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Louisiana Alliance for Simulation-Guided Materials Applications

# Novel bridging ligands based on sugar acids for stabilizing inorganic nanoparticles

Linden Allison[2], Galina Goloverda[1], Vladimir Kolesnichenko[1],
[1]Department of Chemistry, Xavier University, New Orleans, LA 70125
[2]Department of Chemistry, Juniata College, Huntingdon, PA 16652.

## Abstract

Superparamagnetic iron oxide nanoparticles have been utilized in the biomedical field as contrasting agents for MRI. Presently, most contrasting agents are Gadolinium based, which are expensive and have been proven to cause toxic side effects. Utilizing iron oxide nanoparticles can present a less toxic alternative that is just as effective. However, these nanoparticles first need to be encased in an organic coating for biocompatibility. A bridging ligand is required for the nanoparticle to be bound to biomolecules. The bridging ligand explored in this research was based on a class of compounds known as sugar acids, in particular mucic acid. The alpha hydroxyl groups can be protected by binding mucic acid with either nickel or an iron oxide nanoparticle, leaving the beta hydroxyl groups exposed. These exposed hydroxyl groups can then be bound to linkers allowing biomolecules to be attached. Three compounds were synthesized including: nickel phenantrolino mucicate, nickel mucicate, and colloidal iron oxide mucicate. The products were characterized using TGA and ESI-MS.

## Introduction

MRI Contrasting agents work by interacting with water molecules in the body. When a magnetic force and a radiofrequency are applied during an MRI scan, the water molecules are forced into an excited energy state. When a contrast agent is introduced the $T_1$ or $T_2$ relaxation state is shortened allowing the molecules to emit higher energies, producing a sharper image. There are two types of contrasting agents: $T_1$ and $T_2$. Contrasting agents that shorten the $T_1$ relaxation state, or the longitudinal relaxation, create a positive contrast. An example of this is gadolinium based agents, which are the most commonly used today. The other type shortens the $T_2$ relaxation state, or transverse relaxation. These show negative contrast in images. Usually these agents are composed of superparamagnetic nanoparticles. Gadolinium contrasting agents have been found to cause kidney disease and have a short presence in the vascular system, meaning they diffuse very quickly.[1,2] Because of these problems superparamagnetic iron oxide nanoparticles are being explored as alternative agents. By surrounding the iron oxide nanoparticle with certain biomolecules, of variable size, the nanoparticles' function can be tailored for use as both positive and negative contrasting agents.[3] The attached biomolecules would allow for optimal biocompatibility making this a safer option than gadolinium based contrasting agents. However, in order for the biomolecules to be attached to the nanoparticle surface, a bridging ligand and a linker need to be in place. This poster explores the use of sugar acids for novel bridging ligands.

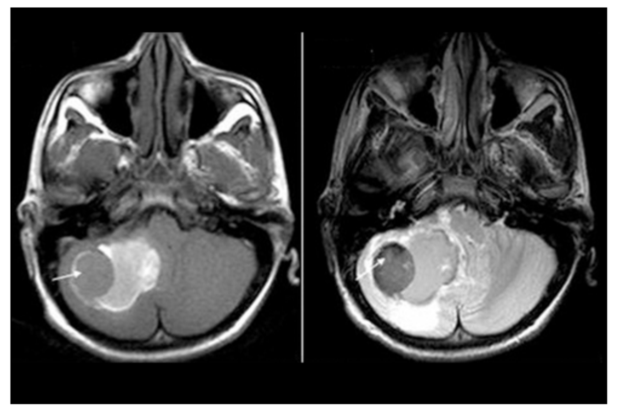

*Figure 1. Left: Image using $T_1$ contrasting agent. Right: Image using $T_2$ contrasting agent*

