J. Phys. Chem. A **1998,** *102,* 3607−3613

Reactivity Indices in Density Functional Theory: A New Evaluation of the Condensed Fukui Function by Numerical Integration

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Received: December 16, 1997; In Final Form: March 2, 1998

The condensed Fukui functions f_k of maleimide (1*H*-pyrrole-2,5-dione) have been calculated using a numerical integration scheme implemented in the deMon program package. The condensed functions show that soft nucleophiles interact with the α carbon atoms, whereas hard nucleophiles interact with the carbonyl carbon atoms, in accordance with the experimental evidence. The present method yields extremely few dispersed values of f_k, whatever the basis sets, the numerical grids, and the exchange-correlation functionals used. Finally, the validity of the method has been successfully tested on a set of organic and organometallic molecules.

1. Introduction

Density functional theory (DFT)[1] provides a very attractive framework for the quantitative description of global and local indices, which allow one to study the reactivity of chemical species.[2−5] Since the electron density distribution $\rho(r)$ contains all of the information on the system in its ground state, chemical reactivity should be reflected in its sensitivity to perturbations. Various electronic reactivity indices related to $\rho(r)$ have been hence identified, such as the Fukui function (softness) $f(r)$,[2,6] the condensed Fukui function f_k,[16] the local softness $s(r)$,[2,7] and the softness kernel $s(r,r')$.[2,6,8] In particular, Yang and Parr[9,10] have shown how calculated $f(r)$ values provide chemical information about properties of molecules. A description of the reactive site within a molecule and the reaction path are obtained from $f(r)$ and f_k, respectively. The condensed Fukui functions are generally extracted from Mulliken population analysis (gross charges) of atoms in a molecule. It is hence not surprising that numerous studies[11−15] concluded that f_k[16] is highly sensitive to both the basis sets and the atomic charge calculation scheme. A better evaluation of the condensed Fukui functions has to be found in order to get values independent from the computational conditions.

Despite the potential importance of the Fukui indices and functions in describing molecular reactivity, the subject of their accurate evaluation has not yet attracted adequate attention in the chemical literature. On the other hand, the field of numerical integration of Hamiltonian elements of polyatomic systems has been an intense subject of research during the past years.[17−19] An attractive method for evaluating the Fukui functions is to take advantage of recent progresses in the numerical integration schemes. The first *rational* method consists *of partitioning* a molecule into atoms and *mapping* the electron density. It provides hints as to where the borderline between vicinal atoms should be set.[20] Such a method does not fit to a picture of nearly spherical atoms but would reproduce the additivity of atomic volumes. A much more elaborate geometrical method has been proposed by Bader et al.,[21−23] who established general conditions for the borderline between atoms as the zero flux of electron density. On the other hand, Parr has introduced an alternative method within the DF framework.[24] In that case, the molecular density is the sum of the atomic densities at every point of the space within the system, where atoms have equal chemical potentials. Electron density is a *local value* that does not distinguish between parts of a molecule, and its decomposition into contributions from individual atoms has not been pursued.

Becke[17] proposed another simple scheme for decomposition of molecular functions into single-center components, so-called *fuzzy cells*. The latter has been largely implemented in DFT codes[25,26] and has been used to calculate the functions $f(r)$ and f_k performed with the deMon program package.[26]

This paper intends to verify the reliability and the accuracy of this method for the calculation of both $f(r)$ and f_k. Section 2 briefly reviews theoretical concepts and computational details, emphasizing the points that are important for the present calculations. Section 3 outlines the main results of test calculations performed on maleimide with different sets of basis sets, numerical grids, and exchange-correlation functionals. Finally, section 4 underlines the interest in using condensed Fukui functions as a reliable tool for studying reactivity or catalytic properties of selected molecules. It is not our purpose to present developments[17−29] in the theory of numerical integration in the present paper.

2. Theory and Computational Details

2.1. Fukui Function as a Reactivity Index. In DFT, the fundamental differential expression for the change in energy from one ground state to another is[2]

$$dE = \mu \, dN + \int \rho(r) \, \delta v(r) \, dr \tag{1}$$

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S1089-5639(98)00521-0 CCC: $15.00

where N, $\rho(r)$, and $\nu(r)$ are the total number of electrons, the density, and the external potential, respectively. The quantity μ is the electronic chemical potential defined as

$$\mu = (\partial E/\partial N)_{\nu(r)} = -\chi \tag{2}$$

The connection with classical chemistry is achieved with the identification of μ as the negative of electronegativity χ. The latter is a property of the state of the system, and it drives electron transfer. It may easily be calculated from the above expression or determined from experiment.

