# KIBABII UNIVERSITY

## UNIVERSITY EXAMINATIONS
## 2020/2021 ACADEMIC YEAR

### THIRD YEAR FIRST SEMESTER
### SUPPLIMENTARY/SPECIAL EXAMINATIONS

**FOR THE DEGREE OF BSC (CHEMISTRY)**

**COURSE CODE:** SCH 317

**COURSE TITLE:** BIOOGANIC AND MEDICINAL CHEMISTRY

**DATE: 12/1/2022** **TIME: 8-10AM**

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**INSTRUCTIONS TO CANDIDATES**
Time: 2 Hours

**Answer question ONE and any other TWO of the remaining**

## QUESTION ONE (30 MARKS)

a) Define the following terms as used in medicinal chemistry **(5 marks)**

i. Hormone

ii. Semiochemicals

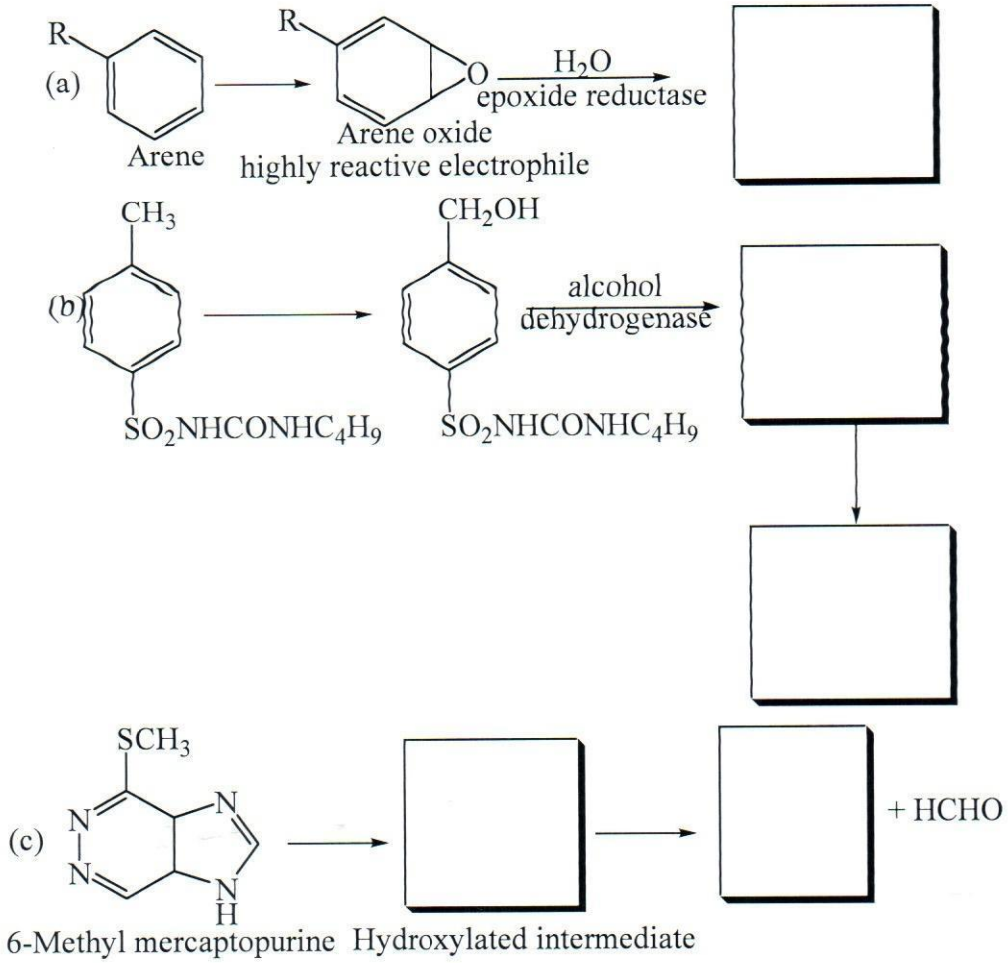
iii. Pheromone

iv. Allelochemicals

v. Pharmakinetics

b) Mention fives ways how drugs interact with DNA **(5 marks)**

c) In Phase I of drug metabolism a polar group is introduced/unmasked to make the drug molecule more water-soluble and less active to be excreted. The majority of metabolites are generated by a common hydroxylating enzyme system known as Cytochrome P450. In the following oxidation reactions provide the intermediate and the final metabolites **(5 marks)**

