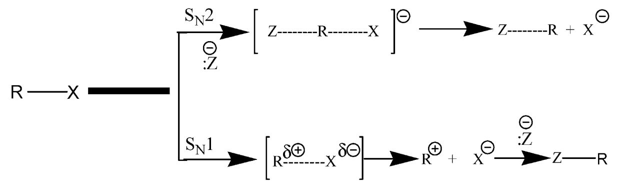


Figure 1. A Scheme of S$_N$1 and S$_N$2 reactions of alkyl halides. Here, Z$^{(-)}$ is the attacking nucleophile Nu$^-$.

where $\rho(\bar{r})$ is the electron density at the site $\bar{r}$, μ is known as the "chemical potential", which is identified as negative of the electronegativity χ[12a]as defined by Iczkowski and Margrave,[12b] and $v(\bar{r})$ is the external potential (i.e., the potential due to the positions of the nuclei plus applied external field, if any) at position $\bar{r}$.

Thus the local softness is such a reactivity parameter, which describes the response of any particular site of a chemical species (in terms of change in electron density ρ) when there is any global change in its chemical potential value. The parameter $s(\bar{r})$ obeys the condition

$$\int s(\bar{r})\, \mathrm{d}\bar{r} = S \tag{2}$$

where S is known as the global softness S of chemical species, which is inversely related to the global hardness η and is defined as follows:[2a]

$$S = \frac{1}{2\eta} = \left(\frac{\partial N}{\partial \mu}\right)_{v(\bar{r})} \tag{3}$$

It turns out that the global hardness is defined as[2a]

$$\eta = \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right)_{v(\bar{r})} = \frac{1}{2}\left(\frac{\partial \mu}{\partial N}\right)_{v(\bar{r})} \tag{4}$$

where E is the total energy, N is the number of electrons of the chemical species.

The operational definitions of η and S are obtained by the finite difference approximation to eq 4 as[2a]

$$\eta = \frac{\mathrm{IP} - \mathrm{EA}}{2} \tag{5}$$

$$S = \frac{1}{\mathrm{IP} - \mathrm{EA}} \tag{6}$$

where IP and EA are the first vertical ionization potential and electron affinity, respectively, of the chemical species.

Rewriting eq 1 and then combining with eq 3 one may write

$$s(\bar{r}) = \left(\frac{\partial \rho(\bar{r})}{\partial N}\right)_{v(\bar{r})}\left(\frac{\partial N}{\partial \mu}\right)_{v(\bar{r})} = f(\bar{r})S = \left(\frac{\partial \mu}{\partial v(\bar{r})}\right)_N S \tag{7}$$

where $f(\bar{r})$ is the Fukui Function indices and was introduced by Parr and Yang.[5] As $s(\bar{r})$ is obtained by simply multiplying $f(\bar{r})$ with the global softness S, the information they hold is same, i.e., sensitivity of the chemical potential of the system to the local external perturbation.[13] However, $s(\bar{r})$ contains some additional information about the global molecular softness.

In general, at some integral value of N_0, the derivative $\partial\rho/\partial N$ may produce three values, i.e., one value from the right, one from the left and an average, three such indices can be obtained as

$$f^+(\bar{r}) = \left(\frac{\partial \rho(\bar{r})}{\partial N}\right)_v^+$$

(derivative as ΔN increases from $N_0 \rightarrow N_0 + \delta$) (8a)

$$f^-(\bar{r}) = \left(\frac{\partial \rho(\bar{r})}{\partial N}\right)_v^-$$

(derivative as ΔN increases from $N_0 - \delta \rightarrow N_0$) (8b)

$$f^0(\bar{r}) = \frac{1}{2}[f^+(\bar{r}) + f^-(\bar{r})]$$

(mean of left and right derivatives) (8c)

When compared with the frontier-electron theory of reactivity as proposed by Fukui and collaborators,[14] we write that[13]

$$f^+(\bar{r}) \approx \rho_{\mathrm{LUMO}}(\bar{r})$$

measures reactivity toward a nucleophilic reagent (9a)

$$f^-(\bar{r}) \approx \rho_{\mathrm{HOMO}}(\bar{r})$$

measures reactivity toward an electrophilic reagent (9b)

$$f^0(\bar{r}) \approx \frac{1}{2}[\rho_{\mathrm{HOMO}}(\bar{r}) + \rho_{\mathrm{LUMO}}(\bar{r})]$$

measures reactivity toward an innocuous (radical) reagent (9c)

here, according to the convention, HOMO represents the "highest occupied molecular orbital" and LUMO the "lowest unoccupied molecular orbital" in the chemical species in question.

Yang and Mortier[15] have proposed approximate atomic $f(\bar{r})$ indices by applying the finite difference approximation to the condensed electronic population on any atom. Thus we have three operational forms of approximate atomic $f(\bar{r})$ indices (from eqs 8a, 8b, and 8c) which, when multiplied by S, provide three different types of local softness for any particular atom k. These can be written as

$$s_k^+ = [\rho_k(N_0 + 1) - \rho_k(N_0)]S$$

(suited for studies of nucleophilic attack) (10a)

$$s_k^- = [\rho_k(N_0) - \rho_k(N_0 - 1)]S$$

(suited for studies of electrophilic attack) (10b)

$$s_k^0 = \frac{1}{2}[\rho_k(N_0 + 1) - \rho_k(N_0 - 1)]S$$

(suited for studies of radical attack) (10c)

where $\rho_k(N_0)$, $\rho_k(N_0 - 1)$, and $\rho_k(N_0 + 1)$ represents the electronic population on atom k for the N_0, $N_0 - 1$, and $N_0 + 1$ electronic systems, respectively.

