

Knorr Pyrazole Synthesis

CHEM HELP *ASAP*

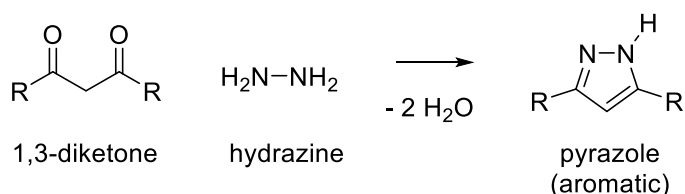
experiment video: <https://youtu.be/3y83OXlytw4>

Purpose

This experiment demonstrates reaction of a β -ketoester with hydrazine to make a pyrazolone ring.

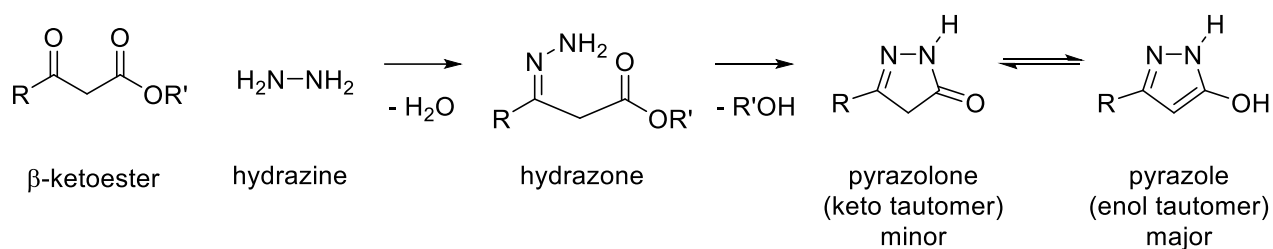
Background

German chemist Ludwig Knorr researched a number of heterocyclic ring systems, including pyrazoles, a five-membered aromatic ring with two adjacent nitrogens (Scheme 1). Knorr found that pyrazoles and related compounds can be readily made through reactions of hydrazines with 1,3-dicarbonyl compounds following the loss of two water molecules. Because of the high reactivity of hydrazine, these reactions tend to be very fast. Furthermore, because the product is aromatic and stable, the yields tend to be high.



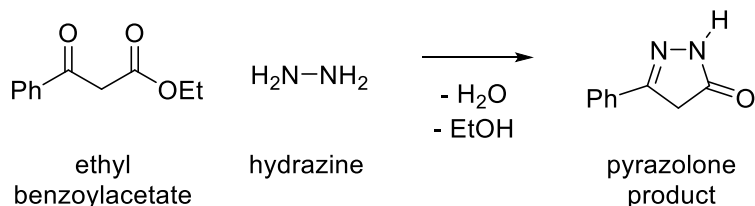
Scheme 1. The Knorr reaction to form pyrazoles

A variation of the Knorr reaction is the condensation of hydrazines with a β -ketoester (Scheme 2). The reaction starts with condensation of the hydrazine with the ketone to form a hydrazone. The other nitrogen then performs an intramolecular substitution on the ester to form the final product, which is called a pyrazolone. Note that pyrazolones of the type shown in Scheme 2 have another tautomeric form that achieves aromaticity of the five-membered ring. While pyrazolones are normally drawn as their keto tautomer, the enol tautomer is generally the major structural form observed in samples.



Scheme 2. A Knorr-type reaction to form pyrazolones

Today's reaction is a pyrazolone synthesis through reaction of a β -ketoester, ethyl benzoylacetate, and phenylhydrazine (Scheme 3). Note that hydrazine is toxic and should be handled with care.



Scheme 3. Today's reaction scheme

Procedure – 2,4-Dihydro-5-phenyl-3H-pyrazol-3-one

Mix ethyl benzoylacetate (3 mmol) and hydrazine hydrate (6 mmol) in a 20-mL scintillation vial. Add 1-propanol (3 mL) and 3 drops of glacial acetic acid. Heat the reaction on a hot plate with stirring at approximately 100°C (hot plate should be slightly over 100°C). After 1 h perform a 3-lane TLC on the experiment with 30% ethyl acetate/70% hexane as the mobile phase and ethyl benzoylacetate as the starting material. Let the reaction continue to heat while the TLC runs. If the ketoester is completely consumed, add water (10 mL) to the hot reaction with stirring. Turn off the hot plate, and allow the reaction to cool slowly and stir rapidly on the slowly-cooling hot plate over 30 min. Filter the reaction mixture with a Buchner funnel. Rinse the collected product with a small amount of water, and allow the solid to air dry. This filtrate should be disposed as lab waste. 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 100% ethyl acetate as the mobile phase. Once you finish your TLC, dispose your mobile phase in a waste container. Interpret the provided NMR spectrum. Record all your observations in your notebook.