Model Answer Paper

AS – 2162

M.Sc (Third Semester) Examination, 2013

Medicinal Chemistry

By

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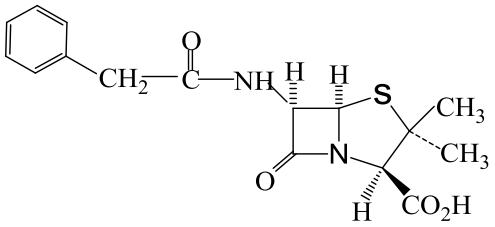
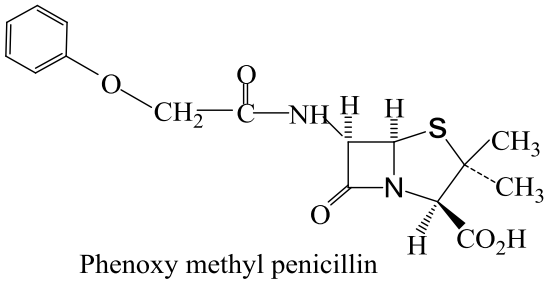
1. (iv) Write the structures of mostly used penicillin for clinical studies. 2

Ans: Mostly used penicillin for clinical studies are (a) benzyl penicillin and (b) phenoxy methyl penicillin.



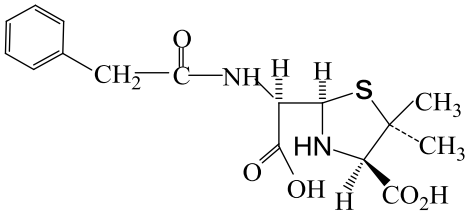
Benzyl penicillin



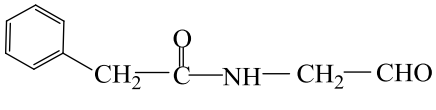
Phenoxy methyl penicillin

(vi) Write the structures of penicilloic acid and penillo aldehyde . 2

Ans:



peniciollic acid



penilloaldehyde

(vii) Write the properties (any four) of cephalosporins 2

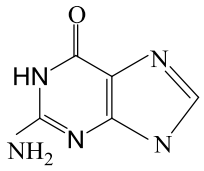
Ans: Properties of cephalosporins

(a) Difficult to isolate and purify because the presence of highly polar side chain.
(b) Relatively stable to acid hydrolysis compared to penicillin G.
(c) Good ratio of activity against gram negative and gram positive bacteria.
(d) Low reactivity (one thousand of penicillin G)

4. (a) Acyclovir owes its structural activity to which part of its structure? What is the structure of the compound it is able to mimic?

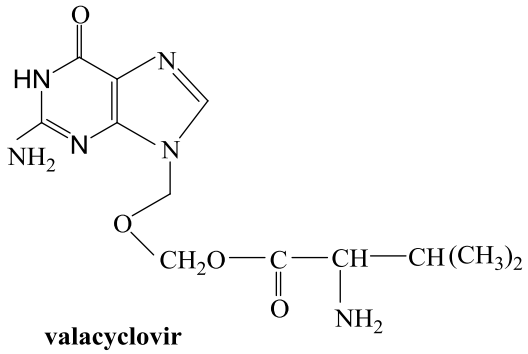
(b) Give the structure of norfloxacin/ciprofloxacin and associate the different regions in the structure with their corresponding activity. 4+4 = 8

Ans: (a) Acyclovir owes its structural activity to the following structure because this parent framework is responsible for the modification of acyclovir and will be responsible for the similar properties which will be responsible to show same activity.

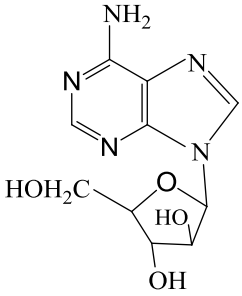


parent structural framework

Acyclovir can mimic the structure with similar activity when the particular compound contains the above parent structural framework with different substituent. Valacyclovir and vidarabine are the compounds which will be mimicked by acyclovir.

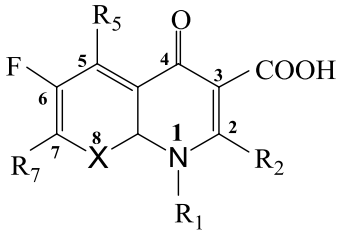


valacyclovir



vidarabine

(b)



X = C ⟶ norfloxacin or ciprofloxacin

X = N ⟶ naphthyridone

this group controls pharmaco kinetics and total activity

Carboxilic acid group must be essential for gyrase binding and bacterial support

F group controls gyrase binding and bacterial potency.