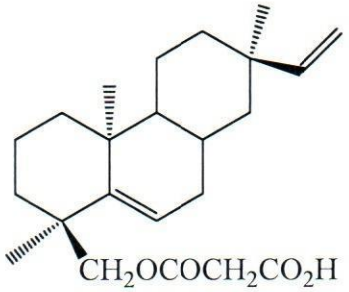


d) Combinatorial chemistry is a very effective tool in drug discovery

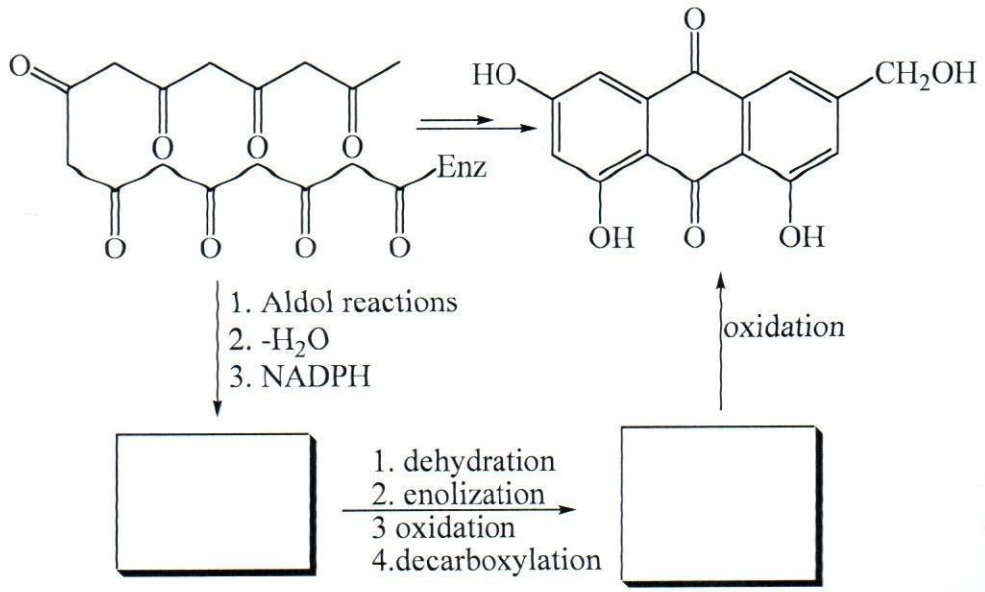
i. Define combinatorial chemistry **(1 mark)**

ii. Explain the working principle of (i) above **(3 marks)**

e) Repeated column chromatography on the stem bark of *Calceolaria pinnifolia* Cav. (Scrophulariaceae) sample from San Juan Province of Argentina produced several terpenoids active against M. tuberculosis on such terpenoid shown below exhibited an MIC value of 4.o μg/mL. Indicate, using bold lines, its constituent isoprene units **(3 marks)**




f) Growing poly-β-keto chain is stabilized on enzyme surface until the chain reaches the required length. The poly-β-keto ester is very reactive – various possibilities for undergoing Claisen or Aldol reactions, dictated by the nature of the enzyme and folding of the substrate. Anthraquinone aloe-emodin is one of such compounds produced from polyketide pathway. Provide its intermediate during its biosynthesis. **(5 marks)**




g) Drug target is a molecule in the body, that is essential to a particular disease process and that could be addressed by a drug to produce a desired therapeutic effect. Name three protein drug targets **(3 marks)**

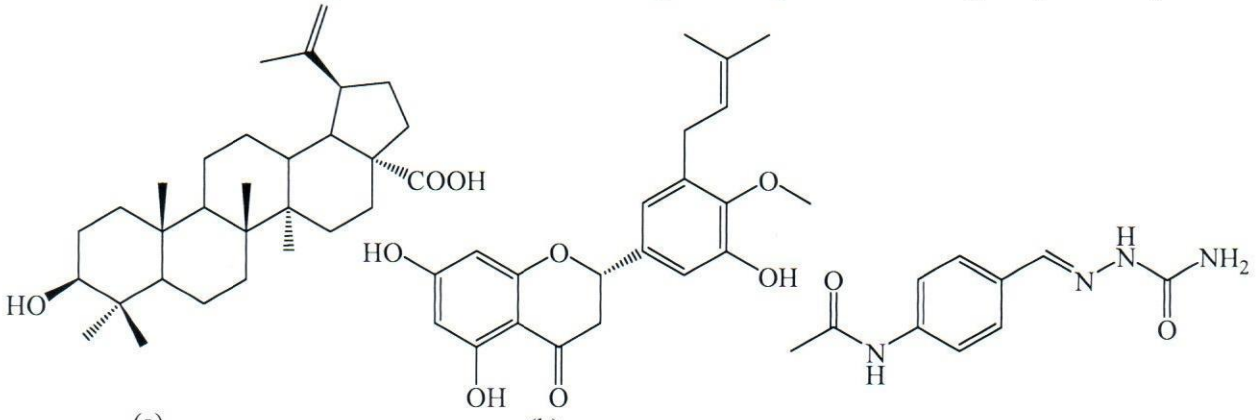
## QUESTION TWO (20 MARKS)

a) Drug targets are macromolecules while drugs are generally much smaller than their targets. Drugs interact with their targets by binding to binding site which typically involve intermolecular bonds

i. Define intermolecular bonds **(1 mark)**

ii. Discuss with relevant diagrams how drugs interacts with active sites by ***ion-dipole bond, hydrogen bond*** and ***dipole-dipole*** interactions **(9 marks)**

