Topics in the June 2008 Exam Paper for CHEM1611

Click on the links for resources on each topic.

2008-J-2:

- Assumed Knowledge
- Chemical Bonding
- Atomic Structure
- The Periodic Table

2008-J-3:

- The Shapes of Molecules
- Intermolecular forces
- Acids and Bases

2008-J-4:

- Acids and Bases
- Heterocyclic Compounds

2008-J-5:

- Alkenes
- Alcohols, Phenols, Ethers and Thiols
- Aldehydes and Ketones
- Carbohydrates

2008-J-6:

- Alkenes

2008-J-7:

- Amino Acids, Peptides and Proteins

2008-J-9:

- Alcohols, Phenols, Ethers and Thiols
- Organic Halogen Compounds

2008-J-10:

- Alkenes
- Aromatic Hydrocarbons
- Aldehydes and Ketones

2008-J-11:

- Carboxylic Acids and Derivatives
- Heterocyclic Compounds

2008-J-13:

- Amino Acids, Peptides and Proteins

Marks

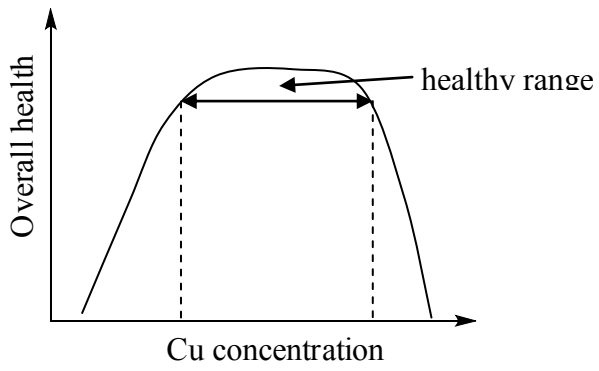
- Complete the following table, giving either the systematic name or the molecular formula as required. **2**

Formula	Systematic name
SO_2	**sulfur dioxide**
$CoCl_2 \cdot 6H_2O$	**cobalt(II) chloride-6-water**
Ag_2CrO_4	silver chromate
$KHCO_3$	potassium hydrogencarbonate

- Complete the following table, providing the ground state electron configuration for each of the following species. **3**

Species	Ground state electron configuration
nitrogen atom	**$1s^2\ 2s^2\ 2p^3$ or [He] $2s^2\ 2p^3$**
chloride ion	**$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6$ or [Ne] $3s^2\ 3p^6$**
manganese(II) ion	**$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 4s^0\ 3d^5$ or [Ar] $4s^0\ 3d^5$**

- Copper is an essential element in human biology, deficiencies leading to blood disorders. Excess copper can occur in cases of poisoning or in Wilson's disease. Draw a graph showing the relationship between overall health and the level of copper in the body and identify the 'healthy' range. **4**



Describe one biological function of copper.

Copper enzymes are involved in electron transport systems due to the ability of copper to change its oxidation state.

In some organisms, copper enzymes are involved in oxygen transport.

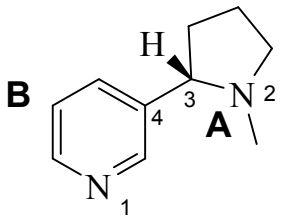
ANSWER CONTINUES ON THE NEXT PAGE

Suggest one approach for treating an excess level of copper.

Treatment with a complexing agent such as EDTA leads to the formation of stable water-soluble complex that can be excreted from the body.

Marks 8

- The molecular structure of nicotine, the addictive component of tobacco, is shown below.



List the types of intermolecular interactions that each of the following sites on nicotine would be involved in when it is dissolved in water.

A – H bonding and dipole-dipole interactions

B – dispersion forces and dipole-induced dipole

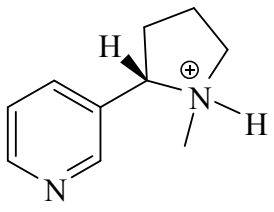
Provide the requested information for each of the indicated atoms in nicotine.

Atom	Geometric arrangement of the electron pairs around the atom	Hybridisation of the atom	Geometry around the atom
N-1	**trigonal planar**	***sp*^{2}**	**bent (~120°)**
N-2	**tetrahedral**	***sp*^{3}**	**trigonal pyramidal**
C-3	**tetrahedral**	***sp*^{3}**	**tetrahedral**
C-4	**trigonal planar**	***sp*^{2}**	**trigonal planar**

The pK_b of N-1 is 10.88 and the pK_b of N-2 is 5.98. Draw the structure of the predominant form of nicotine that exists in the human body at pH 7.4.

