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The Electron Localization Function Signature of the Amide Bond Exhibits Nitrogen Lone Pair Character

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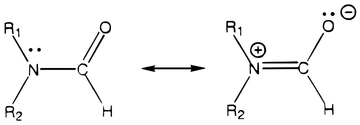
An electron localization function (ELF) study of the amide bond at the B3LYP/6-31+G(d,p)//MP2(FC)/6-31+G(d,p) level shows that the ELF isosurfaces near nitrogen resemble those found in planar ammonia where the lone pair is of necessity localized on the nitrogen atom. This suggests that in the planar form the neutral resonance structure is of considerable importance and gives rise to a characteristic ELF signature for nitrogen in the amide bond and similar settings where the nitrogen lone pair contributes to the bonding.

Introduction

The CN amide bond is a classic example of a resonance stabilized conformation in which the normal tetrahedral structure about nitrogen in amine-like settings is replaced by a planar arrangement allowing lone pair participation in the π-conjugation in the NC═O group. The planar structure is known experimentally and confirmed by studies indicating a significant shortening of and a barrier to rotation about the CN bond. In terms of classical Lewis resonance structures, one has for the planar structure

SCHEME 1



where the energy required to flatten the pyramidal amine structure is more than compensated for by the additional resonance energy provided by the three-atom conjugation. While the ionic resonance form leads to the overall stability of the amide group, in the absence of solvation effects an ionic resonance structure is generally unfavorable relative to a neutral one so that one might well expect the original nitrogen lone pair to tend to remain on nitrogen. As is well-known (and repeated below), this is confirmed by π Mulliken populations and by atoms-in-molecules[1] (AIM) treatments showing a significant charge on nitrogen.

The electron localization function[2−10] (ELF) is a robust descriptor of chemical bonding based on topological analysis of local quantum mechanical functions related to the Pauli exclusion principle. It was first introduced by Becke and Edgecombe[2] and has been developed and applied extensively by Savin and Silvi and their collaborators.[3−10] The local maxima of the function define localization attractors corresponding to core, bonding (located between the core attractors of different atoms) and nonbonding electron pairs and their spatial arrangement. It is of special interest to chemists in that the resulting isosurfaces of ELF density tend to conform to the classical Lewis picture of bonding. In the present work we exhibit the ELF picture of the region surrounding the nitrogen nucleus in a number of representative molecules in which the planar nitrogen setting allows lone pair participation in the bonding; we show that it tends to conform to the localized lone pair picture about nitrogen, is rather unusual and apparently distinctive of nitrogen in amide-like settings.

Becke and Edgecombe[2] pointed out that the conditional pair probability for same spin electrons has the form

$$P_{\text{cond}}^{\sigma\sigma}(\vec{r},s) = \frac{1}{3}\left[\sum_{j}^{\sigma}\left|\nabla\varphi_j\right|^2 - \frac{1}{4}\frac{|\nabla\rho_\sigma|^2}{\rho_\sigma}\right]s^2 + ... \qquad (1)$$

for a spin at point $\vec{r}$ and another a distance s away (averaged over a spherical shell of radius s). The coefficient of the quadratic term is the local Pauli kinetic energy density, the excess kinetic energy electrons have (due to the Pauli exclusion principle) compared to a bosonic system of the same density.[5] When it is small the Fermi hole at $\vec{r}$ is large and one would expect to find pairs of electrons of *opposite* spin in the region; when it is large, the converse is true.

