Computational Study of Ruthenium–Nitrosyl Compounds

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9 Summary

The discovery of the chemical properties related to the physiological and pathophysiological processes of the nitric oxide molecule has advanced scientific research concerning the control of NO availability in the biological environment. Complexes involving ruthenium and other ligands, such as amine and tetraazomacrocycles, have been used as models because they display properties like stability to air oxidation, solubility in water, and low cytotoxicity against host cells.

Given the peculiar properties of nitric oxide, we first conducted a computational experiment based on the molecular orbital diagram of NO (Chapter 3). Then, we performed exercises of computational quantum chemistry involving the mono–cation (NO^+) and mono–anion (NO^-) of NO. These exercises were presented to students at the end of their undergraduate studies or at the beginning of their postgraduate studies.

The students started the experiment by exploring the Lewis structures of NO^+, NO, and NO^- along with the molecular orbital diagram of NO, to obtain a correlation with different properties like bond lengths and atomic charges. Next, they compared the calculated bond lengths and vibrational frequencies with experimental results found in Internet databases, which allowed them to discuss the differences they visualized.

In addition, distinct approximations helped to calculate partial atomic charges. The students verified that it is difficult to determine this parameter because it is not physically observable and does not rely on any quantum mechanical operator to determine its quantity. The dipole moment calculated for NO, 0.153 D, by using B3LYP/6–31+G(d,p) level is close to the most accepted experimental data. This value contrasts with a recent determination of this parameter indicating that the negative charge concentrates on the nitrogen atom.

The students finished the experiment by dealing with two topics of relevant interest to computational chemistry: (i) investigation of the behavior of some properties; for instance, atomic charges and spin densities, in relation to the basis set increment, and (ii) calculation of accurate electronic energies from extrapolation of the basis set pc–n, n = 2–4, to infinity.

Given the relevance of the nitric oxide molecule and the important role of water as solvent in the biological environment, we undertook a computational study of the interaction of NO$^\bullet$, NO$^+$, and NO$^-$ with H$_2$O: [NO$\cdots$H$_2$O]$^\bullet$, **0**$^\bullet$, [NO$\cdots$H$_2$O]$^+$, **0**$^+$, and [NO$\cdots$H$_2$O]$^-$, **0**$^-$ (Chapter 4). The geometries optimized for these clusters indicated that the NO$\cdots$H$_2$O interaction depends on the total charge: (ON$^\bullet\cdots$H–OH), (NO$^-\cdots$H–OH), and (ON$^+\cdots$OH$_2$). The atomic spin densities along with the frontier molecular orbital representation demonstrated that NO goes from **0**$^\bullet$ to **0**$^+$ or **0**$^-$ in the oxidation or reduction processes, respectively, and that both processes occur on the nitrogen atom.

The quantum theory of atoms in molecules (QTAIM), electron localization function (ELF), and natural bond−bond polarizability (NBBP) methods helped to quantify the electronic delocalization level between NO and H$_2$O: **0**$^+$ > **0**$^\bullet$ > **0**$^-$, to show a predominantly ionic character for the intermolecular interactions, but a primarily covalent character for the intramolecular chemical bonds.

Energy analyses carried out by the natural bond orbital (NBO) and localized molecular orbital energy decomposition (LMO–EDA) methods for the interaction between NO and H$_2$O in the complexes **0**$^\bullet$, **0**$^+$, and **0**$^-$ demonstrated a more favorable interaction in **0**$^-$ than in **0**$^+$ and **0**$^\bullet$, as revealed by the former method. However, the latter method indicated more negative total interaction energy for **0**$^+$ in relation to **0**$^-$ and **0**$^\bullet$ because of its predominantly electrostatic component.

Analysis of the electrostatic potential surfaces furnished a clear and direct explanation for the relative position of the monomers. Additionally, this analysis showed that the Coulombic attraction between the water molecule and the charged complexes NO$^+$ and NO$^-$ is larger than in the case of the complexes with NO.

