Supplementary material: Heavy Element Incorporation in Nitroimidazole Radiosensitizers: Molecular-Level Insights into Fragmentation Dynamics

Pamela H.W. Svensson,[1] Lucas Schwob,[2] Oscar Gråsäs,[1] Isaak Unger,[1] Olle Björneholm,[1] Nicusor Timneanu,[1] Rebecka Lindblad,[1] Anna-Lydia Vieli,[1] Vicente Zamudio-Bayer,[3] Martin Timm,[3] Konstantin Hirsch,[3] Carl Caleman,[1,4] and Marta Berholts[5]

[1] *Department of Physics and Astronomy, University of Uppsala, SE-75120 Uppsala, Sweden*
[2] *Deutsches Elektronen-Synchrotron DESY, Notkestr. 85, 22607 Hamburg, Germany*
[3] *Abteilung für Hochempfindliche Röntgenspektroskopie, Helmholtz Zentrum Berlin für Materialien und Energie, 12489 Berlin-Adlershof, Germany*
[4] *Center for Free-Electron Laser Science, DESY, DE-22607 Hamburg, Germany*
[5] *Institute of Physics, University of Tartu, W. Ostwald 1, EST-50411, Tartu, Estonia*

In Fig. S1-Fig. S4, summed ion yields are presented for all four samples together with the partial ion yield curves of the strongest fragments, labeled with their respective m/z. The spectra were recorded at C, N, O 1s-edges and I 3d-edge, correspondingly.

In Table SI and Table SII, we present the assignments for the electronic transitions according to our calculations for C 1s and N 1s NEXAFS spectra, correspondingly.

We can present the time scales for bond dissociation using Molecular Dynamics. The energy of each atom is assigned randomly from the Maxwell-Bolzmann distribution with the corresponding temperature. The temperature was chosen to be 3000K such that the total internal energy at the start of the simulation was roughly 5 eV for a molecule with 20 atoms to account for the vibrational energy generated by non-radiative electron relaxation processes. The de-excitation and Auger decay processes happen on a faster time scale than the movement of the nuclei, therefore the simulation is initiated with the charge delocalized across the valence orbitals.

The input files for the calculation of NEXAFS spectra and Molecular Dynamics can be found at `https://doi.org/10.5281/zenodo.8410026`

In Table SIII, the time scales for the N3-C2 bond dissociation (the bond that connects the nitro group to the imidazole ring) are presented for $NimH^+$ and $INimH^+$ samples at different charge states. It is expected that the most likely outcome after photoionization at the C or N 1s-edges for the $NimH^+$ is the formation of $NimH^{3+}$ final state while at the I 3d-edge, for the $INimH^+$, it is the formation of $INimH^{4+}$ final state. Therefore, comparing the bond breakage resulting in the ejection of NO^+ or $NO_2{}^+$ species in iodinated and non-iodinated nitroimidazole, these states should be compared. The simulation shows that, on average, the time before bond breakage has reduced to approximately 12 fs in iodinated nitroimidazole.

