Theoretical Study of Imidazole···NO Complexes[†]

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A set of weak complexes between imidazole (Imi) and nitric oxide (NO) were calculated with UMP2/6-31++G(d,p) and UMP2/6-311++G(2d,2p) levels of theory. Planar and nonplanar geometries were considered. Complexes of NO and protonated imidazole ($ImiH^+$) were also studied due to the biological important effect of Imi protonation. It was found that ring protonation increases the stability of planar complexes and does not affect significantly nonplanar complexes. The Z−H···XY (Z = C, N and X, Y = N, O) interactions resulted as hydrogen bonds according to Koch and Popelier criteria based on AIM theory. Charge transfer was also found very important for complex stabilization within our theoretical framework. Planar NO···$ImiH^+$ complexes are more stable than those obtained with neutral Imi.

1. Introduction

In recent years, many studies have been devoted to van der Waals (vdW) interactions between nitric oxide (NO) and other molecules.[1−6] This small molecule is used as a benchmark for the study of vdW interactions between radicals and closed-shell molecules.[1] Intermolecular complexes between open-shell and closed-shell species have an important role in chemical reactions, in interstellar cloud collisions, ultracold molecules, and Bose−Einstein condensates.[7] These systems are considerable less understood than similar weak complexes between closed-shell molecules.

Particularly, the complexes between NO and rare gases attracted the attention of experimentalists and theoreticians.[1−4,8] NO is a free radical and its unpaired electron is easily promoted to excited states. The study of its electronic spectra and the changes due to vdW binding provides information about the nature and energetic of these interactions.[1] On the other hand, NO has an important role in biology;[9,10] it is implicated in many physiological functions like neurotransmission, platelet aggregation, regulation of blood pressure, heart contractility, host defense, and others.[11,12]

Many of the NO biological functions are related with its interaction with proteins. Although NO usually reacts with metals in the active site, its diffusion depends on the interaction with amino acids and the amino acidic binding pocket can modulate its function.[13,14] In a previous work, we analyzed the interaction between the amino acids and nitric oxide molecules at semiempirical level.[15] For polar amino acids, the interactions with lateral chains are energetically as stable as or even more stable than the interactions with the backbone atoms. Histidine (His) is a polar amino acid, which can change its charge in the physiological interval of pH. Some proteins related with NO functions, like myoglobins have His in its active site.[16] The basic−acid properties of His are related to the presence of imidazole (Imi) group in its lateral chain. Imi has a structure that allows it to act as both a proton donor and proton acceptor, playing an important role in enzymatic reaction mechanisms, proton transport pathways, and electron transfer. Figure 1 shows the Imi molecule in its neutral (Imi) and protonated ($ImiH^+$) forms. Imi is also present in the structure of nucleotidic bases adenine and guanine.

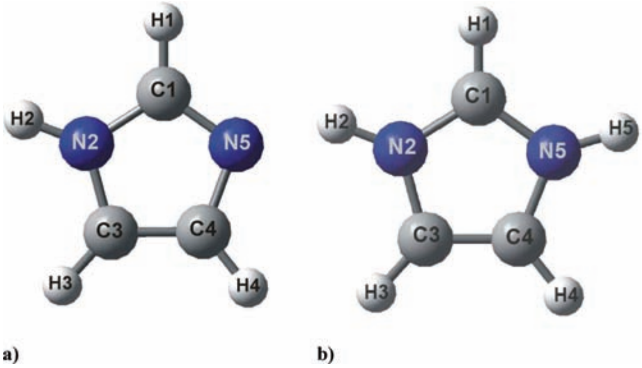

Figure 1. (a) Uncharged (Imi) and (b) Protonated ($ImiH^+$) imidazole.

There are some studies related to the interaction of Imi with small molecules.[17−20] In particular, its interaction with water has been studied.[20] A recent study employing Helium nanodroplets with IR spectroscopy and theoretical calculations, reports a couple of Imi···H_2O complexes with similar populations.[17] In one of these complexes the Imi ring acts as proton donor, and in the other, as proton acceptor. The complexes between charged $ImiH^+$ and water have also been analyzed.[18,21]

Recently, Robinet et al.[22] studied the interactions between models for aromatic lateral chains of amino acids and nitrosium cation (NO^+) and nitroxyl anion (NO^-). They were particularly interested in the formation of half sandwich and sandwich complexes. They established that the NO^+ cation presented stronger interactions than NO^- anion with metil-imidazole.

Imidazole is an aromatic system that can establish different kinds of interactions with NO. This system can be used as a model for open-shell···closed-shell interactions. The aim of this work is to explore different intermolecular complexes that can

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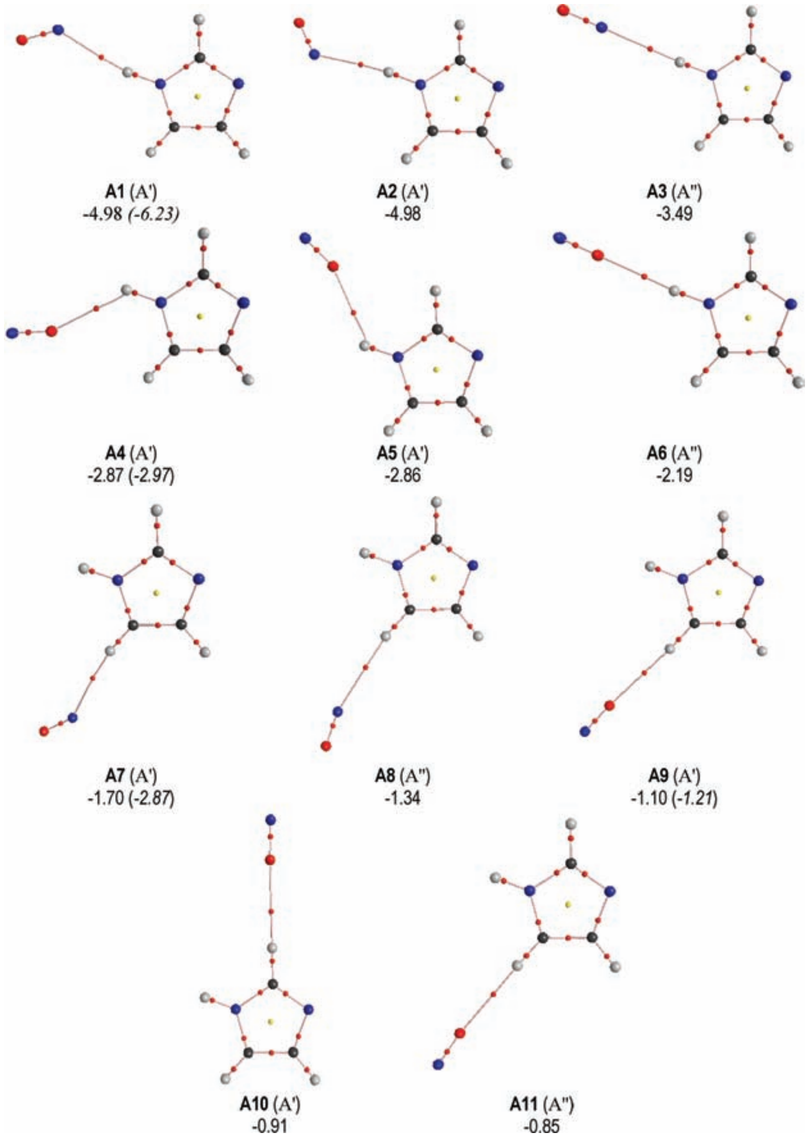


Figure 2. Molecular graphs for Imi···NO planar complexes stabilized by hydrogen bond interactions. The Imi molecule is in the same orientation as in Figure 1. Atoms are represented by the large spheres. The colors corresponding to carbon, nitrogen, oxygen, and hydrogen atoms are gray, blue, red, and white, respectively. Small red spheres are the bond critical points (bcp's), and yellow spheres are the ring critical points (bcp's) of electron densities. Stabilization energies (kJ/mol) are shown at the UMP2(full core)/6-31++G(d,p) level of theory corrected from BSSE. Stabilization energies calculated at the UMP2(full core)/6-311++G(2d,2p) level of theory (BSSE corrected) are shown for the most stable complex of each interaction in italics.

appear between Imi and NO and to analyze the effect of Imi protonation on these interactions, to understand the nature of NO interactions due to its growing interest in biology and for the physical chemistry of weak intermolecular complexes.

