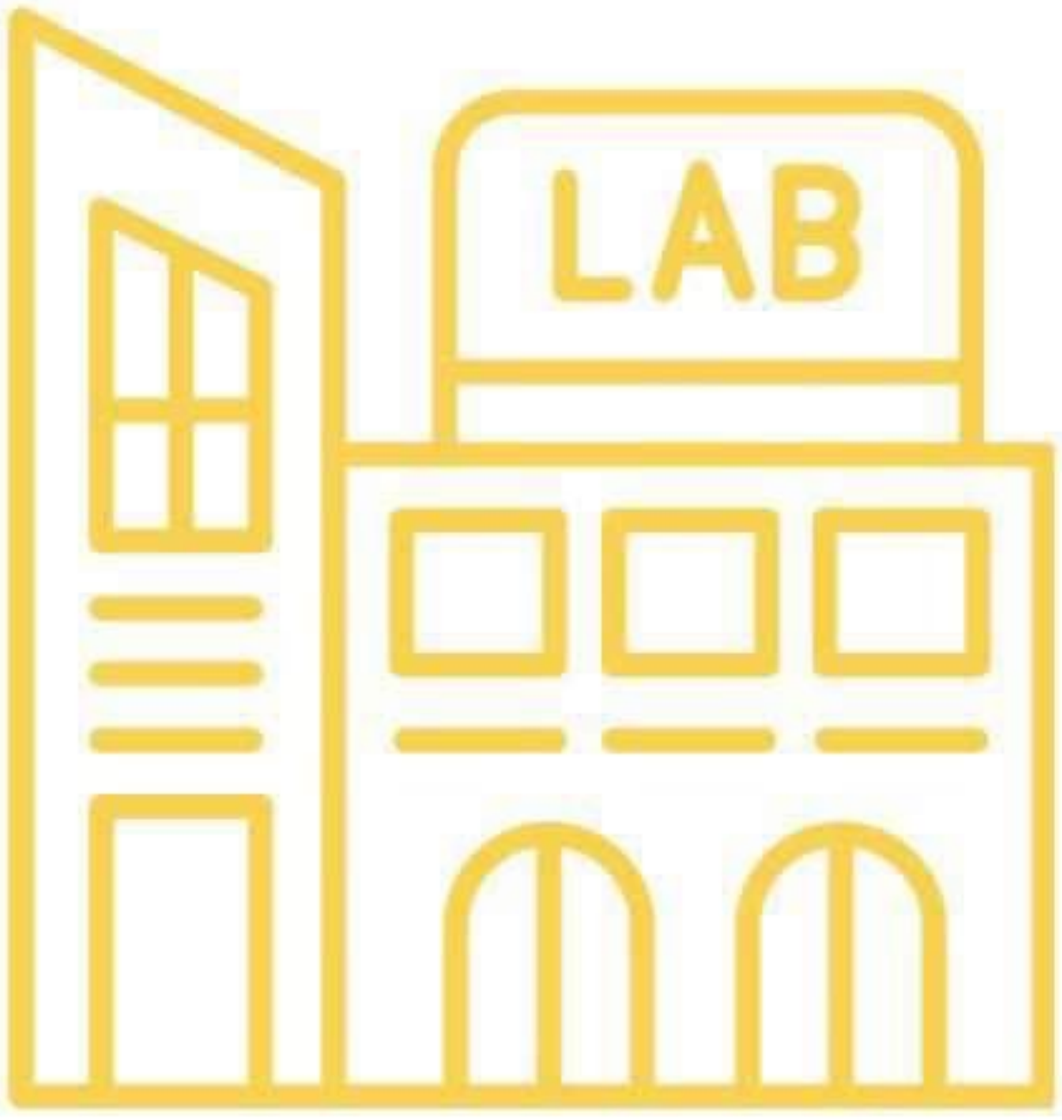


MIRACLE
Academy

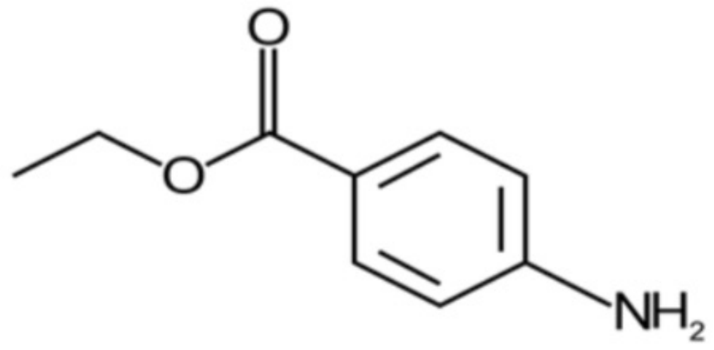
لاب ميدسينال
زميلتكم شيماء ياسين

لجان الدُّفعات

قال تعالى (يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ)

