

تفريغ لاب ميديسنال



المحاضرة: Benzocine Synthesis
(Exp 2)

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لجان الرُفُعات

* الكون بالدنرو وهاي التجربة *



SYNTHESIS OF BENZOCAINE

Ali Salama

التجربة هبيرة

* كحيت كل كلام الدنور على السلايدات

بس يفضل سمعوا الريكور عشان ما

تضيحوا بالتفاعل , موش محب بس

بده تركيز + عشان تشوفوا

الخطوات العملية

بسم الله

* كيف؟ جعل Inhibition لـ Na^+ voltage gated Channel إلى مسؤول عن depolarizing Action potential
ويمنع الـ

Introduction

- Benzocaine is a local anesthetic that works by blocking nerve signals to produce numbness. It is widely used to ease pain from minor skin irritations, sunburn, sore throat, ingrown toenails, hemorrhoids, and vaginal or rectal discomfort, as well as other superficial pains. It may also be applied inside the mouth, nose, throat, vagina, or rectum to reduce discomfort during procedures involving medical instruments such as tubes or speculums.

- Benzocaine is a common ingredient in cough drops and topical pain relievers. It is generally considered safe, but a rare yet serious side effect is methemoglobinemia, a condition that decreases hemoglobin's ability to carry oxygen and can be life-threatening.

← بأدوية الـ
Cough

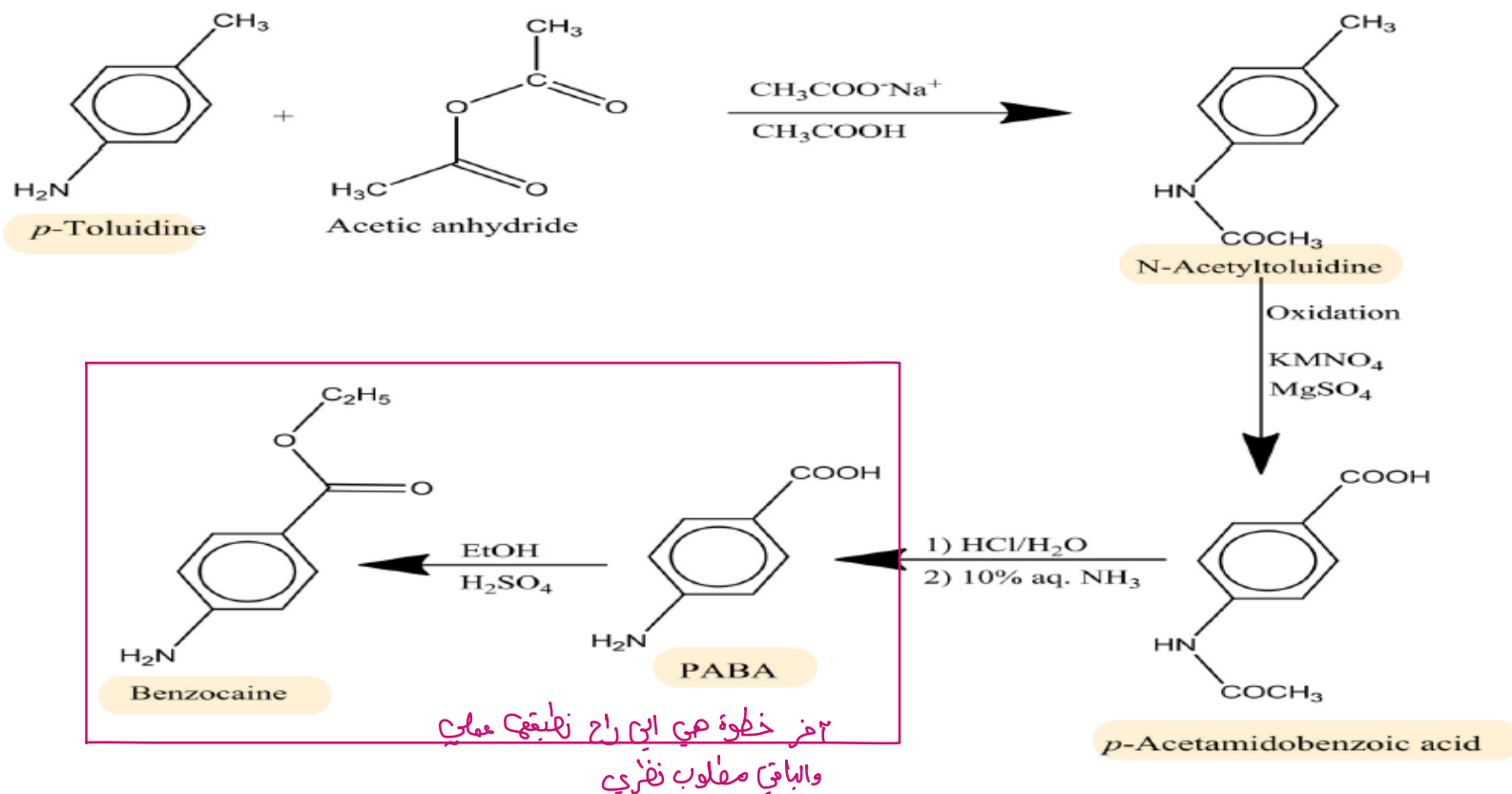
← انه الـ
Hemoglobine
الموجود بالدم
يبدل قارانه
ليحمل الـ O_2