2. Methods and Models

Two kinds of possible minima Imi···NO interactions were considered to reach planar and nonplanar complexes. Moreover, the effect of protonation on the interactions was analyzed. For this reason, the Imi molecule was calculated in its neutral and charged forms (Figure 1). The planar complexes are at least of C_s symmetry and thus two electronic states can be found: A′ and A″. Both states were considered in each case. The nonplanar complexes were generated by locating the NO molecule over the imidazole plane and rotating both molecules. Then, the resulting molecular arrangements were optimized. Configurations where the NO is perpendicular to the Imi plane were also calculated.

Full optimizations as well as frequency calculations for all the examined complexes, employing tight convergence criteria, were performed at the UMP2(full core)/6-31++G(d,p) level of theory. This method of calculation and these basis sets are undoubtedly more reliable for open-shell vdW complexes.[5,6] Moreover, preliminary calculations using the B3LYP method give similar results to those obtained with the MP2 method for planar complexes. However, B3LYP calculations do not reproduce stable nonplanar conformations. The design of density functionals that consider dispersion energy is an active field.[23,24] Their performance to open-shell systems is not completely clear, at least until very recent proposals.[25] The election of the UMP2 method for this study was based on our good experience with this method for CH_4···NO complexes.[5,6] The most stable minima corresponding to each interaction were reoptimized by employing the UMP2(full core)/6-311++G(2d,2p) level of theory. Basis set superposition error (BSSE) was calculated using the counterpoise method proposed by Boys and Bernardi.[26]

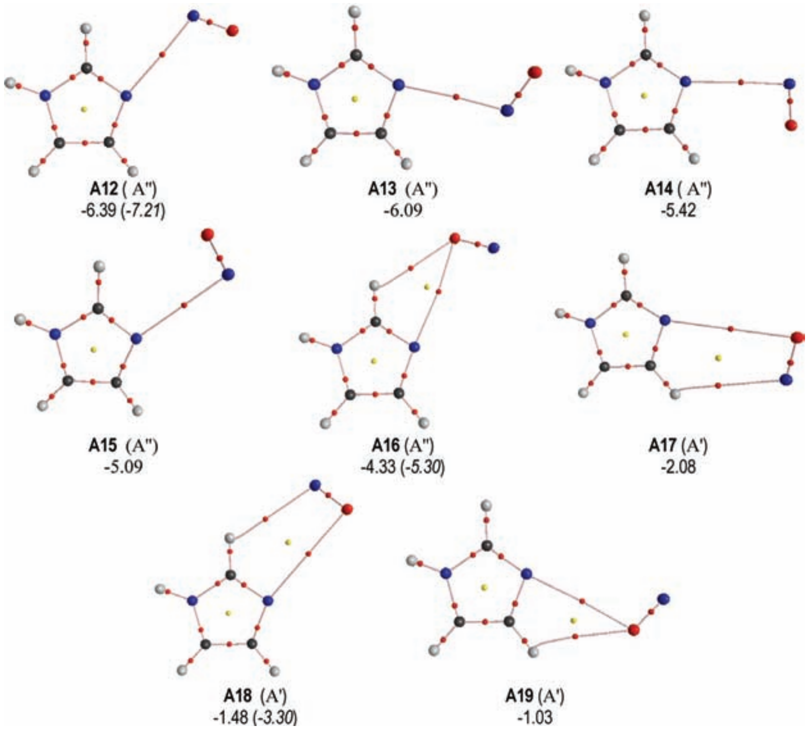


Figure 3. Molecular graphs for planar complexes of Imi···NO stabilized by N···N or N···O interactions. The Imi molecule is in the same orientation as in Figure 1. The colors corresponding to carbon, nitrogen, oxygenn and hydrogen atoms are gray, blue, red, and white, respectively. Small red spheres are the bond critical points (bcp's), and yellow spheres are the ring critical points (rcp's) of electron densities. Stabilization energies (kJ/mol) are shown at the UMP2(full core)/6-31++G(d,p) level of theory corrected from BSSE. Stabilization energies calculated at the UMP2(full core)/6-311++G(2d,2p) level of theory (BSSE corrected) are shown for the most stable complex of each interaction in italics.

All calculations were done using the Gaussian03 program.[27] The stabilization energies were calculated as the difference between the energy of complexes and the sum of the isolated molecules. The spin contamination obtained with UMP2 calculations in all cases is not large (ca. 0.78). All energies shown throughout this paper are the corresponding projected ones (PMP2).

The bonding features of all the studied complexes were analyzed by means of atoms in molecules theory (AIM), which has been widely used to study and characterize H-bonds and weak interactions.[28] The localization of critical points and the calculation of electron densities and the Laplacian at these points are useful tools to study molecular interactions. The number of nonzero eigenvalues of Hessian matrix on a critical point defines its rank (σ) and the sum of the signs of these eigenvalues its signature (λ). The (σ, λ) code can be used to characterized a critical point. According this theory, if a pair of atoms is bonded, there is a path of maximum charge density between them, with a saddle point along the path. This line is called the bond path (bp) and the saddle point as the bond critical point (bcp). Thus, in a bcp, the electron density has a maximum in two directions and a minimum in the third perpendicular direction. A bcp can be described with the code (3, −1). In the middle of a ring is found a point where the electron density has a minimum in two directions and a maximum in the third perpendicular direction. This (3, +1) point is called the ring critical point (rcp). The electron density in the middle of a cage is characterized for a minimum in all directions, called the cage critical point, (3, +3).

