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Revisiting Electroaccepting and Electrodonating Powers: proposals for Local electrophilicity and Local nucleophilicity descriptors

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Abstract

Electrophilicity index, $\mu^2/2\eta$, where μ is the chemical potential, and η is the hardness, has been defined by Parr, Von Szentpaly, and Liu (J. Am. Chem. Soc. 121, 1922 (1999)), as the lowering in energy of an electronic system, during the process in which the chemical potential of the system raises from μ to zero, accepting $-\mu/\eta$ electrons. In this work, it is shown that the electrophilicity index is also a rational choice for measuring nucleophilicity. Indeed, within the grand canonical ensemble, when the chemical potential of a system increases from μ to zero, the system gives away μ/η electrons. During the process, the variation of the grand potential is $\mu^2/2\eta$. Additionally, through the use of a second order Taylor series expansion of the density as a function of the number of electrons, at constant external potential, that depends on the Fukui function and the dual descriptor, the local electrophilicity is defined as the actual variation of the electron density when the system acquires $-\mu/\eta$ electrons, while the local nucleophilicity is similarly defined for the case when the system loses μ/η electrons.

1 – Introduction

The full prediction of the chemical behavior of electronic systems rests upon the capability to assess two important properties, namely the global reactivity and the local selectivity. In Density Functional Theory of Chemical Reactivity (DFT-CR),¹ also coined by its founder conceptual DFT,² both concepts are regarded in terms of successive responses of the electronic energy, to external perturbations.³⁻⁶ During any chemical process, two main perturbations are likely to happen. The reagents are supposed to be able to exchange electrons, and atoms or chemical groups can move, or relocate, constituting eventually the new molecular backbone. The consequences of those modifications in the system are monitored through derivatives of the electron energy with respect to either the number of electrons or the external potential. The former derivatives give rise to global descriptors able to quantify the chemical reactivity of the system. The latter derivatives define local descriptors characterizing the chemical selectivity.

In a great number of chemical reactions, such as oxidations, reductions, acids and bases reactions or in reactions between a nucleophile and an electrophile, the driving force is the stabilization energy due to the exchange of electrons between the interacting fragments. Therefore, it is highly desirable to be able to accurately characterize both the electroaccepting or electrodonating power of electronic systems. It is also quite important to locally characterize this property for hence predicting where, within the molecule, the reaction is likely to take place. Within a time span of almost one century a great deal of work has been dedicated to such a task. These efforts have led to the definitions of several indexes, such as ionization potential, electron affinity, electronegativity,⁷⁻⁹ chemical potential¹⁰ and, lately, the electrophilicity.¹¹ Some local functions have been defined alongside for describing selectivity, for instance the Fukui function,^{12,13} the local softness¹⁴ and the dual descriptor.^{15,16}

Contrary to electrophilicity which is quite well defined in DFT-CR, the characterization of nucleophilicity remains elusive. The assessment of global electrophilicity is based upon the measure of the stabilizing energy a system gets when it becomes saturated with electrons. The whole proposal lies upon the assumption that the chemical potential is always negative. Within this framework, the definition of an absolute nucleophilicity index proved to be a rather thorny topic. Most of the attempts undertaken aimed to define a relative measure of nucleophilicity,¹⁷

however, some absolute definitions have also been proposed.¹⁸ In this work, some arguments are put forward in favor of the use of the electrophilicity as a measure of absolute nucleophilicity. Besides, the local descriptors designed to measure the local electrophilicity and the local nucleophilicity are also proposed. Additionally, the electrodonating and electroaccepting powers are analyzed through the present approach considering the case when the first right and left derivatives of the energy and of the density with respect to the number of electrons are different.

Recently, Liu and collaborators^{19, 20} have proposed a method to determine simultaneously electrophilicity and nucleophilicity values through the use of information gain^{21, 22} or Hirshfeld charges,²³ finding good correlations with experimental scales. However, in the present work we will adopt a different viewpoint, based on the response functions of DFT-CR.

2 – Electroaccepting Power and Local Electrophilicity

2-1. Global Electroaccepting Power

The electrophilicity index,¹¹ hereafter called electroaccepting power has been proposed by Parr and co-workers to characterize the propensity of a system to acquire electrons from its environment. The aim of this section is merely to propose a local counterpart for this index. Thus, the first sub-section is a reminder of the way the electroaccepting power has been established and aims to provide some complementary arguments about its grounds. The second sub-section is dedicated to the proposal of its local counterpart.

The electroaccepting power has been established by calculating the stabilizing energy of a system that acquires enough electrons to be saturated. The number of electrons that saturates a system is obtained by optimization. The variation of the electron energy up to the second order, at constant external potential, $v(\mathbf{r})$, is given as,²⁴

$$\Delta E = \left(\frac{\partial E}{\partial N} \right)_{v(\mathbf{r})} \Delta N + \frac{1}{2} \left(\frac{\partial^2 E}{\partial N^2} \right)_{v(\mathbf{r})} (\Delta N)^2 \quad . \quad (1)$$

It is important to mention that in this equation it has been assumed that the energy is a continuous and differentiable function of the number of electrons. However, it has been shown

that the energy, E , and the electron density, $\rho(\mathbf{r})$, as a function of the number of electrons are given by a series of straight lines connecting the integer values of N .^{25, 26} This situation implies that the first derivative of these two quantities is different when evaluated from the left or from the right, and that the second derivative is equal to zero when evaluated from the left or from the right, and it is not defined for integer number of electrons. Nevertheless, the use of a smooth interpolation of the energy around the integer values of N , that leads to the same value of the first derivative at the integer values of N , when evaluated from the left or from the right, and to a well defined and unique second derivative, has proven to be quite useful to describe many aspects of chemical reactivity.^{1-6, 27-31}

In equation (1), one overlooks the possible variation of the external potential that can occur during the process. The identification of the first N -derivative as the chemical potential¹⁰ (μ) and the second N -derivative as the chemical hardness^{24, 32-34} (η) gives,

$$\Delta E = \mu \Delta N + \frac{1}{2} \eta (\Delta N)^2 \quad (2)$$

The optimum variation of the energy is reached when,

$$\frac{d(\Delta E)}{d(\Delta N)} = 0 = \mu + \eta \Delta N_{\max} \quad (3)$$

Therefore, the maximum number of electrons a system can acquire is

$$\Delta N_{\max} = -\frac{\mu}{\eta} \quad (4)$$

This number is obviously positive since it is now admitted that the chemical hardness is positive while, for an electronically stable system, the chemical potential has to be negative. To our best knowledge, the fact that the chemical potential is negative has never been formally proved. However, one can heuristically provide some arguments.