For N-1, the pK_a of the protonated form (the conjugate acid) is (14.00 – 10.88) = 3.12. As the pH is *higher* than the pK_a, the conjugate acid is deprotonated: *very* little protonation occurs.

For N=2, the pK_a of the protonated form is (14.00 – 5.98) = 8.02. As the pH is *lower* than the pK_a, the conjugate acid form dominates: protonation occurs.

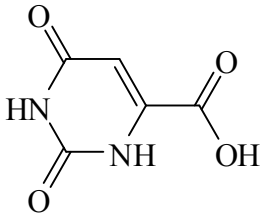


Marks 4

- Lithium salts, especially lithium carbonate, are commonly used in the treatment of bipolar disorder. Write the net ionic equation for the reaction which occurs between lithium carbonate and hydrochloric acid in the stomach.

$Li_2CO_3(s) + 2H^+(aq) \rightarrow 2Li^+(aq) + H_2O(l) + CO_2(g)$

Lithium orotate (as a monohydrate salt, $LiC_5H_3N_2O_4 \cdot H_2O$) is a controversial alternative formulation sold in some health food stores. The orotate ion is the conjugate base of orotic acid, whose structure is shown below.



orotic acid

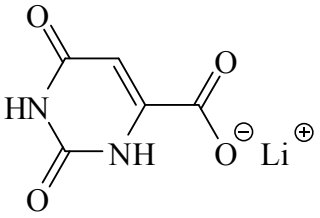
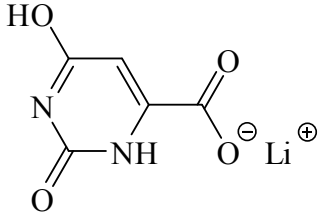
Like the carbonate, lithium orotate is taken orally. Using an equation, comment on any differences between the form in which lithium is bioavailable from these two lithium salts.

When lithium orotate, $LiC_5H_3N_2O_4$, dissolves in water, it forms $Li^+(aq)$ ions and orotate ions:

$LiC_5H_3N_2O_4(s) \rightarrow Li^+(aq) + C_5H_3N_2O_4^-(aq)$

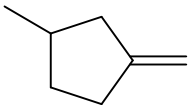
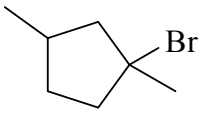
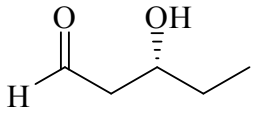
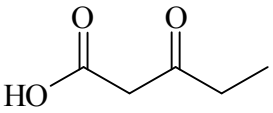
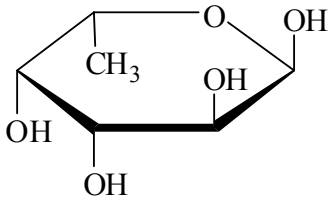
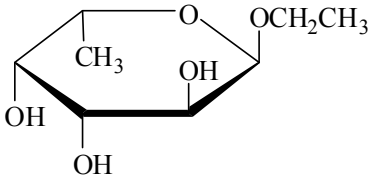
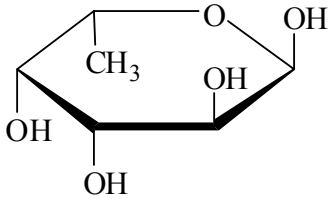
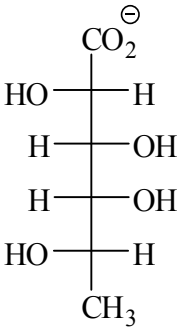
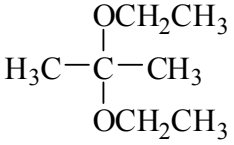
Both lithium carbonate and lithium orotate thus give rise to the same form of lithium, $Li^+(aq)$, when taken orally.

Like three of the bases found in DNA and RNA, orotic acid is a derivative of pyrimidine. Also like those bases, orotic acid and its salts have tautomers. Draw the structural formula of a tautomer of lithium orotate.

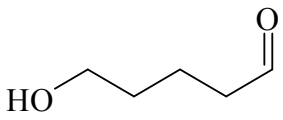
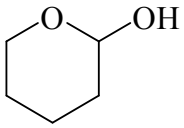
lithium orotate	tautomer of lithium orotate
	

Marks 8

- Complete the following table.