لانه يتحول من

Hemoglobin → Methemoglobin

* إجراءات عالية *

General scheme of synthesis

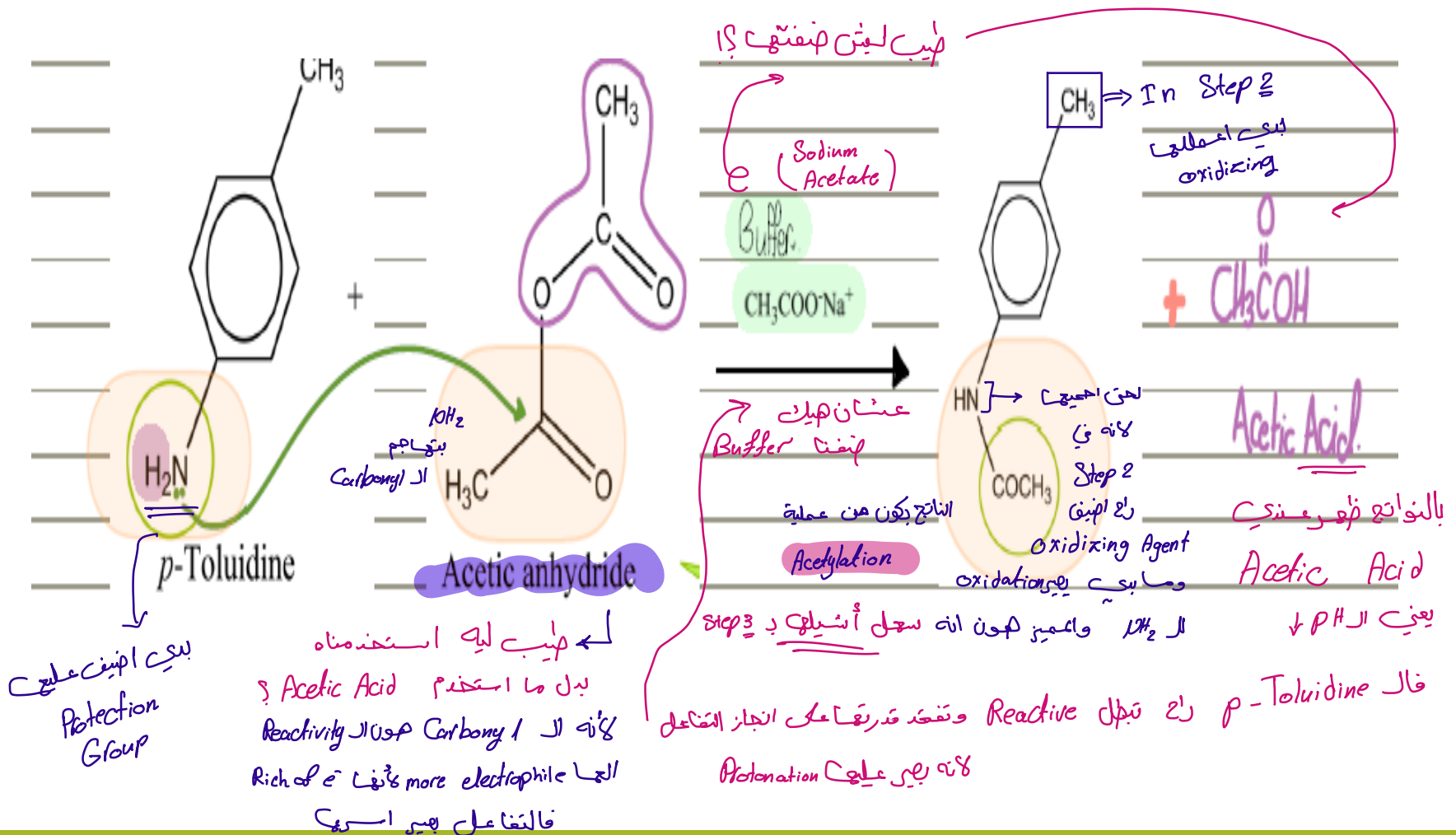


