Exploration into the Synthesis and Reactivity of 3N-Substiuted 4-Quinazolinones

Jessica Lowry, Katrina Nguyen, and Kelly Kim*,

Quinazolinones are heterocyclic organic compounds described as “privileged scaffolds” based on their interesting bioactivity (anti-inflammatory, anti-microbial, etc.) and importance in synthetic development and medicinal chemistry. Due to their promising chemical and biological properties, synthesis of these compounds is worth exploring and improving upon. 4-Quinazolinones, containing alkyl amino *3N* substituents, are particularly interesting, given their ubiquity in bioactive molecules, and are the focus of this project. To synthesize *3N*-substituted 4-quinazolinones for further study, we treated quinazolinones with dihaloalkane electrophiles of varying carbon linker lengths (n = 1 or 2). Once the initial alkylation was complete, the product was then reacted with a primary amine in the presence of potassium carbonate in acetonitrile to effect substitution of the remaining halide. Primary amines differed by their R groups, and included cyclohexylamine, benzylamine, phenethylamine, and 4-methoxyphenethylamine. Our efforts and those of a collaborating team suggest that smaller primary amine R groups and longer dihalide carbon linker chains increased the product yield of novel *3N*-substituted 4-quinazolinones. It also appeared that conversion was higher with dibromo linkers rather than dichloro linkers, perhaps due to the superior leaving group ability of bromine. Additionally, using R groups with longer carbon chains, such as phenethylamine, seemed to increase product yield as well, possibly due to a decrease in steric hindrance. Future work could include trying different R groups on the chosen primary amine, exploring different different bases or solvents, and altering reaction conditions, such as temperature and reagent concentrations. Finally, future work may be done to uncover the bioreactivity of these novel compounds. Overall, our efforts have enabled successful synthesis of *3N*-substituted 4-quinazolinones and produced helpful insights into quinazolinone synthesis, an important area of research with far-reaching applications in the biomedical sciences.