The chemical potential is originally the functional derivative of the energy functional with respect to the electron density, yielding the expression¹

$$\mu = v(\mathbf{r}) + \frac{\delta F_{HK}[\rho]}{\delta \rho(\mathbf{r})} \quad (5)$$

In equation (5), for a molecular system, $v(\mathbf{r})$ stands for the electrostatic potential created by the nuclei and $\delta F_{HK}[\rho]/\delta \rho(\mathbf{r})$ is the functional derivative of the Hohenberg-Kohn universal functional with respect to the electron density. The latter term contains the interaction potential between the electrons, in which electrostatic repulsion prevails. It is obvious that, for an electronically stable system, the magnitude of the repulsion between electrons must be smaller than the electrostatic stabilizing potential created by the nuclei.

$$|v(\mathbf{r})| > \left| \frac{\delta F_{HK}[\rho]}{\delta \rho(\mathbf{r})} \right| \quad (6)$$

Whence, the chemical potential is quite likely to be negative for a stable system.

The maximum variations of the electronic energy can easily be obtained by formally introducing equation (4) into equation (2),

$$\Delta E_{\max} = \mu \Delta N_{\max} + \frac{1}{2} \eta (\Delta N_{\max})^2 \quad (7)$$

At this stage, the analogy proposed by Pearson²⁷ with the basic law of electricity helps understanding the meaning of the two terms of the right hand side of equation (7). Pearson proposed to make a correspondence between the chemical potential and an electric potential (V), between the chemical hardness and an electric resistance (R), and finally between the variation of the number of electrons and an electric current (I). Following this analogy, both terms in equation (7) can be seen as electric powers. Since the chemical potential is negative, the first term is the stabilizing electric power the system gets when it acquires the number of electrons ΔN_{\max} . The second term can be seen as the power dissipated through a “Joule’s Effect” occurring during the transfer of ΔN_{\max} electrons.

The actual introduction of equation (4) into equation (2) gives

$$\Delta E_{\max} = -\frac{\mu^2}{2\eta} \quad (8)$$

As this energy is obviously always negative and corresponds to the stabilizing energy the system gets when it acquires ΔN_{\max} electrons, it has been proposed to use $\omega = \mu^2 / 2\eta$ as a measure of the electrophilicity of the system. The term electroaccepting power also seems quite relevant. This concept has proven to be very useful to understand different aspects of chemical reactivity of a wide variety of systems.^{28, 29, 31}

It is worth pointing out that during the whole process the chemical potential evolves. The variation of the chemical potential is given to first order by,

$$\Delta\mu_{\max} = \eta \Delta N_{\max} = -\mu \quad . \quad (9)$$

Thus, when the process ends, the chemical potential is zero. As discussed previously, the chemical potential for an electronically stable system is negative. For atoms, one can even narrow the range to

$$0 \geq \mu \geq \mu_{\text{F}} \quad , \quad (10)$$

in which μ_{F} is the chemical potential of Fluorine. Therefore, the highest possible variation of the chemical potential is the one that rises up the chemical potential from its initial value to zero. It is the highest possible increase that keeps the system electronically stable. Values higher than zero for the chemical potential appear not to be possible for electronic systems. If the chemical potential were positive, the system would spontaneously lose an electron. It is upon this concept that the electrodonating power is built in section 3. The end of this part is a proposal for a local counterpart of the electroaccepting power.

2-2. Local Electrophilicity

Several attempts have been undertaken to propose a distribution of the electroaccepting power over the system. They generally rest upon the projection of the electroaccepting power index through the Fukui function. In this work, in line with Cedillo and Contreras,³⁵ it has been preferred to assess the actual variation of the electron density when the system acquires the number of electrons ΔN_{\max} . To get this local variation one starts from a full expansion of the electron density variations, at constant external potential, namely,

$$\Delta\rho(\mathbf{r}) = \sum_{i=1}^{\infty} \frac{1}{i!} \left(\frac{\partial^i \rho(\mathbf{r})}{\partial N^i} \right)_{v(\mathbf{r})} (\Delta N)^i = \sum_{i=1}^{\infty} \frac{1}{i!} f^{(i)}(\mathbf{r}) (\Delta N)^i \quad (11)$$

Since $f^{(i)}(\mathbf{r})$ represents the i th derivative of the electron density with respect to the number of electrons at constant external potential, it means that $i=1$ corresponds to the usual Fukui function¹² $f(\mathbf{r})$, $i=2$ corresponds to the dual descriptor^{15, 16} $\Delta f(\mathbf{r})$, and $i \geq 3$ correspond to the hyper-Fukui functions³⁶. Extracting from the sum the first two terms one gets,

$$\Delta\rho(\mathbf{r}) = f(\mathbf{r}) \Delta N + \frac{1}{2} \Delta f(\mathbf{r}) (\Delta N)^2 + \sum_{i=3}^{\infty} \frac{1}{i!} f^{(i)}(\mathbf{r}) (\Delta N)^i \quad (12)$$

The maximum variation of the electron density is obtained by introducing equation (4) into equation (12):

$$\Delta\rho(\mathbf{r})_{Elec} = -\frac{\mu}{\eta} f(\mathbf{r}) + \frac{1}{2} \left(\frac{\mu}{\eta} \right)^2 \Delta f(\mathbf{r}) + \sum_{i=3}^{\infty} \frac{1}{i!} f^{(i)}(\mathbf{r}) \left(-\frac{\mu}{\eta} \right)^i \quad (13)$$

The subindex Elec is used to clarify that the local electronic density changes, in this case, are associated to the concept of local electrophilicity. The main advantage of this new descriptor is that it measures the actual variation of the electron density when the system is saturated with electrons. Besides, because the Fukui function integrates to one, and the dual descriptor and the hyper-Fukui functions integrate to zero, one can see that integrating equation (13) over all space, one finds that

$$\int \Delta\rho(\mathbf{r})_{Elec} d\mathbf{r} = -\frac{\mu}{\eta} = \Delta N_{\max} \quad (14)$$

However, the expression in equation (13) can barely be applied, because of the presence of the hyper-Fukui functions. One can therefore assume that, as long as the magnitude of $|\mu/\eta|$ is lower than 1, equation (13) quickly converges and can be truncated at second order, hence giving

$$\Delta\rho(\mathbf{r})_{Elec} = -\frac{\mu}{\eta} f(\mathbf{r}) + \frac{1}{2} \left(\frac{\mu}{\eta} \right)^2 \Delta f(\mathbf{r}) \quad (15)$$

Thus, equation (15) constitutes a local counterpart of the electrophilicity power and can be called “local electrophilicity”. This quantity may be easily computed using any quantum chemistry software. A relevant aspect of equation (15) is related to the fact that, in addition to the dependence on the Fukui function,³⁷ which corresponds to the natural choice for the distribution of the accepted electrons, the presence of the dual descriptor may also be very important, since this function has been found to play a very important role in the description of certain chemical interactions.³⁸⁻⁴⁶

