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Lewis acidity of NO^+ and NO_2^+ as measured by their affinity to selected bases. An ab initio background study of biological NO release

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Abstract

The very fact that a simple molecule such as NO, can play a key bioregulatory function in a number of physiological responses is simply astonishing in view of the fact that most biologically active molecules are rather complex. In order to understand better the reactivity of NO and its related species, we undertook the study of affinity between $NO^{(+)}$ and $NO_2^{(+)}$ and different inorganic as well as organic bases. For the molecules under study and their derived ionic species, the geometries were fully optimized at the Hartree–Fock level with two basis sets: 3-21G and 6-31 + G(d). Estimation of $X^{(+)}$ affinities at the two basis set used, showed that in gas phase NH_3 is the most basic and H_2S is the least basic of the inorganic bases. For all the three bases, protonation showed a much greater exothermicity than the interaction with NO^+ or NO_2^+. Protonation affinities are in the order of 200 kcal/mol, suggesting a strong bond formation for these species. We observed an increase in the basicity when a methyl group replaced one hydrogen, at both levels of theory. Taken into consideration all the bases studied, both Bronsted and Lewis acidities show a preference for N over O or S. Inorganic species derived from $NO_2^{(+)}$ have stronger bonds than those derived from $NO^{(+)}$ with the exception of those containing S as an heteroatom. The low affinity energy for the nitrosylated sulfur derivatives makes these molecules suitable as reservoirs for the nitrosyl group, thus release and captivation of the group is achieved easily.

Keywords: Nitric oxide; Nitrosonium ion; Nitroniun ion; Lewis acidity; Ab initio study

1. Introduction

Nitric oxide (:N≡O: or simply NO) has a glorious past, an exciting present and an unprecedented future. Table 1 summarizes some historic milestones of NO [1–7] in the past. At present, we are dealing with questions that had been raised during the past 10–15 years. Until the middle of the 1980s nitric oxide had not been considered anything more than an atmospheric pollutant and bacterial metabolite [8]. The identity of NO with the endothelium derived relaxing factor (EDRF) [9] opened up new doors in biochemistry [10,11] that had led to the exciting present situation [12–19]. The very fact that a simple molecule such as NO, can play a key bioregulatory function

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Table 1
Historic milestones in the past of nitric oxide (NO)

Year	Scientist	Happening	Ref.
1620	Jan Baptist van Helmont	NO was prepared for the first time	[1]
1660	Bobert Boyle and Robert Hooke	Synthesis: KNO_3 + C(hot)[a]	[2]
1772	Joseph Priestley	Synthesis: HNO_3 + Metal[b]	[3,4]
1806	J.A. Murray	New name: nitric oxide	[5]
1840	Walter Crum	Synthesis: HNO_3 + H_2SO_4 + Hg	[6]
1908	Fritz Haber	Presence of NO in electric arcs	[7]

[a] In the absence of air.
[b] For example: $3Cu + 8H^+ + 2NO_3 \rightarrow 3Cu^{2+} + 4H_2O + NO$.

in a number of physiological responses [11,20,21] is simply astonishing in view of the fact that most biologically active molecules are rather complex.

Nitric oxide has a very small electron affinity (EA)

$$NO + e^{(-)} \rightarrow NO^{(-)}, \qquad EA = 0.5 \text{ kcal/mol}$$

so that $NO^{(-)}$ is only slightly more stable than NO. In contrast to this NO has a fairly large ionization energy (IE) so that $NO^{(+)}$ is over 200 kcal/mol higher on the energy scale.

$$NO \rightarrow NO^{(+)} + e^{(-)}, \qquad IE = 213.51 \text{ kcal/mol}.$$

The ionization energies of N_2 (which does not have any odd electron in its π valence shell) and that of NO (which has one odd electron in its π valence shell) as well as that of O_2 (which has two odd electrons in its π valence shell) are compared in Fig. 1. Clearly, the reactivity of NO and that of O_2 lies in their open electronic shells. It is interesting to note, that NO is the most easily ionizable of the three.

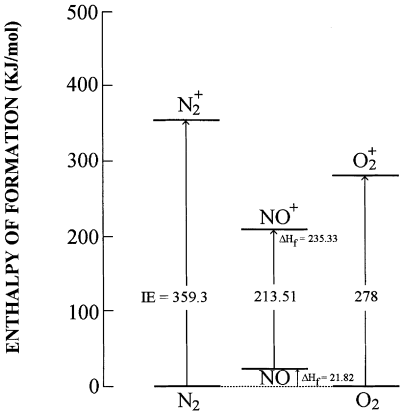


Fig. 1. Ionization energies of N_2, O_2 and NO.

