EXPLORATION INTO THE SYNTHESIS AND REACTIVITY OF 3N-SUBSTITUTED 4-QUINAZOLINONES

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INTRODUCTION

- Quinazolinones are considered "privileged scaffolds" due to their interesting bioactivity, (anti-inflammatory, antifungal, antibacterial, etc.)
- 3N-substituted 4-quinazolinones are particularly interesting due to their ubiquity in bioactive molecules
- Our aim is to explore the synthesis of 3N-substituted 4-quinalzolinones under varying conditions

METHODS

STEP 1: 3N-ALKYLATION OF 4-HYDROXYQUINAZOLINE

- Treated quinazolinone with dihaloalkane electrophiles of varying carbon linker length (n = 1 or 2)
- Starting materials were heated to reflux and stirred under nitrogen gas for 2 hours

STEP 2: AMINATION OF 3N-ALKYLATED QUINAZOLINONE

- Reacted 3N-alkylated product with a primary amine in the presence of potassium carbonate in acetonitrile to effect substitution of the remaining halide
- Primary amines differed in R groups, and included cyclohexylamine, benzylamine, phenethylamine, and 4-methoxyphenylamine

ANALYSIS OF COMPOUNDS

- Synthesized compounds were collected using liquid-liquid extraction and vacuum filtration, and purified via column chromatography
- Crude and purified products were analyzed via silica gel TLC and H1NMR using chloroform-D

RESULTS

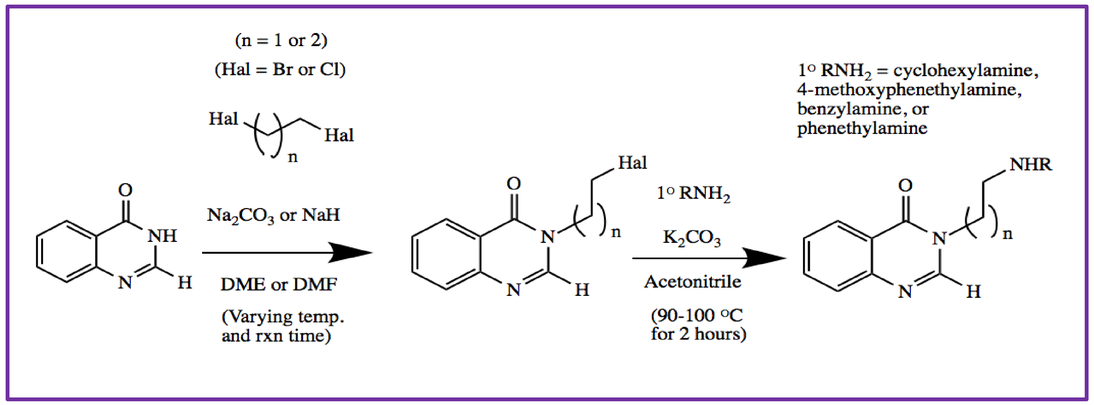
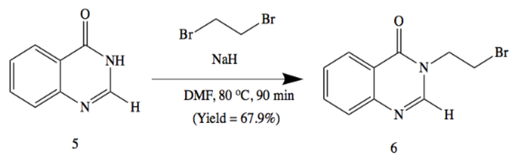
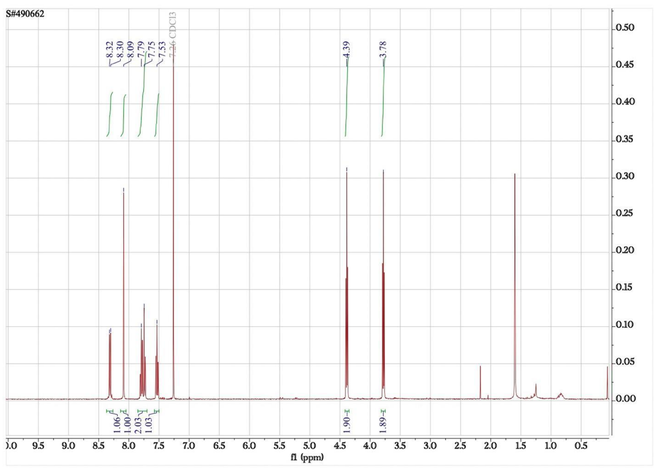


Figure 1: Project Overview

STEP 1 EXPERIMENT: INITIAL 3N-SUBSTITUTION

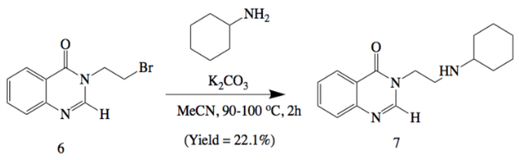


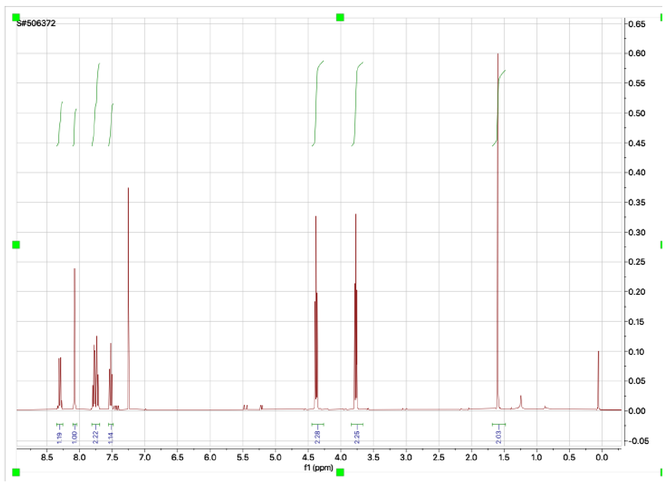


TLC: complete conversion

HNMR:
- Alkane linker: two triplet peaks at ~ 3.8ppm and 4.4 ppm
- Aromatic protons: 5H integration at ~ 7.5pppm

STEP 2 EXPERIMENT: AMINATION OF 3N-ALKYLATED QUINAZOLINONE





TLC: incomplete conversion

HNMR: resembled starting material
- Alkane linker: two triplet peaks at ~ 3.8ppm and 4.4 ppm
- Aromatic protons: 5H integration at ~7.5pppm
- Purification unsuccessful

CONCLUSIONS

- Smaller primary amine R groups and longer dihalide carbon linker chains increased product yield
- Conversion rate increased with dibromo linkers rather than dichloro linkers
- R groups reagents with longer carbon chains, such as phenethylamine, increased conversion

FUTURE WORK

Future work should explore the synthesis of 3N-substituted 4-quinazolinones using primary amines with different R groups, and differing conditions, such as temperature, base identity, solvent identity, and electrophile identity.

Further research could be done to uncover the bioreactivity of novel compounds, and possible medicinal applications.

REFERENCES AND ACKNOWLEDGMENT

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