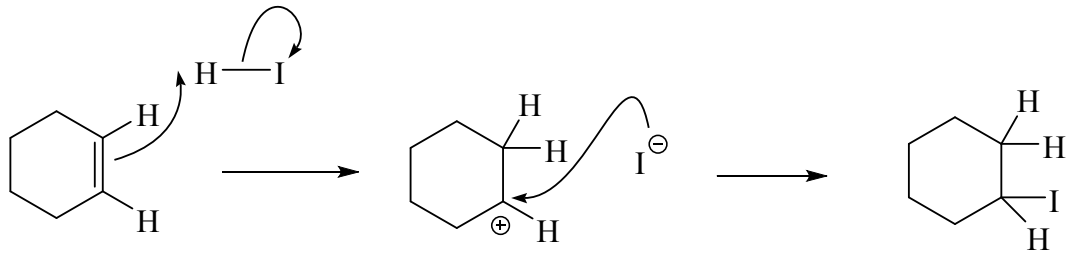
STARTING MATERIAL	REAGENTS/ CONDITIONS	CONSTITUTIONAL FORMULA(S) OF MAJOR ORGANIC PRODUCT(S)
	HBr / CCl_4 (solvent)	 **Markovnikov addition with H adding to less substituted end of double bond**
	$H^{\oplus} / Cr_2O_7^{2\ominus}$	 **Oxidation of aldehyde and alcohol to give non-chiral product**
	**CH_3CH_2OH / catalytic H^+**	
	$[Ag(NH_3)_2]^{\oplus} / OH^{\ominus}$	
	dilute $H^{\oplus}$	 + CH_3CH_2OH **Hydrolysis of acetal**

ANSWER CONTINUES ON NEXT PAGE

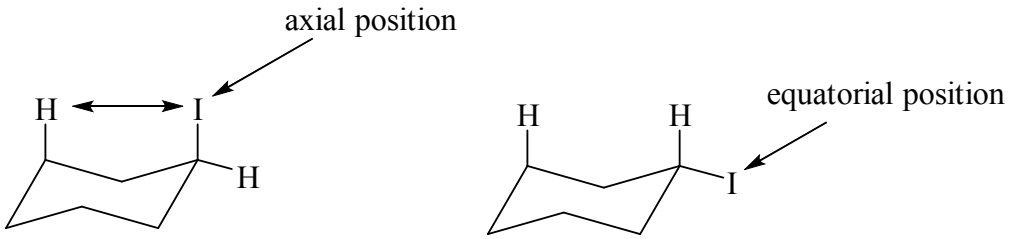
	$H^{\oplus}$ catalyst	

Marks 6

- Cyclohexene undergoes an electrophilic addition reaction with HI in CCl_4 solvent to give iodocyclohexane. Draw the mechanism of this reaction, using curly arrows to indicate the movement of electrons. Include structures for any relevant intermediates.



Draw the two chair conformations of iodocyclohexane and indicate which is likely to be more stable. Briefly explain the reason for your choice.

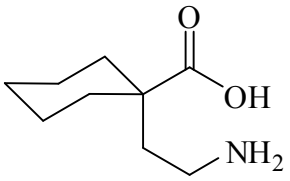


The conformation with the iodine in the equatorial position will be the more stable.

Iodine is a large atom and there are significant 1,3 steric interactions with axial hydrogens when iodine is in the axial position.

Marks 4

- Neurontin® is a pharmaceutical now widely used for the treatment of nerve pain. The structure of the active ingredient in Neurontin, gabapentin, is shown below. The pK_a value for the carboxyl group is 3.68, whilst the pK_b value for the amine group is 3.30.



gabapentin

Explain whether gabapentin can reasonably be described as an amino acid.

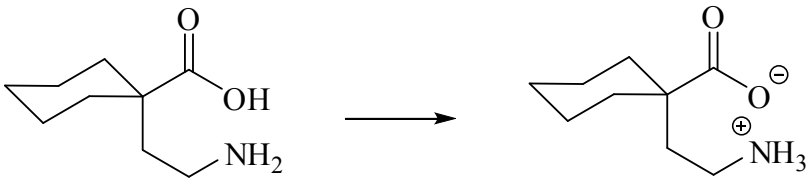
Gabapentin has both an amine and a carboxylic acid functional group, so it is an amino acid.

