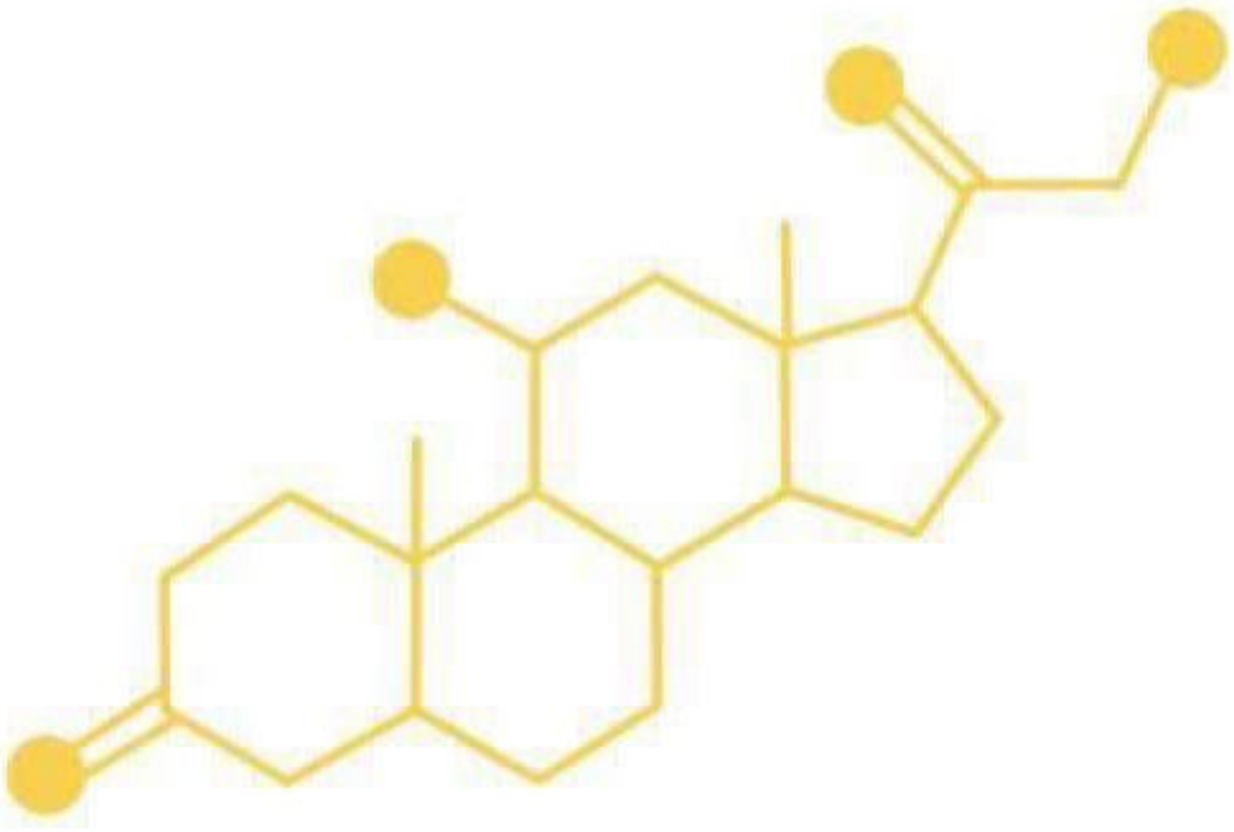


MIRACLE Academy

ميدسينال 2
زميلتكم ريماس الشوابكة

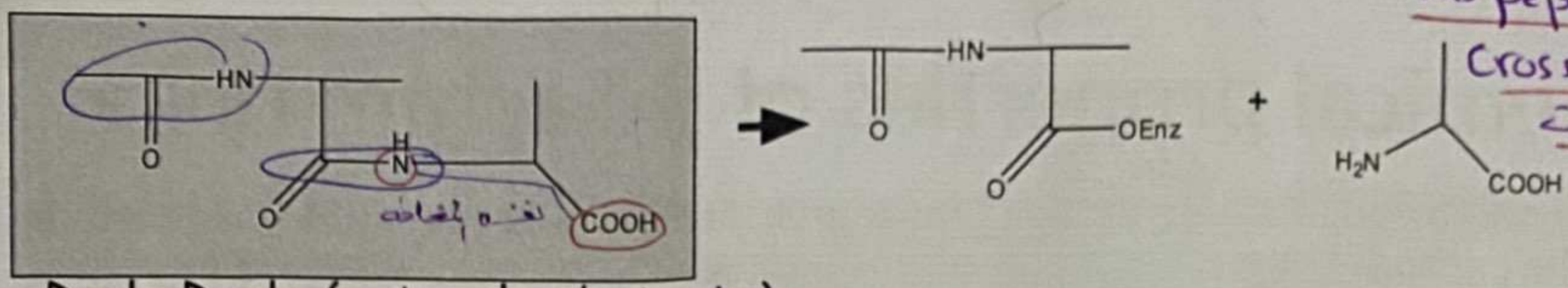
لجان الدُّفعات

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

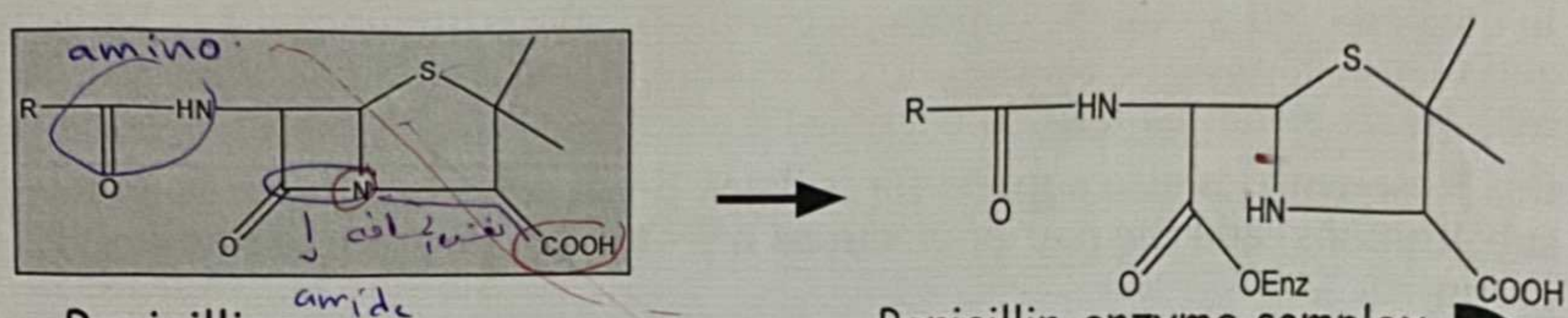
* الـ (Transpeptidase) بفكر الـ Penicillin عبارة عن D-ala-Dala فبروح برتبط فيها وبعمل crossing linkage ← بصير Covelent bond (irreversible) ← بتكون هاي الـ transpeptidase بالبكتيريا غير فعال

فهاد يعني crossing link بيبطل يصير
لانه الـ transpeptidase محبوس ع البقية
Covelent مع الـ Penicilline فهاد الشي
مش راح يصير.

البكتيريا صارت بالنهاية :-
بدون traspepridase
بدون Cross linking
وفتحت ودخلت
عليها ماي
(ضغط اسموزي)
راحت
cell lysis.



D-ala D-ala (natural substrate)



Penicillins

Penicillin-enzyme complex

cross-linking inhibited

The wall become fragile and can no longer prevent the cell from swelling and bursting

Bacterial cell lysis

Excellent selective toxicity

وبصير عندي اشي اسمه "(Cell lysis)" لهيك الـ Penicillin هاي
مش bacteriostatic زي
Sulfonamide
bactericidal هدول

Penicillins :-
بشتغل ع خلايا البكتيريا لانه خلايا الانسان ما بتحتوي ع cellwall
والـ aa ← يستخدمها الانسان هي الـ levo، لكن detro تستخدمها
البكتيريا.

- Penicillin mimic the structure of D-ala-D-ala, because of that the transpeptidase mistakenly bind to it instead of D-ala-D-ala.
- Also this explains the lack of penicillin toxicity, since D-amido acids are not present in human, only the L-amino acids present.
- Also targeting the cross linking in the peptidoglycan biosynthesis which is only present in bacteria explains the selective toxicity.

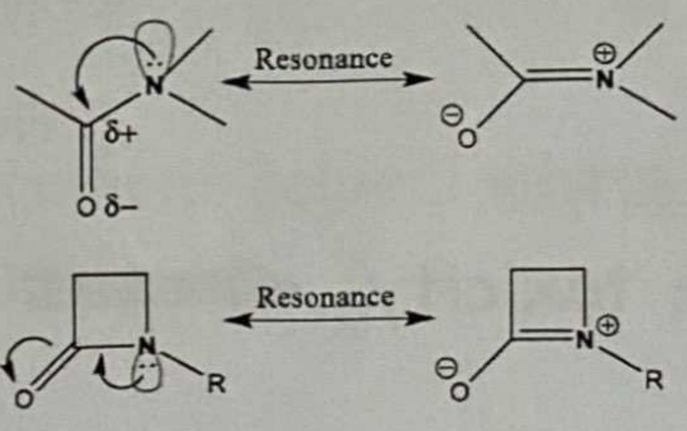
الانسان فيه levo عشان هيك ↓ Penicillin toxicity

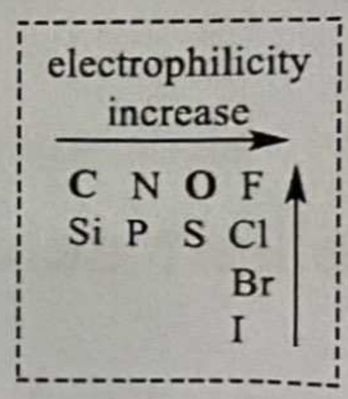
وبالتالي لانه الانسان مش محتاج لـ transpeptidase ولا Cross linking
ولا peptidoglycan واصلا الانسان فش عنده cell wall، فالـ
Selective toxicity → bacterial cells.

شرحته ع لدفتر بالتفصيل ث

chemical properties of β-Lactam ring:

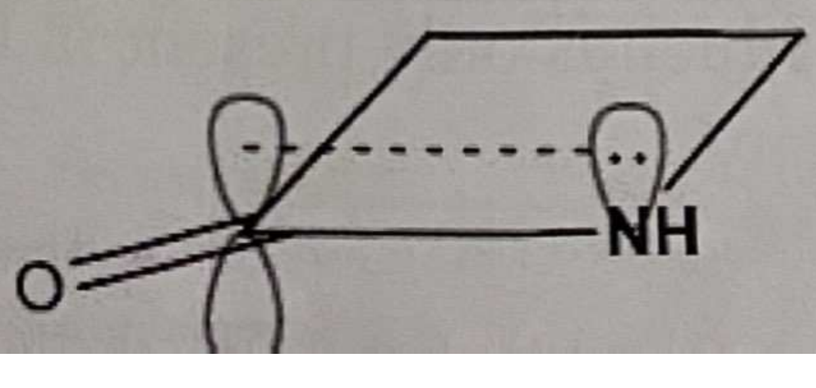
- In the original amide group (Linear amide), the Nitrogen atom that is beside the carbonyl group has a pair of unshared electrons which causes the Resonance between the N and the Carbonyl group (as we see in the periodic table, the O is more electronegative/electrophilic than C so the O in the carbonyl group withdraws electrons to have partial negative charge and C partial positive charge) So this carbonyl system is "Di-polar" and withdraws electrons from N.
- this Resonance is also applied for isolated β-Lactam ring (alone, no other substitutions) and the pair of electrons of N are not far from the carbonyl group





chemical properties of β-Lactam ring:

- Look at the pair of electrons of N in the β-Lactam ring alone
- (**NOTE** that the empty orbital of carbonyl group accepts the pair of electrons of N to make resonance)



No. lecture (2)

قبل ما نبلش نتفرغ هاي المحاضرة خلونا ندعي لـ زميلنا ابهم لحرادات
"اللهم يمّن كتاب ابهم ويسّر حسابه، وثقّل بالحسنات ميزانه، وثبّت على الصّراط أقدامه، وأسكنه في أعلى الجنات، بجوار حبيبك ومصطفاك صلى الله عليه وسلم"
"اللهم احفظ أبهم في بطن القبر مطمئناً وعند قيام الأشهاد آمناً وبجود رضوانك واثقاً، وإلى أعلى درجاتك سابقاً"

بسم الله نبدأ....

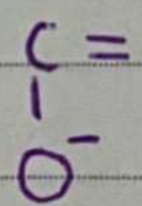
"ليه دائماً بنحكي انه الـ amide بكون moreStable مقارنة بالـ estar"!!!

تفسير الرابطة الاميدية رابطة قوية لسبب معين ← وهو "Resonance"
أقالو الدكاترة توهو

anti orbital → two unshared Pairs of electrons
جلوبل وحربل ن

its more electro negative
carbonyl هاد معناه الـ electron تاعون
مسحوبين لعند الـ O

الـ N بتعطي الـ electron تاعونها
للـ C فبصير بينهم double bond
فهاي العملية بسميها (Resonance)



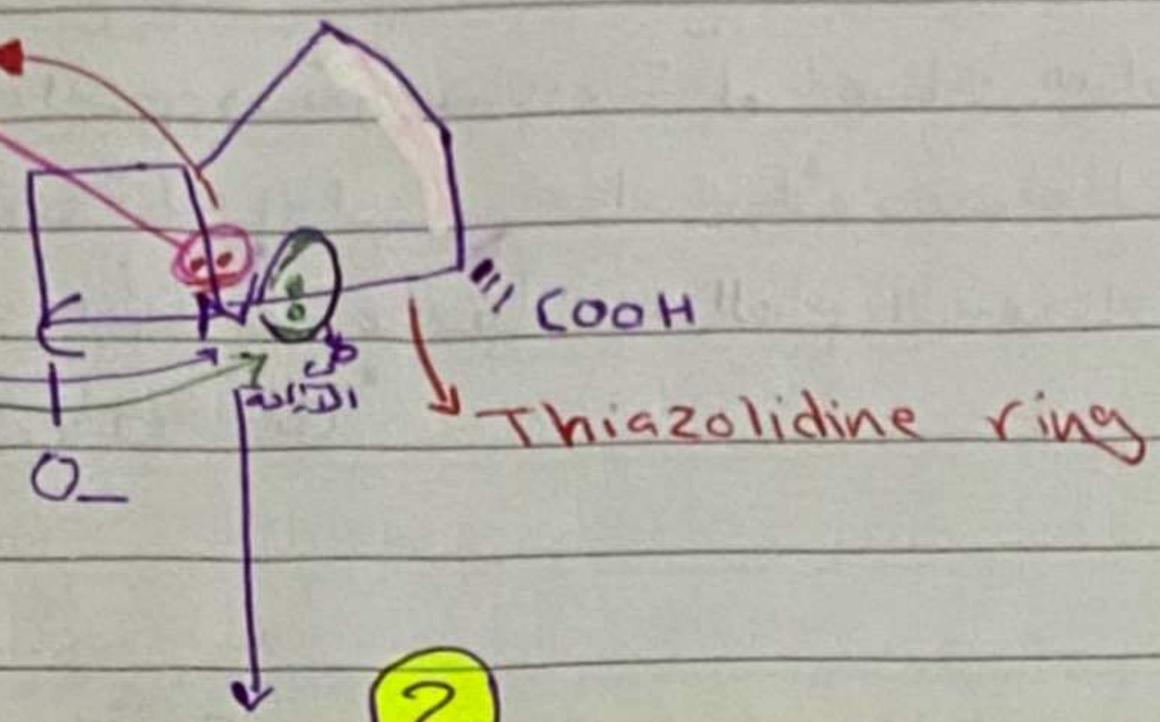
٨ ٥" ٤ ١ افتد بالتفصيل ت

أرقملكم الكلام عشان ما تخربطوا 😂

No.