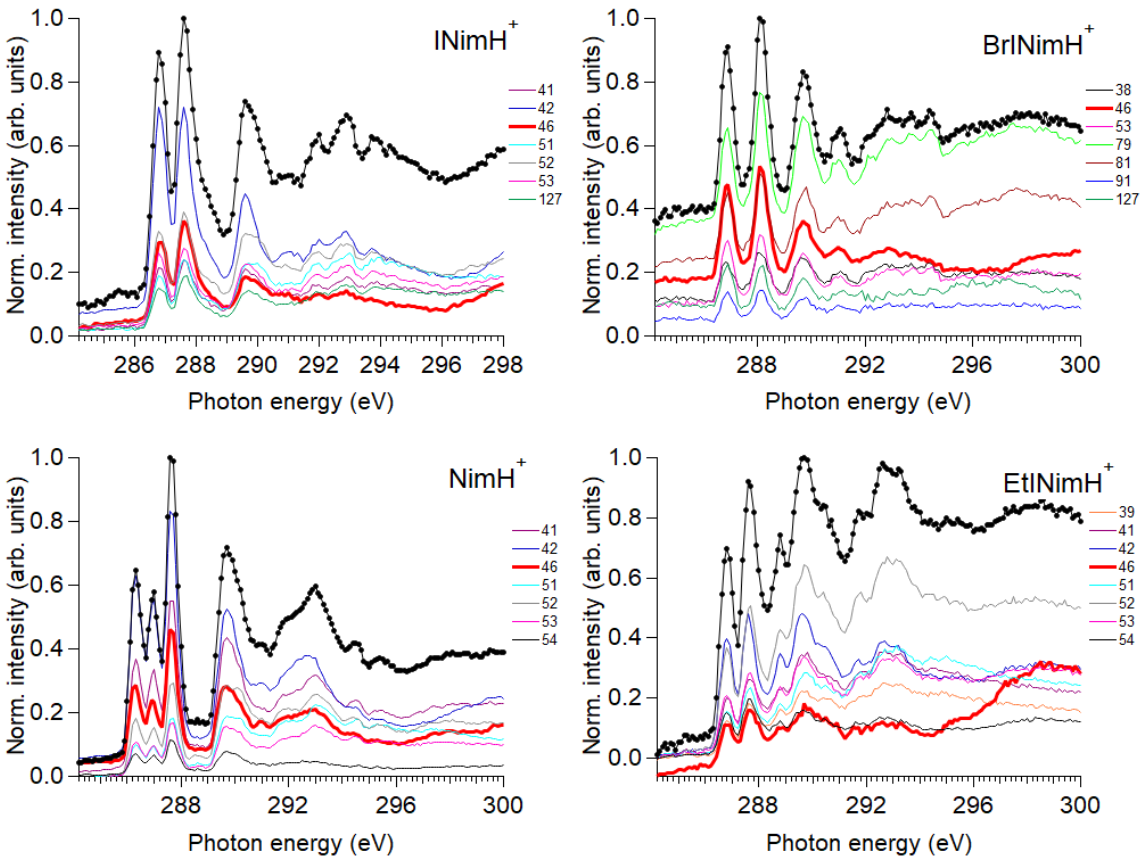

Figure S1. Partial ion yield (PIY) curves plotted with the summed ion yield spectrum (dotted black line) recorded at C 1s edge. The PIYs were multiplied by a factor of 3 for $NimH^+$ and $INimH^+$, and by a factor of 4 for $BrINimH^+$ and $EtINimH^+$. The PIY curves of only the strongest fragments are shown.

