College of Pharmacy	الكلية
Pharmaceutical Chemistry	القسم
Pharmaceutical Organic Chemistry II	المادة باللغة الانجليزية
الكيمياء العضوية الصيدلانية	المادة باللغة العربية
Fourth grade	المرحلة الدراسية
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Paracetamol synthesis	عنوان المحاضرة باللغة الانجليزية
تحضير البراسيتامول	عنوان المحاضرة باللغة العربية
9	رقم المحاضرة
	المصادر والمراجع
Alibhai, M. H., Boyd, D., & Fraser, J. M. (2002). Process for separation of phenol and acetone. WO2002022532A1. Retrieved from	

محتوى المحاضرة

Paracetamol synthesis

Preparation of paracetamol (P-acetamido phenol)

M.wt=151.2(gm/mole)

Acetaminophen is a P- acetamido phenol or it is N-acetyl P-aminophenol or 4-hydroxy acetanilide.

Physical properties:

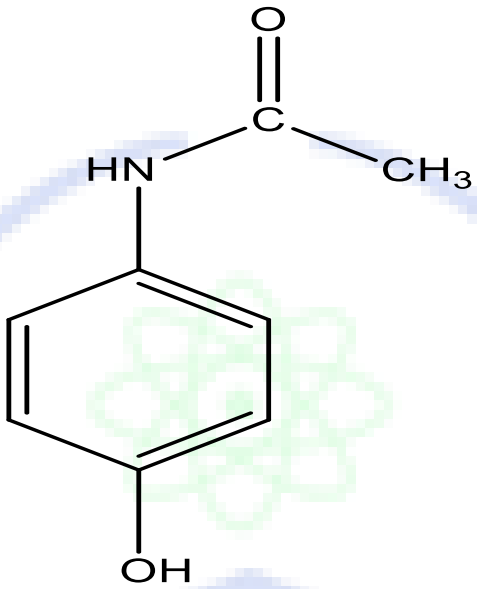
Odorless , white crystals with bitter taste.

M.pt. = 169-172 C0

Solubility: **one part(slightly soluble in water and ether) in 70 parts of water and in 7 parts**

Of alcohol ,soluble in alkali solution(like NaOH),

soluble in boiling water (1:20)

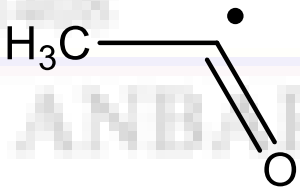


Acetylation methods:

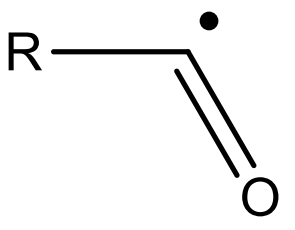
Introduction

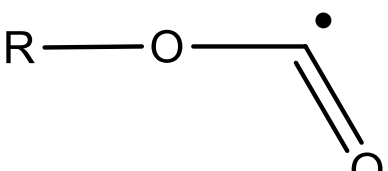
The replacement of '*active hydrogen*' of compounds belonging to the class ROH (phenols or alcohols), in addition to compounds of the category RNH2 and R2NH (*i.e.*, *primary*- and *secondary*-amines may be acetylated directly, whereby the reactive H-atom is

specifically replaced by the acetyl radical "acetylation"



And may be it done by acylation





Also by esterification process

Preparation of paracetamol

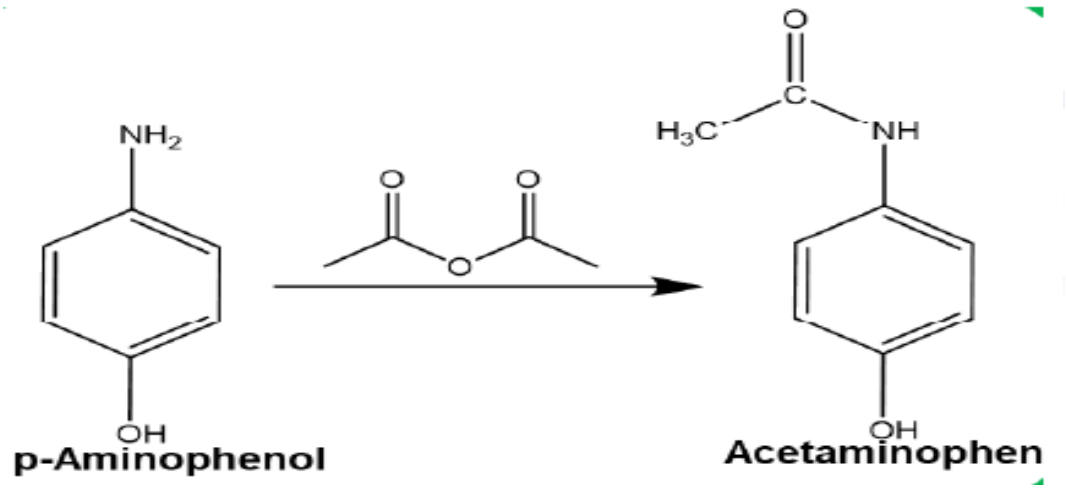
- ***Action and uses:*** **it has analgesic and antipyretic actions but has no anti-inflammatory properties.**
- ***Side effects:*** **like that of acetanilide, affect heart and may cause skin reaction and a jaundice condition (they occur less frequently and less severity) .in doses used for analgesia ,it is relatively safe drug.**
- ***Preparation:*****It may prepared by reduction of P-nitrophenol in glacial acetic acid . acetylation of P-nitrophenol by using acetic anhydride.**

