



CARTHAGE
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Synthesis of Amino Acid Surfactants to Examine Antimicrobial Properties

Iman Deanparvar, Frannie Drake, Dr. David Brownholland

Department of Chemistry, Carthage College



Abstract

Bacteria are rapidly evolving towards antibiotic resistance, necessitating the need for alternative antimicrobial agents. Amino-acid surfactants have generated interest as potential agents due to their biodegradability and effectiveness against bacteria. An ester-linked leucine-based surfactant was previously synthesized and found to exhibit antimicrobial properties. The synthetic procedure for this molecule is being optimized to improve purity and yield. However, the ester linkage is susceptible to hydrolysis. To address this limitation, the surfactant was redesigned with a more stable amide linkage. The synthesis of this amide-linked surfactant is being optimized to improve percent yield. In conjunction with the biology department, the amide-linked surfactant is being analyzed for its antimicrobial properties, and the results will be used to help design new generations of antimicrobial surfactants.

Introduction

- Surfactants are effective antimicrobial agents that target and kill bacteria nonspecifically

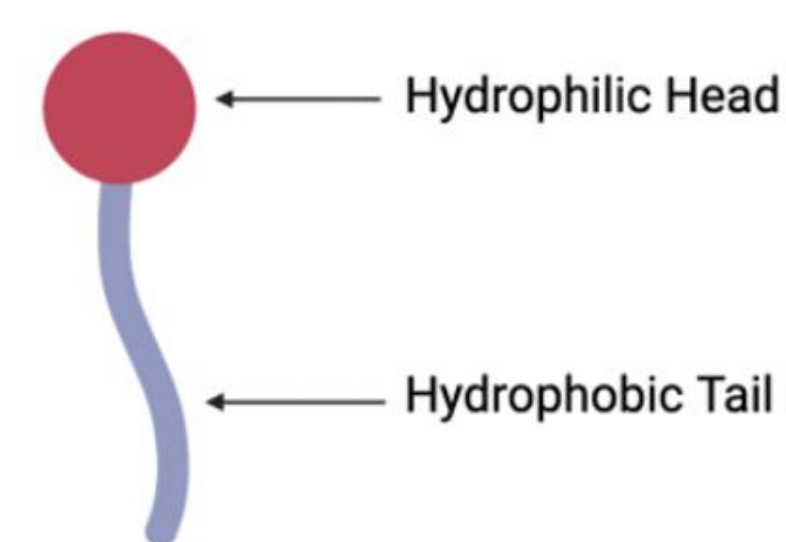


Figure 1. Simplified surfactant molecule with labelled head and tail groups.

- Amino-acid derived surfactants are more environmentally sustainable than their petroleum-based counterparts
- Amino acid L-leucine can be used to form the polar headgroup of the surfactant when linked to a long nonpolar carbon chain
- The first linkage method we attempted was an ester-linkage