It is not an α-amino acid (like those found in proteins) as the amino group is not attached to the carbon next to the COOH group.

Orally-delivered pharmaceutical agents that contain amine functional groups are often prepared as hydrochloride salts, rather than as free amines. Suggest a reason why gabapentin is not delivered as a hydrochloride salt, illustrating your answer with a suitable diagram.

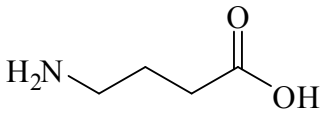
Salt formulations are mainly used to prevent oxidation of the free amine group. The amine group is converted to a quaternary ammonium salt which is more stable.

However, gabapentin already exists in a zwitterionic form at normal pH, with the amine group protonated to form the more stable quaternary ammonium ion.



ANSWER CONTINUES ON THE NEXT PAGE

Gabapentin was originally synthesised as it was anticipated that it would bind to the same receptors as the neurotransmitter GABA (4-aminobutanoic acid). Draw the structure of GABA. Suggest a reason why it might have been anticipated that gabapentin would interact with GABA receptors, and what form such interactions might take.



GABA (4-aminobutanoic acid).

Both GABA and gabapentin have the same basic features - a four carbon chain with a terminal NH_2 and a terminal COOH group. These functional groups are likely to be involved in receptor binding through interactions such as H-bonding.

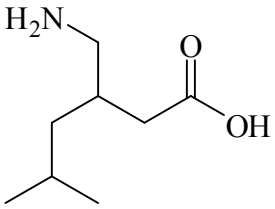
THIS QUESTION CONTINUES ON THE NEXT PAGE.

This expectation has proven to be incorrect, as gabapentin does not interact well with GABA receptors. Suggest a reason why this might be the case.

Marks 4

The bulky cyclohexyl group interferes with the binding of gabapentin at the GABA receptor site. This could be due to either steric reasons (the group is too large to fit into the receptor site) or its hydrophobic nature is a poor match for the equivalent part of the receptor.

Pregabalin (marketed under the trade name Lyrica) has been developed as a successor to gabapentin as it is more potent. Its structure is shown below.



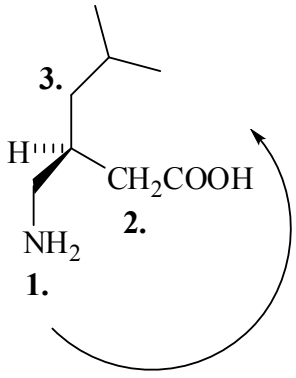
pregabalin

The pharmaceutical formulation contains only the (*S*) enantiomer of pregabalin. Rank the substituents around the stereocentre in decreasing order of priority.

highest priority lowest priority

$-CH_2NH_2$	**$-CH_2COOH$**	**$-CH_2CH(CH_3)_2$**	**–H**

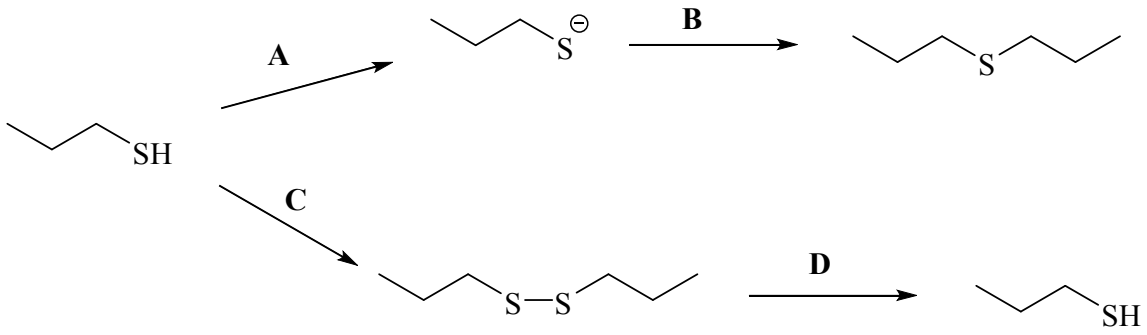
Draw the (*S*) enantiomer of pregabalin.