* وظيفتي الاساسية اننا نعمل Protection لـ NH_2

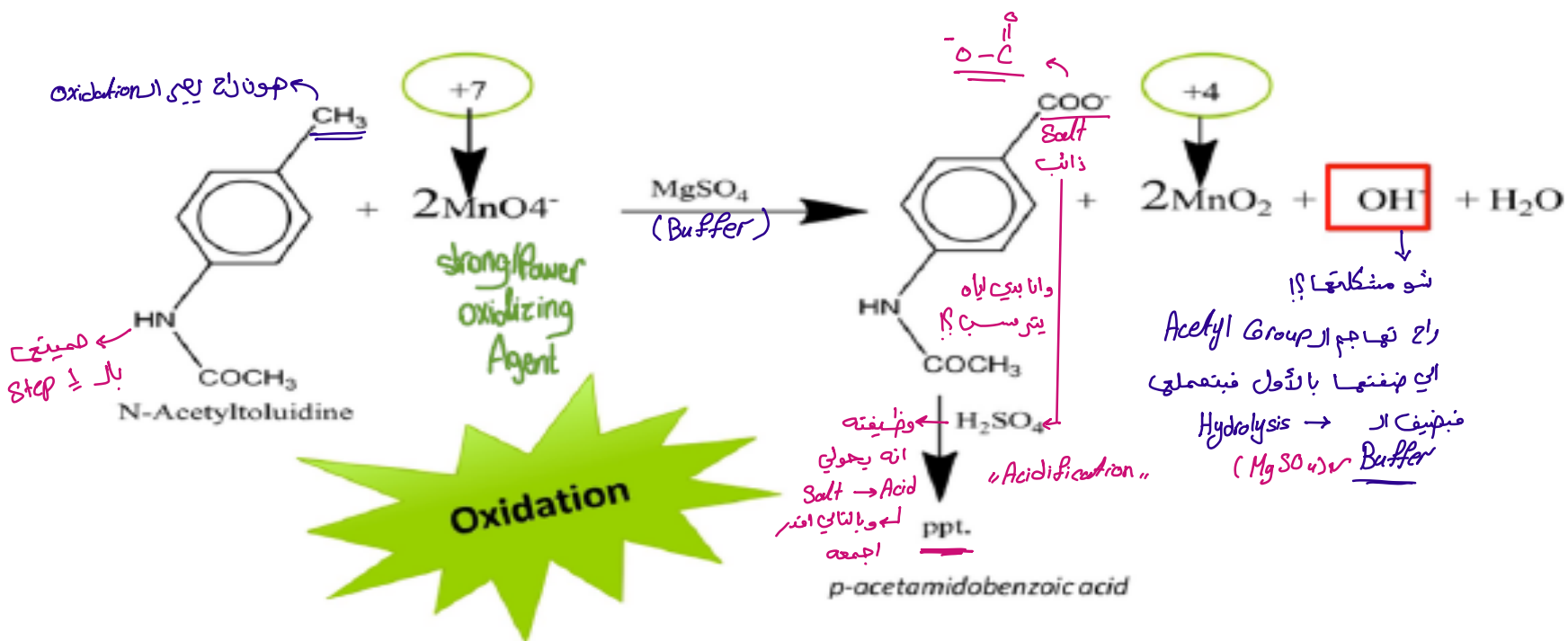
Mechanism of Action :