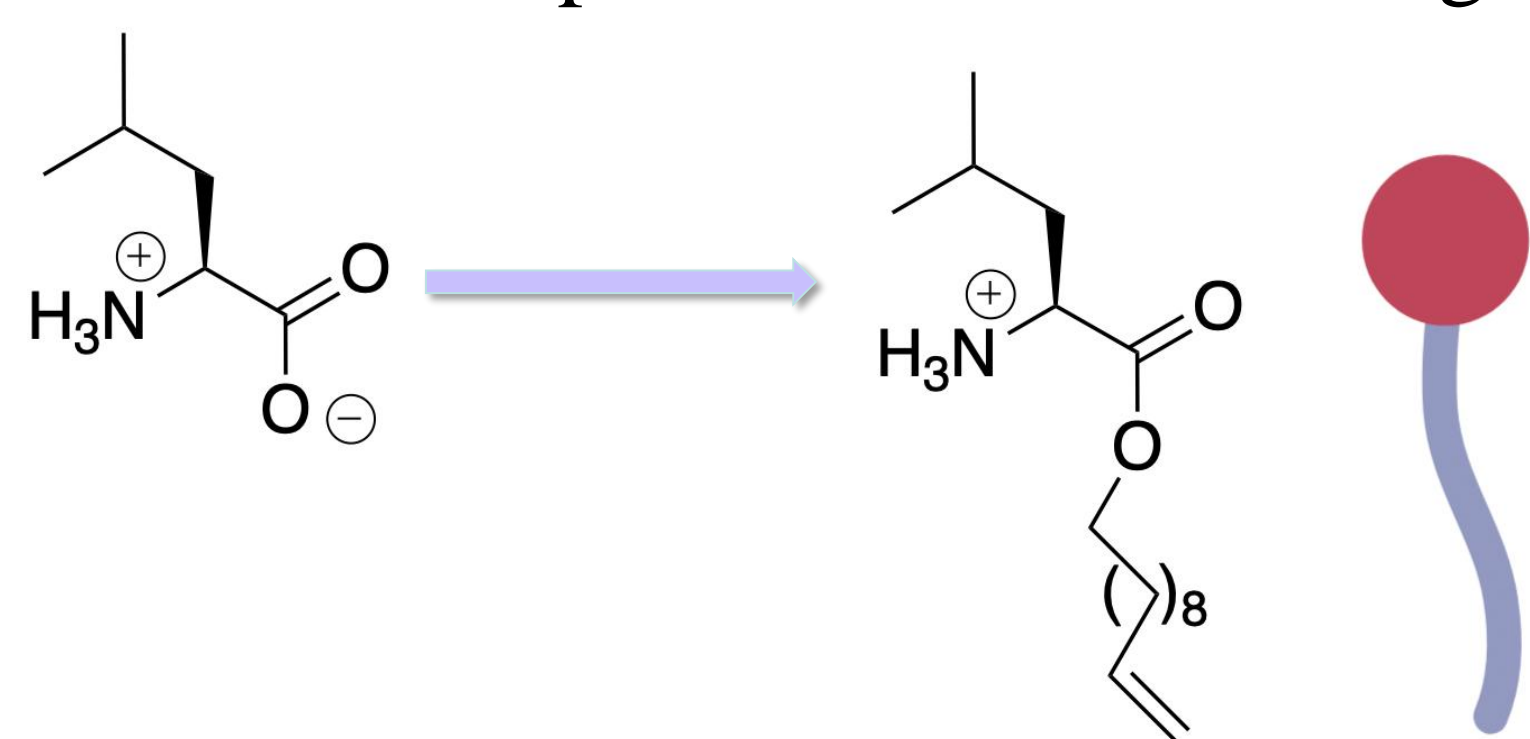


Figure 2. Left: structure of leucine. Right: Ester-linked surfactant with leucine as the polar headgroup.

Synthesis of Ester-Linked Surfactant

- The ester-linked surfactant was synthesized by coupling 10-undecenol with L-leucine using an acid catalyst