1 → 2 → 3 is anticlockwise with 4 at the back: (*S*)

Marks

- Indicate the reagents used in the laboratory to undertake the following transformations. **5**



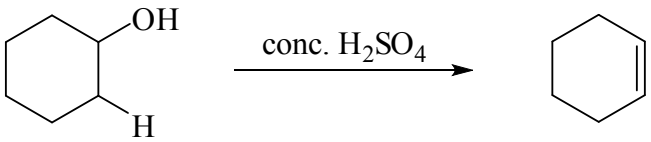
A:	**NaOH**
B:	**$CH_3CH_2CH_2Br$**
C:	**I_2**

Provide a description for transformation **B**.	**nucleophilic substitution**
Provide a description for transformation **D**.	**reduction**

- Define the term "elimination" and illustrate your answer with an equation. **2**

Elimination is the removal of an H^+ and a nucleophile from adjacent atoms, leading to the formation of a double bond between those atoms.

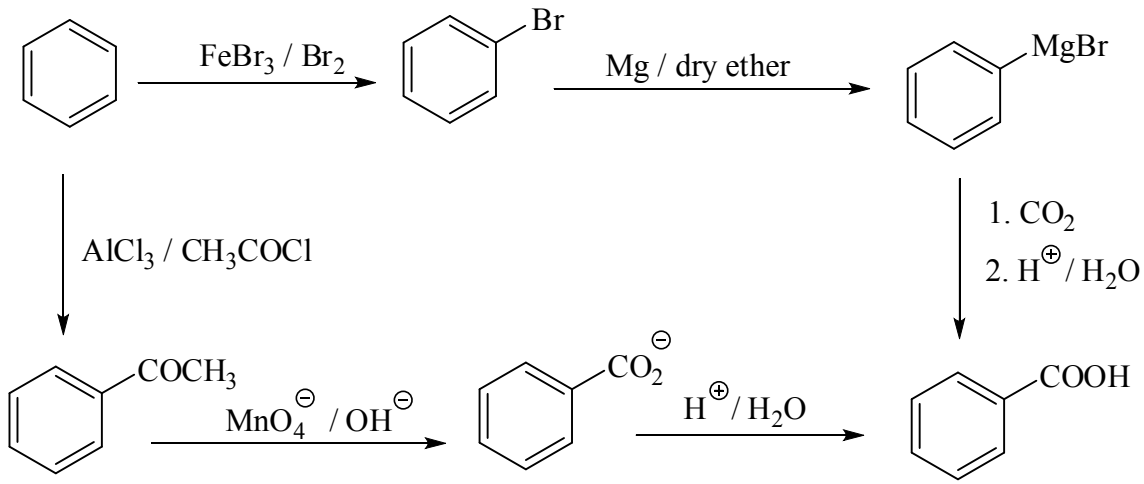
Dehydration is an example of elimination:

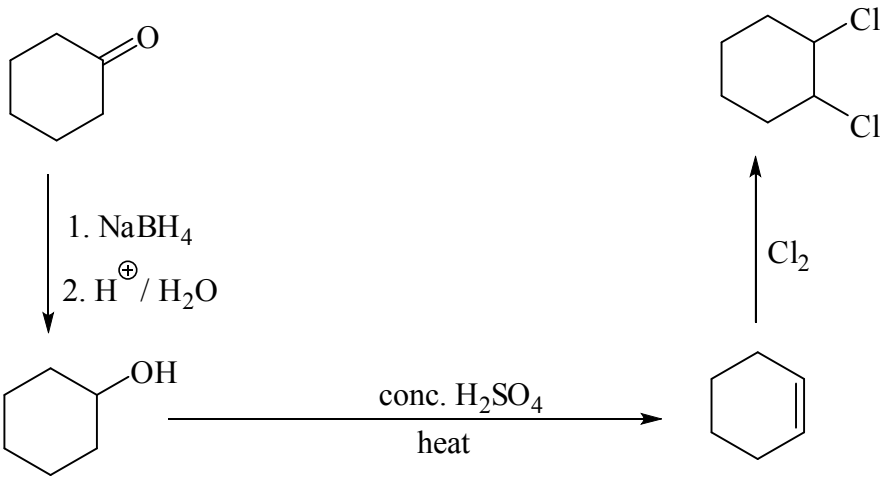


THE REMAINDER OF THIS PAGE IS FOR ROUGH WORKING ONLY.

Marks 7

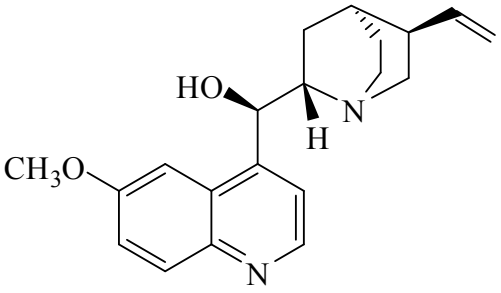
- Show clearly the reagents you would use to carry out the following chemical conversions. Draw constitutional formulas for any intermediate compounds. Note: More than one step is required in both cases.



