Synthesis of an Amphiphilic C_{70} Fullerene Derivative for Biomedical Applications

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Abstract

Hydrophobic drug delivery platforms have been an extensive area of study in previous years due to the emergence of new hydrophobic drugs including the widely used chemotherapy medication Paclitaxel. Such targeted delivery is difficult due to the aqueous environment of the human body, and the hydrophobic nature of the drug. In this work, progress towards a novel hydrophobic drug delivery platform is designed and discussed. The drug delivery platform includes selectively adding anilines that contains an alkyne to the top of a C_{70} cage. The alkyne would undergo a Copper Catalyzed Click Reaction with an azide to attach a water-soluble group. The C_{70} is then predicted to exhibit amphiphilic behavior by clumping together to create a hydrophobic pocket and a hydrophilic surface. The hydrophobic pocket can store and deliver drugs while the hydrophilic surface can interact with the aqueous environment of the human body, as well as interact with the targeted drug delivery site. This work has many applications towards new methods of developing hydrophobic drug delivery properties that can store and deliver hydrophobic drugs.

Background

- Fullerenes are hollow carbon molecules.
- The C_{60} molecules can undergo a wide range of novel chemical reactions by behaving as an electron acceptor.
- Another Fullerene, C_{70}, has a belt region with spherical end
- Because of this geometry, C_{70} has unique reactivity

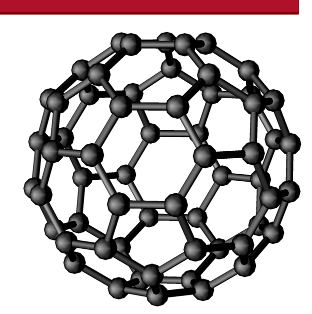


Figure 1. Structure of C_{60} fullerene.

- The curvature in the C_{70} fullerene puts strain on specific carbons on the end caps.
- This strain causes the carbon from rehybridizing upon reaction from sp^2 to sp^3
- This is a driving force for reactivity and specificity of addition reactions

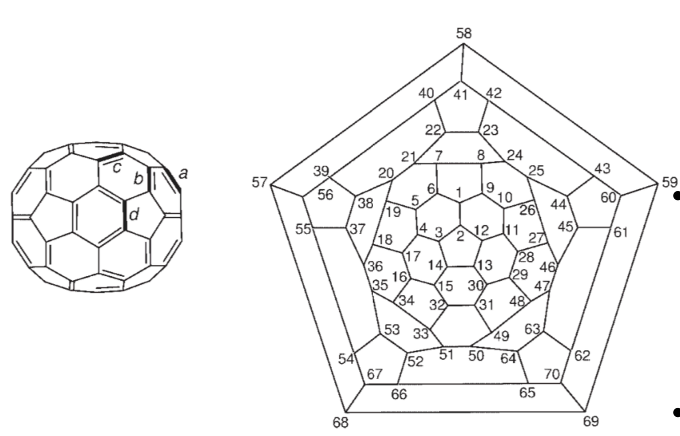


Figure 13.2 The most reactive bonds of C_{70} (left) and numbering scheme of C_{70} (right). (a) C(1)–C(2) (type α), (b) C(5)–C(6) (type β), (c) C(7)–C(21) and (d) C(7)–C(8) bond. Reactivity decreases in the order a > b > c > d.

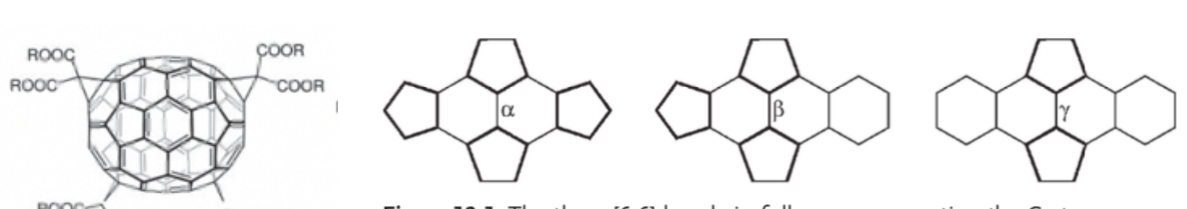


Figure 13.1 The three [6,6]-bonds in fullerenes connecting the C atoms with the highest degree of pyramidalization.

