
# Topic 6: Drug functional groups

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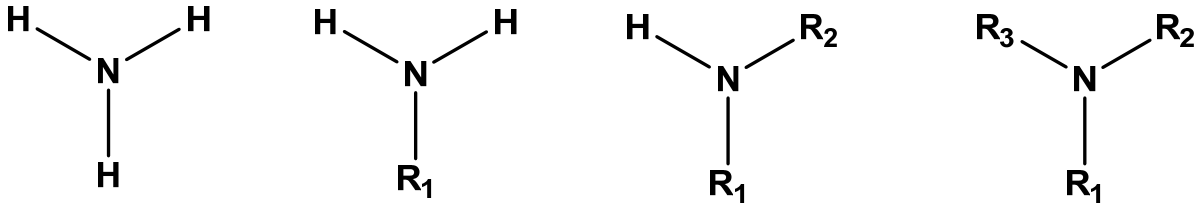
# 1. Nitrogen Containing Functional Groups

➢ The amine group is one of the most important groups responsible for pharmacological activity.

➢ When it bears a positive charge it can exert biological effects through electrostatic interactions with negatively charged groups within proteins.

➢ Amines are derived from ammonia and have the structures of mono-, di- and tri- substituted nitrogen.

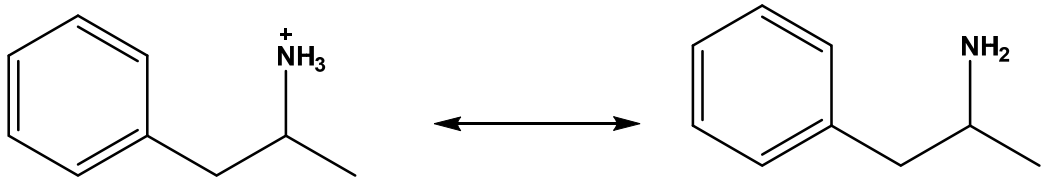
➢The simplest R is $CH_3$ but usually in drug molecules it is a much larger organic structure.




**ammonia** **1° amine** **2° amine** **3° amine**

➢ Amines can carry a positive charge when they accept a proton depending on the pH.

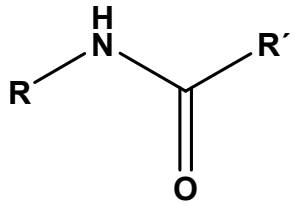
➢ At pH values between 0 and 14.



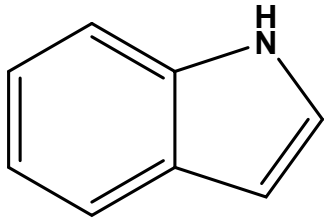

**A**
**Amphitamine pH = 1**
**100% ionised**

**B**
**Amphitamine pH = 14**
**100% unionised**

➢ Nitrogen generally present in drug molecules as basic amine and as nitrogens which do not accept a proton (neutral) such as nitrogens present in amides and indole compounds.

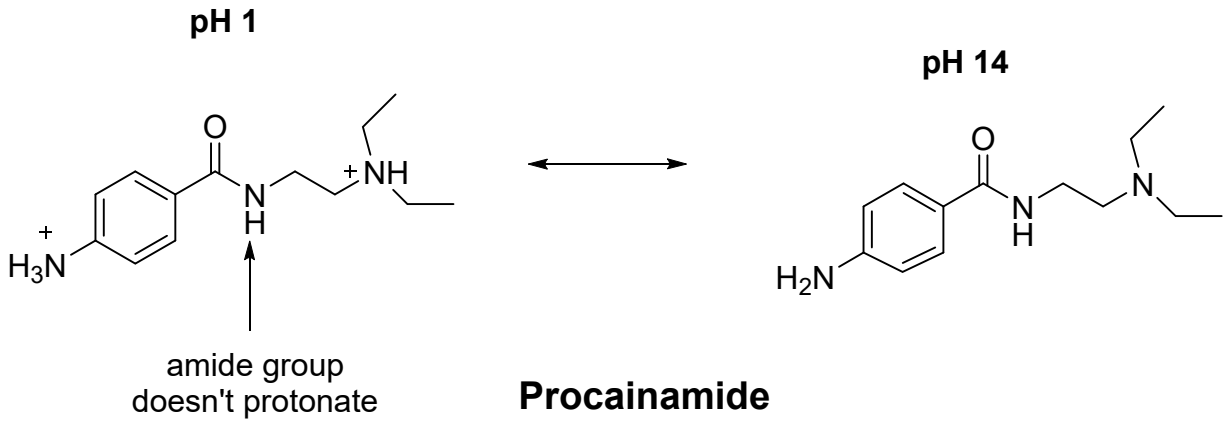



**Amide compound**




**Indole compound**

➢ An example of amide is procainamide, the drug structures at pH 0 and pH 14.




➢ Amide groups contain a carbonyl (or sulfonyl group) next to the nitrogen which pulls electrons away from the nitrogen thus removing its basicity.

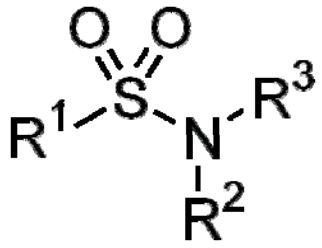
➢ If more than one carbonyl present adjacent to the nitrogen the nitrogen becomes acidic i.e. it will donate a proton rather than accept one.

➢ In the case of sulfonamides and ureides the nitrogen becomes quite strongly acidic.

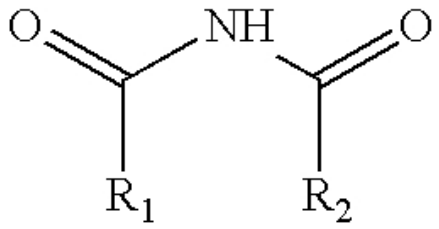
➢ Another type of nitrogen is the quaternary nitrogen which is found in some drugs.

➢ This nitrogen carries a permanent charge and this charge is not affected by the pH.

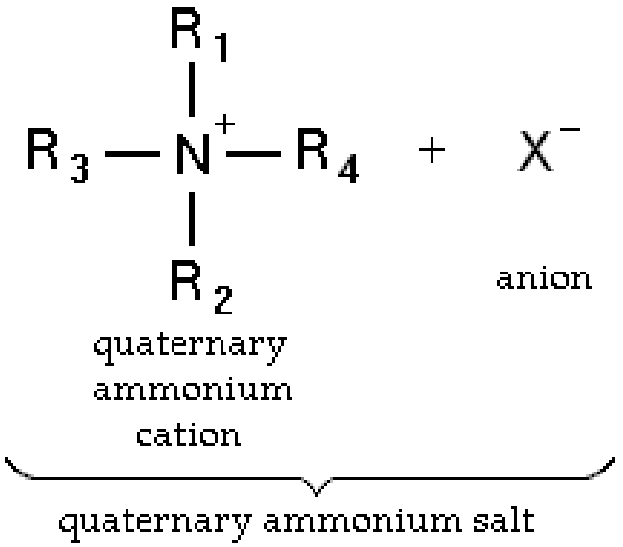
➢ Quaternary ammonium drugs are always in the form of a salt e.g. chloride, bromide, iodide, citrate, mesilate etc.