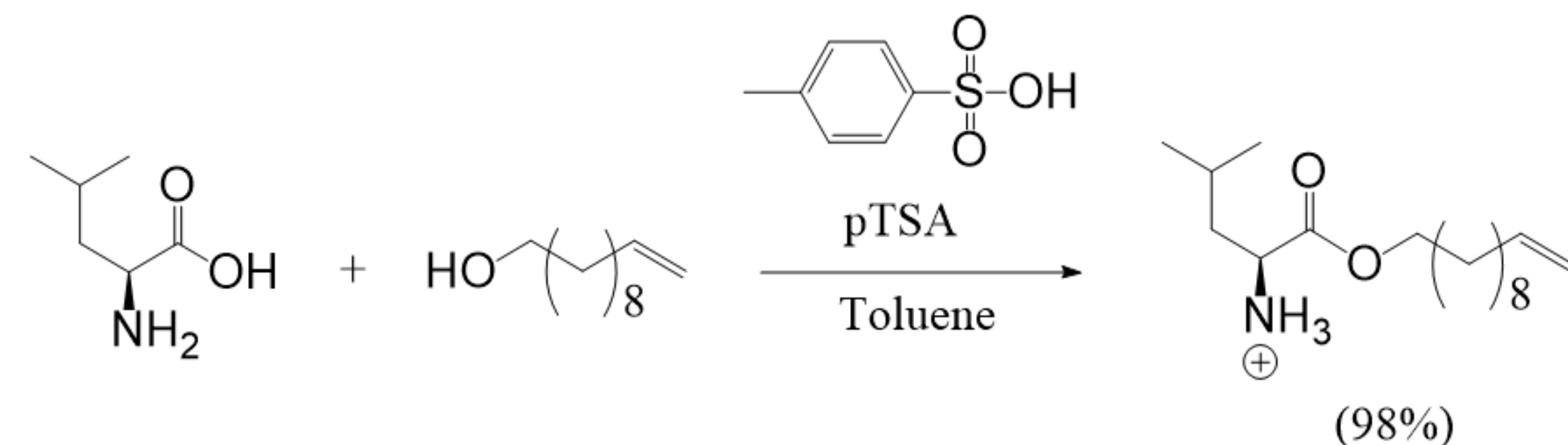


Figure 3. Reaction scheme for the ester-linked surfactant.