- Due to the unique reactivity, novel synthetic reactions can be applied to C_{70} to form biomedical systems with far ranging applications

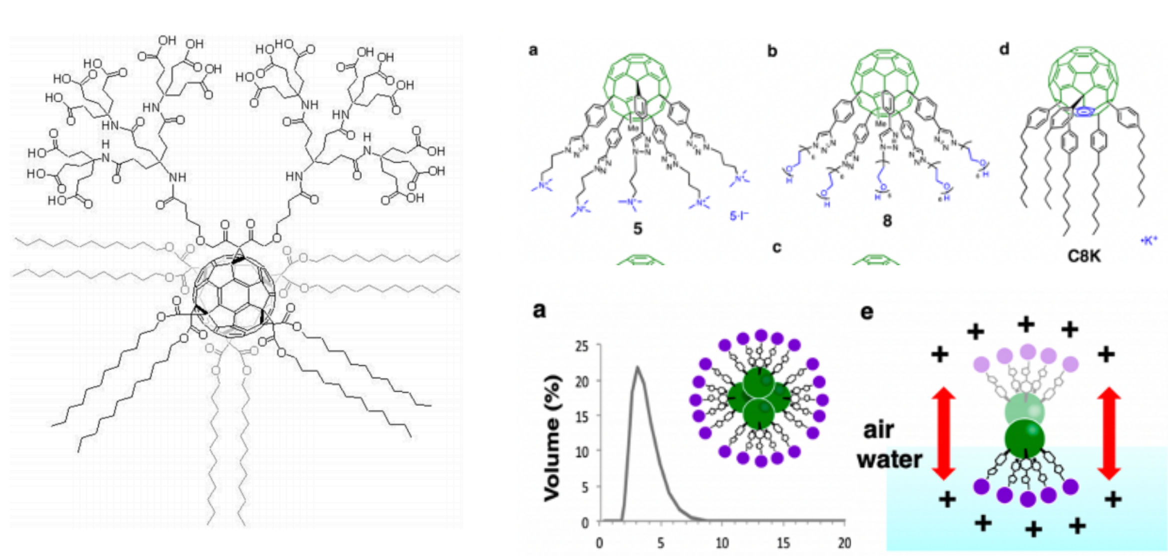
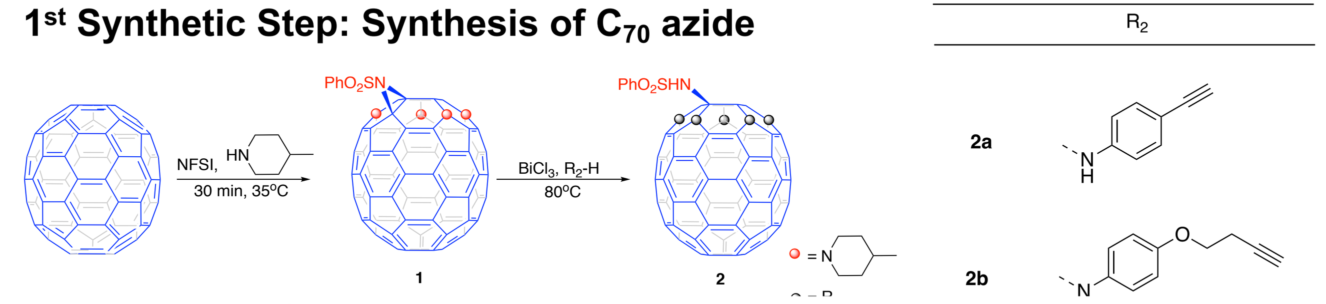
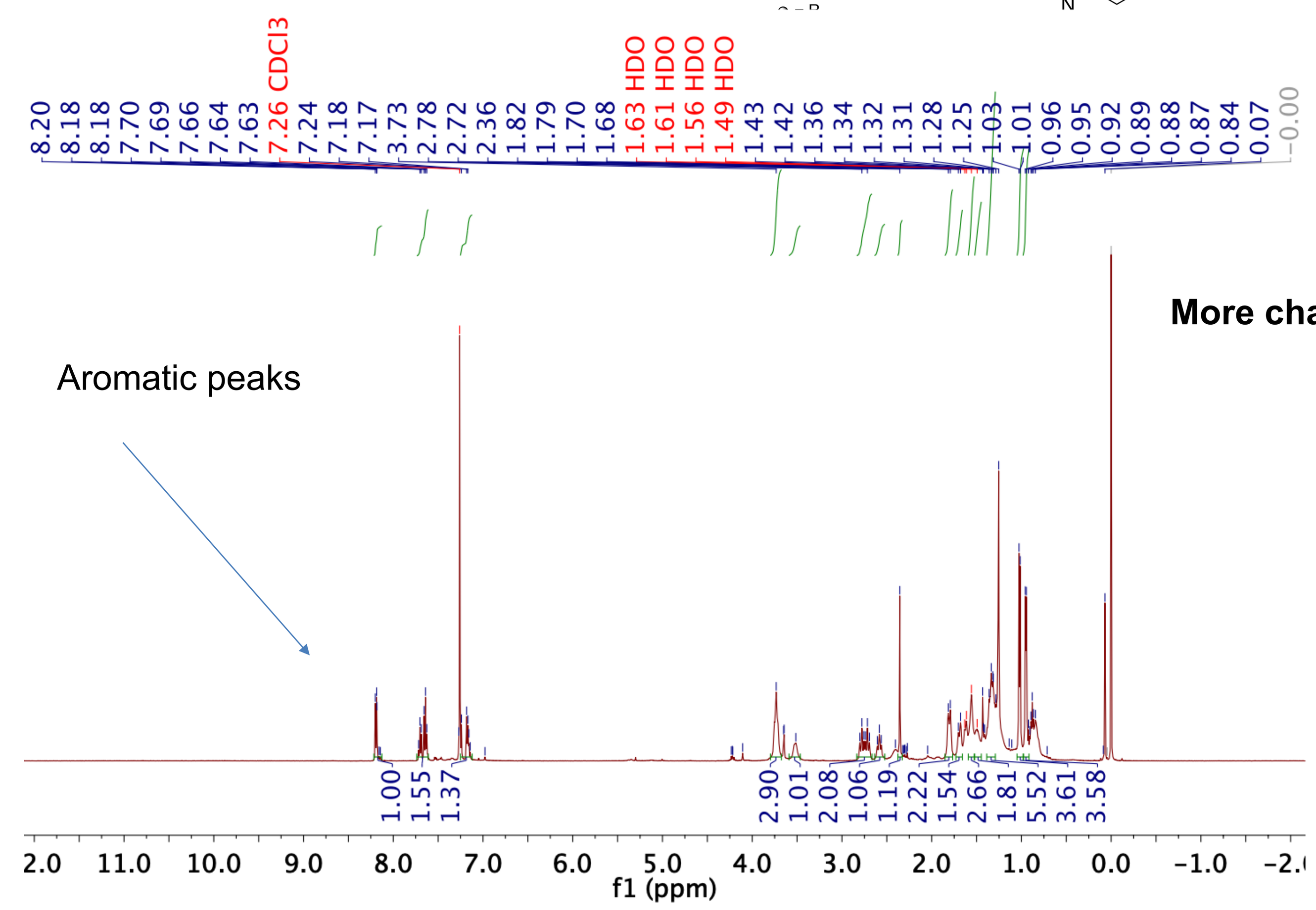