Nucleophilic Addition - Elimination Reaction

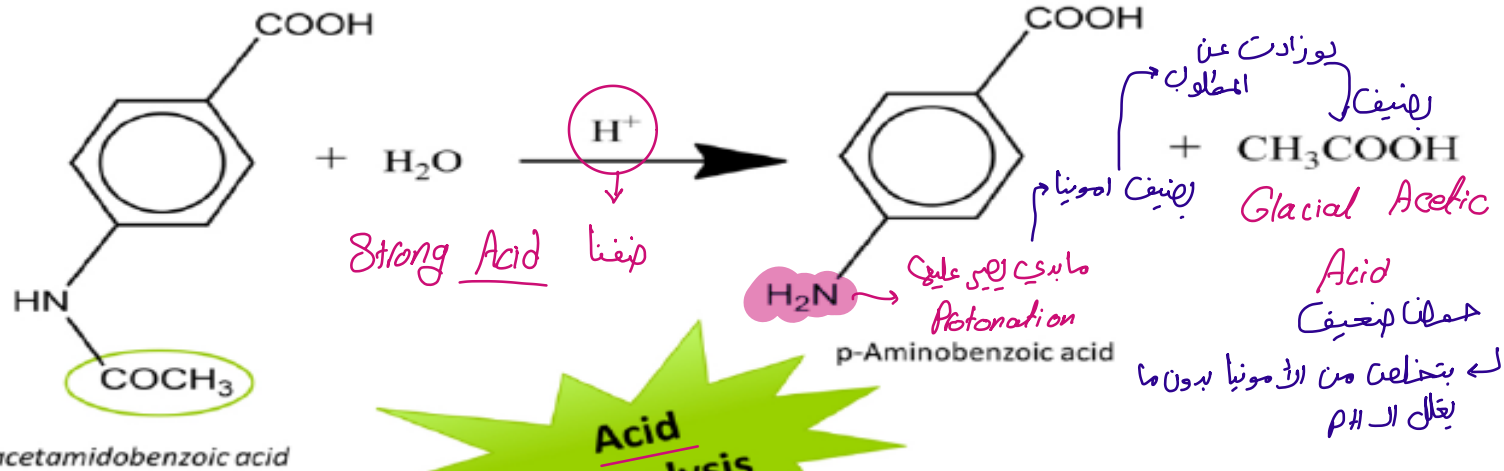
-Step 1 : Synthesis of p Acetotoluidide



Step 2 : Synthesis of p-acetamidobenzoic acid



Step 3 : Synthesis of p-aminobenzoic acid (PABA)



