



DIAZO COMPOUNDS AND pH CONTROL: SEPARATING SIDENCHAINS AND C-TERMINUS

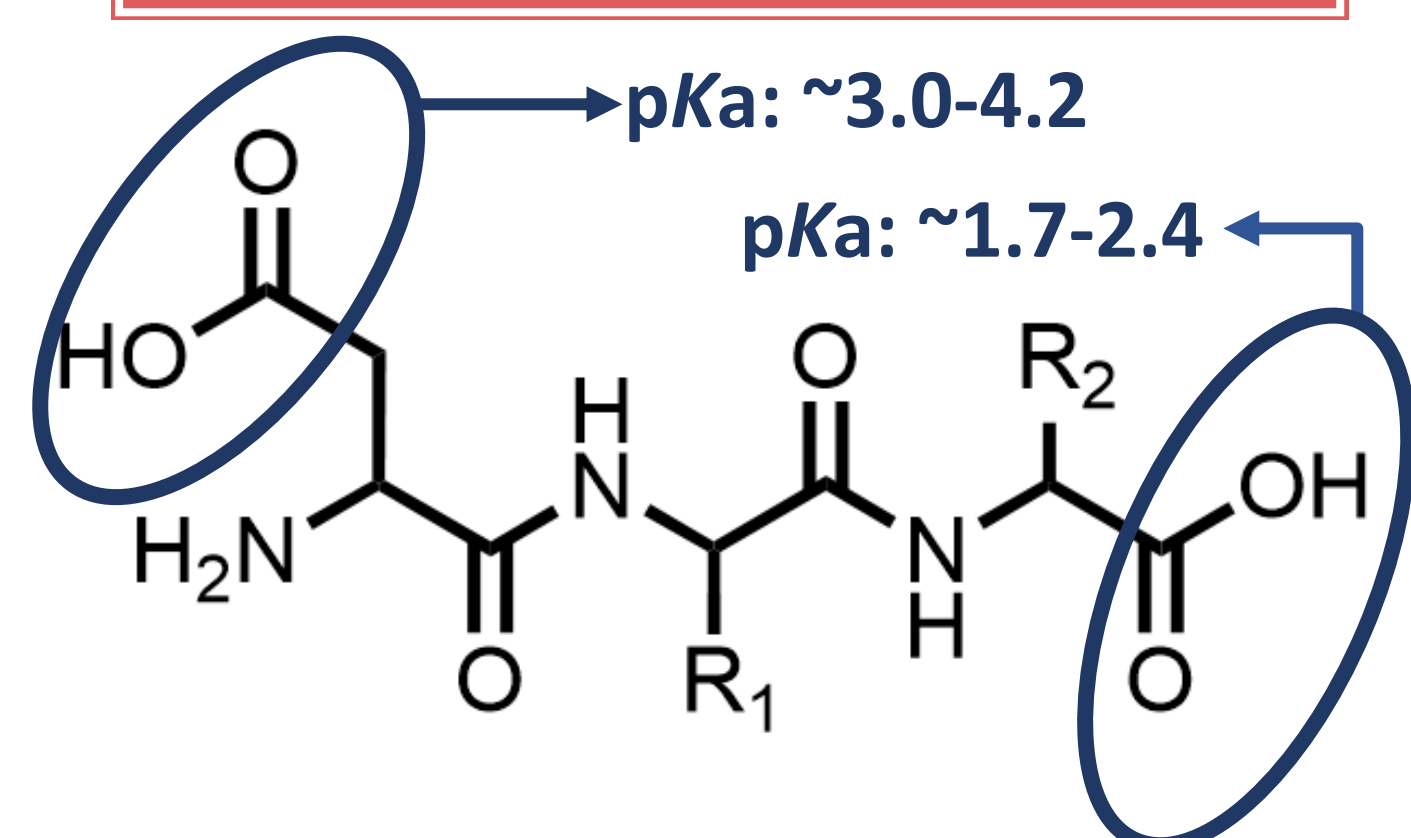
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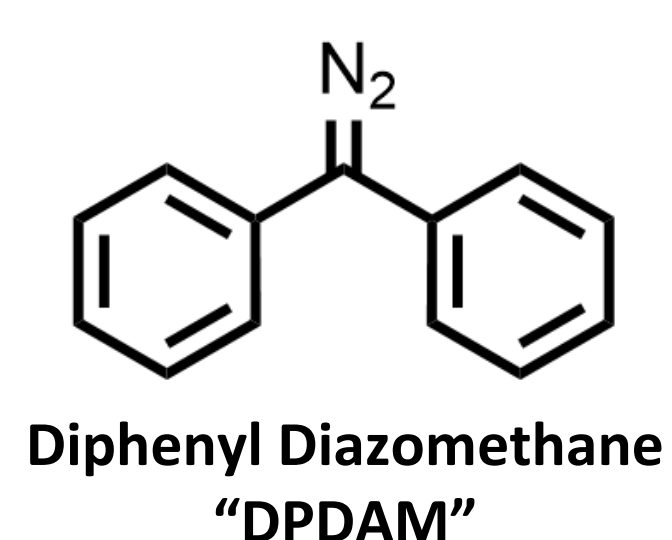
ABSTRACT