Reactivity towards acetylation:

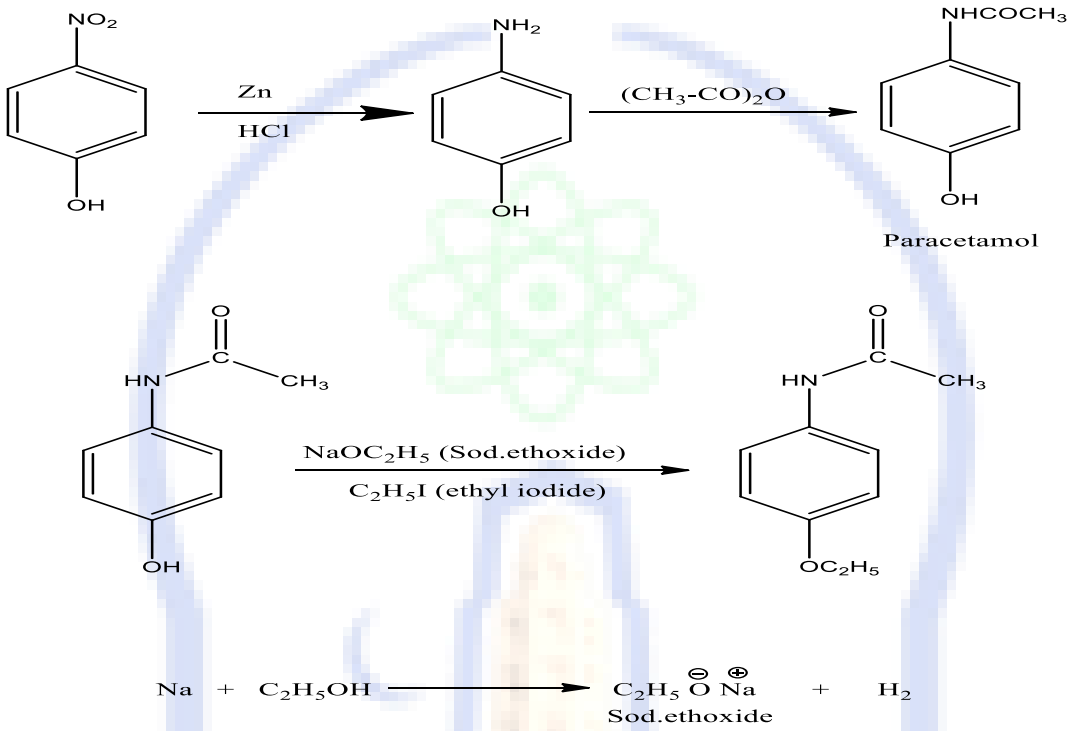
Acetyl chloride > acetic anhydride > acetic acid

The best one: acetic anhydride.

Easily handled, safe and reaction can easily be controlled.



Their characteristic reactions are with nucleophilic reagents, acetic anhydride reacts with compound containing active hydrogen atom to form derivatives containing acetyl group



- ***Physical properties of phenacitin:*** **stable ,white ,glistening crystals or powder.it is odorless and has a slightly bitter taste.**
- ***Solubility:*** **Very slightly soluble in H2O , soluble in alcohol and chloroform but slightly soluble in ether .it is sparingly soluble in boiling H2O it is a neutral compound and will not dissolve in either acids or alkalis.**
- ***Action and uses:*** **it is used widely as an analgesic and antipyretic. the toxic effects are the same as that of acetaminophen (the active form of phenacetin in that it is converted in the body to paracetamol)**
- ***Toxicity:*** **phenacetin may damage the kidneys when used in large dose or for long period of time.**

Precautions:

(1) All glass apparatus which are used in the synthesis must be perfectly dry.
(2) Concentrated sulphuric acid should always be added with great caution.
(3) To complete the reaction mixture it must be warmed at 60°Cfor 20–25 minutes.

Recrystallization:

Dissolve the crude product in 70% (*v/v*) ethanol and warm it to 60°C ; add 2 g of powdered animal charcoal (decolorizing carbon). Filter and concentrate the filtrate over a water-bath. Allow it to cool and large monoclinic crystals will separate out.

The yield of the pure paracetamol (mp 169–170.5°C) is 6.5 g.

Synthesis of chlorobutanol

Procedure:

1-Mix 25 ml acetone in dry conical flask with 10 ml chloroform

2-Cool the mixture (3-7 min).

3-Prepare alcoholic KOH (1.75 gm KOH / 12.5 ml ethanol) & put the mixture in a burette

4-Add this solution (alc. KOH) drop wise from burette on the previous solution within a period of 10 min.

5-Filter the ppt. KCl

6-Evaporate the filtrate on hot plat and then filter

Calculations:

Theoretical yield/Practical yield

Wight of *p*-Aminophenol on acetylation with Volume of acetic anhydride yields Paracetamol = Wight g

Hence, Theoretical yield of Paracetamol = **g**

Reported Practical yield = g

Therefore, Percentage Practical yield = Practical yield Theoretical yield 100 =