

Title: Click Chemistry via Coordination complexes using bis(bipyridyl) azido Complexes of Ruthenium (II)

Mekhala Girish

Abstract: The generation of 1,4 and 1,5 disubstituted triazoles using “Click Chemistry” between terminal alkynes and alkyl and aryl azides catalyzed by Cu (I) is well established. However, a Ruthenium(II) ion coordinated to a triazole ring system has not yet been studied. The synthesis of a bis(azido) bis(bipyridyl) complex of Ru(II) is described here. A complete study of the electronic spectra of this complex confirms that Ru(II) is coordinated to two azido groups in the cis position. The impressive chemical stability of this Ruthenium azido complex makes it an ideal candidate to perform “Click Chemistry” with it on a variety of terminal and substituted alkynes. The reaction of the bisbipyridyl bis(azido) Ruthenium complex with terminal alkynes was investigated. The non activated terminal alkyne failed to react with the bis(azido)Ru(II) complex under the conditions in which the reaction was carried out.

Introduction: The Nobel Laureate, Prof. Barry Sharpless along with Valery Folkin of The Scripps Institute at La Jolla, California and M.G.Finn of the Georgia Institute of Technology were the first to coin the term “Click Chemistry.”⁽¹⁾ The term “Click Chemistry refers to reactions which can be conducted in the laboratory by joining chemical units in a modular fashion. These types of reactions can be conducted under moderate temperatures, produce stereospecific products, have minimal side reactions, produce high yields of products and exhibit large thermodynamic driving force. Considering these factors, and also the budgetary constraints, these types of reactions can be studied and conducted easily with the facilities available in Middlesex County College. “Click Chemistry” approach to synthesis has been widely used to develop a large “warehouse” of compounds which may have potential applications in pharmaceutical^(2,3), biotechnological^(4,5), material science^(6,7) and nanotechnology.

The Huisgen 1,3- dipolar Cycloaddition of substituted alkynes and arynes to azides to produce 1,4 and 1,5 disubstituted triazole ring systems is well known.^(8,9) However, these reactions require elevated temperatures and produce mixtures of regioisomers. A copper (I) catalyzed reaction follows a different mechanism but allows for the production exclusively of the 1,4 – disubstituted triazole ring.⁽⁶⁾ Thus, this can truly be classified as a “Click Chemistry” type reaction since it can be carried out in aqueous media and at room temperature. A Ruthenium catalyzed reaction between azides and substituted alkynes (or arynes) producing exclusively 1,5- disubstituted triazoles is also well established.⁽⁷⁾ The objective of this project is to first synthesize a coordination complex in which a bis(bipyridyl) Ru (II) azido complex and then to attempt to perform a 1,3 dipolar cycloaddition type reaction where this Ru (II) ion coordinates to one or more triazole rings.

Experimental Section:

Instrumentation: Ultraviolet-Visible Spectra were recorded using Genesys 10S UV – VIS Spectrophotometer (Model 610S Serial number 2L5P123002). Spectrograde acetonitrile was used as a reference/blank and also as solvent for the various compounds. IR spectra were

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recorded using Perkin Elmer Infrared Spectrophotometer (Model 710 B Serial 132636). KBr was used to make the pellets of the various samples.

Materials: All solvents and ligands used for the preparation were reagent grade and used without further purification.

Preparation of cis-(bpy)₂RuCl₂. 2H₂O The preparation of this complex was done in the method proposed by T.J. Meyer et.al ⁽¹⁰⁾ to obtain good yields of the compound.

Commercial RuCl₃.2H₂O (1.000 g), bipyridine (1.399 g), and LiCl (1.070 g) and 7.2 mL of reagent grade dimethylformamide (DMF) were measured out and transferred to a two necked round bottom flask. The reaction mixture was purged with Helium gas continuously to create an inert atmosphere. Next an additional 1-2 mL of DMF was used to wash down any reactants adhering to the walls of the flask. The reaction mixture was heated at reflux for the first half hour at 70°C and then at 60 °C for the next 8 hours. It was stirred magnetically throughout this time period. After the reaction mixture cooled to room temperature, 30 mL of reagent grade acetone was added and the contents of the flask were cooled to about 0° C overnight. The product was filtered and the solid was washed with three times with 8.0 mL portions for distilled water followed by three 8.0 mL portions of diethylether. The product was dried using a Glass Frit Suction filtration unit. The yield of the cis-(bpy)₂ RuCl₂. 2H₂O was determined to be 0.9876g.