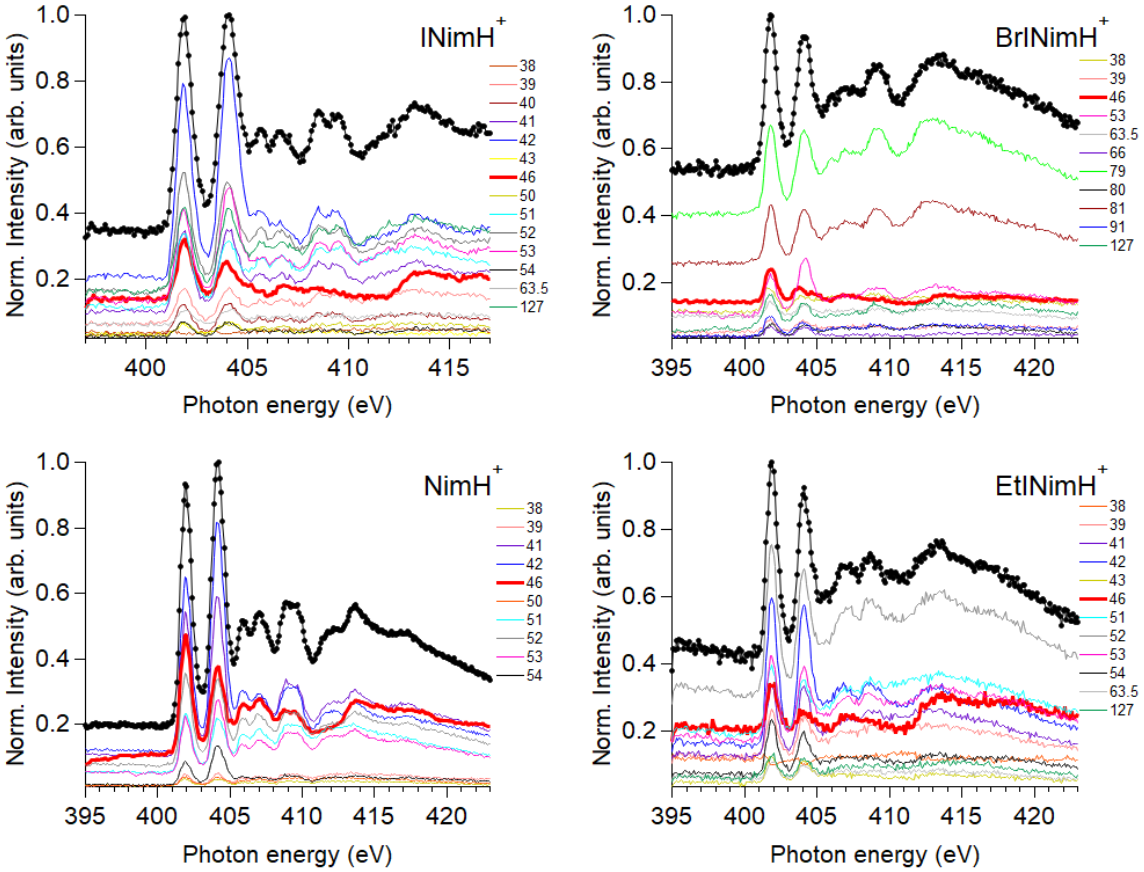

Figure S2. Partial ion yield (PIY) curves plotted with the summed ion yield spectrum (dotted black line) recorded at N 1s edge. The PIYs were multiplied by a factor of 3 for $NimH^+$ and $BrINimH^+$, by a factor of 4 for $INimH^+$, and by a factor of 5 for $EtINimH^+$. The PIY curves of only the strongest fragments are shown.