The first partial derivative of μ with respect to N yields the global hardness (the inverse of global softness S).[2,7] The factor $^1/_2$ originally introduced[30] has been omitted. It follows

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

The finite-difference approximation for this is[2]

$$\eta \cong (I - A) \geq 0 \tag{4}$$

where I and A are the ionization potential and the electron affinity, respectively. This global quantity is sometimes called *absolute* hardness to emphasize the fact that the effective hardness of an atom in a molecule can differ from its atomic hardness.[31] The hardness can be thought of as a resistance to charge transfer, while the softness measures the ease of transfer and is associated with high polarizability.[32]

The frontier orbitals are involved in a quantity called the Fukui function $f(r)$, first introduced in the 1980s by Yang and Parr.[6] They defined $f(r)$ as the partial derivative of $\rho(r)$ with respect to the number of electrons, at constant external potential $\nu(r)$. A Maxwell relation[2] links the chemical potential μ and $f(r)$ as

$$f(r) = \left(\frac{\partial \rho(r)}{\partial N}\right)_{\nu} = \left(\frac{\partial \mu}{\partial \nu(r)}\right)_{N} \tag{5}$$

This assumes that both the chemical potential and the electronic density are differentiable functions of N, while this might be not the case for the exact functional in a finite system.[3,33] Due to the discontinuity of this derivative,[6] Yang and Parr proposed to associate it different reactivity indices. In the case of nucleophilic attack on the system,

$$f^{+}(r) = \left(\frac{\partial \rho(r)}{\partial N}\right)_{V}^{+} \tag{6}$$

In case of an electrophilic attack,

$$f^{-}(r) = \left(\frac{\partial \rho(r)}{\partial N}\right)_{V}^{-} \tag{7}$$

And in the case of a radical attack,

$$f^{0}(r) = \frac{1}{2}\left(\left(\frac{\partial \rho(r)}{\partial N}\right)_{V}^{+} + \left(\frac{\partial \rho(r)}{\partial N}\right)_{V}^{-}\right) = \frac{1}{2}(f^{+}(r) + f^{-}(r)) \tag{8}$$

where the superscripts + and − refer to the right and the left derivatives, respectively. Because the evaluation of these derivatives is quite complicated, Yang and Parr have proposed a finite difference scheme to evaluate $f(r)$,[7,34]

$$f^{+}(r) \cong \rho_{N+1}(r) - \rho_{N}(r) \tag{9}$$

$$f^{-}(r) \cong \rho_{N}(r) - \rho_{N-1}(r) \tag{10}$$

$$f^{0}(r) \cong \frac{1}{2}(\rho_{N+1}(r) - \rho_{N-1}(r)) \tag{11}$$

where $\rho_{N+1}(r)$, $\rho_{N}(r)$, and $\rho_{N-1}(r)$ are the electronic densities of the system with $N + 1$, N, and $N - 1$ electrons, respectively.

Similarly, the finite difference approximation leads to the condensed Fukui functions f_k,[16]

$$f_k^{+} = q_k(N{+}1) - q_k(N) \tag{12}$$

$$f_k^{-} = q_k(N) - q_k(N{-}1) \tag{13}$$

$$f_k^{0} = \frac{1}{2}(q_k(N{+}1) - q_k(N{-}1)) \tag{14}$$

The gross charge q_k of atom k is generally calculated from a Mulliken population analysis and leads to f_k largely depending on the choice of basis set.[11−15] In the present work, integrating the density of each single center of the system has allowed *us* to derive the q_k values.

2.2. Computational Method. The linear combination of the Gaussian-type orbital−model core potential−density functional theory (LCGTO-MCP-DFT) method[35−37] and its corresponding deMon package[26] has been used. The local softness $s(r)$, the Fukui functions $f(r)$, and the condensed Fukui functions f_k of maleimide have been determined through a finite difference scheme. In order to explore consistently the influence of the computational conditions on f_k, a set of six radial grids, three angular grids, five exchange-correlation functionals, and six basis sets have been used in this work. It led to a set of 7650 calculated condensed Fukui functions.

