Experiment 3

Synthesis of 1-Phenylthiourea

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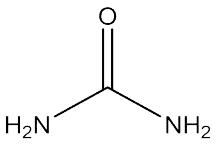
modified by

PURPOSE OF THE EXPERIMENT

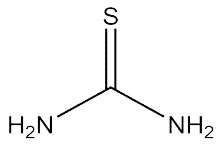
Synthesis of 1-phenylthiourea via two-step reaction and separation with pH controlling

BACKGROUND INFORMATION[1]

Carbonyl substitution and addition reaction are one of the most important categories in chemical industry. One simple example with the carbonyl group is urea. Urea is popular organic compound as first compound that artificially synthesized from inorganic materials by Friedrich Wöhler in 1828. Heated ammonium cyanate decomposes to ammonia and cyanic acid. These two undergo nucleophilic addition followed by tautomeric isomerization and finally produce urea. In a similar way, ammonium thiocyanate can produce thiourea by heating, the sulfur analogue of urea



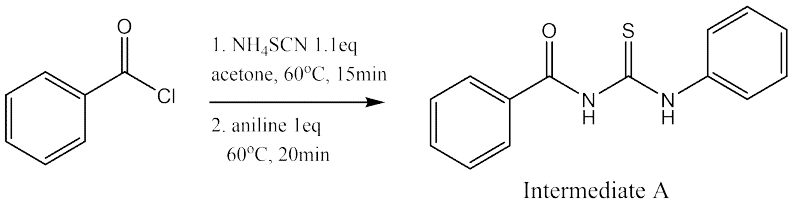
Urea



Thiourea

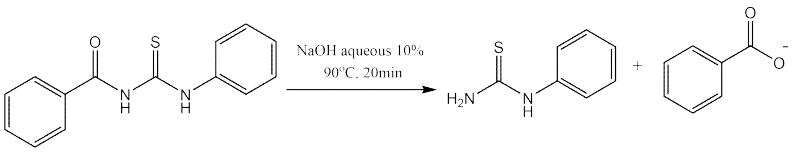
Substituted thiourea are important building blocks in organic synthesis of many heterocyclic compounds, such as thiazoles and benzothiazoles. Recent studied have been performed actively to investigate the potential pharmacological activities of substituted thioureas.

Experiment will progress two steps.



Intermediate A

Benzoyl chloride and ammoniumthiocynate react first, and then aniline addition occurs. The reaction completion can be decided through TLC.



A

Secondly, intermediate cleavage proceeds under base condition. Reaction completion can be decided from TLC analysis, diethyl ether as eluent on silica plates. Benzoate ion and 1-phenylthiourea(product) will be produced. For isolation of product only, pH control have to be applied. Ammonium chloride can make reaction medium to acidify to pH 8.

EXPERIMENTAL PROCEDURE **Two steps synthesis of 1-phenylthiourea**

Reagents and Properties

substance	*quantity*	*molar mass* (*g/mol*)	mmol*	*mp* (*°C*)	bp (*°C*)	*density* (*g/mL*)
Ammonium thiocyanate	0.837g	76.12	11			
Benzoyl chloride	1.16ml	140.6	10			1.21
Acetone	18ml					
Aniline	0.911ml	93.1	10			1.03
NaOH(2.5M)	15ml					
Saturated NH4Cl solution	~10ml					
Diethyl ether(TLC)	~10ml					

experimental stuff (erase later) two-neck round bottom flask(50ml), rbf(50ml)
reflux condensor
100ml beaker
pinch clamp
heating plate
vacuum filtrate
TLC & NMR analysis(Silica plates, chamber, D-CCl3)

PROCEDURE ***Caution***: Wear lab coats and safety goggles at all times while in the lab. Many chemicals are potentially harmful. Prevent contact with your eyes, skin, and clothing. Wearing contact lens is strictly prohibited.

Step 1 ***Caution***:

Experiment should be performed under fume hood. Benzoyl chloride is harzardous if skin contact occurs. Aniline is harmful if inhaled and is a potential methemoglobin-forming agent. Both intermediate and product of this experiment can cause skin irritation, so they must be handled with care.

Charge two-neck round bottom flask(50ml) with 0.837 g(1.1mmol) of ammonium thiocyanate and 1.16ml of benzoyl chloride under magnetic stirring at room temperature.

Connect round bottom flask to reflux condensor and heat at 60℃ for 15 minutes. While the reaction go on, dissolve 0.911ml of aniline to 3ml of acetone.

After 15 minutes, add aniline solution dropwise and continuously heat at 60℃ about 20 minutes more. Monitor aniline consumption with TLC.

Pour the reaction medium into 50ml of room temperature water. Gain precipitation via vacuum filtration and caculate intermediate, A's yield(NMR analysis of intermediate can be added).

Step 2 Add 2.3g of intermediate A(8.9mmol) to 15ml of 2.5M NaOH solution in 50ml round bottom flask and stirr at 90℃ about 20 minutes. Monitor your reaction medium by TLC analysis with diethyl ether eluent. Then cool the reaction flask to room temperature.

Isolation Acidify the reaction medium to pH 8 with saturated ammonium chloride. The precipitation isolates by vacuum filtration and washes with water. Dry your product and calculate final yield.

NMR analysis ***Caution:*** Deutero-Chloroform is toxic and a suspected carcinogen. Dispense it in a fume hood. Wear protective gloves.
Product will dissolve in deutero-chloroform. Obtain the NMR spectrum as directed by your TA.

Pre-Laboratory Questions

1. Summarize all MSDS's of chemicals used in this experiment.
2. Write down the detailed reaction process of 1-phenylthiourea(Need hint?).
3. Search the literature pKa data of benzoic acid and 1-phenylthiourea. What pH would be preferred for isolation of 1-phenylthiourea?

Post-Laboratory Questions

1. Assign peaks in 1H NMR spectra of product.
2. Calculate your intermediate's and product's percentage yield.
3. Why aniline have to be added later than thiocyanate in step 1? Propose one possible reaction if three starting components added simultaneously.