Cycle 1

Multistep Synthesis of Benzocaine

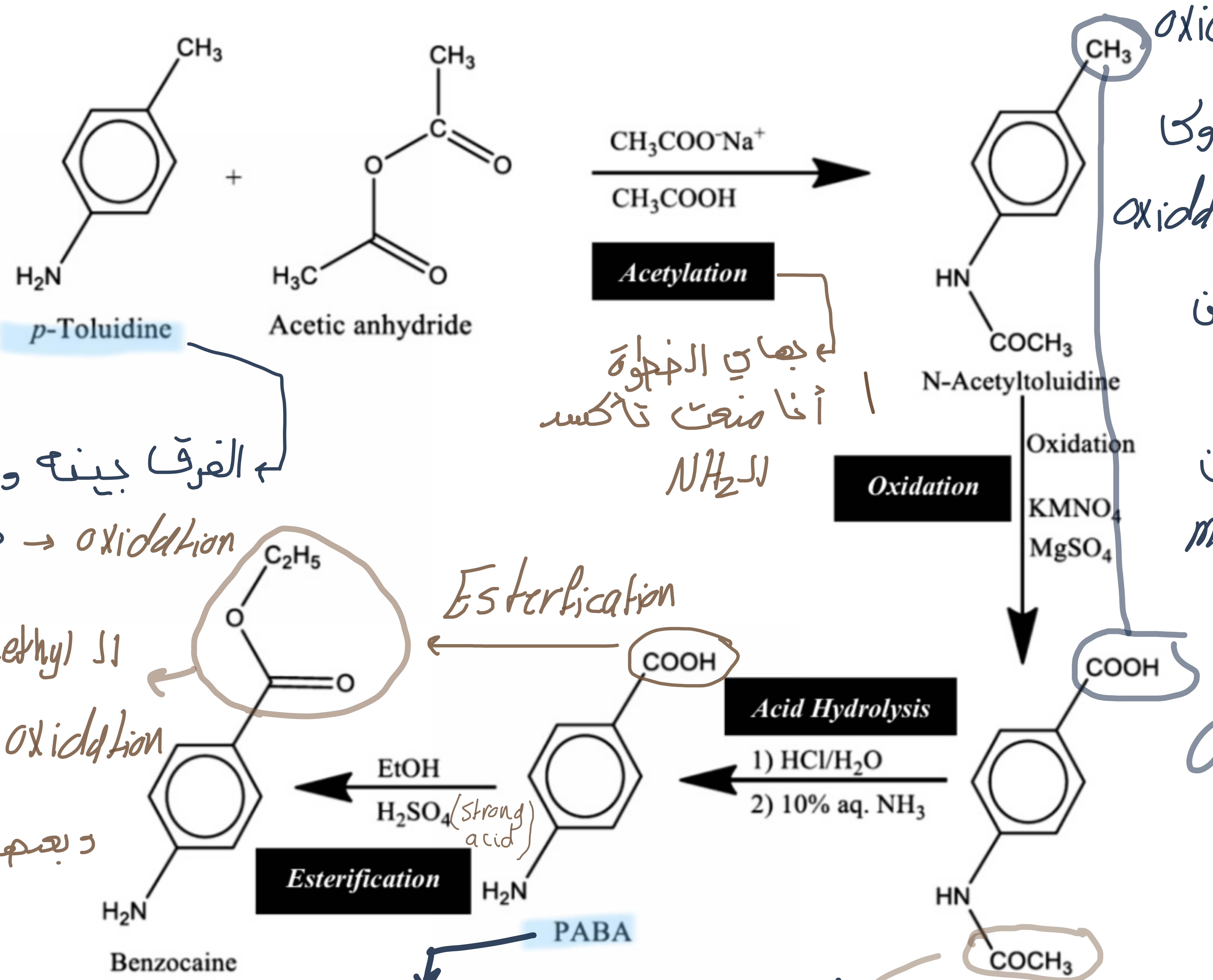


Target Product

- 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.

← حسب ال Scheme بنقدر نصنع ال Benzocaine عن طريق ← P-Toluidine

General scheme of synthesis



← إذا عملت oxidation مباشرة كخطوة أولى لح يصير ال oxidation لل NH_2 والمفروض أمنع ال oxidation لل NH_2، لأنه الهدف يكون على ال methyl

لهيك في الخطوة ا أنا منعت تأكسد ال NH_2

الفرق بينه وبين ال Benzocaine

① methyl group → oxidation