Preparation of [(bpy)₂(py)₂Ru] (BF₄)₂: The preparation of this complex was done in the method proposed by T.J. Meyer et.al ⁽¹⁰⁾ in their paper with minor modifications.

cis- (bpy)₂RuCl₂. 2H₂O (0.2517g) was suspended in about 11 mL of a 1:1 methanol - water solution (by volume). About 100 % molar excess of pyridine (0.5 mL) was added to the above mixture in a drop wise fashion. Helium gas was bubbled through the reaction mixture continuously to deaerate the contents of the flask using a syringe needle. The mixture was refluxed and heated at about 60°C for about 2 hours and magnetically stirred. A 5 mol excess (0.5699 g) of tetraethylammoniumtetrafluoroborate was added to the reaction flask while still under reflux. The heat was switched off and the contents cooled to room temperature. The crystals were then filtered and the solid washed with minimal quantity of ice cold water to remove excess pyridine. The orange crystals were air dried by continuing vacuum filtration using a clean dry flask.

Preparation of (bpy)₂Ru(II) azido complex: About 10 mL of a 1:1 methanol water solution by volume was placed in a flask that had been deaerated with He using a syringe needle. 0.2107 g of cis-(bpy)₂ RuCl₂. 2H₂O was suspended in the above solution. After about 10 minutes of continual bubbling of He through the reaction mixture, a 5 mol excess (0.1401 g) of sodium azide was added to this flask. The contents of the flask were refluxed for about 2 hours at 40°C. The reaction mixture was cooled to room temperature and then placed in a refrigerator overnight at about 0° C to promote crystallization. The dark purple crystals were then filtered the next day

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using copious amounts of ice cold distilled water. The crystals were air dried using vacuum filtration.

Reaction with Silver Nitrate: the compounds bis(bipyridyl)dichloro Ruthenium and bis(bipyridyl)bis(azido) Ruthenium complexes were dissolved in acetonitrile and treated with 2.5 mol. equivalents of silver nitrate solution.

Preparation of Crystals of bis(bipyridyl) bis(azido) Ruthenium was done using the Bilayer Diffusion Crystal growth method using methylene chloride and diethyl ether as the solvent system. 0.0361 g of the complex was weighed and dissolved in 5.0 mL of methylene chloride. Next He was bubbled through the mixture to deaerate it. The mixture was filtered. The filtrate in a test tube was clamped to a stand at a 45 degree angle. Next, about 9 mL of diethyl ether was added to it in a drop wise fashion. The test tube was sealed with a cork and left undisturbed for 3-4 days.

Click Chemistry: A “Click Chemistry” reaction was performed between the azido complex of Ruthenium and phenylacetylene. In a sealed test tube 0.1004 g of bis(bipyridyl)bis(azido)Ru was dissolved in approximately 3 mL of Dimethylformamide. 66.2 μ L of phenylacetylene was added. The test tube was lowered in an oil bath maintained at 100°C.

Results and Discussion: The Ruthenium (III) chloride was refluxed with bipyridine and excess Lithium chloride which served to reduce the Ruthenium (III) ion to Ruthenium (II). Simultaneously two bipyridyls were introduced into the coordination sphere of the ruthenium (II) ion forming an octahedral complex. Here, the chloride ligands are occupying the cis position. Replacement of chloride ions in $(bpy)_2RuCl_2$ with other neutral ligands like pyridine results again in an octahedral complex with the two bipyridyls and two pyridyl ligands satisfying the six coordination number for the metal ion. Here, the complex is precipitated out as a tetrafluoroborate salt which is an orange colored sparingly soluble solid. It is well established ⁽¹¹⁾ that a mono aquo bisbipyridine pyridine Ru (II) ion is formed when $Ru[(bpy)_2(py)_2](ClO_4)_2$ is heated with water at about 95°C. It was assumed that $[(bpy)_2(py)_2Ru](BF_4)_2$ would behave similarly when heated with water. Since water is a labile ligand, it then can be easily replaced by an azido group. But for purposes of saving time and because of budgetary constraints with regards to cost of chemicals, it was decided that the dichlorobis(bipyridyl) Ruthenium in methanol be directly refluxed with sodium azide. The dark purple crystals obtained were insoluble in water. The colors of the various Ru(II) complexes synthesized varied from plum purple to orange to violet. The overall yields for these complexes were reasonably high (about 70-75%).