B. "Relative Electrophilicity" and "Relative Nucleophilicity". Although eqs 10a, 10b, and 10c are found to be very useful in generating the experimentally observed intramolecular reactivity trends in previously studied cases,[16,17] a few deviations have been reported by Roy et al.[18] Based on the condensed FF (local softness) indices, Roy et al. introduced two different local reactivity descriptors, "relative electrophilicity" (s_k^+/s_k^-) and "relative nucleophilicity" (s_k^-/s_k^+) of any particular atom k, to locate the preferable site for nucleophilic and electrophilic attack on it, respectively. The advantage of this new proposition consists of the fact that the individual values of s_k^+ and s_k^- are strongly influenced by the basis set or correlation effects. But the ratio of s_k^+ and s_k^-, involving two differences of electron densities (see eqs 10a and 10b) of the system differing by one in their number of electrons, at constant nuclear framework, is expected to be less sensitive to the basis set and correlation effects.[18] These two newly proposed reactivity descriptors are shown to generate improved intramolecular reactivity trends than those obtained from condensed FF indices.[18,19] The general scheme to employ these two newly proposed local reactivity descriptors for predicting the preferable reactive site is as follows: (i) Choose only the sites (i.e., atoms) having comparable and higher s_k^+ and s_k^- values. (ii) Compare s_k^+/s_k^- and s_k^-/s_k^+ values of these sites only. (iii) If for any site $s_k^+/s_k^- > s_k^-/s_k^+$, then it is the preferred electrophilic and vice versa.

Very recently Roy et al.[20,21] has shown that "relative electrophilicity" (s_k^+/s_k^-) and "relative nucleophilicity" (s_k^-/s_k^+), when evaluated through Hirshfeld's population analysis (HPA) (ref 22) technique, produces the more reliable local reactivity trends than when the same reactivity descriptors are evaluated through MPA[23] technique. Also HPA generates nonnegative condensed FF indices, which is physically more realistic than the negative condensed FF indices generated by MPA and other charge partitioning techniques in some cases. Subsequently, there are several analytical and numerical studies regarding the superiority of HPA over others as a charge partitioning schemes because HPA retains more information of atoms in molecules.[24]

However, the present study demonstrates that even using MPA we can get a reliable local reactivity trends. The technique employed in the present work is as follows.

C. Evaluation of s_k^+ and s_k^- from MPA Based Atomic Charges with Hydrogens Summed on the Heavy Atoms to Which They are Bonded. Normally, while evaluating condensed local softness or condensed FF values, the charge (or condensed electronic population) on individual atoms are considered (the relation between charge on any atom k, i.e., q_k and electronic population on it, i.e., ρ_k is $\rho_k = Z_k - q_k$, where Z_k is the atomic number). When this technique is used along with Mulliken based charge (or population) we encountered a poor local reactivity trend. However, it may be more logical to add the charges on the H-atoms to that of the heavy atoms to which they are bonded. An example may be suitable to make this point clear. While calculating the s_k^+ value of the C-atom in CH_3X (i.e., alkyl halides) it may be more appropriate to add the Mulliken charges of the H-atoms to that of the C-atom. The reason is that the halogen atom (i.e., X) draws the bonding electron density toward itself (i.e., exerts −I effect). As a result positive charge is developed on the C-atom. The electronegativity of the neutral (sp^3 hybridized) carbon atom is higher than that of the hydrogen atom. The development of the partial positive charge will further enhance its electron withdrawing power from the bonded H-atoms toward itself. So the ideal situation would be to evaluate the partial contribution of the attached H-atoms in the process of partial neutralization of the positive charge of the carbon atom: but it is a very complicated procedure as it varies from system to system. Although little bit crude, a good approximation would be to add the charges on the H-atoms to that of the carbon atom to which they are bonded. So, basically we are considering the charge of the $-(CH_3)$ fragment instead of just the charge on the carbon atom itself while evaluating the local reactivity of the carbon atom. So eqs 10a, 10b, and 10c may be rewritten as

$$s_C{}^+ = [\rho_{CH_3}(N_0 + 1) - \rho_{CH_3}(N_0)]S$$

(suited for studies of nucleophilic attack) (11a)

$$s_C{}^- = [\rho_{CH_3}(N_0) - \rho_{CH_3}(N_0 - 1)]S$$

(suited for studies of electrophilic attack) (11b)

$$s_C{}^0 = \frac{1}{2}[\rho_{CH_3}(N_0 + 1) - \rho_{CH_3}(N_0 - 1)]S$$

(suited for studies of radical attack) (11c)

where $\rho_{CH_3}(N_0)$, $\rho_{CH_3}(N_0 - 1)$,and $\rho_{CH_3}(N_0 + 1)$ represents the electronic population on the fragment $-(CH_3)$ for the N_0, $N_0 - 1$, and $N_0 + 1$ electronic systems, respectively. It should be mentioned that similar kind of approaches were adopted by Contreras et al.[25] to evaluate the local reactivity indices within a static reactivity picture.