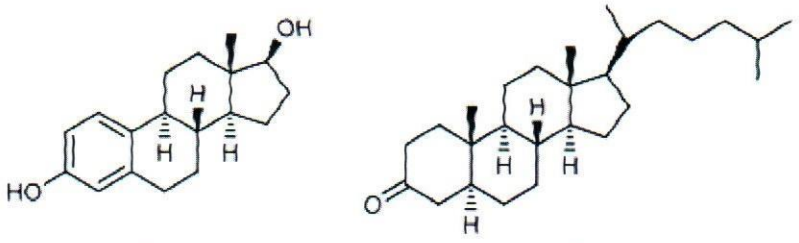
b) In which class of natural product does the following natural products belong **(3 marks)**




(a) (b) (c)

c) Name three factors that affect enzyme activity **(3 marks)**

d) Name the following compounds using IUPAC rules **(4 marks)**

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## QUESTION THREE (20 MARKS)

a) Explain the following terms as used in enzyme as drug target **(5 marks)**

i. Irreversible enzyme inhibitor

ii. Natural substrate

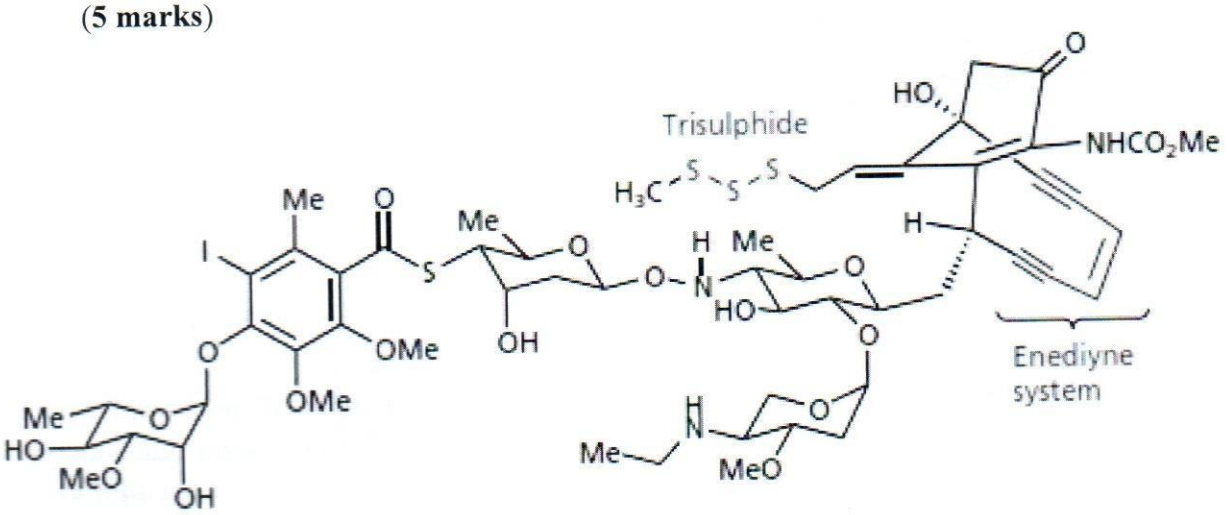
iii. Allosteric binding site

iv. Uncompetitive inhibitor

v. Transition state analogue

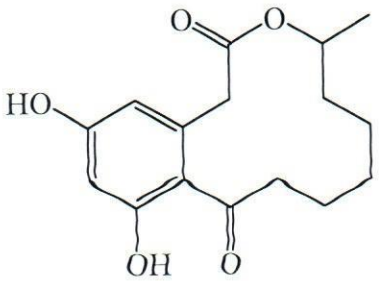
b) Briefly explain lock and key model of enzyme action **(3 marks)**

c) Podophyllotoxins (calicheamicin γ) shown below is anticancer drug that interact with DNA as its target. Explain and provide illustration of its mode of action (**5 marks**)