Figure I Chemical structure of the amphiphilic fullerene(AF-I) monomer. AF-I readily self assembles into buckysomes.

Results

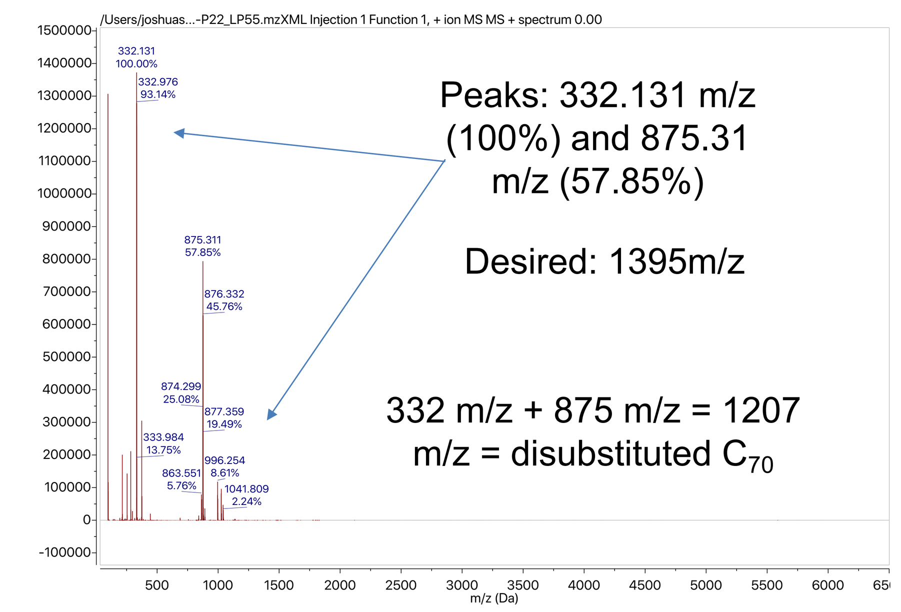
1st Synthetic Step: Synthesis of C_{70} azide



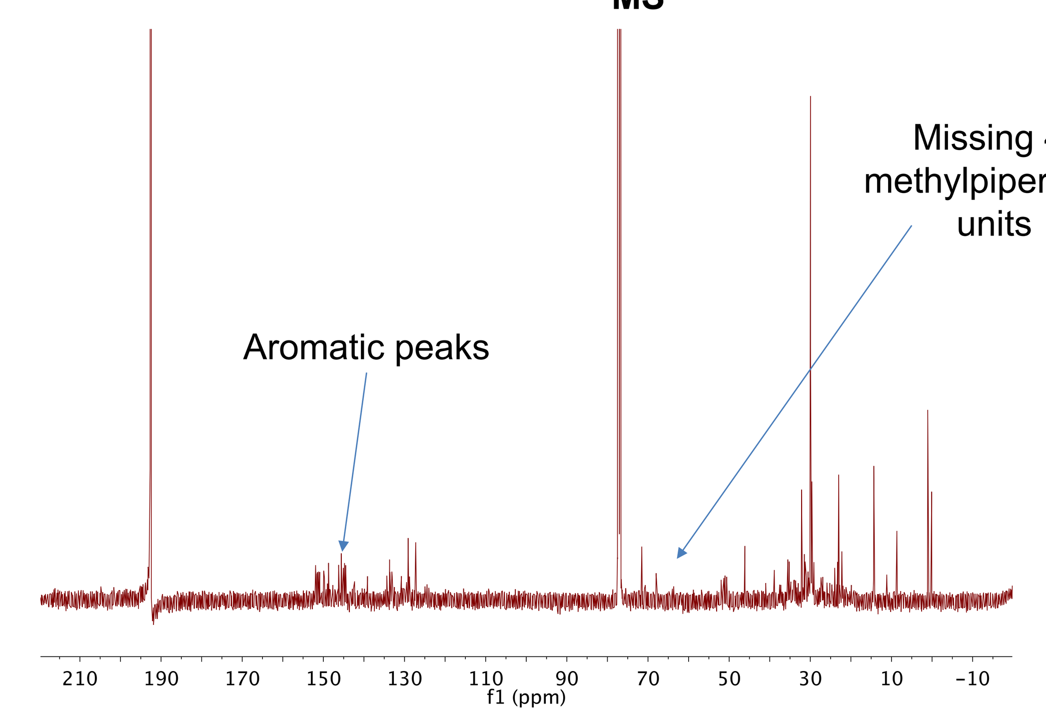


HNMR

More characterization needed!