The gas phase chemistry is, however, modified in solution. The ion $NO^{(+)}$ is available in solution without investment of a large amount of energy in contrast to gas phase where it requires an investment of 213.51 kcal/mol. In a protonating environment the $NO^{(+)}$ transfer from one base to another may well be energetically feasible:

$$Y\text{–}NO + H_3O^{(+)} \rightarrow H\text{–}Y\text{–}NO^{(+)}, \qquad (1)$$

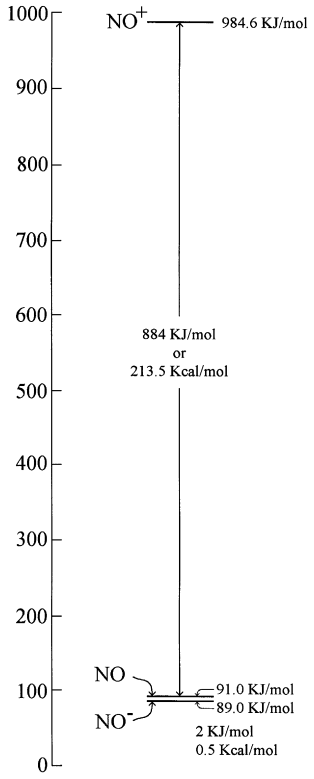


Fig. 2. Relative stabilities of $NO^{(-)}$, NO and $NO^{(+)}$.

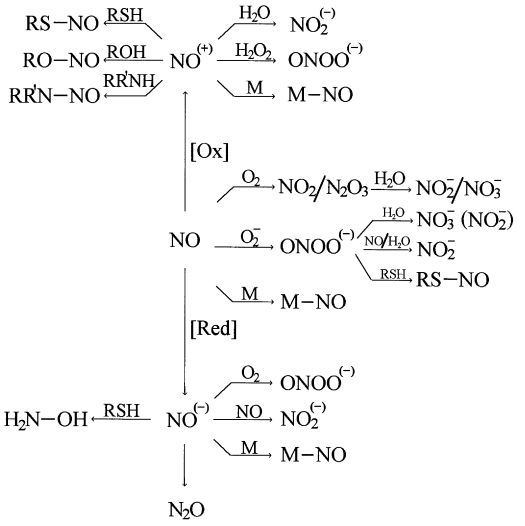


Fig. 3. Overview of chemical reactivities of $NO^{(-)}$, NO and $NO^{(+)}$ in biological systems.

$$H–Y–NO^{(+)} + : Z \rightarrow H–Y + Z–NO^{(+)}. \quad (2)$$

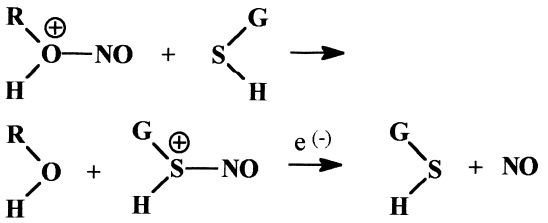
It is not surprising therefore that under biological conditions all three species i.e. $NO^{(+)}$, NO and $NO^{(-)}$ (cf. Fig. 2) jointly may play a role. In fact, all three species may react with a variety of reagents (cf. Fig. 3).

The diatomic molecule, NO, is an intracellular messenger, though the size of the molecule does not predestine this. Yet it is formed biologically in the vascular endothelial cells and by diffusion it relaxes the underlying smooth muscle of the blood vessel walls. In this case the NO release occurs from *N*-hydroyl-L-arginine which is formed by the oxidation of arginine. Overall, the five electron oxidation is catalyzed by the enzyme called NO synthase (NOS) [22,23].

Nitric oxide is also released from nitrate esters (e.g. nitroglycerin) via the formation of an intermediate nitrite ester as illustrated by the Eq. (4):

$$R–O–NO_2 + 2[H] \rightarrow\rightarrow\rightarrow H_2O + R–O–NO \rightarrow\rightarrow \rightarrow NO. \quad (4)$$

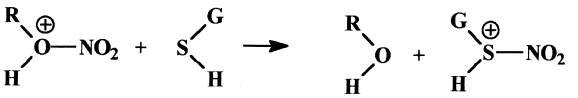
The mechanism of this reaction is strongly debated but one of the proposed mechanisms involves the following steps:



(5)

where GSH stands for glutatione.