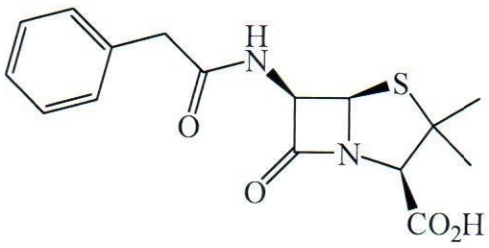

d) Name any three pharmakinetics processes drug undergoes during its administrations (**3 marks**)

e) Indicate, using bold lines, the constituent acetate units in the natural product compound below (**4 marks**)

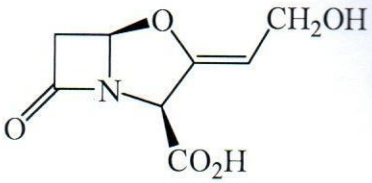



## QUESTION FOUR (20 MARKS)

a) 'Suicide substrates are *bona fide* visitors to an enzyme's active site that become stubborn squatters once they have arrived' Provide illustration of this statement using a suicide substrate *clavulanic acid,* used clinically in antibacterial medications to inhibit the bacterial β-lactamase enzyme in comparison to the mode of action of penicillin G. (**6 marks**)



Penicillin G

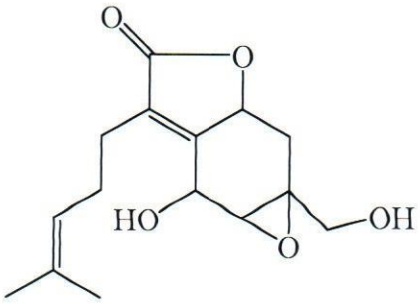


Clavulanic acid

b) Phase II of drug metabolism involve covalent attachment of small polar endogenous molecule to form water-soluble compounds. Highlight four conjugation reactions and their preferred functional group of attachment **(4 marks)**

c) Provide simple procedure on how you would carry out esterification of alcohol and acyl chloride using the principle of combinatorial chemistry **(5 marks)**

d) Identify the isoprene units in paniculide B, a product of tissue culture from *Andrographis paniculata* **(3 marks)**

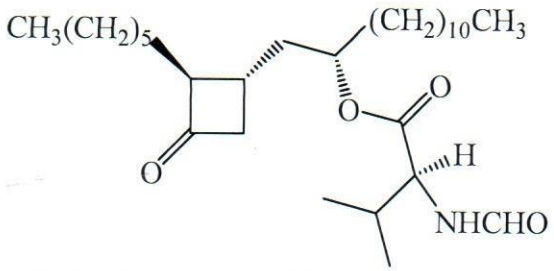


e) State four difference between DNA and RNA **(2 marks)**

## QUESTION FIVE (20 MARKS)

a) Highlight three importance of enzymes **(3 marks)**

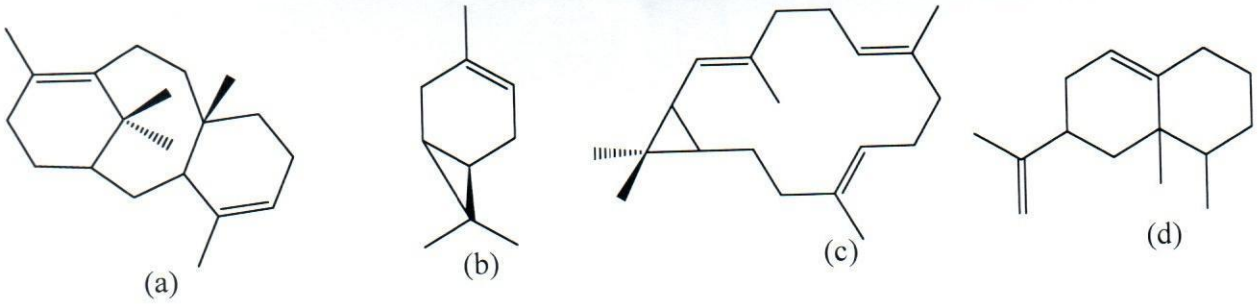
b) Pancreatic lipase is an enzyme responsible for catalyzing the digestion of fats. Orlistat is an anti-obesity drug that target this enzyme. Explain its mode of action on how it binds in the enzyme active site. **(4 marks)**



c) List four disadvantages of injection as route of drug administration **(2 marks)**

d) Name four importance of drug metabolism **(2 marks)**

e) Classify the following terpenes and indicate the number of isoprene units **(4 marks)**




f) Endocrocin is a simple anthraquinone frequently identified in extracts of various fungi. There have been attempts to determine its biosynthetic pathway. The following is one of the proposed pathway. Provide the missing intermediate using the indicated reactions. **(5 marks)**