R_1 ⟶ it is responsible for control the pharmaco kinetics

R_2 ⟶ this group is responsible for closing to the gyrase binding site

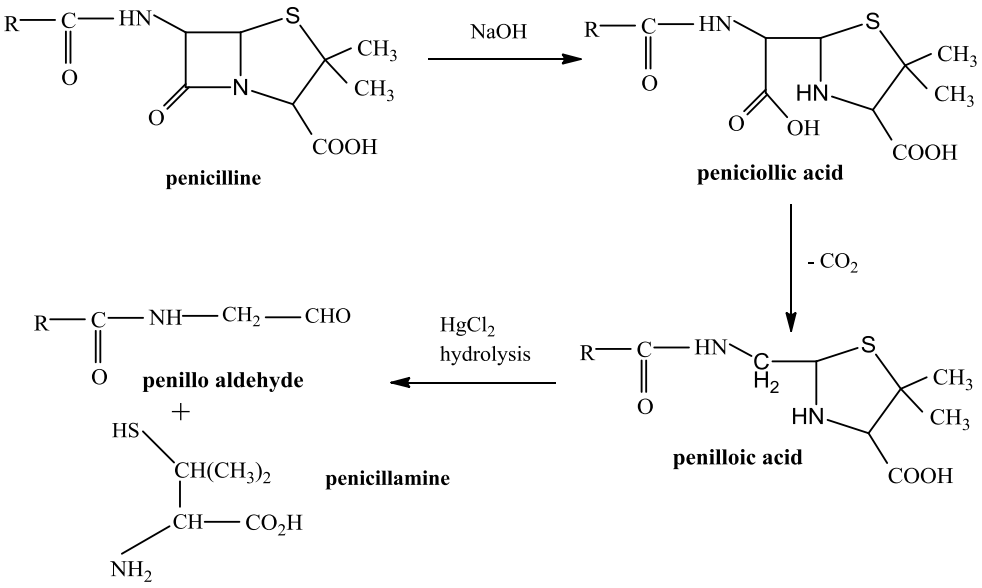
R_5 ⟶ this group controls potential addition of the activity of gram +ve bacteria.

R_7 ⟶ this group is responsible for control potency, spectrum and pharmaco kinetics

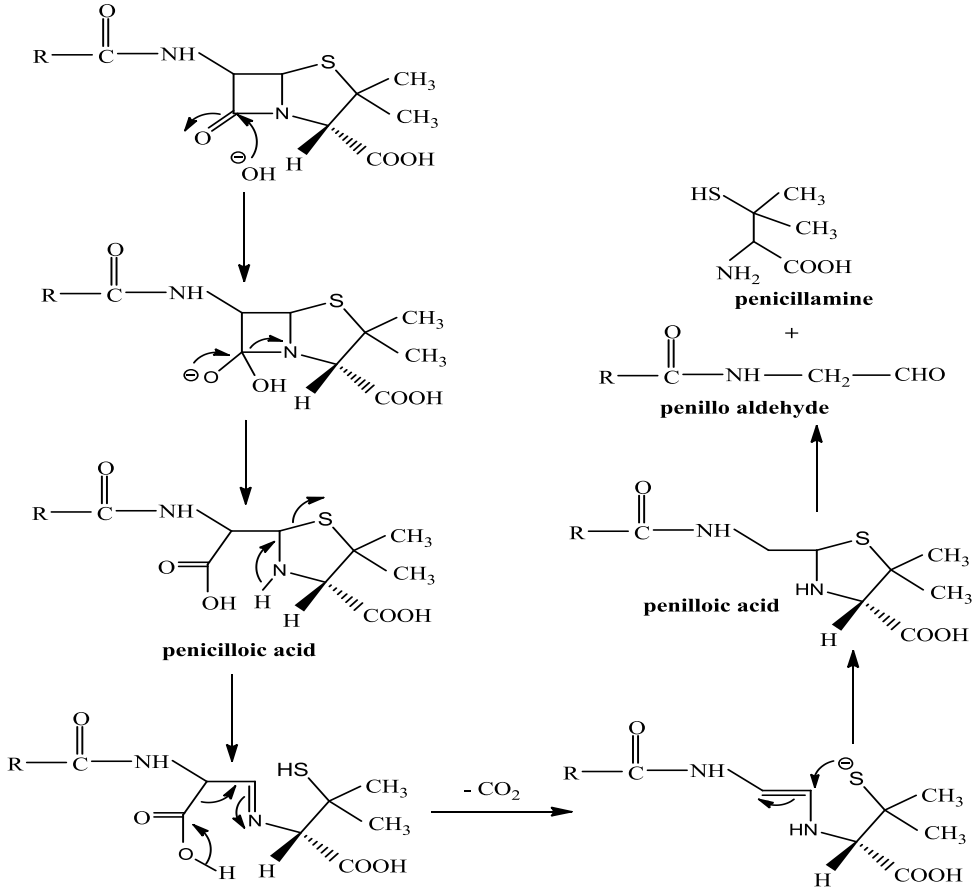
5. (a) Discuss the reaction between benzyl penicillin with sodium hydroxide followed by aqueous mercuric chloride and explain the mechanism.

