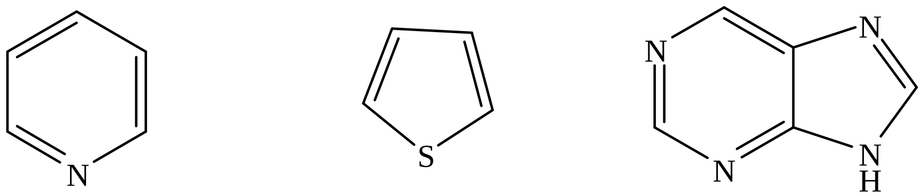
- What are the requirements for a molecule to be aromatic? Give one example of an aromatic heterocycle. 2

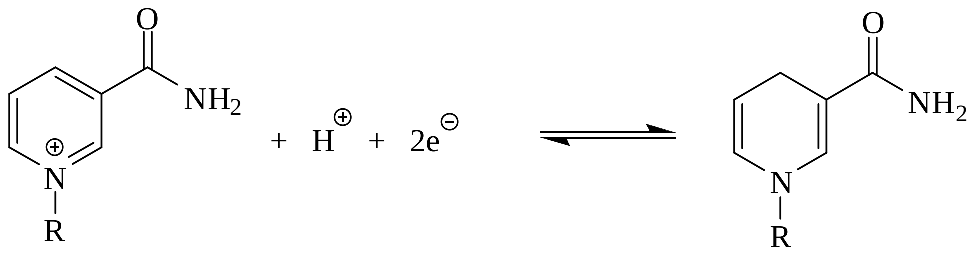
The molecule must be cyclic. The ring system must have a conjugated π bond system. The number of electrons in the π bond system must be 4n+2 where n=integer. All atoms in the ring system must be *sp*^{2} hybridised.

Examples of heterocyclic heterocycles include:



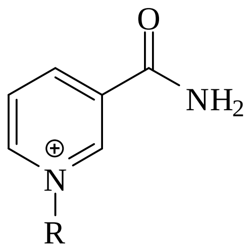
Marks 4

- NAD^+ and NADH are coenzymes used by animals in oxidation and reduction reactions. They are related by the following half-reactions.



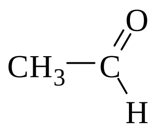
Which of these coenzymes is used in the biological oxidation of ethanol, CH_3CH_2OH?

An oxidizing agent is itself reduced. As shown in the equation, it is NAD^+ which is reducible.



NAD^+

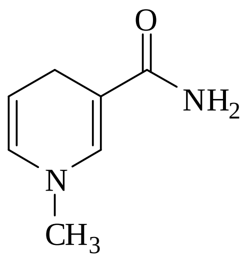
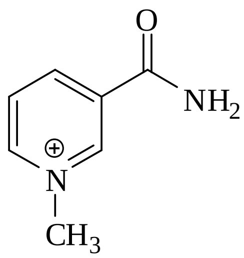
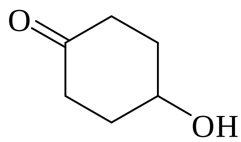
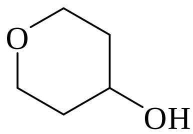
What is the product of the biological oxidation of ethanol, CH_3CH_2OH?



Which of NAD^+ and NADH is aromatic? Give reasons for your answer.

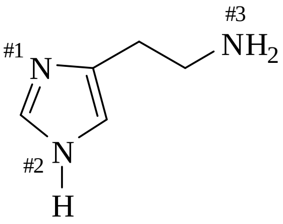
NAD^+ is aromatic. It is cyclic, planar, conjugated, and has $4n+2$ π electrons. NADH is not fully conjugated and is therefore not aromatic.

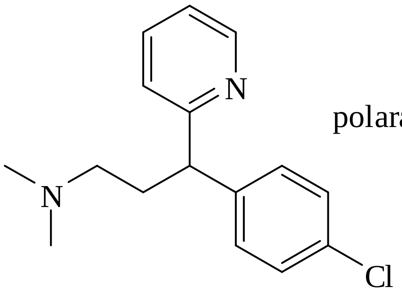
Using a spectroscopic technique, how would you distinguish between the following pairs of compounds? Indicate the observations you would make. 2

Compounds	Technique and observation
 	**^{1}H nmr will detect different numbers of H's attached to the ring. The first compound has 3 olefinic resonances (each 1H) and 1 aliphatic resonance (2H) whilst the second compound has 4 aromatic resonances (each 1H).**
 	**IR. The first compound will give intense absorption at about 1740 cm^{-1} due to the C=O group. The second compound will have no absorption in that region.**

Marks
6

- The structures of histamine and polaramine are shown below.