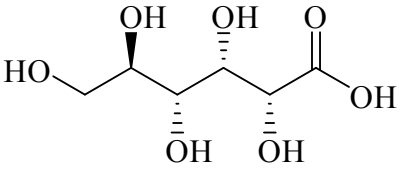


Marks 4

- Quinine has long been used for the treatment of malaria. For an intramuscular injection, quinine is reacted with gluconic acid. Structures and molar masses for these substances are shown below.



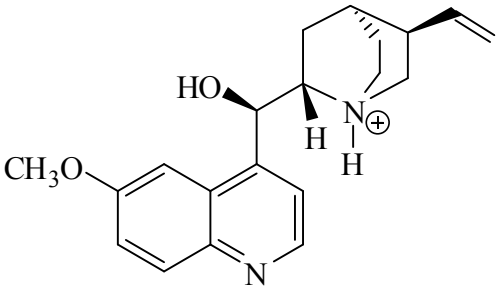
quinine
molar mass 324.41 g mol^{-1}

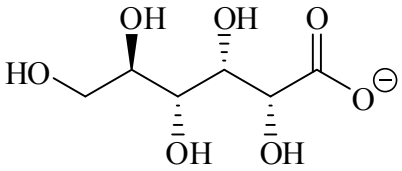


gluconic acid
molar mass 196.16 g mol^{-1}

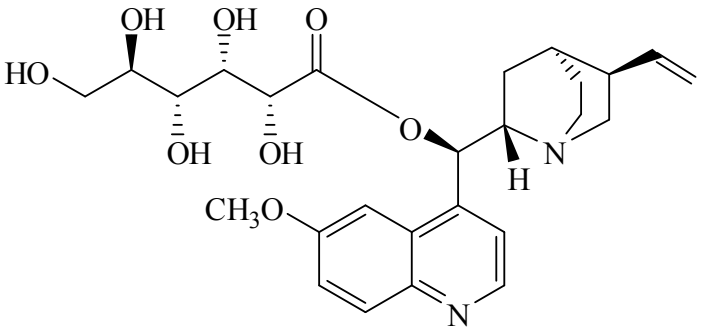
Quinine and gluconic acid can undergo an acid-base reaction to form a salt, or a condensation reaction to form an ester. One molecule of each substance is required for the transformation, and a 160.0 mg dose of quinine gluconate is equivalent to a 100.0 mg dose of quinine. By determining the molar mass of the product formed, or otherwise, determine whether the product formed is an ester or a salt.

The two possible products, and their molar masses, are shown below.





Salt: formed by proton transfer from acid group on gluconic acid to quinine amine, with no loss of mass. Formula $C_{26}H_{26}N_2O_9$ and molar mass 520.57 g mol^{-1}



Ester: formed from acid group on gluconic aicd and –OH group on quinine with elimination of water. Formula $C_{26}H_{24}N_2O_8$ and molar mass 502.56 g mol^{-1}

ANSWER CONTINUES ON THE NEXT PAGE

100.0 mg of quinine corresponds to:

$$\textbf{number of moles} = \frac{\textbf{mass}}{\textbf{molar mass}} = \frac{100.0\times10^{-3}\ \text{g}}{324.41\ \text{g mol}^{-1}} = 3.083 \times 10^{-4}\ \text{mol}$$

160.0 mg of the salt product corresponds to:

$$\textbf{number of moles} = \frac{\textbf{mass}}{\textbf{molar mass}} = \frac{160.0\times10^{-3}\ \text{g}}{520.57\ \text{g mol}^{-1}} = 3.074 \times 10^{-4}\ \text{mol}$$

160.0 mg of the ester product corresponds to:

$$\textbf{number of moles} = \frac{\textbf{mass}}{\textbf{molar mass}} = \frac{160.0\times10^{-3}\ \text{g}}{502.56\ \text{g mol}^{-1}} = 3.184 \times 10^{-4}\ \text{mol}$$

As the dosages are the same, it must be the salt which is being administered.