ال Acetyl Group الي بنفها ب Step 1 بيدي
 أشيلها

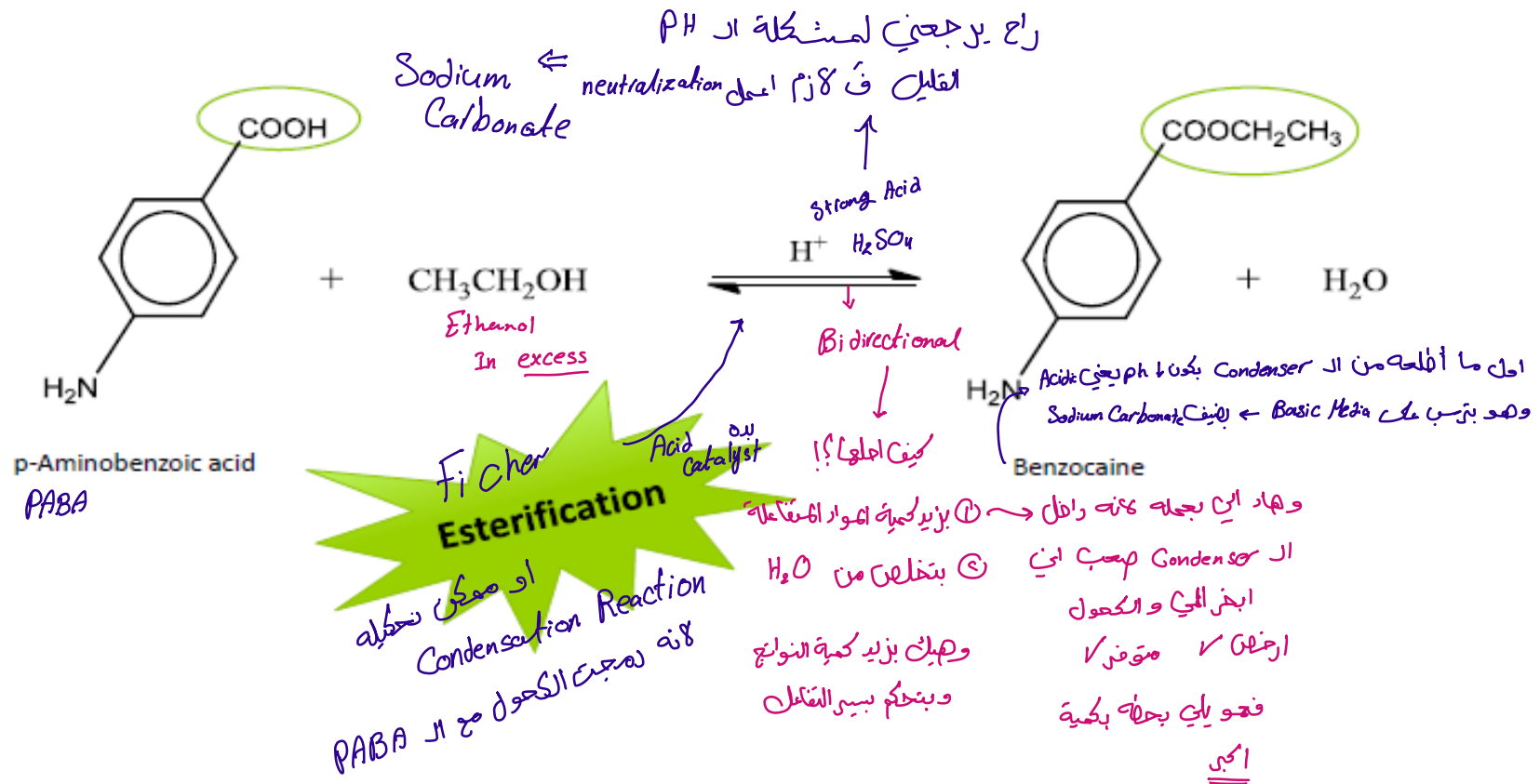
كيب ليش الامونيا NH₃?

لا نغلا Acid Scavenger يعني بتخلع من كل ال Acid الزيادة

لو بنفنت كمية زيادة من الامونيا ← بضعف Glacial acetic acid
 ما بأشعل
 Weak acid
 Acidity

عشان ما تزيد ال Acidity كثر وينزل ال pH
 لبي اعمل Neutralization فبيخدم الامونيا لحن اتخلع
 من ال Acid الزيادة ، عشان ما يهي في Protonation
 على ال Amine Group الي تكونت عندي

Step 4 : Synthesis of Benzocaine



Recrystallization of benzocaine from methanol-water (Mixed-solvent method)

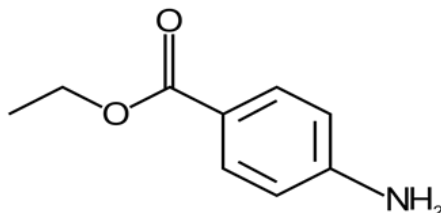
- Mixed-solvent Recrystallization is used when a suitable solvent cannot be found, find a pair of solvents that in combination provide the appropriate solubility properties.
- Our product should be too soluble in one of the solvents for its use alone and too insoluble in the other solvent for its use alone
 → Methanol
- Our product is dissolved at an elevated temperature in the solvent that is more soluble in it, and the other solvent is then added drop wise at elevated temp. until turbidity appears and doesn't clear upon shaking .