Following the scheme proposed by Becke,[17] the three-dimensional space has been divided into weighted atomic subregions, reducing the integration problem to single-center integrations.[37] The Gauss−Legendre quadrature[37,38] and the Lebedev scheme[39] have been used for the radial and for the angular integrations, respectively. The number of radial points per atom (N_{rad}) has been chosen as $N_{\mathrm{rad}} = 32$, 40, 48, 64, 96, and 128. The Lebedev angular integration scheme[39] is known to be very efficient, leading to the highest accuracy for the smallest number of points.[17,37,40] Because the distribution of the electronic density in not uniform, the number of angular points for each radial shell has been enlarged where the angular variation of the density is the largest.[37] The angular grid has been divided in a subset of three numerical grids, (i) medium, (ii) fine, and (iii) extrafine, corresponding to 3000, 5600, and 11000 angular points ($N_{\mathrm{rad}} = 64$), respectively. Goursot et al.[37] have shown that reliable calculated molecular properties can be obtained by combining 64 radial points with the fine angular grid, at least for elements with $Z < 60$. The Vosko−Wilk−Nusair (VWN)[41] and the Xα[42] exchange-correlation potentials have been used in the local approximation. On the other hand, the Becke 1988 exchange[43] coupled to the Perdew−Wang gradient-corrected correlation functionals[44] (Be88−PW91), the Becke 1988 exchange[43] with the Perdew 1986 correlation functionals[45] (Be88−P86), and the Perdew−Wang 1986 exchange[46] coupled to the Perdew 1986 correlation[45] (PW86−P86) have been the three combinations used as nonlocal exchange-correlation functionals. A subset of six basis sets has been used for C, N, O, and H atoms, and the contraction patterns are displayed in Table 1. The structural parameters of maleimide have been taken from a previous work of Méndez et al.[47] and have been kept fixed during all calculations.

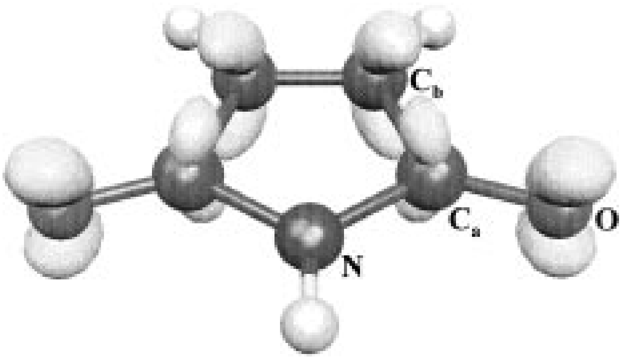

Figure 1. Fukui function $f^+(r)$ isosurfaces for maleimide molecule (0.001 au).

TABLE 1: Combinations of Basis Sets Used in the Calculations of the Condensed Fukui Functions f_k

basis	H	C	N	O
set 1	(41)	(521/41)	(521/41)	(521/41)
set 2	(31/1)	(631/31/1)	(631/31/1)	(631/31/1)
set 3	(311/1)	(6311/311/1)	(6311/311/1)	(6311/311/1)
set 4	(41/1)	(5211/411/1)	(5211/411/1)	(5211/411/1)
set 5	(41/1*)	(621/41/1*)	(621/41/1*)	(621/41/1*)
set 6	(41/1*)	(7111/411/1*)	(7111/411/1*)	(7111/411/1*)

TABLE 2: Condensed Fukui Function[a]

	f_k^+	f_k^-	f_k^0
(a) Determined by Numerical Integration			
C_a	0.0901	0.0715	0.0808
C_b	0.1347	0.0607	0.0977
variance $f_k(C_a)$	6.68×10^{-5}	5.68×10^{-6}	3.85×10^{-6}
variance $f_k(C_b)$	1.13×10^{-5}	7.34×10^{-7}	3.77×10^{-6}
(b) Calculated from Mulliken Population Analysis			
C_a	0.0847	0.0757	0.0802
C_b	0.1438	0.0718	0.1078
variance $f_k(C_a)$	2.05×10^{-3}	1.44×10^{-2}	4.69×10^{-3}
variance $f_k(C_b)$	1.30×10^{-3}	3.78×10^{-3}	1.30×10^{-3}

[a] The values displayed have been averaged on the whole set of data.