Of the 20 canonical amino acids, only aspartic acid (Asp) and glutamic acid (Glu) bear a carboxyl-terminating sidechain. As a result of the peptide bond, proteins also contain a carboxyl terminus (C-terminus) and an amino (N-terminus). The physical properties of the carboxyl functional groups make them a highly versatile functional group capable of engaging in molecular interactions with a wide variety of complementary functional groups. Asp, Glu, and the C-terminus exist as their respective ionized conjugate bases at physiological pH (7.4). This equilibria has limited the number of chemical probes that selectively react with these functional groups. **We demonstrate the ability to separate sidechain and C-terminal reactivity, harnessing the chemoselectivity of diazo compounds and pH control.**

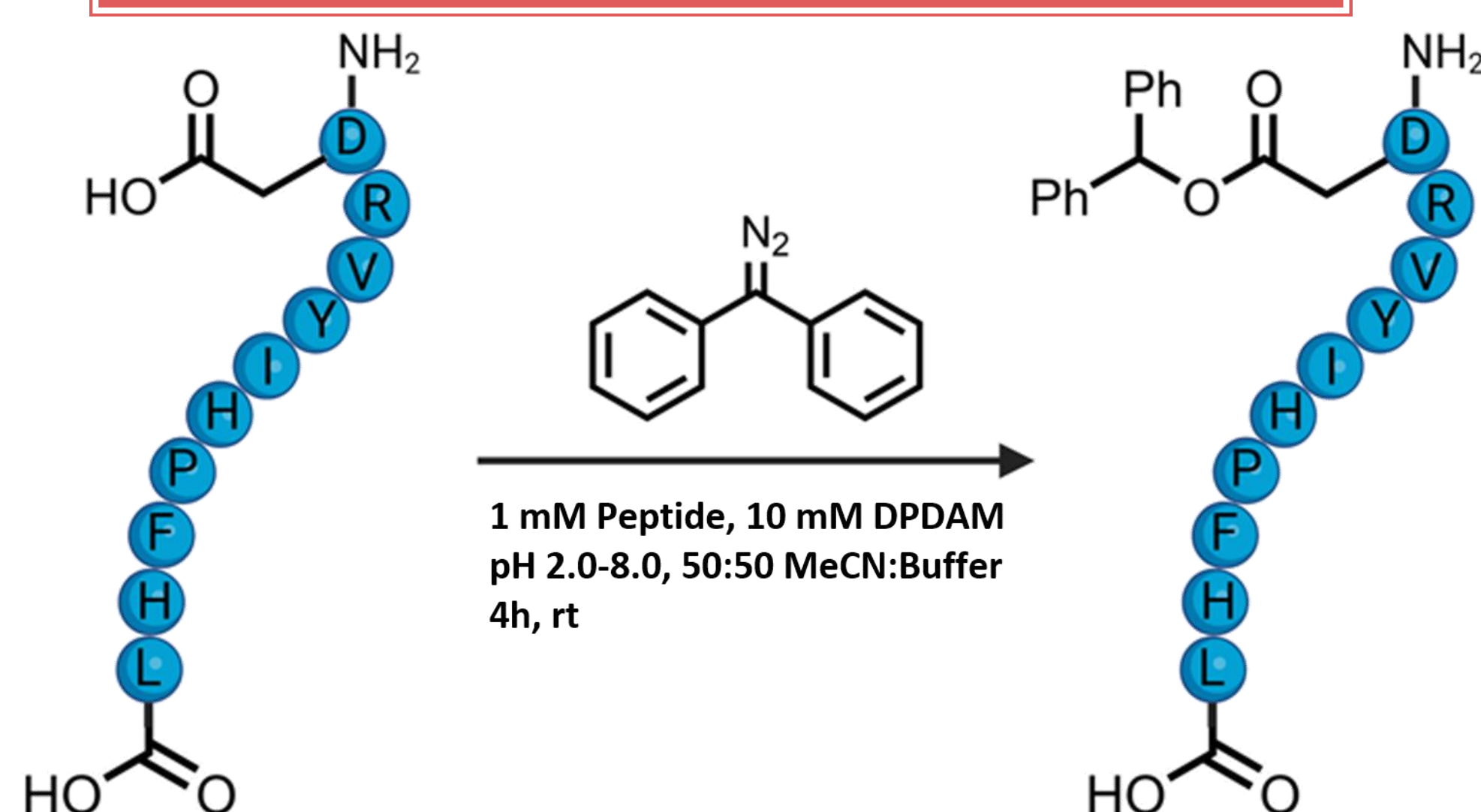
THE DIFFERENCES IN REACTIVITY



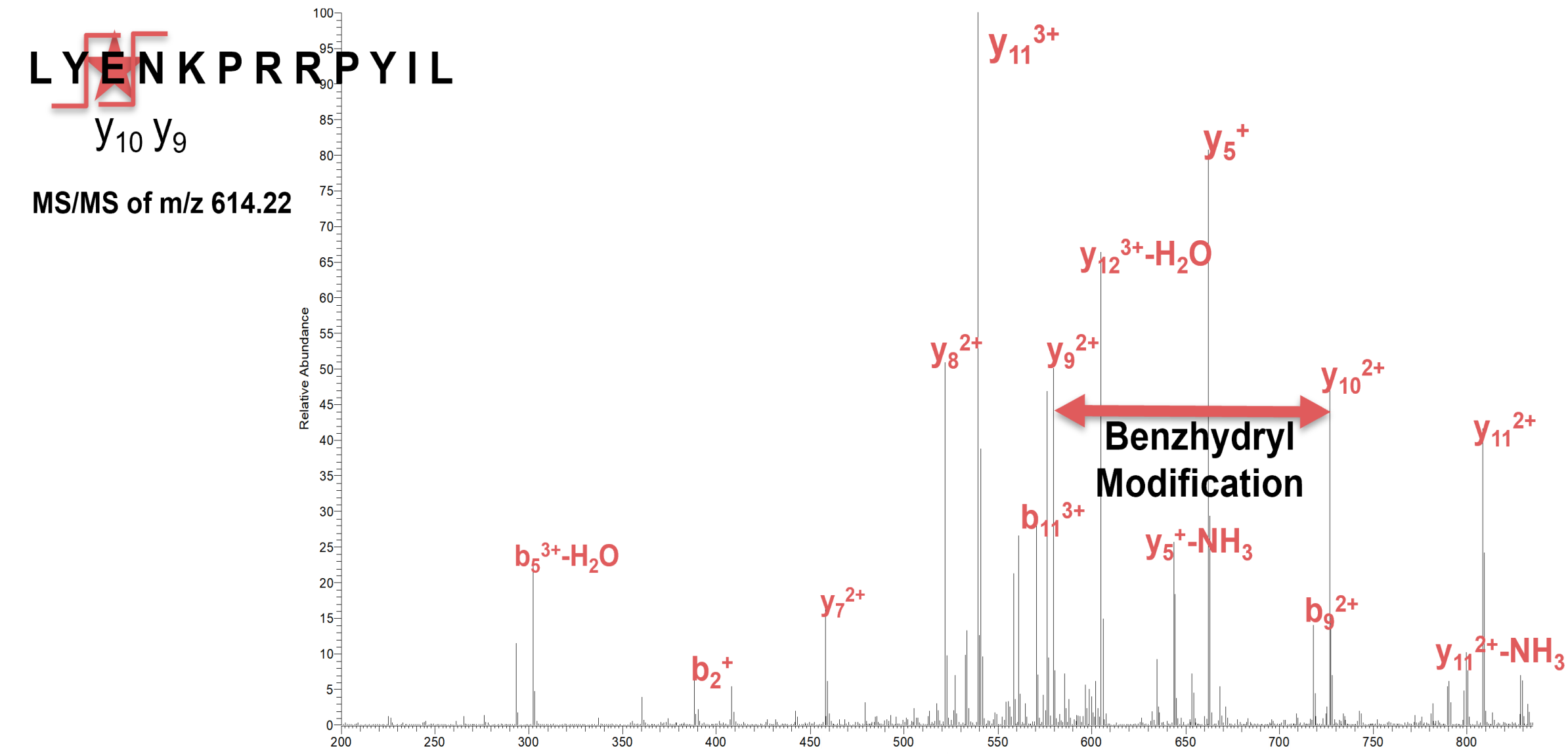
CHEMOSELECTIVE PROBE



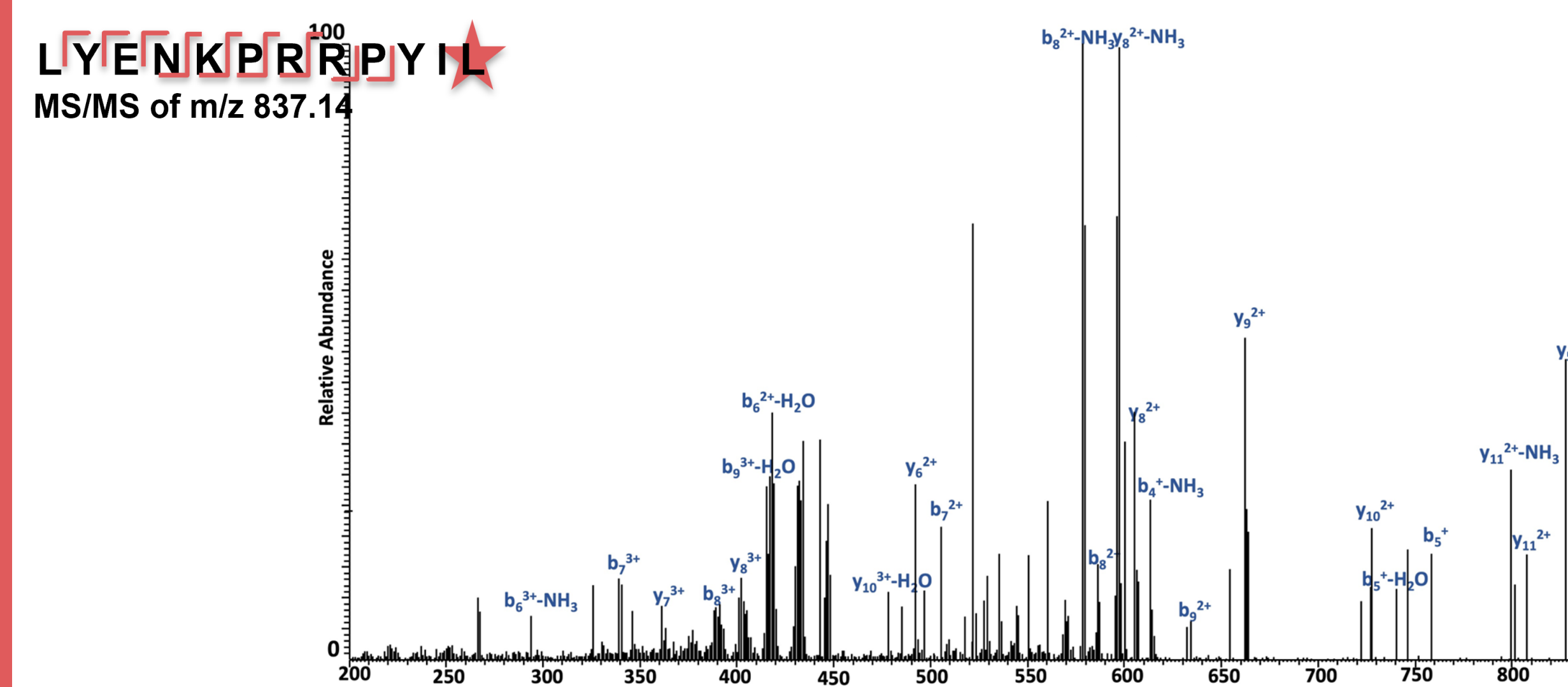
SCREENING CONDITIONS



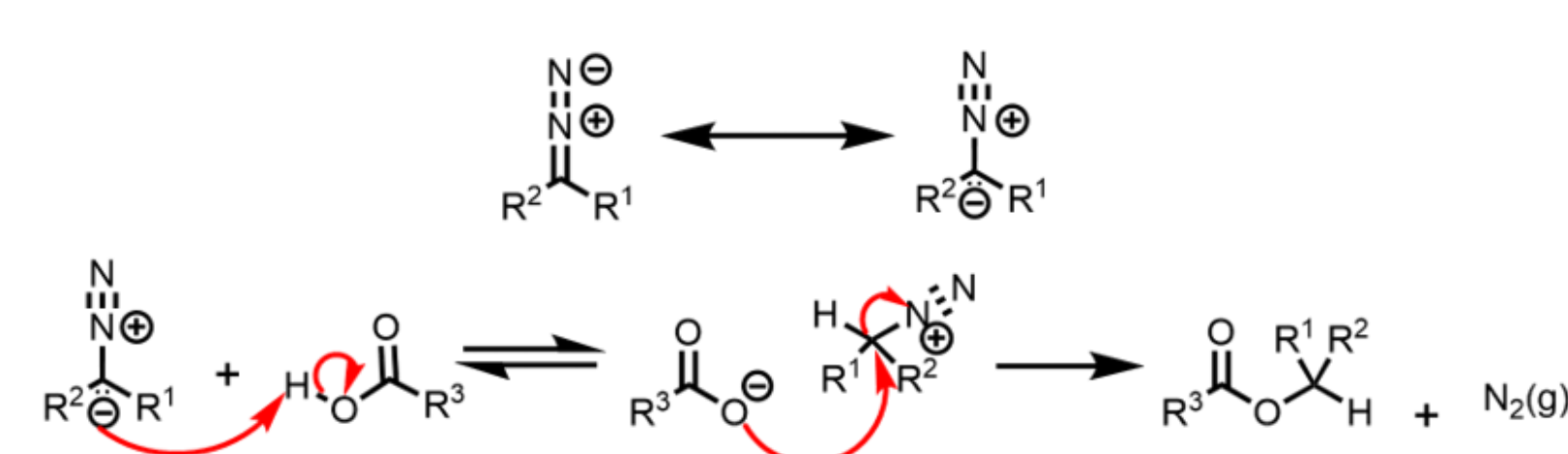
SIDENCHAIN LABELLING AT pH 4.0 CONFIRMED BY MS/MS