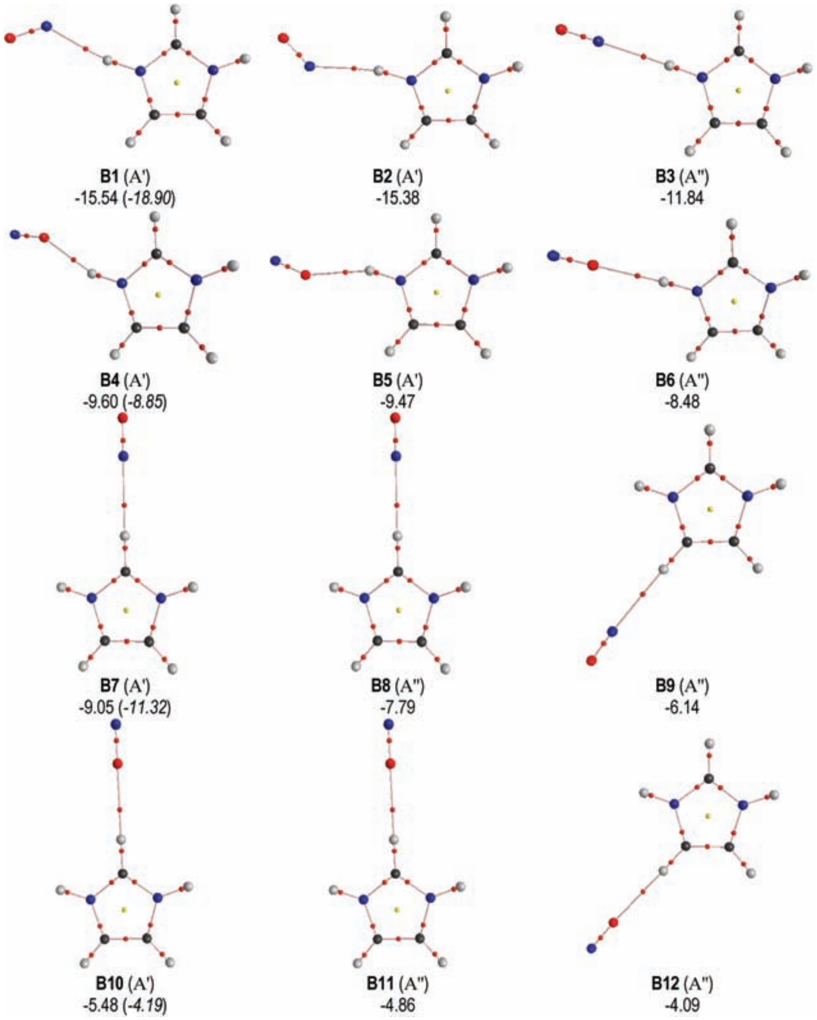
The UMP2 electron densities of the complexes were analyzed using the AIM theory. Critical points were detected and the contour plots of the electron density were visualized.[29] In selected cases, the charges were calculated, and the integrations over atomic basis were performed using PROMEGA algorithm of AIMPAC package, using defaults parameters. The default parameters to integration allow us to calculate the total charge of isolated molecules with an accuracy of 1×10^{-3}, which is enough to our interpretative purposes.

3. Results and Discussion

Both forms, Imi and ImiH$^+$, are planar (Figure 1). The π nature of Imi and NO molecules favors the interactions in the same plane of the ring to obtain planar complexes and in the plane perpendicular to the ring to form π complexes. The protonated form ImiH$^+$, a more symmetrical structure (C_{2v}), presents two kinds of equivalent carbons, C1 and the equivalent C3 and C4, and only one kind of nitrogen (N2 and N5 are also equivalent). Consequently, we will obtain more nonequivalent complexes for Imi than for ImiH$^+$ (19 and 12 planar complexes and 10 and 6 nonplanar complexes, respectively). Planar and nonplanar complexes will be analyzed in individual sections.

a. Planar Complexes. The optimized planar complexes and the stabilization energies (UMP2(full core)/6-31++G(d,p) level of theory) are collected in Figures 2−4. Uncharged complexes are denominated as **A** and charged complexes as **B**, the numbers are ordered according to the stabilization energies. On the basis of AIM framework was found six kinds of interactions between imidazole and NO that determine the stabilities and geometries of these intermolecular complexes. For the ImiH$^+$ complexes, there are only four intermolecular interactions: N−H···N−O, N−H···O−N, C−H···N−O, and C−H···O−N. Additionally, for Imi complexes the N···NO and N···ON interactions appear. Table 1 shows the main topological features of the electron densities in the bcp's for all calculated planar complexes. Intermolecular parameters for each kind of complexes are in Table 2.

The isolated molecules and the complexes were reoptimized at UMP2(full core)/6-311++ G(2d,2p) level of theory. The experimental interatomic distance r(N−O) is 1.151 Å,[30] the



B1 (A') -15.54 (*-18.90*)
B2 (A') -15.38
B3 (A") -11.84
B4 (A') -9.60 (*-8.85*)
B5 (A') -9.47
B6 (A") -8.48
B7 (A') -9.05 (*-11.32*)
B8 (A") -7.79
B9 (A") -6.14
B10 (A') -5.48 (*-4.19*)
B11 (A") -4.86
B12 (A") -4.09

Figure 4. Molecular graphs for $ImiH^+\cdots NO$ planar complexes stabilized by hydrogen bond interactions. The $ImiH^+$ molecule is in the same orientation as in Figure 1. Atoms are represented by the large spheres. The colors corresponding to carbon, nitrogen, oxygen, and hydrogen atoms are gray, blue, red, and white, respectively. Small red spheres are the bond critical points (bcp's), and yellow spheres are the ring critical points (rcp's) of electron densities. Stabilization energies (kJ/mol) are shown at the UMP2(full core)/6- 31++G(d,p) level of theory corrected from BSSE. Stabilization energies calculated at the UMP2(full core)/6- 311++G(2d,2p) level of theory (BSSE corrected) are shown for the most stable complex of each interaction in italics.

predicted value for UMP2(full core)/6-31++G(d,p) is 1.142 Å and is 1.136 Å for UMP2(full core)/6-311++G(2d,2p) level of theory. Both methods tend to underestimate the experimental value, but the largest basis set gives the smaller distance. There is a good agreement between the stabilization energies calculated at both levels (Figures 1 and 2; for more details, see S1 and S2 in the Supporting Information); the largest deviation is obtained for the **A18** (30% taking the BSSE corrected energy at MP2/6-311++G(2d,2p) as reference). The optimized geometries of the complexes with both basis sets are very similar, showing same critical points of electron densities. The only exception is the **A7** complex at the MP2/6-311++G(2d,2p) level of theory in which the geometry obtained is quite different. The complex obtained at the higher level of theory has the NO molecule pointing to the middle of the C3−C4 bond interacting with H3 and H4.

These interactions are favored by the protonation of the imidazole ring; i.e., the stabilization energies of charged complexes are larger than that obtained for the uncharged ones (Figures 1 and 2). For similar interactions, electron densities at intermolecular bcp's for the $ImiH^+\cdots NO$ complexes are larger than those obtained for Imi···NO complexes. For the Imi···NO complexes, the N···X−Y interactions are the most stable, followed by N−H···X−Y and C−H···XY, where X and Y are the N or O atoms. The complexes where X = N are usually more stable than similar complexes with X = O. The larger stabilization of N orientated complexes with respect to the O orientated has also been obtained for other NO···small molecule complexes, like $CH_4\cdots NO$, $H_2O\cdots NO$, $NH_3\cdots NO$, etc.[15] The largest stabilization energies of N orientated complexes are in agreement with the largest electron densities obtained in the intermolecular bcp's.

The N−H···NO interaction appears in complexes: **A1**, **A2**, **A3**, **B1**, **B2**, and **B3** (Figures 1 and 2). The protonation of the imidazole ring produces a decreasing of N−H···NO distance around 0.2 Å, but the angles related with the interaction do not significantly change and the conformation of complexes remains similar for the Imi and ImiH+ complexes. The linear complexes (**A3** and **B3**) are transition states with an electronic state of A′ symmetry, the imaginary frequencies are related with the out-of-plane NO molecule.

A4, **A5**, **A6**, **B4**, **B5**, and **B6** complexes have the N−H···ON interaction (Figures 1 and 2). The geometries of protonated complexes are quite different from those obtained for the Imi complexes (Table 2). The NO molecule has a larger deviation from the N−H line (see ∠NH···O values).

