Synthesis of Paracetamol

Structure

Principle

Procedure

1. Suspend 5.5 gm (0.05 mole of p-aminophenol in 15 ml of water (use tap water) contained in 100 ml conical flask.
2. Add 6 ml of acetic anhydride.
3. Stir (or shake) the mixture vigorously and warm on a water bath, the solid dissolves after 10 min.
4. Cool the flask under tap water.
5. Filter the solid acetyl derivative at the pump and wash with little cold water.
6. Recrystallize from hot water (about 100 ml) and allow to crystallize spontaneously.

Results

On the DRY PRODUCT carry out the following:

- Weigh the dry compound (actual yield).
- Determine the melting point.
- Label the product and submit it your demonstrator.

The label should include:

Product name, actual yield theoretical yield, % yield, melting point and your name.
Synthesis of Aspirin

Structure

Chemical Name

Acetylsalicylic acid.

Pharmacological Use

Analgesic, antipyretic and anti-rheumatic.

Principle

Procedure

1. Place 5 gm (0.3625) of dry salicylic acid and 7 ml (7.5 gm, 0.073 mole) of acetic anhydride in a small dry conical flask.
2. Add 3 drops of H₂SO₄ and rotate the flask to ensure through mixing.
3. Warm the flask on a water bath to about 50–60°C, with stirring, for about 20 min.
4. Cool the flask under tap water then add 75 ml of water, stir well and filter at pump.
5. Dissolve the solid in about 15 ml of hot ethanol, filter then add 35 ml hot water (if solid precipitate at this point, warm the mixture until solution is clear).
6. Allow cooling, needling like crystals of pure aspirin will separate.

Results

On the DRY PRODUCT carry out the following:

- Weigh the dry compound (actual yield).
- Determine the melting point.
- Label the product and submit it your demonstrator.

The label should include: Product name, actual yield theoretical yield, % yield, melting point and student name.
Synthesis of Benzimidazole

Structure

Principle

Uses

As a starting material in the synthesis of a lot of organic and medicinal compounds.

Procedure

Place 6.81 gm (0.062 mole) of o-phenylenediamine in a 100 ml round-bottom flask and add 4.4 gm (4 ml, 0.085 mole) of 90% formic acid. Heat the mixture on a water bath at 100°C for one hour. 20 ml H₂O add 10% NaOH solution slowly, with constant rotation of the flask, until the mixture is just alkaline to litmus paper.

Filter off the crude benzimidazole at pump, wash with ice-cold water. Drain well and wash again with 10 ml cold water. Dissolve the crude product in 150–200 ml of boiling water, add 1 gm of decolorizing carbon and boil for 15 min. Filter rapidly through a pre-heated funnel and flask. Allow to cool, filter off the benzimidazole, wash with 10 ml of cold water and dry at 100°C.

Results

On the DRY PRODUCT carry out the following:

- Weigh the dry compound (actual yield).
- Determine the melting point.
- Label the product and submit it to your demonstrator.
Synthesis of 5,5-Diphenyl Hydantoin

Place 5.3 g (0.025 mole) of benzyl, 3.0 g (0.05 mole) of urea, 15 ml of 30% NaOH solution and 75 ml of C₂H₅OH in a 250-ml round bottomed flask, attach a reflux condenser and boil under reflux using an electric heating mantle for 1½ hour. Cool to room temperature and pour the reaction mixture into 125 ml of water and mix thoroughly. Allow to stand for 15 minutes and then filter under suction to remove an insoluble by-product. Render the filtrate strongly acidic with conc. HCl, cool in ice-water and immediately filter off the precipitated product under suction. Recrystallize at least once from industrial spirit (about 150 ml). Concentrate the solution to 100 ml.
Synthesis of Chloramine T

Structure

Uses

Used as a source of chlorine for sterilization of water.

Principle

1. Toluene-p-sulfonyl chloride $\xrightarrow{\text{Ammonia}}$ Toluene-p-sulfonamide
2. Toluene-p-sulfonamide $\xrightarrow{\text{Ca. hypochlorite, Acetic acid}}$ Dichlormine T
3. Dichlormine T $\xrightarrow{\text{NaOH, H}_2\text{O}}$ Chloramine T
Procedure

Grind 10 gm of toluene-p-sulphonyl chloride into a fine powder. In 100 ml conical flask add 30 ml conc. NH₄OH to the powdered toluene-p-sulphonyl chloride and heat the mixture to boiling for 15 min. (in the fume cupboard). Cool, then filter at pump and recrystallize from boiling water about 200 ml (melting point 138°C).

Prepare about 200 ml of a saturated solution of calcium hypochlorite by grinding a fresh sample of the bleaching powder with water (filter with slight suction).

Dissolve 5 gm of toluene-p-sulfonamide in about 150 ml of calcium hypochlorite solution (heat a little if necessary). Cool in mice, then add 15 ml of 50% acetic acid slowly with stirring until precipitation is complete.

The dichloramine T separates first as a fine emulsion which rapidly forms colorless crystals. Filter the later at pump and wash with little cold water. Drain well and dry immediately between two filter papers. Recrystallize from light petroleum ether (b.pt. 60-80°C) which will give pure dichloramine T (m.pt. 83°C).