3. Methodology and Computational Details

To investigate the reliability of the newly proposed way of evaluating condensed FF (or local softness) values, 18 different alkyl halides are chosen. They are the chlorides, bromides and iodides of six different alkyl groups. These are allyl ($-CH_2$-$CH{=}CH_2$), benzyl ($-CH_2C_6H_5$), ethyl ($-CH_2CH_3$), *n*-propyl ($-CH_2CH_2CH_3$), isopropyl ($-CH(CH_3)_2$), and *tert*-butyl ($-C$-$(CH_3)_3$) groups. Geometries are generated using the CHEM-3D program package[26] For alkyl chlorides and bromides, after optimizing the geometries at lower level (i.e., semiempirical), further reoptimization was done at higher level (RHF/6-31G**) followed by single point calculation at this higher level. However, for alkyl iodides, the reoptimization (followed by single point calculation) was done at RHF/LANL2DZ[27] level because of the unavailability of the 6-31G**[28] basis set for iodine. Both optimization and single point calculations were performed using the Gaussian-98 program package.[29] The pictures of the alkyl halides with the numberings of the atoms are shown in Figure 2. Each of the 18 halides is denoted by an identification number, e.g., $CH_2{=}CH{-}CH_2Cl$ = **1**, $CH_2{=}CH{-}CH_2Br$ = **2**, $C_6H_5CH_2I$ = **6**, etc., for simplicity of discussion in the later part of the article,

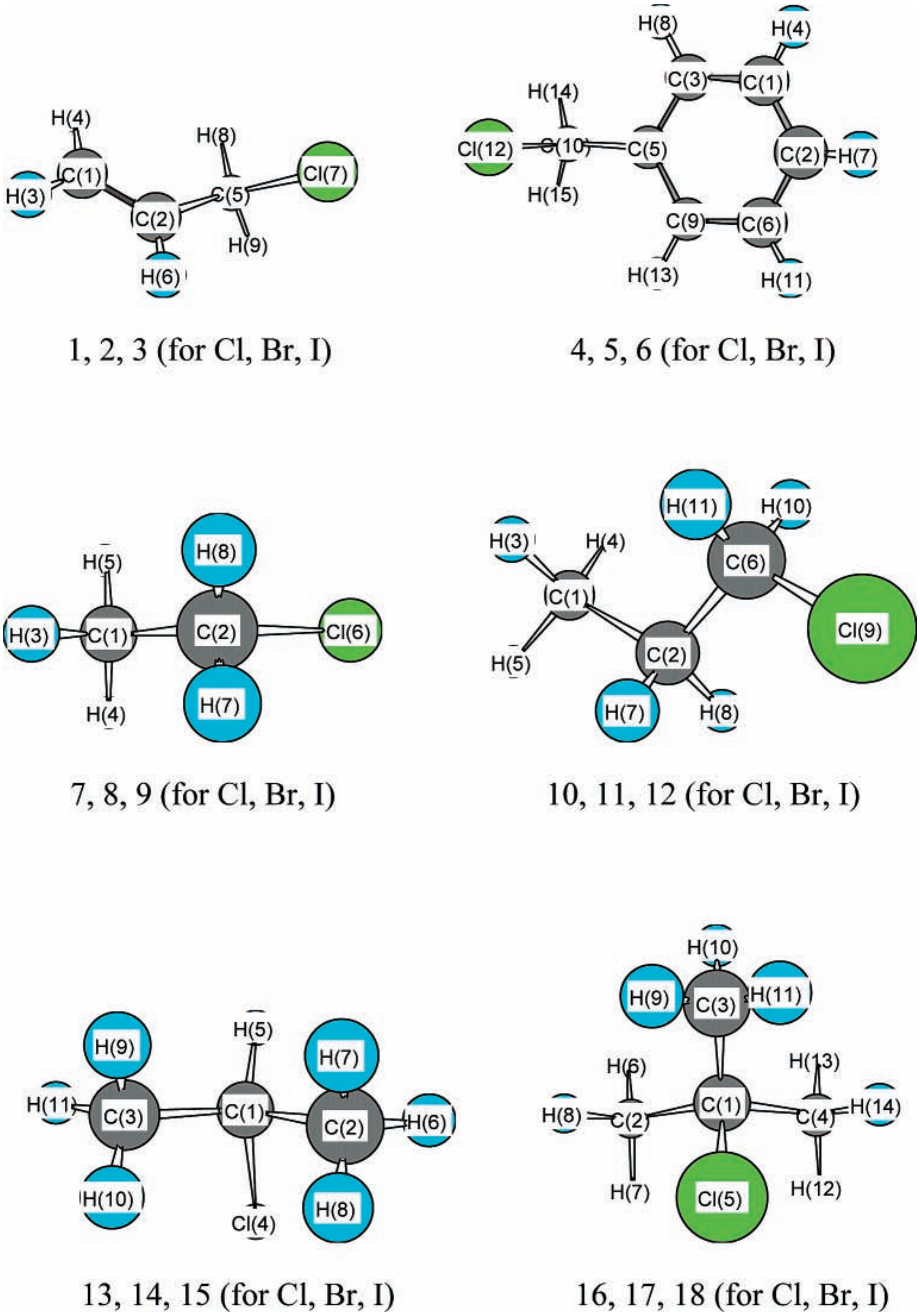
As the nucleophilic substitution reaction in alkyl halides proceeds through a gradual break up of the C−X bond, it can be viewed as if the C−X bond distance is increasing gradually (as this is the rate determining, and hence, the slowest step). To mimic this situation the C−X bond distances are stretched out to larger distances and keeping these fixed the geometries are re-optimized. So, this is some kind of constrained optimization. As the equilibrium C−X bond distances increase in the order C−Cl < C−Br < C−I (also it depends to some extent on the alkyl groups to which they are attached; see Table 3 for the values of the equilibrium C−X distances for each alkyl halides), the following distances are chosen for constrained optimizations:

C−Cl → 2.75, 3.00, and 3.25 Å
C−Br → 2.75, 3.00, 3.25, and 3.50 Å
C−I → 2.75, 3.00, 3.25, 3.50, and 3.75 Å

Note that there is no specific reason to choose only these particular distances and distances other than these can also be chosen.

4. Results and Discussion

A. Electrophilicity of C_{C-X} at Equilibrium Geometry. In Table 1 the list of the atomic charges q_k, s_k^+, and s_k^+/s_k^- values



1, 2, 3 (for Cl, Br, I)

4, 5, 6 (for Cl, Br, I)

7, 8, 9 (for Cl, Br, I)

10, 11, 12 (for Cl, Br, I)

13, 14, 15 (for Cl, Br, I)

16, 17, 18 (for Cl, Br, I)

Figure 2. Alkyl halides (with numbering of atoms) chosen in the present study.

of the C_{C-X} and X_{C-X} (halogen atom bonded to the C−X bond) is demonstrated. These values are for the equilibrium geometries of the alkyl halides. Only for allyl halides (i.e., **1**, **2**, and **3**, see Figure 2) the corresponding values for another carbon atom (i.e., C_1) are also shown. This is because the C_1-atoms in these three halides also exhibit significant nucleophilicity, may be because of the presence of the conjugative allyl double bond. Values obtained through eqs 10a and 10b are tabulated against method-A and those obtained through eqs 11a and 11b are tabulated against method-A′. However, as halogens are monovalent (i.e., no hydrogen is attached to them), the corresponding values are evaluated only through method-A. Similarly, as the C_{C-X} in tertiary butyl halides (i.e., **16**, **17**, and **18**) is not attached to any hydrogen, the values in these cases are also evaluated only through method-A.

It is obvious from the computed values through method-A that in almost all cases the atomic charge (i.e., q_k) on the C_{C-X} is negative. This is physically unrealistic because the −I effect of the halogen atoms in the C−X bond makes C_{C-X} positively charged. These unphysical charges on the C_{C-X} have their effect on s_k^+ and s_k^+/s_k^- values also. In most cases the halogen atoms emerge out to be the most electrophilic ones (i.e., the most preferable site for an attack by a nucleophile, which is again unphysical). Because of the negative values of s_k^+/s_k^- in a few cases (e.g., **5**, **9**, and **12**), it is difficult to compare these values. But the positive and large s_k^+ and s_k^+/s_k^- values of halogen

TABLE 1: Charges (q_k), s_k^+, and s_k^+/s_k^- Values (in Both Methods *A* and *A′*) of Carbon and Halogen Atoms Attached to the C−X (X = Cl, Br, and I) Bonds of the Alkyl Halides Considered in the Present Study[a]

alkyl halides	atomic center	methods					
		A			A′		
		q_k	s_k^+	s_k^+/s_k^-	q_k	s_k^+	s_k^+/s_k^-
1	C_1	−0.2709	0.3410	0.8820	0.0020	0.9695	0.9713
	C_5	−0.3162	−0.1097	0.5230	0.0364	0.2373	1.9310
	Cl	−0.1098	0.4368	1.1198			
2	C_1	−0.2736	0.3041	0.7303	0.0000	0.8020	0.8226
	C_5	−0.2405	−0.0035	0.0204	0.1148	0.4198	2.5158
	Br	−0.1886	0.8066	1.5352			
3	C_1	−0.4467	0.4475	1.5311	−0.0591	0.6878	1.4017
	C_5	−0.7256	−0.0937	7.2218	−0.2210	0.3509	0.9128
	I	0.0430	1.6080	0.8687			
4	C_{10}	−0.3063	−0.0181	0.0748	0.0471	0.2300	1.3293
	Cl	−0.1042	0.3431	0.2579			
5	C_{10}	−0.2284	0.0153	−0.1071	0.1282	0.3485	3.0637
	Br	−0.1890	0.6134	1.4598			
6	C_{10}	−0.8128	−0.0764	0.4593	−0.2975	0.3564	4.6640
	I	0.0393	1.5577	2.2511			
7	C_2	−0.2845	−0.0626	0.2644	0.0515	0.5284	3.0602
	Cl	−0.1201	0.9478	0.6754			
8	C_2	−0.2108	−0.0421	0.3413	0.1274	0.5842	2.5644
	Br	−0.1978	1.0871	0.6933			
9	C_2	−0.6074	−0.1777	−12.5697	−0.1247	0.3232	0.8795
	I	0.0263	1.7235	0.9395			
10	C_6	−0.2870	−0.0287	0.1182	0.0436	0.5303	3.2342
	Cl	−0.1149	0.9182	0.6504			
11	C_6	−0.2051	−0.0143	0.1161	0.1295	0.5903	2.7463
	Br	−0.2009	1.0649	0.6750			
12	C_6	−0.6617	−0.2020	−8.9004	−0.1830	0.3127	0.8263
	I	0.0365	1.7389	0.9536			
13	C_1	−0.2001	−0.0641	0.2446	−0.0296	0.2135	−3.6527
	Cl	−0.1246	0.9445	0.6692			
14	C_1	−0.1208	−0.0674	0.4583	0.0515	0.2380	12.9008
	Br	−0.2118	1.0824	0.6771			
15	C_1	−0.4109	−0.4337	6.9364	−0.1691	−0.1708	−1.3994
	I	0.0028	1.7780	0.9605			
16	C_1	−0.1471	−0.0814	0.3214			
	Cl	−0.1270	0.9395	0.6591			
17	C_1	−0.0656	−0.1017	0.5337			
	Br	−0.2184	1.0835	0.6646			
18	C_1	−0.1958	−0.6906	5.1176			
	I	−0.0124	1.8396	0.9893			