¹H NMR Spectrum of Ester-Linked Surfactant

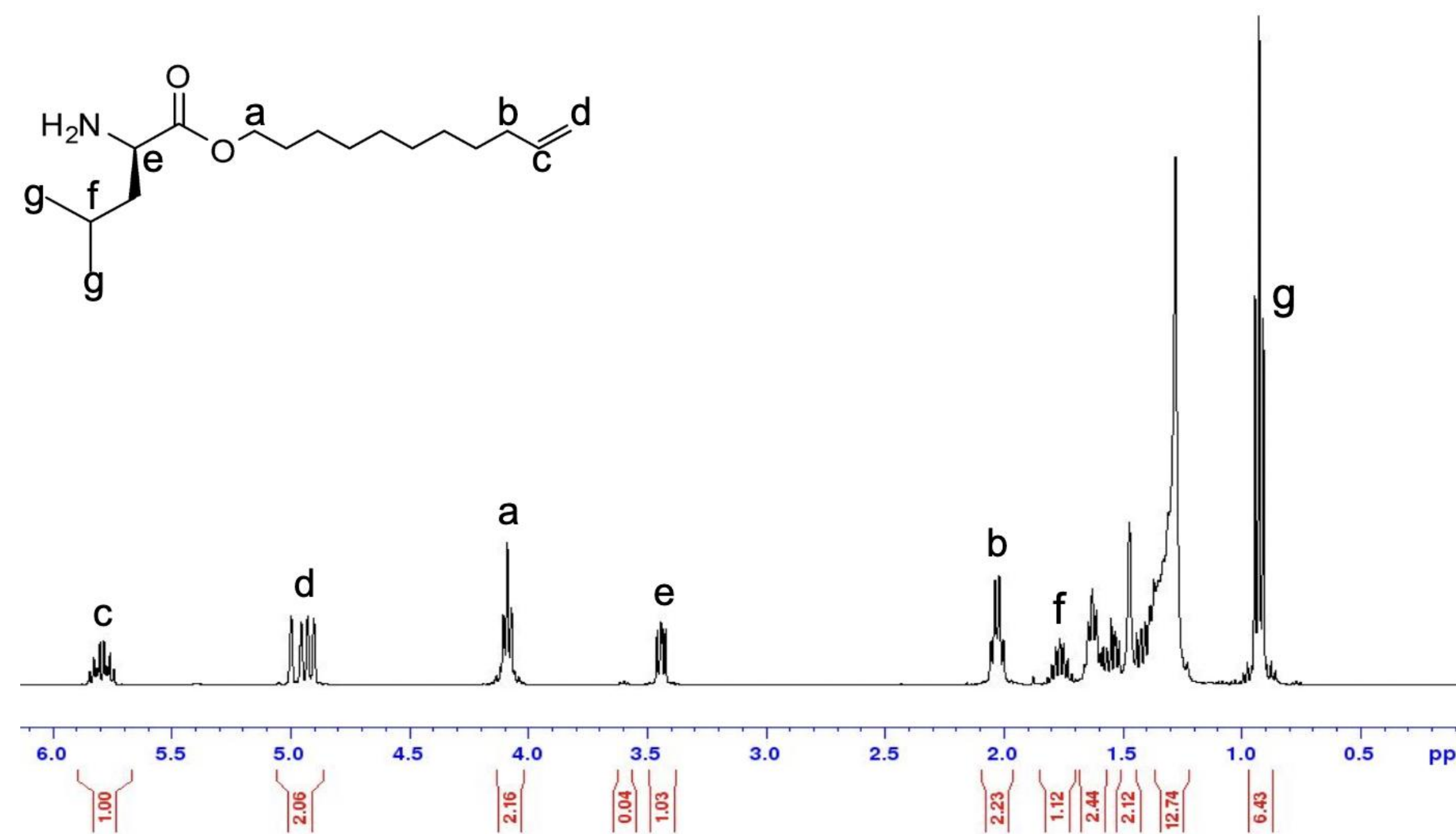


Figure 4. ¹H NMR spectrum (400MHz, CDCl₃) of the ester-linked surfactant product.

Ester vs Amide-Linkage

- To reduce the surfactant's susceptibility to hydrolysis, an amide linkage was designed



Figure 5. Left: ester-linked surfactant with leucine headgroup. Right: amide-linked surfactant with leucine headgroup.

Synthesis of Amide-Linked Surfactant

- To create the amide-linked surfactant, first the carbon chain with a terminal amine needed to be synthesized
- The amine was attached to the L-leucine headgroup

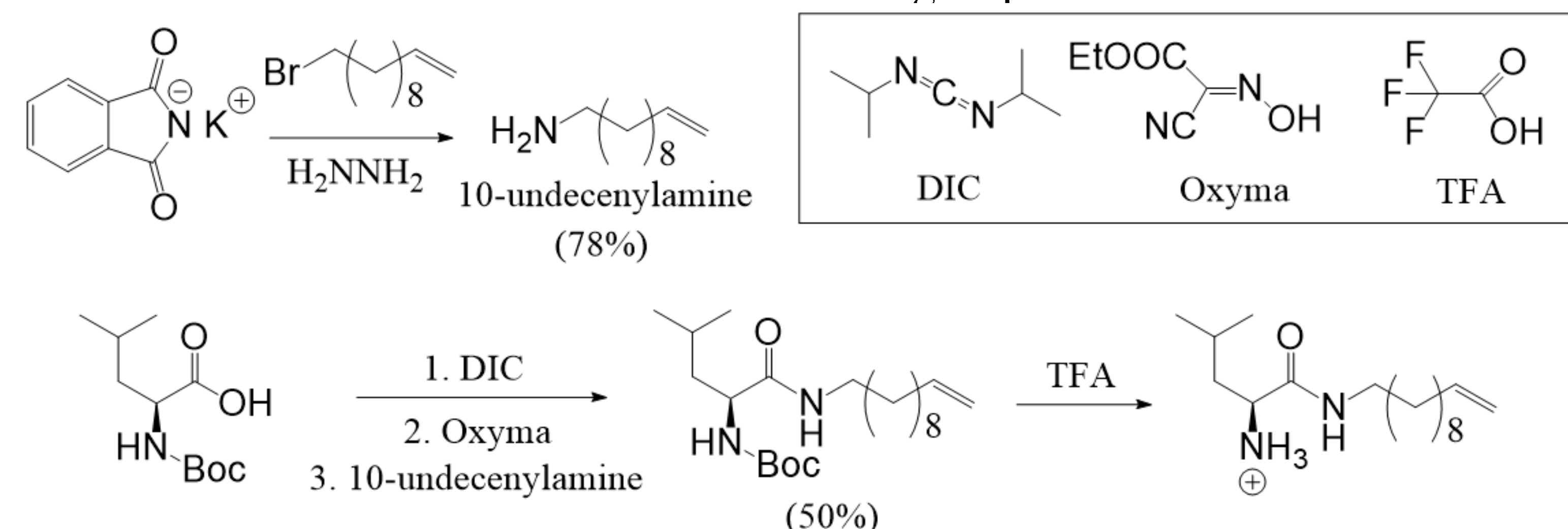


Figure 6. Reaction scheme for the amide-linked surfactant.

