Betty A. and Donald J Baumann Family Scholarship Fund Application Form

1. Name

   Rebecca Zawistowski

2. Chemistry Faculty Research Director

   James T. Fletcher, Ph.D.

3. Research proposed (Please copy proposal into the box below this section. It will expand to include all text. The proposal is not to exceed 500 words and is not to exceed 2 pages. A summary of work already completed should also be included, if appropriate.)

   (Attached, next two pages)

4. Plans for presentation of research results (conference, publication, seminar, etc.)

   I plan to present my current and future results at the 2018 Nebraska Academy of Science meeting next spring.

5. Post-graduate plans (job market, graduate school, medical school, etc.)

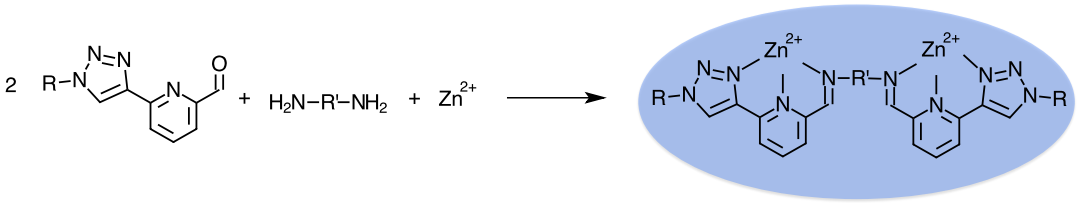
   Upon graduation, I intend to attend graduate school to further my studies in Chemistry. My goal is to do research focusing on biophysical chemistry, specifically using applied physical chemical techniques to study protein structure and activity.

Applicant signature

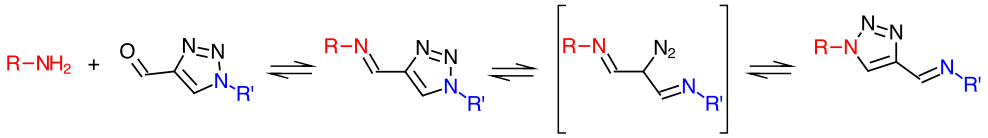
Chemistry research director's signature

L'abbe rearrangements on sold-phase immobilized peptides and chemosensing applications

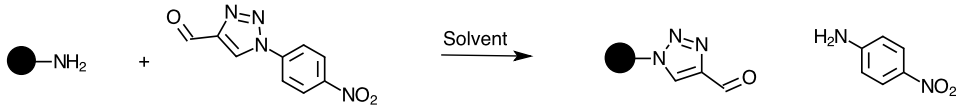
Biogenic amines and metal cations cannot be directly detected spectroscopically by UV-visible absorbance or fluorescence emission measurements. This makes small molecule chromophores attractive for the development of sensors for these analytes.[1,2] Previous research in Dr. Fletcher's lab has shown that triazole-containing compounds can be designed to react with amine analytes and bind specific metals in solution to generate unique colorimetric and/or fluorescent signals. Because of this quality, it has been proposed that triazole-containing compounds could show promise as chemosensors. I previously developed a biogenic diamine sensor using Zn(II), as shown below. For this system, I discovered that fluorescent signal generation required a 2:1:2 ratio between the triazole containing compound, the diamine analyte, and Zn(II).



In a second project, my goal was to develop reaction conditions for immobilizing 4-formyl-1,2,3-triazole compounds onto solid-phase resins via a L'abbe rearrangement. This rearrangement reaction proceeds through the mechanism shown below, and has been used to synthesize 4-formyl-1,2,3-triazoles that would otherwise be sterically hindered.[3]