**Sulfonamide**




**Ureides**



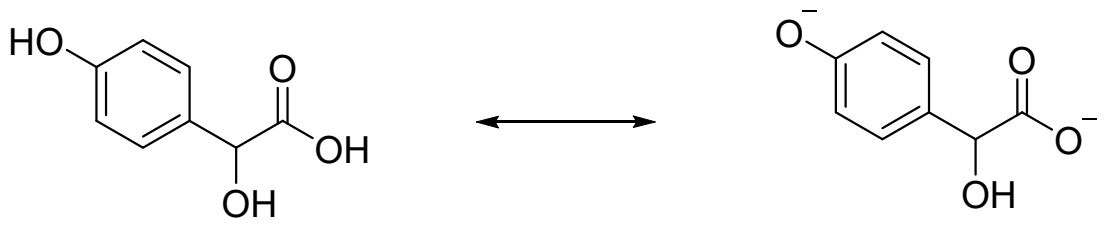
## 2. Oxygen Containing Functional Groups

- The behavior of oxygen is more straightforward than nitrogen

- Oxygen containing compounds can be neutral or acidic but not basic.

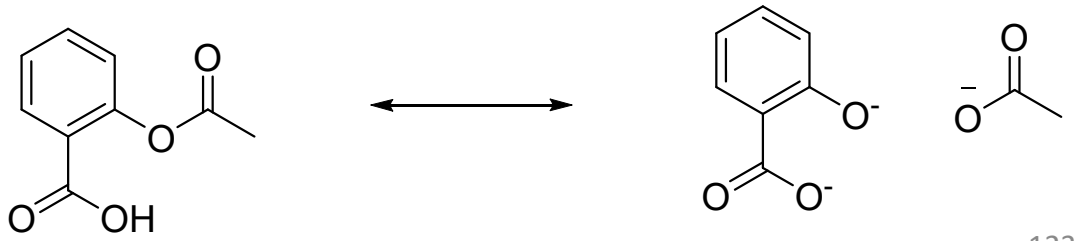
- For example carboxylic acids are acidic, phenols are weakly acidic and alcohols are neutral.

**pH 1** **pH 14**




*p*-hydroxymandelic acid

**pH 1** **pH 14**

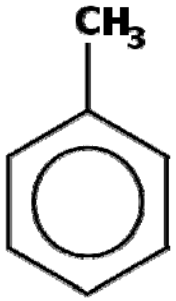



Aspirin

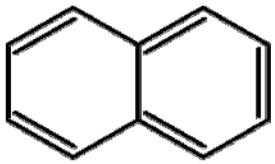
➢ Oxygen containing groups have another two groups which are neutral

• An ether which is neutral and stable to high pH
•An ester which is neutral but unstable to high pH.
• Ethers are also found in some drugs where sulfur is present instead of oxygen and these are termed thioethers.

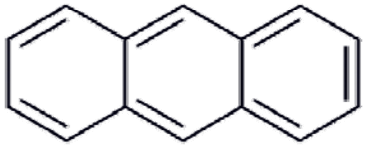
## 3. Aromatic Hydrocarbons



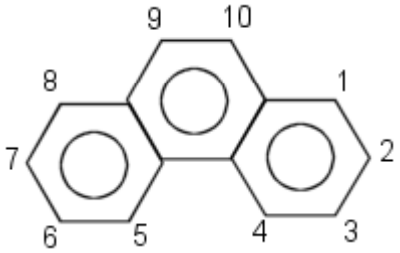

**Toluene**



**Naphthalene**

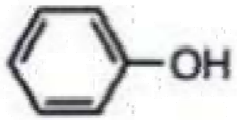
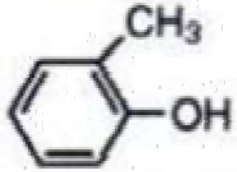
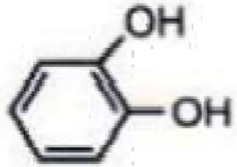
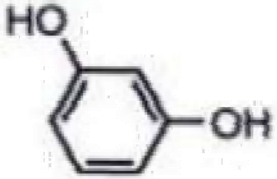


**Anthracene**




**Phenanthrene**

# 4. Phenols

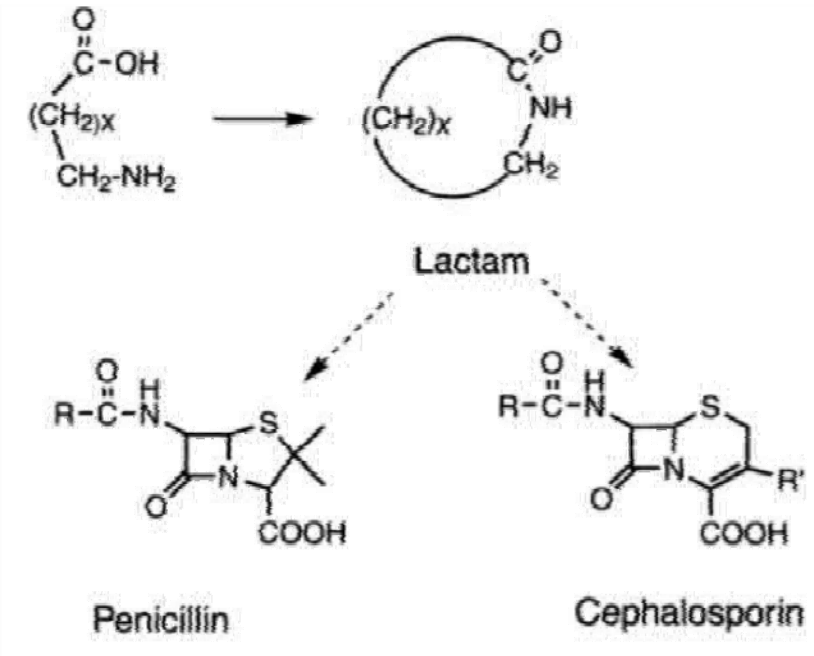
| Structure | Common name | IUPAC name |
|---|---|---|
|  | Carbolic acid | Phenol |
|  | *o*-Cresol | 2-Methylphenol |
|  | *p*-Nitrophenol | 4-Nitrophenol |
|  | Catechol | 1,2-Dihydroxybenzene |
|  | Resorcinol | 1,3-Dihydroxybenzene |
|  | Hydroquinone | 1,4-Dihydroxybenzene |

