

تفريغ لاب ميديسنال



Phenytoin Synthesis
Part 1

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المحاضرة:

الصيدلاني/ة:



لجان الدفوعات

SYNTHESIS OF [PHENYTOIN] PART 1

عبارة عن
Cycles

راح نشغل 3 Steps

Ali Salama

هون

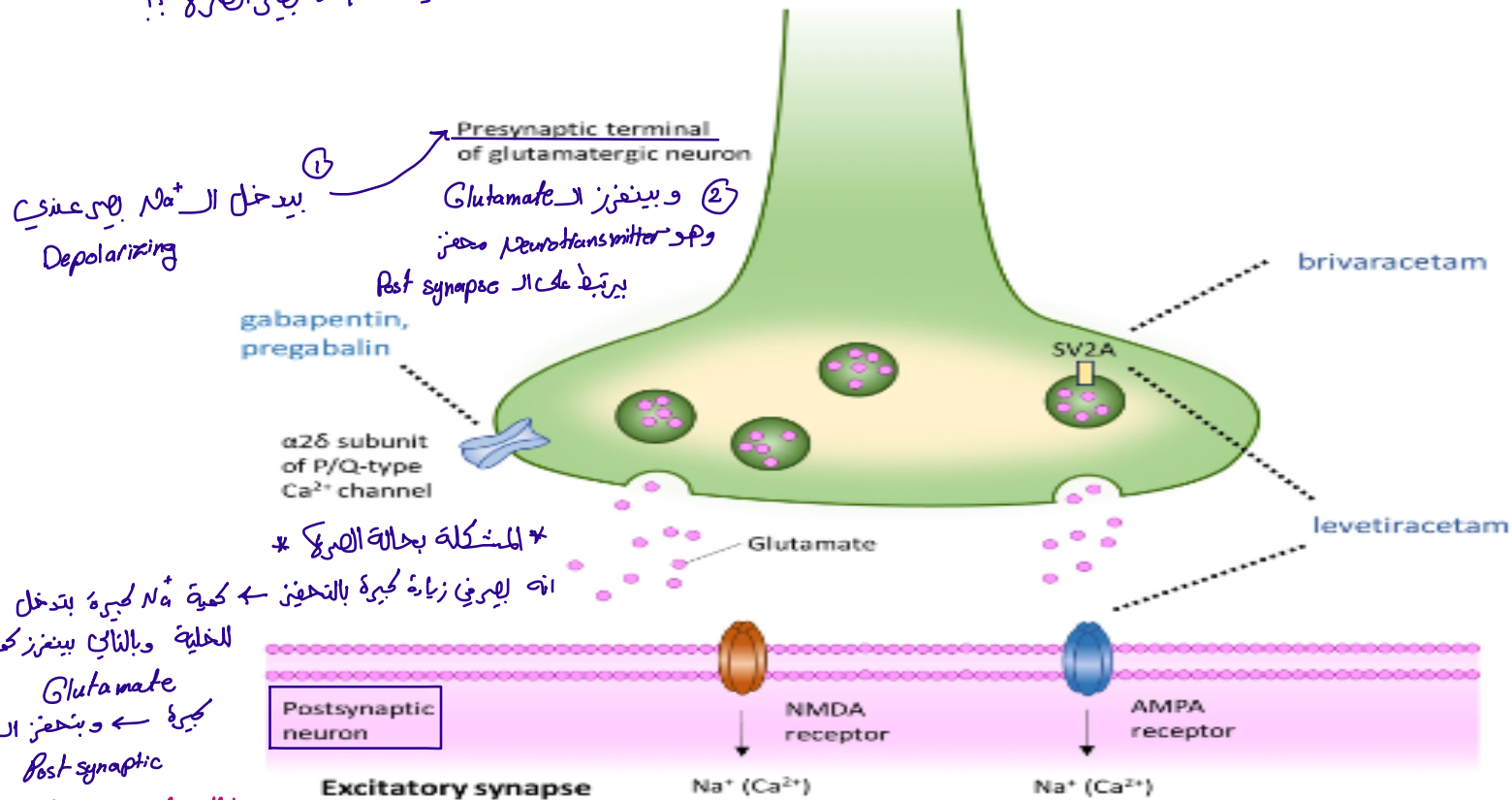
وكل وحدة معقدة على
الي قبلها

Introduction

- Phenytoin ^{مهدئات تشنج} is an anticonvulsant drug used to prevent and control seizures. ^{نوبات الصرع}
- It works by stabilizing neuronal membranes and decreasing excitability. ^{① ②}
- Commonly sold under the brand name Dilantin®. ^{الاسم التجاري}
- It can also be used to manage certain types of cardiac arrhythmias. ^{لأنه يخلل دخول الصوديوم ويمنع من الـ Action Potential}
- Unlike some other antiepileptics, it does not have sedative or hypnotic effects. ^{التي تتميز بالـ Phenytoin عن الباقي}
- Routes of administration include oral and intravenous forms.

