

# Development of Lipoic Acid Derivatives for Environmentally-Friendly Materials

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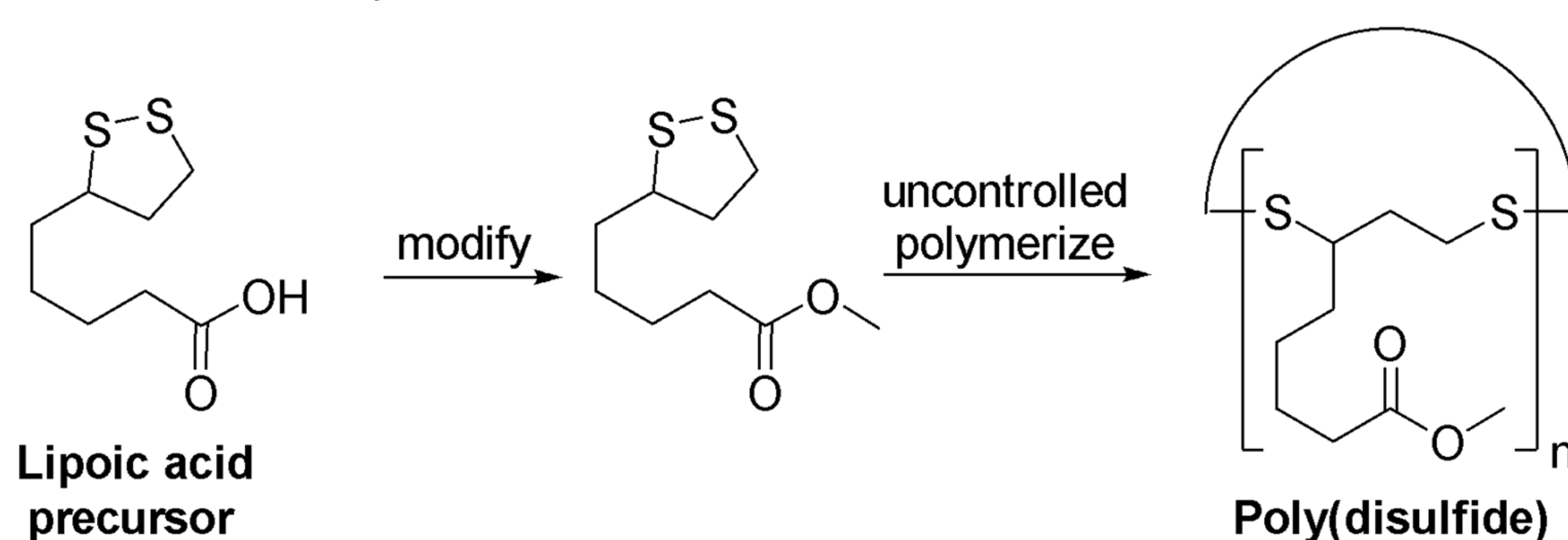
## Introduction:

Plastics are extensively used in day-to-day life. The increase in consumer use is a result of plastics being developed as a cheaper, more durable alternative to other materials. This prized durability, however, has turned out to be a negative, as it has significant impacts on the environment due to current plastics' limited ability to degrade. Furthermore, the materials used to make modern plastics are equally as harmful. Currently, plastic materials are mainly derived from crude oil and natural gases, both of which are usually acquired through means harmful to the environment (creating wastewater, releasing toxic air pollutants and greenhouse gases that can contribute to global warming).<sup>1</sup> As we become more environmentally conscious, the need for environmentally-friendly plastics becomes more evident.

Poly(disulfide)s serve as a potential alternative due to their unique ability to undergo disulfide exchange.<sup>3</sup> As a result of these dynamic bonds, poly(disulfide)s are theoretically interconvertible between their starting materials and their bulk plastics. In addition, disulfide monomers can be found naturally or produced through other environmentally-friendly techniques, improving the overall benefits of such plastics.

## Previous work:

Former group members have completed preliminary studies on this project. Synthetic conditions for modifying lipoic acid have been achieved. However, the resulting structure is a liquid that undergoes non-selective disulfide exchange while being stored (Figure 1). Ultimately, this limits the use of this material.



**Figure 1.** General depiction of the structural modification of lipoic acid followed by the product from uncontrolled polymerization.

