

# Synthesis, Metal-Coordination, and Characterization of Existing and Novel Schiff Base Ligands

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## Introduction

Schiff base ligands have a simple synthesis and a wide variety of applications. Due to this, they are a focus for researchers. Characterized by a carbon-nitrogen double bond in which the nitrogen atom is connected to either an alkyl or aryl group, Schiff base ligands have displayed the potential for vast chemical arrangements during synthesis. Due to the ligands ability to form a variety of structures, they can be manipulated to exhibit favorable properties. As a result of their potential favorable properties, Schiff base ligands are studied for their applications as catalysts and in pharmaceuticals.<sup>1-6</sup> These ligands act as high active catalysts to polymerization. Through the metal-coordination of these ligands, they have demonstrated antibacterial<sup>1</sup> and antiviral<sup>2</sup> properties. Some Schiff base ligands have also demonstrated anticancer<sup>3</sup> effects. Resulting from their simple synthesis and governable properties, Schiff base ligands are desirable in the fields of catalysis and medicine.

Due to the constant use of antibiotics in both animals and humans, bacteria have grown resistant to available antibiotics. As a result, researchers are forced to increase the spectrum of drugs. Schiff base compounds have great flexibility and stability.<sup>3</sup> Thus, scientists are focusing on ways to incorporate Schiff base ligands and their metallic compounds into viable forms of medication.<sup>3</sup> In experimentation, the ligand showed a higher potency than that of current drugs. More so, metal-coordinated complexes show an even higher potency and stability making them ideal for such use.<sup>2-3</sup>

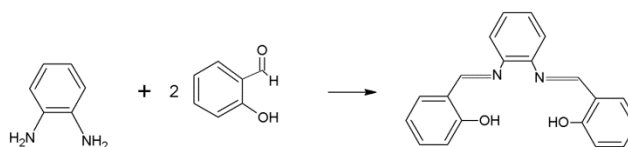
In experimentation, three bacteria samples were used: *Staphylococcus aureus*, *Bacillus subtilis*, and *Escherichia coli*. A commonly used antiseptic, cetrimonium bromide (CTAB), was used as the blank. Schiff base ligands coordinated with iron(III), zinc(II), and nickel(II) were found to be much more active against the bacteria than CTAB.<sup>4</sup> Not only have Schiff base compounds proved to be antibacterial, they are also predicted to have anticancer properties.<sup>5</sup> G-quadruplex DNA is a functionally secondary DNA structure that has recent has shown to inhibit telomere maintenance.<sup>5-6</sup> Thusly, studying the interaction between DNA<sup>7</sup> and metal-coordinated complexes has become a high interest of researchers in recent years.<sup>5-8</sup>

Also, late transition metal catalysts have been one of the highest growing studies in organometallic chemistry.<sup>9</sup> Due to their stability, Schiff

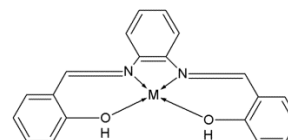
base ligands have been a focus. In experimentation, Schiff base compounds demonstrated greater activity in a wide range of temperature.<sup>9-10</sup> Schiff base ligands have also demonstrated the potential for easily bonding with transition metals.<sup>11</sup> According to the literature, Schiff base compounds not only have the potential for catalysis, but also for the medicinal applications.<sup>7, 9-11</sup>

Though the applications and properties of Schiff base compounds are important, the synthesis has an important aspect in the binding of metals. Considering the near endless potential for Schiff base ligand structure and their metal complexes, the synthesis clearly plays an important part in formation.<sup>12-13</sup> The discovery of a novel Schiff base ligand may lead to new discoveries and applications. Thusly, the focus of this project is to study and characterize Schiff base ligands with the focus of creating a novel complex.

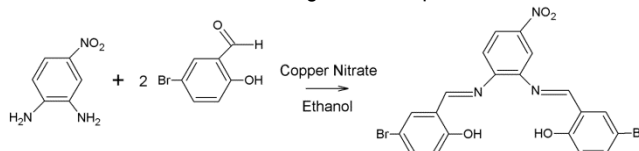
The targeted directive of this project was to synthesize and characterize a novel Schiff based ligand. In general terms, a ligand is a functional group that binds to a metal in order to create a coordination compound. Generally, the ligand will donate one or more pairs of electrons for covalent bonding. **Scheme 1** depicts a pictorial representation of the primary ligand family studied. The metal coordination of the first ligand is represented in **Scheme 2**. The novel ligand that produced, **Scheme 3**, is characterized by some of the same chemical features as a general Schiff base.



**Scheme 1.** N,N'-bis(salicylidene)-3,4-phenylenediimine



**Scheme 2.** Metal-coordinated ligand. "M" represents metal ions



**Scheme 3.** Scheme for novel ligand, N,N'-bis(5-bromosalicylidene)-4-nitro-1,2-phenylenediimine.

By using previous research on Schiff base ligands as a starting place; this project studied the techniques used in synthesis and metal-coordination. Through a literary search, it is evident that multiple techniques are available for ligand synthesis.<sup>14-16</sup> This research planned to further characterize Schiff base ligands and study the synthesis methods. Using the most efficient synthesis, a novel ligand is to be synthesized by the addition of a halogen on the arms of the structure. This ligand is to then be characterized and coordinated with a metal.

In view of this, the project focused on the synthesis, characterization, and metal-coordination of Schiff base ligands. Diligent attention was noted to methods of synthesis, instrumentation, and observation.

## Materials and Methods

The reagents and solvents were not purified or manipulated from their commercial form. Sigma-Aldrich was the primary source for all solvents and reagents. All reactions took place in the same fume hood. Among the instruments used are NMR spectrometer, FT-IR, hydraulic pellet press, and rotary evaporator. Besides the novel ligand, N,N'-bis(5-bromosalicylidene)-4-nitro-1,2-phenylenediamine, all other syntheses were based on previously published methods.<sup>15</sup>

## Results and Conclusion

At the beginning of the project, an article written by Darensborough and his team was used.<sup>15</sup> The main goal of his article was to synthesis novel ligands, mainly Schiff base compounds. Using his article as a starting point, the first experiment was conducted. The first experiment, synthesis of N,N'-bis(salicylidene)-1,2-phenylenediamine, was conducted under two different conditions. The reagents were not further purified or manipulated in either condition. Methanol was the common solvent used in both experiments. The first condition, referred to as Method A, consisted of using a three-neck round bottom flask, condenser, and additional funnel. In Method A, a solution of salicylaldehyde, formic acid, and methanol was slowly dripped into a solution of 1,2-phenylenediamine. The second condition set, Method B, used the same set-up; however, the formic acid was located in the round bottom flask with the salicylaldehyde. Comparing the two products, Method A appears to be a significantly deeper yellow. However, after running <sup>13</sup>C-NMR on each sample, they appear to be the same product. Reacting for the same amount of time, but different order of addition, appears to not make a difference on the chemical structure of the product. From this, it was concluded

that the most successful trial was when the aldehyde was dripped into the amine. The second experiment was looked to Darensborough for guidance. Darensborough used a nitrogen atmosphere to prevent the chromium(II) from oxidizing into chromium(III). One difference between this experiment and that of Darensborough is that when the sodium sulfate was added to the experimental product, the product was absorbed and salt was formed. After many attempts to recover crystals, the experiment was eventually concluded with no product.

The next experiment was conducted because it took a significantly smaller amount time. Instead of taking two days, it took ten hours. For this experiment, DMSO was used as a solvent. This is because DMSO has the ability to dissolve both polar and nonpolar compounds. However, due to its high boiling point of 180°C, it eventually became clear that this was a poor solvent to use because it could not be rotary evaporated. The finished product was allowed to air dry for nearly two weeks before being terminated because the DMSO would not evaporate.

For synthesis of the novel ligand, it was determined that a three hour stir using copper nitrate as a catalyst would be the most effective form of synthesis. Using past experiments as data, this method proved effective for ligands of similar nature. Fortunately, the ligand was synthesized like predicated, and then metal-coordinated.

Excluding metal complexes, results from the NMR instrument were sufficient in characterization of the Schiff base ligands. The metal coppers, mainly that of copper(II), were unable to produce a decisive NMR. This is due to their paramagnetism.<sup>16</sup> Paramagnetism is the presence of unpaired electrons and resulting magnetic moment. This moment therefore causes a disturbance in the magnetics resulting to produce correct resonance. In cases where this occurred, FT-IR spectroscopy was performed to determine the proper metal coordination of the ligand.

Among the methods of synthesis conducted during this experiment, reflux and stirring under various conditions, one method was researched that was not undertaken. This method, mechanochemistry, is solvent free. It uses strictly mechanical forces as a route to synthesis. These forces are used to achieve chemical processing and transformation. The method that was discovered during research required using a mortar and pestle to grind reagents for three hours.<sup>17</sup> Though this seemed like an appealing route to synthesis, it was undertaken due to time constraints. However, further research should be done to test the efficacy of such a method.

Schiff base compounds have a diverse and substantial potential. This project is only a small part of a large and collaborative effort that is necessary to

fully utilize these ligands. Though small, this project was successful in not only characterization and synthesis of many existing Schiff base ligands, but was also successful in synthesizing a novel ligand, bis(5-bromosalicylidene)-4-nitro-1,2-phenylenediamine, and metal complex. Out of the total number of experiments, nine yielded product. From this project, a larger understanding of Schiff base ligands was obtained. Understanding more about efficient synthesis methods will not only lead to the synthesis of more novel ligands, but will help increase the efficiency of such experiments. On top of the synthesis methods conducted during this project, there is the potential for more novel methods of synthesis. Based on the research conducted, the production of novel ligands may depend on the synthesis method used.

Overall, this project should be considered a success. Not only did it reach the goals of synthesizing, characterizing, and metal-coordinating existing ligands, but it also produced a novel ligand and resulting metal complex. A greater understanding of the chemistry behind Schiff base ligands and their synthesis was gathered. From this research, it is hopeful that further research will spawn and continue to understand Schiff base ligands.

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