For a single determinental wave function built from Hartree−Fock or Kohn−Sham orbitals, φ_j, the ELF function of position $\vec{r}$ is *defined* as

$$\eta = \frac{1}{1 + \left(\frac{D}{D_h}\right)^2} \qquad (2)$$

where

$$\mathrm{D} = \frac{1}{2}\sum_{j=1}^{N}|\nabla\varphi_j|^2 - \frac{1}{8}\frac{|\nabla\rho|^2}{\rho}$$

$$D_h = \frac{3}{10}(3\pi^2)^{2/3}\,\rho^{5/3}$$

$$\rho = \sum_{j=1}^{N}|\varphi_j|^2 \qquad (3)$$

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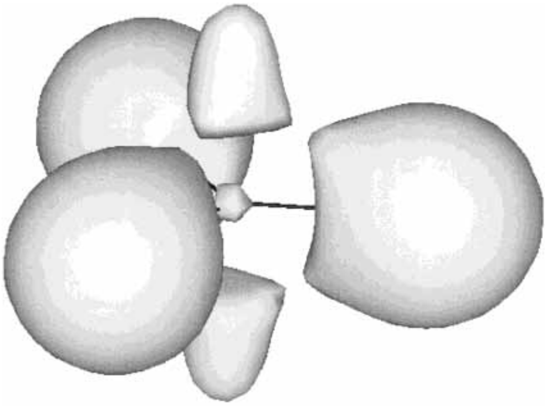

Figure 1. $\eta = 0.853$ isosurfaces for planar ammonia. The lone pair basins are smaller in extent that those of the hydrogens and occur above and below the molecular plane.

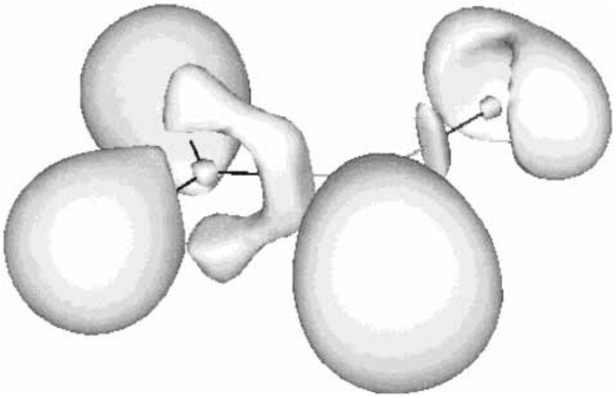

Figure 2. $\eta = 0.835$ isosurfaces for formamide. The nitrogen center is on the left; the carbonyl oxygen core and lone pair basins are found in the right upper back of the figure.

and where the scaling factor was chosen to be the homogeneous electron gas kinetic energy density of a system of the same density. The ELF function can be viewed as a local measure of the Pauli repulsion between electrons due to the exclusion principle and allows one to define regions of space that are associated with different electron pairs in a molecule or solid. The position where ELF attains a maximum value (the attractor) can be used as an electron pair's signature.[8] Indeed, it is the signature of nitrogen in amide-like settings we probe here.

Using the vector field of the gradient of the electron localization function, the topology of the ELF function can be used to define basins within which one or more electron pairs are to be found.[4-6,9] These subsystems are defined in terms of zero flux surfaces; the gradient paths ends at what are called *attractors* within each subsystem. The region of three-dimensional space traversed by all gradient paths that terminate at a given attractor defines the *basin* of the attractor. ELF basins are labeled as either core or valence basins. Core basins contain a nucleus while valence basins do not; hydrogen basins are taken as exceptions since, although they contain a proton, they do represent a shared pair interaction. A valence basin is characterized by its number of connections to core basins, referred to as its synaptic order. Basins are connected if they are bounded by part of a common surface. A simple covalent bond basin would be connected to two core basins and be of synaptic order two; a lone pair basin would be monosynaptic. More complex bonding basins can be polysynaptic.

The population of a basin Ω_i, N_i, is given by integrating the total electron density, $\rho(\vec{r})$, over the basin volume. These populations are particularly important in that they tend

$$N_i = \int_{\Omega_i} \rho(\vec{r})\, \mathrm{d}\vec{r} \tag{4}$$

to reflect delocalization effects and, in the case of bond basins, the bond order.