1

الـelectron هاي مشان
مطينهم للكاربون يزاله (=O)
ح يصيرلهم إزاحة



2

ف بسبب الحلقة الخماسية اللي جنب الـ
[Nitrogen] الـ electron هاي صعبت
صار عليها اسمه
" off set "

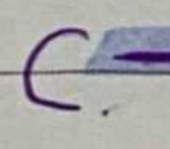
شو عملت؟؟؟

3

بسبب الـ off set بخل يصير في عندي
بخل يصير قبلها B-lactame فال ,resonance.

offset بسبب resonance

٤ أرد اوضح



الـelectron هاي الكترونات بدل ما بتروح ع الكاربون
هي ما راحت, شو عملت؟؟ عملت إزاحة
وخلت هيك الرابطه بين N و C رابطه صعيفه

5

جلب الـ C شو ح يصير عليها؟؟

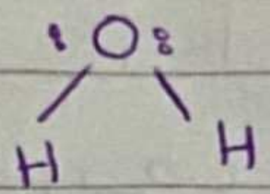
ف صارت هاي الـ C مسحوبة الكترونات تاعتها من O لإنها electronegative
وكمان مسحوبة الكترونات من الـ nitrogen, بسبب off set
على ازاحة

وهيك صارت الـ C [+] يعني فاقدة للكترونات

No.

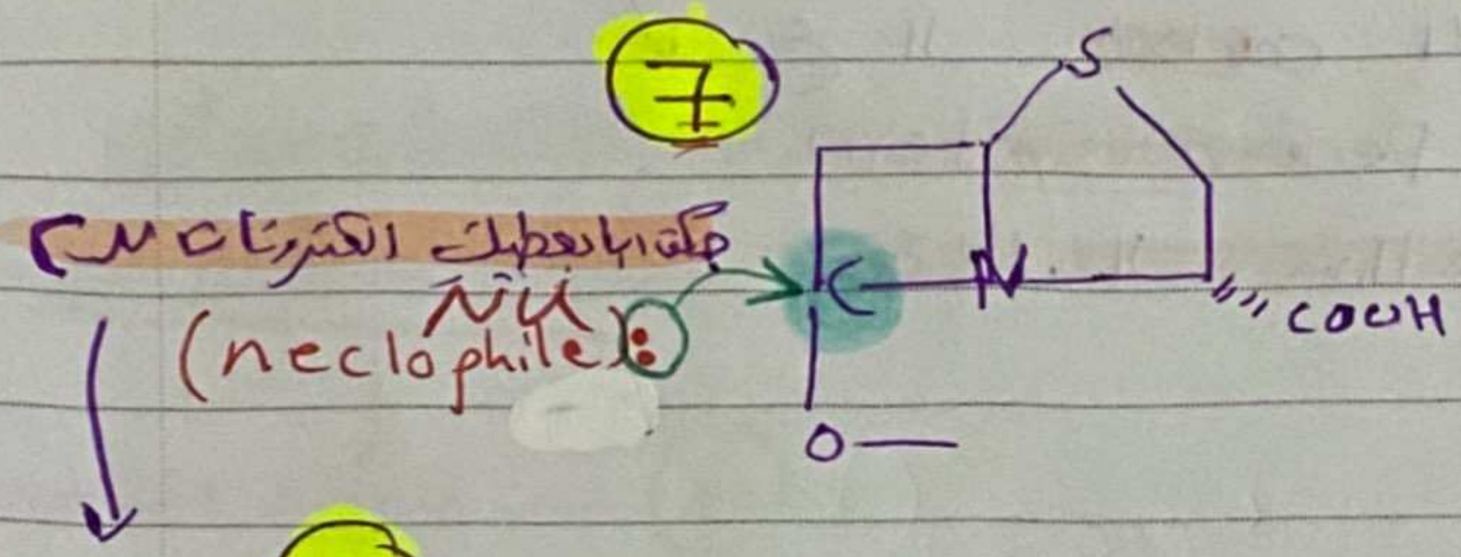
6 وهي هيلئ صارت عرضة أكثر لـ (nucleophilic attack)

ال nucleophile ← هي مادة غنية بالإلكترونات مثل H_2O



فال O لما فقدت الكلترونا وصارت محتاجة للكترونات، اجت ال nucleophile وعطتها انابطبك ال electron

7

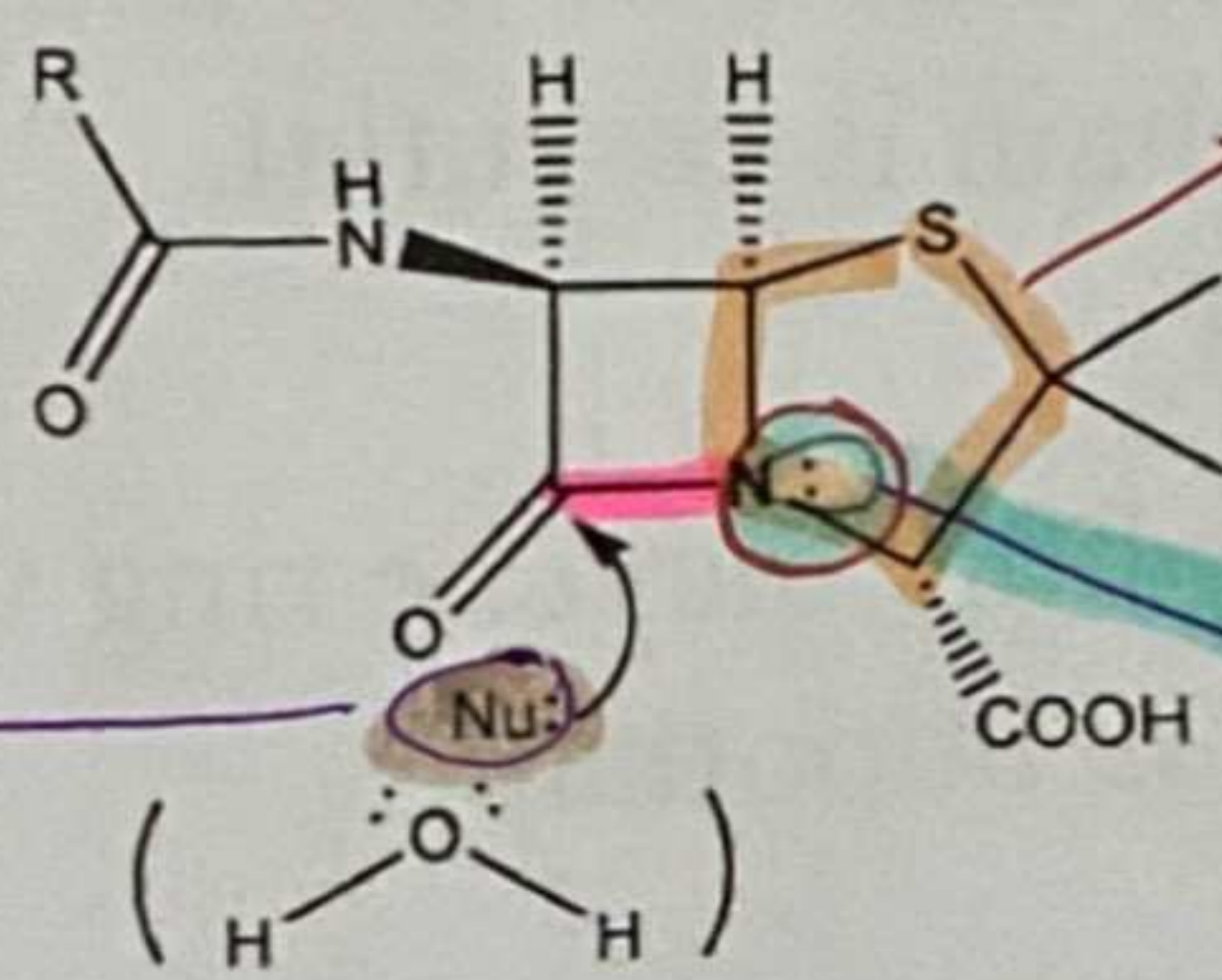


8 هادي شي بتجعلنا رابطه گسرت لرابط الأساسي بالـ system

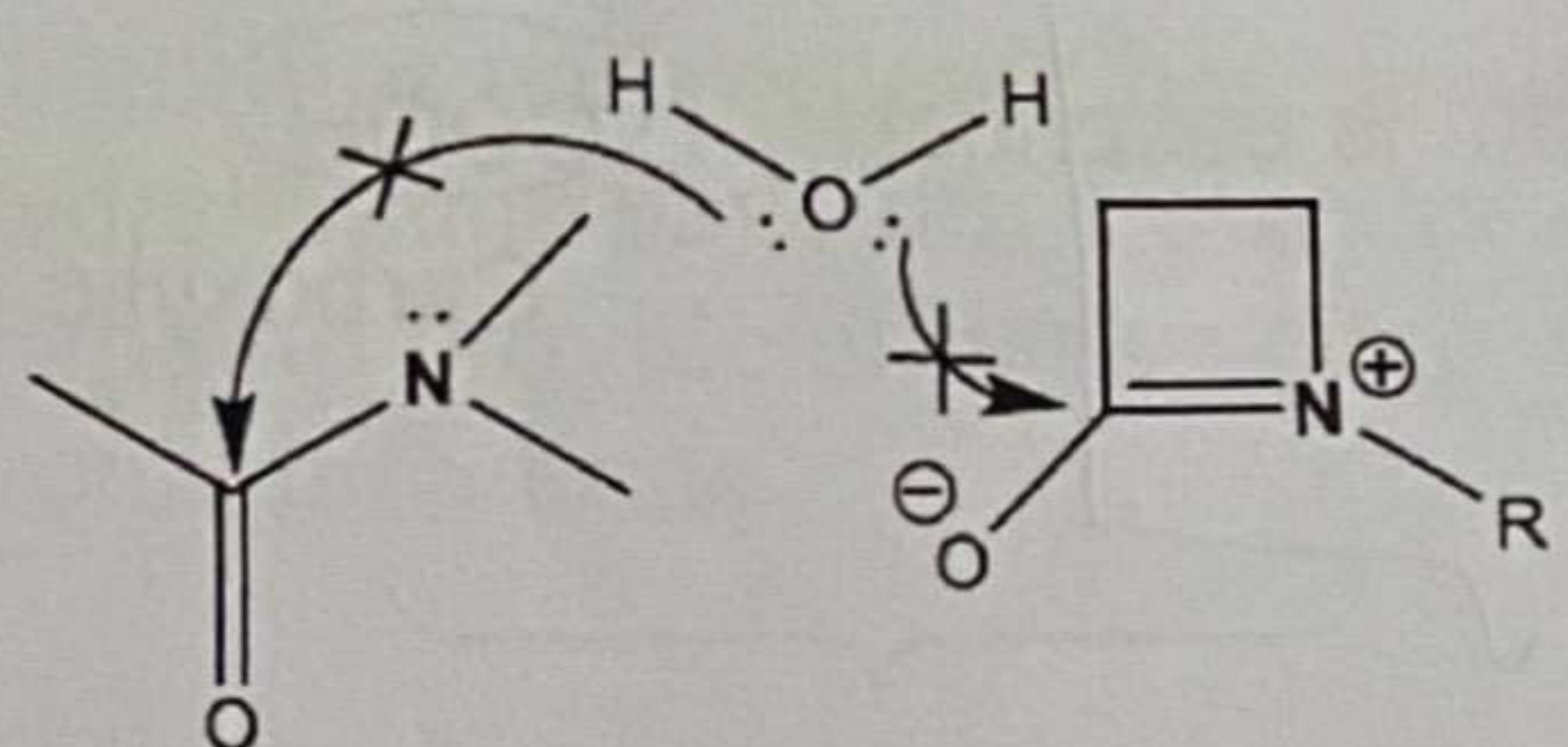
9 وهادا أدى الى تكسر الـ penam system الي هو كان مسؤول عشان الـ transpiptadase يصير "inhibition"

10 فهادي قصة الـ Nucleophilic attack بكون في carbon فاقد لإلكترونات فبتيجي ذرة تعمل مع رابطه ع طول رابطه الـ system الأساسية، وهاد الإشي بؤدي الى تكسر كل الـ system الموجود عشان يصير ineffective.

- BUT when the β-Lactam is involved in the Penam system, and look at it in 3D view,
- the pair of electrons of nitrogen is far from the carbonyl group because the
- Thiazolidine ring bends this pair of electron (**Off-setting**) and the N becomes
- pyramidal (very close to the amines).
- So the Penam is completely different from amide, the carbonyl group is very electrondeficient and easily attacked by a nucleophile such as water (**No resonance** to make this carbonyl rich in electrons and resistant to hydrolysis as in amides that need enzymes to be hydrolyzed).



- **NOTE**: the β-Lactam alone is also resistant to hydrolysis as the amides due to
- resonance but easier than amides (the Nucleophilic attack is more easy).
- For that reason, when one of the penicillins is given orally as solution, it can be used only for one week after dissolving in water due to hydrolysis and must be stored in the fridge to slow down the hydrolysis rate by water (which is a nucleophile, contains two pairs of electrons).
- So all penicillins are unstable in water and tend to breakdown quickly in the aqueous conditions, and for that reason mostly these preparations are made as suspensions not solutions to reduce the water activity. This is also applied for parental penicillins that are given as re-constitutable powders.



No.

