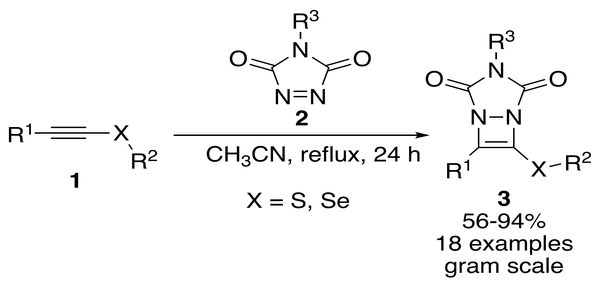
Diazacyclobutenes: A Possible Anti-Parasitic?

Harrison Lapin, Dr. Daniel Whitehead, PhD., Brock Miller.
University of South Carolina School of Medicine Greenville; Clemson University – Chemistry/EPIC; Clemson University – Chemistry/ EPIC

Abstract

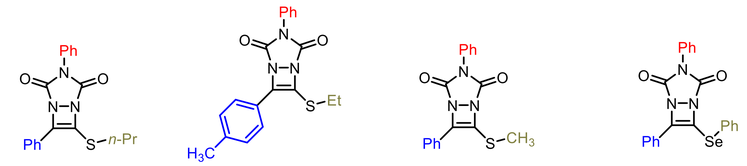
The long journey of drug discovery may be a process many do not consider. This tedious process is extremely important in creating favorable outcomes for patients. The journey of a new drug can start in many different fashions. (1) In this case, it happens to be a random side effect of a chemical compound developed by organic chemist. Recently, the Clemson lab discovered a novel method to synthesize a group of compounds, the diazacyclobutenes. (2) Creating a method of synthesis for these compounds that is efficient and cost-effective is important to consider when the goal is drug discovery. Certain derivatives of the diazacyclobutenes, have shown promise as a compound that can kill certain parasites, including *Trichomonas vaginalis. T. Vaginalis* infected around 2 million individuals in the United States in 2018. (4) The goal is to expand the library of novel diazyclobutene derivatives and investigate their therapeutic effect against *T. Vaginalis.* This process is completed by a 2 or 4 step process depending on if you want to change the bottom or top positions, respectively. The positions are manipulated by changing the substrates used in the reactions (2). The library of novel DCB derivatives has successfully been expanded; however, due to COVID – the testing against *T. Vaginalis* has been halted. It is encouraging that the library of compounds to test against the parasites has been expanded; but, until the parasites and molecules can be cultured together, the anti-parasitic activity of the certain derivatives will not be known at this time.

Diazacyclobutene

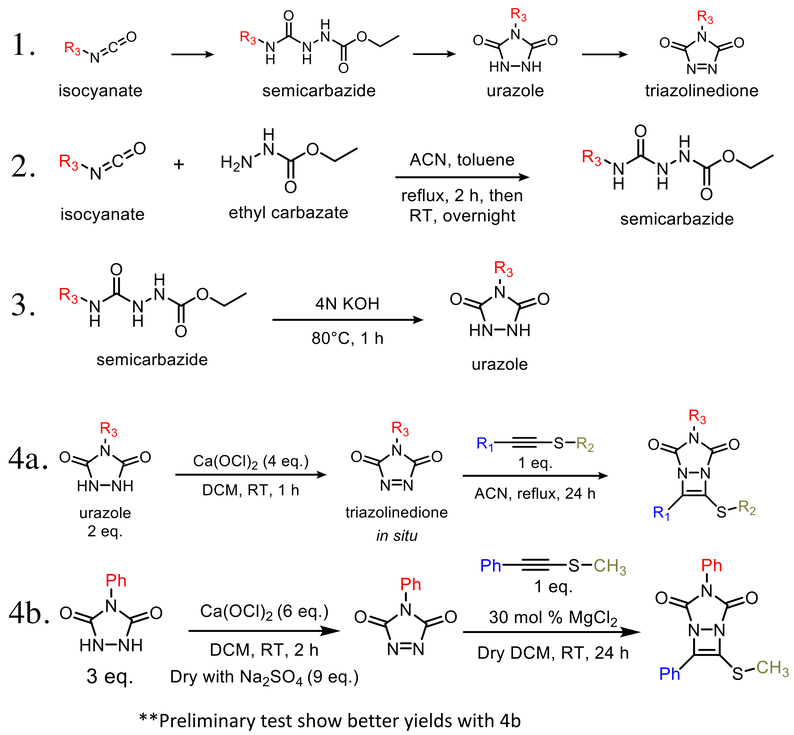


Changing the Side Chains

The fundamental question is: How does changing R1, R2, R3, and X effect this compounds biological activity?

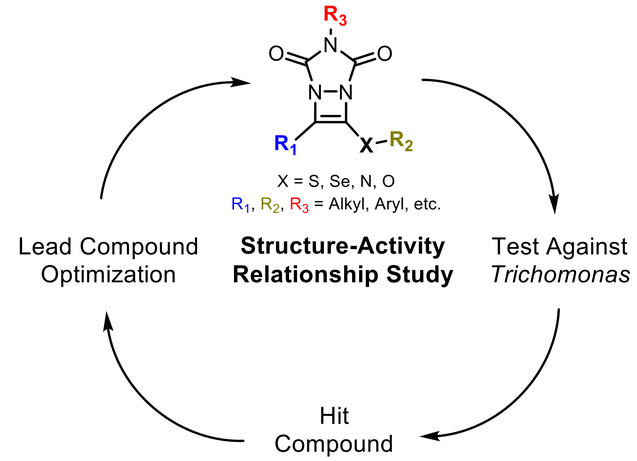


How is this process conducted?



**Preliminary test show better yields with 4b

Method



1. Expand the library of novel diazacyclobutenes with emphasis on the R3 and X position.
2. Testing against *T. vaginalis* to explore hit compounds
3. Edit positions on hit compounds
4. Further optimize hit compounds in order to explore further modifications

Future Goals

- Increase the % yield on lead compounds
- Narrow in on hit compounds and expand similar derivatives
- Continue testing derivatives against *T. vaginalis*
- Send compounds to outside labs for testing against other parasites

Funded by: Clemson- EPIC/ NIH T35 Grant
Contact: hlapin@email.sc.edu