

EXPERIMENT 5

Synthesis of cis- and trans-Diamminedichloroplatinum(II)

REFERENCES

- Singh, M. M.; Szafran, Z.; Pike, R. M. "The Microscale Laboratory", *J. Chem. Educ.* **1990**, *67*, A261-A262.
- Szafran, Z.; Pike, R. M.; Singh, M. M. *Microscale Inorganic Chemistry*, Wiley, New York, 1991, p. 176
- Alderden, R. A.; Hall, M. D.; Hambley, T. W. "The Discovery and Development of Cisplatin", *J. Chem. Educ.* **2006**, *83*, 728-733.

SAFETY RECOMMENDATIONS

Potassium tetrachloroplatinate (IV) (K_2PtCl_4): This compound is harmful if swallowed, inhaled or absorbed through the skin. It is classified as an anticancer agent.

Potassium iodide (KI): Harmful if swallowed, inhaled or absorbed through the skin. It has been shown to have deleterious effects on newborns and on pregnancy.

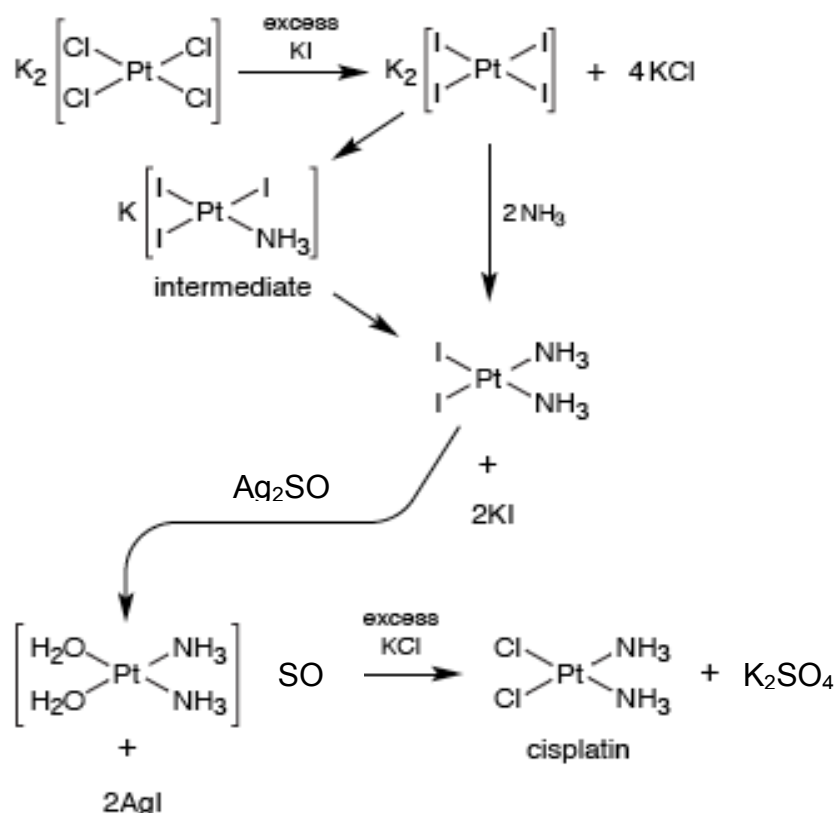
Silver Sulfate (Ag_2SO_4): Silver salts have been found to act as heavy metal poisons.

NOTE: Bright light should be avoided in this experiment since it can minimize the formation of iodoplatinum precipitates.

