



## A Brief Note on the Numerical Stability of Some Local Atomic Static Reactivity Indices. A Hartree-Fock/STO-3G Example

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**Abstract** Local atom reactivity indices need to be numerically stable. This means that, if for example there is not a breaking off of a pi conjugated system or a creation of intramolecular bonds, the numerical values of a local atomic reactivity index should not change notably. Earlier studies with the semiempirical CNDO/2 method showed abnormal numerical variations of the nucleophilic superdelocalizability with conformational changes in p-hydroxy-β-phenylethylamine. Here we explore the variation of the numerical values of the net charge and both superdelocalizabilities in two atoms same molecule but at the HF/STO-3G level. All indices showed numerical stability. These results are discussed.

**Keywords** Hartree-Fock/STO-3G, reactivity indices, superdelocalizabilities, p-hydroxy-β-phenylethylamine

### 1. Introduction

Total atomic net charges (Q), electrophilic (SE) and nucleophilic (SN) superdelocalizabilities are some static atomic reactivity indices which have been employed with success in many formal Quantitative Structure-Activity Relationships studies [1-3]. For a given atom p, the superdelocalizabilities are defined as:

$$S_p = 2.0 \sum_n^{\text{MO}} \sum_j^{\text{AO}} c_{jn}^2 / E_n \quad (1)$$

where  $E_n$  is the energy of the n-th Molecular Orbital (MO),  $c_{jn}$  is an LCAO coefficient and the summation on j runs over the atomic orbitals of atom p contributing to the AO basis set. If we take n over the occupied MOs, we get  $SpE$  and if we conduct the summation over the virtual MOs we get  $SpN$ . The physical meaning of  $SpE$  and  $SpN$  within a molecular system are, respectively, the relative electron-donor and electron-acceptor capabilities of a given atomic center [4]. Note that the eigenvalues of the occupied MOs are negative and that the values of the virtual ones should be positive. Also note that in  $SpE$  the dominant terms are the ones corresponding to the higher occupied MOs. In the case of  $SpN$  the dominant terms are those corresponding to the lowest virtual MOs.

Now, let us consider a series of molecules having a common set of atoms (a common skeleton) and substituents that can function as perturbations on them. The use of the superdelocalizabilities (SDs) has proven to be particularly useful (Razzak and Glen made a serious conceptual mistake when commenting on them [5]). From the theoretical point of view, we should expect that it is expected that, in general that the values of the net charges and superdelocalizabilities do not vary significantly in the various rotamers of a molecular system.



On the other hand, atomic calculations strongly suggest that for neutral systems the numerical Hartree-Fock (HF) equations have not discrete solutions other than the ground-state orbitals: all other eigenvalues lying in the continuum. Therefore, the Virtual Molecular Orbitals (VO) are an artifact of using a finite expansion in the HF equations. Although a severely restricted basis set may accidentally mimic the properties of an excited state, the VOs have no chemical or physical significance. At most they could describe the states of a hypothetical test electron moving in the field of the whole neutral molecule. In minimal basis set calculations, such as the STO-3G one, the valence VOs have their maxima in the same region as the occupied valence orbitals. For these reasons, we can use the VOs and their calculated energies as a rough approximation to the higher SCF orbitals and energies.

Given that SpN is calculated from VO data of a single point SCF calculation, we may face any one of the following problems:

1. One or more VOs have negative eigenvalues.
2. Incorrect VO electronic density distribution.

A preliminary analysis of the first problem indicates that in this case the numerical value of SpN cannot be used because around the energy zero there is an arithmetic cancellation of positive and negative values. The second problem is more complicated to solve because it requires a series of calculations that we are trying to avoid. Anyway, the use of virtual MOs in the Hartree-Fock and Density Functional Theory (DFT) has become a usual working method.

An analysis of the numerical stability of some reactivity indices was conducted longtime ago for the CNDO/2 semi-empirical method [6]. The systems studied were a set of rotamers of p-hydroxy- $\beta$ -phenylethylamine in its neutral and protonated forms. This method employs a minimal basis set of valence Slater AOs with fixed orbital exponents on each atom, its aim being to reproduce as well as possible the results of minimal basis set ab initio SCF-MO calculations. Therefore, for the effect of comparison and to close this theoretical problem, we analyze here the same system above mentioned and the same reactivity indices but within an ab initio formalism and a STO-3G basis set.

## 2. Results and Discussion

The Monstergauss set of programs [7] was used for all calculations, retaining the same geometry as for CNDO/2 studies.

The calculated reactivity indices are shown in Tables 1 and 2. The relative positions of the OH group and the amine chain are referred to by cis and trans; parallel (||) and perpendicular ( $\perp$ ) refer to the position of the substituents in relation to the phenyl ring.

