

Hantzsch Thiazole Synthesis

CHEM HELP **ASAP**

experiment video: <https://youtu.be/0c5z0ob8V3k>

Purpose

The purpose of this experiment is synthesize a thiazole ring system. The crude product will be isolated by simple filtration and is pure enough to be characterized in its crude form.

Background

Ring systems that contain atoms *other than* carbon are called **heterocycles**. The prefix hetero- means “different” – different from carbon. Heterocycles represent a separate branch of organic chemistry with *nitrogen heterocycles* being the largest area of study. Nitrogen heterocycles include small aromatic rings like pyridine (1), pyrrole (2), imidazole (3), isoxazole (4), and thiazole (5) (Figure 1). Rings of this type are frequently found in pharmaceuticals. The chemistry for making aromatic nitrogen heterocycles dates back to the late 1800s because the molecules are stable and prepared from simple reagents.

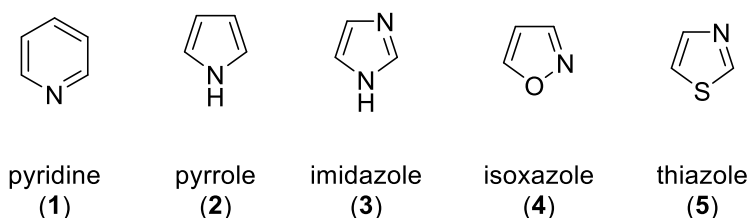
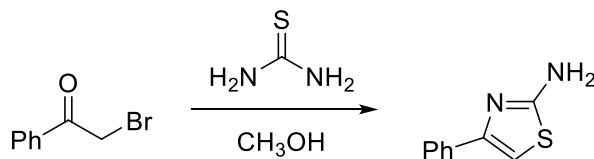


Figure 1. Sample aromatic nitrogen heterocycles

One reaction that forms thiazoles is the Hantzsch thiazole synthesis (Scheme 1). The Hantzsch synthesis reacts a haloketone with a thioamide. Loss of HX and water forms a thiazole ring through a multistep pathway. The reaction starts with an S_N2 reaction and continues with an intramolecular attack by the nitrogen onto the ketone carbonyl to form the ring. The Hantzsch thiazole synthesis tends to be very high yielding and is simple to perform.

This Hantzsch synthesis involves 2-bromoacetophenone and thiourea (Scheme 2). The thiazole product is poorly soluble in water and can be readily precipitated from the reaction.



Scheme 2. Today's reaction scheme

Procedure – 2-amino-4-phenylthiazole

In a 20 mL scintillation vial combine 2-bromoacetophenone (5.0 mmol) and then thiourea (7.5 mmol). Add methanol (5 mL) and a stir bar. Heat the mixture with stirring on a hot plate with a temperature setting of 100° or 1.0. Stir for 30 min. Remove the reaction from heat, and let the solution cool to room temperature. Pour the reaction contents into a 100-mL beaker containing 5% Na₂CO₃ (20 mL) and swirl to mix. Filter the mixture through a Buchner funnel with a 50 mL side-arm flask. Seat the filter paper with water. Use water to rinse the filter cake. Spread the collected solid on a tared watchglass, and let the solid air dry. Once the product is dry, determine the mass of the product. Determine your percent yield. Determine the melting point (melting range – both upper and lower limits) of the product. Take a TLC of the product using 50% ethyl acetate/50% hexane as the mobile phase. Once you finish your TLC, dispose your mobile phase in a waste jug. Interpret the provided NMR spectrum. Record all your observations in your notebook.