TABLE 1: Topological Features of Electron Density (UMP2(full core/6-31++G(d,p)) on bcp's for All Planar Complexes

complexes	interactions	ρ(bcp)	$\nabla^2\rho$(bcp)	ellipticity	*G*(bcp)	*V*(bcp)	|*V*(bcp)|/*G*(bcp)
			Imi···NO Complexes				
A1	N−H···NO	0.011	0.036	0.0103	0.0082	−0.0076	0.93
A2	N−H···NO	0.011	0.036	0.0066	0.0082	−0.0077	0.93
A3	N−H···NO	0.008	0.032	0.1741	0.0066	−0.0055	0.83
A4	N−H···ON	0.008	0.032	0.0825	0.0069	−0.0058	0.85
A5	N−H···ON	0.008	0.032	0.0885	0.0069	−0.0058	0.84
A6	N−H···ON	0.009	0.036	0.0758	0.0078	−0.0069	0.89
A7	C−H···NO	0.006	0.020	0.0485	0.0044	−0.0035	0.80
A8	C−H···NO	0.005	0.020	0.1852	0.0036	−0.0027	0.75
A9	C−H···ON	0.006	0.024	0.0474	0.0049	−0.0040	0.81
A10	C−H···ON	0.006	0.024	0.0439	0.0049	−0.0039	0.81
A11	C−H···ON	0.005	0.024	0.0443	0.0047	−0.0038	0.81
A12	N···NO	0.011	0.040	0.1694	0.0083	−0.0069	0.83
A13	N···NO	0.011	0.040	0.1545	0.0084	−0.0069	0.82
A14	N···NO	0.010	0.036	0.0728	0.0077	−0.0063	0.82
A15	N···NO	0.010	0.036	0.1032	0.0073	−0.0060	0.83
A16	N···ON	0.004	0.016	0.7564	0.0031	−0.0026	0.83
	C−H···ON	0.005	0.020	0.1069	0.0042	−0.0032	0.76
A17	N···ON	0.005	0.016	0.1767	0.0039	−0.0035	0.89
	C−H···ON	0.005	0.020	0.4594	0.0039	−0.0030	0.76
A18	N···ON	0.004	0.014	0.6671	0.0030	−0.0025	0.84
	C−H···NO	0.005	0.020	0.0812	0.0037	−0.0029	0.79
A19	N···ON	0.004	0.016	0.7284	0.0031	−0.0026	0.84
	C−H···NO	0.005	0.016	0.1190	0.0032	−0.0025	0.78
			ImiH$^+$···NO Complexes				
B1	N−H···NO	0.019	0.052	0.0150	0.0127	−0.0125	0.98
B2	N−H···NO	0.019	0.052	0.0170	0.0126	−0.0124	0.98
B3	N−H···NO	0.013	0.048	0.0154	0.0116	−0.0112	0.97
B4	N−H···ON	0.015	0.052	0.0140	0.0127	−0.0122	0.96
B5	N−H···ON	0.015	0.052	0.0140	0.0127	−0.0122	0.96
B6	N−H···ON	0.014	0.052	0.0735	0.0123	−0.0115	0.93
B7	C−H···NO	0.009	0.036	0.1510	0.0075	−0.0063	0.84
B8	C−H···NO	0.009	0.032	0.1716	0.0067	−0.0056	0.83
B9	C−H···NO	0.008	0.028	0.3943	0.0041	−0.0029	0.70
B10	C−H···ON	0.010	0.036	0.0512	0.0084	−0.0075	0.89
B11	C−H···ON	0.009	0.036	0.0697	0.0080	−0.0071	0.89
B12	C−H···ON	0.009	0.032	0.0684	0.0073	−0.0064	0.87

The C−H···NO and C−H···ON interactions can appear due to the contact between the hydrogens bonded to each of three C atoms of imidazole ring and the NO molecule. The complexes between neutral Imi and NO related to C1 and C4 atoms of Imi ring have an angular geometry, allowing the interaction with N5. These complexes are labeled **A18** and **A19**. The **A7**, **A8**, **B7**, **B8**, and **B9** complexes are stabilized only by the C−H···NO interaction (Figure 7). The electron densities in C−H···NO critical points are smaller than those obtained for the N−H···NO interactions. Their values are between 0.005−0.009 au, the largest corresponds to the charged complexes. The N···H distances are larger than those obtained for the similar complexes related to N−H···NO interactions.

The N···NO and N···ON interactions are only found in complexes with uncharged Imi. Some of the complexes stabilized by these interactions have a second interaction (i.e., C−H···NO and C−H···ON interactions). It was found that four complexes are stabilized only by the N···NO interaction: **A12**, **A13**, **A14**, and **A15** complexes. These are slightly more favorable from the energetic point of view than the corresponding N−H···NO interactions in similar Imi complexes, and the electron densities in the bcp between both molecules are also similar. But, for these complexes the distances N···N are larger than those obtained for the N−H···N and N−H···O interactions. In these complexes the *r*(N···N) are between 2.8 and 2.9 Å.

b. Electron Density Analysis. Table 1 shows the values of kinetic (*G*(bcp)) and potential density energies *V*(bcp), and the ratio |*V*(bcp)|/*G*(bcp) between them. According to the local virial formulation

$$\frac{h^2}{4m}\nabla^2\rho(r) = 2G(r) + V(r)$$

In the case of local accumulation of electron density in the bcp, as is found in covalent bonds, $\nabla^2\rho(\text{bcp}) < 0$. For weak interactions (like hydrogen bonds and van der Waals complexes), $\nabla^2\rho(\text{bcp}) > 0$; thus there is a depletion of electron density in the bcp and a local excess of *G*(bcp) with respect to atomic virial. The intermolecular interactions can be classified as closed-shell if $|V(\text{bcp})|/G(\text{bcp}) < 1$ and as shared interaction if $|V(\text{bcp})|/G(\text{bcp}) > 2$; the intermediate case corresponds to $1 < |V(\text{bcp})|/G(\text{bcp}) < 2$.[31] For all calculated interactions, $\nabla^2\rho(\text{bcp})$ is larger than 0, as is typical of weak interactions. At the same time the $|V(\text{bcp})|/(G(\text{bcp}) < 1$ for all studied interactions behaves as typical for closed-shell interactions. The N−H···NO interactions have the largest |*V*(bcp)|/*G*(bcp) values. In the cases of ImiH$^+$···NO complexes, it is near 1; thus these complexes are almost in the limit ($H(\text{bcp}) = V(\text{bcp}) + G(\text{bcp}) = 0$) to intermediate interactions. The ratios are larger for the ImiH$^+$···NO complexes.

The AIM charges for monomers and the most stable complexes of each interaction were calculated at the UMP2(full)/

TABLE 2: Geometrical Parameters for the Most Stable Complexes of Each Interaction[a]

		UMP2(full core)/ 6-31++G(d,p)	UMP2(full core)/ 6-311++G(2d,2p)
		Imi···NO Complexes	
A1	*r*N−O	1.140	1.134
	*r*N···H2	2.341	2.294
	∠H2···N−O	133.1	136.8
	∠N2H2···N	167.6	166.8
A5	*r*N−O	1.145	1.138
	*r*O···H2	2.440	2.456
	∠H2···O−N	157.1	152.8
	∠N2H2···O	130.5	128.5
A7	*r*N−O	1.142	1.136
	*r*N···H3	2.660	2.697
	∠H3···N−O	148.5	168.5
	∠C3−H3···N	168.7	173.2
A9	*r*N−O	1.144	1.137
	*r*O···H3	2.571	2.589
	∠H3···O−N	176.7	179.5
	∠C3−H3···O	177.0	177.7
A12	*r*N−O	1.147	1.139
	*r*N···N5	2.834	2.887
	∠N5···NO	109.5	108.7
A16	*r*N−O	1.143	1.142
	*r*N5···O	3.399	3.204
	∠H1···O−N	133.7	110.8
	∠C1−H1···O	118.2	110.7
	∠N5···ON	52.2	69.6
A18	*r*N−O	1.140	1.135
	*r*H1···N	2.835	2.782
	∠H1···N−O	111.38	108.74
	∠C1−H1···N	120.7	123.0
	∠N5···ON	86.9	89.3
		$ImiH^+$···NO Complexes	
B1	*r*N−O	1.135	1.129
	*r*N···H5	2.111	2.021
	∠H5···N−O	131.6	134.3
	∠N5H5···N	168.8	168.8
B5	*r*N−O	1.151	1.142
	*r*O···H5	2.093	2.046
	∠H5···O−N	152.4	138.5
	∠N5H5···O	158.5	157.7
B7	*r*N−O	1.133	1.128
	*r*N···H1	2.381	2.297
	∠H1···N−O	180.0	180.0
	∠C1−H1···N	180.0	180.0
B10	*r*N−O	1.150	1.142
	*r*O···H1	2.305	2.304
	∠H1···O−N	180.0	180.0
	∠C1−H1···O	180.0	180.0

[a] Intermolecular distances (Å) and angles in degrees.