## 5. Functional Derivatives of Carboxylic Acids

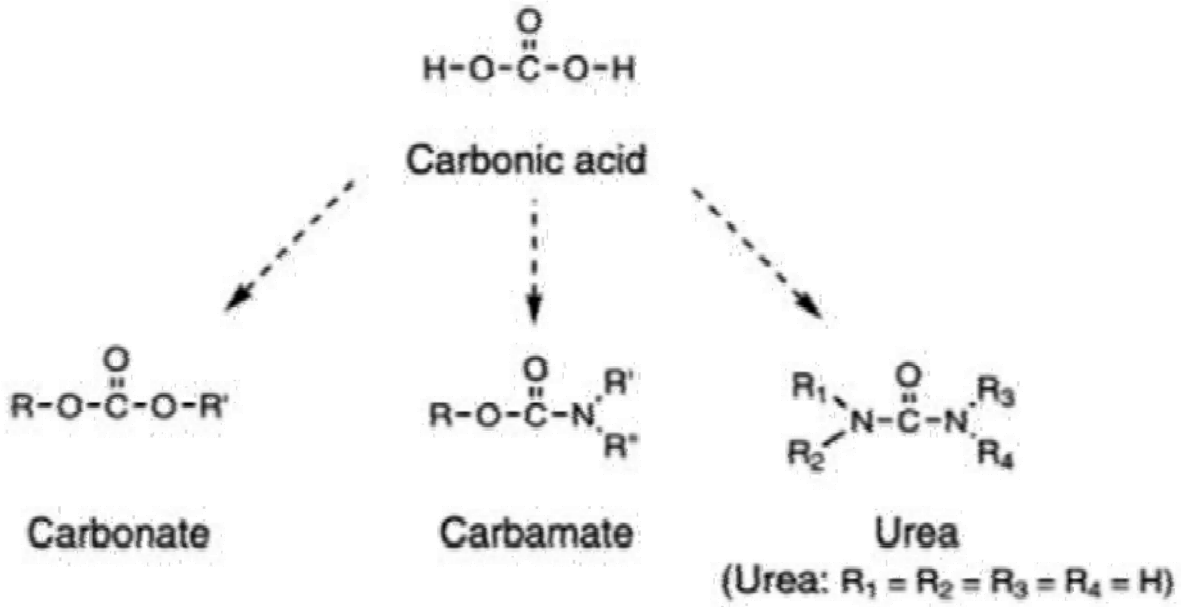
- Ester and amides

- The cyclization of an amine and a carboxylic acid. The resulting amide is known as a lactam. Lactams make up the nucleus or several classes of important drugs.

- the cyclilization of an oxygen and a carboxylic acid the result is lactone ring which is also important in many drugs.



# 6. CARBONATES, CARBAMATES, AND UREAS

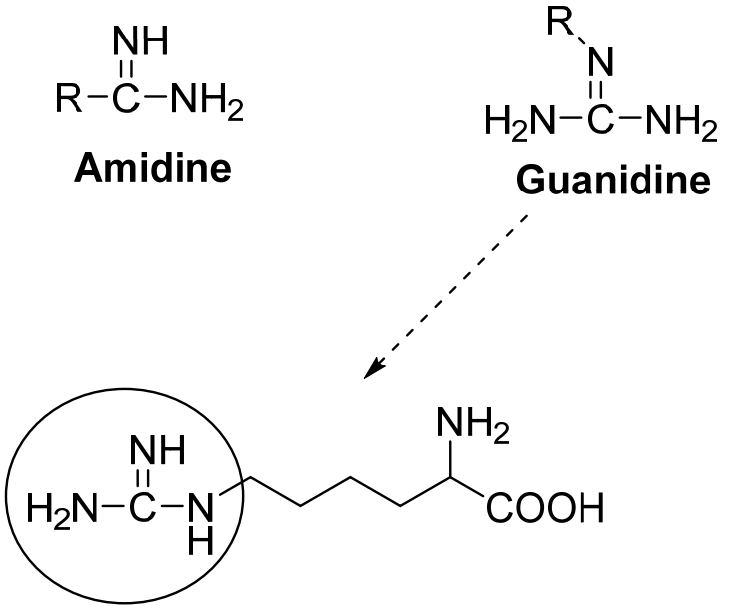


# 7. AMIDINES AND GUANIDINES

➢Amidines are actually a functional derivative of an amide, while the guanidine is a functional derivative of urea.

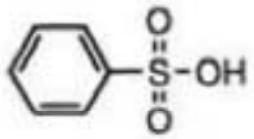
➢ They are found as an integral part of several drug molecules.

➢ The guanidine moiety is an important unit in the naturally occurring amino acid arginine.