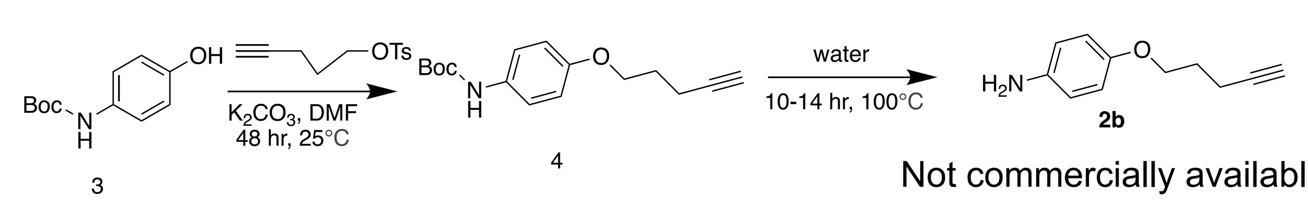


MS



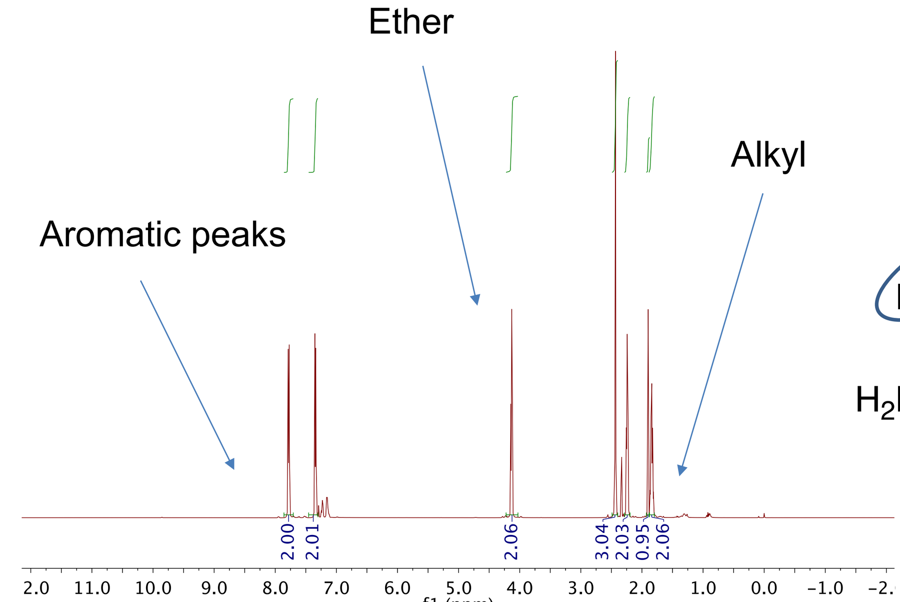
CNMR

Small Molecule Synthesis: 2b



Not commercially available

CNMR: No Ester peak around 170: no Boc deprotected required



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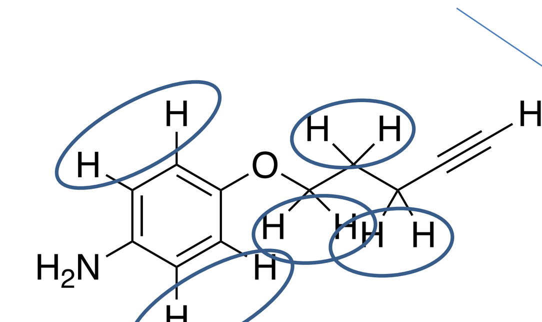