Heat 45 ml of 10% NaOH in a beaker to a temperature of about 80°C. Add 3.5 gm of dichloramine T in a small quantities, stirring the mixture gently after each addition until a clear solution is obtained. Filter the solution if turbid and allow it to cool spontaneously (put in the fridge) filter the crystals with suction, wash with a little amount of saturated sodium chloride solution. Dry upon filter paper or in a dissicator over anhydrous calcium chloride. It may be recrystallized if desired from twice its weight of hot water. It is a salt and has no definite melting point.

Results

On the DRY PRODUCT carry out the following:

• Weigh the dry compound (actual yield).
• Determine the melting point.
• Label the product and submit it your demonstrator.
Synthesis of Dulcin

Structure

\[
\begin{align*}
\text{H}_2\text{C}_2\text{O} & \quad \text{NHCONH}_2 \\
\end{align*}
\]

Chemical name

p-Ethoxyphenylurea

Use

Artificial sweetening agent.

Principle of Synthesis

1) \( \text{H}_2\text{N}=\text{CO}–\text{NH}_2 \quad \rightleftharpoons \quad \text{NH}_4^+\text{NCO}^- \quad \rightleftharpoons \quad \text{H}–\text{N}=\text{C} = \text{O} \)

2) \( \text{C}_2\text{H}_5\text{O} (\text{C}_6\text{H}_4)\text{NH}_2 \quad + \quad \text{H}–\text{N}=\text{C} = \text{O} \quad \rightarrow \quad \text{dulcin} \)

Procedure

In 250 ml r.b.f. place 7 ml of p-phenetidine, 12 gm of urea, and 25 ml of water. To this solution add 5 ml of conc. HCl and about 25 drops of glacial acetic acid. Adjust a reflux condenser, shake the solution well, and boil vigorously for 30 min., until the reaction is complete. At first the dark-colored solution remains clear, but in 15-20 min. the product begins to separate rapidly. When the mixture sets to semisolid crystalline mass, stop the heating at once. After cooling the flask under tap water add 20 ml cold water, cork the flask tightly and shake it thoroughly to make a slurry of the crystals. Collect the product on suction, wash it with cold water and press firmly. Recrystallize from boiling water (~30 ml/gm).
Results

On the **DRY PRODUCT** carry out the following:

- Weigh the dry compound (actual yield).
- Determine the melting point. (The literature melting point = 173-174°C).
- Label the product and submit it your demonstrator.
Synthesis of Benzoic Acid

Structure

\[
\begin{align*}
\text{COOH} \\
\text{C} \\
\end{align*}
\]

Principle

\[
\begin{align*}
\text{CH}_2\text{OH} & \xrightarrow{\text{KMnO}_4 / \text{Na}_2\text{CO}_3 \text{ reflux (60-90 min)}} \text{C} & \xrightarrow{\text{HCl}} \text{COOH} \\
\text{COONa} & & \text{COOH}
\end{align*}
\]

Uses

Preservative.

Procedure

Place 4 gm of anhydrous Na$_2$CO$_3$, 200 ml of water, 9 gm (0.057 mole) of MnO$_4$, 5 gm (4.5 ml, 0.04 mole) of benzyl alcohol and a few chips of porous porcelain in a 500 ml r.b.f.

Boil the mixture gently until the reaction is complete (60–90 min.), i.e. until the liquid running down from the condenser contains no oil drops of unchanged benzyl chloride. Allow to cool, add 50% H$_2$O$_2$ drop-wise with shaking until the color of KMnO$_4$ disappear and filter off the precipitated manganese dioxide. Acidify with conc. HCl, cool and then filter off the precipitated benzoic acid at pump, wash with cold water. Recrystallize from about 200 ml boiling water.

Results

On the DRY PRODUCT carry out the following:

- Weigh the dry compound (actual yield).
- Determine the melting point.
- Label the product and submit it your demonstrator.
Synthesis of Antipyrine

Structure

Chemical Name

1-Phenyl-3-methyl-5-pyrazolone

Uses

As a starting material for the synthesis of many medicinal compounds, such as antipyrine reduces pain and fever in migraines and chronic rheumatism).

Principle

\[
\text{Ethylacetoacetate} + \text{Phenyl hydrazine} \xrightarrow{\text{Heat}} \text{Antipyrine}
\]

\[
\text{N-methylation} \xrightarrow{(\text{CH}_3)_2\text{SO}_4 / \text{NaOH}} \text{1-phenyl-3-methyl-5-pyrazolone}
\]
Procedure for the Synthesis of 5-Pyrazolone Nucleus

In a 250-ml flask, containing 10 ml of redistilled ethylacetoacetate, add 7.3 ml gm of phenyl hydrazine and heat for one hour (on water bath, inside the hood) with occasional stirring until you obtain heavy reddish syrup. Pour the mixture in a beaker and evaporate. Allow the syrup to solidify by stirring with 20 ml ether and filter off the p.p. at pump. Wash, recrystallize from hot water.

Results

On the **DRY PRODUCT** carry out the following:

- Weigh the dry compound (actual yield).
- Determine the melting point.
- Label the product and submit it your demonstrator.