

## نموذج الإجابة الخاص بمادة الكيمياء الضوئية والفراغية

### 415 CHM

#### الجزء الثاني (الكيمياء العضوية الفراغية)

#### الفرقة الرابعة

تاريخ الإمتحان: 18 يناير 2017

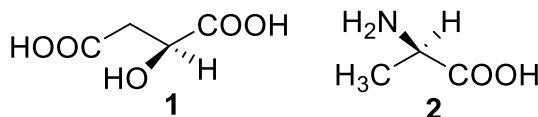
د. بهاء الدين الجندي

#### Section 2: Stereochemistry

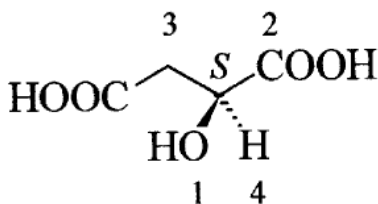
[40 Marks]

3.[20 Marks]

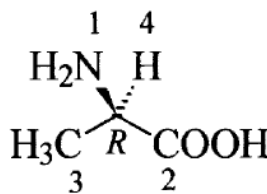
A. Determine the configuration of the isomer of 2-hydroxysuccinic acid (1) and the isomer of the amino acid alanine (2) shown below. [6 Marks]



Answer:



(S)-2-hydroxysuccinic acid

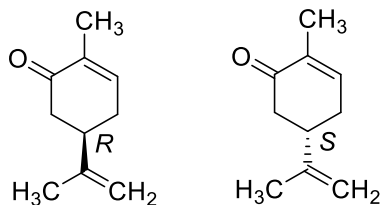


(R)-alanine

1: By application of the CIP rules the order of priority of the atoms directly attached to the chirality centre is  $O > C(O,O,(O)) > C(C,H,H) > H$ . The atom or group of lowest priority, hydrogen in this case, is already oriented away from the observer. Therefore, the sequence of the remaining three groups can be directly deduced from the formula, and these are easily seen to be arranged in a counter-clockwise sense to the observer. It therefore follows that the formula represents (S)-2-hydroxysuccinic acid.

2: The order of priority of the atoms and groups attached to the chirality centre by application of the CIP rules is  $N > C(O,O,(O)) > C(H,H,H) > H$ . The isomer depicted is therefore the unnatural amino acid (*R*)-alanine, more usually referred to as D-alanine.

B. Which of the following properties or methods can be used to distinguish between (*R*)-carvone and (*S*)-carvone? (There are more than one correct choice)[3 Marks]



- a) boiling point      b) UV spectroscopy      c) refractive index      d) melting point  
 e) smell              f) optical rotation      g) dipole moment      h) circular dichroism  
 i) NMR spectroscopy      j) IR spectroscopy

**Answer:**

(*R*)-Carvone and (*S*)-carvone are enantiomers and can be distinguished from each other by their optical rotations, by circular dichroism and by smell. Laevorotatory (*R*)-carvone has a spearmint smell (spearmint = *Mentha spicata*), whilst (*S*)-(+)-carvone has a caraway odor.

C. The chromatographic purification of 1 g of (–)-ethyl lactate with an enantiomeric excess (ee) of 85% yields of the optically pure (–)-enantiomer. Calculate the amount of the (+)-enantiomer that was separated? [6 Marks]

**Answer:**

Since the original compound has an enantiomeric excess of 85%, it contains 85% of the pure enantiomer and 15% of the racemate. Thus for a 1 g sample there is 150 mg of the racemate which must contain 75mg of each enantiomer. Therefore, 75mg = 0.075 g of the (+)-enantiomer must have been separated. The same result can also be obtained using the following equation:

$$\%ee = \frac{|E1 - E2|}{|E1 + E2|} \times 100$$

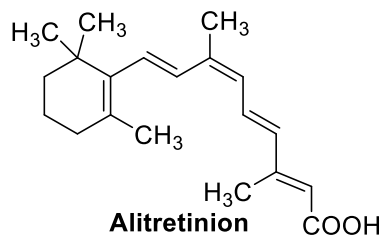
$$E1 + E2 = 1$$

$$\frac{85}{100} = \frac{|E1 - E2|}{1} \times 100$$

$$0,85 = E1 - E2$$

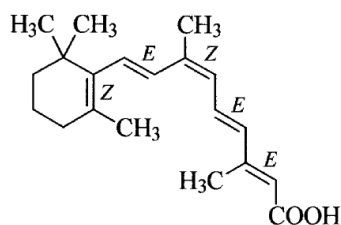
$$E2 = 0,075 \text{ g}$$

D. Determine the configuration of the double bonds in the cytostatic retinoid alitretinoin. How many stereoisomers are possible? [5 Marks]



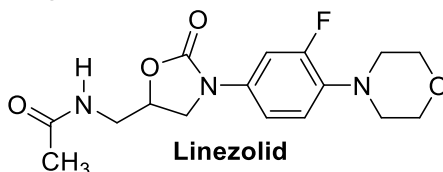
**Answer:**

According to the formula for the calculation of the theoretical number of stereoisomers (configurational isomers),  $x = 2^n$ ,  $2^4 = 16$  (where  $n = 4 =$  the number of stereogenic units) stereoisomers are possible for alitreinoin. Although the molecule contains five double bonds only those in the side chain can be considered, since because of ring strain the double bond in the six-membered ring can only have the Z configuration.



