Daniel S. Jeremiah,
End of Summer Report,
FURSCA. Summer 2024

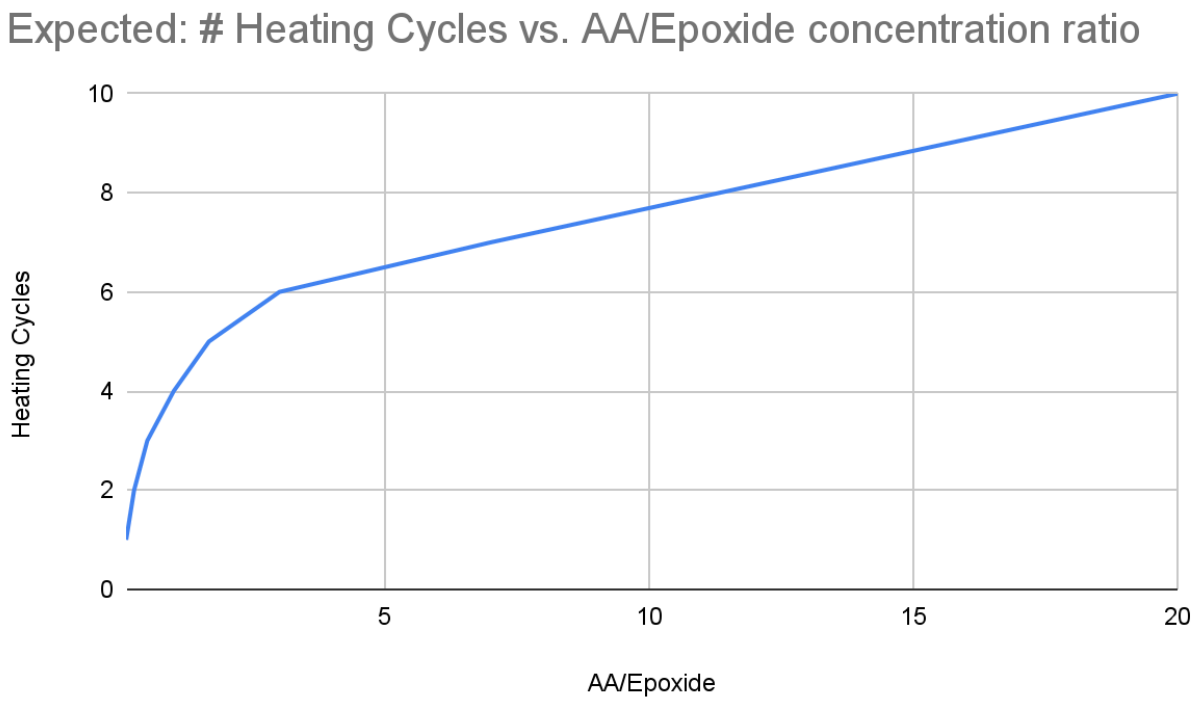
END OF SUMMER FURSCA REPORT, 2024

This summer, my goal was to develop an enantioselective synthesis of beta-aminoalcohols. Previous workers in the Harris lab have developed a catalyst that converts common compounds called epoxides into amino alcohols. This summer, we took the next step in this research, which is to determine if the amino alcohols being produced are racemic or enantio-enriched. That is, do the products exist as two mirror images in equal amounts or predominantly one mirror image? This is called asymmetric synthesis and represents a multi-billion dollar demand due to the high value of these products.

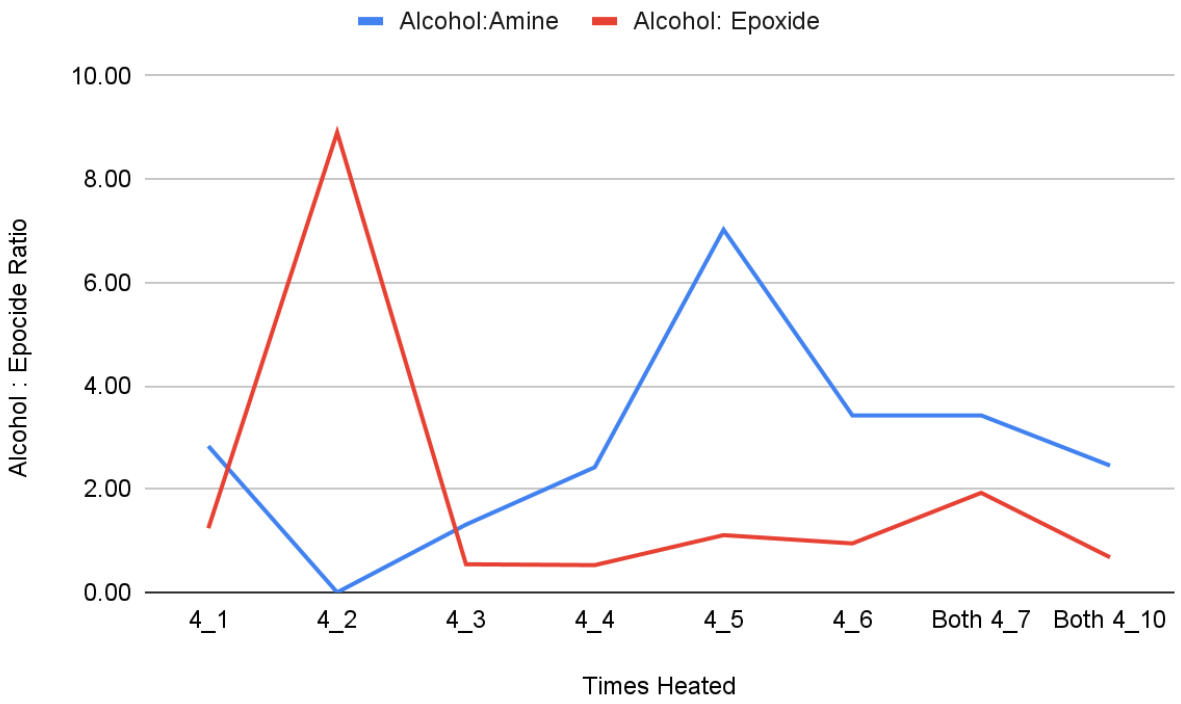
The goal of this project was to ascertain the feasibility of newly optimized reaction conditions generated from the previous semester. These conditions comprising of heating under pressure, reaction time, and reaction solvent, are critical to ensure optimal yield, that is the amount of desired product made, of our reactions.

Results:

Attempts to optimize reaction conditions proved to be more complicated than expected. For context, an increase in reaction products was expected with an increase in reaction heating time and cycles, as shown in the diagram below. As the heating cycles increased, the ratios between starting material and product are expected to be widened showing a reaction on the path to completion.



However, for reasons still being investigated, the results were rather erratic and inconclusive. Further research is needed to determine the reasons for this data.



While the cause of this erratic data is being investigated, I continued my research by synthesizing pure enantiomeric stocks of our desired compound. I spent the rest of my summer replicating the following paper:

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An improved and efficient process for the scalable preparation of optically pure *trans*-2-aminocyclohexanols

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An improved and efficient process has been developed for a green and scalable preparation of optically pure (*1R,2R*)- and (*1S,2S*)-*trans*-2-aminocyclohexanols. The process utilised hot water to promote the aminolysis of cyclohexene oxide by benzylamine to afford racemic *trans*-2-(benzylamino)cyclohexanols, which were resolved by sequential and repeated use of (*R*)- and (*S*)-mandelic acid. Finally, after treatment of the two salts sequentially with HCl and NaOH and recovery of mandelic acid, liberation was achieved of the optically pure *trans*-2-benzylaminoaminocyclohexanols which were smoothly debenzylated using a low loading of a Pd/C catalyst to the *trans*-2-aminocyclohexanols. The synthetic route has been successfully applied to large-scale (1 mol) preparations in good yield.

Keywords: *trans*-2-(benzylamino)cyclohexanol, chiral resolution, enantiopure (*1R,2R*)-*trans*-2-aminocyclohexanol, enantiopure (1S,2S)-*trans*-2-aminocyclohexanol

Enantiopure *trans*-1,2-amino alcohols are versatile synthetic ... involving formation of the amine hydrochlorides with aqueous

This paper demonstrates the scalable synthesis of optically pure beta-amino alcohols via a chiral resolution synthesis. I plan to continue replicating the work found in this paper and continue to synthesize more enantiomerically pure amino alcohols with varying amines while the reaction conditions mentioned earlier are continually optimized. to provide pure standards that will be used in evaluating the enantiomeric excess of our catalyst-synthesized amino alcohols.

Consequently, I intend to present my findings at the college's annual Elkin Isaac research symposium in the spring of next year, as well as the annual American Chemical Society (ACS) meeting.

This summer has further solidified my interest in drug design as well as experimental design, which I will experience in graduate school while I work to obtain my PhD in chemistry. I would like to thank the Robson Family Fellows Endowment for their generous support of my summer research. This project has allowed me to acquire valuable insights into the everchanging field of chemical synthesis and has even inspired me to take up a side project. For this, I am incredibly grateful!