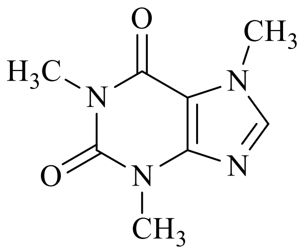
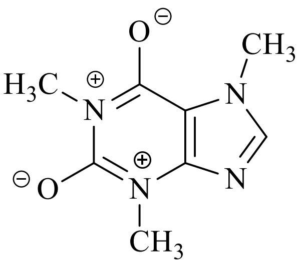
Marks 5

- Shown below is the structure of caffeine.

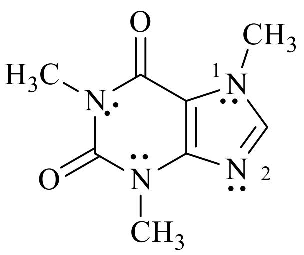


caffeine

Draw the structure of a 10 π−electron aromatic resonance contributor to the structure of caffeine.



Only one of the nitrogen atoms in caffeine is basic. Indicate which of the nitrogen atoms is basic and explain why it is basic and why the others are not.



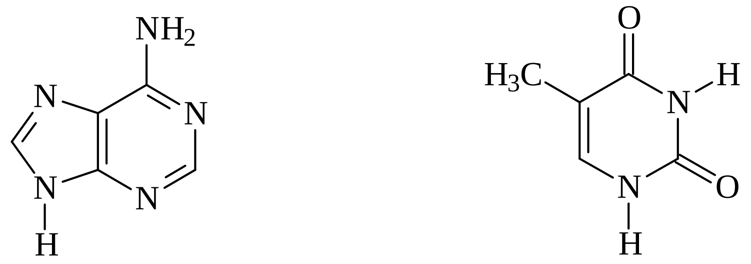
N[1] is *sp*^{2} hybridised. The "lone pair" is in the unhybridised *p* orbital and is part of the aromatic system so is unavailable to act as a proton acceptor.
N[2] is also *sp*^{2} hybridised, but here the lone pair is in the *sp*^{2} hybrid orbital pointing away from the ring system. It is able to act as a proton acceptor, so this N is basic.

The "lone pairs" on the two N's in the 6-membered ring are (at least partially) involved in the resonance stabilisation of the amides and the aromatic system as shown in the first part of this question. These electrons are delocalised and hence not available to act as proton acceptors.

THE REMAINDER OF THIS PAGE IS FOR ROUGH WORKING ONLY.

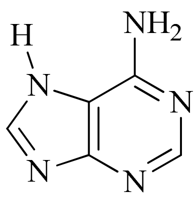
Marks
4

- Adenine and thymine have the structures shown below.



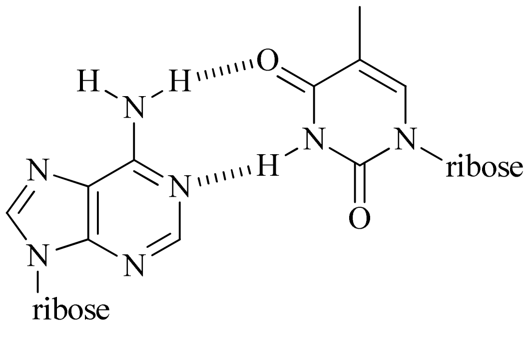
adenine thymine

Draw a tautomer of the shown structure of adenine.



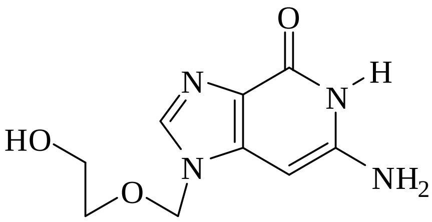
In DNA, adenine forms a "base pair" with thymine. Explain what is meant by "base pair" and indicate the point(s) of interaction between adenine and thymine.

DNA consists of a double strand of polynucleotides. The strands are complementary with C, G, A and T on one strand being paired with G, C, T and A respectively on the other. C (cytosine) and G (guanine) are therefore known as a base pair. Similarly A (adenine) and T (thymine) are another base pair. The two DNA strands are held together by H-bonding between the bases in a base pair.



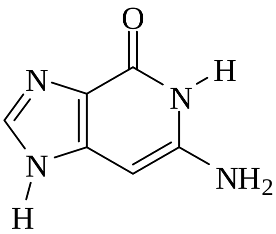
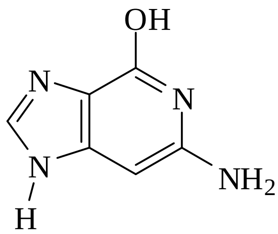
Marks
4

- Acyclovir is an analogue of the nucleoside guanosine, and is used clinically as an antiviral agent.



acyclovir

Hydrolysis of acyclovir gives the nucleic base guanine, a diol and a carbonyl compound. Give the structures of guanine, a tautomer of guanine, and the diol and carbonyl compounds formed.