TABLE 4: AIM Atomic Charges Calculated at UMP2(full core)/6-311++G(2d,2p) for Selected $ImiH^+$···NO Complexes

atom	$ImiH^+$	**B1**	**B5**	**B7**	**B10**
C1	0.94	0.94	0.94	0.93	0.94
N2	−1.11	−1.11	−1.11	−1.11	−1.11
C3	0.40	0.40	0.40	0.40	0.40
C4	0.40	0.40	0.40	0.40	0.40
N5	−1.11	−1.13	−1.12	−1.12	−1.11
H1	0.18	0.17	0.17	0.19	0.19
H2	0.50	0.49	0.49	0.50	0.50
H3	0.15	0.15	0.15	0.15	0.15
H4	0.15	0.15	0.15	0.15	0.15
H5	0.50	0.51	0.51	0.50	0.50
		0.97	0.98	0.99	1.00
N	0.36	0.31	0.43	0.31	0.41
O	−0.36	−0.28	−0.41	−0.30	−0.41
		0.03	0.02	0.01	0.00

6-311++G(2d,2p) level (Tables 3 and 4). The Imi and $ImiH^+$ molecules have negative charges over the N atoms. In the uncharged molecule, the N2 atom has a larger electron density than the N5 atom (−1.13 against −0.95). According to the AIM partition of electron density, the NO molecule has a negative charge of −0.36 over the O atom and +0.36 over the N atom. Other schemes of electron density partition like NBO show the similar results. There is some redistribution of electron density in both monomers due to the formation of the dimers, basically over the atoms involved in the interaction. This effect is larger in the $ImiH^+$ than in the Imi complexes complexes.

In the cases of Imi complexes, the atomic charges of **A7**, **A9**, **A5**, and **A18** complexes are not significantly different from the monomer charges (the changes in charges are of the 0.001 e order of magnitude) and there is not a significant net charge on each unit. The atom directly involved in the interaction increases its electron density with respect to isolated molecules and the other decreases it. For example, the N atom in the **A1** has a charge of 0.34 e, 0.02 e smaller than the charge over N in isolated NO molecule. In this complex, there is a net electron transfer of 0.01 e from the NO radical to the Imi molecule. In the **A12** and **A16** complexes, which are not hydrogen bonded, there is a net electron transfer of 0.01 e from the Imi molecule to the NO radical.

All analyzed complexes of $ImiH^+$ are hydrogen bonded. In agreement with the positive charge on the $ImiH^+$, the electron transfer from NO is more effective in this kind of complex. For the **B1** complex, the most stable complex of $ImiH^+$, there was found the largest electron transfer of 0.03 e from NO to $ImiH^+$. In spite of the change of 0.05 e in NO atomic charges for the **B10** complex, there is not a net electron transfer from Imi to NO.

TABLE 3: AIM Atomic Charges Calculated at UMP2(full core)/6-311++G(2d,2p) for Selected Imi···NO Complexes

atom	Imi	**A1**	**A5**	**A7**	**A9**	**A12**	**A16**	**A18**
C1	0.83	0.83	0.83	0.83	0.83	0.83	0.83	0.83
N2	−1.13	−1.14	−1.14	−1.14	−1.13	−1.13	−1.13	−1.14
C3	0.32	0.31	0.32	0.32	0.32	0.32	0.32	0.31
C4	0.35	0.34	0.34	0.34	0.34	0.34	0.35	0.34
N5	−0.95	−0.95	−0.95	−0.95	−0.95	−0.95	−0.95	−0.94
H1	0.06	0.06	0.06	0.06	0.06	0.07	0.07	0.07
H2	0.42	0.45	0.43	0.42	0.42	0.42	0.42	0.42
H3	0.06	0.05	0.06	0.07	0.07	0.06	0.04	0.06
H4	0.04	0.04	0.04	0.05	0.04	0.05	0.06	0.05
		−0.01	0.00	0.00	0.00	0.01	0.01	0.00
N	0.36	0.34	0.38	0.35	0.37	0.35	0.36	0.34
O	−0.36	−0.33	−0.38	−0.35	−0.37	−0.36	−0.37	−0.34
		0.01	0.00	0.00	0.00	−0.01	−0.01	0.00

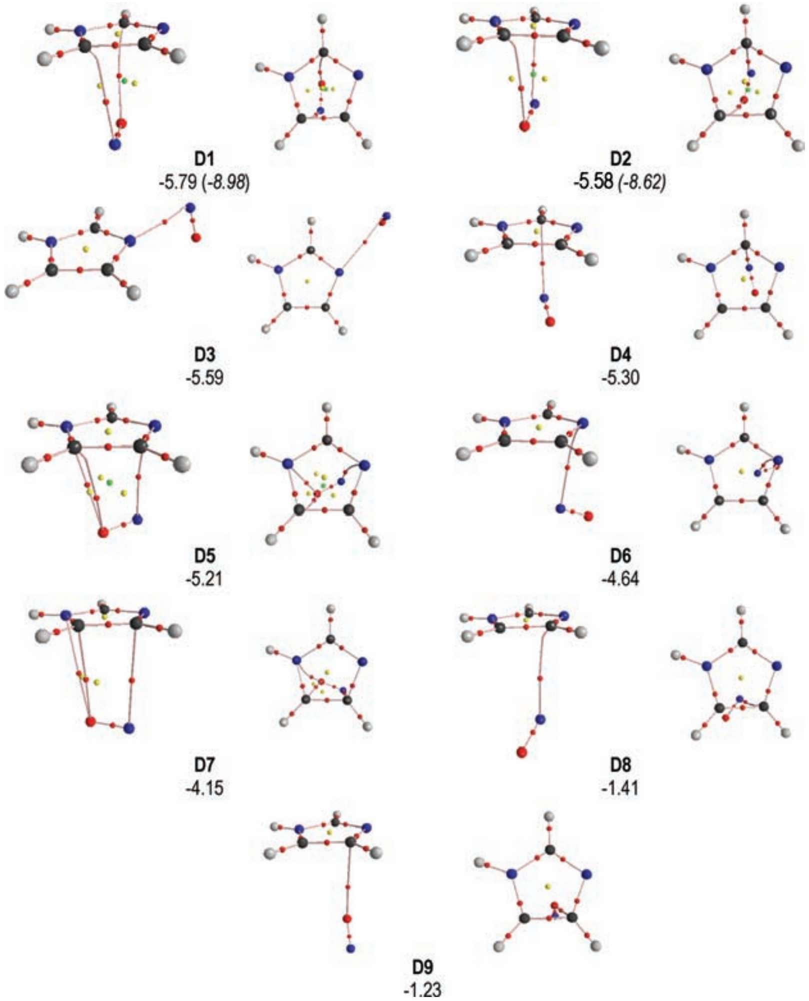


Figure 5. Molecular graphs for nonplanar complexes of Imi···NO. Atoms are represented by the large spheres. The colors corresponding to carbon, nitrogen, oxygen, and hydrogen atoms are gray, blue, red, and white, respectively. Small red spheres are the bond critical points (bcp's), yellow spheres are the ring critical points (rcp's), and green spheres are cage critical points (ccp's) of electron densities. Stabilization energies (kJ/mol) are shown at the UMP2(full core)/6-31++G(d,p) level of theory corrected from BSSE. Stabilization energies calculated at the UMP2(full core)/6-311++G(2d,2p) level of theory (BSSE corrected) are shown for the most stable complex of each interaction in italics.