[a] The s_k^+ values are in atomic units. To identify the atom numberings, see Figure 1, and for explanation in details of methods *A* and *A′*, see the text.

atoms, in most cases, is difficult to explain and seems to be physically unrealistic. For the same reason the negative s_k^+ values of the C_{C-X} in most cases (except **5**) (and thus projecting these to be very week electrophilic center) is a very unphysical outcome.

However, a significant change in the values of q_k, s_k^+, and s_k^+/s_k^- is observed when evaluated through method-A′. Except most of the iodides (i.e., **3**, **6**, **12**, and **15**) and a chloride (i.e., **13**) the charge values appear positive in all cases. The appearance of the negative charge values of the C_{C-X} in alkyl iodides can, most probably, be attributed to the low quality of the basis set (i.e. LANL2DZ) used to compute these values. Thus, we can argue that method-A′ has taken care of the distribution of positive charges on the C_{C-X} (through −I effect, which arises due to the high electronegativity difference between the partially positively charged C_{C-X} and the bonded H-atoms) significantly.

Now when we compare the s_k^+ values of C_{C-X} computed through method-A′ with the s_k^+ values of X_{C-X} (evaluated through method-A) we reach the same unphysical conclusion that the halogen atoms are the stronger electrophilic center. But when the computed s_k^+/s_k^- values (through method-A′ for C_{C-X}) are compared, we found that the C_{C-X} has emerged out to be the strongest electrophilic center in most cases except some alkyl iodides (e.g., **9**, **12**, and **15**) and one alkyl chloride (i.e., **13**). However, it is very difficult to draw any conclusion in case of **13** as in this case, although s_k^+ value is positive, the s_k^+/s_k^- value turns out to be negative because of the negative s_k^- value in the denominator.

In case of tertiary butyl halides (i.e., **16**, **17**, and **18**), as one can use only method A to evaluate the q_k, s_k^+, and s_k^+/s_k^- values (the reason explained earlier), no improvement in the trend is observed. As there is no hydrogen bonded to the C_{C-X} in these three alkyl halides, the only way the positive charge on the C_{C-X} can be distributed is through the other three carbon atoms of the three $-CH_3$ groups attached to it. But unfortunately we cannot take care of that charge dissipation in method-A′.

B. Change of Electrophilicity of C_{C-X} with the Elongation of C−X Bond. As argued in section 3, the C−X bonds of the alkyl halides are gradually elongated to mimic the slow breakup of the bond as the substitution reaction proceeds. The corresponding changes in the values of s_k^+ and s_k^+/s_k^- are demonstrated in Table 2. Because of the interesting trends of s_k^+ and s_k^+/s_k^- values for C_1 and C_5 in the allyl halides (i.e., **1**, **2**, and **3** in Figure 2), they merit separate discussion. Here we see that for allyl chloride and allyl bromide (i.e., **1** and **2**) the C_1 become more and more electrophilic as the C−X bond is elongated

TABLE 2: s_k^+ and s_k^+/s_k^- Values of Carbon and Halogen Atoms Attached to the C−X (X = Cl, Br, and I) Bonds of the Alkyl Halides Considered in the Present Study[a]

