

PF1 Radical cations of base paired nucleosides: models of damage in DNA?

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dGdC radical cations fragment via monomer loss and radical induced sugar damage.

Radicals play key roles in DNA damage via the direct effect of ionising radiation and via indirect effects in which radical attack leads to strand breaks. Inspired by two recent studies that have used CID of metal complexes to generate radical cations of non-covalent complexes of biomolecules [1,2], here we present the first gas phase study on the radical cation of the base pair nucleoside, dGdC. A Finnigan LTQ-FT mass spectrometer equipped with an electrospray ionization source was used to generate a series of doubly charged complexes of the form $[\text{Cu}(\text{A})_x(\text{B})_y]^{2+}$, where $\text{A}=\text{B}=\text{dC}$, dG , dA , dT and $x=0-4$, $y=0-4$ from solutions of copper (II) nitrate and nucleosides. These complexes were subjected to CID, and yielded, amongst others a novel series of radical cation non-covalent complexes. The gas phase chemistry of the base pair dimer dGdC was examined in detail. Three main types of fragmentation reactions were observed: (i) monomer loss to form the radical cation of dG; (ii) monomer loss coupled with proton transfer to form protonated dC; (iii) radical induced sugar fragmentation from the dG site. DFT calculations suggest that these three competing fragmentation reactions have similar reaction endothermicities. The gas phase data are consistent with current models for damage in DNA, whereby initial ionisation at the guanine sites is followed by proton transfer and/or strand breaks.

[1] J.Y. Ke, U.H. Verkerk, P.Y.I. Shek, A.C. Hopkinson, K.W.M. Siu, *J. Phys. Chem. B* 2006, 110: 8517- 8523.

[2] P. Cheng, D.K. Bohme, *J. Phys. Chem. B* 2007, 111: 11075-11082.