Novel Aromatic Bridging Ligands as Nanoparticle Colloid Stabilizing Agents

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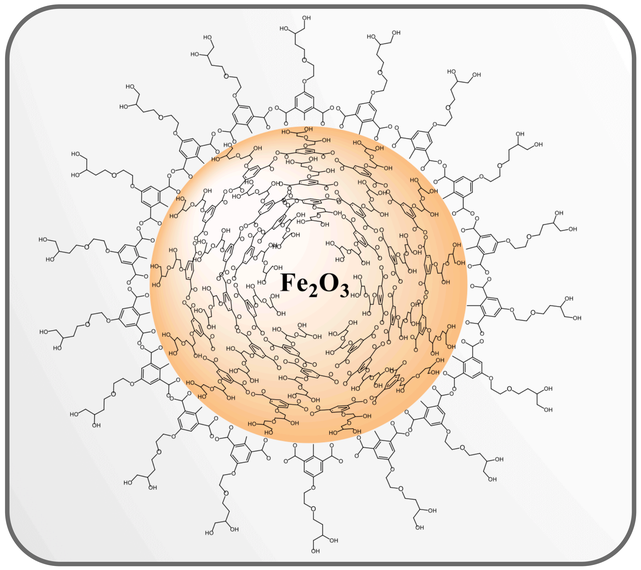
Abstract

Iron oxide nanoparticles are being studied for a variety of biomedical applications such as possible carriers for targeted drug delivery and as a contrasting agent for MRI imaging. The use of iron oxide nanoparticles will require several components to ensure effectiveness in the body. One component required is the binding of the iron oxide nanoparticles to a biological molecule by a linker ligand to improve interaction with the biological makeup. 2,5-dihydroxyisophthalic acid was chosen to be synthesized as a possible linker ligand because it possesses multiple coordination sites for the nanoparticles. 2,5-Dihydroxybenzoic acid was coupled with allyl bromide to produce 5-allyloxy salicylic acid with an average percent yield of 66.5%. This product was then formylated with hexamethylenetetramine to produce 3-formyl-5-prop-2-enoxysalicylic acid with an average percent yield of 62.3%. Oxidation of the product produced 5-alkoxy-2-hydroxyisophthalic acid with a percent yield of 68.7%. The alkoxy tail was then cleaved to produce 2,5-hydroxyisophthalic acid. The acid was then recrystalized from water to improve purity. The structures of the products were confirmed by H' NMR. Moving forward, the addition of various substituents at the 5-hydroxy position on the acid is being optimized for bioconjugation. The pka values of 2,5-hydroxyisophthalic acid will be determined as they are not currently reported.

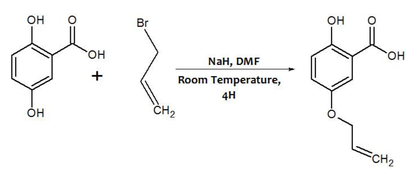
Introduction

Iron oxide nanoparticles are promising agents for novel biomedical applications. In order for these nanoparticles to be compatible in the body, an organic shell is required to provide protection of the agent while optimizing aqueous interaction, biocompatibility, and target specification. Polymers are currently being utilized as organic protecting agents, however, this method leads to an undesired increase in the overall diameter of the complex. Instead, to preserve minimal complex diameter and to secure good mobility and penetrating properties in blood vessels, small capping ligands are being synthesized. These capping ligands are expected to be able to bind strongly to the surface of the nanoparticles while still providing stability. Salicylic acid has already been established as a versatile agent for biomedical applications. It already has biocompatibility while its beta-hydroxycarboxylic acid structure allows for it to be used as a strong ligand for attachment to a nanoparticle. It is hypothesized that using salicylic acid derivatives that have an additional carboxyl group, such as 3-carboxysalicylic acid, will allow the ligand to bind more effectively to the nanoparticles. The proposed 2,5-hydroxyisopthalic would not only have a bridging ligand head group for particle attachment, but also a 5-position site for the desired functionalization and further attachment of a biomolecule.

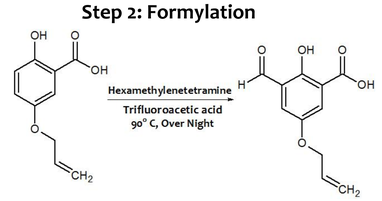


Synthesis

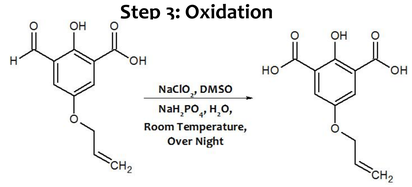
Step 1: Coupling



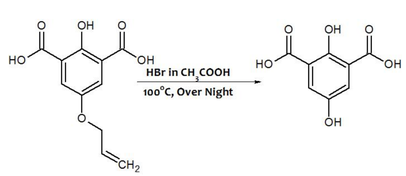
Step 2: Formylation



Step 3: Oxidation



Step 4: Tail Cleavage



Characterization

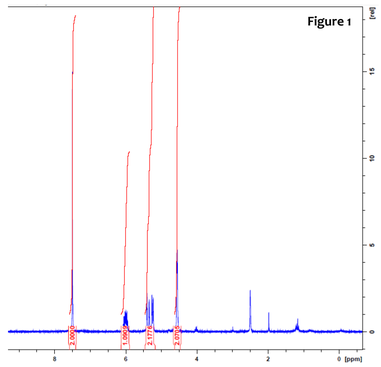


Figure 1 shows the H' NMR confirmation of the production of 5-alkoxy-2-hydroxyisophthalic acid. DMSO was used as the solvent contributing to the 2.5ppm peak.

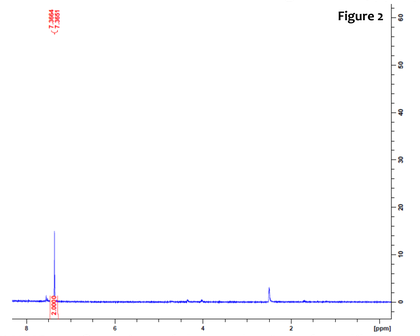


Figure 2 shows the H' NMR confirmation of the production of 2,5-dihydroxyisophthalic acid. DMSO was used as the solvent contributing to the 2.5ppm peak.

Conclusion and Future Goals

- 2,5-hydroxyisophthalic acid was synthesized and characterized by H'NMR
- Optimize the addition of various substituents at the 5-hydroxy position on the acid for biomolecule attachment.
- Characterize isophthalic acid derivatives using UV-Vis spectrophotometry and titration methods.
- React obtained ligands with iron oxide nanoparticles of different sizes, isolate and characterize the adducts, and study their aqueous colloids with Dynamic Light Scattering techniques

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