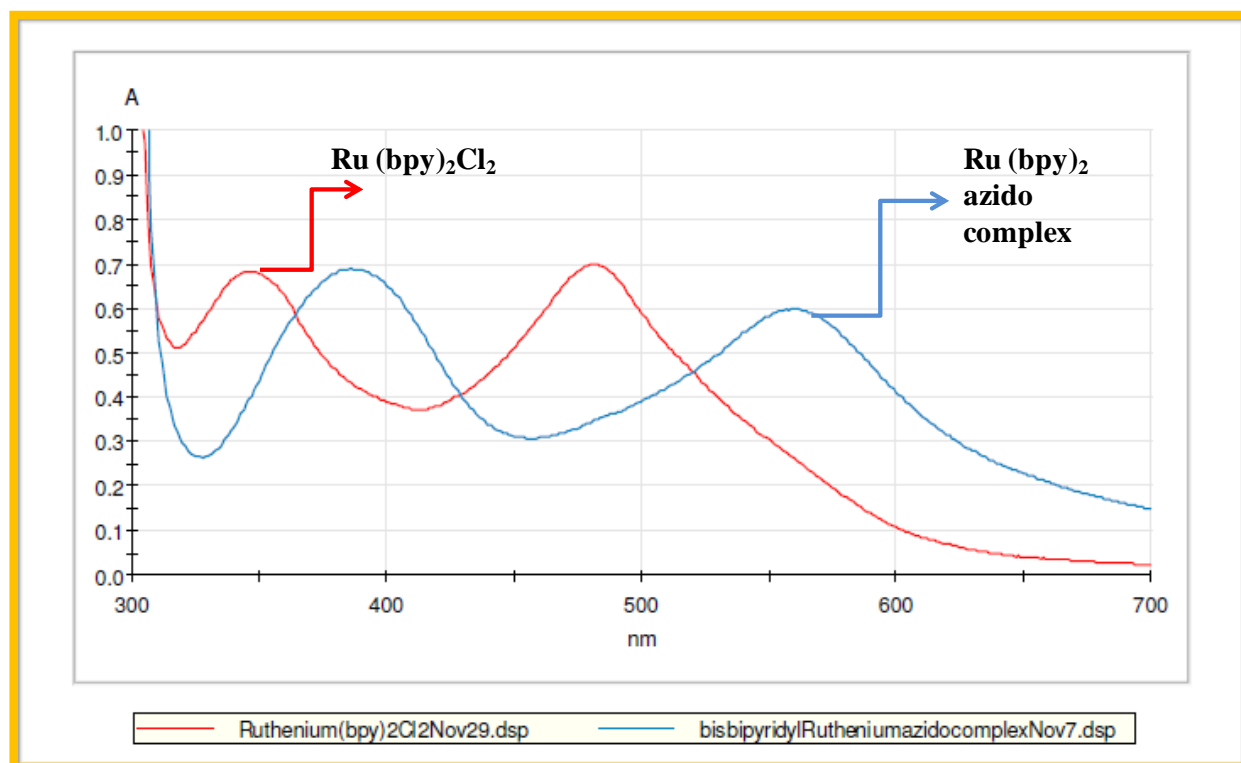


Figure 1: Overlaid UV-Vis spectra of $\text{Ru}(\text{bpy})_2\text{Cl}_2$ and $\text{Ru}(\text{bpy})_2(\text{N}_3)_2$

Figure (1) compares the uv-visible spectrum of dichlorobis(bipyridyl)Ruthenium with the bis(bipyridyl) azido Ruthenium (II) complex using acetonitrile as reference and solvent. As expected the dichlorobis(bipyridyl) Ruthenium (II) complex shows two characteristic peaks at 350 nm and at 490 nm. However, in the bis(bipyridyl) azido $\text{Ru}(\text{II})$ complex it can be seen that these two peaks have shifted to higher wavelengths to 390 nm and 570 nm. This “red shift” to lower energy regions may be consistent with the $\text{Ru}(\text{II})$ ion being coordinated to one or more azide groups.