In this sense, the affinity of $NO^{(+)}$ to oxygen and sulfur is questionable. However, a similar transfer may also occur, at least, in principle, involving the $NO_2^{(+)}$ group:

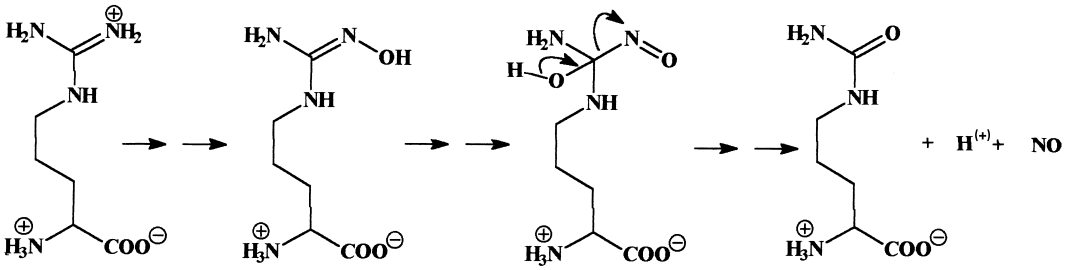


(6)

and therefore the $NO_2^{(+)}$ affinity to heteroatoms such as O and S is also of some interest.

It is of interest to determine whether the extraordinarily diverse biological functions that are currently attributed to NO and related species are consistent with what is known of their chemistry.

NO is a species with an unpaired electron and therefore NO is, by definition, a radical. Nitrosothiols do



(3)

Table 2
Energy values calculated at the two levels of theory: HF/3-21G and HF/6-31 + G(d)) for the ions NO^+, NO_2^+ and the inorganic and organic bases studied

Molecule	*E* (hartree) HF / 3-21G	HF / 6-31 + G(d)
H_3N:	−55.8722035	−56.1894994
H_2O:	−75.5859597	−76.0177432
H_2S:	−396.7046661	−398.6681147
$CH_3(H)_2N$:	−94.6779255	−95.21417294
$CH_3(H)O$:	−114.3956604	−115.04096513
$CH_3(H)S$:	−435.5245598	−437.69754660
$NO^{(+)}$	−128.1377176	−128.9124881
$NO_2^{(+)}$	−202.46006	−203.6778051

occur naturally in human plasma, mainly as the nitrosothiol of human serum albumin. The biosynthesis of nitrosothiols is a matter of controversy. They are not formed by the reaction of NO with thiol at pH 7 as has been suggested. The required nitrosating species would be $NO^{(+)}$ [24]. $NO^{(+)}$ is responsible for a number of electrophilic reactions but it is too reactive to exist in aqueous solution. Thus it would have only a transient existence. Lipton et al. [25] suggested that the oxidized form of NO, the nitrosonium ion ($NO^{(+)}$) as well as NO itself are active in the brain. They also reported that $ONOO^-$ may have a neurotoxic role, perhaps inclusive of nitronium ion (NO_2^+).

In strongly acid solution, $NO^{(+)}$ is responsible for the conversion of a thiol (RSH) into a nitrosothiol (RSNO).

$$RSH + NO^{(+)} \rightarrow RSNO + H^{(+)}. \quad (7)$$

Nitrosothiol can transfer $NO^{(+)}$ to a second thiol or to another nucleophile (transnitrosation).

$$RSNO + R_2S^- \rightarrow RS^- + R_2SNO. \quad (8)$$

Nitroxide ions, $NO^{(-)}$ may result from the ionization of nitroxyl hydride (HNO) or as sometimes referred to 'nitroxyl'.

$$HNO \rightarrow H^+ + NO^{(-)}. \quad (9)$$

The possibility that nitroxide ions ($NO^{(-)}$) have a physiological role has been little explored, although it is quite feasible.

In previous articles we performed a theoretical study on the reaction mechanism of NO formation [26,27]. A mechanism of NO formation was modeled and we performed a configurational and conformational study by the AM1 method [26] and a thermodynamic study by ab initio calculations [27] on reactants, products and intermediates species.

In order to understand better the reactivity of NO and its related species, we undertook the study of affinity between $NO^{(+)}$ and $NO_2^{(+)}$ and a variety of inorganic as well as organic bases.

