

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

1. Name and NetID

Adam Burr

2. Chemistry faculty research director

Dr. James Fletcher

3. Proposal title

Pyridinium-substituted 1,2,3-triazoles

4. Proposal description. Please limit the proposal to about 500 words and include figures as appropriate. Your proposal should briefly outline the overall project and its goal(s). If you have previous results related to your proposed project, concisely summarize those results and describe what you expect to accomplish during the time frame of the scholarship.

Quaternary ammonium compounds (QACs) comprised of N-heterocycles such as cetylpyridinium chloride are common commercial disinfectants. Recently, click-derived 1,2,3-triazolium salts have been shown to display antiseptic properties in a substituent dependent manner. The aim of this study is to prepare pyridinium-substituted 1,2,3-triazole QACs, as well as polyvalent hybrid salts possessing both pyridinium and triazolium subunits, and to evaluate their respective antiseptic properties. Thus far, we've found that under mild conditions, N-benylation at the pyridine subunit can be achieved selectively over N-benylation at the 1,2,3-triazole subunit. Under forcing conditions, N-benylation at both pyridine and 1,2,3-triazole subunits to form a hybrid polyvalent QAC is achievable when 1,5-disubstituted-1,2,3-triazoles are used as the nucleophile (see Figure 1 below).

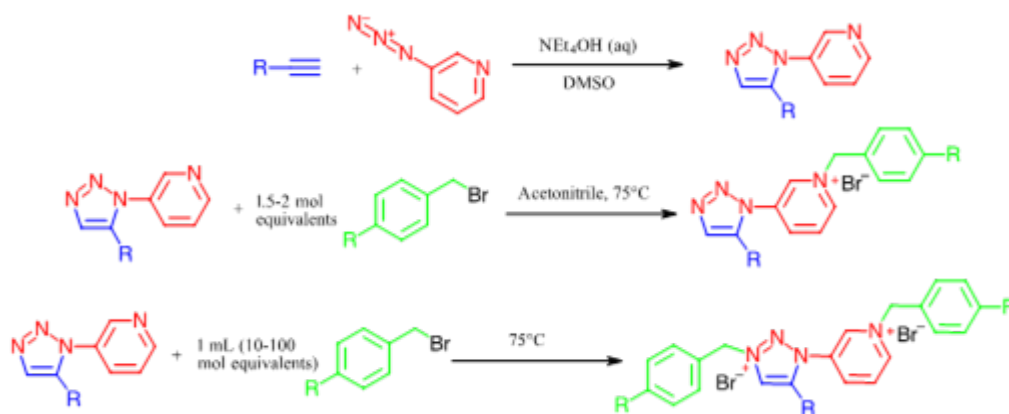


Figure 1. Two step synthesis of generic 1,3,5-disubstituted 1,2,3-triazolium salts containing a pyridinium salt unit. In the first reaction, a terminal alkyne (blue) reacts with a pyridinium-containing azide (red) in the presence of a strong base to form a 1,5-disubstituted 1,2,3-triazole. The second reaction shows nucleophilic substitution of a 1,5-disubstituted-1,2,3-triazole in the presence of 1.5-2 mole equivalents of an electrophile, in which N-benylation at the pyridine subunit was achieved selectively over N-benylation at the 1,2,3-triazole subunit. Finally, the third reaction shows nucleophilic substitution of a 1,5-disubstituted 1,2,3-triazole in the presence of an excess of electrophile, in which N-benylation at both pyridine and 1,2,3-triazole subunits to form a hybrid polyvalent QAC has been achieved.

When comparing the ability of bis-triazole, para-phenyl bridged bis-triazole and para-biphenyl bridged bis-triazole analogs, the efficiency of preparing polyvalent hybrid triazolium products with pyridinium subunits was distance-dependent. Monovalent and polyvalent QACs were evaluated for antiseptic properties against exemplary Gram-positive bacteria (*S. epidermidis* and *B. subtilis*), Gram-negative bacteria (*E. coli* and *K. aerogenes*), and yeast (*C. albicans* and *S. cerevisiae*) using minimum inhibitory concentration (MIC) assays. Micromolar MIC values were observed for select analogs, with overall charge as well as peripheral substituent identity influencing antiseptic potency.

During the timeframe of the scholarship, I plan to synthesize quinine-substituted 1,2,3-triazole QACs to investigate the effects of increased hydrophobicity on the MIC values of these analogs. Furthermore, our synthesis thus far has utilized 3-pyridyl compounds, so I'd like to synthesize analogs containing 2-pyridyl and 4-pyridyl units, if possible. Such a study would be interesting because it would provide insight into the steric effects of N-benylation.

5. Presentation of research results (past and future conferences, publications, seminars, etc.)

Past Presentations:

Burr, Adam J. Antibiotic Peptide Amphiphiles. Oral Presentation given on August 8, 2022 at the 2022 INBRE Conference at Lied Lodge, Nebraska City, NE.

Burr, Adam J, Fletcher, James T. Evaluating the Impact of Overall Charge in Antiseptic Triazolium Salts. Poster presentation given on March 29, 2023 for University Research Week at Creighton University, Omaha, NE.

Burr, Adam J, Fletcher, James T. Evaluating the Impact of Overall Charge in Antiseptic Triazolium Salts. Oral presentation given on April 21, 2023 at the 2023 Nebraska Academy of Sciences Conference at Nebraska Wesleyan University, Lincoln, NE.

Burr, Adam J, Fletcher, James T. Evaluating the Impact of Overall Charge in Antimicrobial Triazolium Salts. Poster presentation given on August 7, 2023 at the 2023 INBRE Conference at Lied Lodge, Nebraska City, NE.

Burr, Adam J, Fletcher, James T. Pyridinium-substituted 1,2,3-triazoles: Synthesis and antiseptic evaluation. Poster presentation given on October 19, 2023 at the 2023 ACS Midwest and Great Lakes Regional Meeting, St. Charles, MO.

Future Presentations:

Burr, Adam J, Fletcher, James T. Pyridinium-substituted 1,2,3-triazoles: Synthesis and antiseptic evaluation. Poster presentation to be given during University Research Week at Creighton University.

Burr, Adam J, Fletcher, James T. Pyridinium-substituted 1,2,3-triazoles: Synthesis and antiseptic evaluation. Oral presentation to be given at the Nebraska Academy of Sciences at Nebraska Wesleyan University, Lincoln, NE.

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

I plan to attend graduate school in pursuit of a Ph.D. in synthetic organic chemistry.

7. Number of semesters involved in research, including current semester (summers count as two semesters)

10 semesters.

8. Anticipated graduation date

May 11, 2024