Introduction

ليه أهدأ بهي الصرع؟!



* المشكلة بحالة الصرع *

انه ليعرفي زيادة كبيرة بالنحفن ← كمية Na^+ كبيرة بتدخل للخلية وبالتالي بينفرز كمية كبيرة ← وبنحفن الـ Glutamate Post synaptic

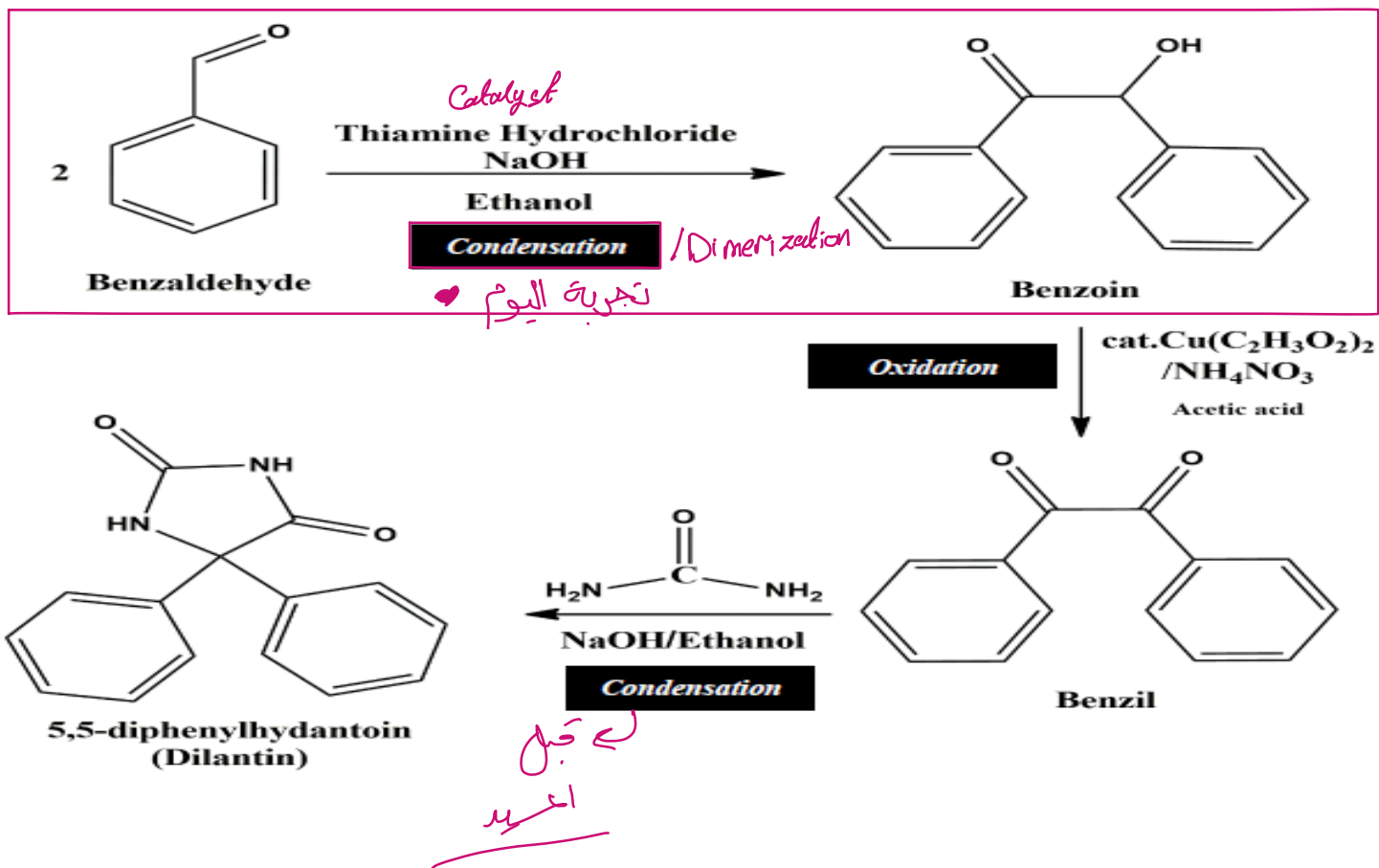
بالتالي أدوية الصرع راح

* تحل Block دخول الـ Na^+

* او بتزيد تركيز GABA «مثبط»