alkyl halides	atomic center	$R_{\mathrm{C-X}}$ (Å)									
		2.75		3.00		3.25		3.50		3.75	
		s_k^+	s_k^+/s_k^-	s_k^+	s_k^+/s_k^-	s_k^+	s_k^+/s_k^-	s_k^+	s_k^+/s_k^-	s_k^+	s_k^+/s_k^-
1	C_1	0.737	1.933	1.031	2.751	1.347	101.168				
		1.721	1.862	2.326	2.430	2.461	−135.525				
	C_5	0.577	133.733	0.916	−25.918	1.348	100.709				
		1.763	5.371	2.378	9.454	2.461	−121.659				
	Cl	1.308	0.372	1.247	0.267	0.443	0.094				
2	C_1	0.579	1.387	0.824	1.747	1.444	2.320	−0.014	0.066		
		1.408	1.449	1.936	1.803	2.602	2.276	0.393	3.106		
	C_5	0.398	2.256	0.676	4.389	1.010	6.611	0.364	0.950		
		1.430	2.483	1.962	3.875	2.605	5.584	0.913	0.907		
	Br	1.593	0.538	1.650	0.419	1.684	0.325	0.741	1.457		
3	C_1	0.740	1.401	0.999	1.520	1.345	1.752	1.770	2.089	2.161	2.176
		1.140	1.275	1.536	1.382	2.059	1.575	2.707	1.862	3.303	1.196
	C_5	−0.089	−0.238	0.126	0.234	0.476	0.710	0.916	1.088	1.352	1.895
		0.656	0.843	1.025	1.098	1.547	1.463	2.191	1.825	2.802	2.416
	I	2.293	0.922	2.534	0.813	2.718	0.679	2.896	0.562	2.954	0.487
4	C_{10}	0.442	−1.899	0.565	−2.740	1.303	−2.172				
		1.220	56.985	1.341	27.993	2.877	−5.877				
	Cl	0.829	1.189	0.619	0.789	0.919	0.147				
5	C_{10}	0.338	−1.304	0.468	−1.673	0.563	−2.090	0.629	−2.879		
		1.068	−48.880	1.203	−32.990	1.313	−25.419	1.389	−1323.181		
	Br	1.118	1.555	0.925	1.046	0.732	0.710	0.571	0.495		
6	C_{10}	−0.064	−0.189	0.186	0.376	0.327	−0.758	0.496	−1.234	1.536	5.423
		0.677	0.957	1.077	1.318	0.912	−4.131	1.070	−5.313	2.929	5.776
	I	2.253	0.894	2.473	0.749	1.419	1.142	1.201	0.849	2.507	0.361
7	C_2	0.651	3.569	1.071	5.840	1.676	6.124				
		0.855	2.734	2.595	3.841	3.723	5.270				
	Cl	1.227	0.448	1.239	0.334	1.331	0.249				
8	C_2	0.406	−0.645	0.829	2.126	1.279	2.665	1.862	3.263		
		1.536	−3.505	2.253	2.616	3.083	3.138	4.167	3.703		
	Br	0.520	0.170	1.643	0.460	1.744	0.378	1.897	0.315		
9	C_2	−0.072	−0.167	0.232	0.360	0.667	0.765	1.208	1.090	1.887	1.373
		0.711	0.879	1.196	1.156	1.854	1.431	2.676	1.699	3.717	1.973
	I	2.312	0.925	2.482	0.818	2.635	0.703	2.853	0.607	3.179	0.529
10	C_6	0.685	4.653	1.120	8.824	1.740	8.804				
		1.883	3.055	2.637	4.522	3.772	6.464				
	Cl	1.222	0.436	1.220	0.320	1.279	0.233				
11	C_6	0.496	1.826	0.874	2.380	1.341	3.101	1.943	4.053		
		1.613	2.336	2.287	2.787	3.137	3.517	4.235	4.362		
	Br	1.569	0.553	1.642	0.450	1.702	0.360	1.808	0.292		
12	C_6	−0.106	−0.239	0.227	0.340	0.702	0.795	1.290	1.170	2.029	1.517
		0.687	0.835	1.197	1.145	1.892	1.481	2.750	1.813	3.842	2.144
	I	2.330	0.935	2.488	0.818	2.621	0.690	2.801	0.586	3.066	0.500
13	C_1	0.606	−5.407	1.062	−16.492	1.512	−6.891				
		1.218	12.822	1.852	22.417	2.363	−21.578				
	Cl	0.990	0.332	0.900	0.211	0.322	0.067				
14	C_1	0.436	6.249	0.821	9.133	1.303	23.867	*b*	*b*		
		1.011	4.066	1.541	5.607	2.192	10.936	*b*	*b*		
	Br	1.329	0.452	1.247	0.328	1.055	0.215	*b*	*b*		
15	C_1	−0.323	−1.442	0.028	0.087	0.511	1.255	1.070	2.383	1.706	10.003
		0.091	0.239	0.533	1.144	1.117	2.022	1.795	3.158	2.576	8.260
	I	2.184	0.849	2.186	0.683	2.131	0.527	2.048	0.399	1.931	0.285
16	C_1	0.515	−2.278	0.842	−1.904	1.178	−2.392				
	Cl	0.862	0.252	0.646	0.159	0.490	0.098				
17	C_1	0.354	−3.320	0.715	−4.213	1.091	−4.754	1.463	−4.942		
	Br	1.153	0.377	0.967	0.247	0.780	0.159	0.620	0.103		
18	C_1	−0.636	−26.200	−0.291	−15.229	0.181	−3.677	0.693	−4.508	1.182	−4.844
	I	2.099	0.797	1.947	0.581	1.711	0.401	1.430	0.266	1.203	0.182

[a] The s_k^+ values are in atomic units. Values in same lines of atomic centers are those evaluated through method *A*, whereas values in lines below are those evaluated through method *A*′. To identify the atom numberings, see Figure 1, and for explanation in detail of methods *A* and *A*′, see the text. [b] Values could not be produced, as the geometry optimization did not converge.

gradually. This is very clearly demonstrated by the s_k^+/s_k^- values of these two atoms when evaluated through method-A′. This anomalous behavior will be explained in the next subsection (i.e., subsection 3C) where we will analyze the change of the global softness values of the systems as the C−X bonds are elongated and will also visualize the pictures of these two halides (i.e., **1** and **2**) at distances 3.25 and 3.50 Å, respectively. For allyl iodide (i.e., **3**), however, the trend is as expected. In this case, although at lower distances s_k^+ and s_k^+/s_k^- values of C_1 are higher than those of C_5 (when evaluated through method-A′), the gap narrows down as the C−I bond is elongated gradually. Finally, at 3.75 Å, the s_k^+/s_k^- value of C_5 is higher than that of C_1, indicating the former to be more electrophilic than the later one.