C-TERMINAL LABELLING AT pH 2.0 CONFIRMED BY MS/MS



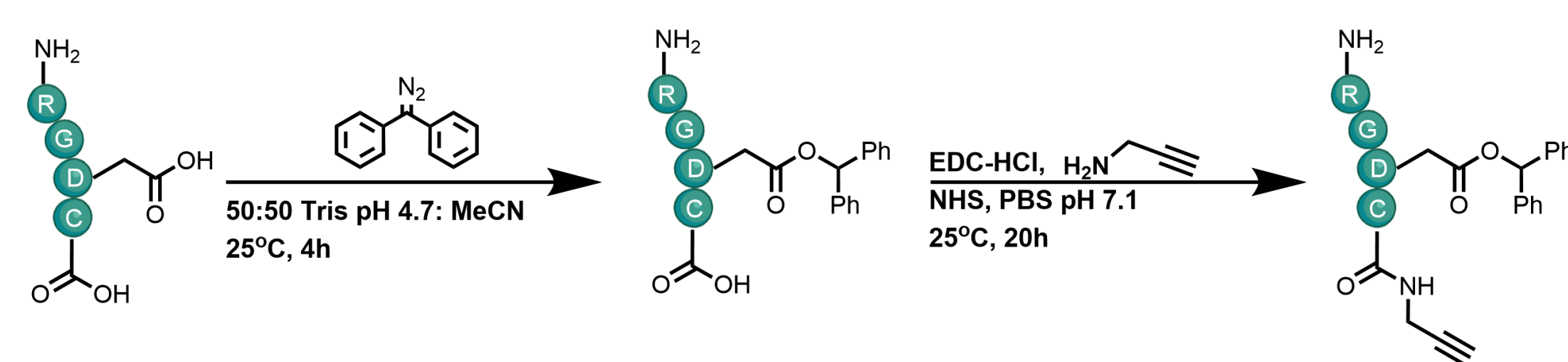
SELECTIVITY DRIVEN BY THE MECHANISM



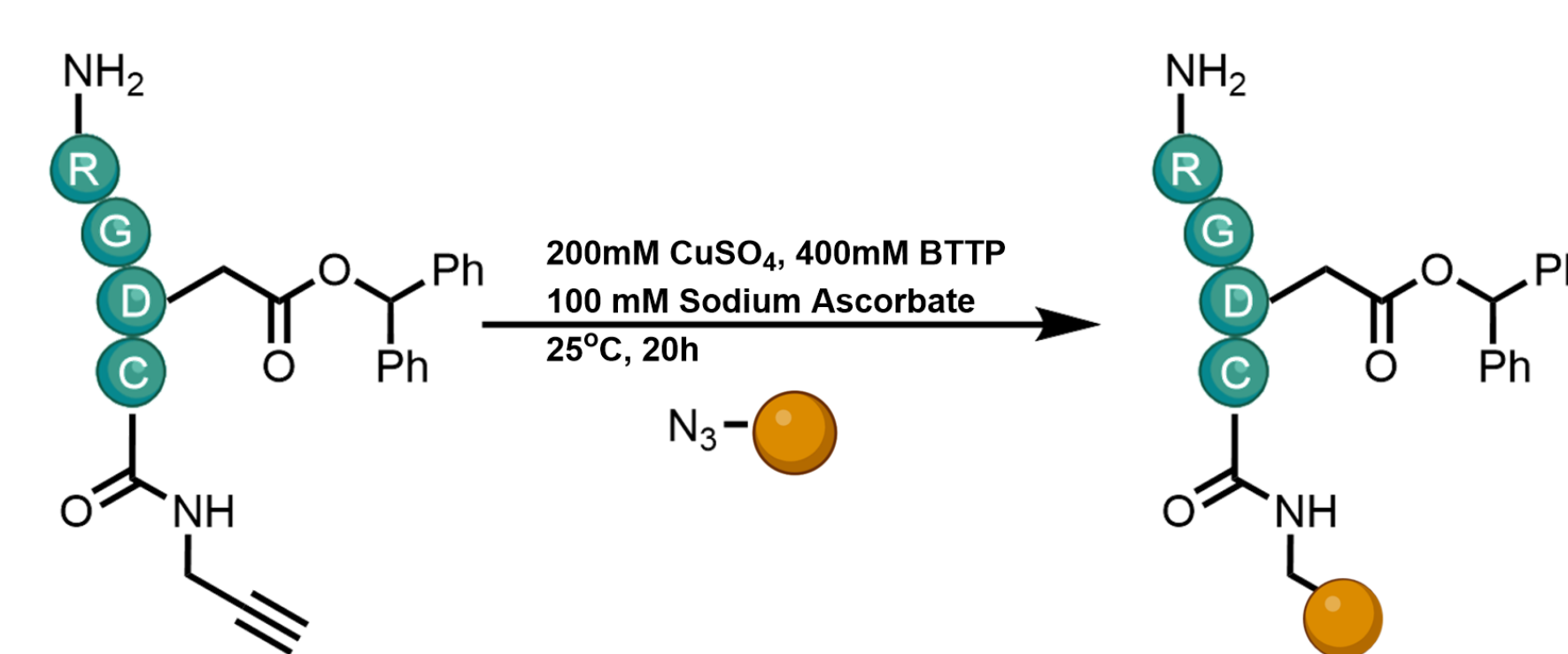
Carboxylic acids (protonated) are able to react.

Carboxylates (deprotonated) are unable to react.