ال methyl تحولت بال oxidation لـ Carboxilc acid وبعدها نعمل Esterification

Esterfication

(strong acid)

oxidation

P-Aminobenzoic acid

هون وصلنا أنه احنا أكسدنا ال methly group وحولناها لـ COOH

ضل علينا تشيل ال group اللي حطيناها لحماية ال NH_2

كيف؟؟ باضافة HCl/H_2O (Acid Hydrolysis)

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

Esterification الخطوة الأخير

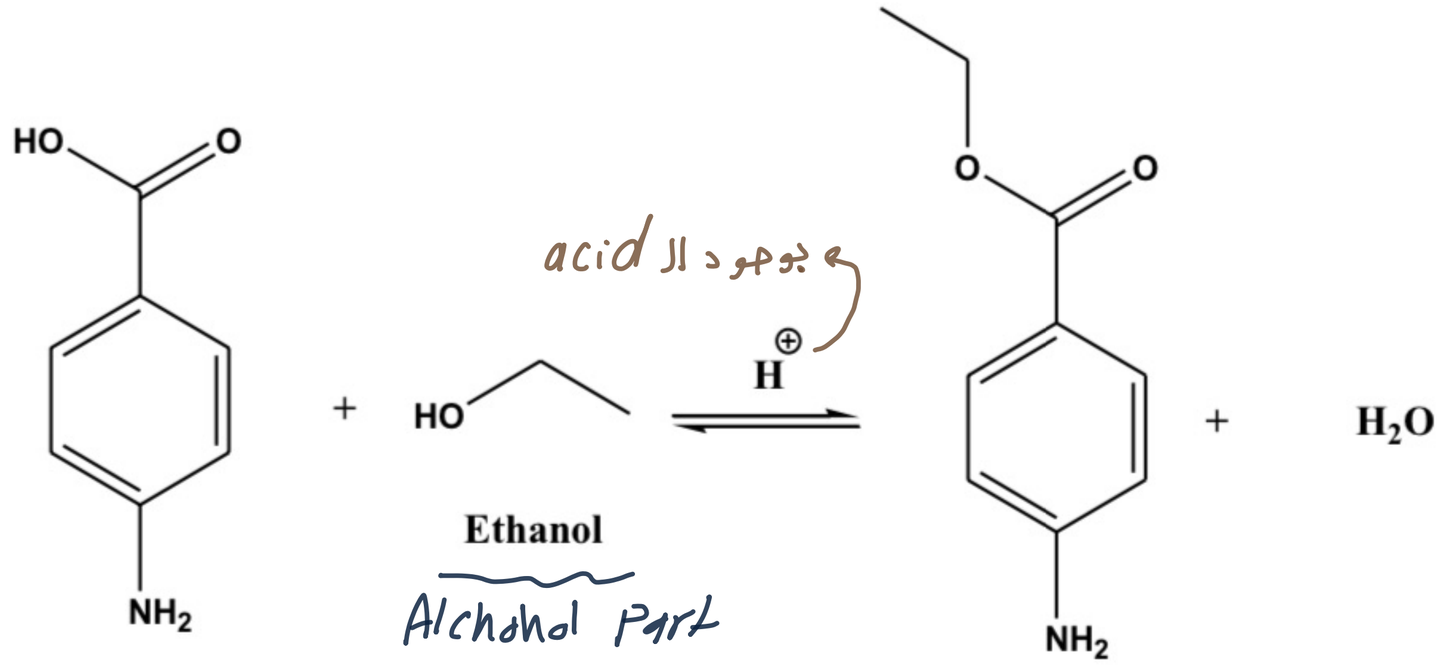
You will see the mechanism only for the forth steps.