There is one similarity in all these three halides. That is the gradual decrease of the electrophilic nature of the halogen atoms

TABLE 3: Global Softness Values *S* of the Studied Alkyl Halides at the Different C−X (X = Cl, Br, and I) Distances (R_{C-X})[a]

alkyl halides		R_{C-X} (in Å)					
		equilibrium	2.75	3.00	3.25	3.50	3.75
1	(1.804)	2.221	4.755	5.908	5.379[b]		
2	(1.972)	2.253	4.395	5.498	6.834	2.367[b]	
3	(2.219)	2.637	4.097	5.092	6.313	7.784	9.071
4	(1.808)	2.150	3.465	3.554	7.318		
5	(1.977)	2.583	3.433	3.577	3.654	3.710	
6	(2.225)	2.864	4.286	5.403	3.739[b]	3.830[b]	9.604
7	(1.799)	1.845	3.961	4.969	6.607		
8	(1.964)	2.075	2.805	4.941	6.178	7.817	
9	(2.205)	2.527	3.777	4.623	5.674	7.022	8.793
10	(1.798)	1.861	4.042	5.072	6.718		
11	(1.962)	2.092	4.043	5.044	6.282	7.923	
12	(2.206)	2.539	3.811	4.671	5.747	7.093	8.862
13	(1.815)	1.887	4.002	5.115	5.325		
14	(1.985)	2.136	4.004	4.905	5.928	*c*	
15	(2.235)	2.611	3.845	4.676	5.677	6.855	8.253
16	(1.834)	1.946	4.194	4.777	5.577		
17	(2.008)	2.203	4.036	4.836	5.705	6.693	
18	(2.268)	2.715	3.917	4.730	5.642	6.636	7.741

[a] The bracketed value next to each alkyl halide is the equilibrium C−X bond distance. All bond distances are in angstroms. The *S* values are in atomic units. [b] Trends are not regular. [c] Optimization did not converge.

as the C−X bonds are elongated. This lowering trend is clearly demonstrated by s_k^+/s_k^- values (and not by s_k^+ values). At large C−X distances the halogen atoms clearly appear to be very weak electrophilic (as the s_k^+/s_k^- values become smaller and smaller than 1) or, to say the other way, strong nucleophilic. The physical reason may be that at large C−X distances the halogen atoms exist almost like halide ions (i.e., X^-) due to heterolytic cleavage of the C−X bond. This typically represents the first step (the slowest rate determining step) of an E1 (unimolecular elimination) or S_N1 (unimolecular substitution) reaction of an alkyl halide.

In case of other halides the trend of s_k^+ and s_k^+/s_k^- values are very similar. Here as the C−X bonds are elongated C_{C-X} become more and more electrophilic and X_{C-X} become stronger nucleophilic. In cases where s_k^+/s_k^- values become negative e.g., **5**, **6**, **8**, **9**, **12**, **13**, **15**, **16**, **17**, and **18** (due to the negative s_k^- values in the denominator), it is very difficult to compare these values. However, in such cases, the comparison of only the s_k^+ values at higher distances makes the argument clear (i.e., C_{C-X} is the stronger electrophilic one).

C. Change of Global Softness with Elongation of C−X Bonds. Although not much related to the present study, the generated results can be considered as a test case of another well-known important chemical principle. This is the principle of maximum hardness (PMH) first proposed by Pearson[2b] and later on proved analytically by Chattaraj et al.[2c] and was tested by different groups on different contexts.[2d] The principle states that "at constant v (potential due to nuclei plus any other external potential), μ (chemical potential), and temperature T a chemical system evolves to a state with maximum hardness, η".[2b] The above statement has a physical interpretation that the stable equilibrium geometry of any chemical species has maximum hardness. Now from the above principle it is expected that as the C−X bonds are stretched the global hardness η should decrease or, in reverse, global softness (i.e., S) should increase (as $\eta = {}^1/_{2S}$). This is exactly what is observed in almost all cases except in **1** (at C−Cl distance 3.25 Å), **2** (at C−Br distance 3.50 Å), and **6** (at C−I distances 3.25 and 3.50 Å). However, when the optimized structures of **1**, **2**, and **6** at the above C−X distances are analyzed, interesting features were discovered. In case of **1** (Figure 3I) the Cl-atom, instead of being attached to only C_5 (with which it was originally bonded), now is attached to both C_1 and C_5 maintaining equal C_1−Cl and C_5−Cl distances (i.e. 3.25 Å). In case of **2** (Figure 3II), the Br-atom, instead of being attached to C_5, is now bonded to only C_1. In this case also the C_5−Br distance is maintained at 3.50 Å. The C_1−Br bond distance (1.965 Å) is now little more than the equilibrium C_5−Br bond distance (values given in Table 3). Although both these phenomena are apparently confusing they can be viewed as the manifestation of the conjugative allyl double bond. This argument becomes stronger when we observe that the bond orders of C_1−C_2 and C_2−C_5 bonds are same (i.e., 1.5) in Figure 3I. In case of 2 the bond orders of C_1−C_2 and C_2−C_5 bonds in Figure 3II are 1.0 and 2.0, respectively, which are the reverse of those at the equilibrium geometry (i.e., 2.0 and 1.0, respectively).