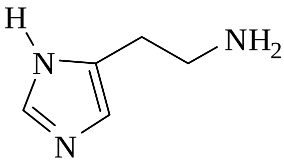




Indicate the hybridisation and geometry of bonds around each of the nitrogen atoms in histamine.

	Hybridisation	Geometry of bonds
N #1:	***sp*^{2}**	**bent**
N #2:	***sp*^{2}**	**trigonal planar**
N #3:	***sp*^{3}**	**trigonal pyramidal**

Draw a tautomer of histamine.



In histamine, only one of the nitrogen atoms in the ring is easily protonated (basic). Indicate which it is and explain why.

N#1 is basic. It has a lone pair directed away from the ring that is *not* involved in the π bonding of the aromatic ring. The lone pair can be used to accept a proton.

The "lone pair" on N#2 *is* part of the aromatic system.

ANSWER CONTINUES ON THE NEXT PAGE

Marks
3

The release of histamine in the body triggers nasal secretions and constriction of airways. Polaramine is one of many anti-histamine compounds used to treat allergies. Explain what structural features of polaramine might make it a suitable anti-histamine agent.

Polaramine has a basic aromatic N and an aliphatic N separated by 5 bonds, as does histamine.

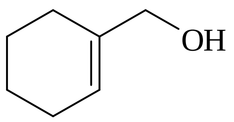
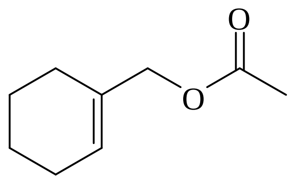
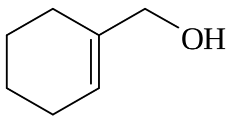
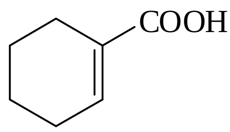
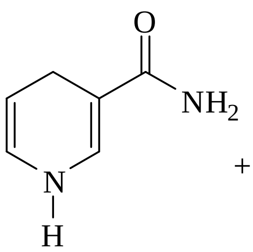
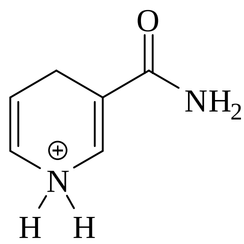
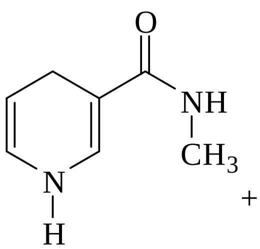
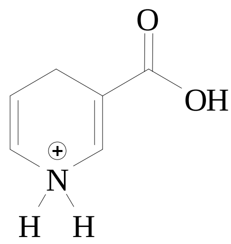
It is therefore likely that it will compete with histamine for the binding sites of certain enzymes in the body and thus block the effects of histamine.

(+)-2-[*p*-Chloro-α-[2-(dimethylamino)ethyl]benzyl]pyridine is another name for polaramine. What does the (+) in this name mean?

The molecule is chiral and rotates plane poarised light in a clockwise direction.

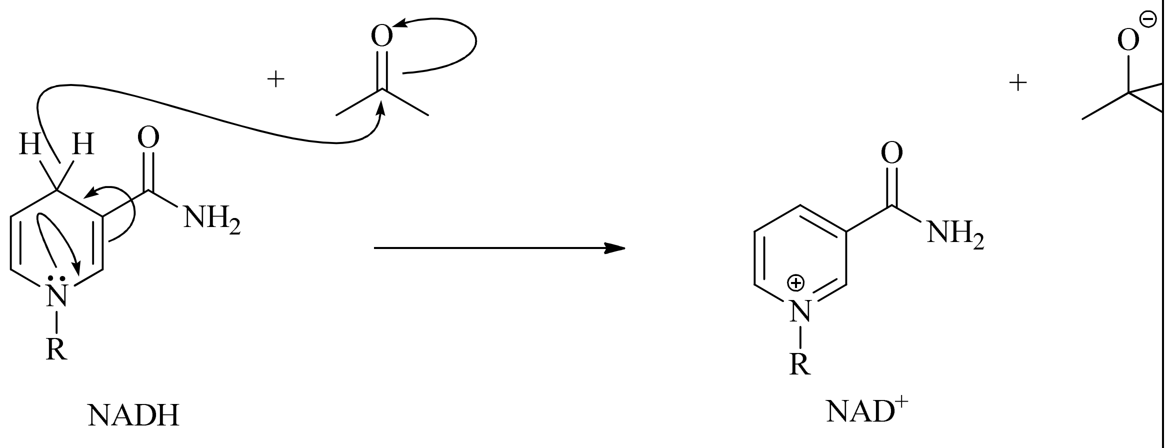
- Indicate the major organic product(s) in the following reactions.

