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Negative ion formation by low energy electron attachment to gas-phase 5-nitrouracil

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ABSTRACT

Dissociative electron attachment (DEA) to gas phase 5-nitrouracil (5NU) is studied using a double focusing sector field mass spectrometer and a hemispherical electron monochromator (HEM) combined with a quadrupole mass spectrometer (QMS). Besides the formation of the long-lived parent anion $5NU^-$, low energy electron impact (<20 eV) leads to a number of anionic fragments. The ion yield for all observed negative ions has been recorded as a function of the incident electron energy. The most dominant negative ion observed was $(5NU–NO_2)^-$, which is produced directly in the ion source and also weakly as a product of a metastable decay of $5NU^-$. These experiments were supported by quantum chemical calculations based on the density functional theory to calculate the electrostatic potential and molecular orbitals.

1. Introduction

One of the major challenges of modern medical research is to discover the most effective method and pharmaceuticals for cancer treatment [1,2]. Radiotherapy, combining the use of ionizing radiation and the incorporation of radiosensitizers within the tumor cells, has been developed as an alternative and/or complementary treatment to the traditional surgery and to chemotherapy. Radiotherapy is based on the assumption that applied ionizing radiation causes DNA damage. However, the methodology for targeting cancerous rather than healthy cells remains uncertain. Energy deposition by high-energy quanta creates many secondary electrons with an average initial kinetic energy up to 20 eV [3,4] which can induce direct damage at selective sites in the DNA leading to single or double strand breaks. Recent research suggests that control of such electron-induced processes may provide a method for targeting cancerous cells by incorporating radiation sensitive molecules in the DNA of such cells, indeed the effectiveness of compounds used as 'radiosensitizers' has been shown to be related to their interaction with low energy electrons [5].

Pyrimidines have a special place in the drugs used for radiotherapy. The modified pyrimidine bases, especially substituted uracil derivatives, have been widely used due to their importance as the constituents of nucleic acids and useful biological activity [6]. 5-Substituted uracils exhibit a significant pharmacological activity and have been used as antitumor, antibacterial and antiviral drugs. The most prominent representatives are: 5-fluorouracil [6,7] and 5-bromouracil [8,9]. It has been shown that the substitution of thymine nucleobase in genetic sequence of cellular DNA does not change the normal gene expression in non-irradiated cell [10]; however, it leads to increased sensitivity of living cells to X-rays (by factor of four) [11]. Apart from the halogen-modified nucleobases several aromatic nitro compounds also show promise as radiosensitizers for overcoming the radioprotection afforded some tumor cells by their lack of oxygen, 'hypoxia' [12]. The effectiveness of these compounds as radiosensitizers has been shown to be related to the electron affinity of their nitro group. Moreover, many derivatives of 5-nitrouracil (5NU) have shown the following effects: antibacterial activity [13], antitumor activity on leukemia cells [14] and inhibitory effect on macrophage [15], while there are many publications concerning the synthesis of new 5NU derivatives which can be considered as promising candidates for pharmacological agents [16].

In order to understand the molecular mechanisms by which radiosensitizers operate, the interaction of low energy electrons with many isolated gas phase halogenated nucleobases has been studied [17–25]. However, to date, experiments on the interaction of slow electrons with 5-nitrouracil are limited to our recent work on vibrational and electronic excitations and negative ion formation [26]. However this was a preliminary study being limited to a

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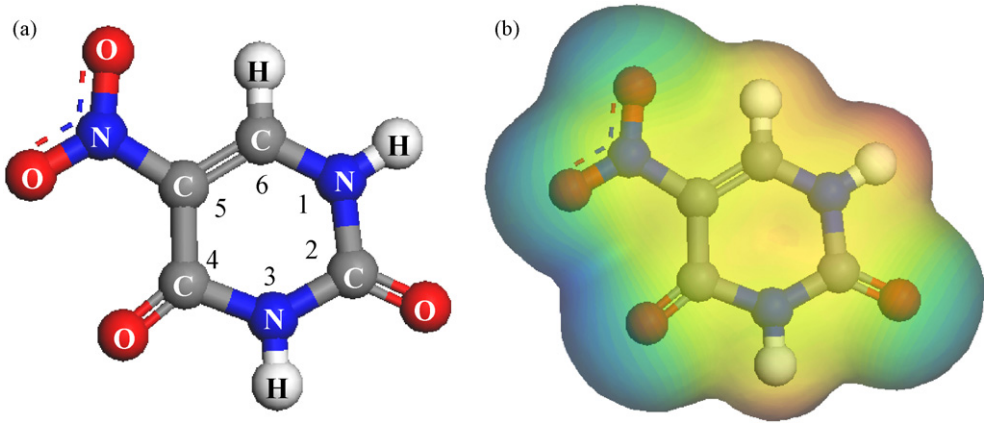

Fig. 1. (a) Molecular structure and (b) the electrostatic potential map of 5-nitrouracil calculated with DMol3 program.

narrow range of electron energy, 0–2 eV and only the three most abundant ions were recorded. In this work we report the results of an extended study on anion production via electron attachment to 5-nitrouracil.