الكلام الي بالعانيوال

مكرر + ال Procedure
موجبات

Cycle 1

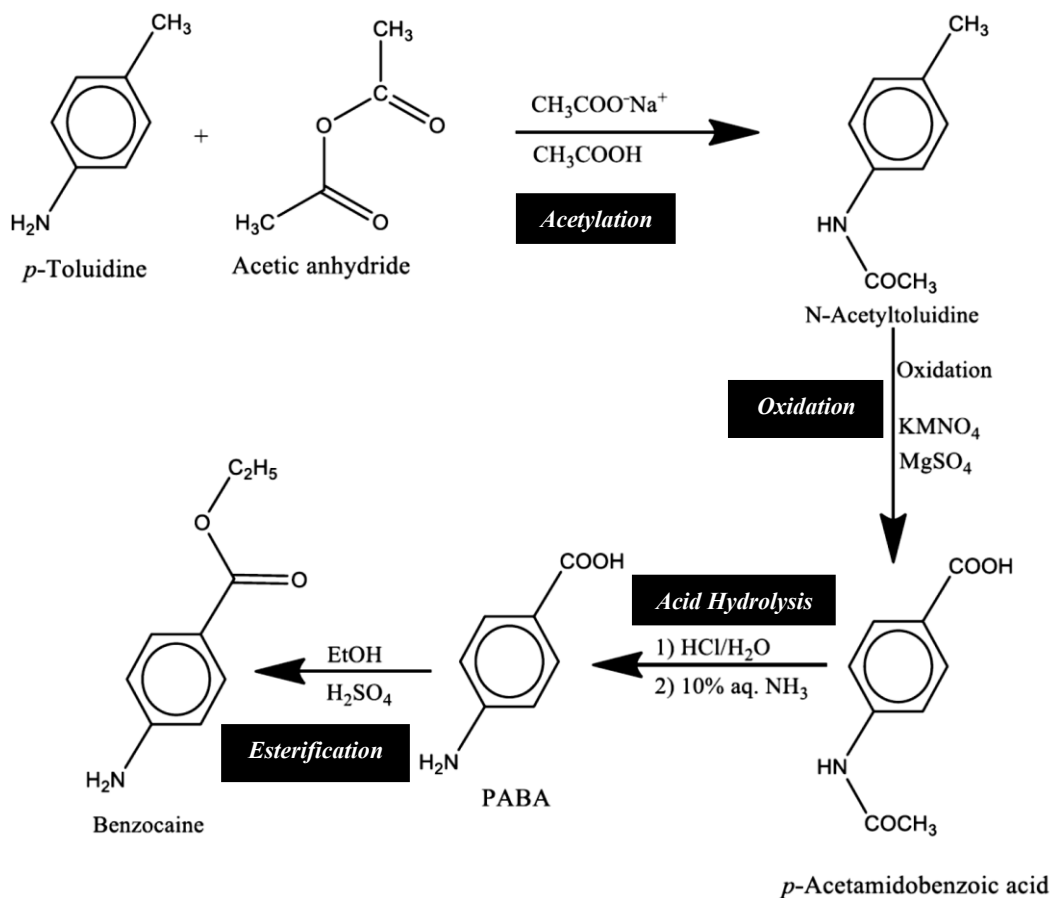
Multistep Synthesis of Benzocaine



Target Product

- Benzocaine is a local anesthetic from the ester family.
- The drug benzocaine is used in multiple forms including lotion, gel, liquid, lozenges, and sprays as a topical pain reliever.
- When Benzocaine is applied in any form, it temporarily numbs or blocks the nerve endings by inhibiting the voltage dependent Na channels on the neuron membrane, which leads to decrease in the amount of pain.

General scheme of synthesis



Four-step synthesis is used to create benzocaine:

Part 1: Synthesis of *p*-Acetotoluidide

Part 2: Synthesis of *p*-Acetamidobenzoic acid

Part 3: Synthesis of *p*-Amino benzoic acid (PABA)