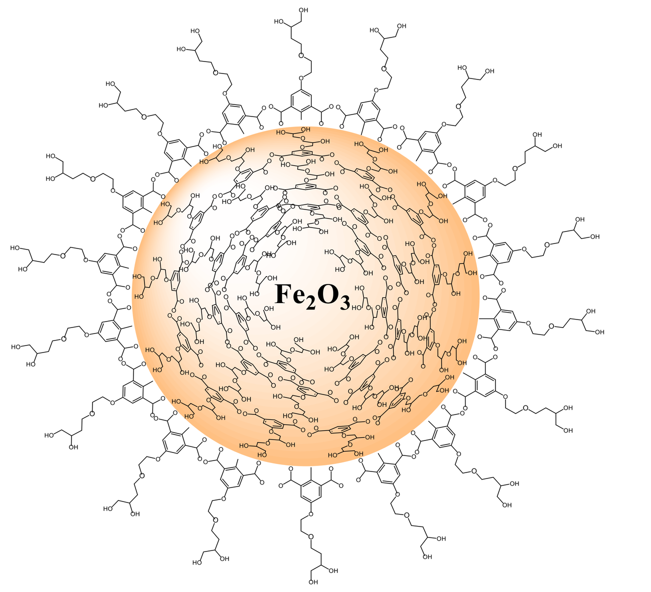


*Figure 2. Iron oxide nanoparticle surrounded by organic coating*

## Synthesis

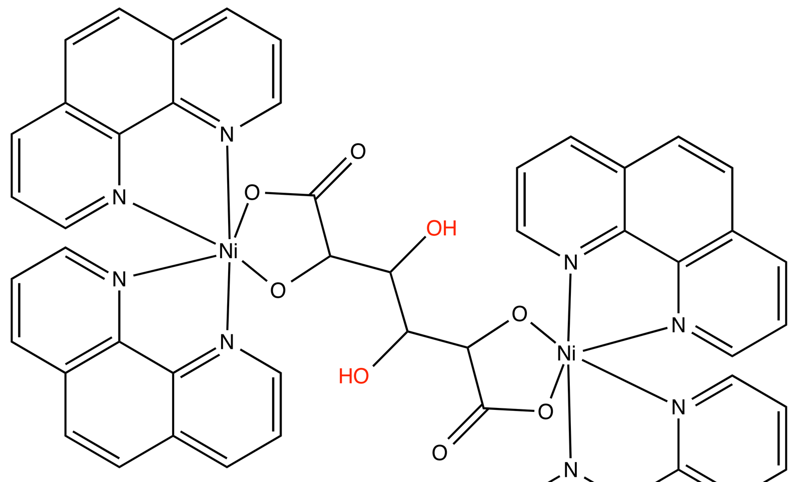


*Figure 3. Nickel Phenantrolino Mucicate*

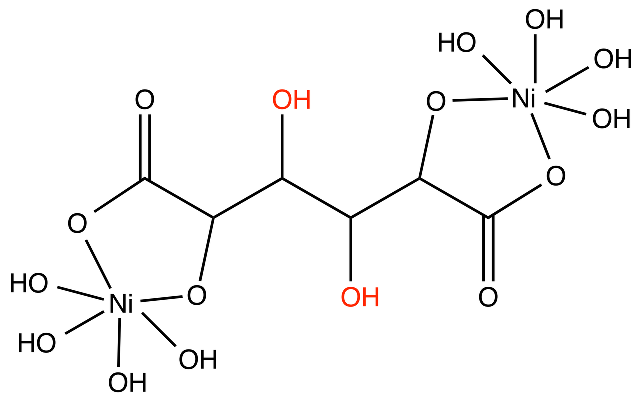


*Figure 4. Nickel Mucicate*

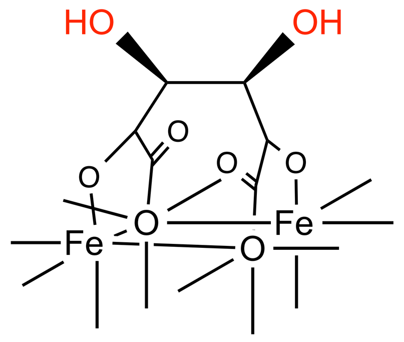


*Figure 5. Colloidal Iron Oxide Mucicate*

Synthesis
- $NiCl_2 \cdot 6H_2O$ was reacted with o-phenantroline hydrate in methanol, this solution was then reacted with mucic acid and DBU forming nickel phenantrolino mucicate and a byproduct of HCl
- Allows the beta hydroxyl groups to be exposed

Results:
- Two products
  - Blue – contained mucic acid
  - Purple – contained phenantroline

Synthesis
- Mucic acid and DBU were reacted with $NiCl_2 \cdot 6H_2O$ in methanol
- Allows the beta hydroxyl groups to be exposed

Results:
- Reacted in a 1:1 ratio instead of a 2:1 ratio forming a coordination polymer

Synthesis
- Mucic acid in diethylene glycol was reacted with colloid solution
- Allows the beta hydroxyl groups to be exposed
- Reaction underway, no current data

## Characterization

Thermo gravimetric analysis (TGA) was used to determine that the nickel mucicate was reacting in a 1:1 ratio, therefore forming a polymeric chain.