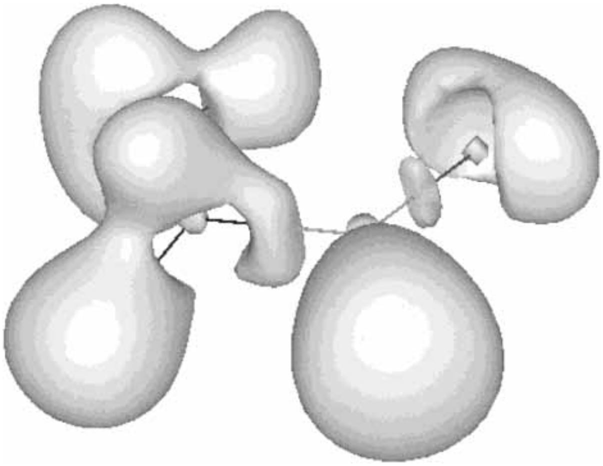

Figure 3. $\eta = 0.830$ isosurfaces for *Z*-formohydroxamic acid. The nitrogen center and the lone pair occupying a tetrahedral site are on the center left (in front of the hydroxyl group basins), and the carbonyl oxygen basins are in the back upper right.

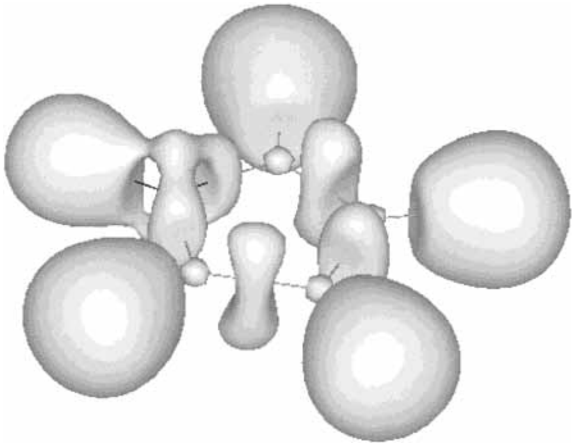

Figure 4. $\eta = 0.800$ isosurfaces for pyrrole. The nitrogen center is in the back upper left of the figure.

Theoretical Details

The ELF calculations were carried out employing the TopMod Package of Noury and co-workers[11] in the B3LYP approach [12,13] with structures optimized at the MP2(FC)/6-31+G(d,p) level. Step sizes of 0.1 au and box sizes that extended 5.0 au from the outermost atomic coordinates in each direction were used. The TopMod package sacrifices some accuracy for efficiency and, according to the authors,[11] is thought to be accurate to a few percent, sufficient for comparative studies. The Mulliken populations were obtained at the MP2(FC)/6-31+G(d,p)//MP2(FC)/6-31+G(d,p) level while the AIM results were obtained in the B3LYP/6-31+G(d,p)//MP2(FC)/6-31+G-(d,p) approach; these calculations were carried out with Gaussian 98.[14]

Results and Discussion

As mentioned in the Introduction, Mulliken gross orbital populations and AIM atomic charges tend to reinforce the

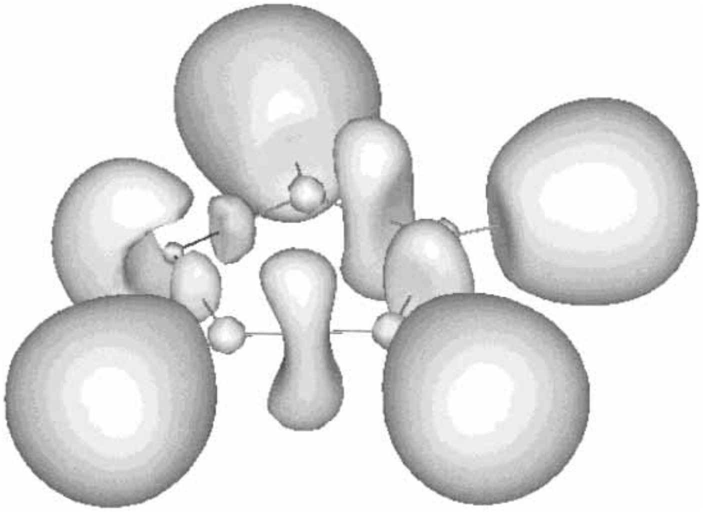

Figure 5. $\eta = 0.820$ isosurfaces for furan. The oxygen center is in the middle left of the figure encompassed in the crescent-shaped lone pair basin.

