Synthesis and Characterization of a Dendrimer to Promote the Formation of Micelles

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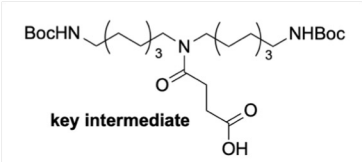
Introduction:

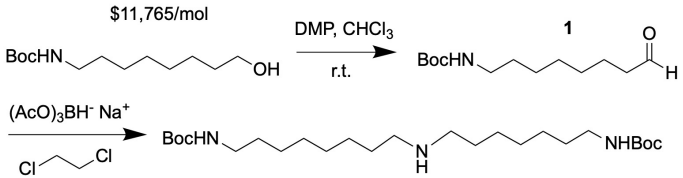
This project aims to synthesize and characterize alkyl phosphate surfactants for the development of a novel drug-delivery nanoparticle. The system consists of surfactants templated around a single 1,5-diaminonapthlane dendrimer core, collectively referred to as a *dendricore micelle*. Conventional surfactant micelles often dissociate under physiological conditions due to their high critical micelle concentrations, limiting their utility [CMC=0.14M in water][1] If successful, this approach could help obtain a stable micelle capable of serving as a potential dual-drug delivery platform, improving therapeutic efficacy and targeting.

Compound **1** was synthesized; however, optimization to its synthesis must be made, as it serves as an important precursor for subsequent dendrimer generations.

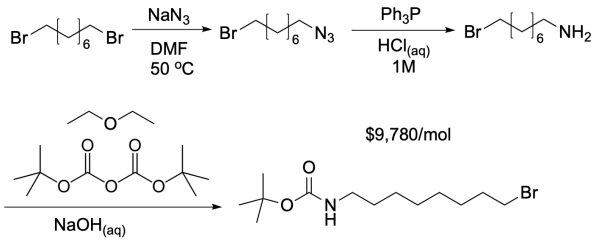
The **key intermediate** shown below is particularly significant because it integrates multiple reactive and protective functionalities, making it a versatile platform for downstream modifications. As such, it is the current focal point of our research as we advance toward nanoparticle assembly.



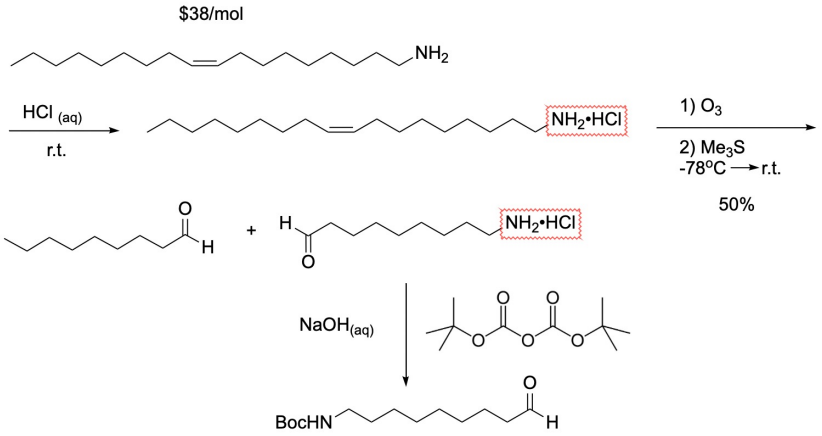
Synthesis of Compound 1 and Subsequent Reaction:

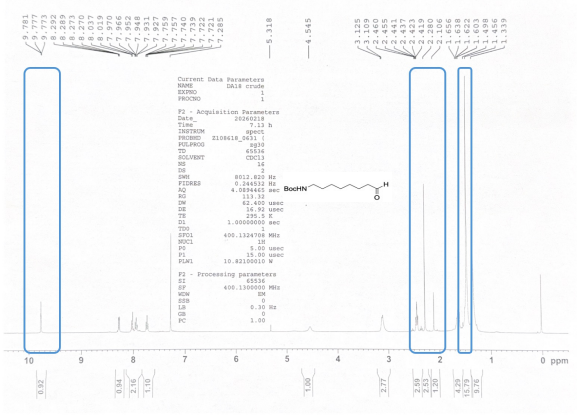


Synthesis of tert-Butyl (8-bromooctyl)carbamate[2]:



Alternate approach to inexpensive reagent:





Future Work:

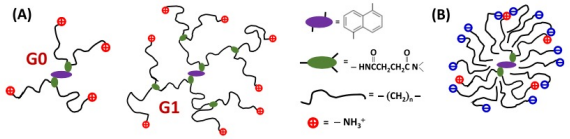


Figure 1: (A) Succinimide dendrimer (SD) of generation 0 (G0) and one (G1) with a naphthalene core, with succinimide branching units, alkyl-chain extensions and amino terminals. **(B)** Proposed self-assembly of MAPs with G0 SD, leading to the formation of a dendricore micelle.

Conclusion:

The NMR spectrum of compound **1** following the DMP oxidation confirmed successful formation of the desired product **1**, although minor impurities remain. Future efforts will focus on improving product purity and incorporating the surfactant into higher dendrimer generations to promote micelle formation.

Acknowledgements:

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References:

1. Arakawa, J.; Pethica, B. Micellization in aqueous-solutions of mono-alkyl phosphate salts. *Journal of Colloid and Interface Science* **1980,** *75,* 441-450.

2. Egbertson, M.; Chang, C.; Duggan, M.; Gould, R.; et al. Nonpeptide fibrinogen receptor antagonists .2. Optimization of a tyrosine template as a mimic for ARG-GLY-ASP. *Journal of Medicinal Chemistry* **1994,** *37* (16), 2537-2551. DOI: 10.1021/jm00042a007