2. Methods

Calculations were performed for the $NO^{(+)}$ and $NO_2^{(+)}$ species, a number of inorganic and organic bases and their complexes. In all cases, geometries were fully optimized at the Hartree–Fock level with two basis sets: 3-21G and 6-31 + G(d). Diffuse functions (denoted by + in the basis set specification) are large size version of s- and p-type functions. These allow orbitals to occupy a larger region in space. Basis sets with diffuse functions are important for systems where electrons are relatively far from the nuclei: molecules with lone pairs, anions and other systems with significant negative charge, molecules in their excited states, systems with low ionization potentials, description of accurate acidities, and so on.

A positive electron affinity (EA) indicates that the anion is stable while a negative EA means that the anion is unstable. The accurate theoretical determination of EAs has proven to be difficult and large basis sets augmented with diffuse and polarization functions is always essential.

In order to obtain the relative Lewis-acid affinities, selected inorganic (NH_3, H_2O, and H_2S) and organic (CH_3–NH_2, CH_3–OH, and CH_3–SH) bases were chosen as model compounds to study the reactivitiness of $NO^{(+)}$ and $NO_2^{(+)}$, two of the possible cationic intermediates generated [24,27] upon the emergence of NO.

3. Results and discussion

Full Hartree–Fock optimization of the molecules under study at the two basis set level chosen was performed and the energy values obtained are summarized in Table 2. In this way the energy values of the reactants were obtained.

Table 3
Energy values and the X^+ affinity for the selected inorganic bases

Conjugate bases	HF/3-21G *E* (hartree)	Affinity (kcal/mol)	HF/6-31 + G(d) *E* (hartree)	Affinity (kcal/mol)
$H_3N–H^{(+)}$	−56.2338557	−226.94	−56.5312766	−214.47
$H_2O–H^{(+)}$	−75.8912281	−191.56	−76.29060497	−171.22
$H_2S–H^{(+)}$	−396.9521627	−155.31	−398.94274698	−172.33
$H_3N–NO^{(+)}$	−184.0855497	−47.46	−185.14391612	−26.31
$H_2O–NO^{(+)}$	−203.7802851	−35.52	−204.9641473	−21.08
H_2 S–$NO^{(+)}$	−524.8686029	−16.45	−527.5997118	−11.99
$H_3N–NO_2^{(+)}$	−258.4185130	−54.15	−259.9162743	−30.73
$H_2O–NO_2^{(+)}$	−278.0966544	−31.77	−279.7338086	−24.01
H_2 S–$NO_2^{(+)}$	−599.1862273	−13.49	−602.35177112	−3.67

3.1. H^+, NO^+ and NO_2^+ affinity

To determine the protonation energy (i.e. proton affinity) of the inorganic and organic bases, we performed calculations on the protonated forms (the conjugated acids) of the selected bases. Energies of protonation reactions, in gaseous phase, provide a direct measure for the intrinsic basicities of molecules.

In order to measure the nitrosylation and nitration energy of a number of bases (Z:) which could interact with the species $NO^{(+)}$ and $NO_2^{(+)}$, calculations were performed for the newly formed complexes: $Z–NO^{(+)}$ and $Z–NO_2^{(+)}$. As the energy of H^+ is zero, on the quantum mechanical scale, the proton affinities (A_H^+) were obtained from the energy differences between the neutral and protonated species.

$$Z: + H^{(+)} \rightarrow Z–H^{(+)}, \quad (10a)$$

$$A_{H+} = E[Z–H^{(+)}] - E[Z:]. \quad (10b)$$

The $NO^{(+)}$ and $NO_2^{(+)}$ affinity (A_{NO_+} and $A_{NO_2^+}$) is the energy released (ΔE) upon complexation and can be calculated as the energy difference between the nitrosylated molecule and the sum of the computed energies of the neutral base plus the energy for $NO^{(+)}$ or $NO_2^{(+)}$

$$Z: + NO^{(+)} \rightarrow Z–NO^{(+)}, \quad (11a)$$

$$A_{NO^+} = E[Z–NO^{(+)}] - \{E[Z:] + E[NO^{(+)}]\}, \quad (11b)$$

$$Z: + NO_2^{(+)} \rightarrow Z–NO_2^{(+)}, \quad (12a)$$

$$A_{NO_2^+} = E[Z–NO^{(+)}] - \{E[Z:] + E[NO_2^{(+)}]\}. \quad (12b)$$

Table 3 provides $X^{(+)}$ affinities, where $X^{(+)} = H^{(+)}$ or $NO^{(+)}$ or $NO_2^{(+)}$ at the two basis set used, for the inorganic bases. In gas phase NH_3 is the most basic and H_2S is the least basic of these compounds. For all the three bases, protonation showed a much greater exothermicity than the interaction with $NO^{(+)}$ or