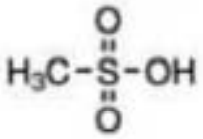



**Arginine**

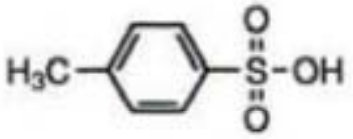
# 8. Sulfonic Acids and Sulfonamides



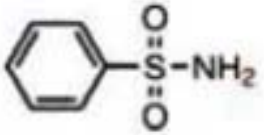
Benzene sulfonic acid



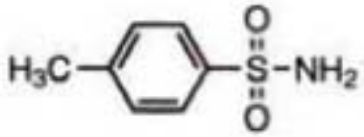
Methane sulfonic acid



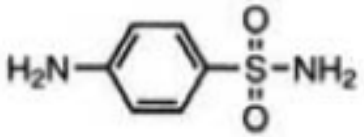
*p* -Toluene sulfonic acid



Common: Benzene sulfonamide
IUPAC: Benzene sulfonamide

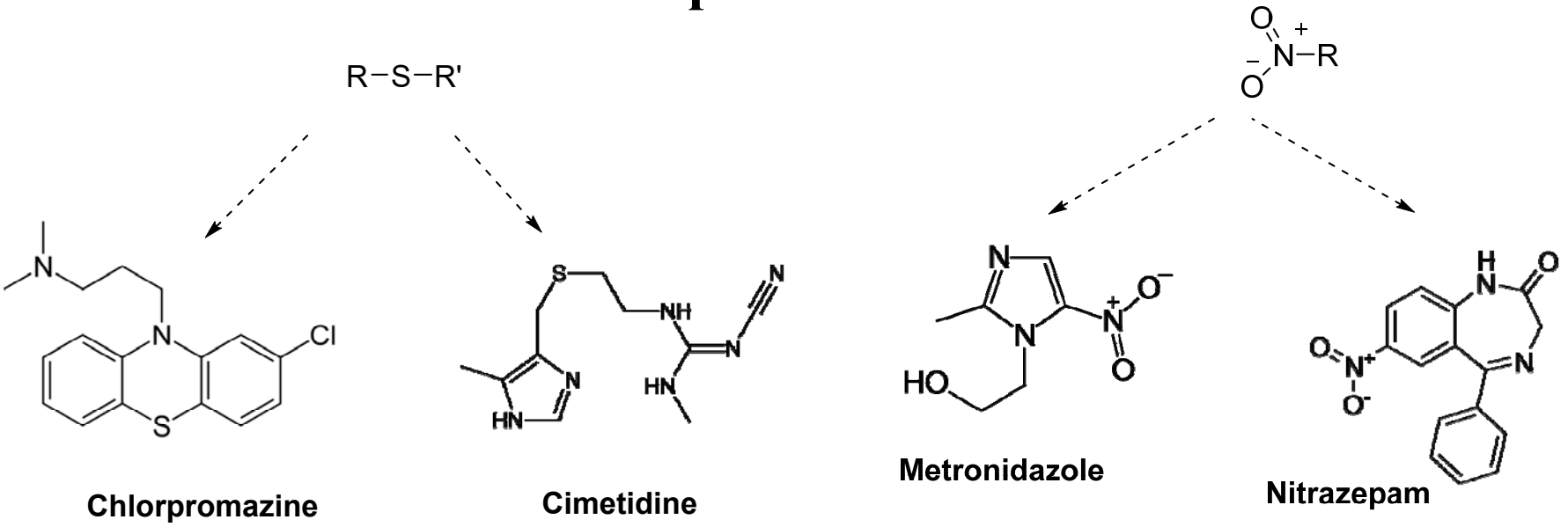


Common: *p* -Toluene sulfonamide
IUPAC: 4-Methylbenzene sulfonamide



Common: *p* -Aminobenzene sulfonamide
Sulfanilamide
IUPAC: 4-Aminobenzene sulfonamide

## 9. Thioethers and Nitro Groups



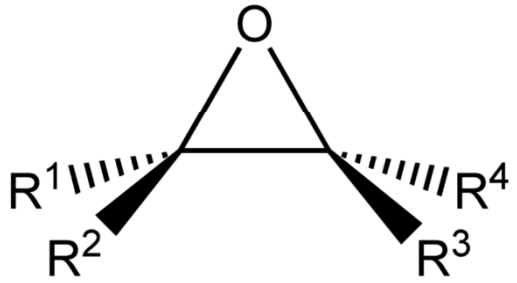

## 10. Heterocycles

➢Heterocycles are defined as cyclic molecules that contain one or more heteroatoms in a ring.

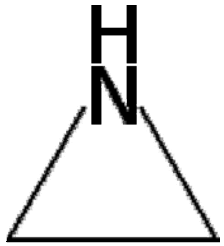
➢ A heteroatom is an atom other than carbon. It would be impossible to introduce all of the possible heterocycles that are of medicinal value so a selected number of monocyclic, bicyclic, and tricyclic rings

# 10.1. THREE-MEMBERED RING HETEROCYCLES

➢ A saturated three-membered ring containing oxygen is known as the oxirane, the presence of these molecules also referred as epoxide.




➢ A saturated three-membered ring containing nitrogen is known as the azridine ring.

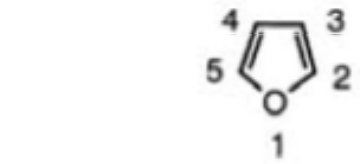


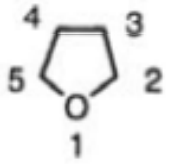
## 10.2. FOUR-MEMBERED RING HETEROCYCLES

➢ Only one derivative of a four-membered ring heterocycle that will be mentioned here ; the β Lactam.

## 10.3. FIVE-MEMBERED RING HETEROCYCLES

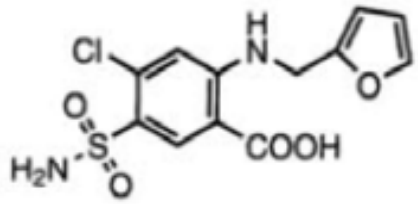
➢ Two common five-membered ring heterocycles are furan and tetrahydrofuran.



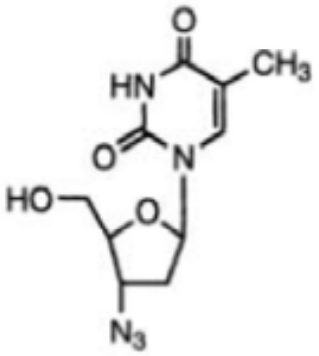




Common: Furan — Tetrahydrofuran (THF)