neutral resonance structure shown on the left-hand side of Scheme 1. Calculations done here at the MP2(FC)/6-31+G-(d,p)//MP2(FC)/6-31+G(d,p) level on formamide yield for nitrogen, carbon, and oxygen gross π populations of 1.73, 0.78, and 1.42, respectively; the carbon and oxygen populations are not largely modified from their values in H_2CO of 0.71 and 1.26. Likewise, a B3LYP/6-31+G(d,p)//MP2(FC)/6-31+G(d,p) AIM calculation yields atomic charges of -1.26, $+1.54$, and -1.19 for nitrogen, carbon, and oxygen, respectively. As we shall see, the ELF isosurfaces and basin populations conform with this picture.

ELF isosurfaces for typical single and double bonds are located in the bond region with some displacement from the center point due to bond polarization effects. Single bond basins tend to be more spherical in shape, while the situations characterized as a $\sigma - \pi$ double bonds show more of an ellipsoidal shape extending above and below the local molecular plane. Hydrogen basins are generally centered near protons, and lone pair basins are generally spherical and in those regions of space predicted by simple pictures of chemical bonding. For example, in tetrahedral NH_3 the lone pair basin defines the C_3 symmetry axis with an attractor located some 0.78 Å above the nitrogen core. In pyridine the nitrogen lone pair occupies an in-plane position some 0.72 Å from nitrogen and is not part of the π system.

The effect we shall see is best introduced by considering the $\eta = 0.853$ ELF isosurfaces for *planar* NH_3 shown in Figure 1. Krokidis, Noury, and Silvi[15] carried out the first ELF investigation of this system when they looked at the ammonia inversion as an example of an elementary chemical process. The hydrogen basins are apparent and we note the presence of *two* lone pair basins, one above and one below the nitrogen core attractor at distances of 0.67 Å. This picture is easy to understand. In tetrahedral NH_3 the lone pair electrons have "their own space" and take up essentially a tetrahedral site about nitrogen with a basin population of 2.01. In planar NH_3 the symmetry of the situation demands that the probability of finding a lone pair above the plane be matched by an equal probability below the plane, each basin with a population of 1.16 electrons. The lone pair regions in the planar molecule have caused a transfer of some 0.31 electrons from the hydrogen basins to those of the lone pairs.

Figure 2 shows the $\eta = 0.835$ isosurfaces for formamide. We note the typical two lone pair basins for oxygen (in the right upper back of the figure), a CN bond basin between nitrogen and carbon, and planar-ammonia-like lone pair basins above and below the molecular plane about nitrogen. These latter two basins have not yet separated at the ELF level shown in the figure but do so ultimately, leading to three attractors. Clearly, the nitrogen lone pair structure on the left-hand side of Scheme 1 is revealed. The situation for *N*-methylacetamide (not shown) is similar.

Formohydroxamic acid in the *Z* configuration (both oxygens on the same side of the molecule) is an important model for biological Fe(III) chelators (siderophores).[16] While the amide group is nearly planar, overall the molecule is noticeable nonplanar due to the presence of the hydroxyl group on nitrogen. The $\eta = 0.83$ isosurfaces for this molecule are shown in Figure 3. Here the CN bond basin is apparent but now, due to the overall nonplanarity of the molecule, the nitrogen lone pair basin occupies essentially a tetrahedral site about nitrogen. In the fully planar O-acid anion of this molecule, $^{-}$ONHCHO, a picture (not shown) emerges much like that shown for formamide in Figure 2 but now the lone pair and CN basin bonding electrons form a $\supset$-crescent-shaped basin but with only one attractor.