INTRODUCTION

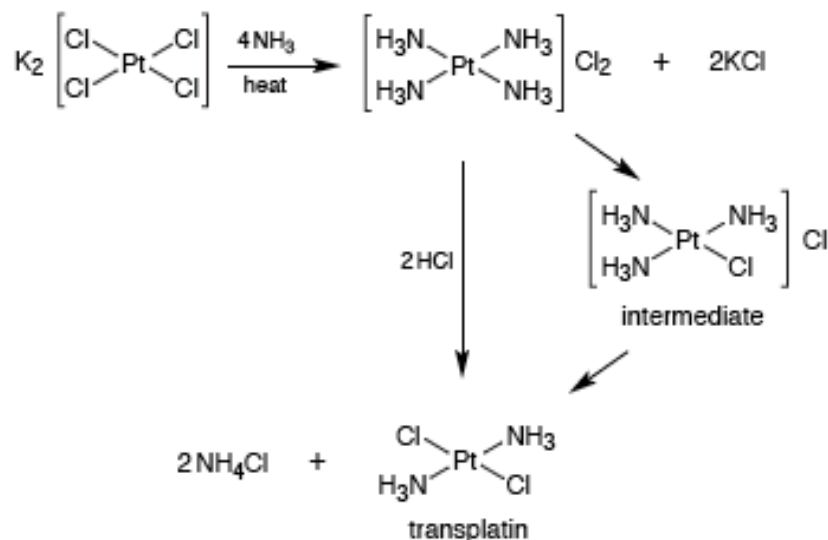
Platinum(II) complexes have been extensively studied as anticancer agents. One particularly effective anticancer drug is *cis*-Diamminedchloroplatinum(II) (Cisplatin), discovered at Michigan State University by Barnett Rosenberg in 1969. In this experiment, a number of Pt(II) complexes are synthesized, resulting in the synthesis of both Cisplatin and Transplatin.

The synthesis of Cisplatin is described in Scheme 1.



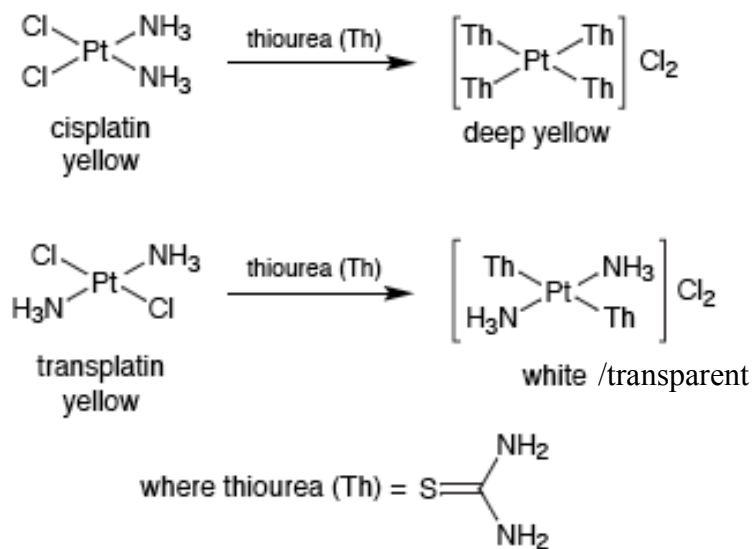
Scheme 1: Synthesis of Cisplatin

In a more direct approach, described in Scheme 2, we will next synthesize Transplatin.



Scheme 2: Synthesis of Transplatin

Finally, we will perform the Kurnakow test (Scheme 3), a method developed in 1894 by Kurnakow that allows us to distinguish between the cis and trans isomers of square planar complexes.



Scheme 3: The Kurnakow test

PROCEDURE

IMPORTANT NOTE: During both lab periods, make sure you put any waste (solid or liquid, including all washings and anything else you collect) to the Pt-waste container.

1st LAB PERIOD

Preparation of *cis*-Diamminediiodoplatinum(II)

In a 10 mL beaker equipped with a stirring bar place 125 mg of potassium tetrachloroplatinate (K_2PtCl_4). Using a micro-syringe add 200 μ L of water and heat the solution with stirring in an oil bath to 40 °C. Add a solution of 300 mg of KI in 500 μ L of warm water. (Upon addition the solution should change from red-brown to dark brown). Heat the mixture to 70 °C with continuous stirring. DO NOT OVERHEAT the solution! As soon as you reach 70 °C cool the mixture to room temperature.