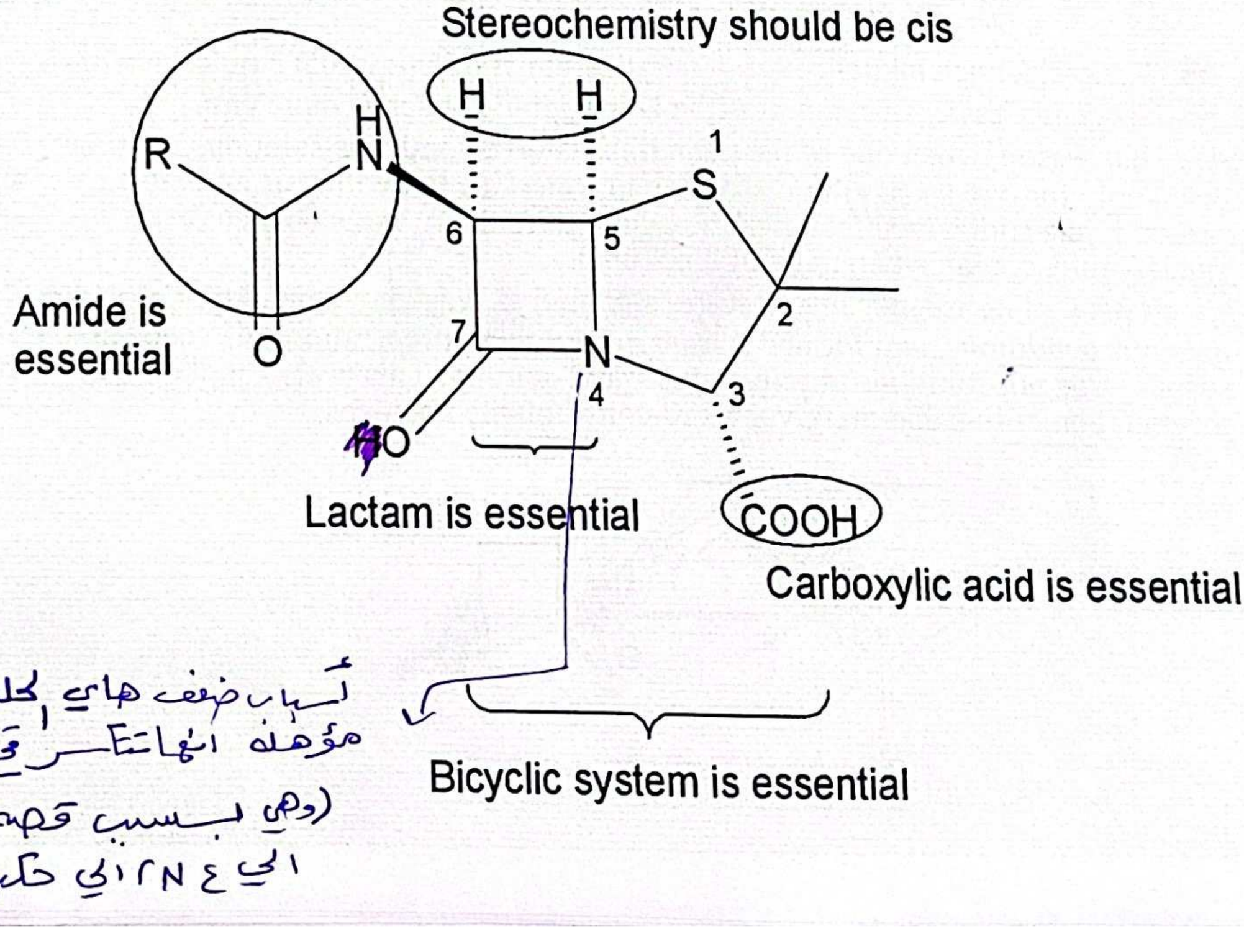
* ليه المضادات الحيوية تاعت الاطفال بتكون
Pencilline [oral]

Solution. على شكل "Suspension" يتم تحضيرها
وبيبقى جوا الـ Suspension بالصيدلية بكون
للمريض جاهز. داخل الثلاجة. (عشان ما يقل فى
الجو) (Nucliophilic attack)
لأنه أثناء تفاعل المضاد الحيوي nucliophile
nucliophilic attack
مع الـ carbon اللي جوا الحلقة بتاعته
Penam system.
وبيقل الـ penicillin فعال

Structure-activity relationships of penicillins (SAR)

- The strained β-lactam ring is essential.
- The free carboxylic acid is essential (the carboxylate ion binds to the charged nitrogen of the lysine at the active site.
- The bicyclic system is essential.
- The acylamino side chain is essential.
- Sulfur is not essential.
- The stereochemistry of the bicyclic ring with respect to the acylamino side chain is important.

Structure-activity relationships of penicillins



Reasons for the acid sensitivity of penicillin G:

- Ring strain: due to the large angle and torsional strain exist, acid catalyzed ring opening will relief these strains.
- A highly reactive β-lactam carbonyl group:
- This amide bond is exceptionally unstable compared to the normal amide, because it is a 4-membered ring this will increase the angular and torsional strain

Chemical degradation and properties

- The early penicillins were yellow to brown in color and very unstable so refrigeration was required to maintain activity for short time
- Unpleasant taste
- Strongly dextrorotay
- Most penicillins are acidic Pka=2.5-3.0 some are amphoteric
- The free acids are not suitable for parentral or oral administration Na and K salts are suitable to allow both oral and parentral administration.
- Some salts of penicillins with organic bases such as Benzathine, Procaine and Hydrabamine have limited water solubility and so they are suitable as depot to provide effective conc. Of penicillin for long time to treat chronic infections

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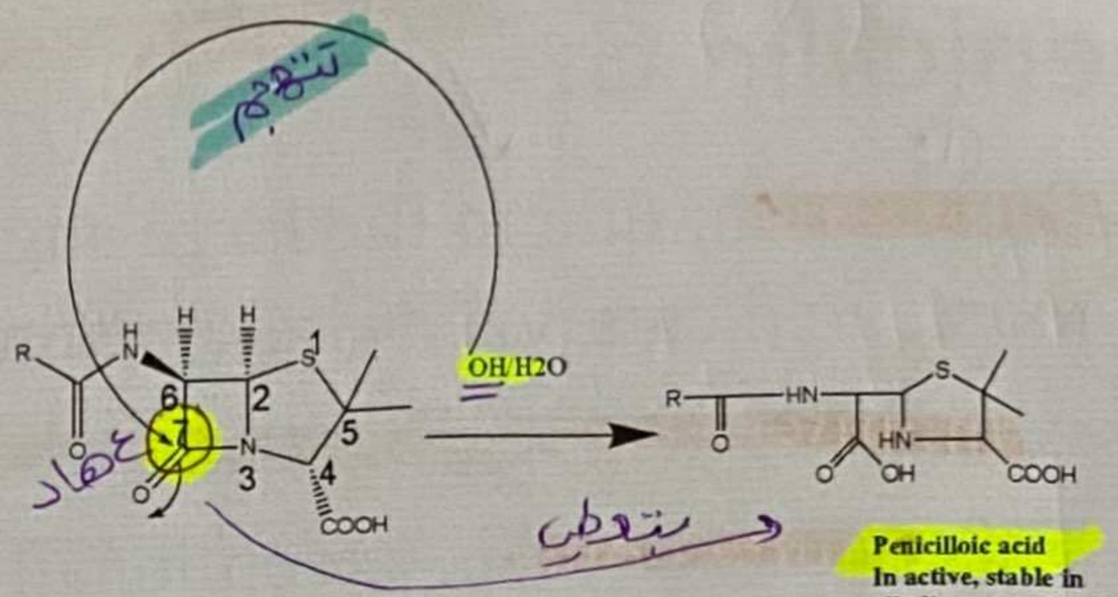
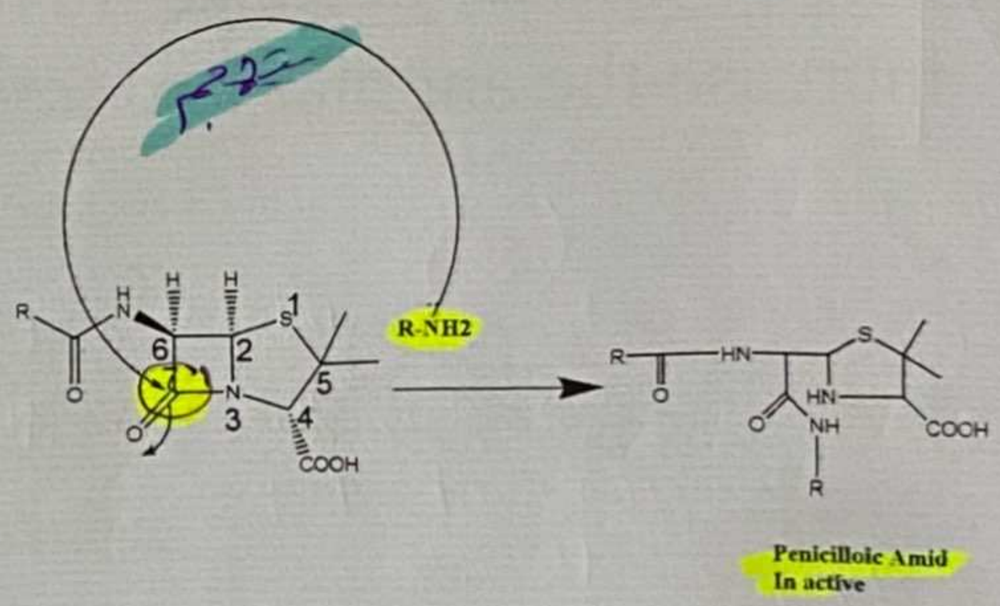
Chemical reactivity

1. reactions with nucleophiles –OH, H_2O, NH_2-OH, R-NH_2, R-OH, and body proteins

- 1. reaction with –OH



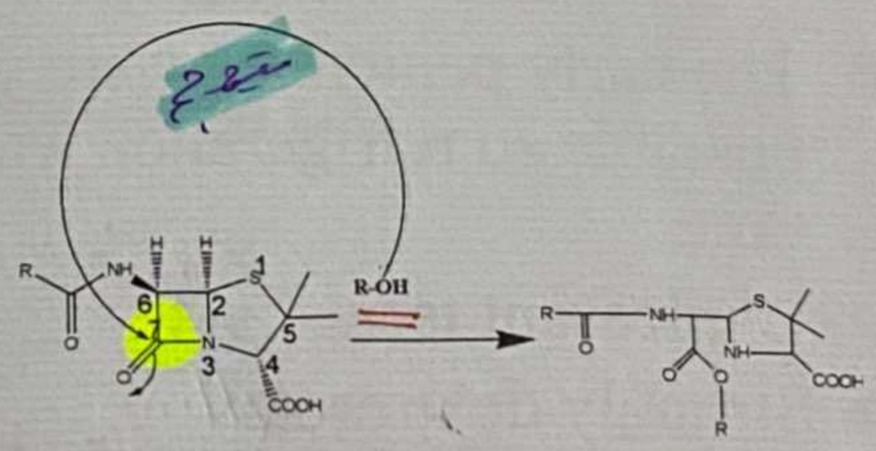
2. Reaction with alkyl amines



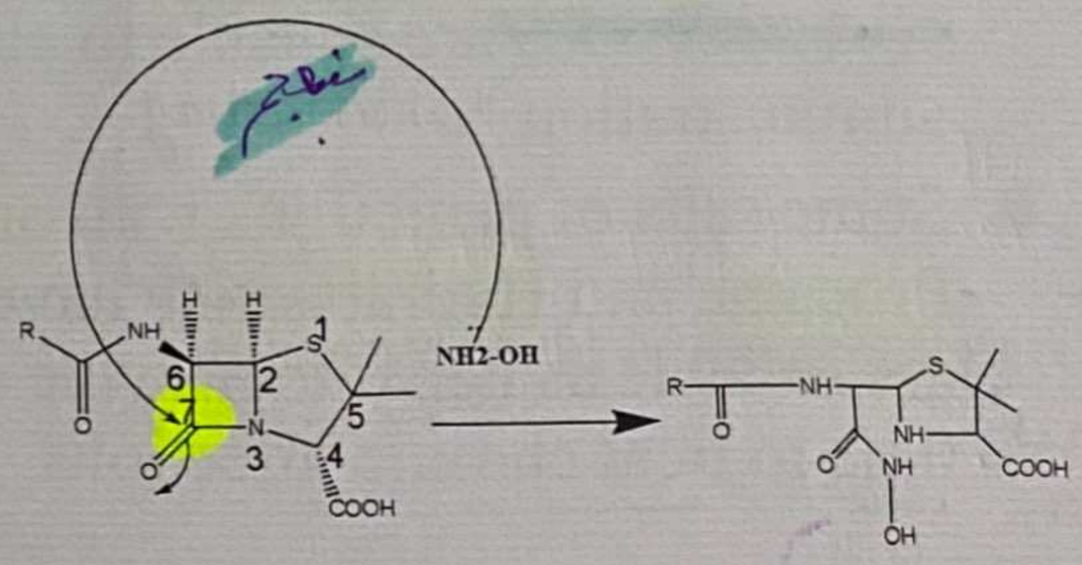
Chemical reactivity

1. reactions with nucleophiles –OH, H_2O, NH_2-OH, R-NH_2, R-OH, and body proteins