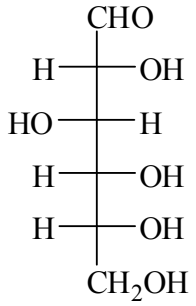
Suggest two reasons why it might be important to know whether quinine gluconate is a salt or an ester.

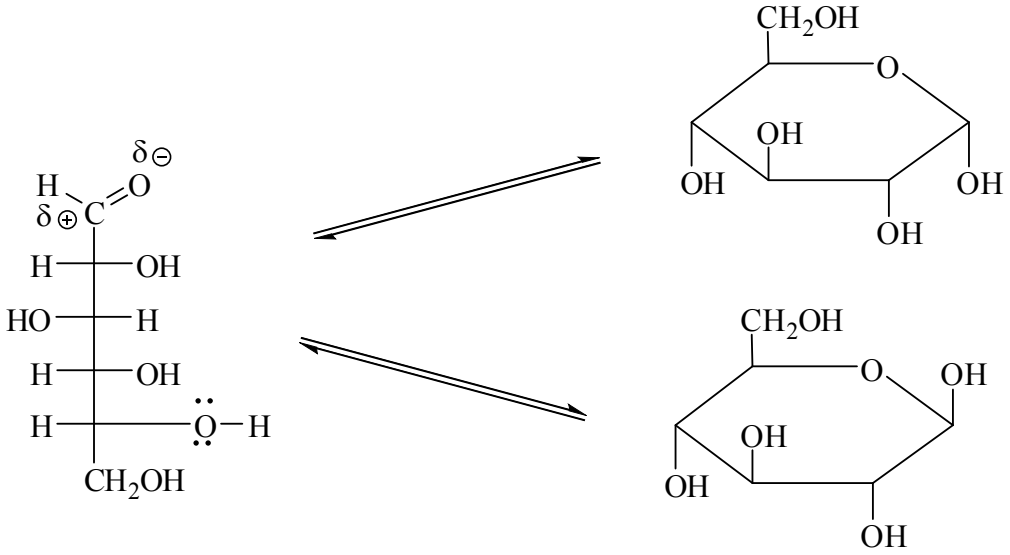
- **So that the correct dosage can be delivered.**
- **The ester form may need to be given orally to allow it to hydrolyse (to give the free quinine) in the digestive tract.**

THIS QUESTION CONTINUES ON THE NEXT PAGE.

Marks 3

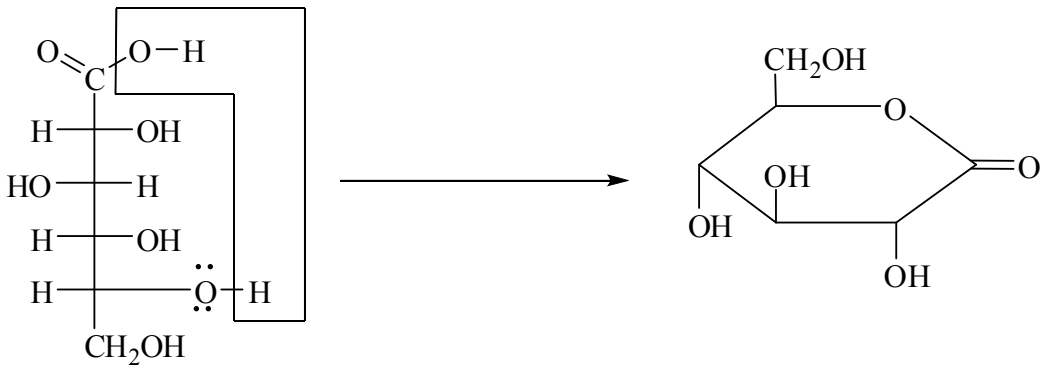
Gluconic acid is formed in biological systems by the oxidation of glucose, which can exist as both an open-chain form and as cyclic forms. The Fischer projection for the open-chain form of D-glucose is shown on the right. Illustrate the formation of the cyclic forms of glucose, and discuss whether gluconic acid can form similar cyclic forms.





The formation of cyclic forms of glucose is due to the reversible reaction between the OH on C5 and the aldehyde group on C1 to form the hemiacetal function group.

