"Position" does matter : the photofragmentation of the nitroimidazole isomers

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Synopsis Experimental and theoretical spectroscopic methods have been combined to disentangle the fundamental mechanism of VUV induced fragmentation of the three isomers of nitroimidazole radiosensitisers.

Radiotherapy is one of main techniques used in cancer treatment and radiosensitizers are drugs used to selectively improve its effectiveness against tumour cells. Misonidazole and Nimorazole are two radiosensitizers with similar chemical structure. However clinical trials have shown that they have different efficiency in the tumor treatment. In order to understand why this happens we have studied the photofragmentation of 2-nitroimidazole and 4(5)-nitroimidazole, which are the "building blocks" of Misonidazole and Nimorazole, respectively.
To the purpose time of flight mass spectrometry has been used to investigate the fragmentation of these molecules. These measurements have been then extended via the determination of the Appearance Energies (AE) of the different fragments and by Photelectrons-Photoions Coincidences (PEPICO) experiments using synchrotron radiation [1]. To interpret the results DFT calculations [1] have been also performed.
The mas spectra of the two molecules display many similar features and relative intensities, but also a few intriguing peculiarities. The most striking differences are the fragments at m/z 55^+ and 56^+, present exclusively in 4(5)NI and 2NI, respectively, and the fragment at m/z 83^+, which is one of the leading fragmentation channels in 2NI, but is almost absent in the 4(5)NI sample.The results of mass spectrometry are confirmed by the photoelectron–photoion coincidence measurements.

Based on DFT calculations, a model is proposed which fully explains such differences, and reveals the subtle fragmentation mechanisms leading to the release of neutral species like NO, CO and HCN. The present results

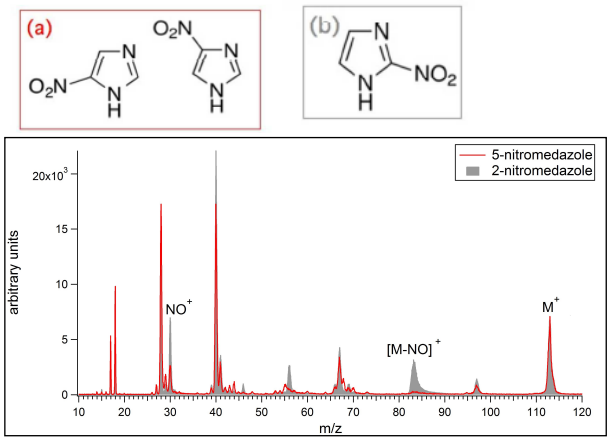

Figure 1. Mass Spectra of 4(5)-nitroimidazole (red line and scheme a) and 2-nitroimidazole (grey area and scheme b) molecules measured with a He lamp.

suggest that the products of decomposition of the different nitroimidazole isomers migth play a role in determining their distinctive degrees of effectiveness in radiotherapy.

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References

[1] P. Bolognesi et al. J Chem Phys Comm. 145, 191102 (2016)

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