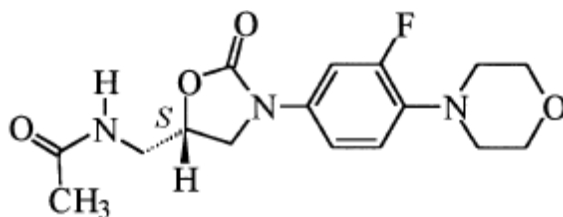
**4. [20 Marks]**

A. The antibiotic linezolid is the pure S enantiomer. Draw the structural formula of the molecule with this configuration. [5 Marks]

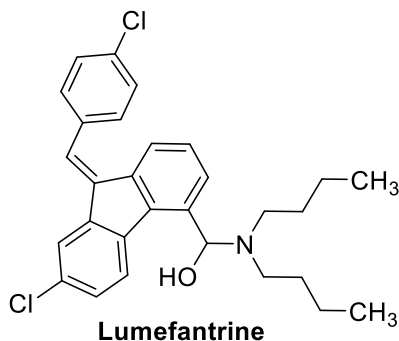


**Answer:**

Linezolid contains a chirality centre in the oxazolidinone ring. The ring oxygen atom has the highest priority and the methylene group attached to the nitrogen atom with two neighbouring carbon atoms has a higher priority than the methylene group attached to the nitrogen atom with only one neighbouring carbon atom. However, since the sequence is clockwise in the formula given, the hydrogen atom must be drawn with a bold (forward projecting) wedged bond to produce the S configuration.

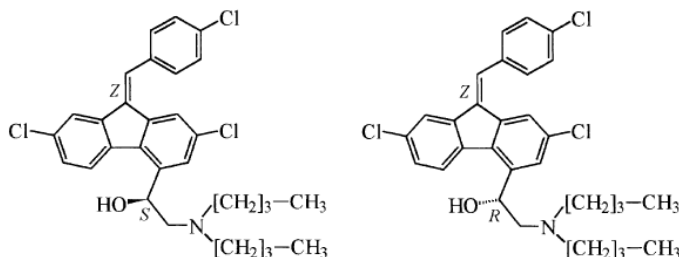


B. Mark the stereogenic units in lumefantrine (an antimalarial drug) and state how many compounds can be represented by this formula. How many stereoisomers in principle are possible with this constitution? [5 Marks]



**Answer:**

Lumefantrine contains two stereogenic units, i.e., a Z-configured double bond and a chirality centre whose configuration in the formula given is unspecified. As a result, the formula represents two compounds (enantiomers) with R, Z and S, Z configuration, respectively. Both are present in the racemic pharmaceutical. There are formally  $2^2 = 4$  isomers possible with this constitution; in addition to the isomers of lumefantrine there are also two others with an E-configured double bond.



C. Answer only two of the following questions: [10 Marks]

- I. Define chiral pool synthesis and what is the main advantage of using this strategy?
- II. What is chiral auxiliary and why synthetic chemists use chiral auxiliaries?
- III. What is enzymatic resolution, give an example for this method?

**Answer:**

- I. Chiral pool synthesis is a strategy that aims to improve the efficiency of chiral synthesis. It starts the organic synthesis of a complex enantiopure chemical compound from a stock of readily available enantiopure substances. Common chiral starting materials include monosaccharides and amino acids. The built-in chirality is then preserved in the remainder of the reaction sequence.

This strategy is especially helpful if the desired molecule bears a great resemblance to cheap enantiopure natural products. Otherwise, a long, tortuous synthesis involving many steps with attendant losses in yield may be required. At times, it may be difficult to find a suitable enantiopure starting material; other techniques may prove more fruitful.

General methods used in chiral pool synthesis are the use of protecting groups, and functional group interconversion (FGI).

- II. A chiral auxiliary is a stereogenic group or unit that is temporarily incorporated into an organic compound in order to control the stereochemical outcome of the synthesis. The chirality present in the auxiliary can bias the stereoselectivity of one or more subsequent reactions. The auxiliary can then be typically recovered for future use. Most biological molecules and pharmaceutical targets exist as one of two possible enantiomers; consequently, chemical syntheses of natural products and pharmaceutical agents are frequently designed to obtain the target in enantiomerically pure form. Chiral auxiliaries are one of many strategies available to synthetic chemists to selectively produce the desired stereoisomer of a given compound.
- III. Enzymatic resolution: Resolution of a mixture of enantiomers based on the selective reaction of one of them under conditions of enzyme catalysis. This approach, involves treating a racemic mixture with an enzyme that catalyzes the reaction of only one of the enantiomers. Some of the most commonly used ones are lipases and esterases enzymes that catalyze the hydrolysis of esters. In a typical procedure one enantiomer of the acetate ester of a racemic alcohol undergoes hydrolysis and the other is left unchanged when hydrolyzed in the presence of an esterase from hog liver. High yields of the enantiomerically pure alcohol and enantiomerically pure ester are regularly achieved

All best wishes,  
Dr. Eman Gad El-Karim  
Dr. Bahaa El-Gendy