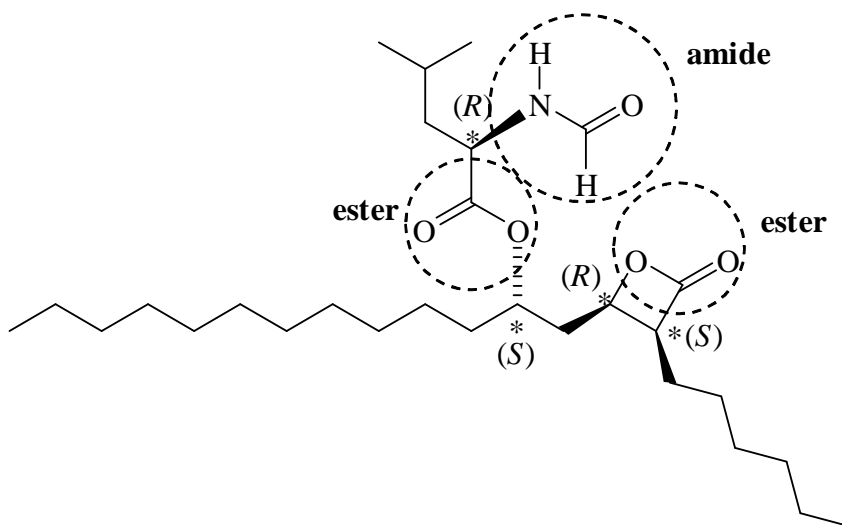


- Orlistat (shown below) is a drug for obesity management which acts by inhibiting the absorption of dietary fats.



Is it likely to be soluble in water? Why?

The molecule contains long-chain hydrocarbon areas which are hydrophilic. Although oxygen atoms are present, there are no O-H groups to allow H-bonding. The molecule is thus unlikely to be soluble in water.

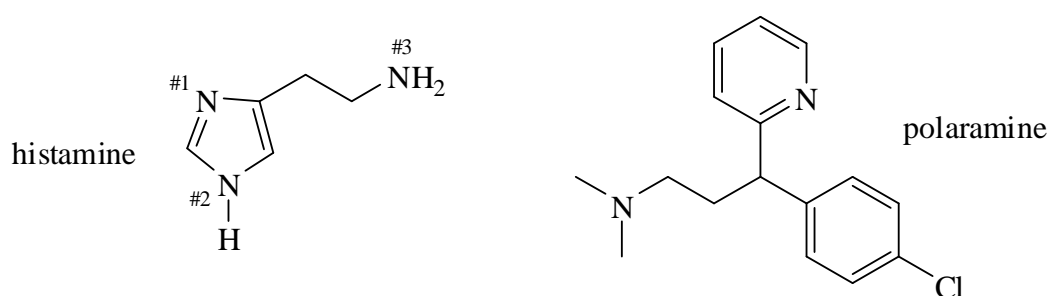
Indicate on the above structure all stereogenic centres. Select one of these centres and clearly assign its stereochemical configuration.

Name the functional groups present in orlistat.

Ester \times 2 and amide (see structure).

Marks
6

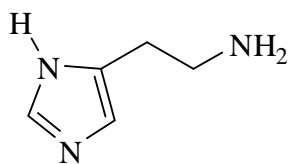
- The structures of histamine and polaramine are shown below.



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 polarised light in a clockwise direction.