IUPAC: Oxole — Oxolane



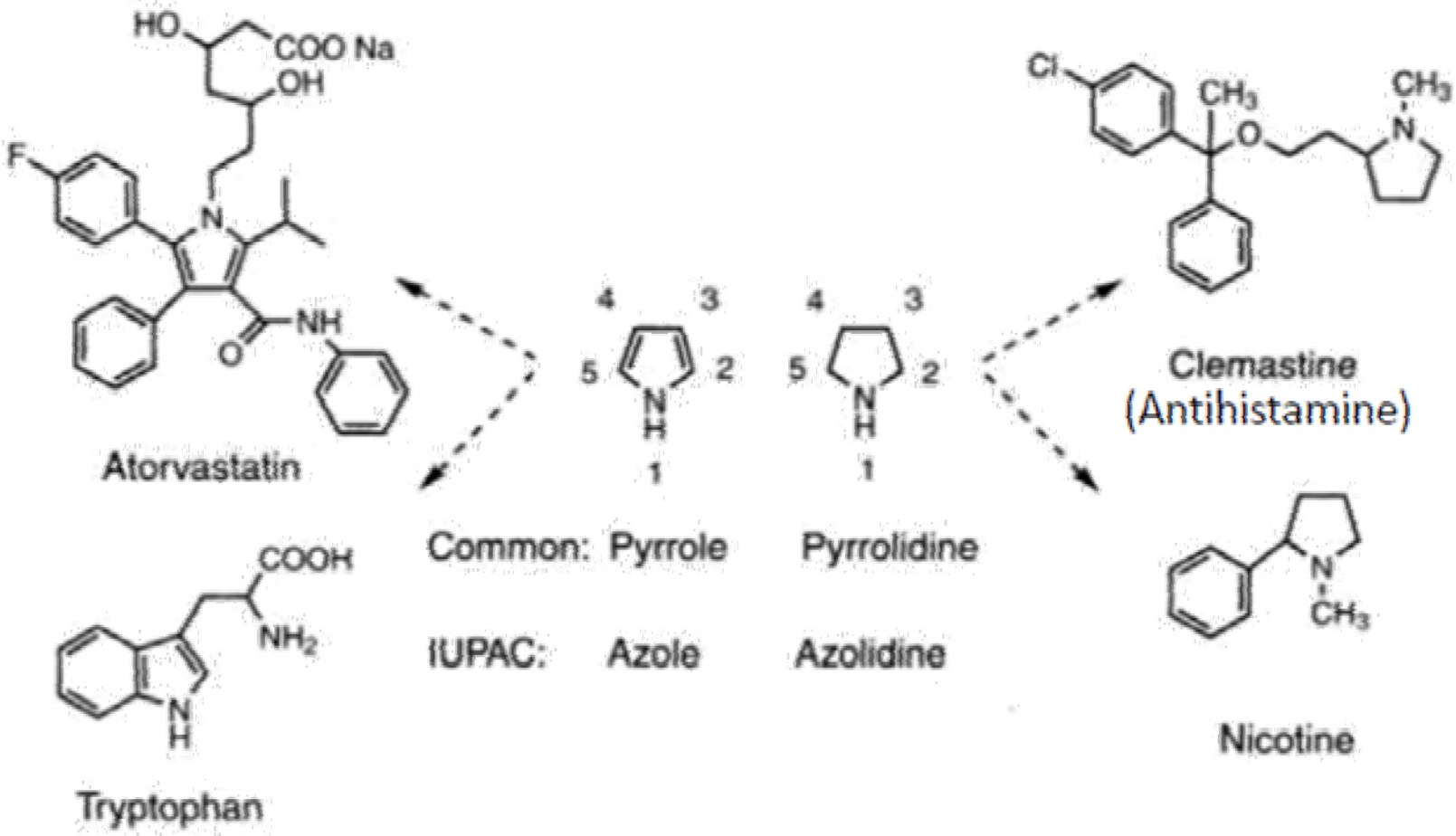

Furosemide



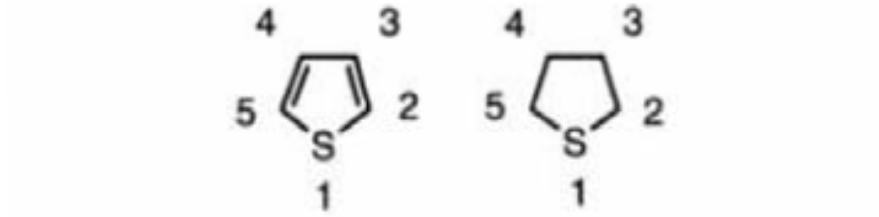

AZT

**Azidothymidine (zidovudine)**

➢ Two common five-membered ring hetrerocycles containing nitrogen are pyrrole and pyrrolidine

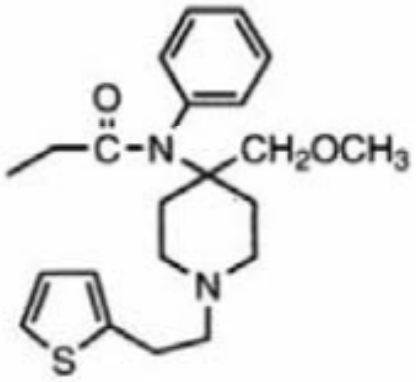


➢ Two sulfur-containing heterocycles, thiophene and tetrahydrothiophene

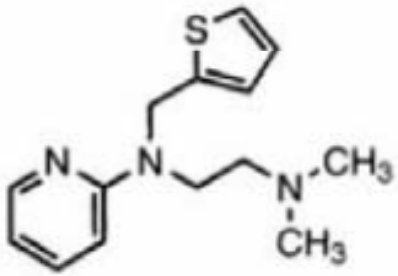



Common: Thiophene Tetrahydrothiophene

IUPAC: Thiole Thiolane

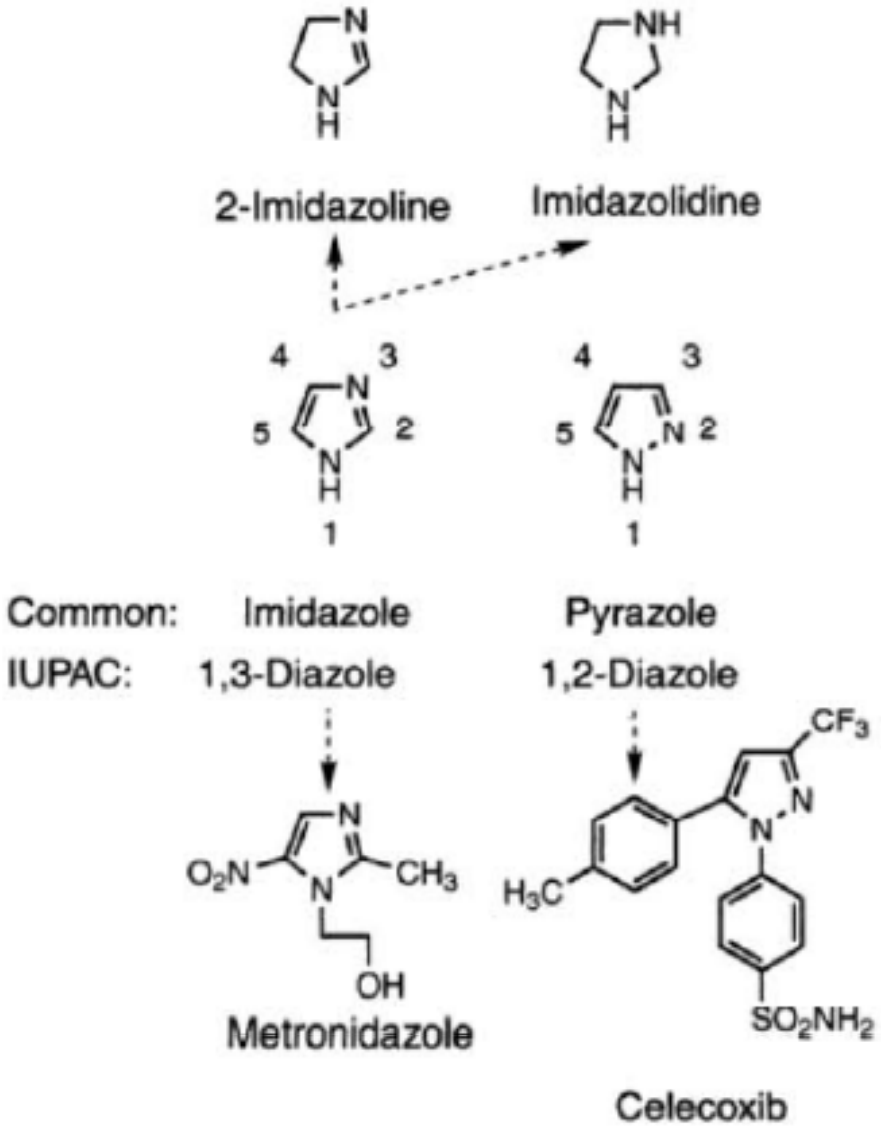



Sufentanil
(Opoid analgesic)

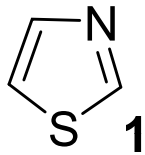



Methapyrilene
(Antihistamine)

➢ Two important dinitrogen heterocycles are found in medicinal agents; these are imidazole and pyrazole