في ال lab ما اشتغلنا غير الخطوة الأخيرة لأنه ال PABA متوفر عندي ورغم هيك الخطوات السابقة مطلوبة منا.

Experiment 1

Multistep Synthesis of Benzocaine

Part 4: Benzocaine synthesis



p- aminobenzoic acid

PABA

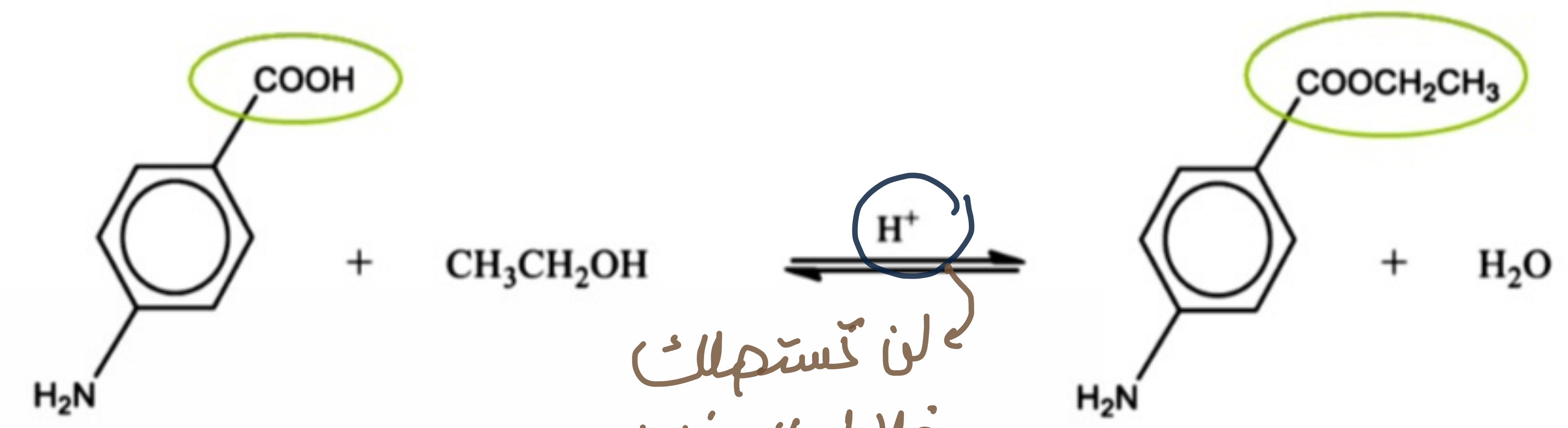
Ethyl p-aminobenzoate
(Benzocaine)

- 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.