Electron transfer between both molecules depends on the nature of the involved interactions. For the Z−H···X−Y interactions (where Z = C or N and X, Y = N or O) an electron transfer can appear from the NO to Imi molecule. Consequently, these interactions are more favorable for charged $\mathrm{ImiH^+}$ complexes. For the complexes stabilized by the Z···X−Y interactions, the Imi ring acts as electron donor and electron transfer is from the ring to the NO molecule.

Can these Z−H···X−Y interactions be classified as hydrogen bonds? The classification of intermolecular complexes as hydrogen bonded is controversial. On the basis of AIM framework Koch and Popelier had established a set of criteria valid to many hydrogen bonded complexes.[32] Do these interactions fill these criteria for hydrogen bonding? First, they have the right topology of the gradient vector field. The bond paths linked the involved atoms, and they are almost coincident with the line between the involved atoms. The majority of the complexes have only one bcp between the monomers. The **A16**, **A17**, **A18**, and **A19** complexes have two interactions: N···O and C−H···NO or C−H···ON. In these cases an rcp guaranteeing a consistent topology also appears (Figure 3). The electron densities in the bcp's are between 0.005−0.019 au for Z−H···NO and 0.005−0.015 au for Z−H···ON complexes. These values are in the range of typical hydrogen bonds (0.002−0.034 au). The stabilization energies show a good linear correlation to electron density on the bcp's ($R = -0.88$ for Z−H···NO complexes and $R = -0.98$ for Z−H···ON complexes; see S3 and S4 in Supporting Information). A larger electron density in the bcp's corresponds to more stable complexes. For these complexes, the $\nabla^2\rho(\mathrm{bcp}) > 0$, and a good correlation to stabilization energies was found. Another criterion satisfied by these complexes is a loss of charge over the H atom involved in the interaction. On the other hand, an electron transfer from the acceptor to the donor is usually found in hydrogen bonded systems.

The planar Z−H···XY complexes formed with imidazole and its protonated form can be classified as hydrogen bonds. These complexes have the topological parameters of electron density in the range of typical hydrogen bonds found between closed-shell molecules. The electronic state of the most stabilizing Z−H···XY interactions is A′; thus the unpaired orbital is symmetrical with respect to the aromatic ring plane. This orbital can be on the line of interaction and it can participate in the hydrogen bond. Previous investigations about the interactions between open-shell (OH, F, NH_2, and HO_2 radicals) and closed-shell molecules do not show a significant influence of unpaired orbital.[33,34] Nevertheless, the analysis of these intermolecular

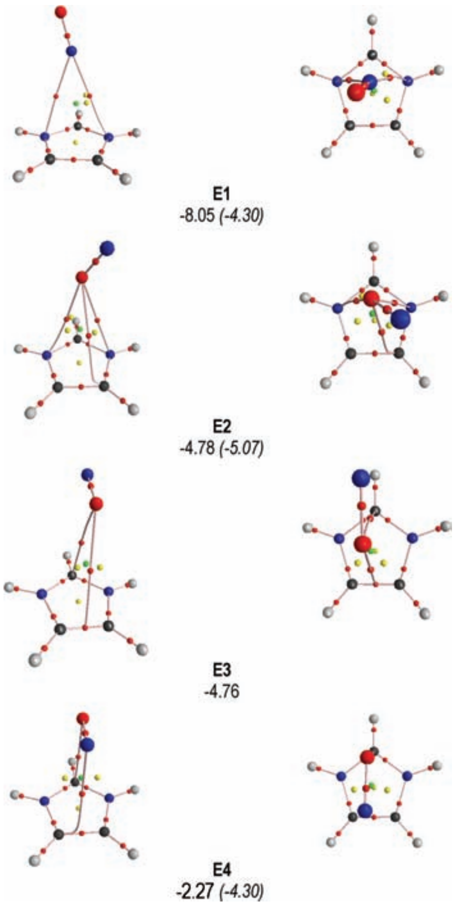


Figure 6. Molecular graphs for nonplanar complexes of $ImiH^{+}\cdots NO$. Atoms are represented by the large spheres. The colors corresponding to carbon, nitrogen, oxygen, and hydrogen atoms are gray, blue, red, and white, respectively. Small red spheres are the bond critical points (bcp's), yellow spheres are the ring critical points (rcp's), and green spheres are cage critical points (ccp's) of electron densities. Stabilization energies (kJ/mol) are shown at the UMP2(full core)/6-31++G(d,p) level of theory corrected from BSSE. Stabilization energies calculated at the UMP2(full core)/6-311++G(2d,2p) level of theory (BSSE corrected) are shown for the most stable complex of each interaction in italics.

complexes and others formed by NO and a closed-shell partner suggests a different situation.

c. Nonplanar Complexes. Two different patterns of nonplanar complexes were found. In some complexes one of the NO atoms is pointing to the Imi molecule. There are others where the NO molecule is almost parallel to the aromatic ring. The nonplanar $ImiH^{+}$ complexes can be symmetrical with respect to the plane perpendicular to the aromatic ring. In these cases the corresponding A′ and A″ complexes can also be considered by employing a monodeterminantal method like UMP2. The loss of symmetry to a nonplanar nuclear configuration can produce a mixing of these states or the predominance of one of them. Symmetrical and nonsymmetrical complexes with respect to the perpendicular plane to the Imi ring will be analyzed.