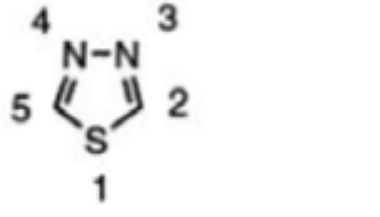


- Heterocycles with nitrogen and sulfur called 1,3-Thiazole

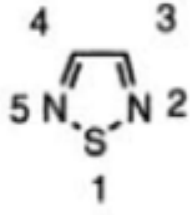



**1,3-Thiazole**

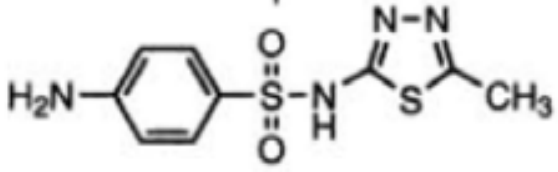
- Complex Five-Membered Heterocycles



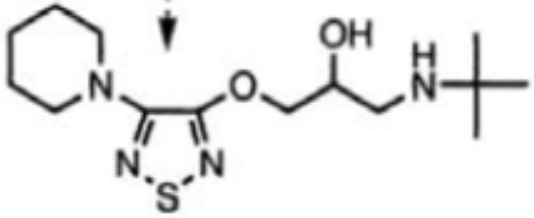

**1,3,4-Thiadiazole**



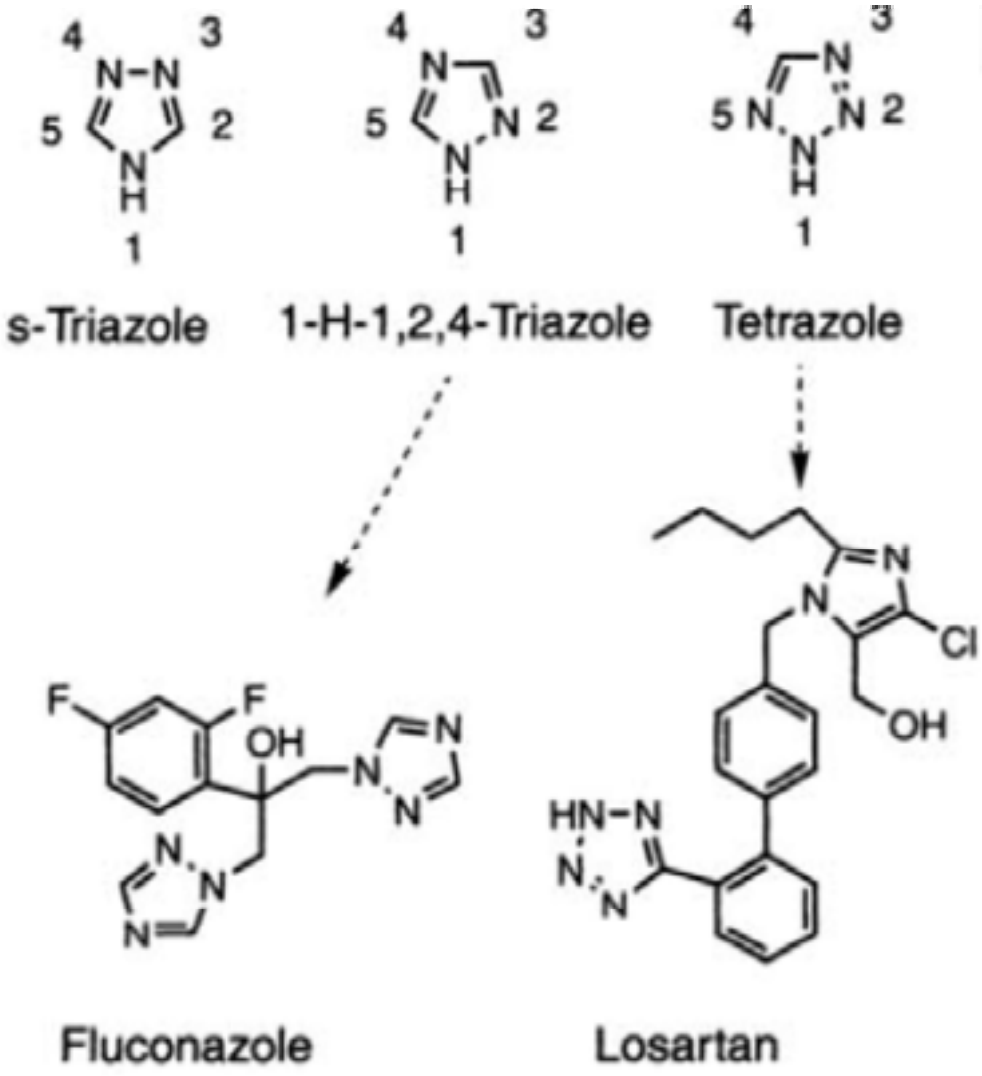

**1,2,5-Thiadiazole**



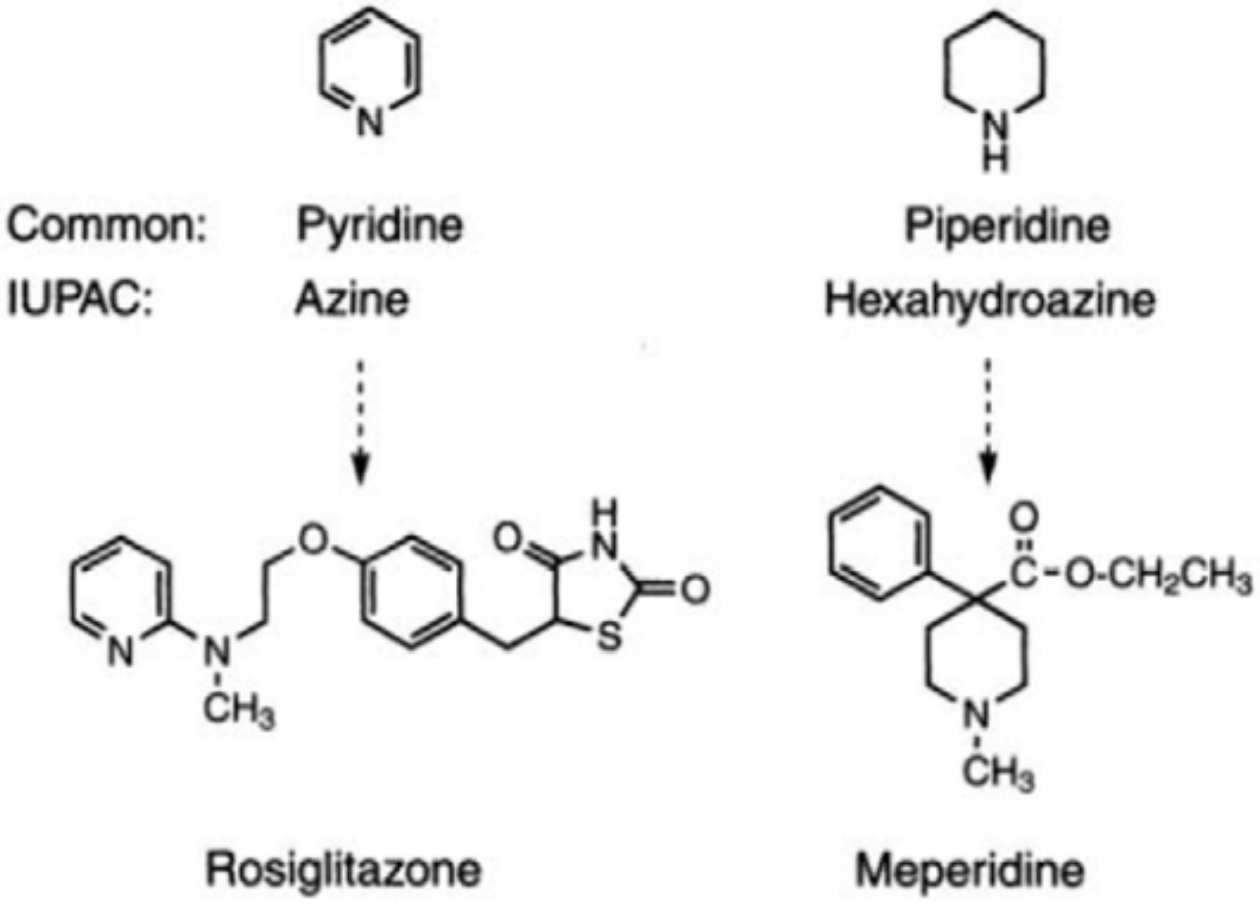

**Sulfamethizole**

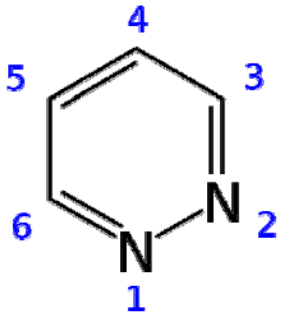



**Timolol**

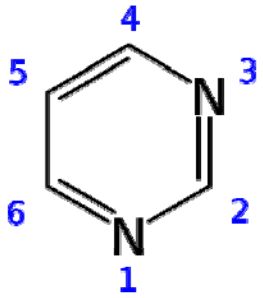