* وهدأ بهي الـ Glutamate *

General scheme of synthesis



Step 1 :benzoin condensation

- Benzoin is produced by dimerization of 2 molecules of benzaldehyde, The benzoin condensation is in fact a dimerization and not a condensation because a small molecule like water is not released in this reaction

- This reaction doesn't occur spontaneously. *عشان التفاعل يمشي بسرعة* It needs a catalyst to render the aldehydic carbon acidic so that it can be deprotonated and function as a nucleophile to attack the second benzaldehyde carbon.

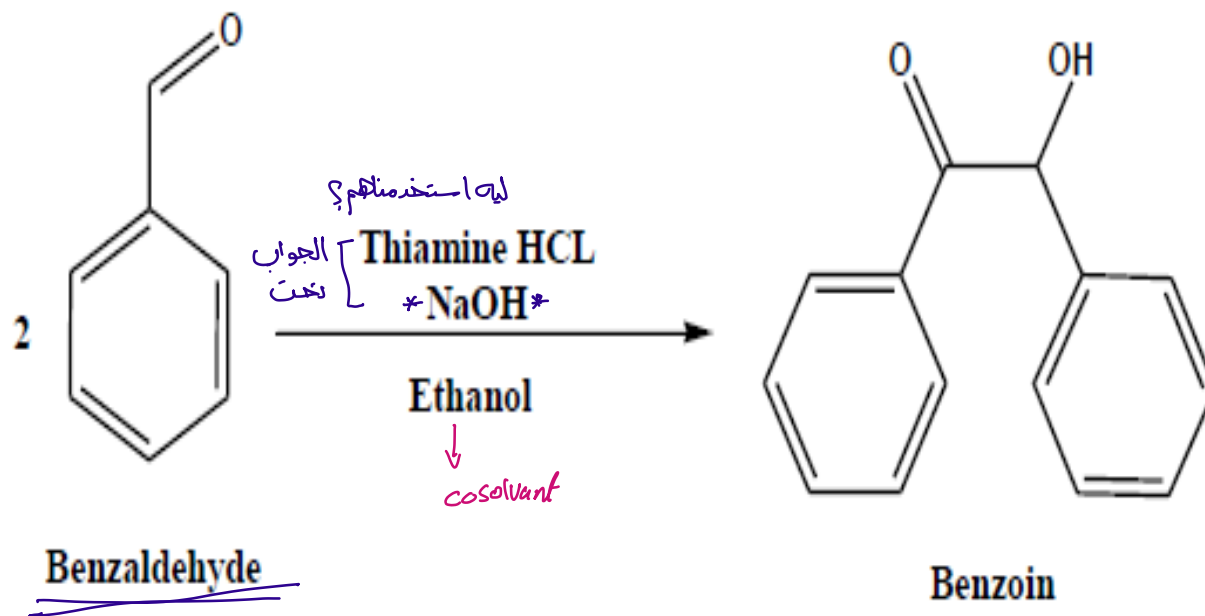
لا
يملك كاتاليزا يستعمله
زمن

- Cyanide* [$K+C \rightleftharpoons N^-$] can use as a catalytic reagent use at 75°C (give faster rate) but they are extremely poisonous *بجعل درجات حرارة عالية* very toxic

لا
الكاتاليز
الحيوية

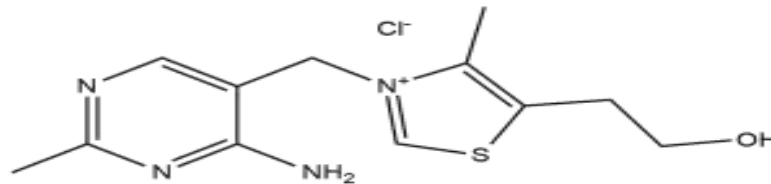
- Thiamine (contains a thiazole unit) is the catalyst was used here at Room temp, (give very slow rate). *عشان يركب التفاعل
overnight*