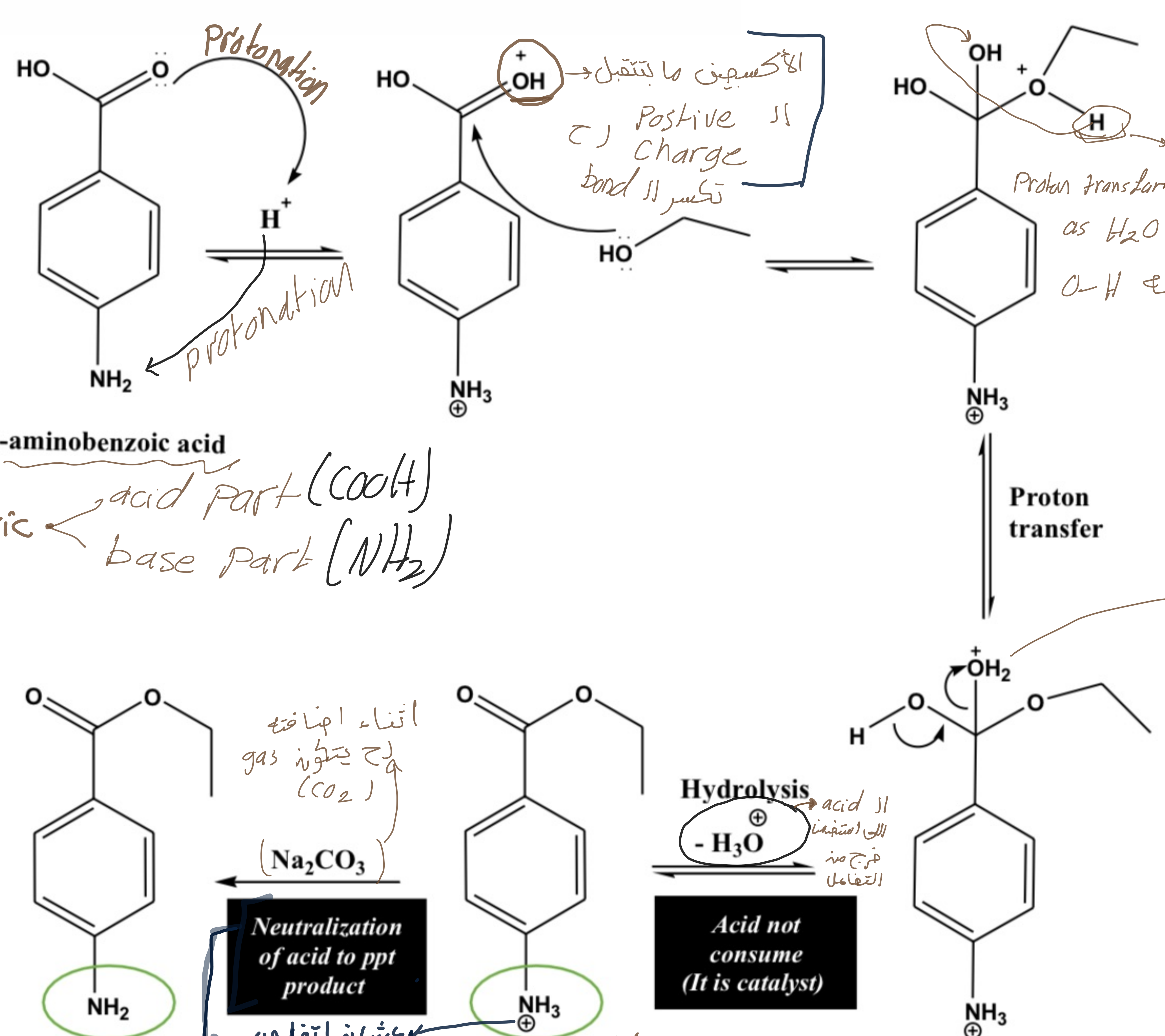
5 *Assignment*

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 :

1. - *Use excess from the reactants*
2. - *Remove water from reaction mixture as it is formed*

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 1 hour.
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 combined organic layers over anhydrous magnesium sulfate *[drying agent]*.(1)
3. Remove the dichloromethane by distillation using a steam bath as a heat source.
4. Then recrystallize the residue from methanol-water [**Mixed solvent recrystallization**‡].(2)

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

(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.

	Weight (gm)	M.P
Benzocaine		

2 *Brain storming Question*

2.1 Discus the reason behind doing extraction in DCM, and define the component for each layer.

2.2 Discus the reason behind adding drying agent for the organic layer.

*Refer to appendix V: Boiling chips
‡Refer to appendix III: Recrystallization-Mixed solvent recrystallization.
**Refer to appendix VII: Extraction.