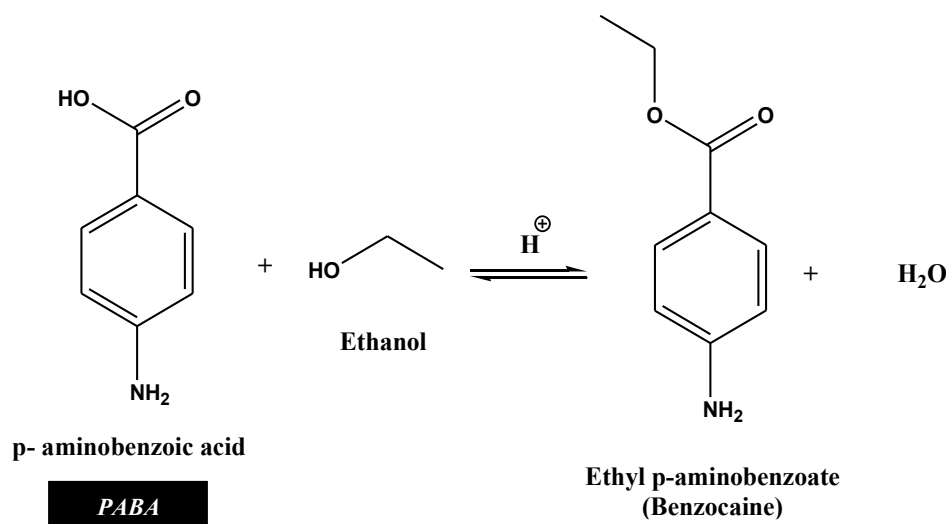
Part 4: Synthesis of Benzocaine

You will see the mechanism only for the forth steps.

Experiment 1

Multistep Synthesis of Benzocaine

Part 4: Benzocaine synthesis

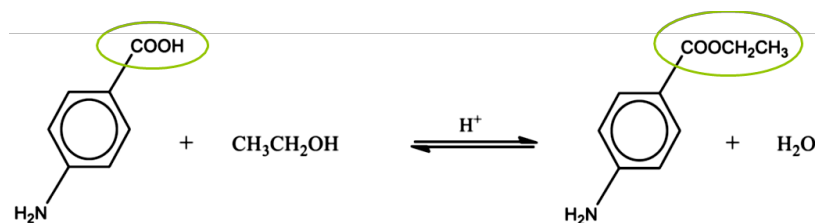


- Benzocaine is synthesized through the Fischer esterification of p-aminobenzoic acid (PABA) and ethanol, using sulfuric acid as a catalyst.
- PABA: is amphoteric that has weak acidic and weak basic properties.