Table 4
Energy values and the X^+ affinity for the selected organic bases

Molecule	HF / 3-21G E (hartree)	Affinity (kcal/mol)	HF / 6-31 + G(d) E (hartree)	Affinity (kcal/mol)
$CH_3(H)_2$ N–$H^{(+)}$	−95.0559815	−237.23	−95.57415901	−225.895
CH_3 (H)O–H $^{(+)}$	−114.7248392	−206.56	−115.34065957	−188.06
CH_3 (H) S–H $^{(+)}$	−435.80288896	−174.65	−438.00182490	−190.94
$CH_3(H)_2$N –NO $^{(+)}$	−222.9099292	−59.17	−224.17528915	−30.51
CH_3 (H)O–NO $^{(+)}$	−242.5978972	−40.49	−243.99052700	−23.26
CH_3 (H) S–NO $^{(+)}$	−563.7019561	−24.90	−566.64228550	−20.24
$CH_3(H)_2$N–$NO_2^{(+)}$	−297.25449633	−73.40	−298.96795643	−47.68
CH_3 (H)O–$NO_2^{(+)}$	−316.91998826	−40.26	−318.75889460	−25.18
CH_3(H)S–$NO_2^{(+)}$	−638.0128895	−17.73	−641.40489820	−18.54

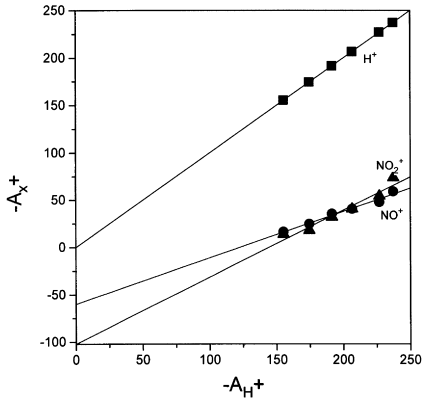


Fig. 4. Variation of Lewis acid ($X^+ = NO^{(+)}$ and $NO_2^{(+)}$) affinity: A_{X^+} with proton ($H^{(+)}$) affinity: A_{H^+} of selected bases calculated at HF/3-21 G level of theory. NB: m measures the Lewis acidity of X^+ with respect to proton Bronsted acidity at HF/3-21 G level of theory.

$NO_2^{(+)}$. Protonation affinities are in the order of 200 kcal/mol, suggesting a strong bond formation for these species. For all the three $X^{(+)}$ species the affinities decrease with the electronegativity of the heteroatom, as expected. Both nitrosylating and nitrating species showed similar affinities to the same heteroatom.

Although the same ordering of the affinity was maintained by the two sets of calculations performed, the affinity values are different with a larger effect on the nitrosylated species.

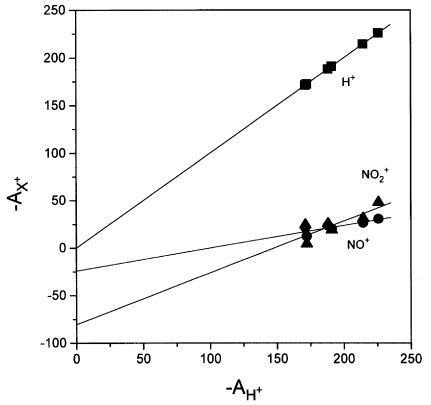


Fig. 5. Variation of Lewis acid ($X^+ = NO^{(+)}$ and $NO_2^{(+)}$) affinity: A_{X^+} with proton ($H^{(+)}$) affinity: A_{H^+} of selected bases calculated at HF/6-31 + G(d) level of theory. NB: m measures the Lewis acidity of X^+ with respect to proton Bronsted acidity at HF/6-31 + G(d) level of theory.

Only in the case of H_2S was a higher $H^{(+)}$ affinity value achieved with 6-31 + G(d) than with 3-21G calculations.

Electron donor substituents, such as the methyl group can easily modify the protonation capacity of the compounds. We performed affinity calculation on a set of organic bases where heteroatoms N, O, and S, were compared with the corresponding inorganic bases. Table 4 shows the energy values and the $X^{(+)}$ affinity for the selected organic bases.

Comparison of the data in Tables 3 and 4 clearly indicates an increase in the basicity when a methyl group replaces one hydrogen, at both levels of theory.

