

Suppression of electron-induced degradation in methylated nitroimidazoles

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Abstract: Nitroimidazoles are efficiently decomposed by low energy electrons. This process, known as dissociative electron attachment (DEA), is believed to account, at least partly, for the radiosensitizing bioactivity of nitroimidazoles [1,2]. Since the DEA reactions are typically initiated by the formation of transient negative ions, or resonances, obtaining the anion spectra of nitroimidazoles is a key step to better understand their electron-induced degradation, and ultimately their application as sensitizers in the radiation and heavy-ion treatment of cancer cells.

The recently reported DEA measurements of Tanzer *et al.* [3] revealed that 4-nitroimidazole (4NI) has a very rich fragmentation spectrum below 2V, comprising single-bond cleavages and more complex reactions. Despite the low collision energies, several dissociation channels were observed, producing the H, OH and NO₂ radicals, besides HNO₂ and CN⁻. However, the most striking experimental result was the complete suppression of these reactions in 1-methyl-4-nitroimidazole (1M4NI), along with a significant quenching of higher energy dissociation reactions, around 3 eV. The DEA suppression was also observed for 1-methyl-5-nitroimidazole (1M5NI) in subsequent experiments [4]. As the DEA yields show a series of narrow peaks for H abstraction below 1 eV, Tanzer *et al.* consistently argued that vibrational Feshbach resonances (VFRs) would trigger the H-elimination reaction. Since the methylation at the N1 site would be expected to completely quench this reaction, in view of the unfavorable energetics of C–H bond cleavages, those authors further considered that VFRs would also be doorways for more complex reactions, involving the cleavage of the C4–NO₂ bond.

We report a theoretical study on the anion state spectra of 4NI, 1M4NI and 1M5NI, based on electron scattering and bound state calculations. Our results point out five anion states that would be relevant for the DEA dynamics in 4NI, namely a dipole bound state (DBS), a valence bound state and three resonances, the latter formed by electron attachment into either π^* or σ^* virtual orbitals. While the DBS binding energy and the fundamental frequency of the ν_{NH} stretch mode are consistent with the VFR progression for H elimination, as previously suggested, our calculations strongly indicate that a π^* shape resonance would be the initial step for the cleavage of both the N1–H and C4–NO₂ bonds around 1.5 eV. The calculated integral cross sections,



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obtained with the Schwinger Multichannel Method [5] at the equilibrium geometries of the target molecules, also point out that the lifetime of the π^* resonance is about four times smaller in 1M4NI and 1M5NI than in 4NI. We believe the shorter-lived resonances, which strongly favor autoionization with respect to vibrational relaxation in the methylated species, would be responsible for the observed DEA suppression around 1.5 eV. Our results are also consistent with the DEA signals for several fragments around 3 eV, where we found a higher lying π^* resonance.

Key-words: Rediosensitizers; Radiation Therapy, Resonances, Dissociative Electron Attachment; Electron Scattering.

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