Accordingly, we investigated the complexes *cis*–[RuCl(NO)(NH$_3$)$_4$]$^+$, **1**; *cis*–[RuCl(NO)(NH$_3$)$_4$]$^{2+}$, **2**; *cis*–[RuCl(NO)(NH$_3$)$_4$]$^{3+}$, **3**; *trans*–[RuCl(NO)(NH$_3$)$_4$]$^+$, **4**; *trans*–[RuCl(NO)(NH$_3$)$_4$]$^{2+}$, **5**; *trans*–[RuCl(NO)(NH$_3$)$_4$]$^{3+}$, **6**; [Ru(NO)(NH$_3$)$_5$]$^+$, **7**; [Ru(NO)(NH$_3$)$_5$]$^{2+}$, **8**; and [Ru(NO)(NH$_3$)$_5$]$^{3+}$, **9** to improve our understanding of the nature of Ru–NO chemical bond and of the influence of the total charge, nature, and relative position of simple ligands on NO release from these complexes (Chapter 5).

According to the analysis of charges conducted by the QTAIM and NBO methods along with the molecular orbital representation, the first chemical reduction of complexes **3** and **6** to complexes **2** and **5**, respectively, occurs in the π orbital of Cl, whereas the second reduction, from complexes **2** and **5** to complexes **1** and **4**,

respectively, and the overall reduction process complex **9** → complex **8** → complex **7** takes place in the π^* orbital of NO.

In addition, geometric parameters, wavenumbers related to bond stretching, and analysis of electron density by the QTAIM and NBO methods showed that the thermodynamic stability of the Ru–NO bond in complexes **1**–**6** increases in the first reduction (on going from total charge 3+ to 2+), but it decreases in the second reduction (on going from 2+ to 1+). For complexes **7**–**9**, the stability of the Ru–NO bond decreases in the first reduction, but it increases in the second reduction. This is because interaction between NO$^-$ and Ru is more favorable in complex **7** than interaction between NO and Ru in complex **8**. For N–O, the bond order decreases upon reduction of the total charge in the three classes of complexes: **1**–**3**, **4**–**6**, and **7**–**9**.

For the complexes containing the chlorine atom, it is possible to observe that the chloride group increases the electron density and provides a more favorable electrostatic interaction in the Ru–NO bond as compared to the complexes containing amine only. The results also indicate increased stability of the Ru–NO bond in complexes **1**–**3** as compared to complexes **4**–**6**. As a result, the electrostatic interaction between Cl and NO is larger in complexes **1** and **3** as compared to complexes **4** and **6**, respectively.

We investigated the influence of the Effective Core Potential (ECP) in relation to the treatment involving all the electrons along the scalar relativistic effects obtained by the second–order Douglas–Kroll–Hess (DKH2) approximation by analyzing the geometric parameters of complexes **1**–**9** and *trans*–[RuCl(NO)(NH$_3$)$_4$], **10**. By using the ECP basis set, we determined the energies of reduction (**A**: **2**→**1**, **B**: **3**→**2**, **C**: **5**→**4**, **D**: **6**→**5**, **E**: **8**→**7**, and **F**: **9**→**8**), isomerization (**G**: **1**→**4**, **H**: **2**→**5**, and **I**: **3**→**6**), and Cl$^-$ negative *trans* influence (**J**: **7**+Cl$^-$→**10**+NH$_3$, **K**: **8**+Cl$^-$→**5**+NH$_3$, and **L**: **9**+Cl$^-$→**6**+NH$_3$) with the computational methods: RI–MP2, RI–SCS–MP2, OO–RI–MP2, OO–RI–SCS–MP2, M06–L, M06, M06–2X, M06–HF, BP86–D3BJ, BP86, B2PLYP, LC–wPBE, and B3LYP. We adopted the CCSD(T) method as reference (Chapter 6).

For the statistical analysis, we used the following parameters: minimal negative deviation, $D_{neg}(Min)$; maximum positive deviation, $D_{pos}(Max)$; medium absolute deviation, MAD; and root–mean–square, RMS. In addition to these results, we used values relative to the computational model used as reference, CCSD(T)/def2–TZVP, or even a comparison with the experimental results.

The geometric parameters obtained with ECP were very close to the values obtained with DKH2 — we achieved MARD values of 1.4 and 0.4% for the bond

lengths and angles, respectively. Besides that, the calculated data had MARD values close to 4% as compared to the X–ray experimental results for bond lengths and MARD values close to 3% for the bond angles. These results are acceptable, despite deviation intervals of (–5%) – 9% for r, and (–5%) – 7% for <.