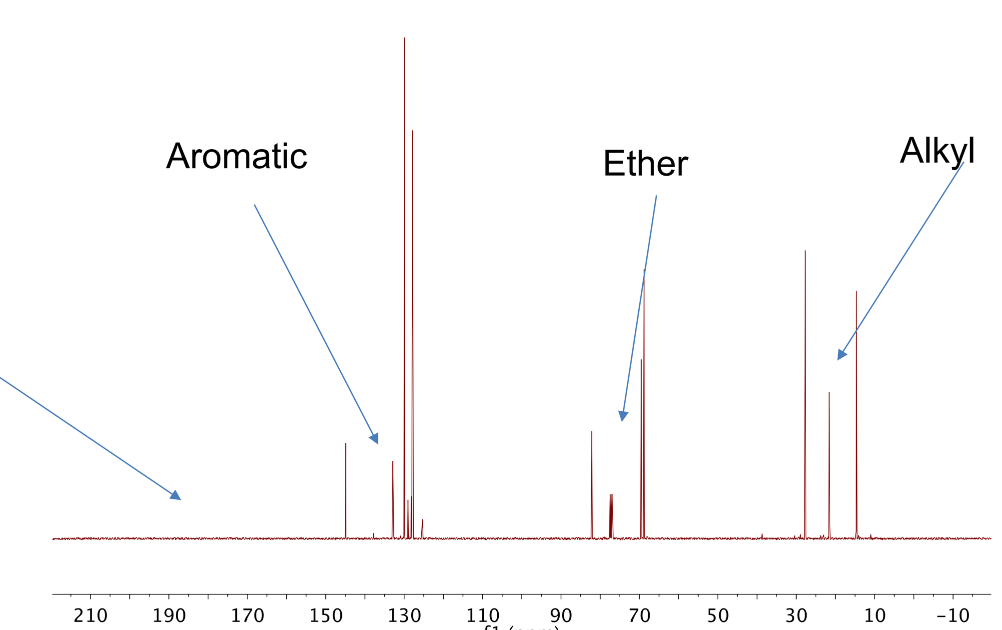

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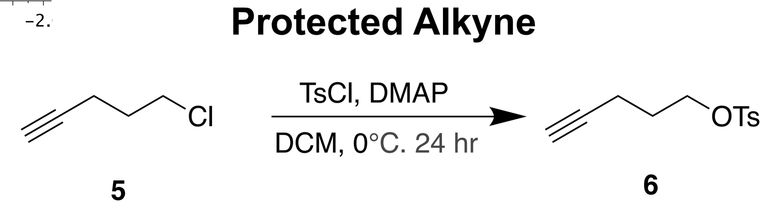
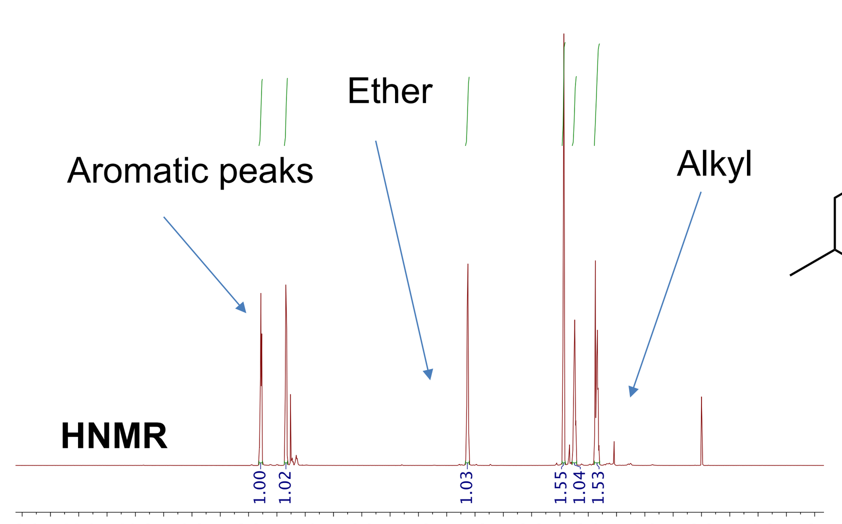
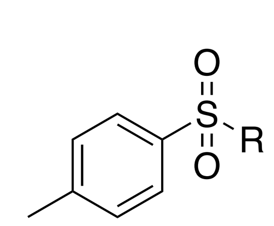
Small Molecule Synthesis: Protected Alkyne