(b) Explain the stability of penicillin depending on different *ortho* substituent aryl groups of side chain towards β-lactamase. 5+3 = 8

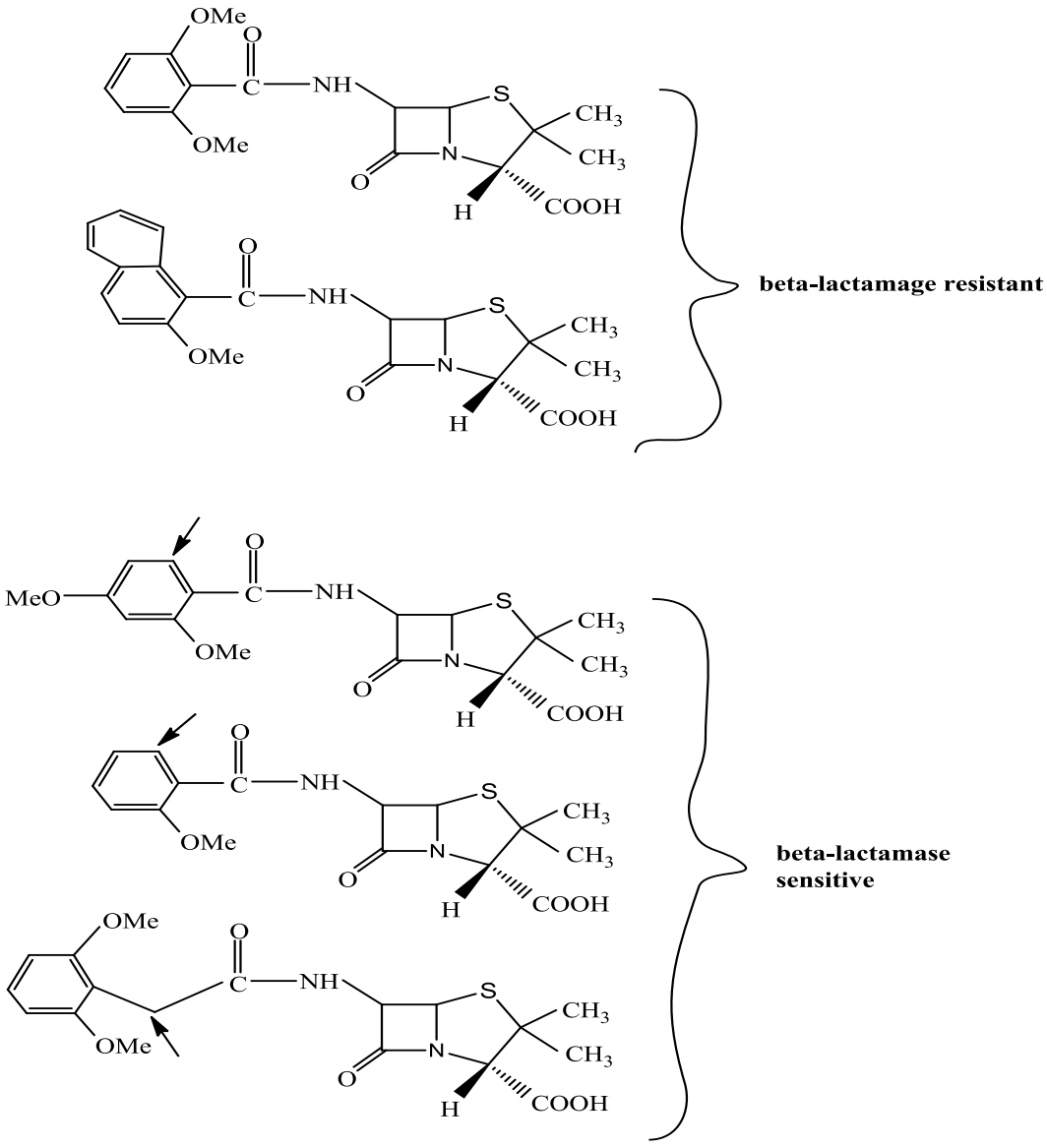
Ans: (a) The products are penicillamine and penillo aldehyde for the reaction between benzyl penicillin with sodium hydroxide followed by aqueous mercuric chloride.