s-Triazole
1-H-1,2,4-Triazole
Tetrazole
Fluconazole
Losartan

# 10.4. SIX-MEMBERED RING HETEROCYCLES

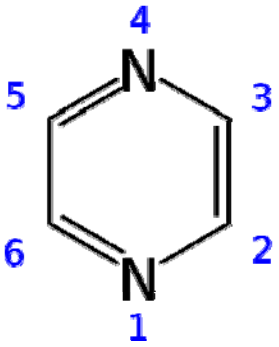




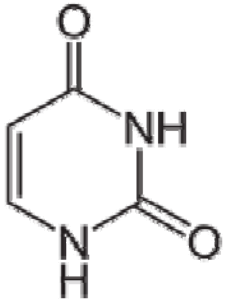

**pyridazine**



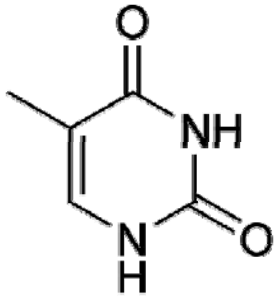

**pyrimidine**



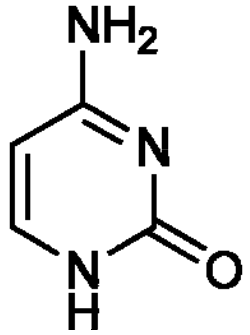

**pyrazine**




**Uracil**

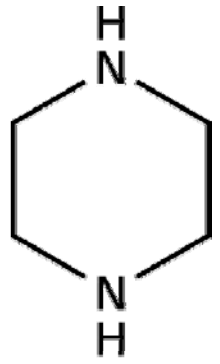



**Thymine**

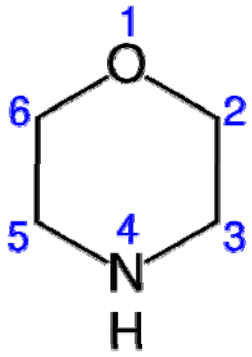



**Cytosine**

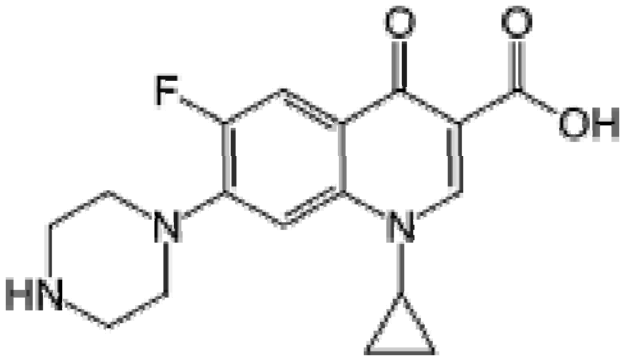
# 10.5. SATURATED SIX·MEMBERED HETEROCYCLES