**Table 1:** Reactivity indices of the carbon (OH) atom for some rotamers of the p-hydroxy- $\beta$ -phenylethylamine (au)

| Form       | Position of OH and ethylamine groups | Qc   | Sc <sup>E</sup> | Sc <sup>N</sup> |
|------------|--------------------------------------|------|-----------------|-----------------|
| Basic      | N  , O $\perp$                       | 0.12 | -161.95         | 485.55          |
|            | cis, N $\perp$ , O $\perp$           | 0.12 | -161.67         | 486.37          |
|            | trans, N $\perp$ , O $\perp$         | 0.12 | -161.70         | 486.30          |
|            | cis, N  , O                          | 0.13 | -156.61         | 488.58          |
|            | trans, N  , O                        | 0.13 | -156.66         | 488.37          |
|            | N $\perp$ , O                        | 0.13 | -156.35         | 489.37          |
| Protonated | N  , O $\perp$                       | 0.14 | -127.70         | 618.46          |
|            | cis, N $\perp$ , O $\perp$           | 0.14 | -127.27         | 622.56          |
|            | trans, N $\perp$ , O $\perp$         | 0.14 | -127.31         | 622.20          |
|            | cis, N  , O                          | 0.15 | -123.82         | 617.03          |
|            | trans, N  , O                        | 0.15 | -123.85         | 616.72          |
|            | N $\perp$ , O                        | 0.15 | -123.42         | 620.39          |



**Table 2:** Reactivity indices of the nitrogen atom for some rotamers of the p-hydroxy- $\beta$ -phenylethylamine (au)

| Form       | Position of OH and ethylamine groups | $Q_N$ | $S_N^E$ | $S_N^N$ |
|------------|--------------------------------------|-------|---------|---------|
| Basic      | N  , O $\perp$                       | -0.36 | -276.80 | 321.95  |
|            | cis, N $\perp$ , O $\perp$           | -0.35 | -276.14 | 321.86  |
|            | trans, N $\perp$ , O $\perp$         | -0.35 | -276.67 | 321.39  |
|            | cis, N  , O                          | -0.35 | -276.48 | 321.50  |
|            | trans, N  , O                        | -0.34 | -276.82 | 321.20  |
|            | N $\perp$ , O                        | -0.35 | -277.52 | 321.81  |
| Protonated | N  , O $\perp$                       | -0.30 | -118.52 | 930.43  |
|            | cis, N $\perp$ , O $\perp$           | -0.30 | -118.74 | 931.91  |
|            | trans, N $\perp$ , O $\perp$         | -0.30 | -118.83 | 929.07  |
|            | cis, N  , O                          | -0.29 | -118.65 | 926.84  |
|            | trans, N  , O                        | -0.30 | -118.71 | 924.94  |
|            | N $\perp$ , O                        | -0.30 | -119.03 | 924.76  |

As can be seen in the Tables, the trends of the STO-3G results for the basic rotamers are like the CNDO/2 trends reported in Ref. 6. There are only relatively slight changes in the net charge and SE values of the carbon atom in some rotamers due to the loss of electronic conjugation between the oxygen atom and the phenyl ring. The phenomenon is also present in the protonated rotamers. It may be noted that the net charge on the carbon atom does not vary significantly when passing from the neutral to the protonated form. As expected, the relative electron donating capacity of the C atom diminishes by about 22%, while the electron-acceptor capacity rises by about 27%. This is due to the influence of the protonation on the molecular electrostatic potential surrounding the molecule (i.e., the protonated form is better able to interact with electron-donating systems).

Table 2 shows that the nitrogen atom electron-accepting capacity rises by about 289%, while its electron-donating capacity diminished by about 43%. All the above results are in perfect agreement with chemical intuition, which suggests that the most profound changes in the SD values must occur at the substituted site (the N atom here).

Interestingly, and contrasting with the results of CNDO/2 studies, the SN index of the protonated rotamers does not show abnormal changes in value when passing from one rotamer to the other. From the theoretical point of view, the values of these three reactivity indices must not be highly dependent on the conformation. The only exceptions to this rule are when rotamers differ in the presence or absence of intramolecular interactions and/or electron conjugation. Effectively, they are related directly (Q) or indirectly (SE and SN) to the atomic charge density, the last two also being related to the molecular orbital energies. In general, the MO energies are bounded in the sense that their value must lie between zero and the highest experimental atomic ionization potential value. Then, if we add more MOs (by adding more substituents), their energies begin to be more closely stacked, appearing at the limit of this process as bands or band-like MOs. As this is not the case here, we may expect a continuous behavior of the value of the indices with the substituent rotation. Moreover, if the atomic indices belong to atoms that are not directly involved in the rotation, we may expect a still better continuous behavior. We see that this is the case for the STO-3G reactivity indices but not for the CNDO/2's SN.

An explanation is that, in ab initio methods and within a Koopman description, the virtual MO energies tend to be more unstable (more positive). However, at the Hartree-Fock limit (i.e., without correlation), virtual eigenvalues could be close to the real ones, but they will be upper bound to them. This implies that the SN values will be always positive. On the other hand, in semiempirical methods the eigenvalues come from a methodology that is not strictly variational. Therefore, the eigenvalues may be positive or negative.

Finally, the CNDO/2 and STO-3G basis sets being different, it is expected that the orbital description should vary, i.e., different stable geometries will be obtained. Therefore, a symmetry-dependent description of the eigenvalues may be different due to the different spatial-orbital interaction.



Now, regarding the number of VOs contributing to SN, it is different for different molecular systems. This originated from the fact that the total number of molecular orbitals is equal to the total number of atomic orbitals forming the basis set, the number of VOs being of  $(N-e/2)$ , where  $N$  and  $e$  are, respectively, the total number of MOs and electrons. On the other hand, from the definition of the SDs we can see that the main term contribution to them comes from the higher occupied MOs (SE) and the lower VOs (SN). Therefore, as the difference in the number of VOs corresponded to the highest energy ones, no important source of error appears.

The problem of VOs with positive and negative energies is common in Hartree-Fock and DFT calculations of large molecular systems. It is suggested here that the inclusion of medium effects (solvent) in single point calculations after full geometry optimization may give better results than in vacuo calculations.

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