Electron-induced dissociation of a potential radiosensitizer: 5-trifluoromethanesulfonyl-uracil

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The incorporation of halouracils into DNA enhances its radiosensitivity towards high-energy radiation. The reactivity of these compounds to low-energy electrons (LEEs) plays a crucial role in the sensitization process[1]. The current gas-phase study assesses the propensity of a recently synthesized potential radiosensitizer, 5-trifluoromethanesulfonyl-uracil (OTfU), to undergo dissociative electron attachment (DEA) in the electron energy range between ~0-14 eV[2]. OTfU is a derivative of uracil substituted with a triflate (OTf) group at the C_5-position (see Fig. 1), which substantially increases its ability to go through effective electron-induced dissociation[3]. The measurements were carried out using a hemispherical electron monochromator coupled with a quadrupole mass spectrometer. We report a variety of fragments formed either by simple bond cleavages (e.g. dehydrogenation or formation of the triflate anion, OTf^-) or by complex multi-bond rearrangements leading to a complete decomposition of the molecule. The most favorable DEA channel corresponds to the formation of OTf^- as well as the reactive uracil-5-yl radical by the cleavage of the O–C_5 bond in uracil occurring mainly through a sharp resonance at 0 eV and other resonances (0.14, 1.05 and 3.65 eV) well below the threshold for electronic excitation. The dehydrogenated parent anion, $(OTfU–H)^-$, is formed by the capture of electrons with energies below 2 eV. The latter reactions are mainly driven by the large electron affinity of the triflate anion (5.5 eV). Furthermore, the thermodynamic thresholds of the DEA reactions were predicted theoretically at the M06-2X/aug-cc-pvtz level both at the standard state and at a very low pressure of $3 \cdot 10^{-8}$ mbar to represent the experimental conditions. Ultimately, this study endorses OTfU as a potential radiosensitizing agent with further implications in tumor chemoradiotherapy.

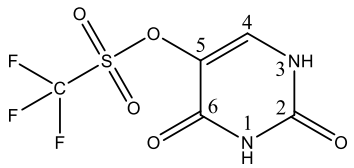

Fig. 1. *Chemical structure of 5-trifluoromethanesulfonyl-uracil.*

References

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