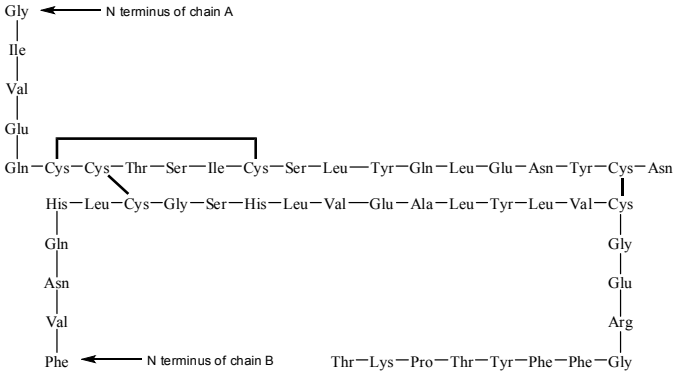
Carboxylic acids do not form hemiacetals, so no similar cyclic forms exist for gluconic acid. However, acids and alcohols can form esters, so a different type of cyclic compound is possible. (Cyclic esters are often called lactones.)

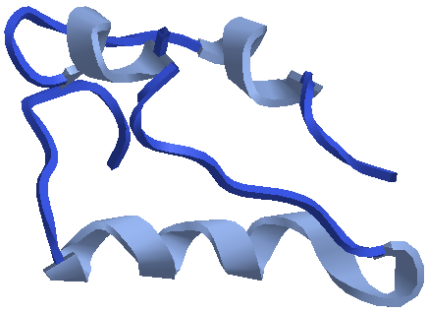


THE REMAINDER OF THIS PAGE IS FOR ROUGH WORKING ONLY.

Marks 4

- Insulin is an important hormone involved in the regulation of glucose availability in the body. It consists of two peptide chains, one consisting of 21 amino acids (the "A" chain) and one of 30 amino acids (the "B" chain). Below are two representations of insulin, one showing the amino acid sequence and the other a stylised ribbon diagram.





Define the terms *primary structure, secondary structure* and *tertiary structure* in relation to proteins. Illustrate your answer with appropriate diagram(s) and by making reference to the representations shown above.

The primary structure is the order of sequence of the amino acids in the chain. The amino acids are linked with covalent bonds, specifically by the formation of amide functional groups. (Shown in structure on left.)

The secondary structure refers to the way segments of the peptide chain orient themselves into regular patterns such as α-helices and/or β-pleated sheets because of H-bonding. The structure on the right shows some α-helices connected together by sections of amino acid chains with neither of these structures. There are no β-pleated sheets in insulin.

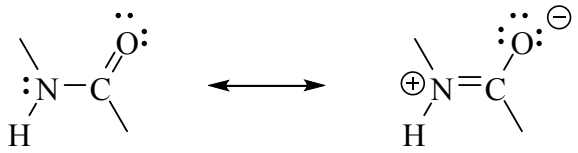
The tertiary structure refers to the way the entire protein coils into a 3-dimensional structure. This is due to disulfide bridges between cysteine (cys) residues, hydrophilic interactions between the protein and solvent (water) and dispersion forces between separate hydrophobic parts of the protein. The positions of the two disulfide bridges is clearly shown in the structure on the left. The basic 3D shape of the protein is shown in the ribbon diagram.

THIS QUESTION CONTINUES ON THE NEXT PAGE.

The peptide links in a protein chain are said to be *resonance stabilised*. Use a diagram to explain what is meant by this term, and indicate one important consequence relating to protein structure and one important consequence relating to the chemistry of proteins.

Marks 4

Resonance occurs when two or more Lewis structures can be drawn for the same compound. In such cases, the true structure is none of those drawn, but rather a weighted average of all of them.



The amide functional group has two major resonance contributors as shown. As a consequence of resonance, the peptide bond is rigid, planar and strong.

Consequence for structure: This rigidity and the charge on the oxygen are ideal for the formation of α-helices and β-pleated sheets via H-bonding.

Consequence for chemistry: The involvement of the N lone pair in resonance, means that the N is unavailable for protonation and is non-basic. The peptide bond is therefore relatively inert.

Modern medicine now uses insulin analogues (where one or more of the amino acid residues has been changed) in the treatment of diabetes. In one such analogue, glargine insulin, the changes have increased the isoelectric point of the enzyme from 5.4 to 6.7, thereby reducing its solubility at physiological pH. Explain how changes in the primary amino acid sequence can alter the pI and solubility of the analogue without altering its interaction with blood-glucose.

Changing surface amino acids (for example by changing charged groups to uncharged or polar groups to non-polar) alters the pI and hence the solubility of the protein.

As long as the residues changed are not near the active site and do not change its shape, the mode of action of the enzyme is not affected.