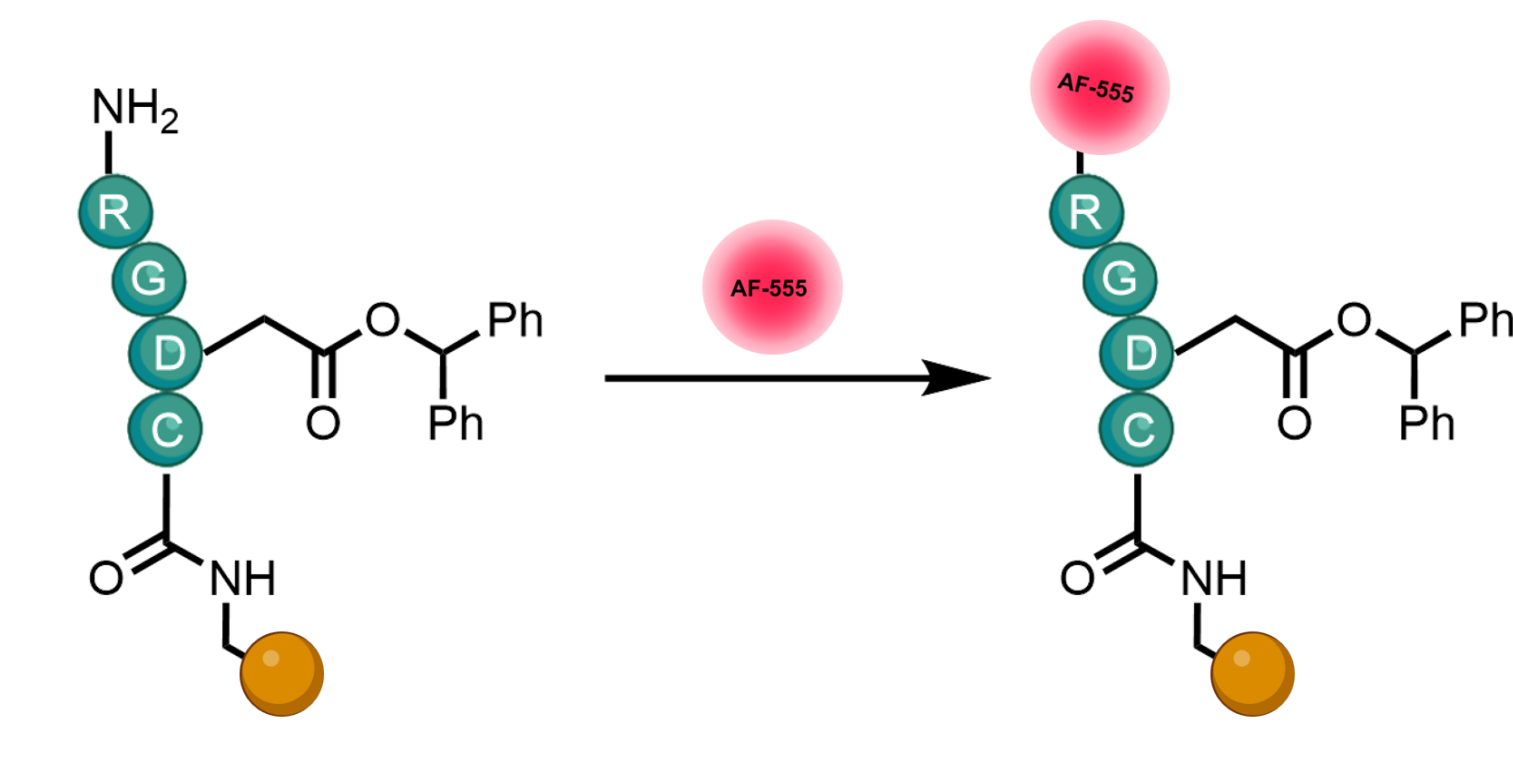
pH CONTROL ENABLES SELECTIVE MODIFICATION OF C-TERMINUS