Another important aspect of the present definition as given by equation (15), is related to the fact that since the process refers to the acceptance of charge by the system, one could expect that the regions where $\Delta\rho(\mathbf{r})_{Elec}$ is large and positive will correspond to the regions where the accepted charge will accumulate, indicating that these are the most electrophilic sites where a nucleophilic attack may occur. Thus, since the chemical potential is negative the distribution of the electrons transferred to the system will lead to large increments of charge in those sites where the Fukui function and the dual descriptor are large and positive, but it may also lead to small or no increase of charge in some sites, depending on the magnitude and sign of the Fukui function⁴⁷⁻⁵¹ and the dual descriptor.^{15, 16} One can even imagine that some sites can lower their electron densities.⁴⁷⁻⁵¹ For these latter sites, $\Delta\rho(\mathbf{r})_{Elec}$ is negative and therefore they have to comply with

$$\Delta f(\mathbf{r}) < \frac{2\eta}{\mu} f(\mathbf{r}) \quad , \quad (16)$$

that requires the values of the dual descriptor to be negative and of high magnitude in regions where the Fukui function is large and positive. All these conditions are in total agreement with what is known about the meaning of the sign of the dual descriptor.

An interesting interpretation of the chemical meaning of equation (15), comes from rewriting it as

$$\Delta\rho(\mathbf{r})_{Elec} = S [\chi f(\mathbf{r}) + \omega \Delta f(\mathbf{r})] \quad , \quad (17)$$

in which S stands for the global softness of the molecular system, while χ symbolises its global electronegativity. The descriptors involved in equation (17) are those one would expect for an index designed to provide a local measure of electrophilicity. The local electrophilicity is the

product of global softness by a local index constituted by a combination of the Fukui function and the dual descriptor. Both local descriptors are also weighted by a global descriptor, namely the electronegativity and the electrophilicity. It is well known that the higher the global softness is, the better the molecule is inclined to exchange electrons. The involvement of global softness as a part of local electrophilicity makes sense. Now, the first part of the local response is the product of the Fukui function times the electronegativity. The first term between brackets can be seen as a casting of the electronegativity over the molecule, some sort of distribution over the molecule of the global electronegativity. This first term can be called local electronegativity. The higher the local electronegativity in a given point in space, the more electrophilic the site will be. On the other hand, the second term is a distribution of the electrophilicity or electroaccepting power over the molecule through the dual descriptor. The term has been coined multiphilic descriptor⁵² by Chattaraj and collaborators. The multiphilic descriptor acts obviously as an enhancer for the local electronegativity. Positions where the multiphilic descriptor is positive are likely positions for a nucleophile to attack. Thus, the present analysis provides additional support to the multiphilic descriptor, which was proposed several years ago. It is also noteworthy that this interpretation of both terms corresponds to the case when the Fukui function and the dual descriptor are large and positive. The sites where $\Delta\rho(\mathbf{r})_{Elec}$ is positive, but small, and the sites where it is negative because of the Fukui function, or because of the dual descriptor, or because of both, should be interpreted as non-electrophilic sites.

3 - Electrodonating Power and Local Nucleophilicity

3-1. Global Electrodonating Power

As already presented in the previous part, Parr and co-workers have introduced a new electrophilicity index based upon the stabilizing energy a system experiences when it is saturated with electrons. This index and some of its extensions^{18, 52-54} have been quite successful for comparing the electrophilicity differences between molecules. The aim of this section is two fold, first to show that the grand canonical analogous of the electrophilicity index provides a way to define an electrodonating power, and second, to propose a local projection of this electron donation.

The grand canonical ensemble⁵⁵ is built from a Legendre transform^{56, 57} of the electronic energy. The conjugated function is called the grand potential and is defined as,

$$\Omega = E - N \mu_N \quad . \quad (18)$$

Where Ω represents the grand potential, E the electronic energy, N the number of electrons and finally μ_N is the chemical potential of a system with N electrons. In this context, the grand potential represents the difference between the electron energy of a system with N electrons and the energy of these N electrons having each the same energy μ_N .

In the grand canonical ensemble, the chemical reactivity is characterized in terms of successive derivatives of the grand potential with respect to both the external potential and the chemical potential. Interestingly, the local descriptors defined within this ensemble combine reactivity and selectivity information making them perfect for comparing the same atomic site within a set of molecules.

Within this ensemble, the mean number of electrons of an electronic system is determined by the value of its chemical potential. This can be easily shown from one of Maxwell's relations,⁵⁸

$$-\left(\frac{\delta \langle N \rangle}{\delta v(\mathbf{r})}\right)_{\mu} = \left(\frac{\partial \rho(\mathbf{r})}{\partial \mu}\right)_{v(\mathbf{r})} = s(\mathbf{r}) \quad . \quad (19)$$

The integral form of equation (19) is

$$\delta \langle N \rangle = - \int s(\mathbf{r}) \delta v(\mathbf{r}) d\mathbf{r} = -S \int f(\mathbf{r}) \delta v(\mathbf{r}) d\mathbf{r} = -\frac{\delta \mu}{\eta} \quad . \quad (20)$$

Thus, according to the direction of the chemical potential variation, the mean number of electrons can either increase or decrease. Indeed, if the chemical potential increases (decreases) the mean number of electrons decreases (increases), since the chemical hardness is always positive. These changes in the mean number of electrons may provide a way to define at the same time electrophilicity and nucleophilicity powers.

Yet, another way to get the result targeted is to use an alternative construction of the grand potential based upon a Legendre transform of the electronic energy as a function of the variation of the electron number, $\Delta N = N - N_0$, in which N_0 stands for the initial number of electrons of the considered system. In this context, the conjugate function of the electron energy would be

$$\Omega = E - \mu \Delta N \quad . \quad (21)$$

The successive derivatives of this alternative grand potential are the same as for the classical grand potential, except for the first derivative with respect to the chemical potential that is now $-\Delta N$.