3. Results and Discussion

3.1. Importance of the Computational Conditions on the Values of f_k. A set of 7650 f_k values (full data are available on request from the authors) was obtained by numerical integration for all combinations by varying the basis sets, the radial and the angular grids, and the exchange-correlation functionals. Within this context, we considered the behavior of the maleimide molecule with respect to nucleophilic attack. The experimental evidence shows that generally soft nucleophiles interact with the maleimide C atoms located at the α positions, (C_b), whereas hard nucleophiles interact with the carbonyl carbons (C_a).[48] The f_k value of each atom in a molecule reflects its relative softness.[2,9] Figure 1 displays isosurfaces of $f(r)$. It shows that the surface is more extended at C_b than at C_a. It indicates that the tendency of C_b for accepting electrons during the nucleophilic attack on maleimide is stronger than the carbonyl carbon atom. Moreover, the shape of $f^+(r)$ suggests that nucleophilic reagents approach the carbon atoms from the direction almost perpendicular to the molecular plane. Parts a and b of Table 2 display the calculated values of f_k. They show that f_C^+ takes a larger value at the α carbon than at the carbonyl carbon atom, suggesting that the latter is the hardest.[47] This is in agreement with the experimental findings.[48] The f_C values obtained by numerical integration are similar to those based on the Mulliken population analysis, but the dispersion of the latter is larger.

Although the dispersion of the computed f_k^+ is very small ($\sim 10^{-6}$), we performed a simplified analysis of variance of the data in order to establish the importance of the sources of dispersion of the number obtained. For the sake of clarity, parts a−d of Table 3 display only the values at the C atoms, namely, f_C^+. A careful analysis of the data shows that the values of f_C^+ are very similar for each subset of data. We have to point out that the value of the variance never exceeds 10^{-5}. Whereas the radial and angular grids do not contribute to a statistically significant dispersion (see Table 3a,b), the first source of

TABLE 3: Condensed Fukui Function Determined by Numerical Integration

(a) Effects of the Radial Grid

	32 points	40 points	48 points	64 points	96 points	128 points
$f_k^+(C_a)$	0.0901	0.0899	0.0903	0.0903	0.0904	0.0901
$f_k^+(C_b)$	0.1348	0.1347	0.1347	0.1347	0.1349	0.1345
variance $f_k^+(C_a)$	6.85×10^{-6}	6.53×10^{-6}	6.74×10^{-6}	6.71×10^{-6}	6.73×10^{-6}	6.85×10^{-6}
variance $f_k^+(C_b)$	1.09×10^{-5}	1.11×10^{-5}	1.17×10^{-5}	1.18×10^{-5}	1.14×10^{-5}	1.18×10^{-5}

(b) Effects of the Angular Grid on f_k

	medium	fine	extra-fine		medium	fine	extra-fine
f_k^+(Ca)	0.0901	0.0899	0.0904	variance $f_k^+(C_a)$	5.49×10^{-6}	7.13×10^{-6}	7.31×10^{-6}
$f_k^+C_b)$	0.1370	0.1337	0.1335	variance $f_k^+(C_b)$	9.66×10^{-6}	8.10×10^{-6}	8.85×10^{-6}

(c) Effects of the Basis Set on f_k

	basis set 1	basis set 2	basis set 3	basis set 4	basis set 5	basis set 6
$f_k^+(C_a)$	0.0935	0.0918	0.0871	0.0881	0.0910	0.0898
$f_k^+(C_b)$	0.1312	0.1366	0.1325	0.1332	0.1392	0.1362
variance $f_k^+(C_a)$	9.53×10^{-7}	7.25×10^{-7}	1.72×10^{-6}	3.77×10^{-6}	7.08×10^{-7}	8.36×10^{-7}
variance $f_k^+(C_b)$	3.00×10^{-6}	2.13×10^{-6}	5.31×10^{-6}	2.07×10^{-6}	3.11×10^{-6}	3.79×10^{-6}