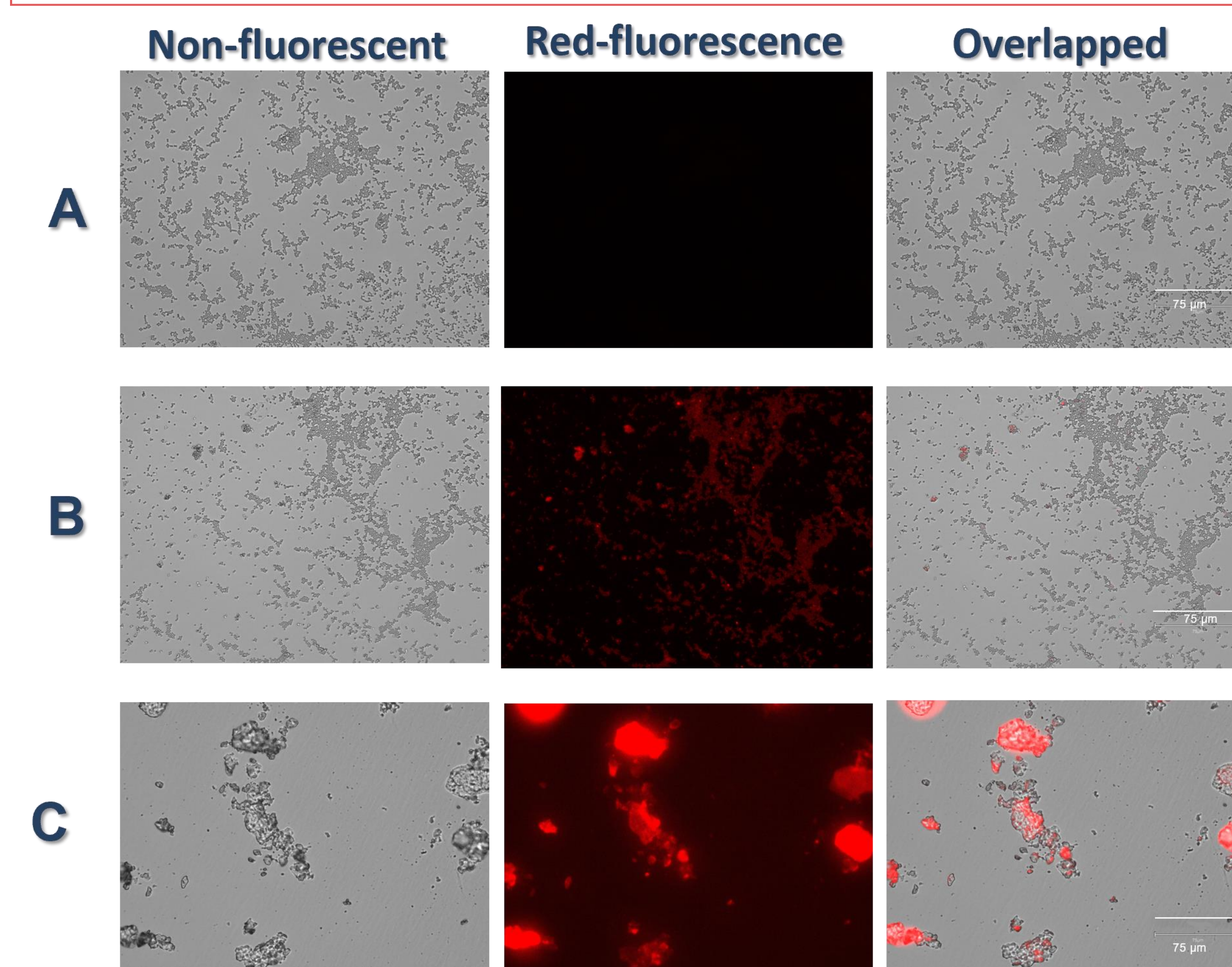
PROPARGYL AMINE ENABLES IMMOBILIZATION



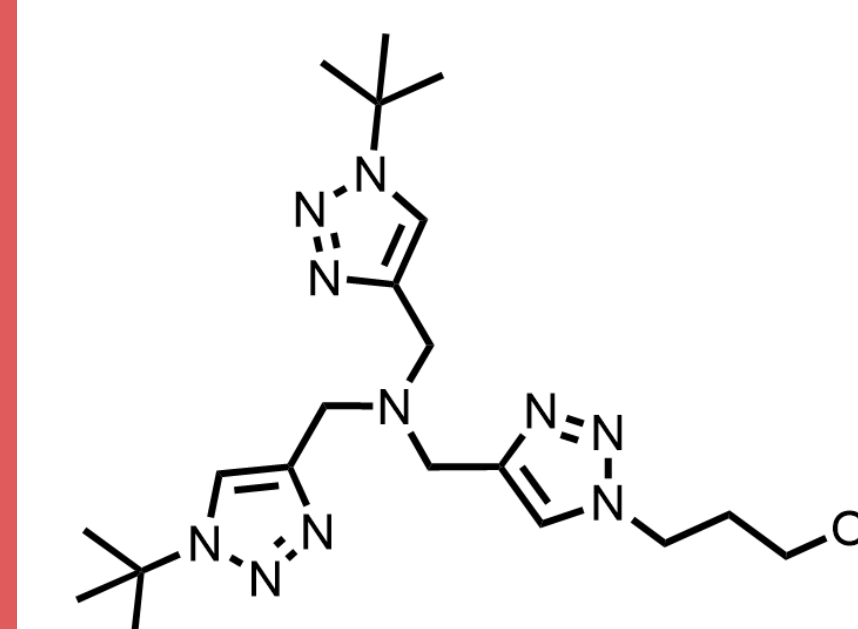
QC BY REACTION WITH FLUOROPHORE



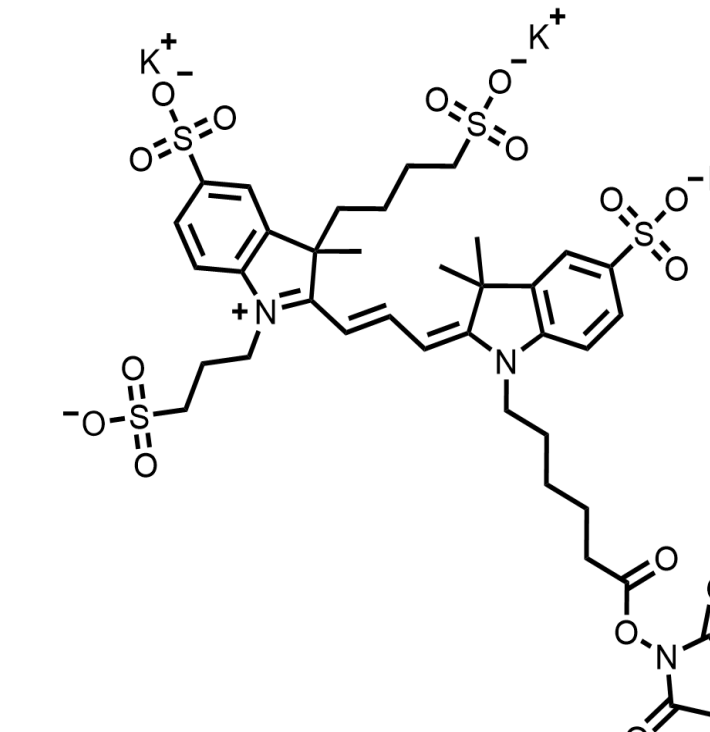
RESULT CONFIRMED WITH EPIFLUORESCENT MICROSCOPY