To recover the electrodonating power as it has been defined by Gázquez and co-workers, one follows the same methodology as Parr and co-workers did for the electroaccepting power. The variation of the grand potential, at constant external potential, up to the second order reads

$$\Delta\Omega = -\Delta N \Delta\mu - \frac{1}{2} S (\Delta\mu)^2 \quad . \quad (22)$$

The optimal variation of the grand potential with respect to a change of the chemical potential corresponding to the maximum number of electrons that the system can exchange with the bath is given by,

$$-\frac{d(\Delta\Omega)}{d(\Delta\mu)} = \Delta N + S \Delta\mu = 0 \quad , \quad (23)$$

which gives

$$-\frac{\Delta\mu}{\eta} = \Delta N \quad . \quad (24)$$

The meaning of equation (24) is quite obvious, it merely indicates the quantity of electrons either gained or lost for a specific variation of the chemical potential. When the chemical potential increases, the system gives away electrons to its surroundings, while when the chemical potential decreases the system withdraws electrons from the environment. The introduction of equation (24) into equation (22) provides an expression for the optimal variation of the grand potential

$$\Delta\Omega = \frac{(\Delta\mu)^2}{\eta} - \frac{1}{2} \frac{(\Delta\mu)^2}{\eta} = \frac{(\Delta\mu)^2}{2\eta} \quad (25)$$

Interestingly, whatever the sign of chemical potential variations, the magnitude of the variations of the grand potential are identical and always positive. Using the same line of arguments as for the electroaccepting power, the maximum variation of the chemical potential that keeps the electronic system stable is $-\mu$. Again, this process leads the chemical potential to increase from its initial μ value to zero. In this case equations (24) and (25) become

$$\Delta N_{\max} = \frac{\mu}{\eta} \quad , \quad (26)$$

and

$$\Delta\Omega_{\max} = \frac{\mu^2}{2\eta} \quad . \quad (27)$$

As the chemical potential for a stable system is negative, and since the chemical hardness is always positive, the variation of the number of electron is negative meaning that the natural tendency is to lose a fraction of electrons. However, since the change in the grand potential needed for this process is positive (equation (27)), it implies that the lower this grand potential energy is, the easier the system gives away its electrons. Therefore one can propose that the quantity $\mu^2/2\eta$ defines the electrodonating power and it can be seen as a measure of the nucleophilicity of the system. The change in the energy associated to this process is

$$\Delta E = \frac{3}{2} \frac{\mu^2}{\eta} \quad . \quad (28)$$

In summary, within the canonical ensemble, the electroaccepting power is defined in terms of the stabilizing energy change of a system when it acquires the maximum number of electrons $\Delta N_{\max} = -\mu/\eta$. During this process, the chemical potential increases up to zero. On the other hand, within the grand canonical ensemble, the nucleophilicity index is defined in terms of the destabilizing grand potential change needed to raise the chemical potential up to zero. During this process the number of electrons of the system decreases by $\Delta N_{\max} = \mu/\eta$.

3-2. Local Nucleophilicity

Following the same argumentation as we did in the second section, one can monitor the local variation of the electron density during the process. Thus, substituting equation (26) in equation (12) one finds that,

$$\Delta\rho(\mathbf{r})_{Nuc} = \frac{\mu}{\eta} f(\mathbf{r}) + \frac{1}{2} \left(\frac{\mu}{\eta} \right)^2 \Delta f(\mathbf{r}) + \sum_{i=3}^{\infty} \frac{1}{i!} f^{(i)}(\mathbf{r}) \left(\frac{\mu}{\eta} \right)^i, \quad (29)$$

which corresponds to the maximum variation of the density when the system donates charge because its chemical potential varies from its initial μ value to zero. The subindex Nuc is used to clarify that the local electronic density changes, in this case, are associated to the concept of local nucleophilicity.

As before, because the Fukui function integrates to one, and the dual descriptor and the hyper-Fukui functions integrate to zero, one can see that the integral of equation (29) over all space, leads to

$$\int \Delta\rho(\mathbf{r})_{Nuc} d\mathbf{r} = \frac{\mu}{\eta} = \Delta N_{\max}. \quad (30)$$

That is, as expected, the integral corresponds to the number of electrons donated by the system.

Proceeding in the same way as it was done for the local electrophilicity, we assume that in equation (29), third and higher order terms are small, in comparison with the first and second order terms, so that it may be simplified to

$$\Delta\rho(\mathbf{r})_{Nuc} = \frac{\mu}{\eta} f(\mathbf{r}) + \frac{1}{2} \left(\frac{\mu}{\eta} \right)^2 \Delta f(\mathbf{r}) \quad (31)$$

It is important to note that equation (31) has a similar structure to equation (15), however there are relevant differences, because in the case of the local nucleophilicity the process refers to the donation of charge by the system, thus one could expect that the regions where $\Delta\rho(\mathbf{r})_{Nuc}$ is large and negative will correspond to the regions from where the donated charge will be

withdrawn, indicating that these are the most nucleophilic sites where an electrophilic attack may occur. Thus, since the chemical potential is negative the distribution of the electrons donated by the system will lead to large decrements of charge in those sites where the Fukui function is large and positive, and the dual descriptor is negative and also large, but it may also lead to small or no decrement of charge in some sites, depending on the magnitude and sign of the Fukui function and the dual descriptor. As in the case of the local electrophilicity, there may be sites that will increase their electron densities. These latter sites, for which $\Delta\rho(\mathbf{r})_{Nuc}$ is positive, comply with

$$\Delta f(\mathbf{r}) > -\frac{2\eta}{\mu} f(\mathbf{r}) \quad , \quad (32)$$

that requires the values of the dual descriptor to be positive and of high magnitude in regions where the Fukui function is large and positive. Thus, as in the case of the local electrophilicity, all the conditions regarding the local nucleophilicity are in total agreement with what is known about the meaning of the sign of the dual descriptor.

Similar to equation (17), one can rewrite equation (31) as

$$\Delta\rho(\mathbf{r})_{Nuc} = S \left[-\chi f(\mathbf{r}) + \omega \Delta f(\mathbf{r}) \right] \quad . \quad (33)$$

Recalling that in the case of the local nucleophilicity we are dealing with an electron donating process, one can perform an analysis that is quite similar to the one established for the local electrophilicity. The main difference arises from the minus sign in the first term of the right hand side of equation (33), which indicates that sites with a high and positive local electronegativity are the ones that present the largest contribution to the donating process. The second term acts as an enhancer for the donating power. However, in this case, the enhancement comes from the positions where the dual descriptor is negative and large, which are the positions for an electrophilic attack. The sites where $\Delta\rho(\mathbf{r})_{Nuc}$ is negative, but small in magnitude, and the sites where it is positive because of the Fukui function, or because of the dual descriptor, or because of both, should be interpreted as non-nucleophilic sites.

4 – Left and right derivatives

As mentioned before, in the analysis presented in the previous sections we have not taken into account that due to the behavior of the energy and of the density as a function of the number of electrons the derivatives around an integer number of electrons are different when taken from the left or from the right. This situation is also important from the chemical perspective, since one could expect that the response of a molecular system to charge acceptance is different from its response to charge donation. The development of the electrodonating and electroaccepting powers was, precisely, based on this differentiation^{18, 59}.