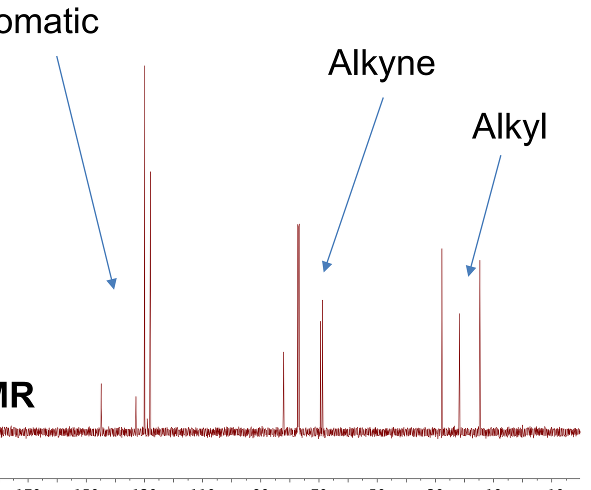




HNMR



Tosyl



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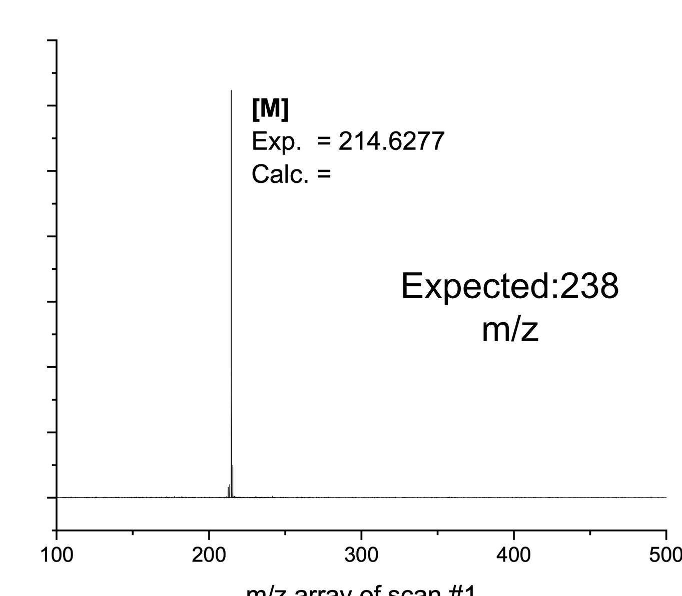
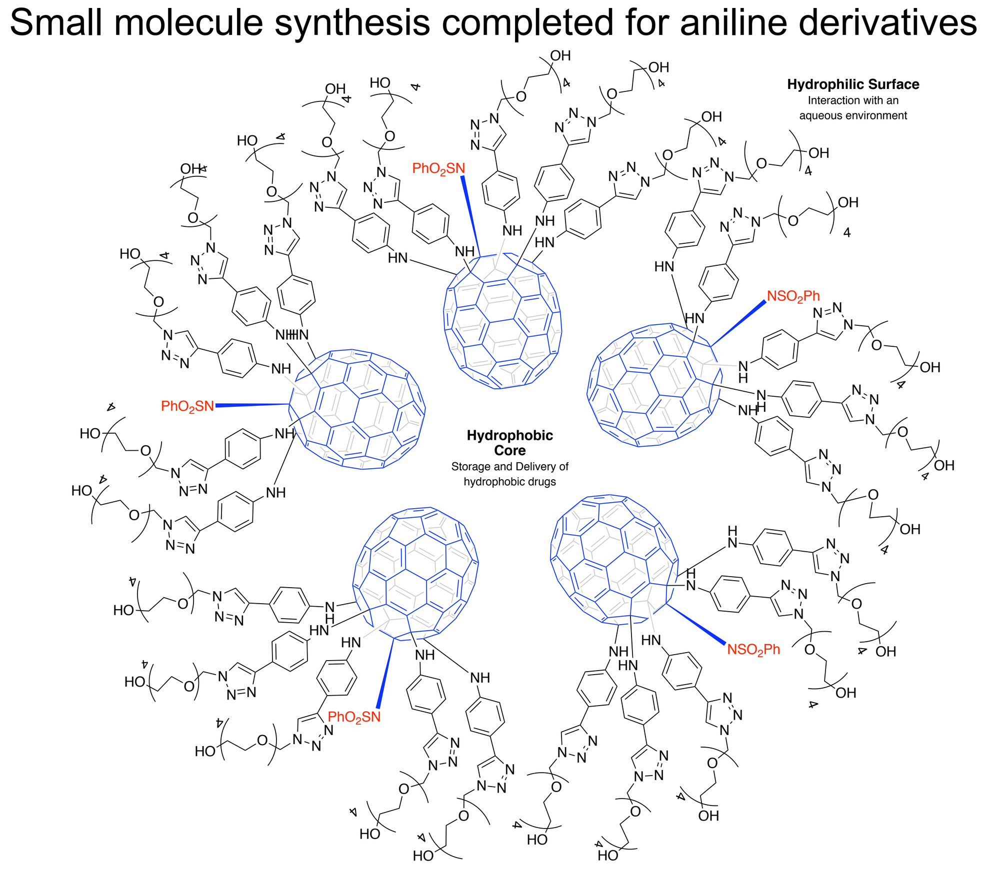