## Our goal:

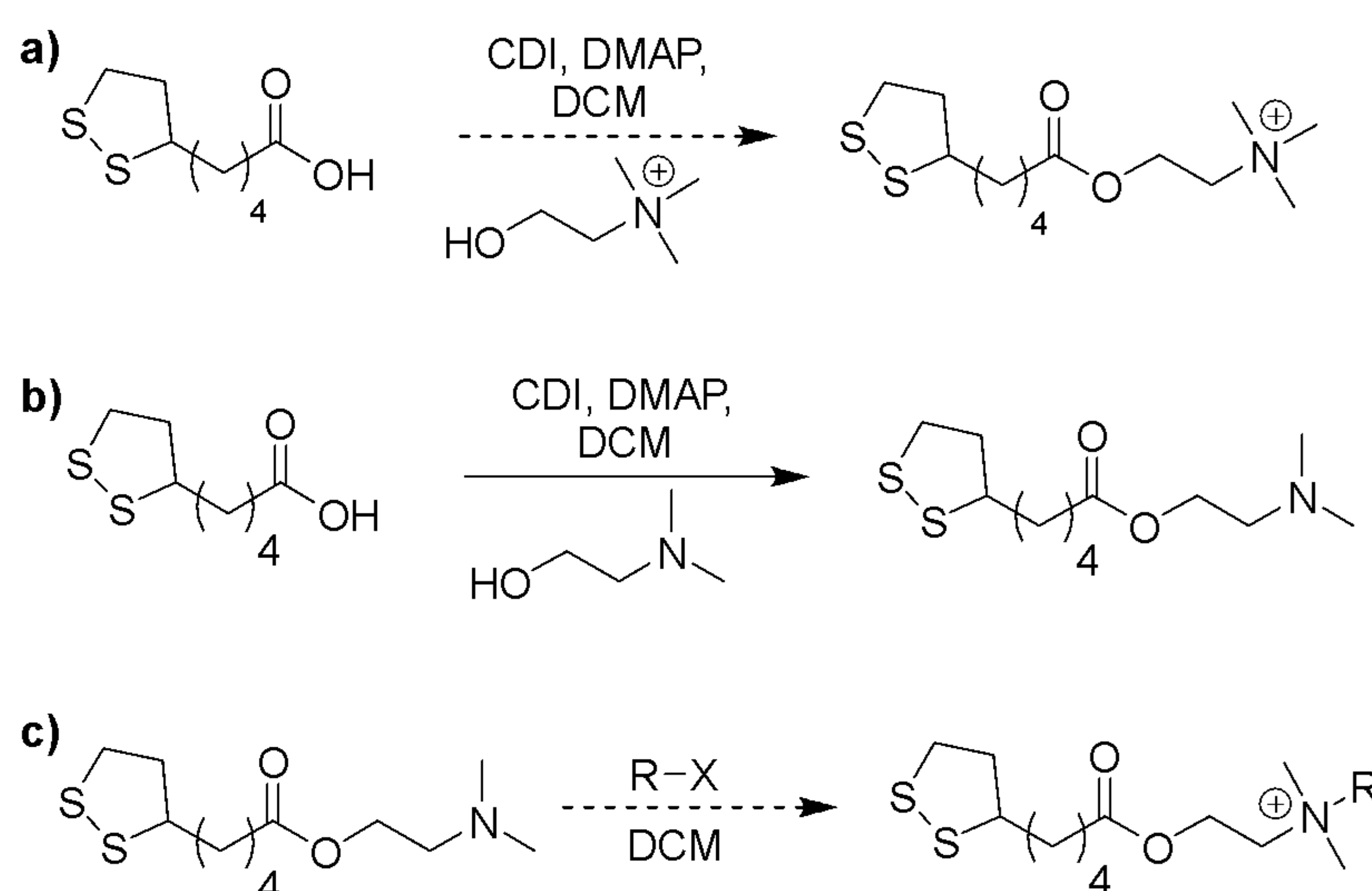
Our goal was to develop a method to synthesize a more stable disulfide monomer that could be stored for longer periods of time. This new feature will allow us to control the conditions for polymerization better and ideally provide additional control over the physical properties of the resulting material.

To accomplish this task our goal was to functionalize lipoic acid with a cationic amine. As a salt, the monomer is more likely to be a solid, preventing side reactions from occurring during storage.