- 3. reaction with Alcohol



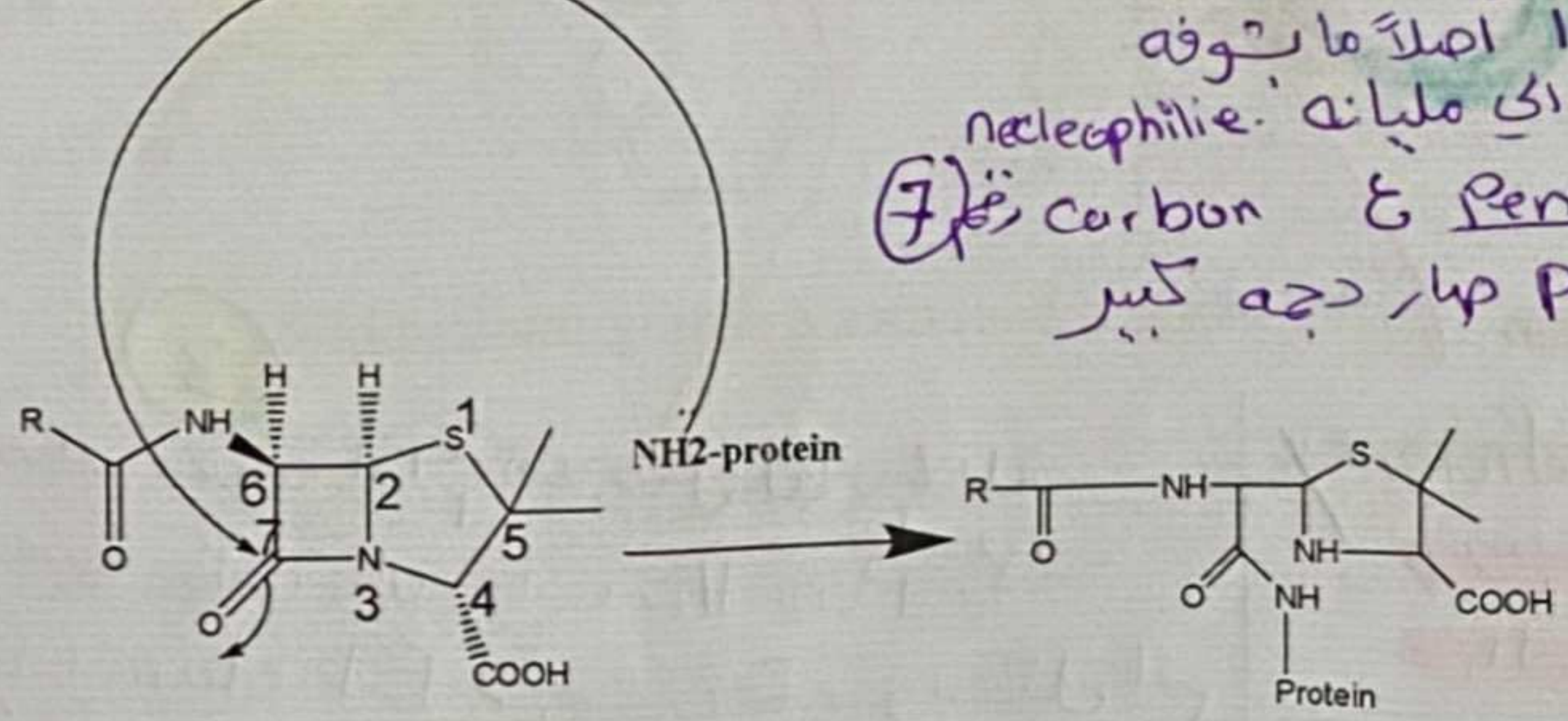
4. Reaction with hydroxyl amine



1. reactions with nucleophiles –OH, H_2O, NH_2-OH, R-NH_2, R-OH, and body proteins

- 5. reaction with body proteins: the nucleophilic attack on B-lactam rings by body proteins (specific) generate penicilloyl proteins that are suspected to be the reason for the allergic reactions to penicillins

متى بتصير حساسية الـ Penicillen ؟؟ طيب أول اشي اصلاً بدي تعرفوا انه الـ Penicillen صغير فالـ Immune system اصلاً ما بشوفه ولكن اذا اجت بروتينات الدم الي مليانة nucleophile وهجمت ع الـ carbon (7) تبع Penicilline فهيك الـ Penicilline صار حجمه كبير وهيك صار الـ Immune system يشوفه، لانه صار عبارة عن Protein مرتبط بـ Penicilline.



اذا كنت بالصيدلية فا تبيع لدواء من راسك 🙂 اذا مش متأكد اذا اعرف ماعنده حساسية أو لا Penicillin ← عكس هادا يكون معه حساسية دعوة طبيب هاد للدواء

Chemical reactivity

2. reactions with Acids

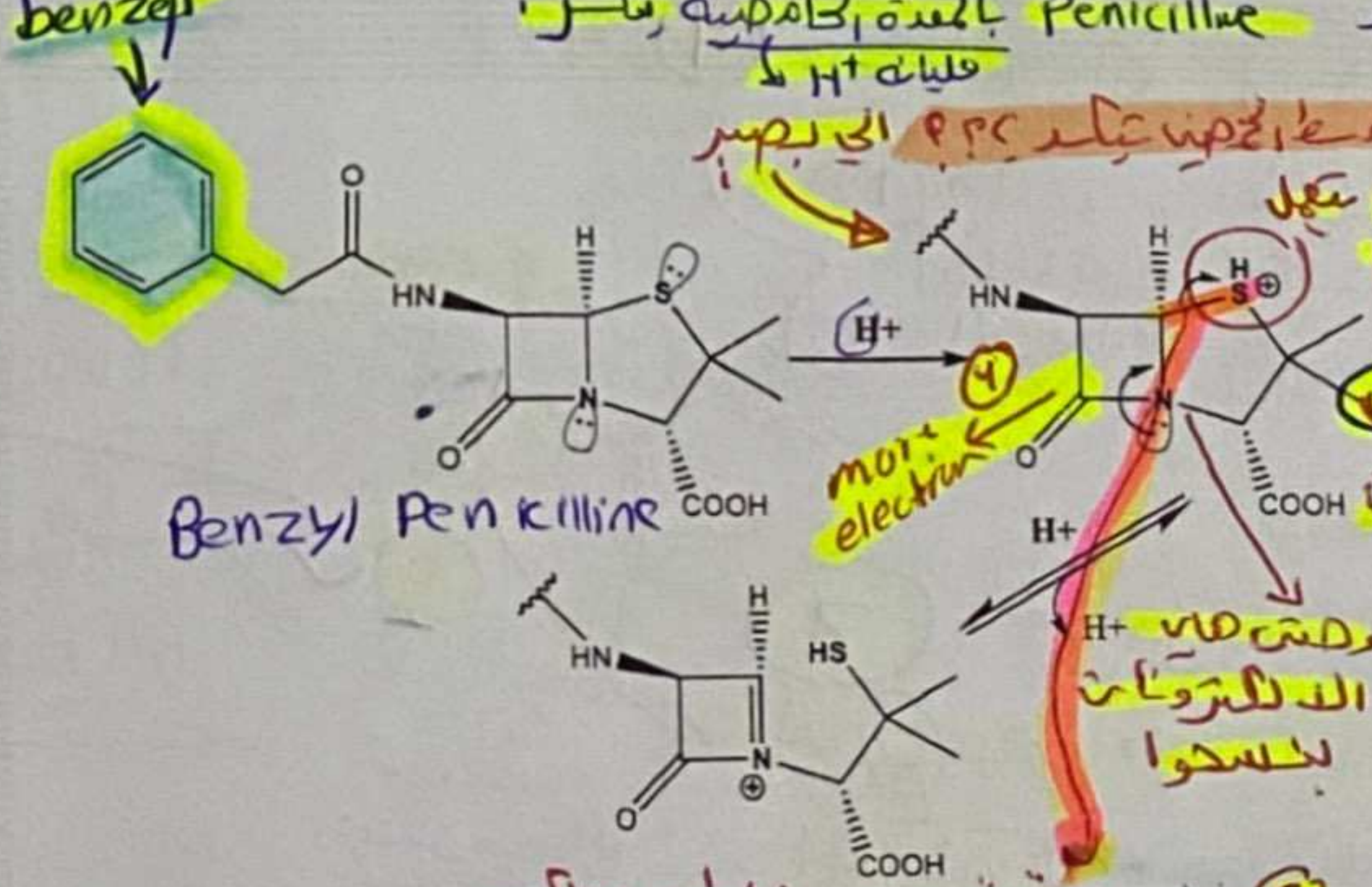
شو الي بصير بالوسط الحمضي لما ناخذ الـ benzyl Penicilline

- In strongly acidic media (PH<3), penicillins undergo complex series of reactions as in the following:
- First step (reversible)

هل الـ H^+ كان ← neucliphile ؟؟ (8)
طب لما انه H^+ ما بقدر يهجم ع الـ Carbonyl الي هون، كيف ليه لما ناخذ Penicilline بالمعدة الحامضية رح تتكسر، مليانة H^+

protination of the sulfur atom will occur then a partial positive charge will be formed on S and becomes a good leaving group, the pair of electrons of N will move causing the structure to become with a thiol group and a double bond, and the N becomes quaternary with a positive charge.

الـ sulfor لما ذرات ع ... مرتبط و ... بتتكسر الرابطة

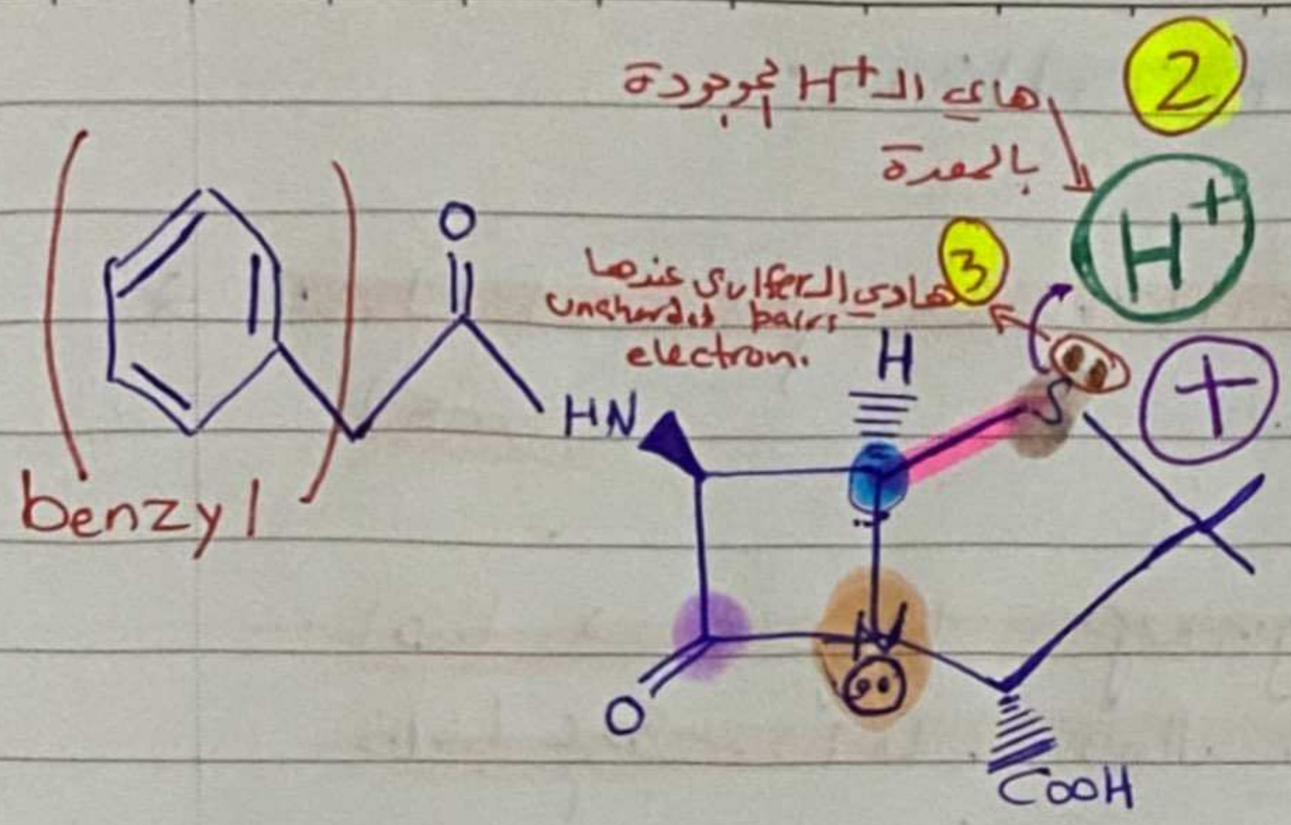


هاد لتفاعل الاول ع عجل نكمل ع سلايد الي بعد هاد.

(5) ومنشان توصل هاي الرابطة بتتكسر. [كسر بالوسط الحمضي] مش بسبب nucleophilic attack بسبب الـ Proteration

أرحم الكلدون ☺

شو بصير بالوسط الحمضي لما ناخد Benzyl Penicillin. No



1 المعروف انه Penicill عكس الوسط الحامضي يعني يتكسر بالمعدة (Protination) الي بدصير هون

2 الـ Sulfer بتعطي الالكترونات لـ H^+ وهيك صار عليها شحنة (+) Positive

3 هيي منطقة بتسحب الالكترونات، اهميتكم من ريت لتشوف الي عليها لون بينك

شو حيصير

4 خليت الكربونة الي لونتها باللون أزرق برضه مش مرتاحة ورح تسحب الالكترونات الي عند الـ N والي هي اصلاً اصلاً مش مرتاحة

5 وهيك كل الإلكترونات مسحوبة باتجاة الـ Sulfer

وصارت الكربونة هاي اكثر ضعفاً

6 بروح لمربك بكسر الرابطة بين Sulfer والـ Blactam وهاي الرابطة ممكن ترجع تتكون عندي لهيك في سهين ع سلايدات [Reversible reaction]

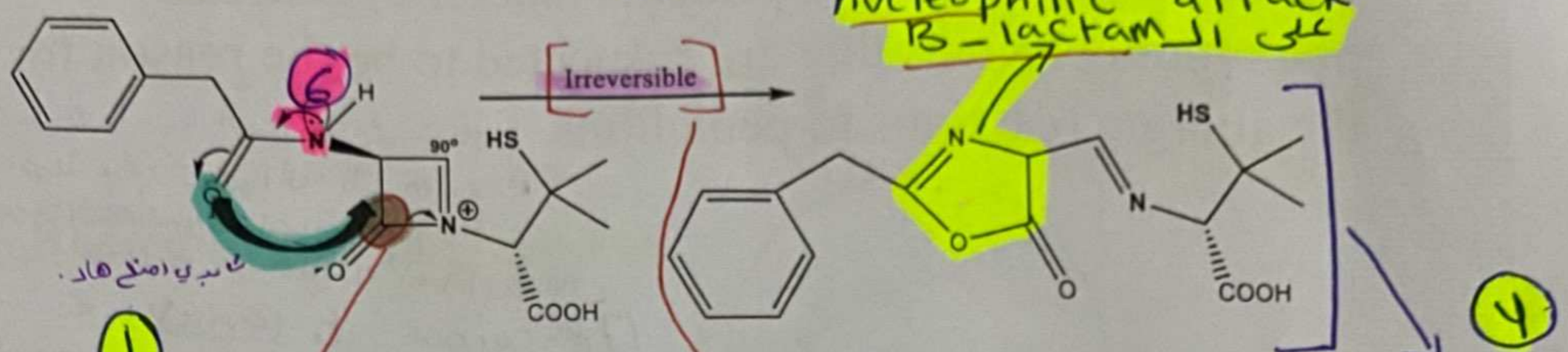
7 سهين آخر ستركز بالسلايدات وصلنا انه لو وصل لوسط قاعدي OH هيي وصل لحد معاي هيك رح يرد يرجع زي ما كان أول شي.