The next step was to measure the Infrared spectra of these complexes using KBr as reference. The IR spectra (Figure 2) of dichlorobis(bipyridyl) ruthenium, bipyridine and bis(bipyridyl) azido Ruthenium complexes were measured. The azido complex showed a characteristic absorption peak at around 2000 cm^{-1} which confirms the presence of the azide group in the complex. All three IR spectra showed absorption peaks at around 1400 cm^{-1} which is consistent with the stretching frequency of the bipyridyl system. It can be clearly concluded by looking at the spectra, that the aromatic bending frequency has shifted to lower wave numbers in the coordinated bipyridine complexes due to π back bonding versus the pure bipyridine. The electronic and IR spectra confirm that one or two azide groups are coordinated to the Ruthenium (II) ion.

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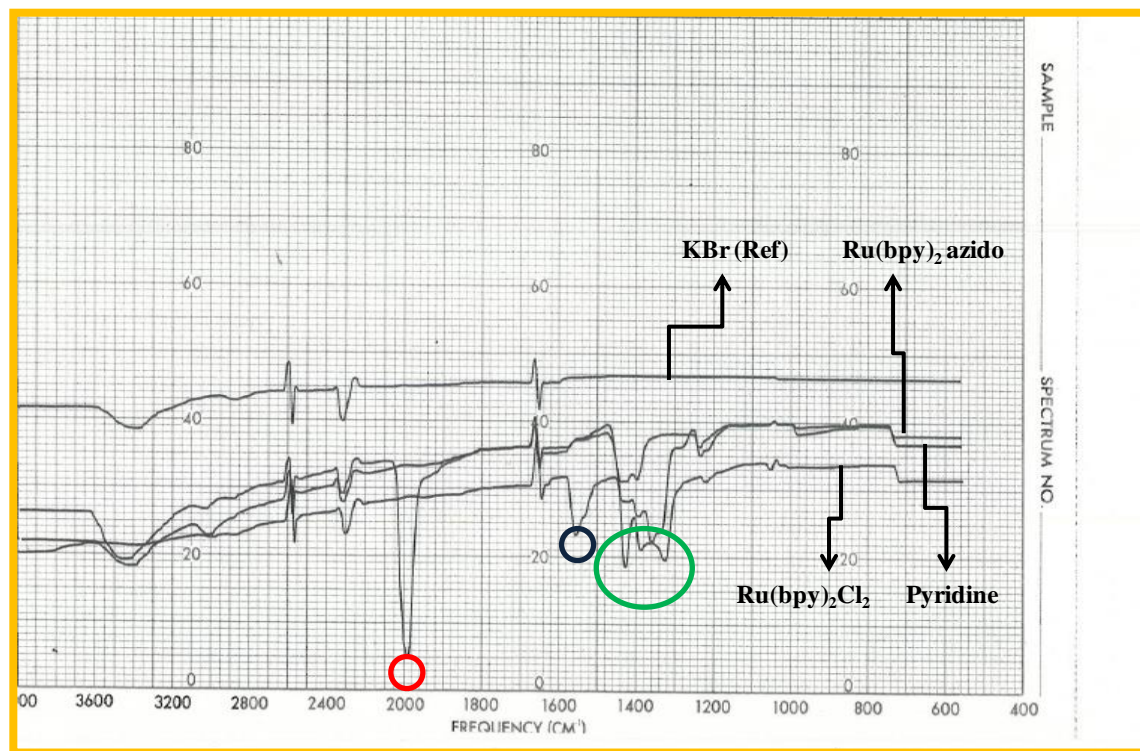


Figure 2: Overlaid IR spectra of bipyridine, $\text{Ru}(\text{bpy})_2\text{Cl}_2$ and $\text{Ru}(\text{bpy})_2(\text{N}_3)_2$ in KBr

The question next arose whether the Ruthenium azido complex is a mono or a diazo compound.