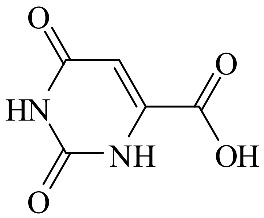
guanine	tautomer of guanine
	
the diol	the carbonyl compound
$HOCH_2CH_2OH$	**CH_2O**

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

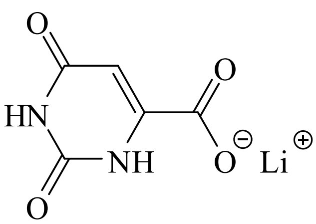
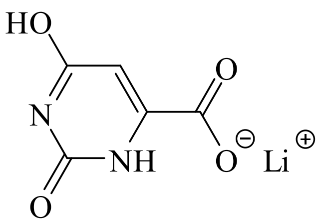
Like the carbonate, lithium orotate is taken orally. Using an equation, comment on any differences between the form in which lithium is bioavailable from these two lithium salts.

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

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

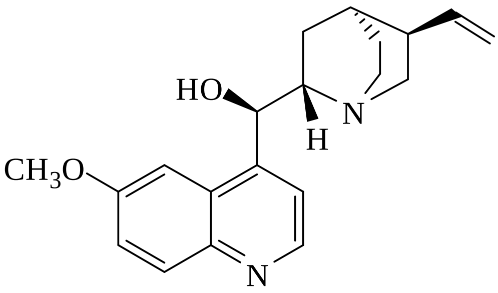
Both lithium carbonate and lithium orotate thus give rise to the same form of lithium, $Li^+(aq)$, when taken orally.

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.

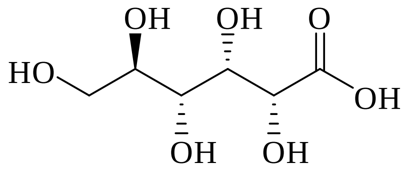
lithium orotate	tautomer of lithium orotate
	

Marks 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.



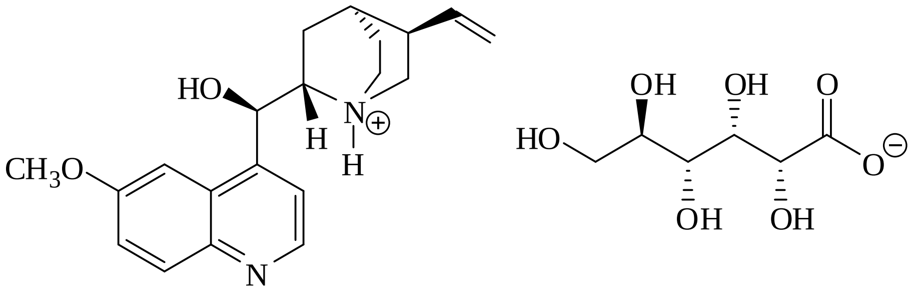
quinine
molar mass 324.41 g mol^{-1}



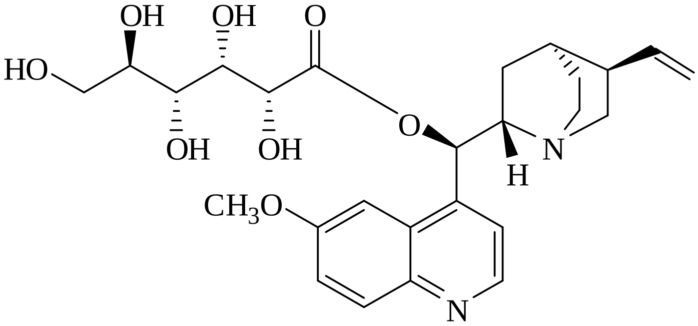
gluconic acid
molar mass 196.16 g mol^{-1}

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:

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

160.0 mg of the salt product corresponds to:

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

160.0 mg of the ester product corresponds to:

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

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

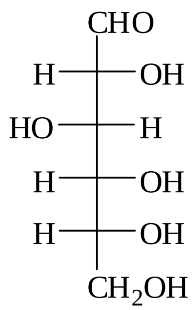
Suggest two reasons why it might be important to know whether quinine gluconate is a salt or an ester.