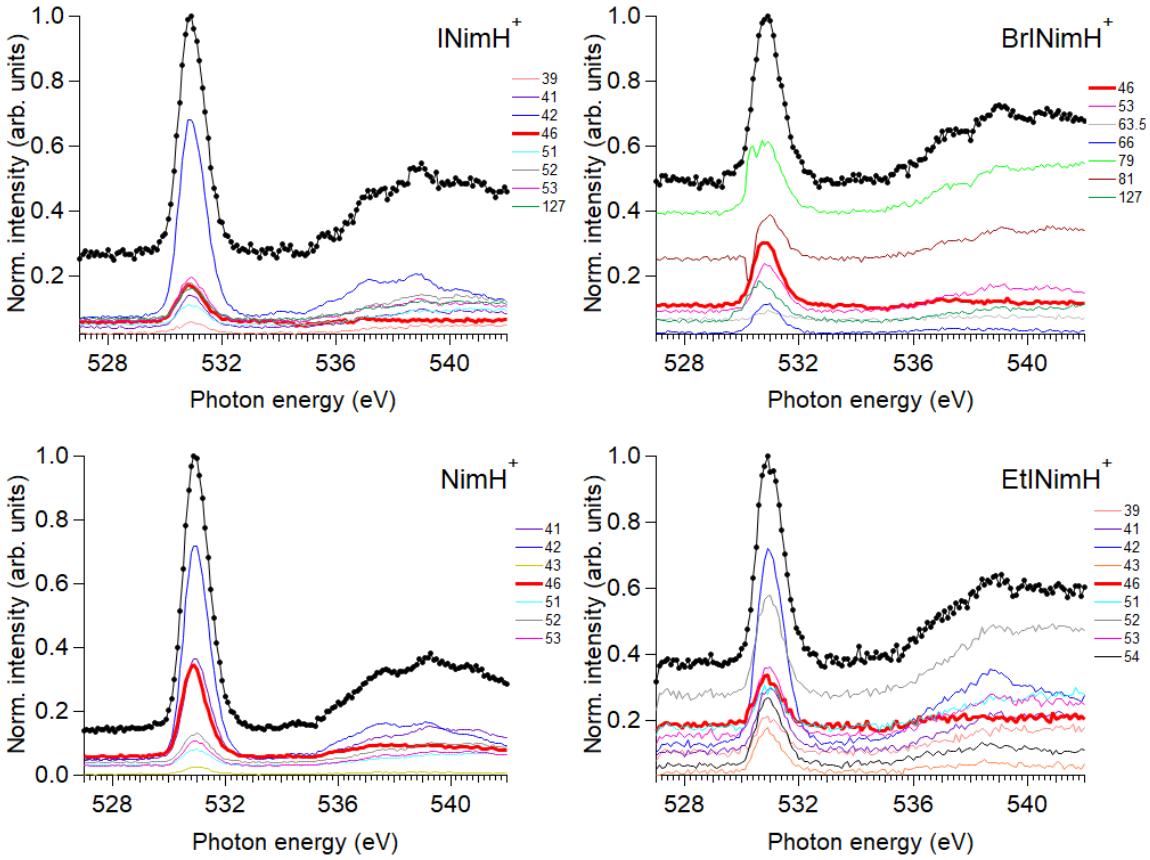

Figure S3. Partial ion yield (PIY) curves plotted with the summed ion yield spectrum (dotted black line) recorded at O 1s edge. The PIYs were multiplied by a factor of 2 for $NimH^+$ and $INimH^+$, by a factor of 3 for $BrINimH^+$, and by a factor of 5 for $EtINimH^+$. The PIY curves of only the strongest fragments are shown.

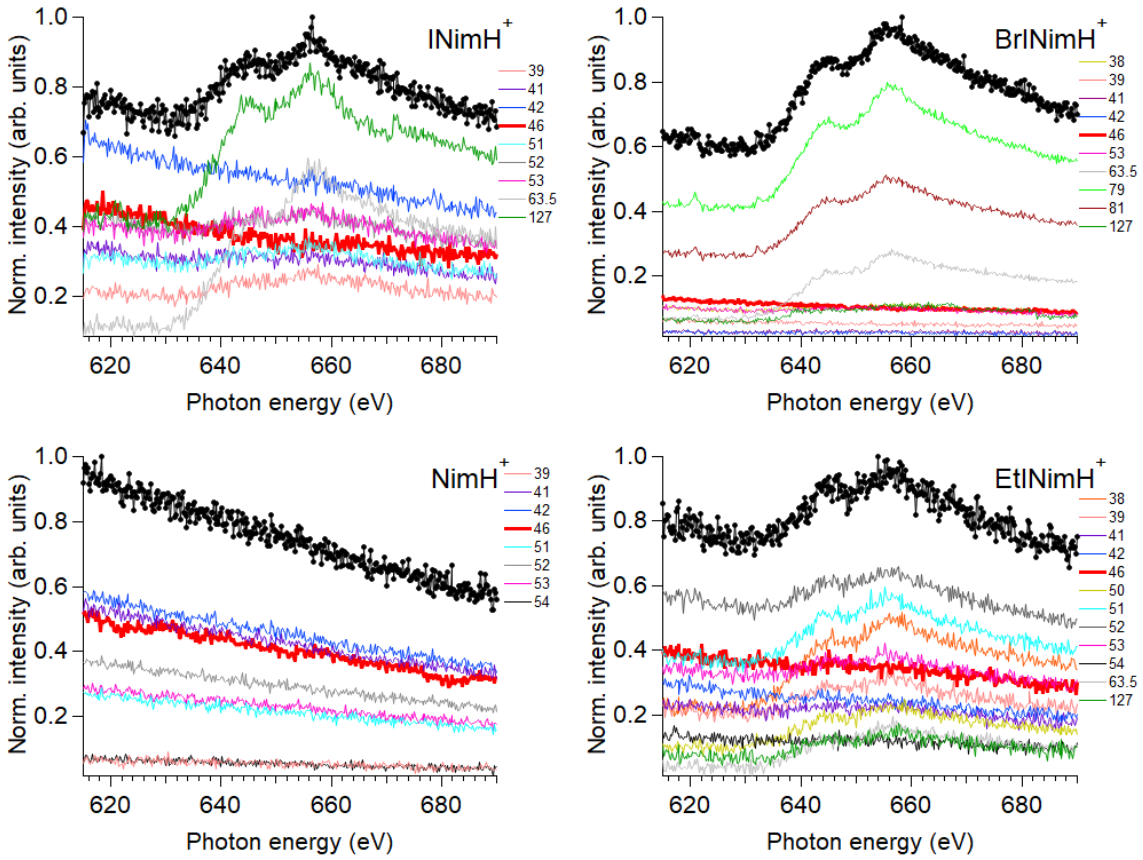

Figure S4. Partial ion yield (PIY) curves plotted with the summed ion yield spectrum (dotted black line) recorded at I 3d. The PIYs were multiplied by a factor of 5 for $INimH^+$ and $EtINimH^+$, by a factor of 3 for $NimH^+$, and by a factor of 2.5 for $BrINimH^+$. The PIY curves of only the strongest fragments are shown.