Filter the solution using a Hirsch funnel to remove any solid impurities. (Use a few drops of water to make the transfer as quantitative as possible)

Using a syringe, add 500 μ L of a 2.0 M NH_3 solution dropwise to the filtrate and stir. As soon as the ammonia is added, fine yellow crystals of *cis*-diamminediiodoplatinum(II) should precipitate. If the supernatant liquid is still dark yellow in color, add a few more drops of ammonia to complete the reaction. Allow the beaker to stand for an additional 20 min at room temperature. Filter the yellow crystalline compound using a Hirsch funnel. Wash the product with 500 μ L ice-cold ethanol, followed by 1 mL ether (use these wash liquids to transfer as much as possible from the beaker to the filter). Air dry the compound and determine the percentage yield.

Obtain the IR spectrum of the product.

Preparation of *cis*-Diamminedchloroplatinum(II), Cisplatin

In a 25 mL beaker containing a magnetic stirring bar, prepare a solution of 63 mg of silver sulfate in 10 mL of water. Add 100 mg of the *cis*-diiodo derivative you prepared before, in SMALL PORTIONS, to this silver solution. (**Note:** The diiodo derivative might remain suspended at the

surface of the solution. If this occurs, stir the solution vigorously with a spatula, making sure that all the compound is well wetted.)

Heat the suspension, with stirring on a sand bath (70-80 °C) for 10-12 min. Filter the mixture to separate the precipitate of AgI.

Concentrate the filtrate over an oil bath, while stirring, to ~2 mL. Treat this solution with 330 mg of KCl. Heat the mixture using an oil bath at 70-80 °C for 2-3 min. Bright yellow crystals of *cis*-diamminedichloroplatinum(II) should precipitate out. The heating is continued for an additional 5-8 min. Cool the mixture to 0 °C in an ice-water bath. Filter the product using a Hirsch funnel. Wash the crystals with 500 µL of ethanol followed by 1 mL of ether and dry them. Determine the percentage yield.

Obtain the IR spectra of the compound and compare it with your previous product.

2nd LAB PERIOD

Preparation of *trans*-Diamminedichloroplatinum(II), Transplatin

In a 10 mL beaker containing a magnetic stir bar dissolve 42 mg of K₂PtCl₄ in a solution of 25 µL of conc. HCl and 750 µL of water. Heat the solution to a gentle boil, while stirring, using an oil bath. Slowly, add 80 µL of concentrated aqueous ammonia to the boiling solution. The solution at this point should be pale yellow. [Avoid adding excess ammonia to prevent the formation of a green product, [Pt(NH₃)₄][PtCl₄] (Magnus's green salt). If any green precipitate forms, filter it using a Pasteur pipet filter.

Reduce the volume of the solution almost to dryness, cool the mass and add 4 mL of 6 M HCl. Evaporate the mixture to about 200-400 µL and cool the mass in an ice bath. Light yellow crystals of the *trans* isomer separate out. Filter the fine crystals using a Hirsch funnel and air-dry the crystals.

Obtain the IR spectra of the compound and compare it with your previous product.

The Kurnakow test

In test tubes, place minimum amount of *cis*- and *trans*-Diamminedchloroplatinum(II) (a few milligrams should be enough). In each tube add minimum amount of DI water, enough to completely dissolve the crystals. After you get clear solutions, record the observed colors. In each tube add a few drops of the saturated Thiourea solution (3-5 drops) and swirl the solution over a warm oil bath (if the color does not change within 5 min add a few more drops of thiourea).

Record the color change for both *cis*- and *trans*-Diamminedchloroplatinum(II) solutions.

In your report, address the following points:

1. Explain / Assign the peaks of your IR spectra (compare the spectra of the different compounds).
2. Explain the different routes to the *trans*- and *cis*- isomers (your knowledge of the *trans*-effect will aid you).
3. *Cis* geometry is maintained in the reaction step:



Explain why.

4. All complexes prepared in this experiment are square planar in geometry. Why is this a favorable geometry for Pt(II)?
5. Explain the results of the Kurnakow test.
6. Provide a brief description of the anticancer role of cisplatin.