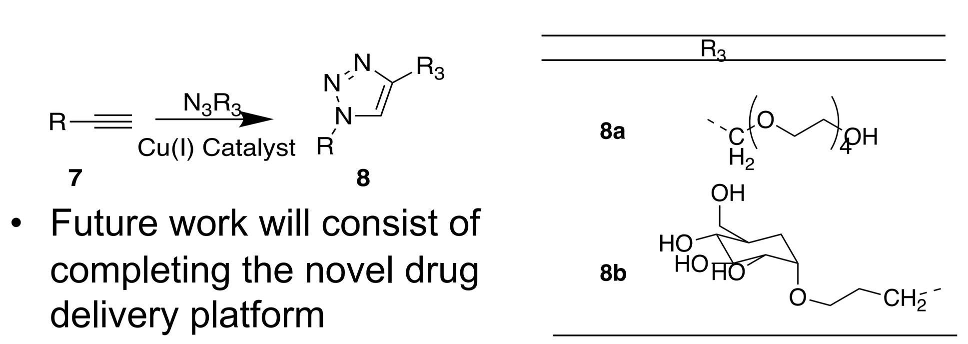
MS

Summary

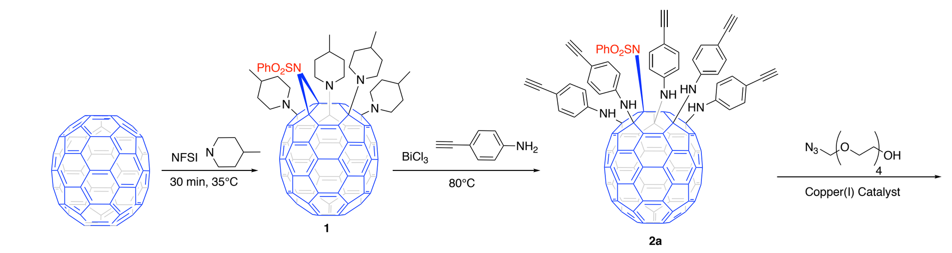
- Extended C_{70} reaction conditions to form a novel drug delivery platform
- More Characterization is needed on the C70 reaction
- Small molecule synthesis completed for aniline derivatives

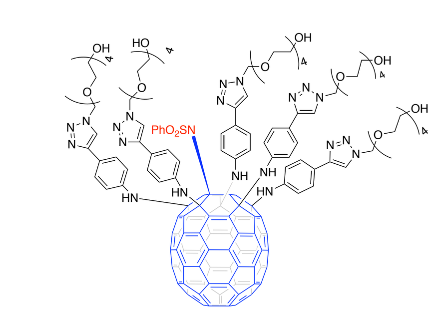


Future Direction



- Future work will consist of completing the novel drug delivery platform





- Future studies will include testing capabilities of drug delivery system such as payload capacity, target delivery.

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