Taken into consideration all the bases studied, both Bronsted and Lewis acidities show a preference for N over O or S. Positive values of the affinities provide a measure of the energy required to brake the interaction between the Bronsted or Lewis acid and the base. The large H^+ affinity values suggest the formation of strong covalent bonds. The smaller $NO^{(+)}$ and $NO_2^{(+)}$ affinity values show relatively weak bonds typical of Lewis complexes.

Consistently stronger interaction was observed for $NO_2^{(+)}$ than for $NO^{(+)}$. These observations are comparable for the two basis sets used in the present study.

Figs. 4 and 5 show the dependence of the affinity for the Lewis acid ($NO^{(+)}$, $NO_2^{(+)}$) against the H^+ affinity at HF/3-21G and HF/6-31 + G(d), respectively. In all cases, N has a higher affinity than O and its affinity is higher than that of sulfur, as expected. This observation is valid for both inorganic as well as organic bases.

Of course when A_{H^+} is plotted against A_{H^+} at any level of theory (cf. Figs. 4 and 5) one obtains a straight line with unit slope and zero vertical intercept. However, when any Lewis acid affinity, such as A_{NO^+} or $A_{NO_2^+}$, is plotted against A_{H^+} we obtain a general straight line:

$$A_{X^+} = mA_{H^+} + A^0_{X^+}. \tag{13}$$

Here, the slope is less than unity ($m < 1$) and the vertical intercept $A^0_{X^+}$ is negative. This negative intercept is the measure of the Lewis complex instability when the base is so extremely weak that even protonation is thermoneutral

$$B : +H^{(+)} \rightarrow BH^{(+)} \qquad \Delta E = A^+_H = 0.0. \tag{14}$$

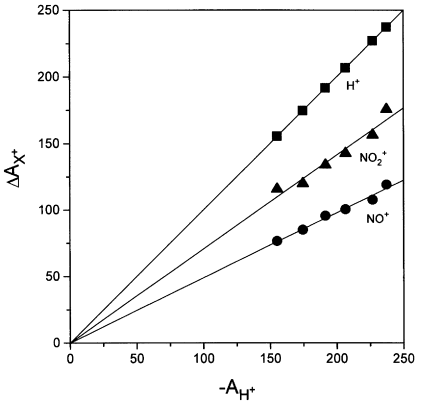


Fig. 6. Variation of relative Lewis acidity ΔA_{X^+} with proton affinity (A_{H^+}) for selected inorganic and organic bases at HF/3-21 level of theory.

If we shift the straight line vertically for $NO^{(+)}$ and $NO_2^{(+)}$ so that they pass through the origin then we effectively are plotting ΔA_{NO^+} and $\Delta A_{NO_2^+}$ against ΔA_{H^+}, which is, of course, the same as A_{H^+}

$$\{A_{NO^+} - A^0_{NO^+}\} = \Delta A_{NO^+} = mA_{H^+}, \quad (15)$$

$$\{A_{NO_2^+} - A^0_{NO_2^+}\} = \Delta A_{NO_2^+} = mA_{H^+}. \quad (16)$$

From such plots it is inmediately obvious that the slope of the straight lines (m) is a measure of the Lewis acidity as shown at the HF/3-21 G (Fig. 6)

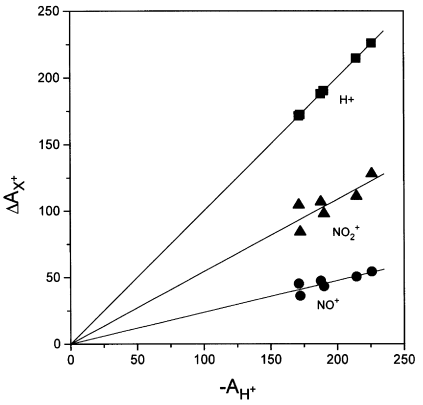


Fig. 7. Variation of relative Lewis acidity ΔA_{X^+} with proton affinity (A_{H^+}) for selected inorganic and organic bases at HF/6-31 + G(d) level of theory.

Table 5
A comparison of Lewis acidity (m)[a] of $NO^{(+)}$ and $NO_2^{(+)}$ as computed at HF /3-21G and HF /6-31 + G(d) level of theory

Species	m HF / 3-21G	HF / 6-31 + G(d)
$H^{(+)}$	1.000	1.000
$NO^{(+)}$	0.682	0.544
$NO_2^{(+)}$	0.477	0.239

[a] The values are relative to the acidity of $H^{(+)}$ which is taken to be unity (or 100 %).

and HF/6-31 + G(d) (Fig. 7) levels of theory. The fitted m values are summarized in Table 5.