(d) Effects of the Exchange-Correlation Functionals on f_k

	VWN	Xα	PW86−P86	Be88−P86	Be88−PW91
$f_k^+(C_a)$	0.0914	0.0891	0.0900	0.0903	0.0900
$f_k^+(C_b)$	0.1339	0.1354	0.1347	0.1344	0.1351
variance $f_k^+(C_a)$	5.06×10^{-6}	8.29×10^{-6}	4.94×10^{-6}	6.53×10^{-6}	5.04×10^{-6}
variance $f_k^+(C_b)$	9.22×10^{-6}	8.83×10^{-6}	1.31×10^{-5}	1.18×10^{-5}	1.44×10^{-5}

TABLE 4: Condensed Fukui Function of Various Chemicals Determined by Numerical Integration

(a) Formaldehyde

elements	f_k^+	f_k^-	f_k^0
C	0.4004	0.1836	0.2920
O	0.2435	0.4570	0.3503
H	0.1789	0.1797	0.1793

(b) Hydroxylamine

elements	f_k^+	f_k^-	f_k^0
N	0.0797	0.3953	0.2375
O	0.2614	0.2394	0.2504
H[a]	0.3821	0.1108	0.2465
H[b]	0.1378	0.1273	0.1325
H[b]	0.1378	0.1273	0.1325

(c) Maleic Anhydride

elements	f_k^+	f_k^-	f_k^0
C_a[c]	0.0898	0.0756	0.0827
C_b[b]	0.1337	0.0617	0.0977

(d) Pd(phosphine)(imine)

	C	$C_{trans-N}$	$C_{trans-P}$
f_k^+	0.0389	0.0441	0.0646

[a] Bonded to the O atom. [b] Bonded to the N atom. [c] In C═O. [d] Bonded to C═O.

scattering comes from the basis set. Table 3c shows that the basis sets leading to the less scattered values are either the largest one or the smaller one, more contracted. The reason of such behavior is not clear. The second source of dispersion is the exchange-correlation functional. The scattering is slightly larger for the softest carbon atoms when nonlocal corrections are included, while this trend does not emerge for the carbonyl carbon atoms. This is probably due to the fact that soft atoms have more diffuse electronic densities than hard atoms.

The covariance of the sample is roughly 10% of the variance of the data. The same trend is observed for both f_k^0 and f_k^-, whatever atom is taken into account in the molecule (N, O, H). It suggests that the sample values are independent;[49] i.e. the values of the condensed Fukui functions do not depend on the computational conditions. The stability of the f_k values to changes in the computational details is very gratifying; it concerns both the numerical parameters, such as basis sets or numerical grids, and the physical model through the choice of the exchange-correlation functional. This last point corroborates the work of Langenaeker et al.[50] who have shown that the electron correlation has a reduced influence on the Fukui function.

3.2. Condensed Fukui Function for Selected Molecules. We first discuss formaldehyde, a simple system extensively studied in past years.[9,51,52] The structure has been optimized at the DFT−BP86 level using *set 4 (Table 1)* as the basis sets. The condensed Fukui functions are displayed in Table 4a. The acid- and base-catalyzed hydration mechanisms of aldehydes[51] show that for the acid-catalyzed hydration, H^+ electrophilic attack at oxygen should occur ($f_O^- > f_C^-$), and for the base-catalyzed mechanism, OH^- nucleophilic attack at carbon should occur ($f_C^+ > f_O^+$). The Fukui functions $f(r)$ lead to the same conclusions but give more information about the reaction path.[2,9] Isosurfaces of $f(r)$ are displayed in Figure 2a,b. From Figure 2a, it can be seen that the surface is more extended at the carbon atom than at the oxygen atom. This means that the tendency of the carbon atom for accepting electrons during nucleophilic attack on H_2CO is stronger than the oxygen atom. In addition, the shape of $f^+(r)$ suggests that nucleophilic reagents approach the carbon atom in formaldehyde from the direction almost perpendicular to the molecular plane. The calculated angle attack is 115°. This result is in excellent agreement with the work of Bürgi et al.[52] who found an angle of 109°. On the other hand, Figure 2b suggests that the direction of the electrophilic attack lies in the molecular plane and is directed toward the lone pairs of the oxygen atom.