Step 1 :benzoin condensation



Step 1 :benzoin condensation

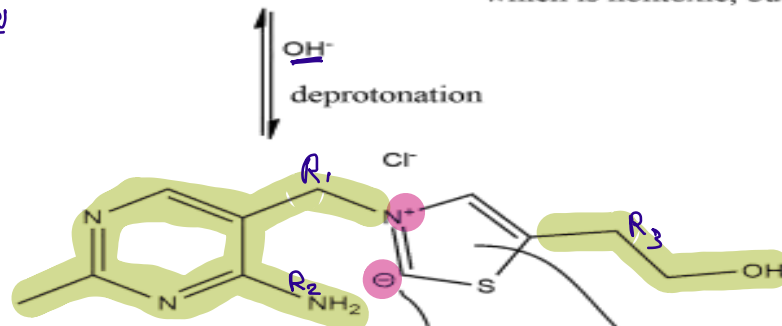
- First: Formation of the catalyst (Ylide*):



Thiamine_HCl

Thiamine is vitamin B1 which is nontoxic, but heat sensitive

as a catalyst لازم عشان يشتغل
Strong Base بوجود NaOH $\rightarrow$ OH^- $\downarrow$ $-\text{H}$
deprotonation
يس عليه



وهو (+-) zwitterion ion
بمعنى المركب لكن جديرين عن بعض شوي
يعني اسمه zwitterion ion
بمعنى Thiamine glide او glider
لانه على ذرتين متريين من
يعني

هي الي بتعطي
(A nucleophile)
راح تحفز وجمع من
Benzaldehyde
Strong

Thiazolonium ion (is the catalyst)