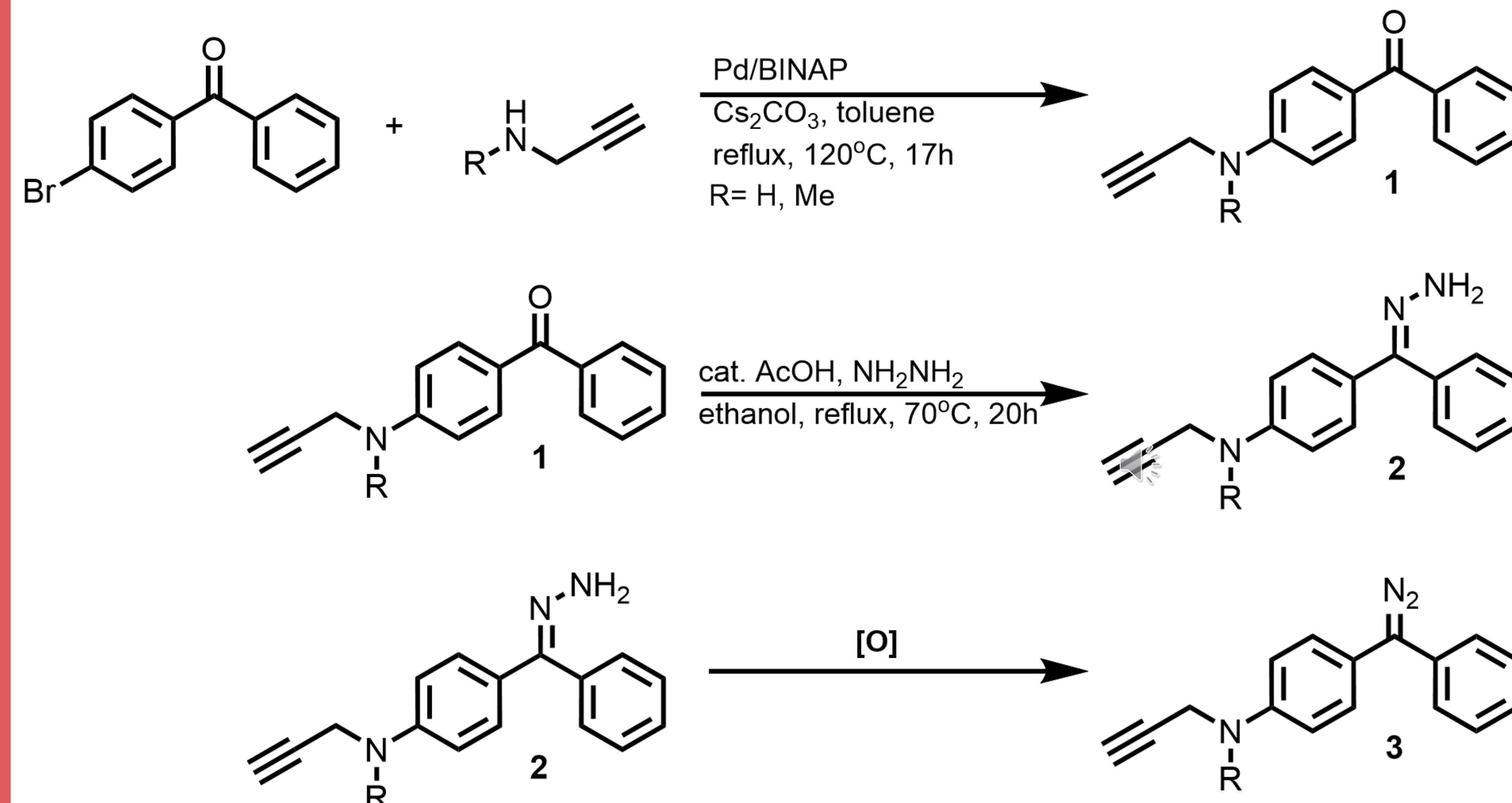
BTTP



AF-555



DEVELOPMENT OF A C-TERMINAL SELECTIVE PROBE



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REFERENCES

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