Mechanism:



(b) The stability of penicillins towards β-lactamase is influenced by the bulk of the acyl group attached to the primary amine. β-lactamase will be resistant when the penicillin aromatic ring is attached directly to the side chain carbonyl and the both *ortho* position of the aromatic ring are substituted by methoxy groups. Movement of one of the methoxy groups to the para position or replacing one of them by hydrogen resulted an analogue to β-lactamases. Putting a methylene group between the aromatic ring will be also sensitive to β-lactamases.



6. Give the complete description of Actinomycin D analogs that are possible. Give structure. What is the fundamental requirement for biological activity mimicking the natural actinomycin? 6+2 = 8

Ans: Actinomycin D or dactinomycin is the first antibiotic as showing anticancer activity. Actinomycin D has two pentapeptide lactones attached to an aromatic actinocin (phenoxazinone) structure. It is capable of intercalating DNA binds preferably between guanine and cytosine residues on a single DNA strand. This interaction results in DNA elongation and distortion. The actinomycin D orients itself perpendicular to the main DNA axis allowing the pentapeptide lactone units to bind to residue in the minor grove of DNA through hydrophobic and hydrogen bonds. Actinomycin D has three parts in structure (a) pentapeptide chains (b) actinocin or phenoxazine ring system (c) p-benzoquinone imine. In pentapeptide lactone rings five amino acids are involved which are sarine, methyl valine, threonine, valine and proline.

The binding of the actinocin D and ploypeptide lactone portions to DNA is cooperative means that the binding of one unit facilitates the binding of others. This significantly enhances drug DNA affinity. The para-benzoquinone segment of actinomycin D renders the molecule vulnerable to NADPH reductase. Here the loss of aromatic methyl group results in a loss of activities.

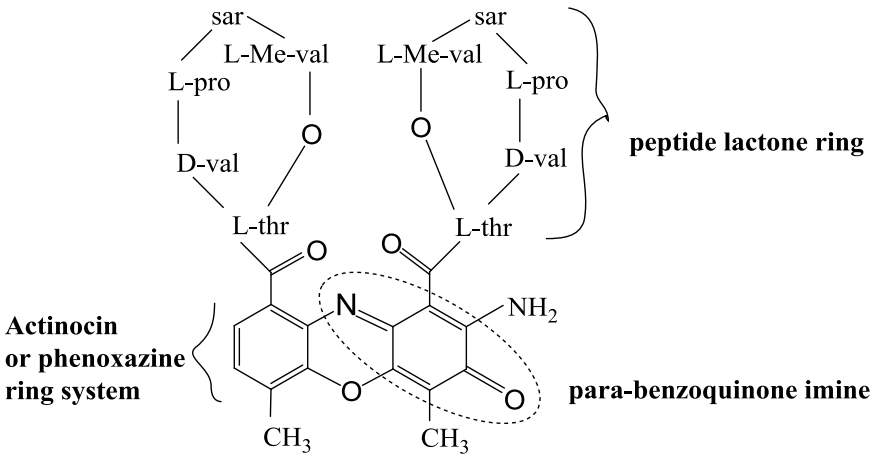
The common side effects: (i) Low white blood levels and increase risk of infection

(ii) Low red blood cell levels – increase risk of anemia.

(iii) Nausea and vomiting

(iv) Sores in the mouth.

Less common side effects: (i) Fatigue, (ii) Liver damage (iii) Loss of appetite (iv) Fever



Actinomycin D

From the structure of actinomycin D, it is found that there are three parts in this structural framework (a) pentapeptide lactone ring (b) actinocin ring system and (c) para-benzoquinone imine. The compounds which contains these three framework together with some other modification by using different structure then the activity or mimic property will very be very closely similar as other anti cancer agents like natural actinomycin D as for example anthracyclines.