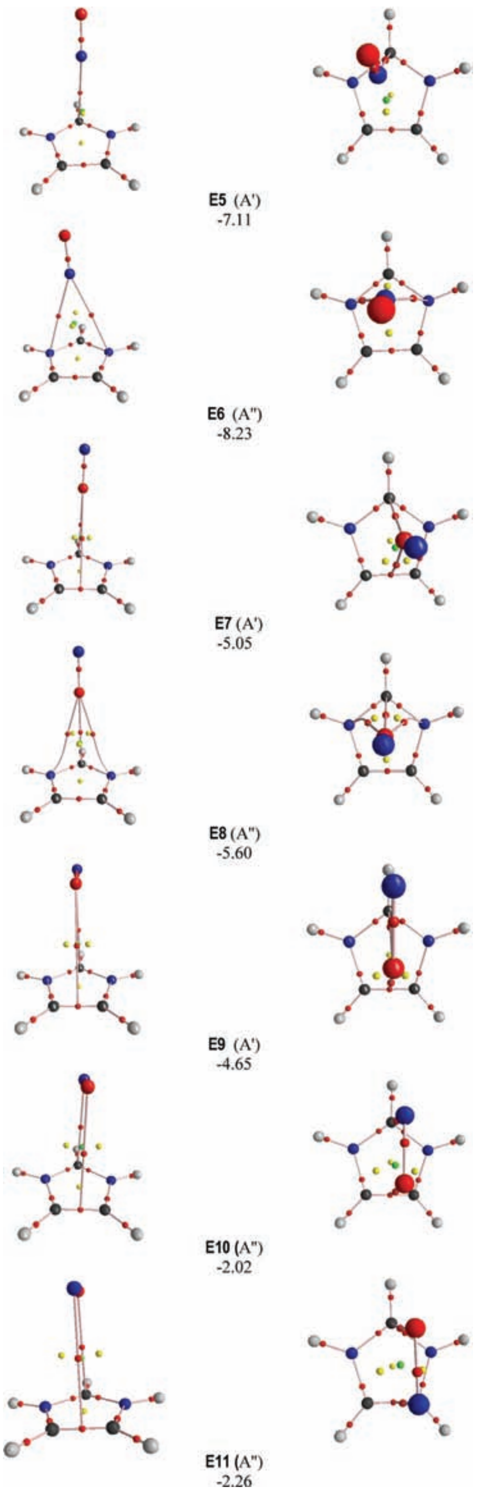


Figure 7. Molecular graphs for nonplanar complexes of $ImiH^{+}\cdots NO$. These complexes are symmetrical with respect to the plane that bisects the protonated imidazole molecule. Atoms are represented by the large spheres. The colors corresponding to carbon, nitrogen, oxygen, and hydrogen atom are gray, blue, red, and white, respectively. Small red spheres are the bond critical points (bcp's), yellow spheres are the ring critical points (rcp's), and green spheres are cage critical points (ccp's) of electron densities. Stabilization energies (kJ/mol) are shown at the UMP2(full core)/6- 31++G(d,p) level of theory corrected from BSSE. Stabilization energies calculated at the UMP2(full core)/6-311++G(2d,2p) level of theory (BSSE corrected) are shown for the most stable complex of each interaction in italics.

The geometries of nonplanar complexes are shown in Figure 5−7. **D** and **E** letters were used to denominate the unprotonated and protonated complexes. Their stabilization energies are listed in Figures 6 and 7. In some complexes, there are many bond paths between both molecules (namely **D1**, **D2**, **D5**, **D7**, **E1**, **E2**, **E3**, and **E4** complexes). For other complexes (**D3**, **D4**, **D6**, **D8**, and **D9**) there is only one bond path. Four types of interactions were found: $C\cdots NO$, $C\cdots ON$, $N\cdots NO$, and $N\cdots ON$. Neither of these interactions involves the H atoms of the imidazole ring. These interactions have smaller values of electron densities on the bcp's as is found for very weak

TABLE 5: Topological Features of Electron Densities (UMP2(full core)/6-31++G(d,p)) on bcp's for Nonplanar Complexes

complexes	interactions	ρ(bcp)	$\nabla^2\rho$(bcp)	ellipticity	G(bcp)	V(bcp)	$\lvert V$(bcp)$\rvert/G$(bcp)
Imi···NO Complexes							
D1	C1···ON	0.008	0.031	2.5149	0.0068	−0.0060	0.87
	C3···NO	0.012	0.037	1.1265	0.0076	−0.0060	0.79
D2	C1···NO	0.010	0.034	0.3206	0.0069	−0.0054	0.79
	C3···ON	0.007	0.023	1.7389	0.0052	−0.0045	0.87
D3	N5···NO	0.010	0.035	0.0380	0.0075	−0.0063	0.84
D4	C1···NO	0.008	0.030	0.5785	0.0061	−0.0047	0.78
D5	N2···ON	0.006	0.022	1.5663	0.0051	−0.0046	0.91
	C3···ON	0.006	0.022	3.1502	0.0048	−0.0041	0.86
	N5···NO	0.007	0.024	1.1773	0.0052	−0.0043	0.82
D6	N5···NO	0.009	0.029	1.5091	0.0066	−0.0060	0.91
D7	N2···ON	0.006	0.021	4.2092	0.0050	−0.0046	0.93
	C3···ON	0.006	0.023	13.7197	0.0051	−0.0044	0.87
	C4···NO	0.008	0.023	0.6360	0.0051	−0.0044	0.87
D8	C4···NO	0.008	0.026	1.2752	0.0053	−0.0043	0.80
D9	C4···ON	0.006	0.021	1.0687	0.0046	−0.0039	0.86
ImiH^+···NO Complexes							
E1	N2···NO	0.007	0.023	1.1102	0.0053	−0.0048	0.91
	N5···NO	0.006	0.023	5.2658	0.0051	−0.0044	0.87
E2	N2···ON	0.006	0.025	5.1738	0.0056	−0.0049	0.88
	N5···ON	0.007	0.024	1.8220	0.0055	−0.0050	0.92
	C4···ON	0.006	0.023	6.3164	0.0051	−0.0043	0.85
E3	C1···ON	0.005	0.022	0.6931	0.0048	−0.0038	0.79
	bcp(C3−C4)···ON	0.005	0.019	7.6025	0.0040	−0.0033	0.83
E4	C1···ON	0.007	0.028	1.6265	0.0061	−0.0051	0.85
	C3···NO	0.007	0.022	1.7286	0.0046	−0.0036	0.78
C_s Complexes							
E5	C1···NO	0.006	0.023	1.2293	0.0048	−0.0039	0.81
E6	N2···NO	0.007	0.023	1.4664	0.0051	−0.0046	0.90
	N5···NO	0.007	0.023	1.4664	0.0051	−0.0046	0.90
E7	C1···ON	0.006	0.026	3.1461	0.0057	−0.0047	0.82
	bcp(C3−C4)···ON	0.005	0.021	1.1655	0.0044	−0.0037	0.84
E8	C1···ON	0.006	0.027	16.131	0.0058	−0.0048	0.83
	N2···ON	0.006	0.025	8.5036	0.0055	−0.0048	0.87
	N5···ON	0.006	0.025	8.5036	0.0055	−0.0048	0.87
E9	C1···ON	0.005	0.022	0.3078	0.0047	−0.0039	0.83
	bcp(C3−C4)···ON	0.004	0.018	7.7393	0.0040	−0.0033	0.83
E10	C1···NO	0.007	0.027	0.6694	0.0056	−0.0043	0.77
	bcp(C3−C4)···ON	0.005	0.019	2.1946	0.0040	−0.0033	0.83
E11	C1···ON	0.007	0.028	1.6351	0.0061	−0.0051	0.84
	bcp(C3−C4)···NO	0.007	0.023	1.8584	0.0046	−0.0036	0.78

interactions. The larger values of electron densities on bcp's are found for the N···NO interactions. At the same time, these interactions have the largest covalent nature with $|V$(bcp)$|/G$(bcp) near unity. Electron densities in N···NO bcp's are slightly larger than those found in N···ON bcp's. It is also found that the C···NO interactions have larger electron densities on the bcp's than C···ON.

The N···NO interactions in these complexes have smaller electron densities in the bcp's than those obtained for similar interactions in planar complexes (Table 5). Ellipticities are large (with the exception of **D3** complex), showing an accumulation of electron densities in one of directions perpendicular to the interaction line. Consequently, these interactions have a considerable π nature.

The uncorrected BSSE stabilization energies are slightly larger than those obtained for the neutral complexes. Nevertheless, the stabilization energies (BSSE corrected) of nonplanar complexes of Imi···NO and ImiH^+···NO at UMP2(full core)/6-31++G(d,p) are similar.

For the Imi···NO complexes, **D1** and **D2** complexes are the most stable (stabilization energies of −5.79 and −5.58 kJ/mol calculated at UMP2/6-31++G(d,p); the values at the UMP2/6-311++G(2d,2p) level of theory are −8.98 and −8.62 kJ/mol, respectively). The geometry and the topology of their electron densities are similar, but the orientation of NO is reversed. There are two critical points between both molecules. For the **D1** complex, the interactions are related to the C1···ON and the C3···NO bond paths. C1···NO and the C3···ON interactions are found for the **D2** complex. A pair of ring critical points and a corresponding cage critical point also appear in the perpendicular direction of the Imi plane.

