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TOWARDS LOW ENERGY CID OF FIXED CHARGE PEPTIDE RADICAL CATIONS

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Several chemical strategies have been developed to generate radical peptide ions in the gas phase.[1-5] Introduction of a neutral peptide coordinated to a copper(II) complex, which, upon CID leads to oxidative dissociation of the peptide to yield the corresponding radical cation has been the most widely studied,[1] with a key aim being to devise ternary complexes which ultimately yield radical cations from a large range of peptides. Unfortunately, upon CID of these copper(II) complexes several competing reactions may occur. While some of these may be avoided by judicious choice of auxiliary ligand, the Lewis acidity of the metal ion typically results in the peptide binding as a zwitterion. This leads to competitive amide bond cleavage of the coordinated peptide *via* a mobile proton pathway.

The installation of a functional group containing a bond susceptible to homolytic cleavage represents an alternative strategy for the production of peptide radicals.[3-5] Our group has examined several peptides containing serine nitrate esters which produce a peptide radical *via* loss of a nitrite radical.[5] Unfortunately, protonated peptides containing serine nitrates esters, undergo preferential loss of HNO_3 rather than unmasking the radical site. Thus, peptide radical formation is prevented in both the metal mediated and organic functionalization strategies by competing mobile proton pathways. Installation of a fixed charge in the peptide removes the troublesome mobile proton and allows selective radical formation, *via* both metal mediated oxidative dissociation[6] and organic functionalization. The presence of the fixed charge also allows the opportunity to examine radical driven fragmentation without competing charge directed chemistry. This presentation will describe our ongoing work aimed at developing an efficient derivatization strategy to allow the modification of a peptide *via* installation of a fixed charge nitrate ester derivative.

[1] Chu, I. K.; Rodriquez, C. F.; Lau, T. C.; Hopkinson, A. C.; Siu, K. W. M. *J. Phys. Chem. B* **2000**, *104*, 3393-3397.

[2] Barlow, C. K.; McFadyen, W. D.; O'Hair, R. A. J. *J. Am. Chem. Soc.* **2005**, *127*, 6109-6115.

[3] Hodyss, R.; Cox, H. A.; Beauchamp, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 12436-12437.

[4] Masterson, D. S.; Yin, H.; Chacon, A.; Hachey, D. L.; Norris, J. L.; Porter, N. A. *J. Am. Chem. Soc.* **2004**, *126*, 720-721.

[5] Wee, S.; Mortimer, A.; Moran, D.; Wright, A.; Barlow, C. K.; O'Hair, R. A. J.; Radom, L.; Easton, C. J. *Chem. Comm.* **2006**, 4233-4235.

[6] Karnezis, A.; Barlow Christopher, K.; O'Hair Richard, A. J.; McFadyen, W. D. *Rapid Commun. Mass Spectrom.* **2006**, *20*, 2865-70.