3.2. Charge variation

Table 6 shows the variation of net charge over the heteroatom of the cation in comparison with the neutral molecule at the 6-31 + G(d) theory level for the inorganic and organic species.

Protonation of the heteroatom for the inorganic

Table 6
Variation of net charge over heteroatom of the cations in comparison with the bases at the 6-31 + G(d)

Molecule	Charge on heteroatoms (a.u)
H_3N:	−1.142
$H_3N–H^{(+)}$	−1.064
$H_3N–NO^{(+)}$	−1.279
$H_3N–NO_2^{(+)}$	−1.030
H_2O:	−0.99
$H_2O–H^{(+)}$	−0.887
$H_2O–NO^{(+)}$	−1.084
$H_2O–NO_2^{(+)}$	−1.120
H_2S:	−0.214
$H_2S–H^{(+)}$	0.238
$H_2S–NO^{(+)}$	−0.250
$H_2S–NO_2^{(+)}$	0.363
$CH_3(H)_2N$:	−0.9
$CH_3(H)_2NH^{(+)}$	−0.998
$CH_3(H)_2N–NO^{(+)}$	−0.950
$CH_3(H)_2N–NO_2^{(+)}$	−0.852
$CH_3(H)O$:	−0.746
$CH_3(H)O–H^{(+)}$	−0.784
$CH_3(H)O–NO^{(+)}$	−0.854
$CH_3(H)ONO_2^{(+)}$	−0.897
$CH_3(H)S$:	−0.052
$CH_3(H)S–H^{(+)}$	0.372
$CH_3(H)S–NO^{(+)}$	−0.16
$CH_3(H)S–NO_2^{(+)}$	0.657

Table 7
Variation on the net charge of N and O from $NO^{(+)}$ and $NO_2^{(+)}$ alone or in combination with inorganic bases and X–N distance of $X–NO^{(+)}$, $X–NO_2^{(+)}$ computed at the HF/6-31 + G(d) level of theory

Molecule	Net atomic charge for NO^+ (a.u)		Distance (Å)	Net atomic charge for NO_2^+ (a.u)			Distance (Å)
	N	O	X–NO $^{(+)}$	N	O	O	X–NO_2 $^{(+)}$
NO $^{(+)}$	0.435	0.565	–	–	–	–	–
$NO_2^{(+)}$	–	–	–	1.290	−0.145	−0.145	–
$H_3N–NO$ $^{(+)}$	0.448	0.458	2.268	–	–	–	–
$H_3N–NO_2^{(+)}$	–	–	–	0.518	−0.067	−0.109	1.514
$H_2O–NO^{(+)}$	0.446	0.120	2.169	–	–	–	–
$H_2O–NO_2^{(+)}$	–	–	–	0.780	0.113	0.113	2.460
H_2 S–NO $^{(+)}$	0.422	0.485	2.855	–	–	–	–
H_2 S–$NO_2^{(+)}$	–	–	–	0.287	−0.085	−0.084	1.930

base decreases the net negative charge of the heteroatom, as expected. In contrast, while NO^+ increases the negative charge over the heteroatom and $NO_2^{(+)}$, in general, decreases the negative charge, except for Oxygen (Table 6). Net atomic charge over the heteroatom for organic bases is lower than that for their corresponding inorganic bases (Table 6).

It is interesting to note that while the addition of $NO^{(+)}$ to the bases renders more negative charge over the heteroatom, addition of the $NO_2^{(+)}$ species has the opposite effect.

Net atomic charges over the N and O atoms of $NO^{(+)}$ and $NO_2^{(+)}$ alone or as substituents for inorganic and organic bases are shown in Table 7 and 8. These tables show the effect of the substituents on charge distribution.

On the isolated species, $NO^{(+)}$ has the positive charge distributed over the N and O atoms. For $NO^{(+)}$ substituted species, no major effect is observed over the N atom, but an important decrease over the O charge is observed for $H_2O–NO^{(+)}$ or $CH_3.(H_2)N–NO^{(+)}$. In all cases, addition of $NO^{(+)}$ to any of the bases became more negative the net atomic charge over the heteroatom (Tables 5–7). Obviously, the positive charge of $NO^{(+)}$ has to be distributed along the atoms within the molecules and it seems to be transferred to the H or CH_3 moieties.