The geometry of **D5** allows three interactions N2···ON, N5···NO, and C3···ON. Three ring critical points and a cage also appear (see Figures). The **D7** complex is similar to **D5**, but the position of NO is slightly different and the N5···NO is substituted by the C4···NO interaction.

The rest of unprotonated Imi···NO complexes are stabilized by only one interaction. **D3** and **D6** have stabilization energies of −5.59 and −4.64 kJ/mol, respectively. These complexes have the interactions N5···NO, but they differ in the NO orientation. For **D3** the bond path is almost in the plane of the Imi ring. In the case of the **D6** complex, the N···N bond path is almost perpendicular to this plane. Although both interactions have similar electron densities on the bcp's, their ellipticies are very different (0.0380 for **D3** and 1.5663 for **D6**, which has a π nature). **D4**, **D8**, and **D9** complexes are stabilized by the interactions C1···NO, C4···NO, and C4···ON, respectively.

TABLE 6: AIM Atomic Charges Calculated at UMP2(full core)/6-311++G(2d,2p) for Selected Nonplanar Complexes

atom	**D1**	**D2**	**E1**	**E2**	**E3**
C1	0.83	0.84	0.94	0.95	0.94
N2	−1.13	−1.14	−1.11	−1.11	−1.11
C3	0.32	0.32	0.40	0.40	0.40
C4	0.35	0.35	0.41	0.40	0.40
N5	−0.94	−0.95	−1.11	−1.11	−1.11
H1	0.07	0.07	0.17	0.18	0.18
H2	0.43	0.43	0.50	0.50	0.50
H3	0.06	0.06	0.15	0.15	0.16
H4	0.05	0.04	0.15	0.15	0.16
H5			0.50	0.50	0.50
	0.04	0.02	1.00	1.01	1.01
N	0.32	0.35	0.31	0.40	−0.36
O	−0.36	−0.37	−0.31	−0.41	0.35
	−0.04	−0.02	0.00	−0.01	−0.01

Four ImiH^{+}···NO complexes were found without symmetry constraints on the optimization. These complexes **E1**, **E2**, **E3**, and **E4** show similar geometrical patterns to unprotonated ones. For protonated Imi, complexes with NO pointing to the middle of the ring (**E1** and **E2**) are more stable than where the NO is parallel tothe ring (**E3** and **E4**). **E1** (the N atom of NO in the direction of the middle of the ring) has a pair of N···N interactions (N2···N and N5···N). For this complex the NO molecule is almost on the symmetry plane of ImiH^{+}. The constrained optimization of **E1** produces the complexes **E5** and **E6** corresponding to the A′ and A″ electronic states. Both complexes are minima on the potential energy surfaces. Their stabilization energies are −7.11 and −8.23 kJ/mol, respectively. The most stable complex, **E6**, is very similar to **E1**; they have similar stabilization energies (−8.05 kJ/mol) and the same critical points. They represent the same structure. Their differences are related to the optimization criteria and the planarity of PES. The **E5** complex has only one bcp with the Imi molecule and related to the interaction C1···N, which has a smaller electron density, and it is consequently weaker. The **E2** complex has a pair of N···O interactions (N2···O and N5···O), and additionally, an interaction between O and C3···C4 is also found. Symmetrical nuclear configurations related to **E2** are shown in Figure 7 (**E7** and **E8** complexes). For the **E8** complex, the A″ electronic state is again the most stable and it has a topology of electron density similar to that of **E2.**

The geometries of the **E3** and **E4** complexes are similar to the geometries of the unprotonated Imi for the **D1** and **D2** complexes, respectively. In the case of the **E3** complex, no interaction of the Imi ring with the N atom of the NO molecule is found. There were a couple of bond paths with the O atom (one with C1 atom and the other with the bcp in the middle of C3−C4 bond). When the symmetry is forced, the obtained complexes **E9** and **E10** (electronic states A′ and A″, respectively) are transition states with very small imaginary frequencies. The most stable complex, **E9**, has a stabilization energy of −4.65 kJ/mol and the barrier to the **E3** minima is only 0.11 kJ/mol.

Complex **E4** is too similar to the corresponding symmetrical complex **E11**. In this case, the complex with A″ electronic state converges to the **E8** complex.

For these complexes, there is not a significant effect of protonation on the stabilization of the complexes. The stabilization energies of ImiH^{+}···NO complexes are similar to those obtained for the unprotonated ones. At the same time, planar ImiH^{+}···NO complexes appear as the most stable of all studied.

Table 6 shows the values of AIM charges over all atoms in the complexes **D1**, **D2**, **E1**, **E2**, and **E3**. For these complexes (with the exception of **E1**) there is a charge transfer from the molecule of Imi to the NO molecule. These complexes are all stabilized by Z···X−Y (with X, Y = N or O) and are similar to the case of planar complexes stabilized by this kind of interaction. Here was found an electron transfer from the Imi molecule (charged or not) to the NO. This transfer is more effective for neutral Imi.

4. Conclusions

We have performed in this paper a study of complexes between imidazole and nitric oxide. The effect of protonation of the imidazole molecule was also considered. These molecules establish weak interactions, which can have biological significance. On the other hand, these complexes can be seen as models for interactions between closed-shell and open-shell molecules, especially for open-shell molecules where the spin density is distributed on different atoms.

The potential energy surfaces of open-shell systems are complex because, among other reasons, there are many electronic states with similar energies. To analyze these systems, the theoretical models should consider different electronic states. In our case, two electronic states were considered for planar complexes and, consequently, many stable structures were obtained and must be considered. They have similar stabilization energies and can be populated at relatively low temperature. Then, entropy seems to be important for these systems and can be affected by a dynamical equilibrium between different stable structures at room temperature.

It is well-known that the NO molecule can act as either a Lewis acid or a base. Both kinds of behaviors were found in the studied complexes. For those stabilized by Z−H···X−Y (X, Y = N or O) interactions appearing in planar complexes, NO acts as a Lewis base employing its unpaired electron or lone pairs. For these complexes a charge transfer from NO to the Imi molecule can be shown. According to the Koch and Popelier criteria for hydrogen bonding, the Z−H···X−Y interactions in these systems can be classified as hydrogen bonds. These complexes have topologies on their electron densities that are similar to those obtained in intermolecular complexes between closed-shell molecules. Nevertheless, the unpaired electron seems to be important in the stabilization of these complexes. The electron density of NO is distributed over both atoms and each Z−H···N−O interaction corresponds to a similar Z−H···ON complex. However, as the spin density over N is larger than the electron density on the O atom, Z−H···N−O complexes are more stable than similar Z−H···ON complexes.

The larger stability of N−H···X−Y with respect to the C−H···X−Y interactions can be understood if a simple qualitative donor−acceptor picture is employed. The energies of localized N−H antibonding orbitals are more similar to the energies of bonding orbitals of NO. Consequently, as the protonation of Imi reduces the energy of Imi antibonding orbitals, the Z−H···X−Y interactions in protonated complexes are more stable than in neutral ones.

The complexes stabilized by C···NO, C···ON, N···NO, and N···ON interactions show the ability of NO to act as a Lewis acid. Consequently, a charge transfer from Imi to NO can be found. The low energy unoccupied orbitals of the NO molecule receive electron density from double occupied orbitals of the Imi molecule. These double occupied orbitals can be on the ring plane or in the plane perpendicular to the aromatic ring.

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Supporting Information Available: Tables of stabilization energies and graphs of stabilization energies vs electron densities. This material is available free of charge via the Internet at http://pubs.acs.org.

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