## Experimental and Results:

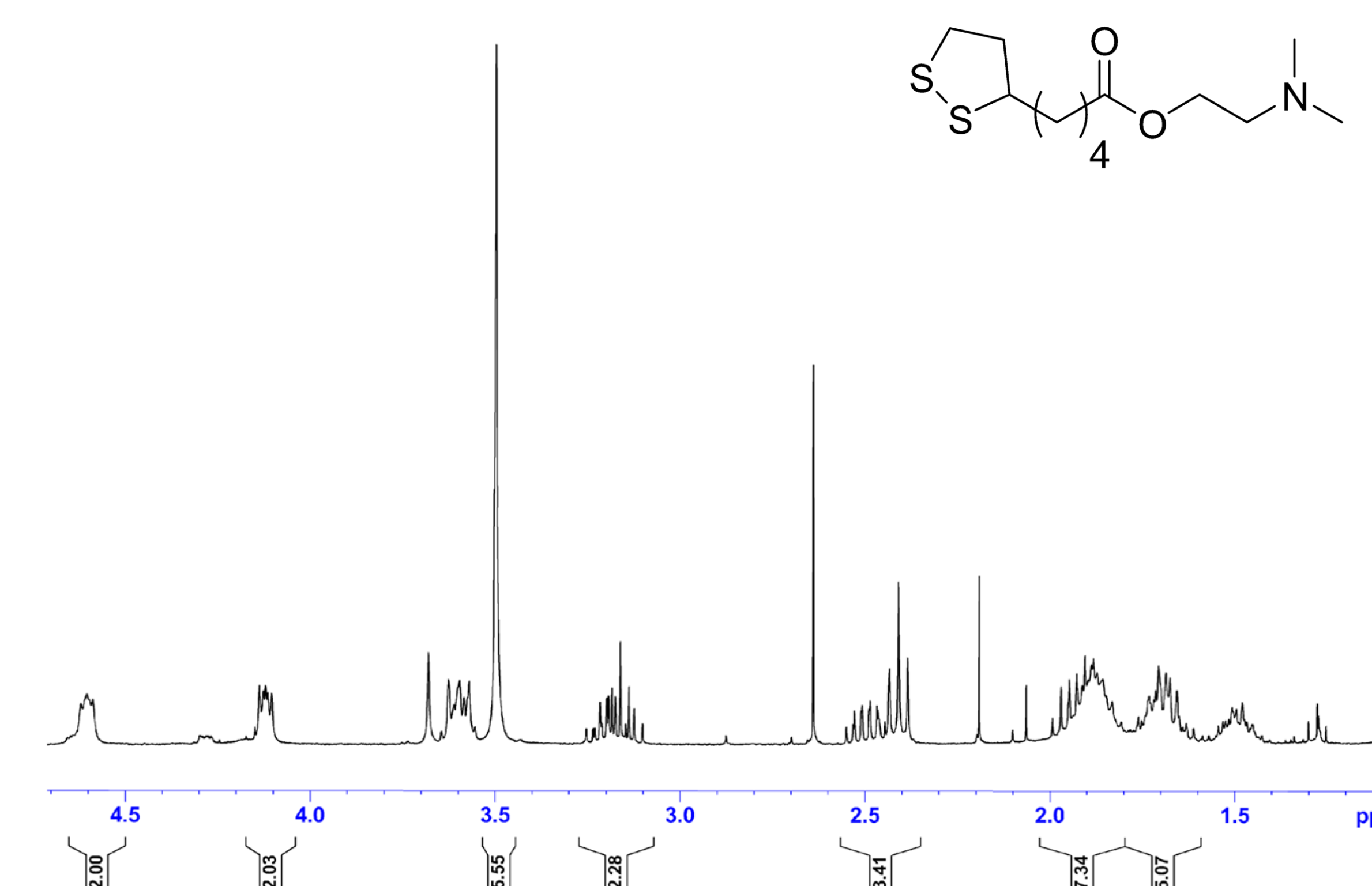
A variety of conditions were used in an effort to functionalize the carboxylic acid. Typically, we performed an esterification reaction using coupling conditions (Scheme 1a and b).

**Scheme 1.** Reaction conditions used to synthesize the desired cationic lipoic acid derivative. CDI = 1,1'-Carbonyldiimidazole, DMAP = 4-Dimethylaminopyridine, DCM = dichloromethane. In reaction sequence c), R is an alkyl chain of varying length, and X is iodine or bromine.



Initially, we attempted to use choline chloride as our alcohol for the esterification reaction (scheme 1a). However, the solubility of the choline chloride was poor, which hindered the success of the reaction. Despite trying a variety of solvents, we were not able to produce the desired product successfully through this route.

Subsequently, we attempted to form the ester bond before generating the cationic nitrogen. To accomplish this transformation, we used traditional coupling conditions with dimethylaminoethanol (Scheme 1b). This reaction proved to be successful, as identified by NMR analysis (Figure 2).



**Figure 2.** Proton NMR of the functionalized lipoic acid derivative

With a successful route to the desired intermediate, we turned our attention to forming the cationic nitrogen via an S<sub>N</sub>2 alkylation. Initially, we used methyl iodide as our electrophile. This reaction was unsuccessful; we believe the iodide generated *in situ* reacted with the disulfide to produce undesired products. As a result, we attempted the same reaction using 1-bromopropane instead and are currently analyzing the outcomes of that reaction.

## Conclusion:

While our initial attempt at forming the desired charged structure was unsuccessful, we have identified a synthetic route that shows promise. We were able to successfully produce the precursor to the desired product. We plan on continuing our substitution reactions in an effort to produce the final product.

## References:

- 1) Meneses, R. A. M. *Heliyon*, **2022**, *8*, e09028.
- 2) Chen, G.-Q. *Chem. Rev.*, **2011**, *112*, 2081-2099.
- 3) Pal, S.; et. al. *Science*, **2024**, *385*, 877-883.