The anomalous trend of the global softness values of **6** at C−I distances 3.25 and 3.50 Å is not still clear. An inspection of the optimized geometries at these two distances does not reveal any change in the original structure (except, of course, the expected change in bond distances, bond angles and dihedral angles). Perhaps the topology of the electron density distributions in these two cases makes the systems more soft.

5. Conclusion

In the present study a new method (except only one case of previous use by Contreras et al.[25]) of evaluating the DFT based

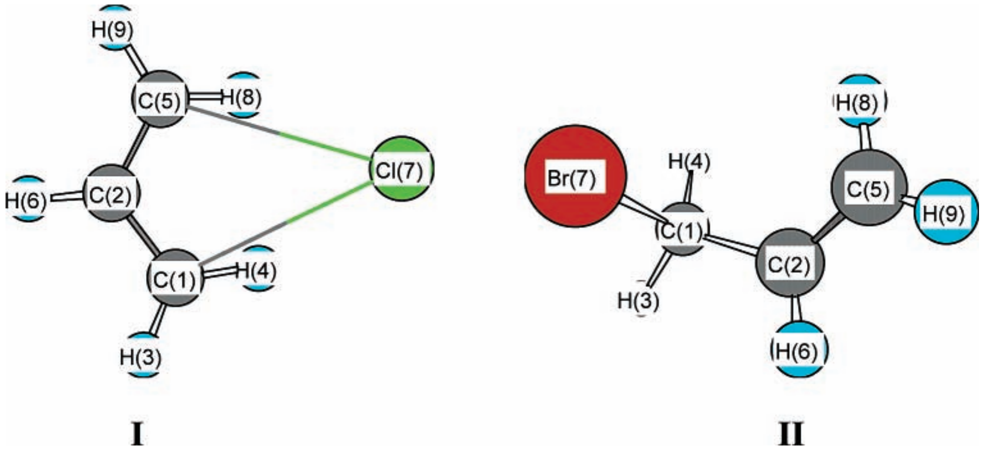


Figure 3. The typical geometries attained by allyl chloride (i.e., I) and allyl bromide (i.e., II) at large (i.e., elongated) C−X distances. For details see the text.

local reactivity descriptors (i.e., s_k^+, s_k^-, and s_k^0) is proposed. The method suggests that instead of using the atomic charges on the individual atoms to evaluate the mentioned descriptors (as it is done in the conventional way using eqs 10a, 10b, and 10c), more appropriate would be to add the charges of the H-atoms to those of the heavy atoms with which they are bonded (i.e., using eqs 11a, 11b, and 11c). It is argued that if the values are evaluated through this new method then charge dissipation of the heavy atoms to the H-atoms (through inductive effect arising out of the electronegativity difference) can be taken care of. The s_k^+ and s_k^+/s_k^- values evaluated through this new method have been found to be more reliable in predicting the strongest electrophilic centers in the chosen alkyl halides even when MPA scheme has been used. Those centers are the C_{C-X}, which are attacked by the Nu^- in a nucleophilic substitution reaction. Also, it is shown that the strongest electrophilic nature of the C_{C-X} become more distinct when the C−X bond is stretched gradually, thus mimicking the progress of the substitution reaction. The unreliable trends in cases of few alkyl iodides have been attributed to the poor basis sets (LANL2DZ) chosen for the study of alkyl iodides.

As a secondary part, the present study shows that PMH holds true when the C−X bonds are stretched. The apparent irregular global softness trends of allyl chloride, i.e., **1**, and allyl bromide, i.e., **2**, have been attributed to the formation of new structures at large C−X distances.

Right now, it is not clear to the author why the *S* values of benzyl iodide, i.e., **6**, at C−I distances of 3.25 and 3.50 Å are smaller than those of 2.75 and 3.00 Å. Repeated geometry optimizations starting with different geometries and applying different optimization conditions could not correct the trends (although there is very minor changes in the numerical values depending upon the optimization conditions). It is conjectured that the topology of the electron density distribution at these two geometries might have made the systems harder (or less soft).

The new method of evaluating the s_k^+, s_k^-, and s_k^0 values has its limitations in the present level. It cannot take into account the charge dissipation of one heavy atom to another heavy atom with which it is bonded. That is why the s_k^+ values of the C_{C-X} in equilibrium geometry of tertiary butyl halides (i.e., **16**, **17**, and **18**) are very unreliable. Although at large C−X distances the reliability of s_k^+ values of C_{C-X} of these alkyl halides improved significantly, further development in this area is warranted.

Acknowledgment. The author is grateful to his colleagues at Birla Institute of Technology and Science (BITS), Pilani, for helpful discussions from time to time.

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