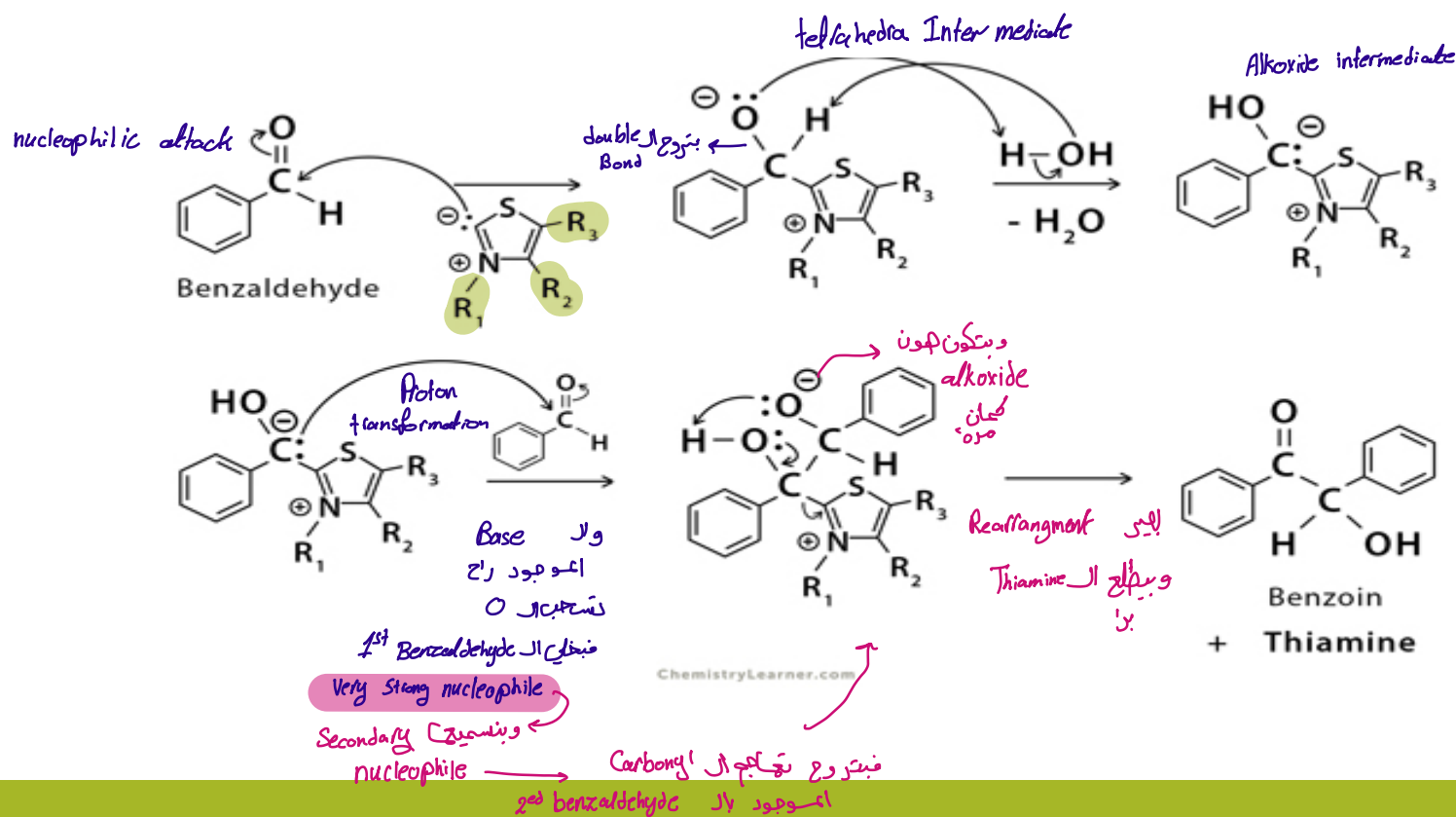
عشان نختار ال Structure

بالسلايد الجايع عنا 3R

حددتهم بنفس لون الملاحظة

Step 1 :benzoin condensation

- Second: The condensation reaction start with umpolung† to the carbonyl center of benzaldehyde



! Important note

- Water is required in this reaction BUT in specific amount:

Critical point

1. Too much water will force benzaldehyde out of the solution preventing an

مازاد يستغل عنا كويس

efficient reaction.

2. Too little water prevents thiamine-HCl from dissolving.

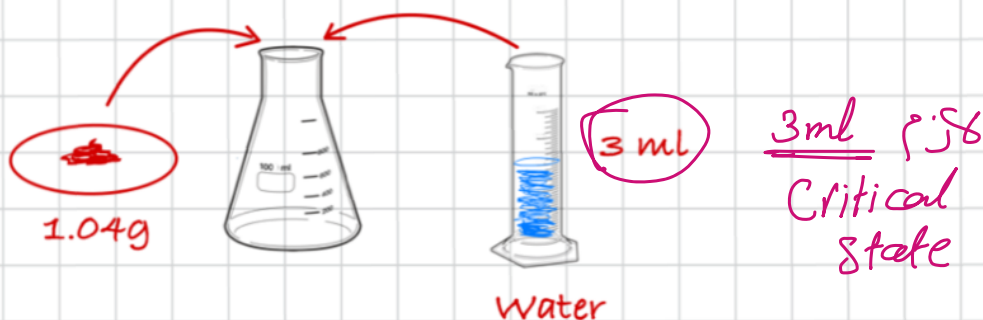
Phenytoin synthesis

Experiment 1: Benzoin Condensation

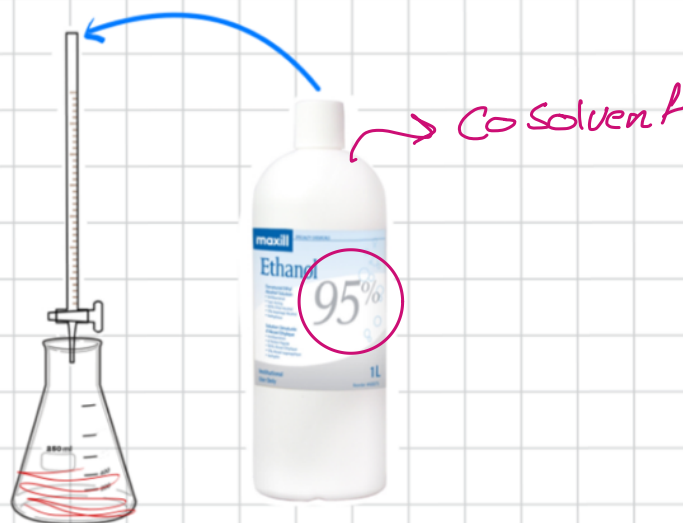
- ① weigh 1.04g of thiamine hydrochloride



- ② In a 100 ml Erlenmeyer flask add 1.04 grams of thiamine hydrochloride and add to it 3 ml of water and shake well until the thiamine hydrochloride totally dissolved.