2. Experimental setup

Two apparatus were used in the present studies, a high-resolution double sector field mass spectrometer (VG-ZAB) and a hemispherical electron monochromator (HEM) in combination with a quadrupole mass spectrometer (QMS). Only a brief description of the experimental arrangements is given here, since more details can be found in Ref. [27]. The VG-ZAB apparatus is utilized for measurements requiring high mass resolution, high sensitivity and the HEM instrument for high electron energy resolution.

The neutral target beam is produced by a resistively heated oven containing 5-nitrouracil powder operated at a temperature of 150 °C. The sample was purchased from Sigma–Aldrich with a stated purity of 98% and used without further purification.

In the case of the VG-ZAB apparatus, an effusive beam of 5NU is introduced into a Nier-type ion source where it is crossed with the electron beam. The energy resolution of the electron beam is approximately 0.8 eV at an electron current of 10 μA. The anions formed in the ion source were extracted by a weak electric field and accelerated through a potential drop of 5 kV into the mass spectrometer. The utilized mass spectrometer has a reversed geometry, i.e., magnetic sector field followed by the electric sector field. Additionally, by using this apparatus metastable decay upon dissociative electron attachment (DEA) can be measured. Metastable dissociation in the field-free region between the magnetic and electric sector is studied by mass-analyzed ion kinetic energy scans (MIKE) [28].

The electron beam formed in HEM is set at an energy resolution of about 100 meV and an electron current of 15–25 nA. The effusive beam of 5NU is crossed perpendicularly by the electron beam. Negative ions formed in the collision chamber are extracted by a weak electric field towards the entrance of the QMS. Anion yields were recorded as a function of the electron energy. The electron energy scale is calibrated by means of well-known Cl^- signal from DEA to CCl_4 yielding a narrow peak near zero eV and a weak peak located at 0.8 eV [29]. In both cases, the mass selected negative ions were detected by a channeltron detector.

3. Quantum chemical calculations

To support the experimental work electrostatic potential and molecular orbitals were calculated using the DMol3 software from Accelrys Software Inc. [30]. Quantum chemical calculations based on the use of the density functional theory have been performed. A geometry optimization was performed to determine the minimum-energy structure of a molecule, starting from the initial geometry entered. After the geometry is minimized, other properties are computed. DMol3 supports several non-local exchange and correlation functionals. In the present calculations, the Becke exchange functional (B88) is used in conjunction with the Lee–Yang–Parr correlation functional (BLYP). This so-called generalized gradient corrected (GGA) functional, by Perdew and Wang (P91) was derived by considering low- and high-density regimes and by enforcing various summation rules [30]. The electrostatic potential map and molecular orbitals of 5NU were calculated using the double numerical plus polarization (DNP) basis set, i.e., functions with angular momentum one higher than that of highest occupied orbital in free atom.

4. Results and discussion

4.1. Electron attachment

In contrast to the uracil nucleobase [31], low energy electron impact on 5-nitrouracil (Fig. 1a) induces the formation of the parent negative ion $(5NU)^-$ observed within a very narrow resonance at zero eV, shown in Fig. 2. Additionally, Fig. 2 presents the negative mass spectrum for the region of the parent ion obtained by

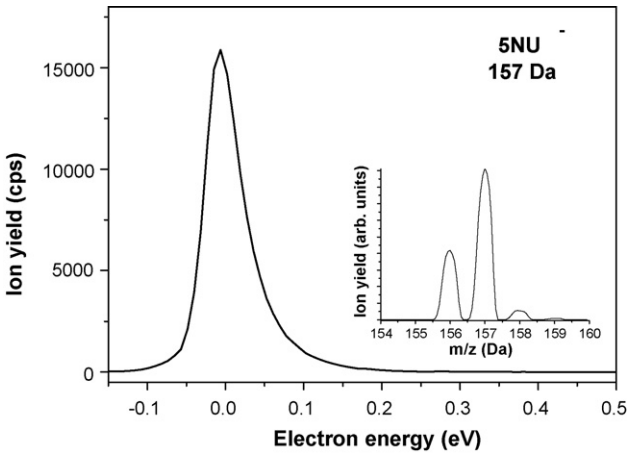

Fig. 2. The anion yield observed for the molecular parent anion $(5NU)^-$. The insert graph shows the anion mass spectrum for the region of the parent anion obtained at 0 eV electron energy.