Marks
4

 + CH_3COCl ⟶	
 + $Cr_2O_7^{2\ominus}$ / $H^{\oplus}$ ⟶	
 + cold dilute $H^{\oplus}$ / H_2O ⟶	
 + hot conc. $H^{\oplus}$ / H_2O ⟶	 + $CH_3\overset{\oplus}{N}H_3$

- NADH is the most important reducing agent in Nature. It is itself oxidised to NAD^+. Complete the scheme below by:
  (a) drawing in curly arrows to show the movement of electrons during the first step in the reduction of acetone with NADH, and
  (b) drawing the structure of NAD^+.

3



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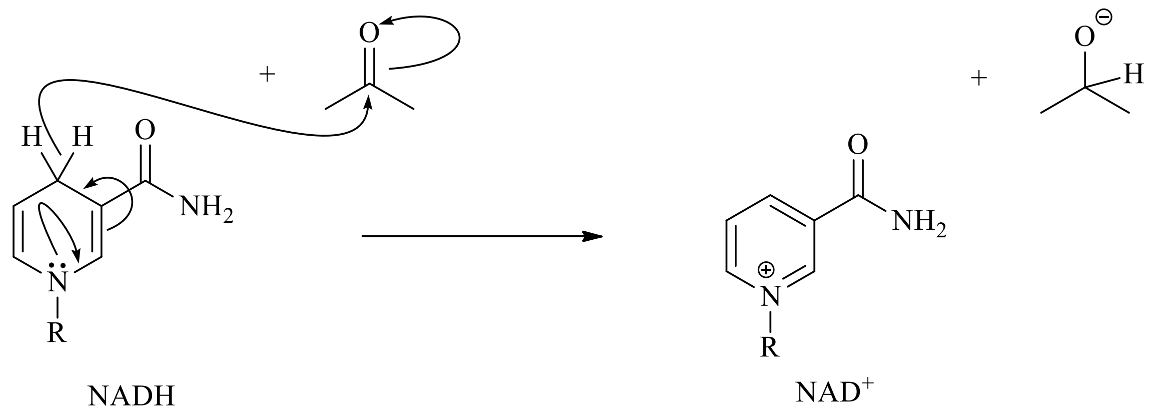
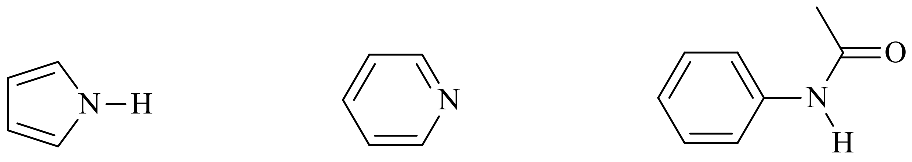
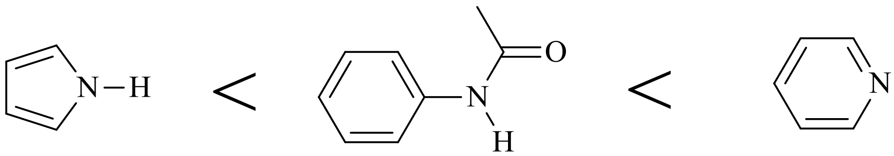
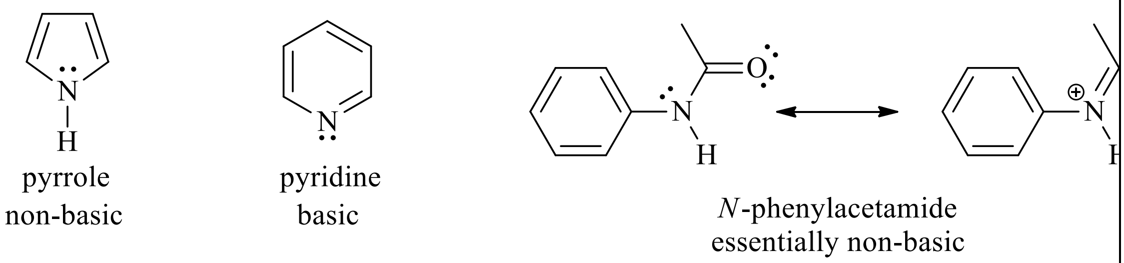


- Rank the following compounds in order of base strength and explain your reasoning. You may use diagrams to assist your explanation. **3**



Order of base strength is:





Pyridine is the most basic as the lone pair of electrons on nitrogen is available to bond with H^+.

Pyrrole is the least basic as the "lone pair" of electrons on nitrogen is part of the aromatic π-electron system and is delocalised around the ring. It is not available for bonding with H^+ ions.

N-Phenylacetamide is essentially non-basic as the lone pair of electrons is involved in resonance forms (including delocalisation of the positive charge into the aromatic ring, which is not shown).