Concerning the reaction energies, the B2PLYP method gave the closest values in relation to those obtained by CCSD(T) in **A**–**I**, whereas B3LYP showed the best performance in the proposed chemical reactions **J**–**L**.

We also studied the nature of the Ru–NO and Ru–NO$_2$ bonds in the compound *fac*–[Ru(NO)Cl$_2$(κ^3N^4,N^8,N^{11}(1–carboxypropyl)cyclam)]$^+$ as well as its derivatives obtained upon changes in pH by the computational model B3LYP/cc–pVDZ with pseudopotential ECP28MDF for ruthenium. The electronic structure was analyzed with the aid of the density overlap regions indicator (DORI), QTAIM, ELF, and NBO methods (Chapter 7).

The DORI method identified a region where the electron density of Ru and NO or NO$_2^-$ overlapped, which indicated the presence of the Ru–NO or Ru–NO$_2$ chemical bond. The QTAIM and ELF methods showed that these bonds have low covalent character. Investigation of the electron density demonstrated that the number of electrons shared between Ru and NO increases on going from complex **11** to complex **12**, when the carboxyl group is deprotonated. However, this number decreases with increasing pH and formation of complex **13**, from deprotonation of N(**2**), and complex **14**, with conversion of Ru–NO to Ru–NO$_2$.

By using NBO, we also observed interaction between the localized d$_\pi$ orbitals of Ru and the π^* orbital of NO or NO$_2^-$. This interaction is related to the π backdonation process, which is more favorable to the stabilization of complexes **11**–**14** than the interaction between the σ NBOs of NO or NO$_2^-$ with the d$_\sigma$ orbital of Ru, associated with the σ donation route. Successively, the second–order stabilization energy involving the NBOs with π symmetry increases on going from complex **11** to complex **12** due to the decreased energy difference and increased overlap between these localized orbitals. The opposite trend is observed on going from complex **12** to complexes **13** and **14**, in agreement with previous results.

We examined the Ru–NO bond mechanism in the complex *trans*–[RuCl(NO)(NH$_3$)$_4$]$^{2+}$ (Chapter 8). Then, we obtained the geometry of this compound and the bond dissociation energy (–ΔE) of the decompositions *trans*–[RuCl(NH$_3$)$_4$]$^+$ + NO$^+$, *trans*–[RuCl(NH$_3$)$_4$]$^{2+}$ + NO, and *trans*–[RuCl(NH$_3$)$_4$]$^{3+}$ + NO$^-$ by using the

computational models ZORA–BP86/TZ2P and BP86/TZ2P, to evaluate how the ZORA approximation influenced treatment of the relativistic effects. Both computational models agreed well with the geometric parameters obtained by X–ray diffraction in the literature. Nevertheless, the values of $-\Delta E$ were significantly different, and we adopted the more accurate ZORA–BP86/TZ2P model in the subsequent discussions.

The dissociation $trans$–$[RuCl(NH_3)_4]^+$ + NO^+ gave the lowest $-\Delta E$, which agreed with a value for the Ru–N–O bond angle close to 180º and is typical of $trans$–$[Ru(NO)L(NH_3)_4]^{n+}$ that are EPR silent. We used this decomposition along with the Kohn–Sham molecular orbital theory in combination with the energy decomposition analysis (EDA) to highlight some important characteristics of the Ru–NO bond mechanism.

Investigation of the negative $trans$ influence of the Cl^- group on Ru–NO revealed a stabilizing effect on for the interaction between $trans$–$[RuCl(NH_3)_4]^+$ and NO^+ — in this structure, the interaction term of the π orbitals counterbalances the electrostatic repulsion and the Pauli repulsion. We also studied the Ru–NO bond in the absence of the Cl^- group for $trans$–$[Ru(NH_3)_4]^{2+}$ and NO^+. The interaction is repulsive because electrostatic repulsion predominates in relation to the attractive contribution of the interaction of the π orbitals. We also analyzed the Ru–Cl bond in the absence of NO^+ for $trans$–$[Ru(NH_3)_4]^{2+}$ and Cl^-. The interaction is attractive due to the considerable value of the favorable electrostatic term.

Investigation of the synergism between the processes of σ donation and π backdonation present in Ru–NO showed that this synergism accounts for an increased stability of this bond. The π component is essential for maintenance of this chemical bond.