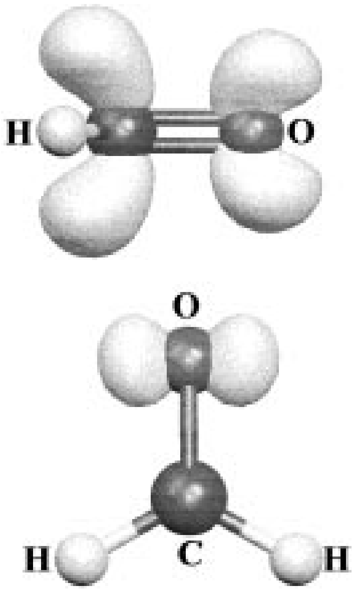

Figure 2. Fukui function $f^+(r)$ (a, top) and $f^-(r)$ (b, bottom) isosurfaces for H_2CO molecule (0.001 au).

Molecules that contain several reactive sites are optimal candidates for testing the current method. Hydroxylamine and maleic anhydride (furan-2,5-dione) are one of such candidates that exhibit different regioselectivities with respect to electrophilic and nucleophilic attacks, respectively. Protonated species are known to be crucial intermediates for ion−molecule reactions in space chemistry. Though not yet identified in the list of NO containing interstellar molecules, hydroxylamine is an interesting system that possesses two competitive sites of protonation. Recently, this reaction has been extensively investigated by Boulet et al.[53] using high levels of post-Hartree−Fock treatments and DFT. They have shown that the *N-protonated* form is more stable than the *O-protonated* form by roughly 25.0 kcal/mol. We have calculated the condensed Fukui functions on a structure optimized at the DFT−BP86 level using *set 4 (Table 1)* as the basis sets. The f_k values are displayed in Table 4b. It is shown that f_N^- is larger than f_O^-, suggesting the most electrophilic site at the nitrogen atom. As described above, the direction of the attack is indicated by the Fukui function, displayed in Figure 3. It can be seen that the shape of the isosurface is more extended at the nitrogen atom. This suggests that an electrophilic reagent should approach the nitrogen atom in hydroxylamine in the NOH plane. Unfortunately, experimental findings are unavailable in this case.

Maleic anhydride and maleimide molecules are similar systems, and both have different reactive regions with respect to nucleophilic attacks. We have calculated the condensed Fukui functions on structures optimized at the DFT−BP86 level using *set 4 (Table 1)* as the basis sets. Table 4c and Figure 4 display the calculated f_k values and isosurfaces of $f(r)$, respectively. The condensed Fukui functions calculated for maleic anhydride lead to identical conclusions as for maleimide, discussed in the previous section. Hard nucleophiles react with the carbonilic group, while soft nucleophiles react with the α

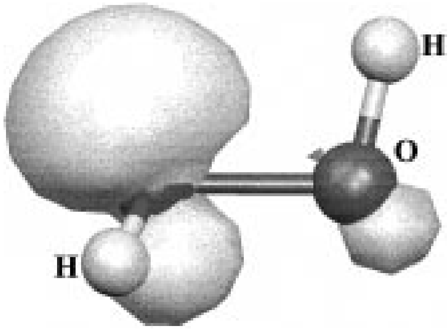

Figure 3. Fukui function $f^-(r)$ isosurfaces for hydroxylamine molecule (0.001 au).

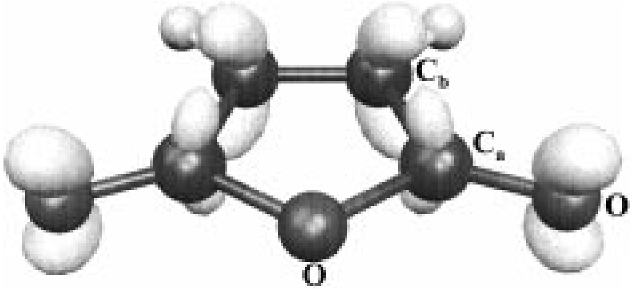

Figure 4. Fukui function $f^+(r)$ isosurfaces for maleic anhydride molecule (0.001 au).

carbon. The calculated f_C^+ values do not only exhibit differences in softness for the two kinds of carbon atoms in the two molecules but also suggest that the carbonyl group in maleic anhydride is slightly harder than in maleimide ($f_{C^+\ \mathrm{Maleimide}} > f_{C^+\ \mathrm{Anhydride}}$). This suggests to us that the condensed Fukui function gives a good description of both the intrinsic and the relative reactivity within a molecule. However, this encouraging result has to be confirmed by specific studies.