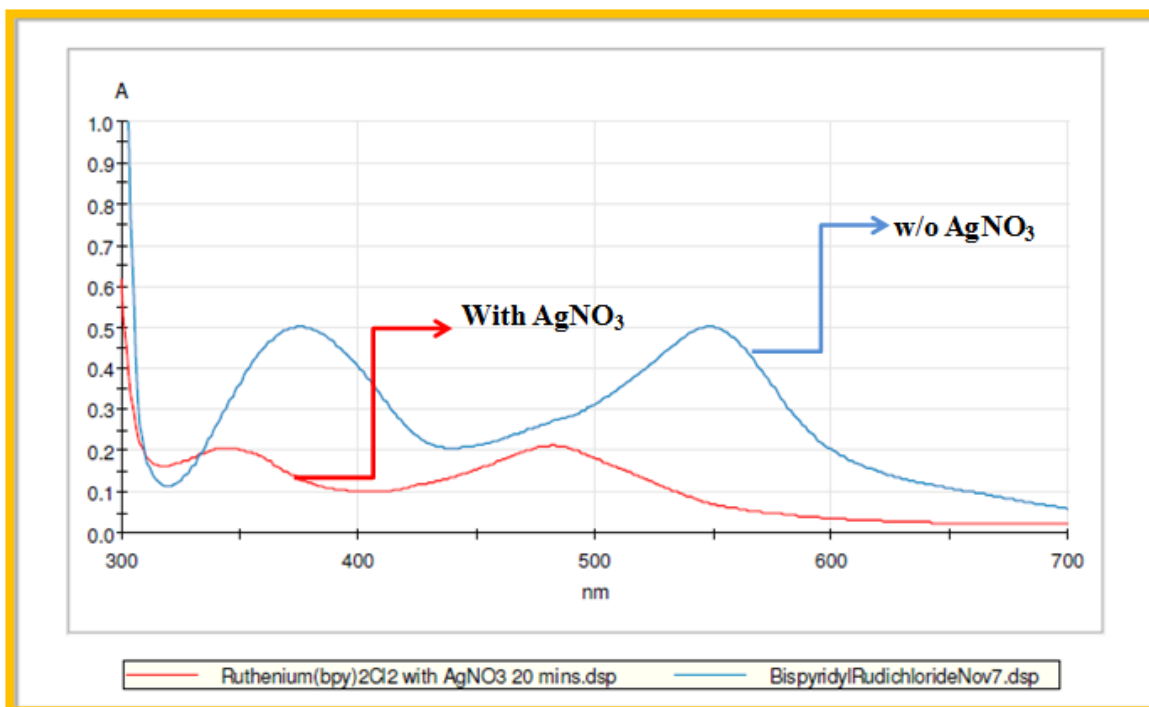


Figure 3: Overlaid UV- Vis spectra of $\text{Ru}(\text{bpy})_2\text{Cl}_2$ with & without AgNO_3 in CH_3CN

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In other words, whether one or both of the chloride ligands in the dichlorobis(bipyridyl) Ruthenium complex were replaced. The dichloro and the azido ruthenium complexes in acetonitrile were separately treated with 2.5 mole equivalents of 0.1 M silver nitrate solution. The dichlorobis(bipyridyl) complex produced a white precipitate which could be seen on centrifugation. In this case, Ag^+ ion was able to abstract the chloride ions from the dichloro complex precipitating it out as AgCl . The UV-Vis spectra of this compound after addition of silver nitrate were studied. The shift of the dichlorobis(bipyridyl) Ruthenium complex peaks to lower wavelength is consistent with the acetonitrile solvent being bonded to Ru^{2+} which is already well established. However, addition of AgNO_3 to the azido complex did not produce any white precipitate, instead the solution turned brown with black particles floating in the test tube. In spite of centrifugation, the precipitate did not settle. The absence of formation of white AgCl precipitate in this case indicates that the azido complex is a di azido complex. In other words, both chloride ligands in the original dichlorobis(bipyridyl) Ruthenium have been most likely replaced by azide groups. The redox potential of the diazido complex is lower than that of the dichlorobis(bipyridyl) Ruthenium complex confirming that azide cannot be stripped by Ag^+ ions instead is oxidized by Ag^+ to probably Ru^{3+} . The UV-Vis spectra of this compound after addition of silver nitrate was studied and presented a complex pattern. In the first few minutes of addition of silver nitrate, the two peaks corresponding to Ru^{2+} appear to be disappearing. The spectrum was monitored at 20 minutes, 40 minutes and three days after addition of silver nitrate.