¹H NMR Spectra for Amide-Linked Surfactant

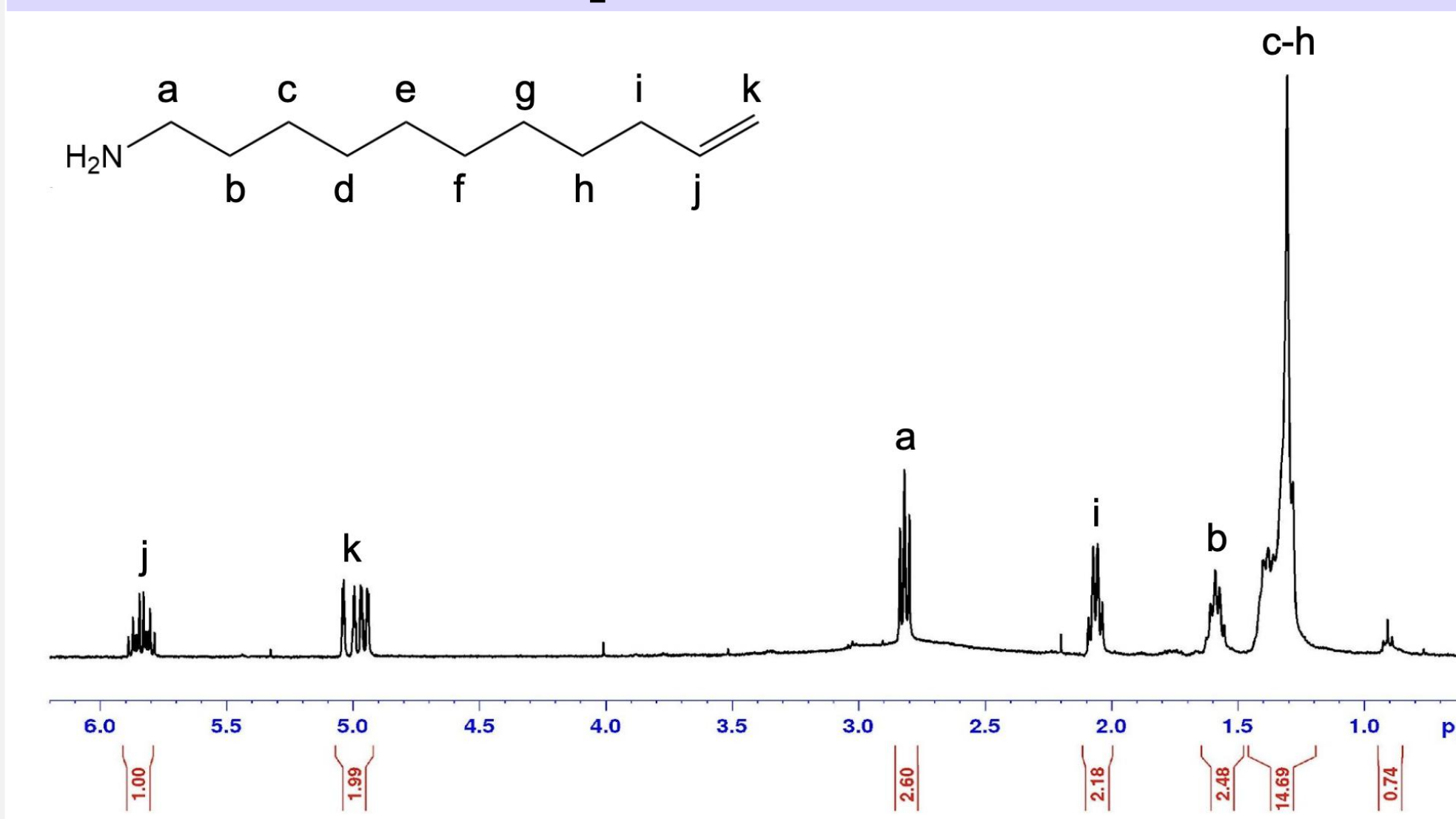
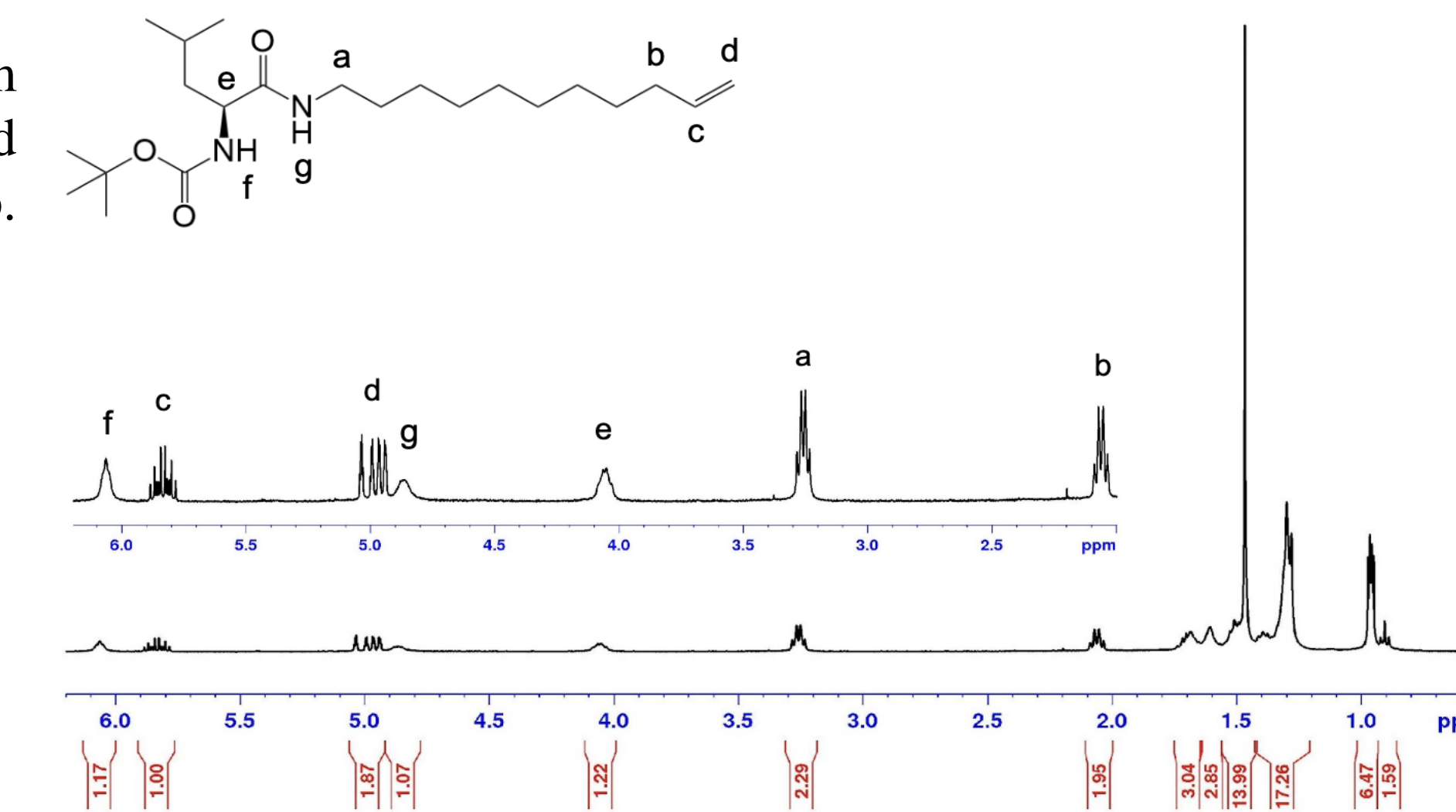


Figure 7. ¹H NMR spectrum (400MHz, CDCl₃) of 10-undecenylamine.

Figure 8. ¹H NMR spectrum (400MHz, CDCl₃) of amide-linked surfactant with protecting group.



Conclusions & Next Steps

- Ester-linked surfactant synthesized with 98% yield, but purification is tedious, and product degrades over time
- Protected amide product successfully coupled, though purification left only 50% yield
- Amide-linked surfactant will be deprotected and screened for antimicrobial properties
- Modifications to amino-acid headgroup: histidine

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