N-Alkylation of 2 Chloro-quinazolinone for the preparation of Di-substituted Quinazoline derivatives.

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INTRODUCTION

- Chagas is an inflammatory infectious disease caused by a group of parasites of the protozoan Trypanosoma cruzi, It is commonly found in Latin America, especially in poor and rural areas and affects about 8 million people [1]

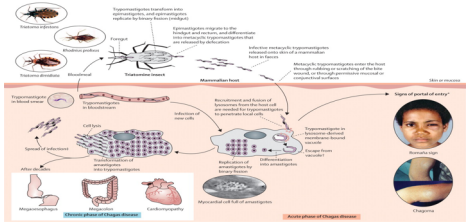


Figure 1. Overview of T. Cruzi life cycle and chronic phases of Chagas disease

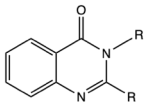


Figure 2. The heterocyclic fused rings quinazoline has constituted a crucial scaffold to obtain molecules with biological activities [2]

Objective

- Establishing an optimized synthesis pathway toward bioactive quinazolinone.
- Testing the reaction with different leaving groups, bases, solvents, and coupling reagents to gather higher yield and more efficient bioactive target compound.

Bioactive Quinazolinones: Synthetic Approach

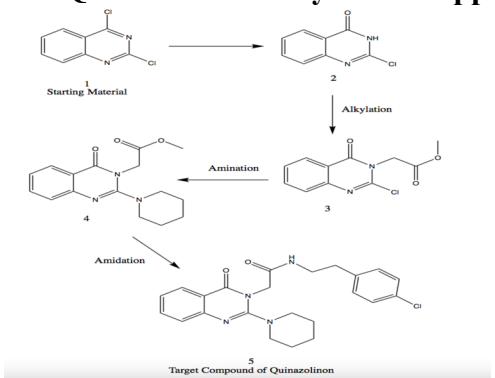


Figure 3. Overall three step forward synthesis of bioactive quinazolinone derivatives [3]

METHODS AND RESULTS

Synthesis of our desired quinazolinone product starts with preparation of the oxidized quinazolinone core, which then undergoes alkylation with methyl-2-bromo acetate via substitution reaction in order to form the desired alkylated precursor. Alkylation completes the first major step in the synthesis of our bioactive treatment and the precursor goes on to be varied in unique conditions in order to generate a widespread of structurally different derivatives of bioactive quinazolinone.

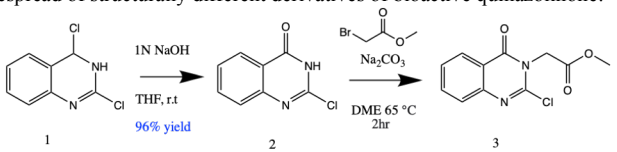


Figure 4. Installation of N-Alkylation of 2 Chloro-quinazolinone

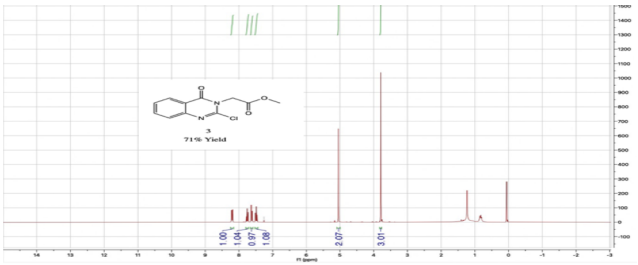
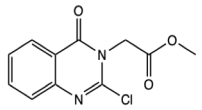


Figure 5. H-NMR data of the successful synthesis of the N-alkylation of Chloro-quinazolinone by affording methyl-2-bromoacetate in good yield 71%

Data summary



3
71% Yield

Figure 6. Alkylated N- Methyl Acetyl-2- chloro quinazoline-4-one for preparation of animated quinazolinone

	Crude product (unpurified)
Mass	54 mg
% yield	71.2%
Appearance	White solid
Rf value & TLC solvent	Rf = 0.82; 1:1 EtoAc/hexane
NMR solvent	Acetone-d6

Future direction

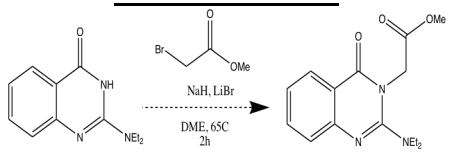


Figure 7. Planned preparation of **7** from aminated quinazolinone core **6**

Alkylation of aminated quinazolinone experiment using different bases (NaOH, or NaH in LiBr)
- If optimizing alkylation reaction synthesizes quinazolinone more efficiently, then it will produce a new compound to study Chagas. This study also contributes to the drug library that provides researchers information to value the potential of using quinazolinone for medicinal benefit.
- Other chemists can use this knowledge to alkylate Quinazolinone for studying another disease.

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- UW Seattle NMR facility

REFERENCE

1. CDC-Centers for Disease Control; Prevention. CDC - Chagas Disease - Detailed Fact Sheet. **2009**.

2. Bollini, M.; Bruno, A. M.; María E. Niño; Casal, J. J.; Sasiambarrena, L. D.; Damián A.G. Valdez; Battini, L.; Puente, V. R.; María E. Lombardo Synthesis, 2D-QSAR Studies and Biological Evaluation of Quinazoline Derivatives as Potent Anti-Trypanosoma cruzi Agents. *Medicinal Chemistry; MC* **2019**, *15*, 265-276.

3. Kim, K. (n.d.). Research Projects in Organic Synthesis. Retrieved March 18, 2022, from https://canvas.uw.edu/courses/1523397/files/86200417?module_item_id=14784165