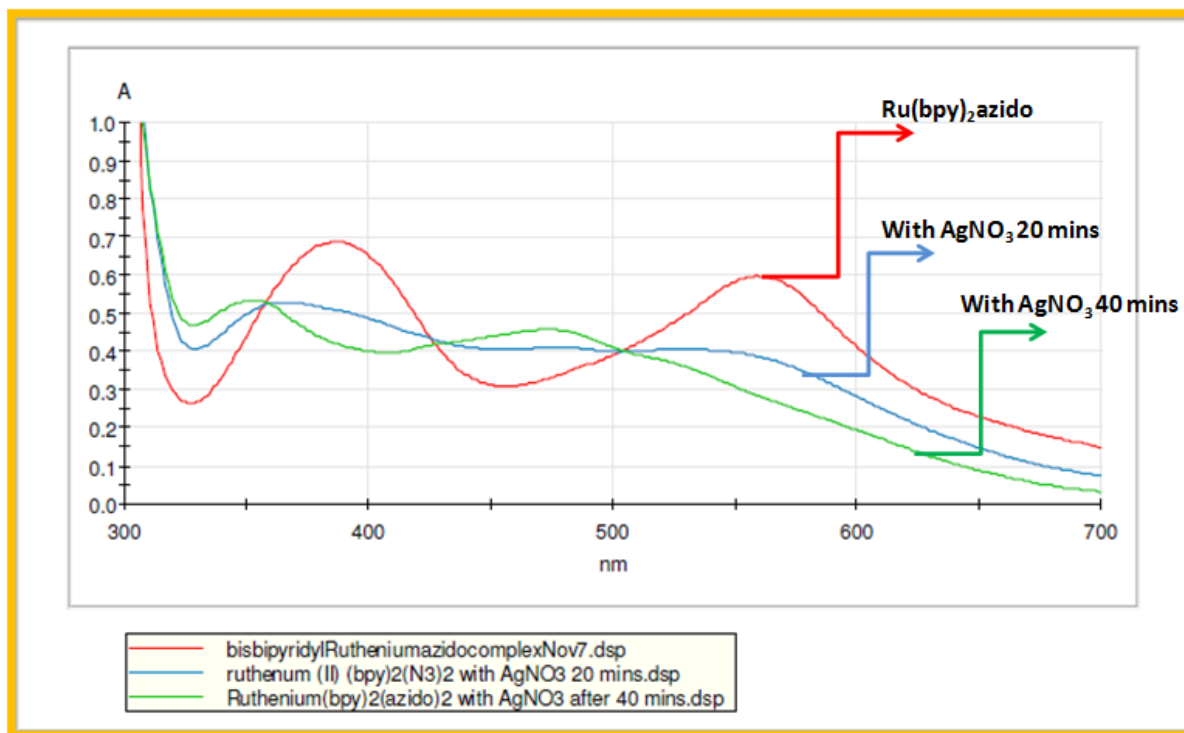


Figure 4: Overlaid UV-Vis spectra of $\text{Ru}(\text{bpy})_2(\text{N}_3)_2$ with and without addition of AgNO_3 in CH_3CN

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At the end of 3 days, the peaks corresponding to Ru(II) have completely disappeared. Instead, two peaks shifted to lower wavelengths could be seen. Also, the two peaks appear to be flattening out with time.

The preparation of crystals using the Bilayer Diffusion method resulted in extremely small crystals which were difficult to harvest. The principle behind this method of crystallization is that the azido complex is highly soluble in methylene chloride but is insoluble in diethyl ether. However, the two solvents are highly miscible with each other. With time, the more dense solvent (methylene chloride) diffuses into the less dense solvent (diethylether) causing the crystals to separate out at the interface. This part needs to be repeated using a different solvent system and also a smaller test tube.

The results of the “Click Chemistry” between the bis(bipyridyl)bis(azido) Ru complex and phenylacetylene in DMF as solvent was not successful. Proof of this was obtained by comparing the UV-Vis spectra of the original azido complex as well as the reaction mixture between the azido complex and phenylacetylene. As can be seen from figure (5) the two spectra perfectly overlap. This shows that the “Click Chemistry” between the azido complex and phenylacetylene was unsuccessful and that the bis(bipyridyl)bis(azido) Ruthenium complex did not react.

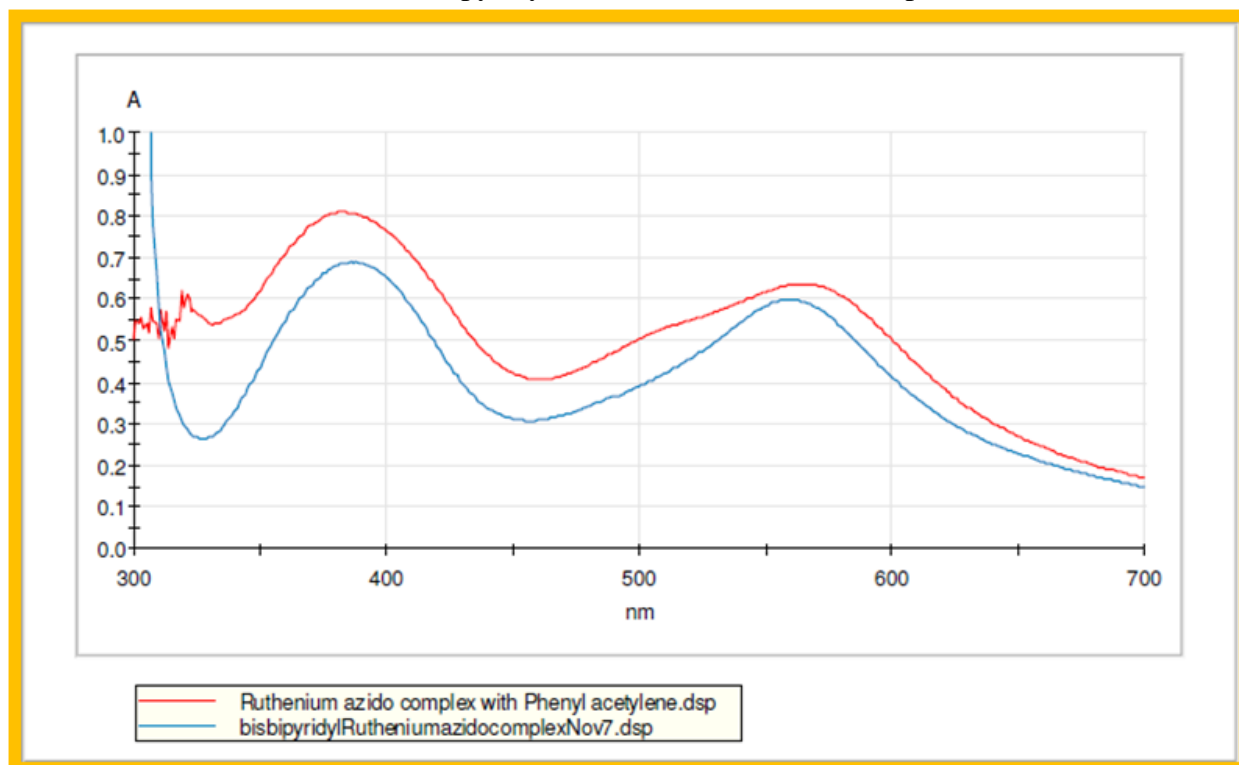


Figure 5: Overlaid UV- Vis spectra of $\text{Ru}(\text{bpy})_2(\text{N}_3)_2$ and after reacting with Phenylacetylene

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Conclusion: Based on UV- vis, Infra Red and data from the silver nitrate reactions, it can be concluded that the complex is a diazo compound of Ruthenium with formula $(bpy)_2(N_3)_2 Ru$. However, pure crystals of this complex need to first synthesized using a better solvent system using the Bilayer diffusion method. Elemental analysis of this compound needs to be accomplished. The next step would be to conclusively prove beyond a reasonable doubt that it is a diazo compound is to characterize it via X-ray Crystallography. The reaction between this diazo complex of Ruthenium (II) and stoichiometric amounts of silver nitrate needs to be studied in greater detail and also needs to be carefully monitored with passage of time. Finally, the reaction between this diazo complex and substituted alkynes needs to be done in the presence of Cu (I) as catalyst. This needs to be done in order to see if the Ru ion is able to coordinate with the alkynes/aryne and form a Ruthenium coordinated triazole system.

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