Preparation of Paracetamol from 4-aminophenol and Ethanoic anhydride

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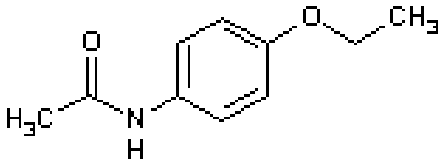
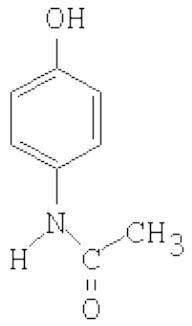
Abstract:
In this experiment I have synthesized Paracetamol from 4-aminophenol and ethanoic anhydride.

Introduction:
Paracetamol or acetaminophen is a very widely used analgesic and antipyretic. It is a relatively safe drug though toxicity has been observed with very high doses. Pure paracetamol is a white crystalline solid which melts at 169o C.It is sparingly soluble in cold water but in hot water it's solubility is about 5g/100mL. It is quite soluble in ethanol (14g/100mL). The drug phenacetin was formerly used an antipyretic to relieve fever. But long term use of phenacetin caused kidney damage. In 1893 Joseph von Merking discovered paracetamol which was found to be not only a good antipyretic but also a much safer one than phenacetin.



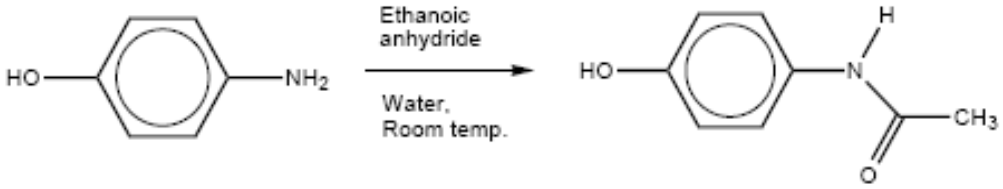
N-(4-Ethoxyphenyl)acetamide



Paracetamol

Synthesis:

- In this experiment paracetamol was prepared starting from 4-aminophenol.



Preparing *N*-(4-hydroxyphenyl)ethanamide – Paracetamol

STEPS:
1.1.0 g of 4-aminophenol and 9 cm3 of distilled water was placed in a 50 cm^3 conical flask and stirred briskly at room temperature, in order to suspend the solid in the water.

2. In a fume cupboard, 1.1 cm^3 (1.17 g) of ethanoic anhydride was added to the stirred suspension and gently shaken to mix. The solid got dissolved after about 30 seconds. Shaking was continued until a precipitate was formed.

3. After 10 minutes the solid was filtered off under suction, washed with a little cold water and dried (0.83g; 60%).

4. The product was purified by crystallisation from distilled water, by dissolving the crude product in the minimum of distilled water at about 80 °C

5. The clear solution was allowed to cool slowly to room temperature and the recrystallised product was collected by suction filtration.

6. The recrystallised product was dried between filter papers, and the yield was determined.

7. The melting point of the dry, recrystallised product was also noted.

Discussions:

Choice of the starting material:

Starting material for any synthesis should be such that it is easily available.

Phenol though easily available, was not used as a starting material because of the difficulty of separation of the isomers after nitration and the subsequent reduction.

So 4-aminophenol was used as the starting point.

Precautions:

Though $-NH_2$ is more nucleophilic than –OH, excess Ac_2O should be avoided as there is chance of double acetylation of 4-aminophenol.

Also high temperature is to be avoided.

Percentage Yield:

The yield was about 45% of the theoretical yield.

Conclusion and Utility:

The yield of paracetamol by this method is considerable. To improve the yield further, the filtration should have been done at further low temperature.

Regarding utility, the product prepared is of immense medical use.

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