Thus, for charge donation processes, equation (2) should be rewritten as

$$\Delta E = \mu^- \Delta N^- + \frac{1}{2} \eta^- (\Delta N^-)^2, \quad (34)$$

while the expression for the charge density should be written as

$$\Delta \rho(\mathbf{r}) = f^-(\mathbf{r}) \Delta N^- + \frac{1}{2} \Delta f^-(\mathbf{r}) (\Delta N^-)^2, \quad (35)$$

indicating that if the reference system has N_0 electrons, $\Delta N \leq 0$, and the first and second derivatives are taken from the left. For charge acceptance processes, the corresponding expressions are

$$\Delta E = \mu^+ \Delta N^+ + \frac{1}{2} \eta^+ (\Delta N^+)^2, \quad (36)$$

and

$$\Delta \rho(\mathbf{r}) = f^+(\mathbf{r}) \Delta N^+ + \frac{1}{2} \Delta f^+(\mathbf{r}) (\Delta N^+)^2, \quad (37)$$

indicating that if the reference system has N_0 electrons, $\Delta N \geq 0$, and the first and second derivatives are taken from the right.

Thus, equation (2) corresponds to a smooth interpolation in which the first derivative of the energy with respect to the number of electrons, the chemical potential, evaluated at N_0 , is approximated by the average of the left and right first derivatives, that is,

$$\mu = \frac{1}{2}(\mu^- + \mu^+) \quad , \quad (38)$$

while the second derivative of the energy with respect to the number of electrons, the hardness, evaluated at N_0 , is approximated by the difference between the right and left first derivatives,

$$\eta = \mu^+ - \mu^- \quad . \quad (39)$$

According to the grand canonical ensemble to describe systems with a fractional particle number at 0 K, $\mu^- = -I$ and $\mu^+ = -A$, so that according to equations (38) and (39), $\mu = -(I + A)/2$ and $\eta = I - A$, which are the expressions normally used to determine the chemical potential and the hardness of a species.

On the other hand, the equivalent expressions for the derivatives of the charge density contained in equations (15) and (31) are

$$f(\mathbf{r}) = \frac{1}{2}(f^-(\mathbf{r}) + f^+(\mathbf{r})) \quad , \quad (40)$$

and

$$\Delta f(\mathbf{r}) = f^+(\mathbf{r}) - f^-(\mathbf{r}) \quad . \quad (41)$$

Thus, when one introduces a smooth interpolation for the first and second derivatives of the energy and the density, the response of the system to charge acceptance is the same as the response to charge donation. In the case of the energy, this approximation implies, according to equation (8) for the electroaccepting power, and according to equation (27) for the electrodonating power, that the quantity $\mu^2 / 2\eta$ provides a measure of these two powers. Although it is important to note that in the case of the electroaccepting power, the larger the value of this quantity, the greater the electroaccepting power, while in the case of the electrodonating power, the smaller the value of this quantity, the greater the electrodonating power. On the other hand, for the local quantities it is interesting to write the expressions with $f(\mathbf{r})$ and $\Delta f(\mathbf{r})$ given by equations (40) and (41), that is, for equation (15) one has that

$$\Delta\rho(\mathbf{r})_{Elec} = -\frac{\mu(f^+(\mathbf{r})+f^-(\mathbf{r}))}{\eta} + \frac{1}{2}\left(\frac{\mu}{\eta}\right)^2 (f^+(\mathbf{r})-f^-(\mathbf{r})) , \quad (42)$$

and for equation (31) one has that

$$\Delta\rho(\mathbf{r})_{Nuc} = \frac{\mu(f^+(\mathbf{r})+f^-(\mathbf{r}))}{\eta} + \frac{1}{2}\left(\frac{\mu}{\eta}\right)^2 (f^+(\mathbf{r})-f^-(\mathbf{r})) . \quad (43)$$

In both expressions μ is given by equation (38), and η is given by equation (39).

Now, since the chemical potential is negative, one can see that the two contributions of $f^+(\mathbf{r})$ in equation (42) add up, while the two contributions of $f^-(\mathbf{r})$ subtract up. This situation implies that the contribution to $\Delta\rho(\mathbf{r})_{Elec}$ from $f^+(\mathbf{r})$ with the presence of the first and second order terms is increased, with respect to having kept only the first term of the expansion of the electronic density change. On the other hand, the fact that the two contributions of $f^-(\mathbf{r})$ subtract up, implies that the contribution to $\Delta\rho(\mathbf{r})_{Elec}$ from $f^-(\mathbf{r})$ with the presence of the first and second order terms is decreased, with respect to having kept only the first term of the expansion of the electronic density change. Now, in the case of equation (43) the contributions to $\Delta\rho(\mathbf{r})_{Nuc}$ are the opposite, that is, since the first term is negative, then the presence of the first and second order terms of the expansion lead to an increment in the contribution of $f^-(\mathbf{r})$ and to a decrement in the contribution of $f^+(\mathbf{r})$, with respect to what one obtains if the expansion would have been truncated after the first order term.

Now, since the differentiation of the response of a system to charge acceptance and charge donation may be important from the chemical perspective, an alternative approach, as the one adopted in the analysis of the electrodonating and electroaccepting powers, could consist in differentiating the first derivative of the energy, and the first derivative of the density, but using for the second derivative of the energy, the smooth interpolation given by equation (39), and for the second derivative of the electronic density, the smooth interpolation given by equation (41). Through this approach, the electrophilicity, or electroaccepting power, according to equation (8) would be given by

$$\omega^+ = \frac{(\mu^+)^2}{2\eta} \quad , \quad (44)$$

while the electrodonating power, according to equation (27) would be given by

$$\omega^- = \frac{(\mu^-)^2}{2\eta} \quad . \quad (45)$$

On the other hand, for the local electrophilicity, equation (42) becomes

$$\Delta\rho(\mathbf{r})_{Elec} = -\frac{\mu^+}{\eta} f^+(\mathbf{r}) + \frac{1}{2} \left(\frac{\mu^+}{\eta} \right)^2 (f^+(\mathbf{r}) - f^-(\mathbf{r})) \quad , \quad (46)$$

while for the local nucleophilicity, equation (43) becomes

$$\Delta\rho(\mathbf{r})_{Nuc} = \frac{\mu^-}{\eta} f^-(\mathbf{r}) + \frac{1}{2} \left(\frac{\mu^-}{\eta} \right)^2 (f^+(\mathbf{r}) - f^-(\mathbf{r})) \quad . \quad (47)$$

Thus, an analysis of these two relationships as the one previously carried out in relation with equations (42) and (43), shows that in the case of equation (46) for the local electrophilicity, the contribution from $f^+(\mathbf{r})$ will be even greater to that in equation (42), while the contribution from $f^-(\mathbf{r})$ will also be larger. In the case of equation (47) for the local nucleophilicity, something similar will happen, with the roles of $f^+(\mathbf{r})$ and $f^-(\mathbf{r})$ interchanged.