smile for life

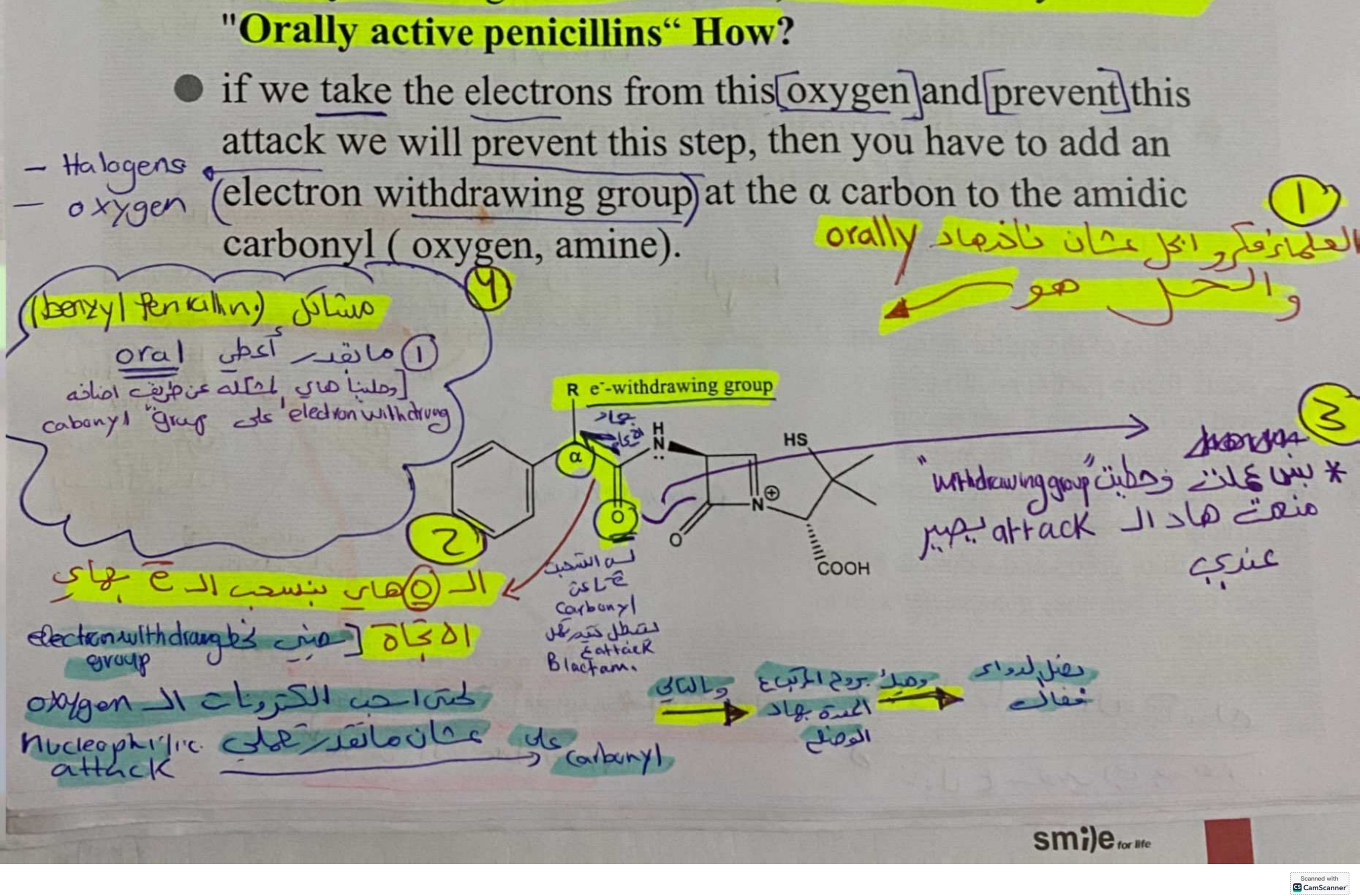
Chemical reactivity

2. reactions with Acids

- Second step (irreversible)



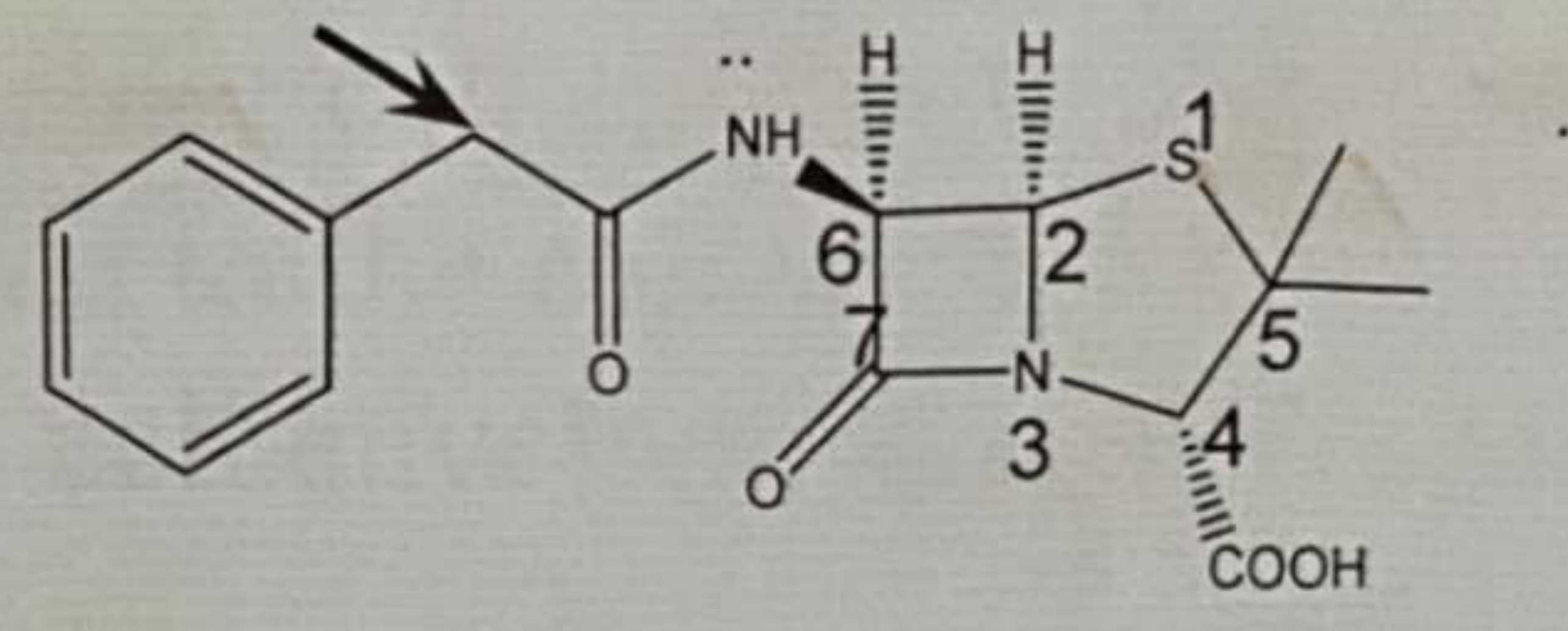
- And by knowing this mechanism, we can actually make **"Orally active penicillins" How?**
- if we take the electrons from this oxygen and prevent this attack we will prevent this step, then you have to add an (electron withdrawing group) at the α carbon to the amidic carbonyl (oxygen, amine).



Acid sensitivity of penicillins

- Electron withdrawing groups in the α-position of Benzyl penicillin will improve acid stability clearly

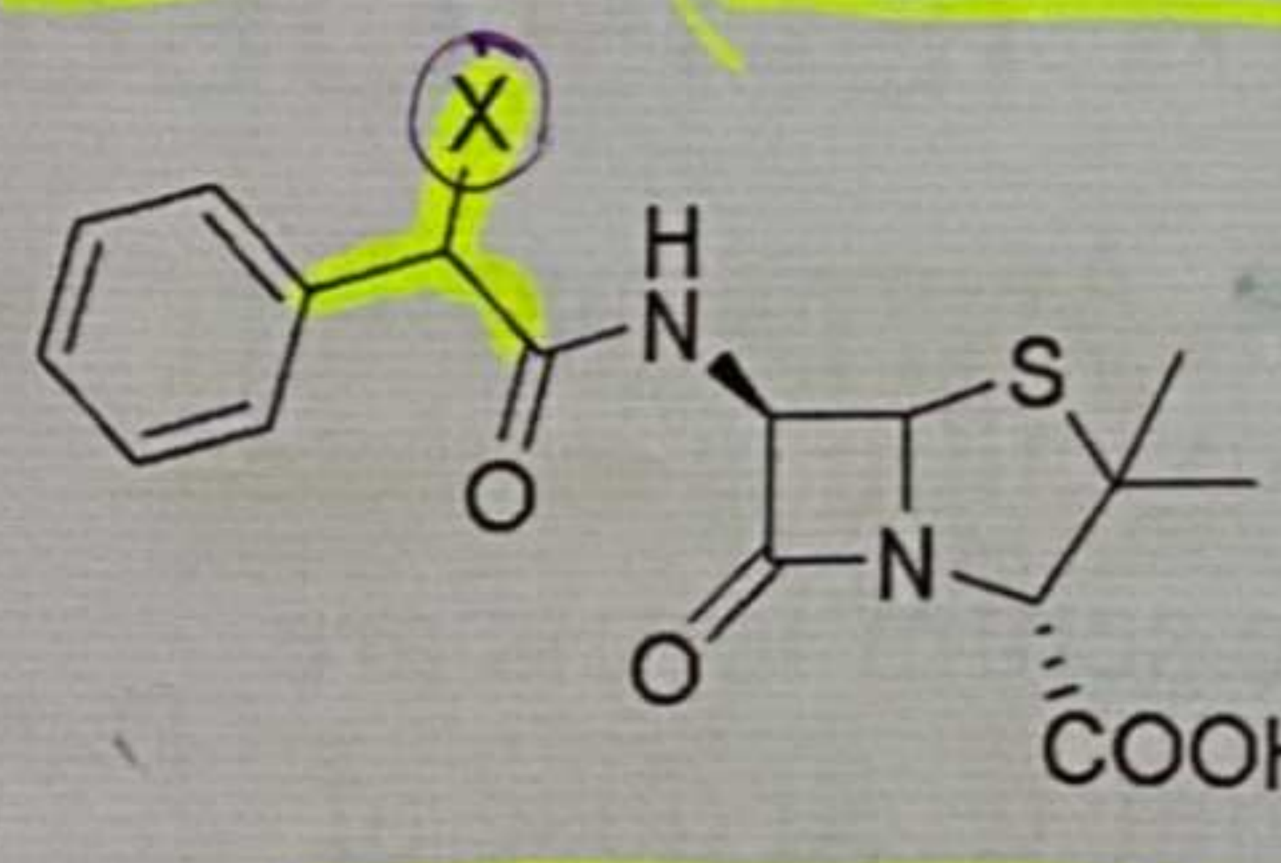
α-position



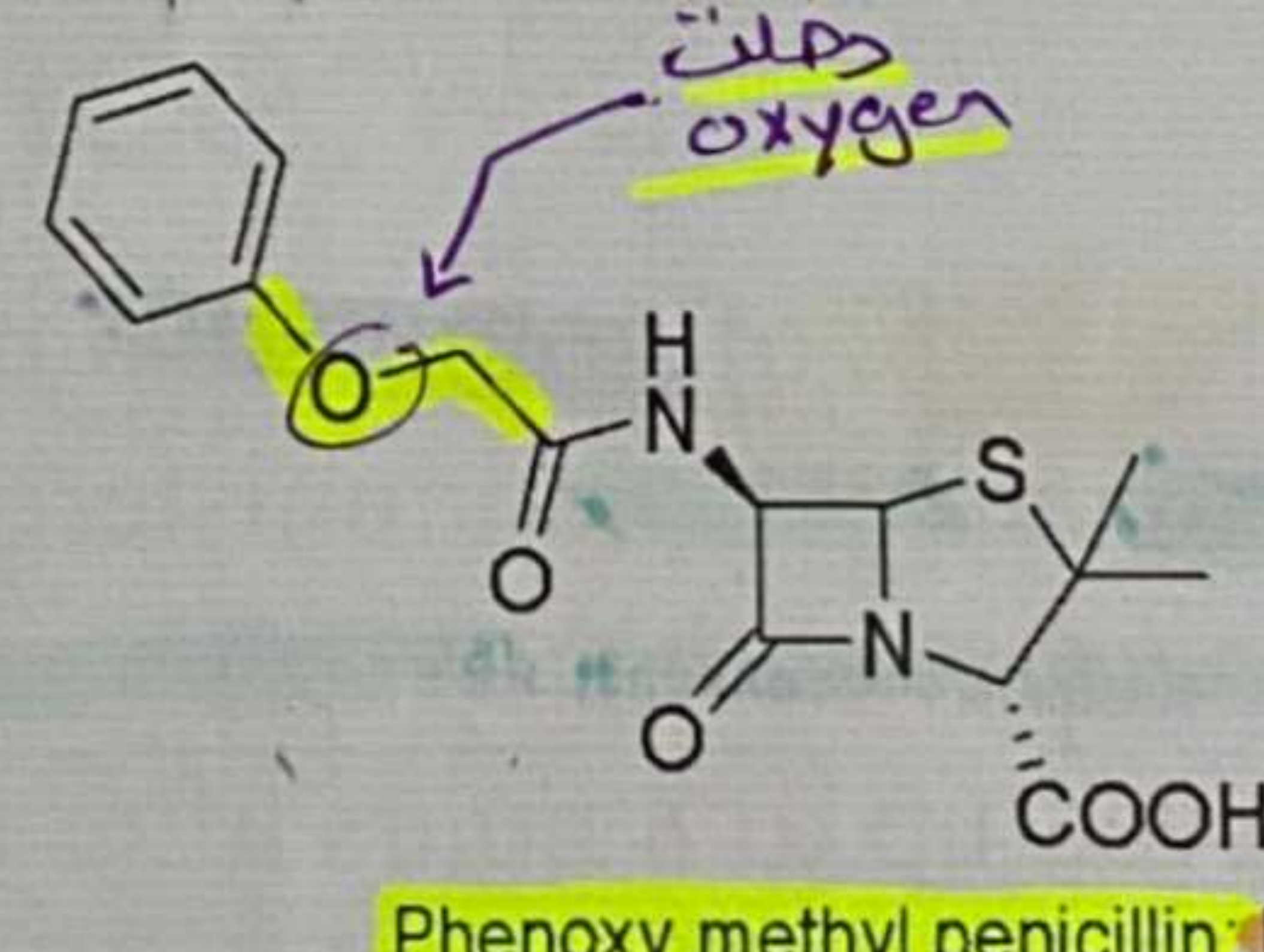
((ē withdrawing group تشوف امثله بس ندي أحط
عشان يصير اكثر stable وبقدر اخذوا orally))

Acid sensitivity of penicillins

Accordingly the following compounds are significantly more stable than Benzyl penicillin:

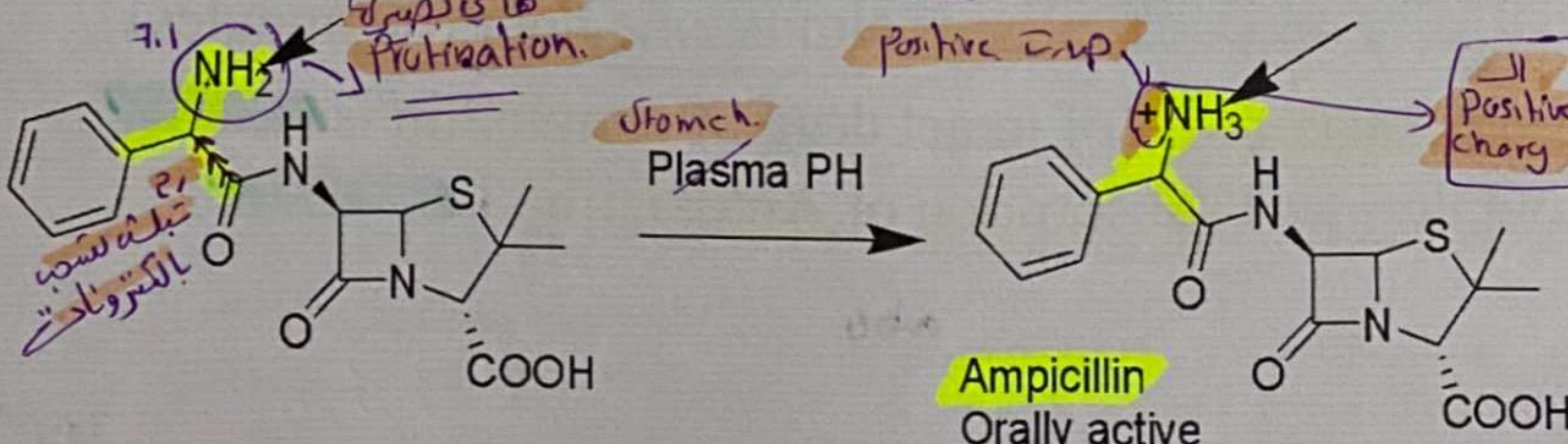


alpha - Halo benzyl penicillin (X=Cl, Br, I)



Phenoxy methyl penicillin: Penicllin V
Acid resistant
can be given orally

Stomch.
In plasma PH NH2 will become ionized to NH3+ so it will become electron withdrawing



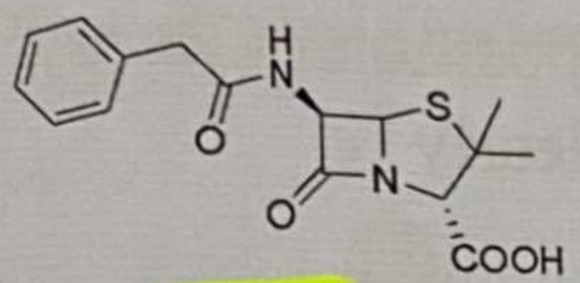
Ampicillin
Orally active

الـ Positive charge تعطي solubility وهيك تشتغل على الـ gram(-)

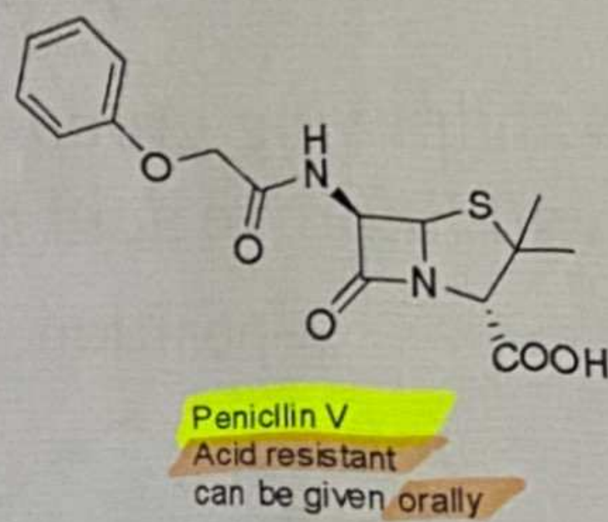
كان هيك بالفحص ... والتهابات بالبطن ... نعطي ampicillin او amoxicillin

Gram(-) ... benzyl penicillin ...

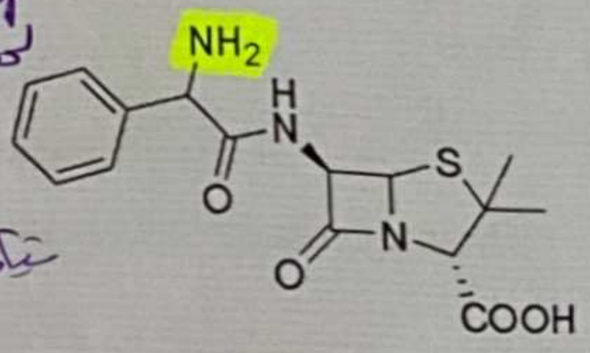
Acid resistant Penicillins



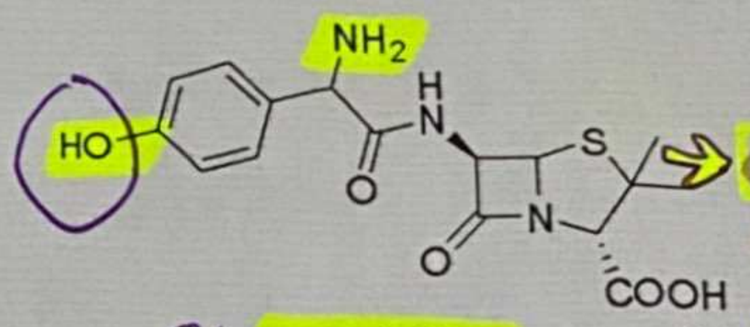
Penicllin G
Acid labile
Can not be given orally



Penicllin V
Acid resistant
can be given orally



Ampicillin
Acid resistant
Orally active
6 hr



8 hr Amoxicillin
Acid stable
Orally active
(longer half life)

Amoxicillin: given once each 8 hours (longer half life).
Ampicillin: given once each 6 hours

Aminopenicillins ← Ampicillin , Amoxicillin

- The half-life of amoxicillin is 61.3 minutes. Approximately 60% of an orally administered dose of amoxicillin is excreted in the urine within 6 to 8 hours. Detectable serum levels are observed up to 8 hours after an orally administered dose of amoxicillin. Since most of the amoxicillin is excreted unchanged in the urine, its excretion can be delayed by concurrent administration of probenecid.
- The half-life of amoxicillin is almost one hour (60 minutes)
- But the % absorption of intact drug of Ampicillin is 30-50% meanwhile The % absorption of Amoxicillin is 75-90%

30-50 %
75-90 %

Bacterial Resistance:

- Two types:
- 1. Natural (innate) resistance, this is particularly important in gram negative (G-) bacteria mediated by the reduced permeability of the outer cell envelope of Gram negative bacilli which is linked to the cell wall via the peptidoglycan, such cell envelope is not present is gram positive bacteria
- 2. Other normally resistant bacteria can develop resistance by generating resistance enzymes by mutation or natural selection

Bacterial Resistance:

- The second type of enzymatic resistance is the most common resistance mechanism.
- The resistant enzymes are collectively known as " penicillinases" and are of two general types:
- 1. B-lactamases (most important)
- 2. Acylases

طبليه !! Panicillinase اسمها

صلاتك يا النبي الابداع بالرسم

Penicillin بأسماء بأنواع

أكثرها بأنواع الـ B-lactam

هي الإنزيمات اللي تقوم بتكسير الـ Penicillin ويصبح غير فعال

β-lactamase (Penicillinase):

- β-lactamase break the β-lactam ring, they are either chromosomal or plasmid, constitutive or inducible depending on particular species:
  - Gram +ve *S.aureus*: 1. *inducible* β-lactamase
    2. synthesized at cell wall and released extracellularly
    95% of *S.aureus* became resistant to penicillins
  - Gram –ve bacillic 1. constitutive R-factor
    2. Cytoplasmic enzymes

Again β-lactamase from different species are different in structure and properties.

هي الإنزيمات اللي تقوم بتكسير

β-lactamase (Penicillinase):

- Gram +ve bacteria normally release β-lactamase to outside of the cell that will cleave penicillin before reaching the bacteria.
- Gram –ve bacteria release β-lactamase into the periplasmic space, which again will cleave penicillin before reaching the plasma membrane.
- Penicillin has to reach the plasma membrane where the transpeptidase present to do its antibacterial action.
- Most of gram –ve bacteria are β-lactamase producing bacteria

ماتخربطوا بين هدول الانزيمات {

Transpeptidase (target) :- هو الي بيجمع Dala Dala بعمل تشبيك لل bacteria لحتى تبني ال cell wall

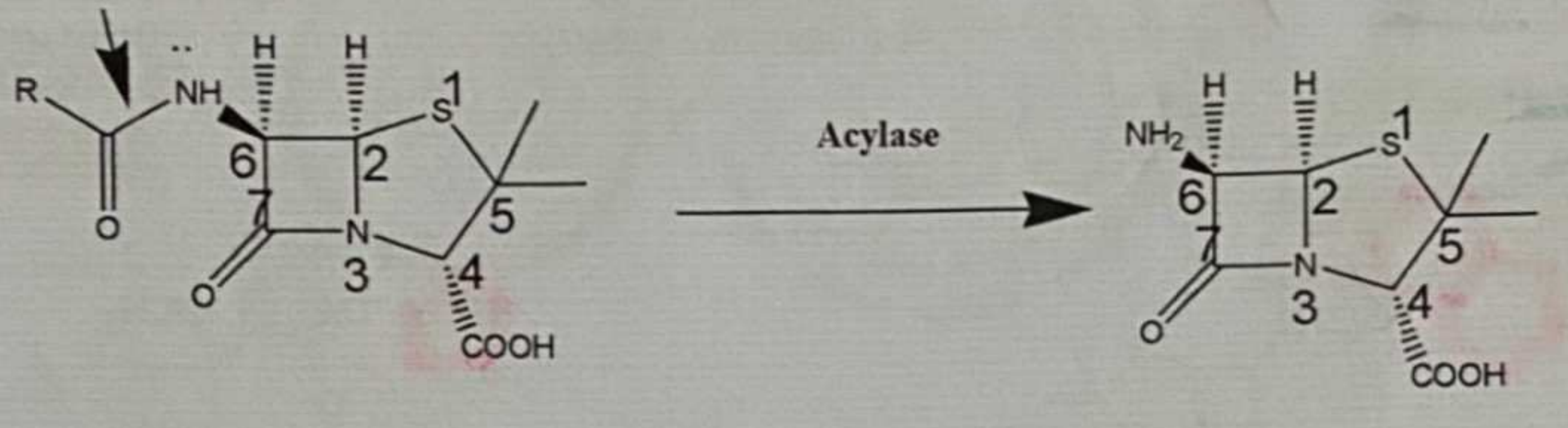
2. Acylases

B-lactamace :- لما تطلق ال bacterial مثير يكسر ال Penicillnase (Penicillinase) قبل مايتوصل عليه (بكسر Beta ring)

- These enzymes can hydrolyze the acylamino-side chain of penicillins

⇒ [ال acylase بشبه ال (B-lactamase)] ⇐

(B-lactamase) بيشتغل ع B-lactam ring وبكسرها — acylase بشتغل ع acyle group وبكسروها



6-Amino penicillanic Acid (6-APA)

كتير اعمل

Rules to create Pinicillinase resistant Penicillins

احيانا بنبدل كلمة B_lactamase بـ Pinicillinase :-

- Increase the steric bulk at the α-carbon on the acyl-amino group enhances good penicillins activity
- Antibacterial activity is enhanced when the α-carbon is part of aromatic ring, so based on these points we can conclude that Ortho substituted aromatic ring should produce excellent β-lactamase resistance
- See the following slide for examples.

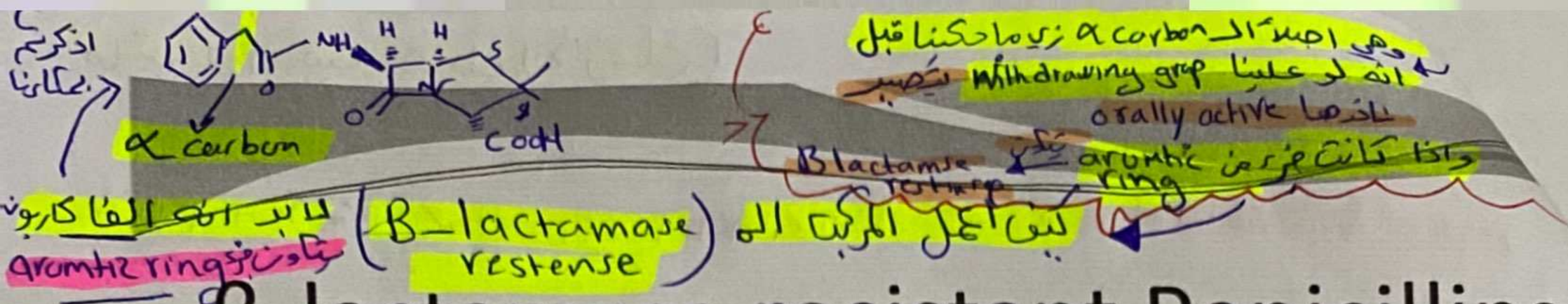
كتير اعمل Penicillinase resistant Penicillins :-

بدي ال Penicillinase الموجود خارج ال extra cellular لما يدخل في مركبي الي هو ال Penicilline بدي اياه يرتد "ليه يدخل جوا ال binding bocket تاعت ال Pencellnase ويكسر "!!!

انا بدي ال Penicillinase يخبط فيه ويرتد ← اروح احط bulk group.