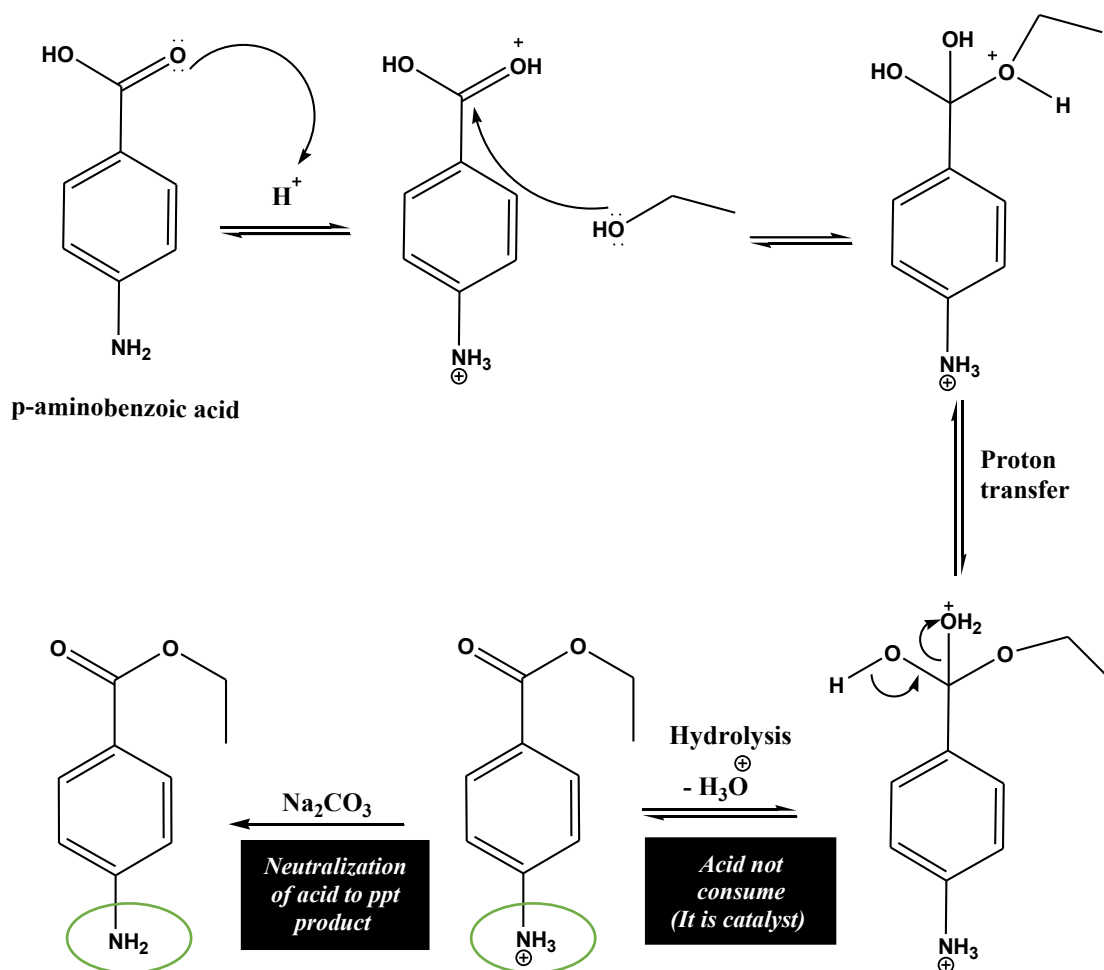
5 Assignment

5.1 Find a commercial synthesis pathway of PABA.

Mechanism



- This reaction is called **Fischer esterification reaction**: a type of **condensation** reaction (*both way reaction- limited yield*)
- It is acid catalyzed (*it not consume in the reaction*).
- It proceeds very slowly in absence of strong acids as HCl or H₂SO₄.



To increase the ester yield :

- Use excess from the reactants
- Remove water from reaction mixture as it is formed

جکنا عینہ

Procedure

1. In a 100 ml round-bottomed flask place 1.32 g of PABA, 10 ml of ethanol, and 1 ml of sulfuric acid (add cautiously). Add a couple of boiling chips* then attach a reflux condenser and heat under reflux for

20 - 30 min ~~1 hour~~

عشان أحلوه منه التفاعل بيتغير الكحول ويجمع ليكتشف ويكمل التفاعل

بيتغير اللون و بيحصل White ppt

2. Cool the solution to room temperature, neutralize with 10% sodium carbonate (foaming), and extract** with two 10-ml portions of dichloromethane (DCM) [use separatory funnel in extraction]. Then dry the

عادي لو ضفت معها زيادة عادي لانها ما بتفرغ ال pH كئي

combined organic layers over anhydrous magnesium sulfate [drying agent].⁽¹⁾

* ما عملناها موجود Benzocaine فالمي (Diluted) بس هو ما بنوب [drying agent] مينج فيها ؟!

3. Remove the dichloromethane by distillation using a steam bath as a heat source.

organic solvent → بخرد

← بدل معه organic solvent فبوا ال separatory funnel وبعدين 2 layers

4. Then recrystallize the residue from methanol-water [Mixed solvent recrystallization].⁽²⁾

← رصيفه على اهرام Benzocaine + methanol → Clear
بعد اضافة H₂O (dropwise) وبعدين بسجنه على Hot Plate Benzocaine يترسب

- (1) Add 3-4 gm of anhydrous magnesium sulfate, swirl the mixture for about 5 minutes, and then remove it by gravity filtration.

لـ بخره ب ice Bath وبعدين Scrub ال flask ب glass Rod

- (2) Add 5 ml portions of methanol (with heating) until all the amount is dissolved, then add water drop wise until the solution becomes turbid, after that cool it in an ice bath to complete crystallization.

↓
بتكون ال Crystals ← بخلها filtration

	Weight (gm)	M.P
Benzocaine		

2 Brain storming Question

- 2.1 Discuss the reason behind doing extraction in DCM, and define the component for each layer.
- 2.2 Discuss the reason behind adding drying agent for the organic layer.

*Refer to appendix V: Boiling chips ما بخله

†Refer to appendix III: Recrystallization-Mixed solvent recrystallization.

**Refer to appendix VII: Extraction.