It is interesting to note that if $f^+(\mathbf{r})$ is approximated by the density of the lowest unoccupied molecular orbital, $\rho_{LUMO}(\mathbf{r})$, and if $f^-(\mathbf{r})$ is approximated by the density of the highest occupied molecular orbital, $\rho_{HOMO}(\mathbf{r})$, equations (46) and (47) become

$$\Delta\rho(\mathbf{r})_{Elec} \approx -\frac{\mu^+}{\eta} \rho_{LUMO}(\mathbf{r}) + \frac{1}{2} \left(\frac{\mu^+}{\eta} \right)^2 (\rho_{LUMO}(\mathbf{r}) - \rho_{HOMO}(\mathbf{r})) \quad , \quad (48)$$

and

$$\Delta\rho(\mathbf{r})_{Nuc} \approx \frac{\mu^-}{\eta} \rho_{HOMO}(\mathbf{r}) + \frac{1}{2} \left(\frac{\mu^-}{\eta} \right)^2 (\rho_{LUMO}(\mathbf{r}) - \rho_{HOMO}(\mathbf{r})) \quad . \quad (49)$$

These expressions show that the local electrophilicity and the local nucleophilicity depend on both frontier orbitals, the HOMO and the LUMO.

5 – Application to some organic compounds

In order to test if the theoretical developments proposed in this work are able to reproduce correctly chemical reactivity and selectivity, they have been calculated for several organic compounds. Thus, $\Delta\rho(\mathbf{r})_{Nuc}$ and $\Delta\rho(\mathbf{r})_{Elec}$ have been computed for acetaldehyde and for a set of butyl-lithiums. Additionally, the local nucleophilicity has also been determined for two aromatic compounds, namely ortho-toluidine and ortho-nitro-toluene. The whole set of molecules has been selected because of their well known reactivity and selectivity trends. Besides, some of them exhibit an unambiguous ambiphilic character.

All the molecules have been fully optimized at PBE0/6-311G+(d,p) level of theory with Gaussian⁶⁰. The computations of both local electrophilicity and local nucleophilicity have been performed through equations (48) and (49), respectively. That is, the Fukui functions and the dual descriptor have been calculated through the frozen core approximation for simplicity. Additionally, to support the isosurface analysis, we have also calculated the condensed to atom values of the Fukui functions and the dual descriptor, which are given by

$$\Delta\rho_k^{Elec} = -\frac{\mu^+}{\eta} f_k^+ + \frac{1}{2} \left(\frac{\mu^+}{\eta} \right)^2 (f_k^+ - f_k^-) \quad , \quad (50)$$

and

$$\Delta\rho_k^{Nuc} = \frac{\mu^-}{\eta} f_k^- + \frac{1}{2} \left(\frac{\mu^-}{\eta} \right)^2 (f_k^+ - f_k^-), \quad (51)$$

with

$$f_k^- = q_k^{N-1} - q_k^N \quad , \quad (52)$$

and

$$f_k^+ = q_k^N - q_k^{N+1} \quad , \quad (53)$$

where q_k^N , q_k^{N-1} and q_k^{N+1} represent the net atomic charges of the k th atom in the molecule with N , $N-1$ and $N+1$ electrons, respectively. Note that since the sum of f_k^- or the sum of f_k^+ over all the atoms in a molecule is equal to one, then

$$\Delta N^{Elec} = \sum_k \Delta \rho_k^{Elec} = -\frac{\mu^+}{\eta} \quad , \quad (54)$$

and

$$\Delta N^{Nuc} = \sum_k \Delta \rho_k^{Nuc} = \frac{\mu^-}{\eta} \quad , \quad (55)$$

The net atomic charges of equations (52) and (53) were obtained through the Hirshfeld scheme.²³

i) Acetaldehyde

Acetaldehyde, just like other aldehydes and ketones displays a rich chemical reactivity⁶¹. The carbon of the carbonyl moiety is targeted by nucleophiles yielding enolate ions. On the other hand, the oxygen of the carbonyl group is able to complex metal cations and is easily protonated. Finally, the hydrogens borne by the carbon neighbor to the carbonyl (generally called alpha carbon) are acids and therefore mildly labile. Both local electrophilicity and nucleophilicity have been calculated and maps are displayed in Figures 1 and 2, respectively. Acetaldehyde atoms numbering is also represented in Figures 1 and 2. One can see from Figure 1 that the maximum of the local electrophilicity functions are located on the carbonyl carbon and to a lower extent on the oxygen. Condensed values given in Table 1 confirm this trend. Local electrophilicity on carbon is 0.022e while the one on oxygen is 0.015e. These results are in total agreement in relation with carbon, but are a bit unexpected for oxygen. The result on oxygen is very likely due to contribution of the π^* density to the electrophilic Fukui function. This contribution is obviously not completely cancelled by the contribution of the dual descriptor. Indeed the condensed value of the dual descriptor on oxygen is obviously negative since oxygen is rich in electrons and basically a nucleophile. As a consequence the dual descriptor contributes to locally decrease the condensed value of the electrophilicity power on oxygen.

From the map of the local nucleophilicity presented in Figure 2, it is observed that the main contribution comes from oxygen, confirming this way that oxygen is mainly targeted by cations. The condensed values are in total agreement with this conclusion, since oxygen exhibits the highest value. In fact, the condensed value on the oxygen (-0.30e) represents more than 40% of the maximum density that would be given away ($\Delta N^{Nuc} = -0.653e$) during an electrophilic attack.

ii) n-butyl-lithium, sec-butyl-lithium and ter-butyl-lithium

Butyl-lithium compounds are widely used in organic chemistry as bases and as nucleophiles. The chemical behavior of these molecules is mainly due to the highly polarized bond between the terminal carbon and the lithium atom.⁶² Local electrophilicity and local nucleophilicity functions for this set of compounds are displayed in Figures 3 and 4 with an isosurface value of 0.002 au. Experimental knowledge indicates that the electrophilicity moiety for these compounds is exclusively centered on the lithium atom. The local electrophilicity map represented on Figures 3a, 3b and 3c acutely reproduces this trend. It is clearly observed on these pictures that local electrophilicity is exclusively centered on the lithium for ter-butyl and sec-butyl and in a lower extent for n-butyl. For the latter compound, a part of the electrophilicity is located along the carbon-lithium bond. The condensed values are in full agreement with this observation. For the series n-butyl, sec-butyl, ter-butyl one finds 0.157e, 0.166e, and 0.197e, respectively.