For $NO_2^{(+)}$ ion, the positive charge is over the N atom and, as a consequence of the interaction, the charge over the heteroatom is more affected.

From all the bases studied, those derived from S, the less electronegative atom, suffers stronger effects over nitrosylation. The X–N distance varies from 1.514 for the $NH_3–NO_2^+$ to 2.855 for the $H_2S–NO^+$. This observation together with the affinity values obtained, confirm that covalent bonds are formed only for proton, while all the others form relatively weak Lewis complexes (Table 6).

Table 8
Variation on the net charge of N and O from $NO^{(+)}$ and $NO_2^{(+)}$ alone or combination with organic bases and N-O distance of $X-NO^{(+)}$, $X–NO_2^{(+)}$ computed at the HF/6-31 + G(d) level of theory

Molecule	Net atomic charge for $NO^{(+)}$ (a.u)		Distance (Å)	Net atomic charge for $NO_2^{(+)}$ (a.u)			Distance (Å)
	N	O	X–NO $^{(+)}$	N	O	O	X–$NO_2^{(+)}$
$NO^{(+)}$	0.435	0.565	–	–	–	–	–
$NO_2^{(+)}$	–	–	–	1.290	−0.143	−0.143	–
$CH_3(H)_2N–NO$ $^{(+)}$	0.323	0.105	2.248	–	–	–	–
$CH_3(H)_2N–NO_2^{(+)}$	–	–	–	0.505	−0.126	−0.114	2.222
CH_3 (H)O–$NO^{(+)}$	0.435	0.504	2.241	–	–	–	–
CH_3 (H)O$NO_2^{(+)}$	–	–	–	0.752	0.123	0.11	2.413
CH_3 (H) S–$NO^{(+)}$	0.394	0.418	2.626	–	–	–	–
CH_3(H)S–$NO_2^{(+)}$	–	–	–	0.174	−0.111	−0.110	1.851

Table 9
Nitrosylated and nitrated species ordered according to their net charge on N

Molecule	$NO^{(+)}$	$NO_2^{(+)}$
$NO^{(+)}$	0.435	–
$NO_2^{(+)}$	–	1.290
$H_2O–NO_2^{(+)}$	–	0.780
$CH_3(H)O–NO_2^{(+)}$	–	0.752
$H_3N–NO_2^{(+)}$	–	0.518
$CH_3(H)_2N–NO_2^{(+)}$	–	0.504
$H_3N–NO^{(+)}$	0.448	–
$H_2O–NO^{(+)}$	0.446	–
$CH_3(H)O–NO^{(+)}$	0.435	–
$H_2S–NO^{(+)}$	0.422	–
$CH_3(H)S–NO^{(+)}$	0.394	–
$CH_3(H)_2N–NO^{(+)}$	0.323	–
H_2 S–$NO_2^{(+)}$	–	0.287
$CH_3(H)S–NO_2^{(+)}$	–	0.174

The net charge over the N atom of $NO^{(+)}$ and $NO_2^{(+)}$ substituted compounds is a measure of the acidity of the formed species. Table 9 provides the different protonated species ordered by their net atomic charge of the N from nitrosylated species. It can be observed that inorganic species derived from $NO_2^{(+)}$ are stronger than those derived from $NO^{(+)}$ with exception of those containing S as heteroatom.

4. Conclusions

We studied the interaction between different NO ionic species that might appear consequently to NO formation and a number of bases with the aim to provide an insight into the possible biological mechanism underlying the existence of such nascent species.

In the gas phase we found that NH_3 is the most basic species and H_2S is the least basic of these compounds. For all the three inorganic bases, protonation showed a much greater exothermicity than the interaction with $NO^{(+)}$ or $NO_2^{(+)}$. Protonation affinities are in the order of 200 kcal/mol, suggesting a strong bond formation for these species and the possibility of a covalent bond.

As expected, affinities decrease with the electronegativity of the heteroatom. This fact could have a biological significance, as the protein RS–NO has a greater stability (15,26,27) and therefore, generation of NO is limited. The low affinity energy for the thionitrosylated species make these molecules suitable as reservoirs for the nitrosyl group, thus, release and captivation of the group is achieved easily.

Electron donor substituents, such as the methyl group can easily modify the protonation capacity of the compounds. The decrease on the charge over the heteroatom owing to the presence of a methyl group could suggest that largest groups could have a similar effect. In this sense, in biological media, the transferring of nascent nitroso species to complex bio-organic molecules becomes realistic if the availability of the NO is secured.

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