Although obviously not an amide, planar pyrrole, C_4H_4NH, has nitrogen in the same kind of setting with three in-plane bonds and the lone pair occupying space above and below the molecular plane. Figure 4 shows the $\eta = 0.80$ isosurfaces for pyrrole, and the same type of picture emerges as for formamide, this time with two CN bond basins in the ring; these basins ultimately lead to four attractors. Related five membered rings where lone pair participation in bonding might be expected differ from pyrrole. Phosphole, C_4H_4PH, is nonplanar with essentially a tetrahedral arrangement about phosphorus; the phosphorus lone pair predictably occupies a tetrahedral site. The $\eta = 0.820$ isosurfaces for furan, C_4H_4O, are shown in Figure 5, and one see that the oxygen lone pairs do fold over the oxygen core but now with the $\subset$-crescent pointing away from the OC ring; in furan there is but one attractor for the two lone pairs. Thiophene, C_4H_4S, resembles furan in the overall structure of its ELF isosurfaces, although the lone pairs there are in two equivalent basins (two attractors).

The quantitative aspects of the pertinent nitrogen compounds are given in Table 1 where the *V*(N) lone pair and adjacent bond basin populations are given along with the distance of the *V*(N) basin(s) from the nitrogen nucleus. The largest lone pair population is that of NH_3 in which the lone pair is obviously completely localized on nitrogen. In pyrrole the nitrogen lone pair population is reduced as charge is delocalized into the

TABLE 1: Nitrogen Bond and Lone Pair Basin Populations and Distances (r_{lp}, in Å) of the Lone Pair Attractors from the Amide Nitrogen Core[a]

molecule	*V*(N)	*V*(CN)	*V*(NO)	r_{lp}
NH_3	2.01			0.78
planar NH_3	1.16 (2)			0.67
formamide	0.87 (2)	2.10		0.65
N-methylformamide	1.01 (2)	2.05[b]		0.65
pyrrole	0.67 (2)	2.05		0.63
formohydroxamic acid[c]	1.74	2.43	0.96	0.69
formohydroxamic acid anion[d]		4.23	1.13	

[a] *V*(N) is associated with the nitrogen lone pair(s) while *V*(CN) and *V*(NO) relate to the CN and NO bond basins. Two basins for *V*(N) are indicated by the number two in parentheses. [b] The population between nitrogen and the methyl carbon, *V*(N,CH_3), is equal to 1.64. [c] This is the *Z* conformation of HONHCHO. [d] This is the *Z* conformation of the O-acid form, $^-$ONHCHO.

conjugated five-membered ring. In formohydroxamic acid there is only one lone pair basin as it occupies a basically tetrahedral site about nitrogen. In the O-acid anion of this molecule there is only one attractor and we see that the population associated with that basin is essentially equal to the sum of the *V*(N) and *V*(CN) basins in the undissociated acid, as expected. The distance from the nitrogen nuclei to the lone pair attractors is roughly constant with the distances in NH_3 and formohydroxamic acid being larger for the lone pair occupying a tetrahedral-like site. In those cases where two lone pair attractors are present, the $V(N)-C(N)-V'(N)$ angles are 167°, 166°, and 176° for formamide, *N*-methylformamide, and pyrrole, respectively, the lone pair attractors being moved slightly toward the CN bond basin(s).

Summary

The electron localization function description of chemical bonding provides very useful qualitative and quantitative information regarding regions of space where pairs of electrons are to be found. It provides a signature of the bond or lone pair involved. The electron localization function (ELF) study here of situations where the nitrogen lone pair is involved in bonding shows that the ELF isosurfaces near nitrogen resemble those found in planar ammonia where the lone pair is localized on the nitrogen atom. This suggests that in amides the neutral resonance form with lone pairs situated on the nitrogen atom is of considerable importance and gives rise to a characteristic ELF signature for the amide bond.

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