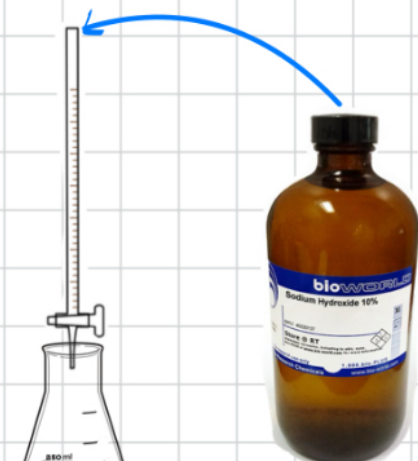


- ③ fill a burette with 95% ethanol, then start adding 8ml to the Erlenmeyer flask and shake well.



④ fill a burette with 10% sodium hydroxide, then start adding 3 ml to the Erlenmeyer flask and shake well.

بجود
Thiamine → ylide



پیرا دی کت
سفر

⑤ finally, fill a burette with benzaldehyde, then start adding 7 ml to the Erlenmeyer flask and shake well.

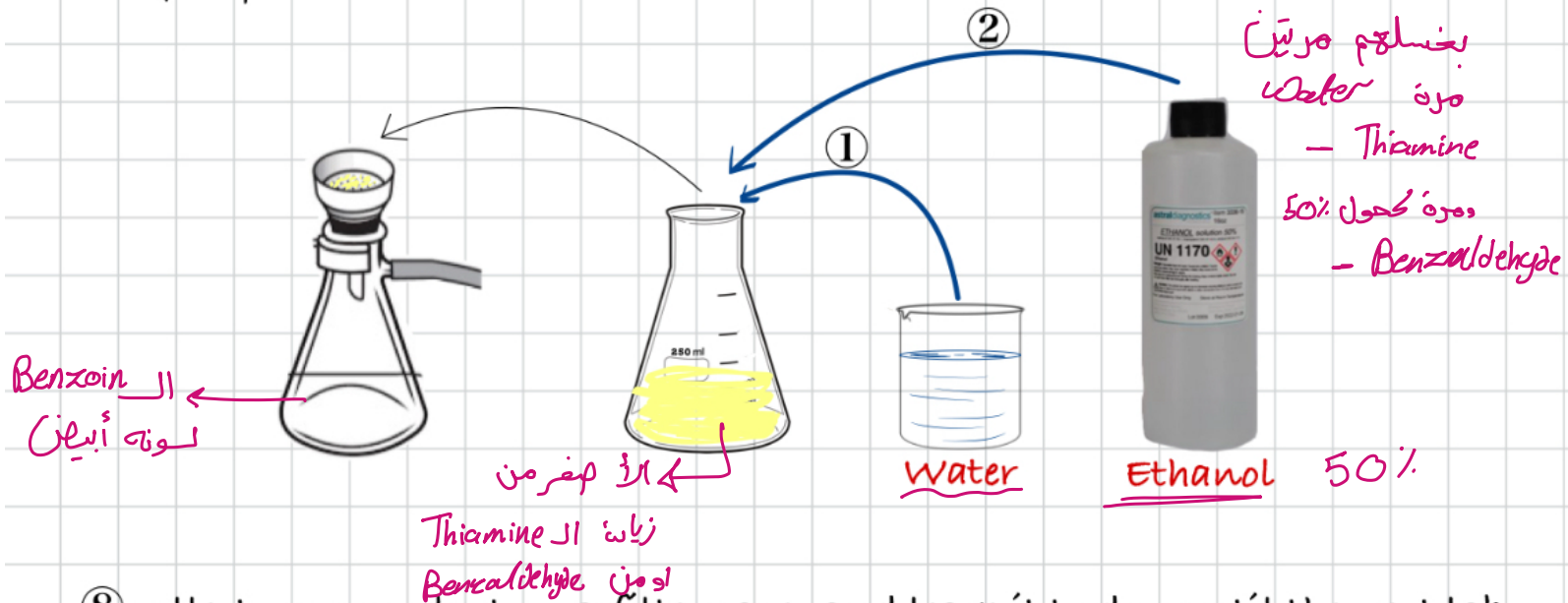


⑥ close the flask with parafilm



Overnight بزرگ

⑦ prepare for suction filtration rinse with water then 7ml of 50% ethanol to get rid of impurities as thiamine



⑧ collect your product on a filter paper and leave it to dry until the next lab.

في فيديو على بالديفئة ١٦