On the other hand, the global nucleophilicity (Figures 4a, 4b and 4c) is expected to increase from n-butyl-lithium to ter-butyl-lithium.⁶³ Indeed, alkyl radicals are electron donating groups and contribute to the charge accumulation on carbon bonded to lithium. This trend is perfectly reproduced by ΔN^{Nuc} which is -0.780e, -0.782e, -0.793e for n-, sec- and ter-butyl-lithium, respectively. The condensed values are unfortunately not as good. The condensed values for the carbon linked to lithium are exhibiting an increase from -0.29e to -0.25e and -0.23e when one goes from n-butyl-lithium to ter-butyl-lithium. However, one would have expected a decrease (an increase in absolute value). This is likely due to a failure of the condensed values, since, as already observed, the global nucleophilicity does increase as expected. The failure is

likely due to an incorrect description of the condensed charges (Hirshfeld charges) because of the capability of the electron density to be spread on the alkyls groups bonded to the terminal carbon.

iii) Aromatic compounds

The last set of molecules is composed by two aromatic compounds. These chemicals, namely toluidine and ortho-nitro-toluene, have been chosen for their high selectivity ratio with respect to Aromatic Electrophilic Substitution (AES). Experimental results show that the product of AES for ortho-toluidine and ortho-nitro-toluene are very specific. Only the para derivative with respect to the exocyclic amino group is formed for the former,⁶⁴ while the latter give yield only to the *meta* with respect to the nitro group.⁶⁵ The results for these molecules are presented in Figures 5 and 6. The atom numbering is also displayed in both figures. During an AES both compounds act as nucleophiles and are targeted by electrophiles. Thus, for AES the relevant descriptor is the local nucleophilicity, which one can see that reproduces satisfactorily the experimental reactivity. For toluidine, the second highest condensed value is observed for the *para* carbon with respect to the amino group, with a value of -0.106e, the highest value being observed for the exocyclic nitrogen (-0.120e). One also observes some density located on the ipso carbon and the *ortho* carbon.⁶⁶ These are also expected and in agreement with experimental results. For ortho-nitrotoluene, the local nucleophilicity is centered on quite different atoms. Indeed, the highest condensed value is observed for the *meta* carbon (-0.162e), numbered C3 in Figure 6. The only other significant value is exhibited by carbon C6. The condensed value on carbon C6 is much lower than that of carbon C3 (-0.125e). The whole reactivity is therefore well reproduced by the local nucleophilicity descriptor.

6 – Conclusions

In this work, the concepts of electroaccepting power and electrodonating power have been revisited. Thus, the analysis of Parr and coworkers based in the canonical ensemble, to define the electrophilicity or electroaccepting power in terms of the stabilization process associated with the number of electrons that a system may accept, at constant external potential, when its chemical potential rises from μ to zero, is used within the grand-canonical ensemble, to define the nucleophilicity or electrodonating power in terms of the destabilization process associated with

the number of electrons that a system may donate, at constant external potential, when its chemical potential rises from μ to zero. In the canonical ensemble the energy change is given by $-\mu^2/2\eta$, while in the grand canonical ensemble the grand potential change is given by $\mu^2/2\eta$. Therefore, these results indicate that the quantity $\mu^2/2\eta$ is a rational choice for both concepts.

Additionally, it has been proposed that the local definitions associated to these concepts can be established through the actual changes of the electron density when it accepts $-\mu/\eta$ electrons, for the case of the local electrophilicity or local electroaccepting power, or when it donates μ/η electrons, for the case of the local nucleophilicity or local electrodonating power.

Previous definitions of the local electrophilicity and of the local nucleophilicity have been based on the use of the Fukui function to distribute the global property over the molecule. In the present work we have preferred to define these two quantities through the changes up to second order in the electronic density, so that the Fukui function and the dual descriptor are considered. The presence of the latter has two important consequences. The first one is that although $f^+(\mathbf{r})$ is the Fukui function for charge acceptance and $f^-(\mathbf{r})$ is the Fukui function for charge donation, equations (42) and (43) or equations (46) and (47), indicate that the local electrophilicity and the local nucleophilicity depend on both. The second one is that although $\Delta\rho(\mathbf{r})_{Elec}$ and $\Delta\rho(\mathbf{r})_{Nuc}$ depend on both Fukui functions, $f^+(\mathbf{r})$ has a greater weight in the local electrophilicity, and $f^-(\mathbf{r})$ has a greater weight in the local nucleophilicity as it could have been inferred on the basis of their chemical meaning. The same situation applies to equations (48) and (49), the local electrophilicity has a larger component of the LUMO, and the local nucleophilicity has a larger component of the HOMO, as it can be expected in association with the processes of charge acceptance and charge donation.

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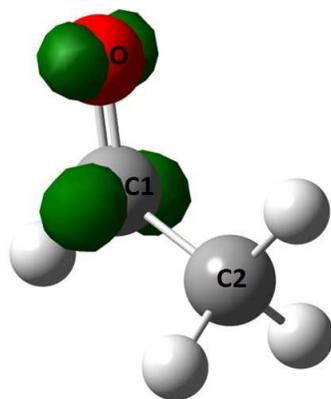


Figure 1. Local electrophilicity isosurface (0.002 au) for acetaldehyde.

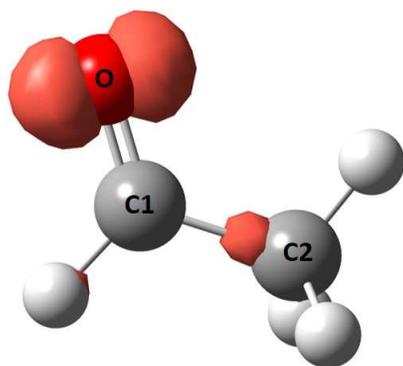


Figure 2. Local nucleophilicity isosurface (0.002 au) for acetaldehyde.