The mass spectrum of both the purple and blue products obtained in the nickel phenantrolino mucicate synthesis, determined that the blue product contained mucic acid with no phenantroline, while the purple product contained phenantroline with no mucic acid.

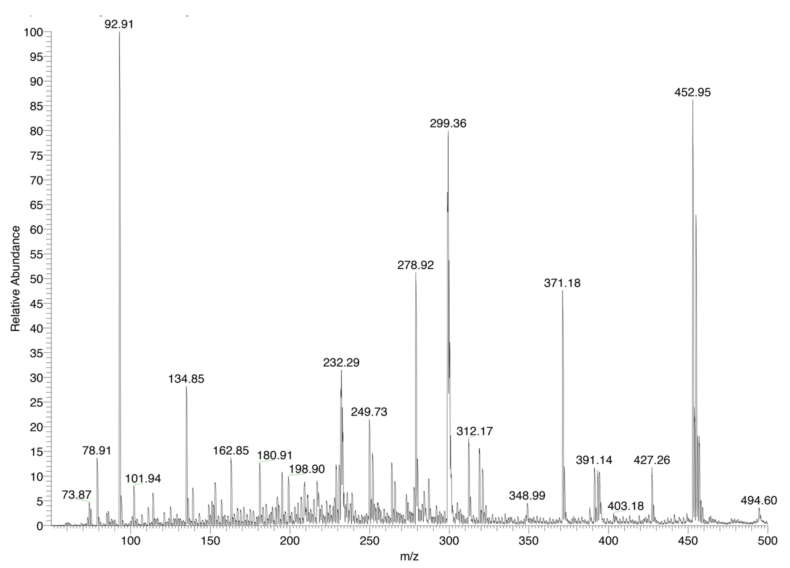


*Figure 6. The mass spec of blue product in HCl*

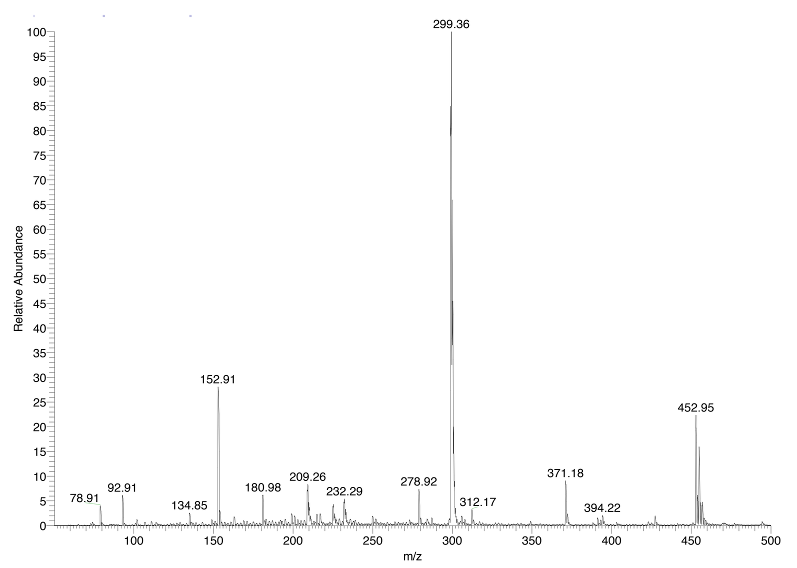


*Figure 7. The mass spec of purple product in HCl*

## Conclusion and Future Work

- Nickel phenantrolino mucicate was not synthesized. Instead two separate products were isolated and characterized:
  - A blue product containing mucic acid, which was confirmed through ESI-MS
  - A purple product containing phenantroline, which was confirmed through ESI-MS
- Nickel mucicate was synthesized and characterized to find that the nickel and mucic acid was reacting in a 1:1 ratio to form a polymer chain.
- Colloidal iron oxide mucicate was synthesized

In the future we would like to proceed with an organic synthesis step where various linkers will be attached once the beta hydroxyl groups are successfully functionalized. This allows for the biomolecules and the nanoparticles to be connected.

## References

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## Acknowledgements

This material is based upon work supported by the National Science Foundation under the NSF EPSCoR Cooperative Agreement No. EPS-1003897 with additional support from the Louisiana Board of Regents.

- LA-Sigma
- Xavier University
- Jonathon Watson
- Rajesh Komati
- Huy Do