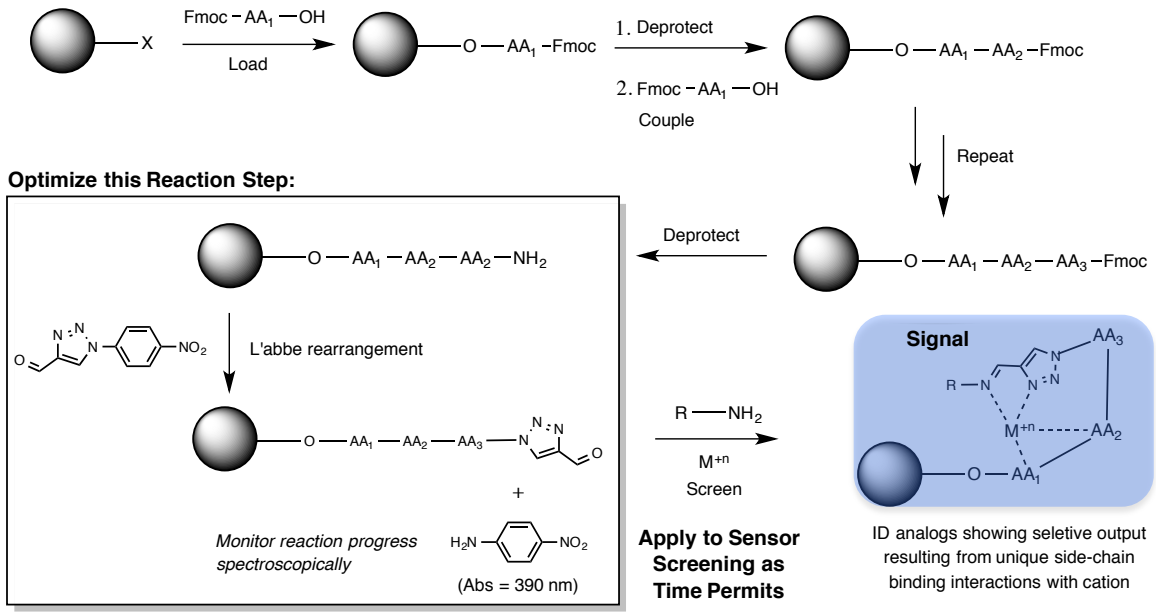


My project showed that this reaction can also be used to prepare resin-bound formyltriazoles, and that the 4-nitroaniline byproduct from this rearrangement produces a yellow color (390 nm), which can be used to monitor reaction progress spectroscopically. I optimized this reaction by surveying the impact of resin identity, solvent identity, stoichiometry and temperature on reaction rate and progress. Results showed that the reaction was fastest using TentaGel resin in DMSO solvent, and that a 2:1 ratio of aldehyde to amine functionality was the optimal stoichiometry.



My next goal in the project is to apply immobilized formyltriazole compounds towards chemosensing applications. I propose using a high-throughput screening approach for evaluating resin-bound peptide-functionalized formyltriazoles to identify new sensor candidates. Once prepared, solutions containing analytes of interest can be repeatedly washed over the resins in order to accumulate the colorimetric and/or fluorescent quality on resin.

For the Baumann proposal, I propose to develop reaction conditions that can be used to prepare 4-formyl-1,2,3-triazole functionalized peptides. I will prepare simple di-, tri- and tetrapeptides on several resins and establish optimal reaction conditions for derivatizing the peptides with a formyltriazole unit by L'abbe rearrangement using 1-(4-nitrophenyl)-4-formyl-1,2,3-triazole. As with my previous resin experiments, I will optimize this reaction by altering resin identity, solvent identity, stoichiometry and temperature and monitoring it spectroscopically.



Once this reaction has been optimized, I will apply those conditions to preparing a small library of di-, tri- and/or tetrapeptides and screen them on-resin against different amine and metal cation combinations, looking for resin beads that give color changes or fluorescent signals. By using solid phase peptide synthesis techniques, several hundred unique functionalized peptides can be efficiently synthesized and tested simultaneously. The peptides producing desirable signals will be selected and cleaved off of resin. They can then be analyzed with LCMS to be identified from the library and prepared by direct synthesis to validate the screen.

References:

[1]Domaille, D. W., Que, E. L., & Chang, C. J. (2008). Synthetic fluorescent sensors for studying the cell biology of metals. Nature chemical biology, 4(3), 168-175.

[2]Lee, B., Scopelliti, R., & Severin, K. (2011). A molecular probe for the optical detection of biogenic amines. Chemical Communications, 47(34), 9639-9641.

[3]L'abbé, G., & Van Essche, G. (1991). Synthesis of 4-keto substituted 1-alkyl-1,2,3-triazoles from 5-substituted 1-phenyl-1,2,3-triazole-4-carbaldehydes. Bulletin des Sociétés Chimiques Belges, 100.