We conclude by exploring a catalytic system. In the field of enantioselective catalysis, bidentate C_2 symmetric ligands have proven to be extremely versatile.[54] Their square planar complexes are dissymmetric and have two *trans*-sites electronically equivalent. The diastereoselective addition of prochiral substrates is thus governed by steric requirements of the ligand and the substrate. The resulting complex is asymmetric, and further reaction often proceeds to yield enantiomerically enriched products. More recently, chiral bidentate ligands with two different donors have attracted attention. Here, a prochiral substrate is desymmetrized not only by steric factors but also through the electronic asymmetry induced by the bidentate ligand.[55−57] A major breakthrough was achieved in palladium-catalyzed functionalization of allylic substrates,[58] catalyzed by {Pd(phosphine)(imine)} complexes.[59−67] For a symmetrical 1,3-disubstituted allyl coordinated in an η^3-mode, attack at C1 or C3 yields the opposite enantiomers. Therefore, the site of nucleophilic attack determines chirality of the product, provided the catalytically active complex shows a single reactive geometry. In the following, the carbon atoms C1 and C3 are distinguished via the different donor atoms in the *trans*-position and are called $C_{trans-P}$ and $C_{trans-N}$, respectively. However, under reaction conditions, the rotation of the allyl averages both sites with respect to the electronic asymmetry and thus precludes a direct and unambiguous correlation between the site of attack and the observed configuration of the product (see Figure 5a). Recently there has been accumulating indirect evidence that a nucleophilic attack on coordinated allyls occurs at $C_{trans-P}$.[61,64,67] Theoretical analyses, both at the extended Hückel[68] and DFT[69] approximation levels, have rationalized these observations.