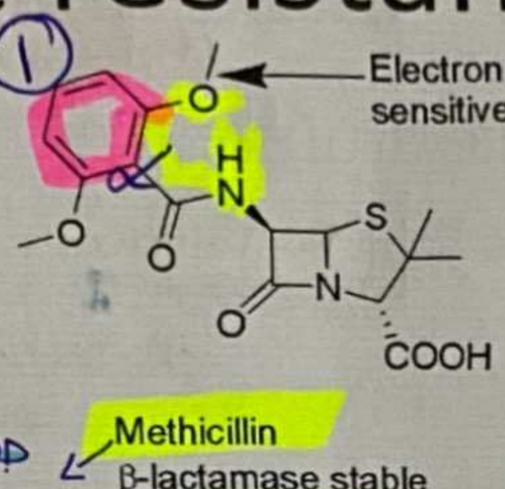
توضح بالسلايد الي بعد هاي

β-lactamase resistant Penicillins

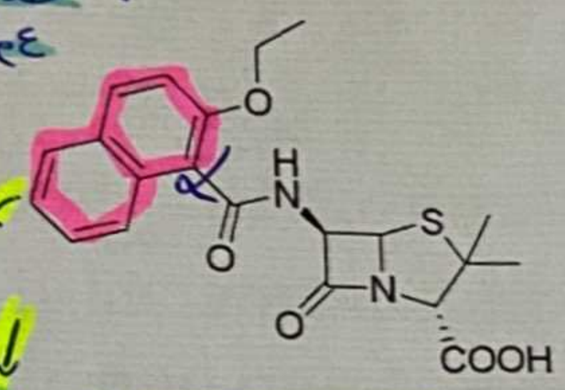


MERS في عندي كمريا

Methicin restense



(electrodonating group)

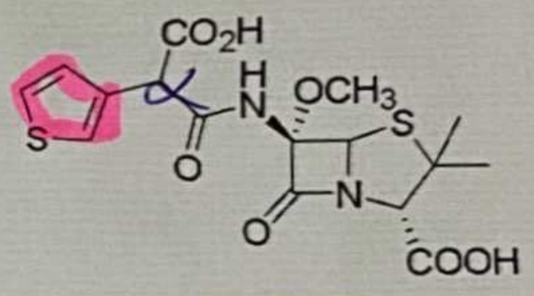


Methicillin
β-lactamase stable
Acid sensitive (why?)

Nafcillin
β-lactamase stable
Acid sensitive

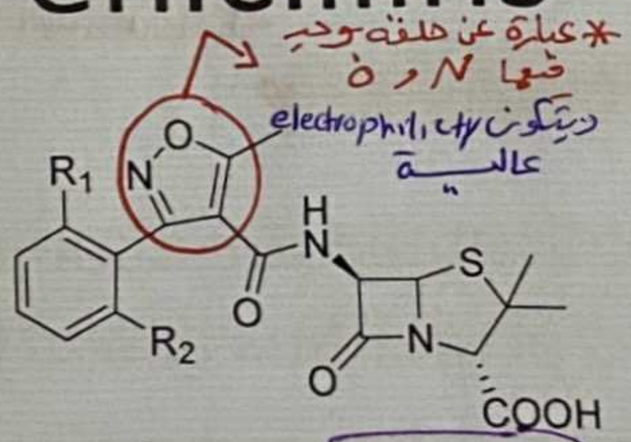
B-lactamase restinse
Wide receptrum
Water Soluble

Ticarcillin Orally inactive,
Broad spectrum and
β-lactamase sensitive
given with clavulinic acid



~~Temocillin~~
Ticarcillin

Isoxazoyl Penicillins



$R_1, R_2 = H$	Oxacillin
$R_1 = Cl, R_2 = H$	Cloxacillin
$R_1 = Cl, R_2 = F$	Flucloxacillin
$R_1, R_2 = Cl$	Dicloxacillin

Flucloxacillin: (how to think and analyze)

- Bulky which means β-lactamase resistant
- E-withdrawing which means acid stable
- α-carbon is part of an aromatic ring which means good activity

- Bulkier substituents are required for small sized heterocycles to give good anti-β-lactamase activity
- Acid stable due to the electron withdrawing effect of the isoxazole ring.
- Used against *S.aureus* resistant bacteria.
- Most penicillinase-resistant penicillins are less active than Penicillin G or Phenoxymethyl penicillin (V) against most non-β-lactamase procedures that are normally sensitive to penicillins, increasing α carbon bulkiness is with price
- Penicillinase-resistant penicillins tend to be bulky and lipophilic with poor penetration into Gram negative bacteria cell envelope

No.

Isoxazoyl penicillins

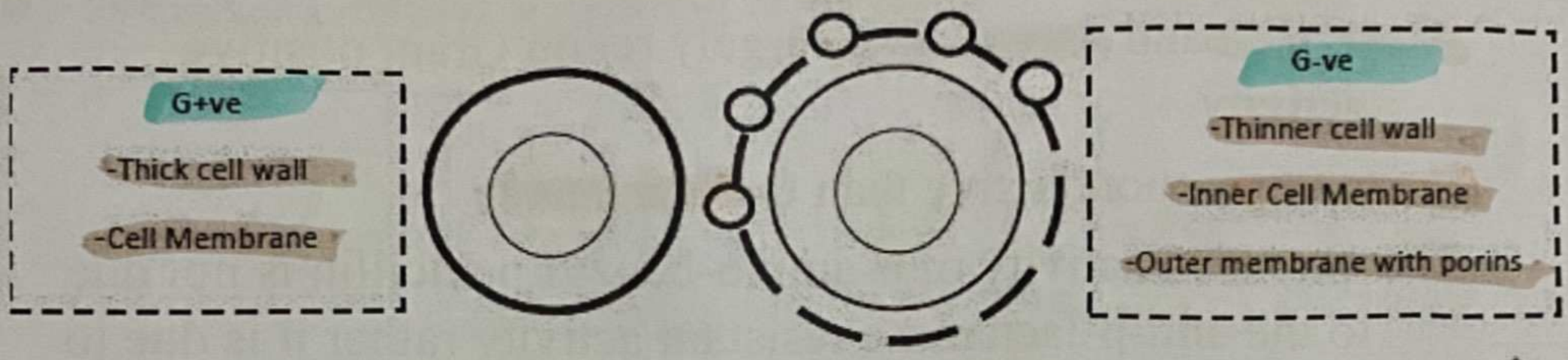
* يفضل استخدام Penicillin G أفضل لانه فعال اكثر

- اما بالنسبة ل bulk group الفا كاربون خلينا عربي أقل فعاليه وخلينا اكرب Narrow

بالبلكتور بتوف هو كابه لـ (oral) ويكون
↓ عطي B-lactamase resistance

oxacillin / cloxacillin.

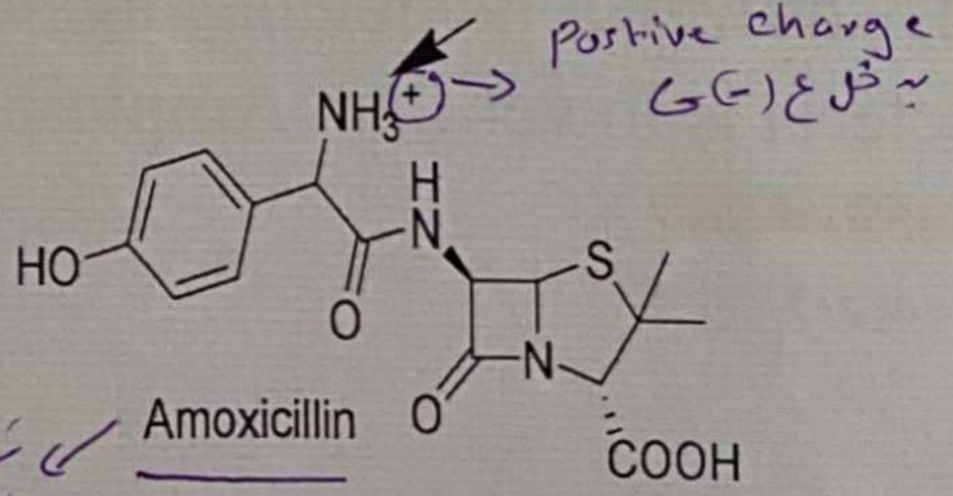
flucloxacillin / Dicloxacillin.



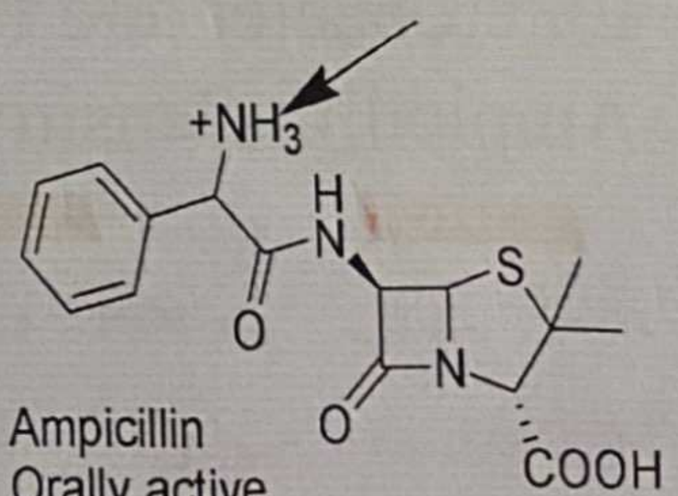
Broad Spectrum Penicillins

- Very important finding is the fact that substitution of α-carbon with polar or ionized group will produce wide spectrum of activity including Gram negative bacteria It works against (Pseudomonas , E.coli , Haemophilus influenza , …)

In plasma PH NH2 will become ionized to NH3+



Amoxicillin



Ampicillin
Orally active

Broad Spectrum Penicillins

Ampicillin and Amoxicillin are effective against Gram negative genera E.Coli, Klebsiella, Haemophila Salmonella, Shiegella and some proteus

Ampicillin and Amoxicillin largely retain Gram positive activity

D-isomer is more active than the L-isomer

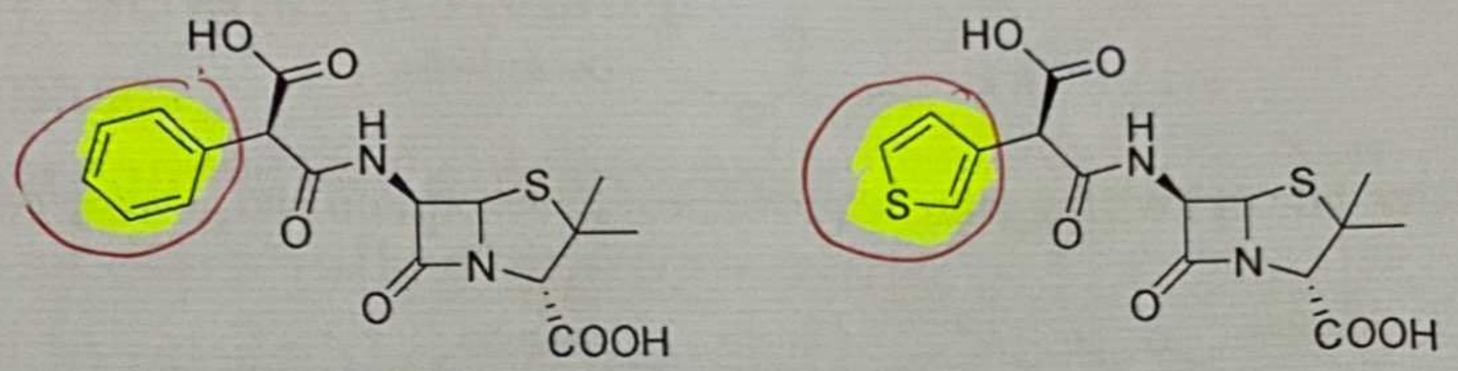
The extended activity of α-amino-benzyl-penicillin is not due to the anti-β-lactamase resistant activity rather it is due to the hydrophillic nature of the molecule which enables it to penetrate the outer cell-envelope through the porin channels

Broad Spectrum Penicillins

- α-OH also expand the activity but they are less active than the α-NH2 derivatives and less acid-stable than the α-amino group
- α-COOH has wide spectrum activity including all the bacteria that are α-NH2 sensitive as well as gram negative bacilli of the genera "**Pseudomonas,** Klebsiella, Enterobacter and Proteus" however its potency against Ampicillin-Sensitive bacteria is lower than Ampicillin

Carboxypenicillins

- They have a carboxylic acid at the □-carbon of the acyl side chain.
- They have broad spectrum activity.

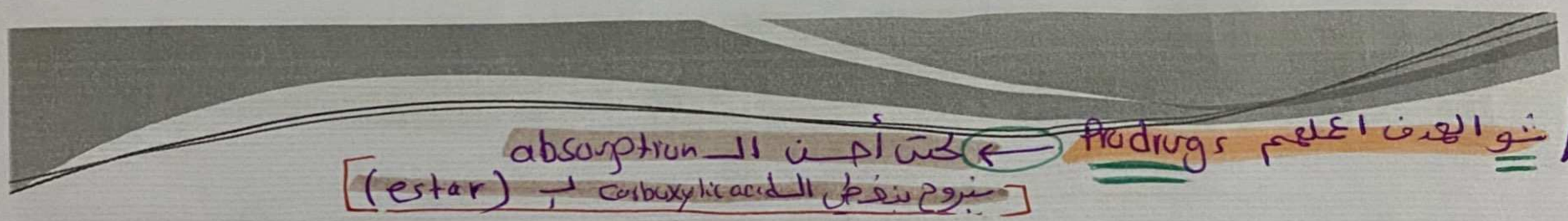


Carbenicillin (1)

Ticarcillin (2)

ما بناخدها orally

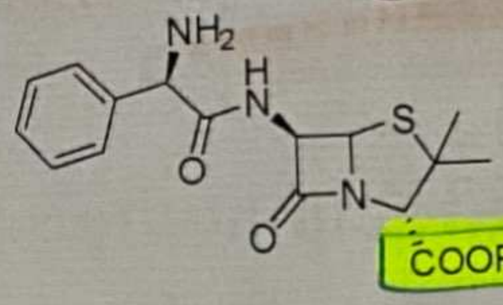
لانه الـ carboxylic acid بتأثر بالمعدة



Ampicillin and amoxicillin prodrugs

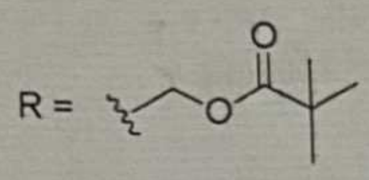
- Ampicillin and amoxicillin are Poorly absorbed through the mucus membrane, this is due to the fact that they formed a zwitter ionic molecule at physiological pH (they contain a carboxylic acid and an amino group in their structure.
- The oral bioavailability can be improved by masking one of them, mainly the carboxylic acid…. By preparing a prodrug esters.