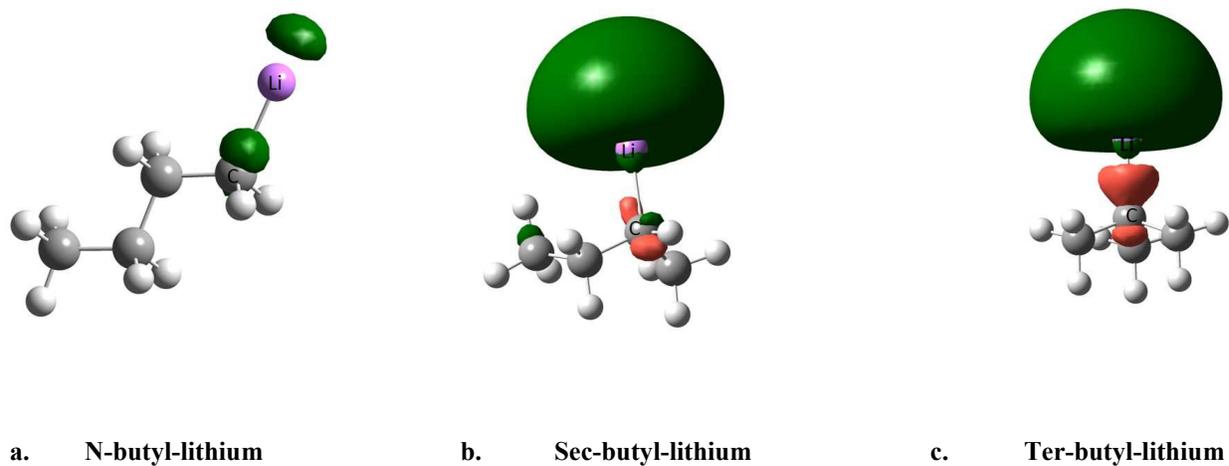


Figure 3. Local electrophilicity isosurfaces (0.002 au).

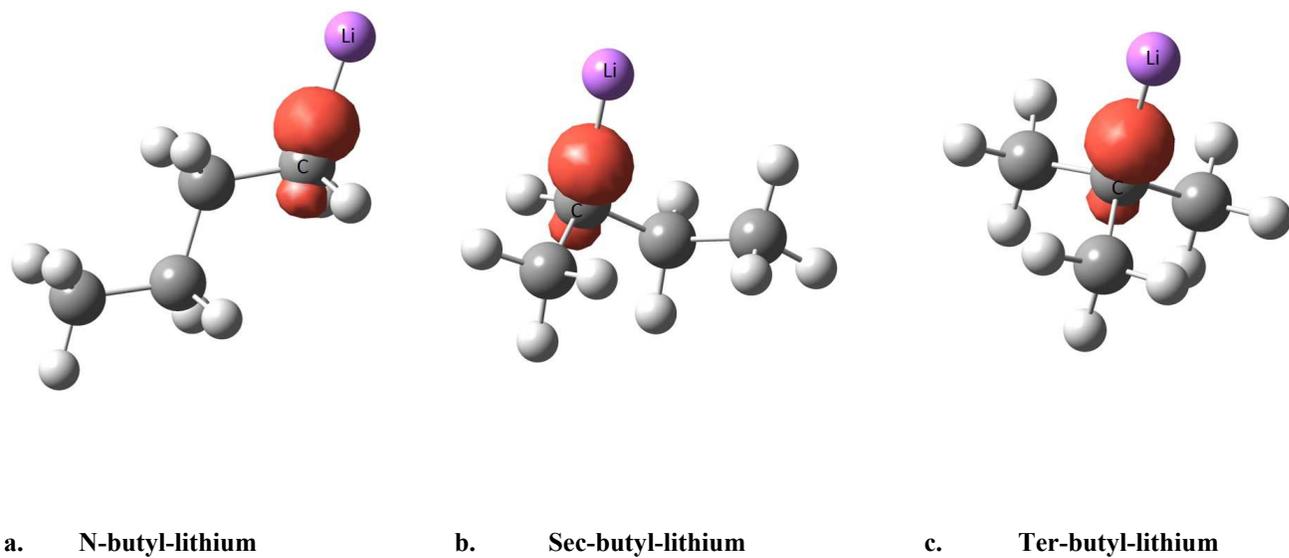


Figure 4. Local nucleophilicity isosurfaces (0.002 au).

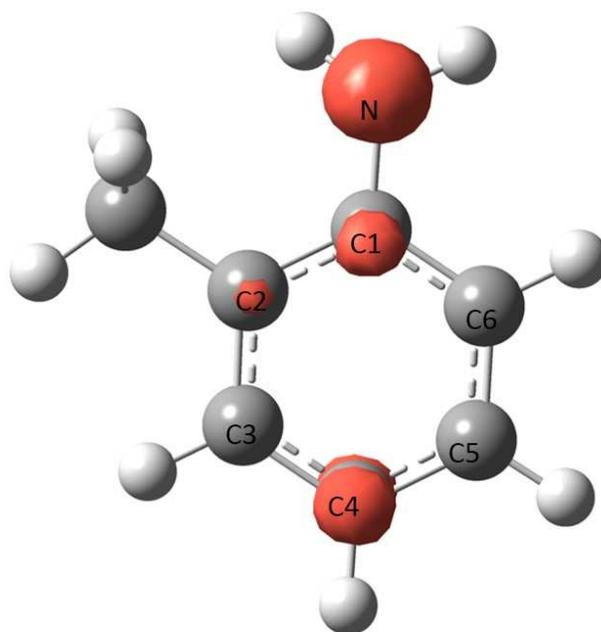


Figure 5. Local nucleophilicity isosurface (0.002 au) of toluidine (ortho-amino-toluene).

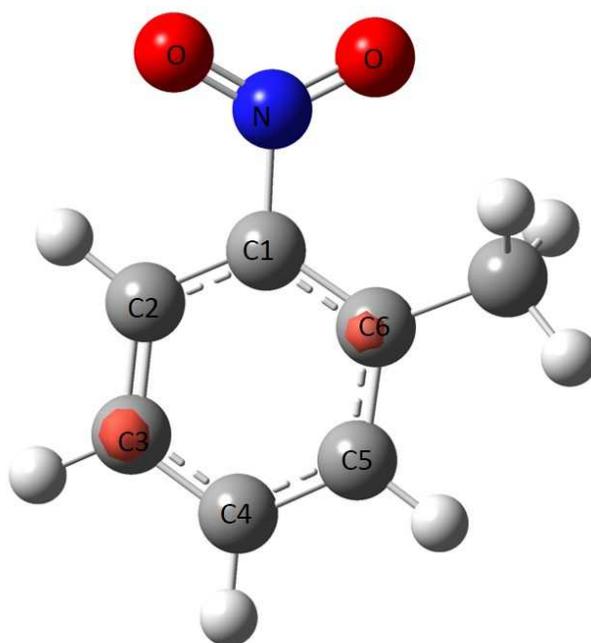


Figure 6. Local nucleophilicity isosurface (0.002 au) of ortho-nitro-toluene.

Table 1. Condensed Values of electrophilicity and nucleophilicity of acetaldehyde. Values in electrons.

Atom	$\Delta\rho_k^{Nuc}$	$\Delta\rho_k^{Elec}$
C1	-0.173	0.022
C2	-0.065	0.005
O	-0.302	0.015
	ΔN^{Nuc}	ΔN^{Elec}
	-0.653	0.066