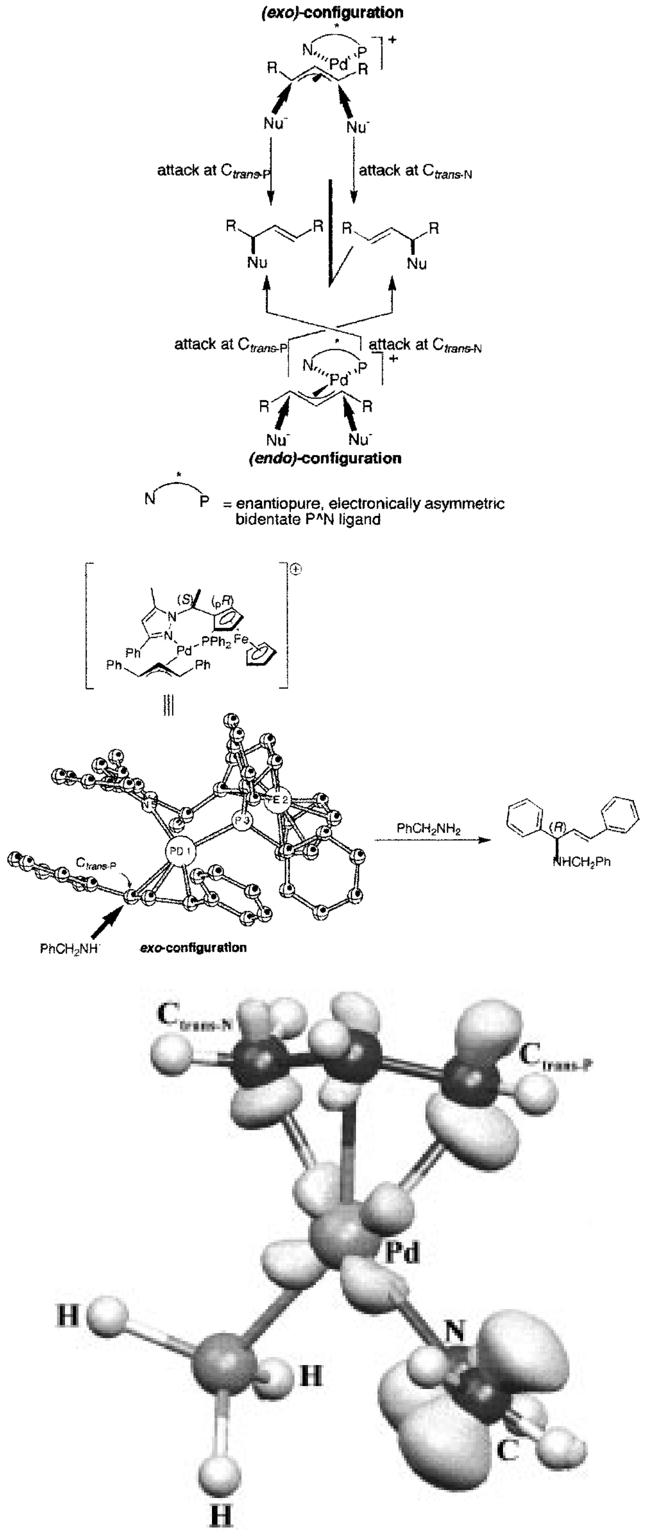

Figure 5. (a, top) Four possible nucleophilic attacks on the diphenylallyl coordinated to the electronically asymmetric {Pd(phosphine)(imine)} fragment. (b, middle) Nucleophilic attack at the $C_{trans-P}$ in the *exo*-{Pd(phosphine)(imine)(allyl)}$^+$, yielding the (*R*) product. (c, bottom) Fukui function $f^+(r)$ isosurfaces for the catalyst precursor (0.001 au).

Mechanistic considerations for the palladium-catalyzed allylic alkylation point toward an early transition state, and therefore, the most electrophilic center of the coordinated allyl in the ground state reacts, leading to the major enantiomer of the product.[70,71] Calculations on related systems reveal that the reaction is frontier orbital controlled rather than charge controlled, since this latter would yield a nucleophilic attack on the central carbon.[72]

The reactivity indices we have implemented are ideally suited to predict the site of nucleophilic attack on coordinated allyls as the site of reactivity and, thus, the enantioselectivity are largely determined by the relative electrophilicity of $C_{trans-P}$ vs $C_{trans-N}$.

For the calculations, we used a simplified model of the catalyst precursor depicted in Figure 5b. Its structure was recently reported by Togni et al.[67] The P and Pd atoms were described by basis sets having the contraction patterns P(6321/521/1) and Pd(633321/53211/531). The remaining of the system has been depicted by *set 4*. In a typical enantioselective catalytic allylic amination experiment, the catalyst with absolute configuration $(S)-({}_{p}R)$ (see Figure 5b) yields predominantly a product with absolute (*R*)-configuration (enantiomeric excess = 95%). This product can either arise from a nucleophilic attack at $C_{trans-P}$ in the *exo* configuration or at $C_{trans-N}$ in the *endo* configuration (see Figure 5a). Keeping the geometry frozen, the phosphine donor was modeled by a PH_3 and the pyrazole was modeled by an imine $HN{=}CH_2$. From both our reactivity index computations (see Table 4d) and Fukui functions (see Figure 5c), it appears clearly that the $C_{trans-P}$ is more electrophilic than $C_{trans-N}$. The carbon atom coordinated to the nitrogen atom has a smaller value of f_k than the $C_{trans-P}$, and it is not taken into account. Considering that the isolated aminated product has an (*R*) absolute configuration, we can unambiguously conclude that the nucleophilic attack occurs at $C_{trans-P}$ on the *exo* configurated allylic intermediate (see Figure 5b).

4. Conclusion

We have shown how calculated Fukui functions provide useful chemical information about the properties of molecules. The reactive site within a molecule may be identified from the condensed Fukui functions and the reaction path from the Fukui function isosurfaces. The values of f_k are usually derived from a Mulliken population analysis, which is very sensitive to the basis sets. The present study shows that the numerical integration provides reliable results independent from the computational conditions. Although the present method was applied to a reduced set of molecules, it reveals a fast and efficient tool for understanding and predicting the electronically controlled chemical reactivity.

Acknowledgment. The authors are grateful to Professor D. R. Salahub for providing a copy of the deMon program and to Professor C. Daul, M. Grigorov, and P. Boulet, for fruitful discussions. Financial support by the Swiss National Science Foundation is gratefully acknowledged.

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