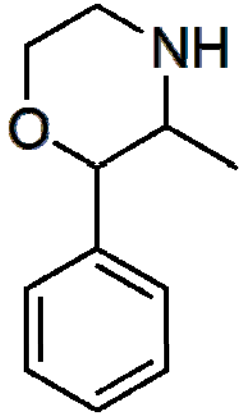

**Piperazine**




**Morpholine**

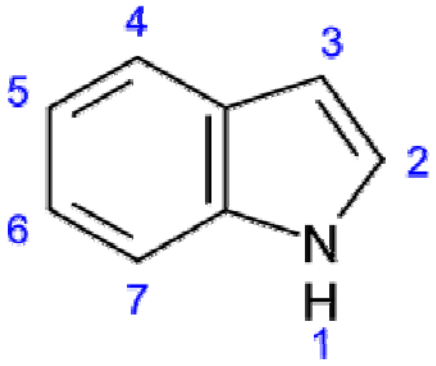



**Ciprofloxacin**

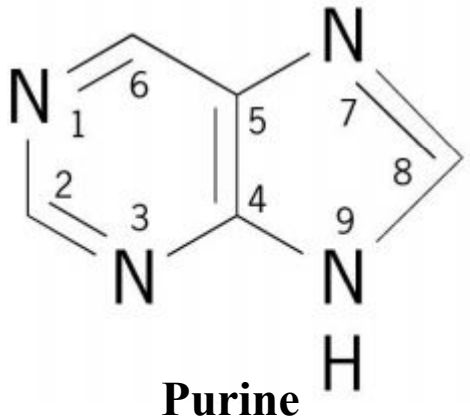



**Phenmetrazine**

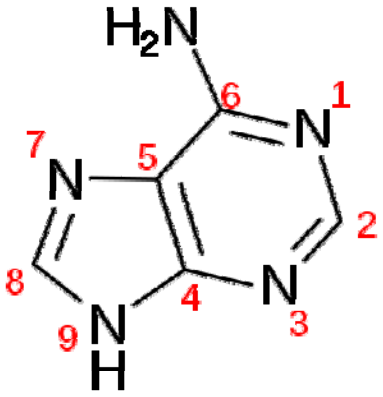
# 10.6. BICYCLIC HETEROCYCLES RINGS



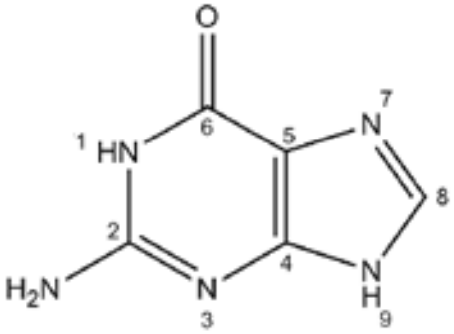

**Indole**



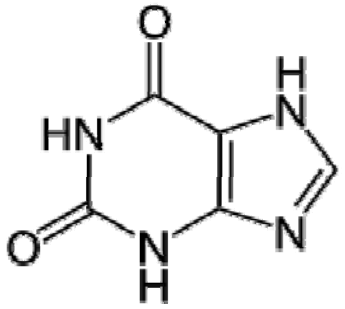

**Purine**



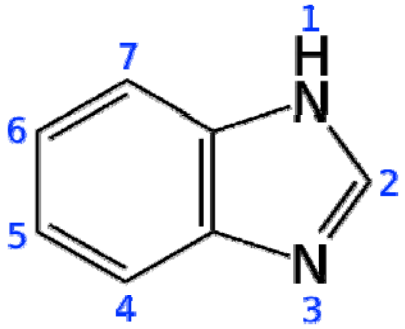

**Adenine**



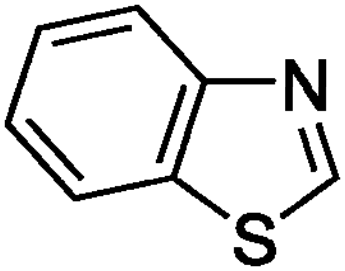

Guanine



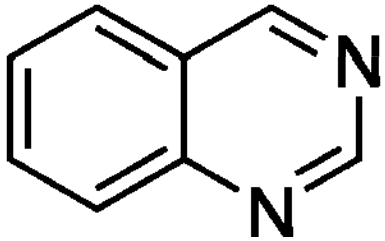

**Xanthine**



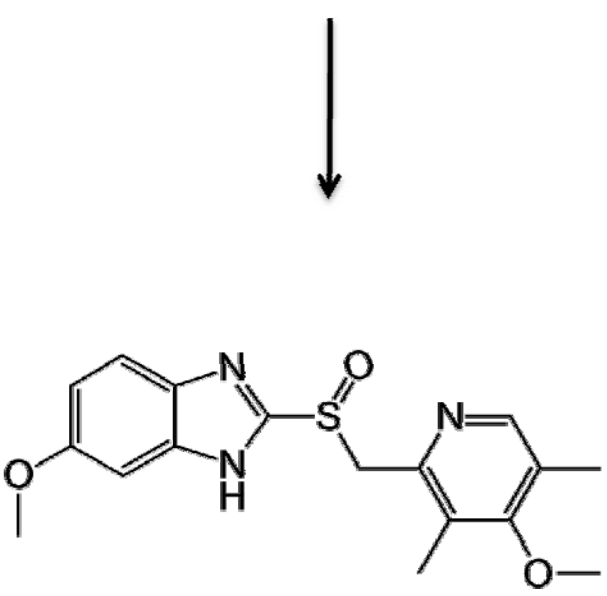

**Benzimidazole**



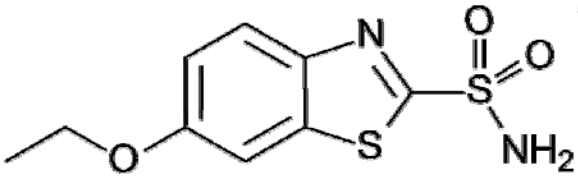

**Benzothiazole**



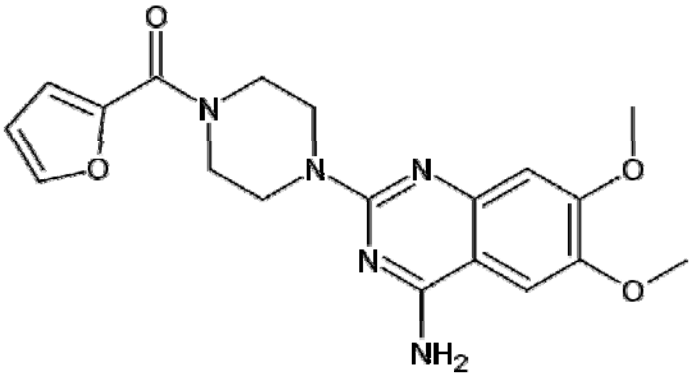

**Quinazoline**




**Omeprazole**

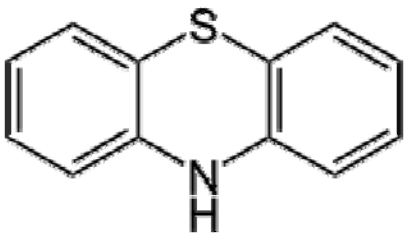



**Ethoxzolamide**

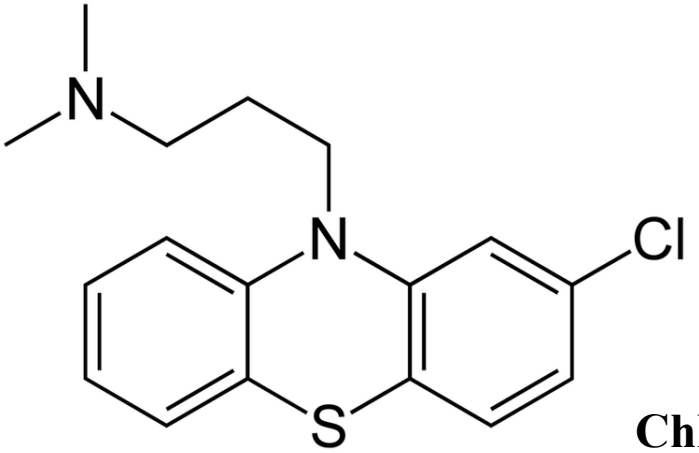



**Prazocin**

# 10.7. TRICYCLIC HETEROCYCLES RINGS




**Phenothiazine**




**Chlorpromazine**