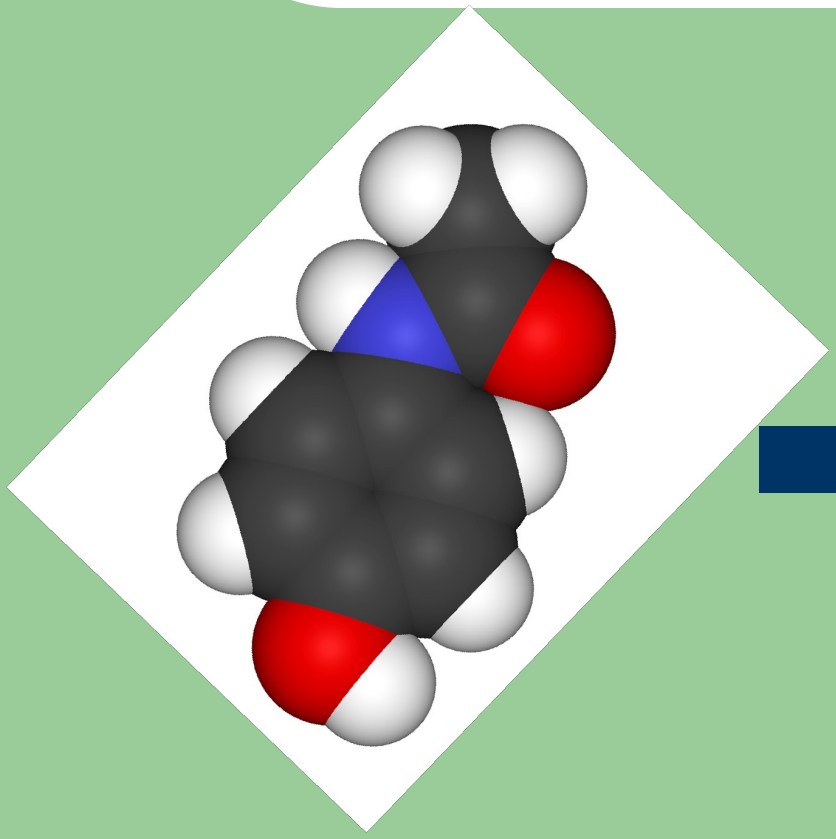
Preparation of Paracetamol from 4-aminophenol and Ethanoic anhydride



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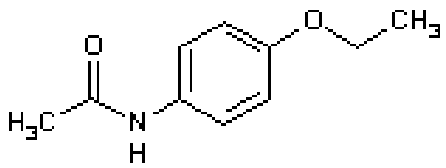
What is paracetamol?

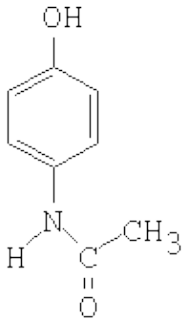
- Paracetamol or acetaminophen is a very widely used analgesic and antipyretic. It is a relatively safe drug though toxicity has been observed with very high doses.
- Pure paracetamol is a white crystalline solid which melts at 169^{o} C.It is sparingly soluble in cold water but in hot water it's solubility is about 5g/100mL. It is quite soluble in ethanol (14g/100mL).

Background history:

- 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.



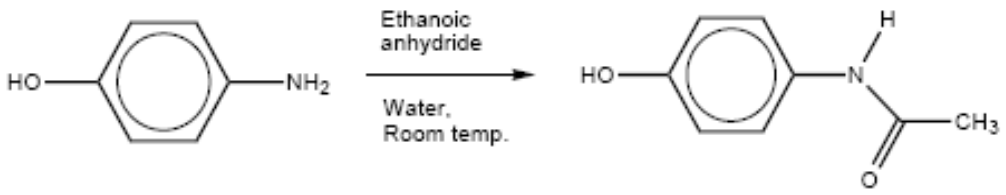
N-(4-Ethoxyphenyl)acetamide



Paracetamol

Synthesis:

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



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

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.

Isolation and Purification:

- The product was isolated by suction filtration and purified by recrystallisation from distilled water.
- The recrystallised product was dried by gentle warming.

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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Thank You.