Table SI. Observed electronic transitions at C 1s edge obtained from NEXAFS calculations of the four molecules. Peaks labeled as 1' are mainly dominated by transitions from C1, C2, or C3 to LUMO in each molecular system. Peak 2' show a mixing of transitions from C1, C2, C3, and C6 to LUMO, +1 and small contributions of LUMO+4. In peak 3' C1 and C3 are mainly excited except in EtINimH$^+$ where the third peak has an additional contribution from C6.

label		NimH+		INimH+
1'	286,35	C3 → LUMO	286,81	C1 → LUMO
			286,88	C3 → LUMO
2'	286,92	C2 → LUMO	287,57	C2 → LUMO, +1
			287,83	C3 → LUMO+1
3'	287,63	C3 → LUMO+1	288,36	C3 → LUMO+2
	287,87	C1 → LUMO+1		
4'	288,84	C1 → LUMO+1	288,97	C4 → LUMO+5
	289,43	C3 → LUMO+3	289,24	C1 → LUMO+4
	289,56	C2 → LUMO+3	289,35	C4 → LUMO+8
	289,63	C3 → LUMO+2	289,72	C3 → LUMO+4
			289,73	C4 → LUMO+7
label		BrINimH+		EtINimH+
1'	286,74	C2 → LUMO	286,71	C2 → LUMO
	286,94	C3 → LUMO	286,87	C3 → LUMO
2'	288	C2→ LUMO+1	287,26	C6 → LUMO+4
	288,03	C2 → LUMO+2	287,61	C1 → LUMO
	288,34	C1 → LUMO+1	287,99	C3 → LUMO+1
3'	289,29	C3→ LUMO+3, C2 → LUMO+4	288,38	C6 → LUMO+8
	289,67	C1 → LUMO+2	288,51	C1 → LUMO
	289,94	C3 → LUMO+4		
4'	290,76	C1 → LUMO+2	288,83	C4 → LUMO+5
	291,18	C2 → LUMO+7	289,02	C6 → LUMO+10
			289,15	C6 → LUMO+9
			289,27	C2 → LUMO+3
			289,53	C4 → LUMO+8
			289,60	C6 → LUMO+12
			289,62	C5 → LUMO+5

Table SII. Excitations observed in N 1s-edge calculations of $NimH^+$ and $INimH^+$. Peak 1' includes transitions mainly from N1 or N2 to LUMO and LUMO+1. Peak 2' is dominated by transitions from N3 and shows the highest probability of occupying the LUMO. Excitations within Peak 3' and 4' target a mix of orbitals of LUMO+3, +4, +5, +6.

label		$NimH^+$		$INimH^+$
1'	401,67	N2 → LUMO	401,73	N1 → LUMO
	402,20	N1 → LUMO	402,12	N2 → LUMO, +1
	402,26	N1 → LUMO+1	402,43	N2 → LUMO, +1
	402,67	N2 → LUMO+1		
2'	404,02	N3 → LUMO	403,95	N3 → LUMO
	404,66	N1 → LUMO+2		
3'	405,94	N1 → LUMO+4	404,91	N2 → LUMO+3
	405,94	N1 → LUMO+6	404,95	N1 → LUMO+3
4'	407,81	N3 → LUMO+3	405,79	N1 → LUMO+5, +6
			405,88	N2 → LUMO+5

Table SIII. Time in femtoseconds until the N3-C2 bond is broken. Each cell represents one simulation and the mean value is presented in bold at the bottom. Introducing the iodine atom to the system pushes the production of the NO^+ or $NO_2{}^+$ species to longer time scales for the same charge state. However, shorter time scales are achieved approaching I 3d-edge.

$NimH^{3+}$	$INimH^{3+}$	$INimH^{4+}$
56	337	966
59	-	166
134	111	63
78	341,5	379
344,5	124,5	75,5
125,5	121,5	429
91,5	-	21
275	-	-
466	439,5	448,5
-	149	140,5
85	375	102,5
410,5	513	66,5
95,5	222	80,5
139	112,5	45,5
250,5	81	84,5
99,5	247	84
155,5	88	68,5
225,5	367,5	225,5
-	231	140,5
551	-	34
202,31	**241,31**	**190,55**