Ampicillin prodrugs

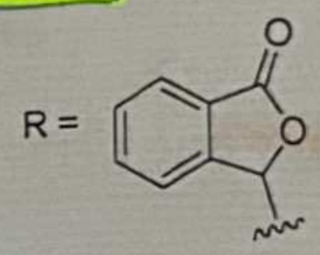


1 * نقوم بتعطيه ال (Carboxylic acid) بـ أي (estar bond)

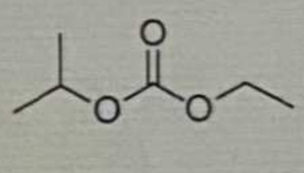
2 وبعد ما يصير الـ hydrolysis بكسر الـ estar bond بواسطة estrase enzyme وبالتالي يرجع الـ Penicillin active form اللي الـ



Pivampicillin

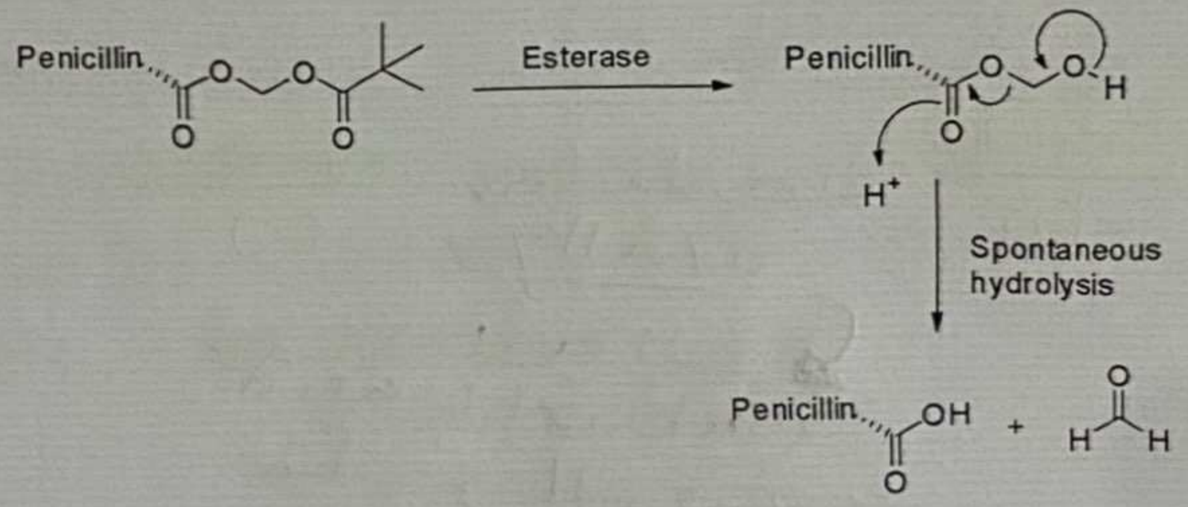


Talampicillin

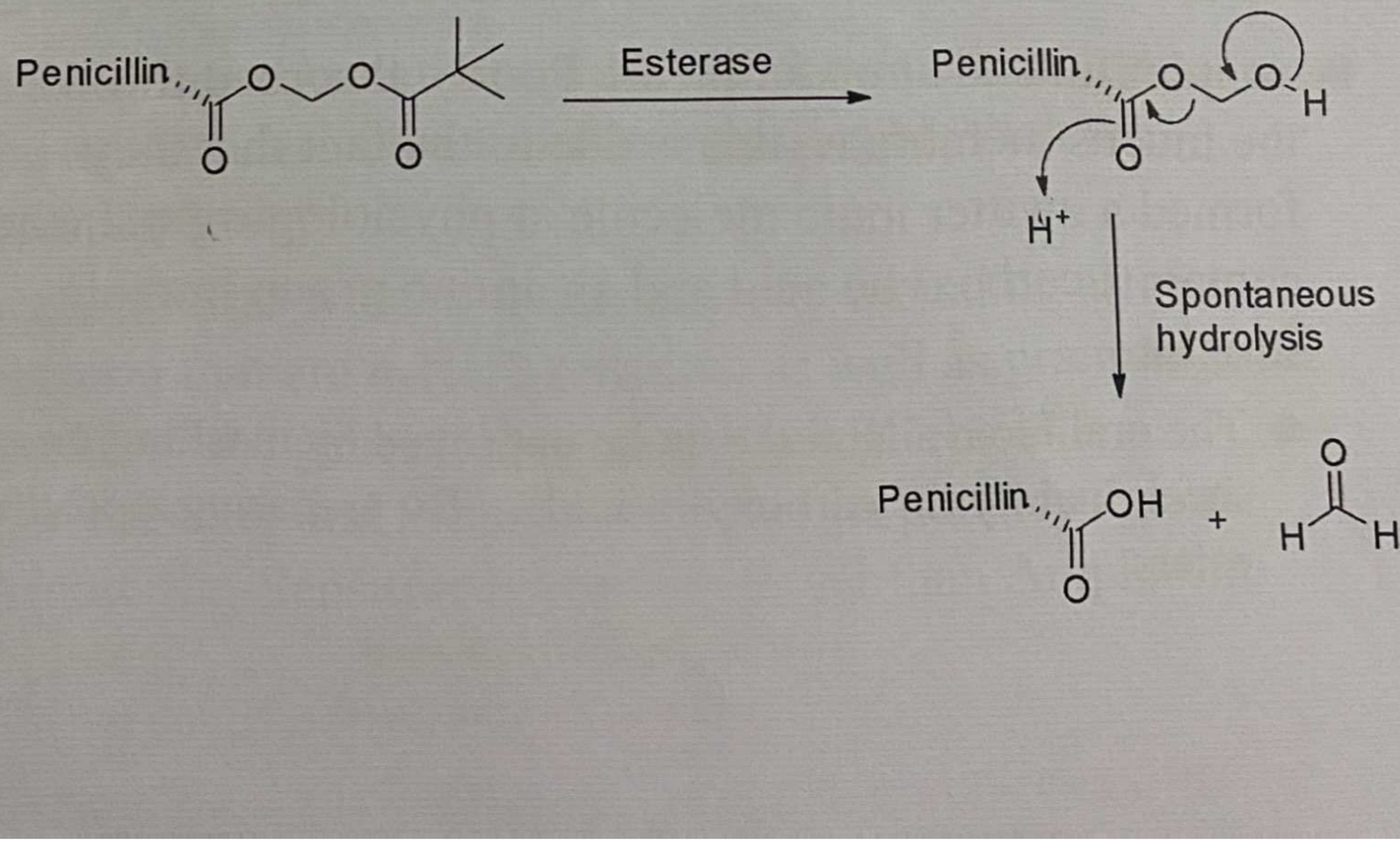


Bacampicillin

- The methyl ester did not give the same improvement in absorption and activity (why?).

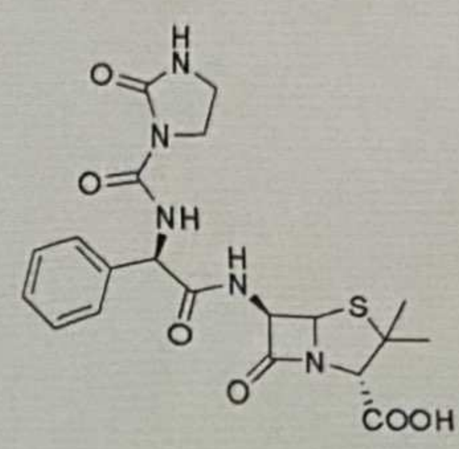


توضيح التأثير:

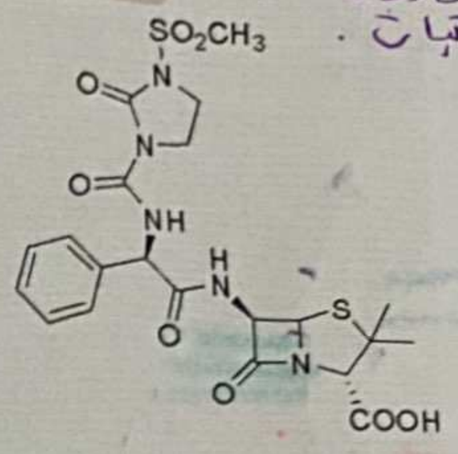


Ureidopenicillins

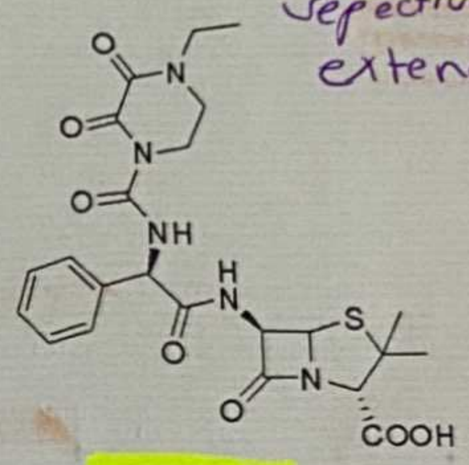
- They all have a urea group at the □-carbon in the acyl side chain.
- They have better activity compared to amoxicillin and they are more resistant to β-lactamase.
- Used parenterally for gram –ve infections especially *P.aeruginosa.*
- the ureido group though to mimic Some of the peptidoglycan structure, which means that it can bind to penicillin-binding protein



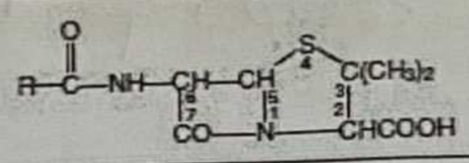
Azlocillin

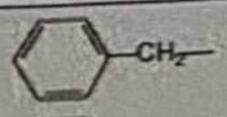
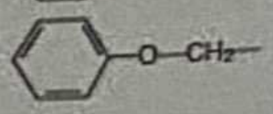
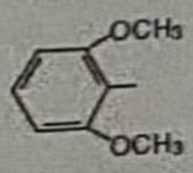
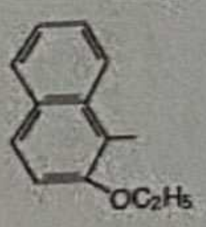
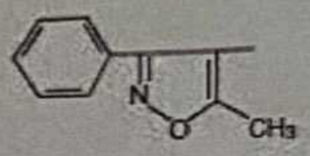
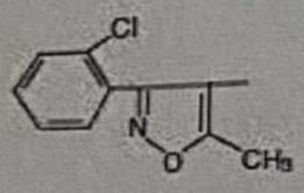
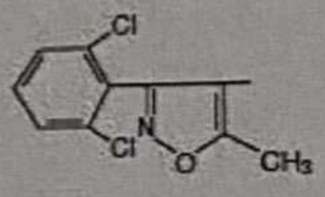
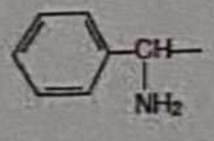


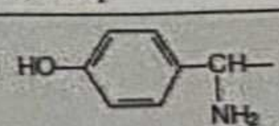
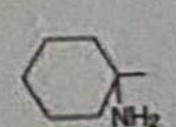
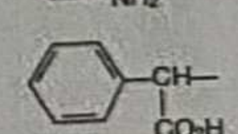
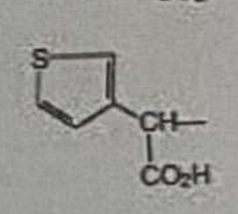
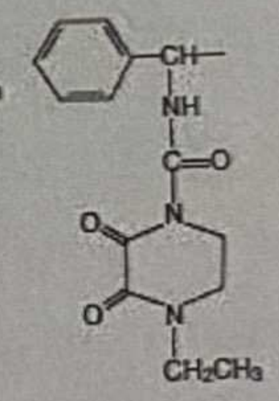
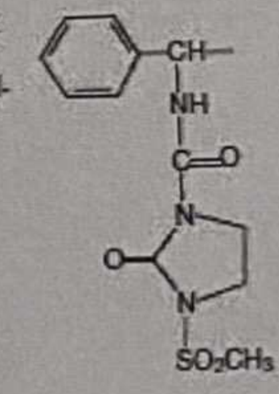
Mezlocillin



Piperacillin



Generic Name	Chemical Name	R Group
Penicillin G	Benzylpenicillin	
Penicillin V	Phenoxymethylpenicillin	
Methicillin	2,6-Dimethoxyphenyl-penicillin	
Nafcillin	2-Ethoxy-1-naphthyl-penicillin	
Oxacillin	5-Methyl-3-phenyl-4-isoxazolylpenicillin	
Cloxacillin	5-Methyl-3-(2-chlorophenyl)-4-isoxazolylpenicillin	
Dicloxacillin	5-Methyl-3-(2,6-dichlorophenyl)-4-isoxazolylpenicillin	
Ampicillin	D-α-Aminobenzyl-penicillin	

Generic Name	Chemical Name	R Group
Amoxicillin	D-α-Amino-p-hydroxybenzylpenicillin	
Cyclacillin	1-Aminocyclohexyl-penicillin	
Carbenicillin	α-Carboxybenzyl-penicillin	
Ticarcillin	α-Carboxy-3-thienyl-penicillin	
Piperacillin	α-(4-Ethyl-2,3-dioxo-1-piperazinylcarbonyl-amino)benzylpenicillin	
Mezlocillin	α-(1-Methanesulfonyl-2-oxoimidazolidino-carbonylamino)benzyl-penicillin	

ليه Narrow ؟؟
لأنه أنا كبرت الحجم تاعها بطلت تقدر تعبر
الـ (Porin)

كان ع الفاكربون aromatic ring

كان ع الفاكربون isoxazoyl

بسبب اضافه amingroup صارت Broad.

TABLE 8.3 Classification and Properties of Penicillins

Penicillin	Source	Acid Resistance	Oral Absorption (%)	Plasma Protein Binding (%)	β-Lactamase Resistance (*S. aureus*)	Spectrum of Activity	Clinical Use
Benzylpenicillin	Biosynthetic	Poor	Poor (20)	50–60	No	Intermediate	Multipurpose
Penicillin V	Biosynthetic	Good	Good (60)	55–80	No	Intermediate	Multipurpose
Methicillin	Semisynthetic	Poor	None	30–40	Yes	Narrow	Limited use
Nafcillin	Semisynthetic	Fair	Variable	90	Yes	Narrow	Limited use
Oxacillin	Semisynthetic	Good	Fair (30)	85–94	Yes	Narrow	Limited use
Cloxacillin	Semisynthetic	Good	Good (50)	88–96	Yes	Narrow	Limited use
Dicloxacillin	Semisynthetic	Good	Good (50)	95–98	Yes	Narrow	Limited use
Ampicillin	Semisynthetic	Good	Fair (40)	20–25	No	Broad	Multipurpose
Amoxicillin	Semisynthetic	Good	Good (75)	20–25	No	Broad	Multipurpose
Carbenicillin	Semisynthetic	Poor	None	50–60	No	Extended	Limited use
Ticarcillin	Semisynthetic	Poor	None	45	No	Extended	Limited use
Mezlocillin	Semisynthetic	Poor	Nil	50	No	Extended	Limited use
Piperacillin	Semisynthetic	Poor	Nil	50	No	Extended	Limited use

متى حكي انه extended ؟؟
بس بأثر المركب P. aeruginosa.
والي هم (4 مركبات فوق) الج
وكل الـ extended ما بأخذهم (orally)
لانه أنا عم بضيف عليها (water soluble group)

ليه Broad؟
بسبب اضافة
الـ
amino group