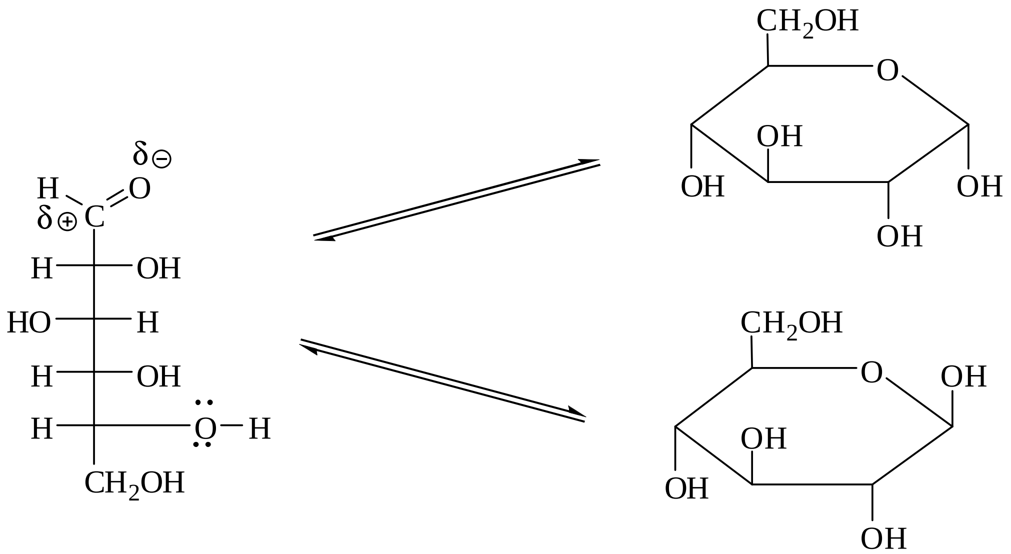
- **So that the correct dosage can be delivered.**
- **The ester form may need to be given orally to allow it to hydrolyse (to give the free quinine) in the digestive tract.**

ANSWER CONTINUES ON THE NEXT PAGE.

Marks
3

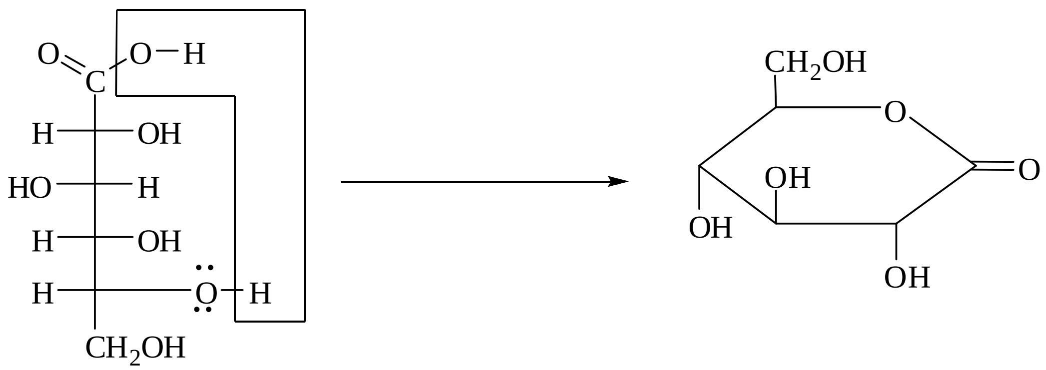
Gluconic acid is formed in biological systems by the oxidation of glucose, which can exist as both an open-chain form and as cyclic forms. The Fischer projection for the open-chain form of D-glucose is shown on the right. Illustrate the formation of the cyclic forms of glucose, and discuss whether gluconic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



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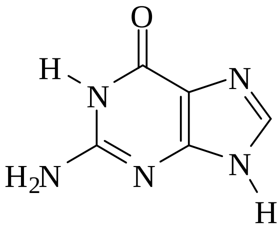
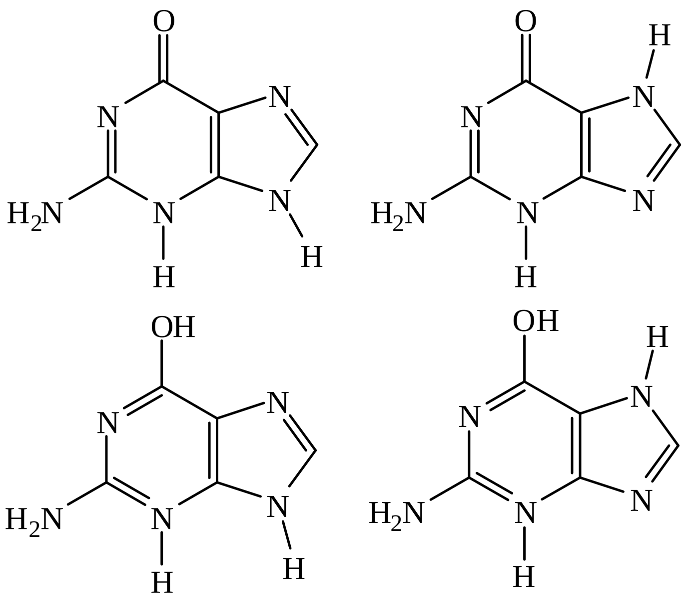
Marks

- The nucleic base guanine is drawn below as a keto tautomer. Draw two other tautomers of guanine. **2**

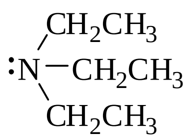


Tautomers include:



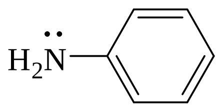
- The pK_b's of two nitrogen-containing compounds are given below. Explain the difference in basicity of these two compounds. **3**

A



pK_b = 2.99

B



pK_b = 9.37

The pK_b of B is higher meaning that it is *less* basic. This is due to delocalization of the nitrogen lone pair onto the aromatic ring. This stabilization of the lone pair decreases its availability to donate to a proton.

The delocalization may be represented by resonance contributions of the form: