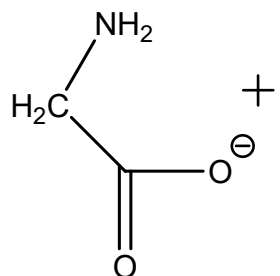


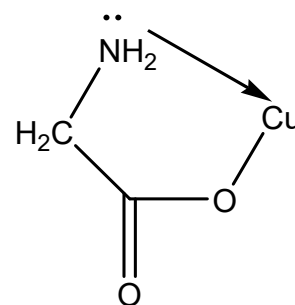
Effect of Chelation on biological activity

❖ The compounds that are obtained by donating electrons to metal ion with the formation of ring structures are called chelates.

e.g. glycine forms chelate with Cu^{+2} .

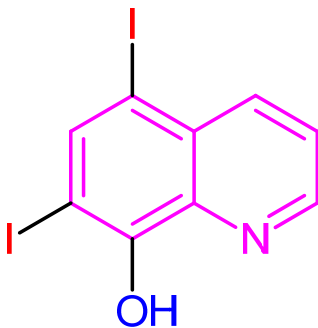


Glycine anion



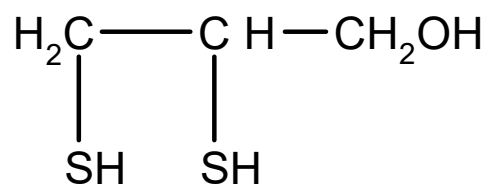
Glycine- copper chelate

❖ Iodoquinol and its analogues acts as antiamebic agents by complexing with iron and copper.

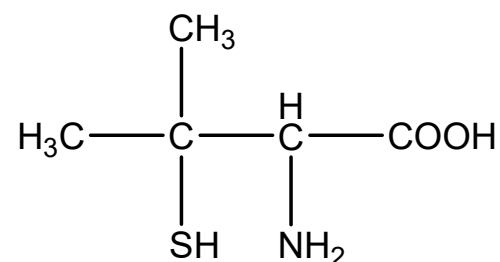


❖ Chelating agents are used as antidote. e.g. Deferoxanamine is used as antidote for iron poisoning.

❖ Dimercaprol is used in the treatment of lead poisoning. L-penicillamine is used in the treatment of copper poisoning.

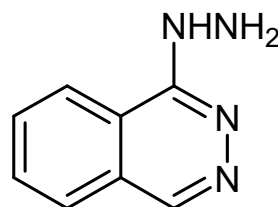


Dimercaprol



L-penicillamine

❖ Undesirable side effects are caused by drugs that chelates with metal. Eg hydralazine an antihypertensive agent causes anaemia due to chelation of the drug with iron.



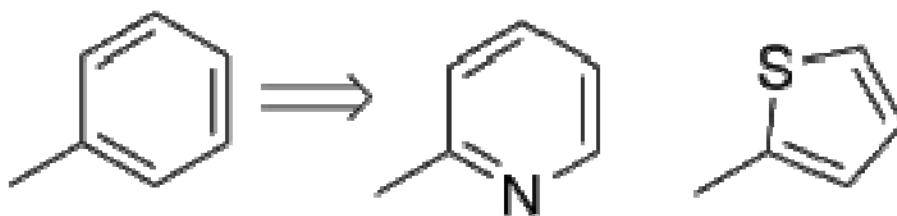
Hydralazine

Effect of Bioisosterism on biological activity

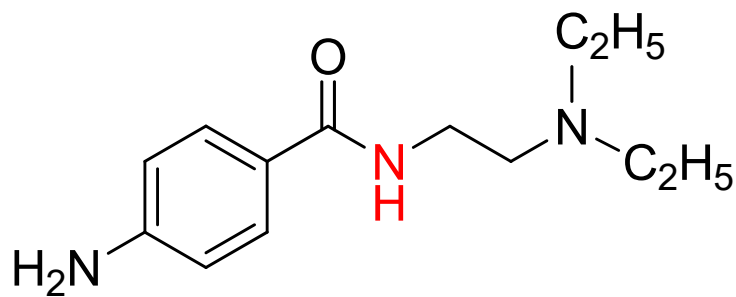
- ❖ In medicinal chemistry, **bioisosteres** are chemical substituents or groups with **similar physical or chemical properties** which produce broadly similar **biological properties** to another chemical compound.
- ❖ In drug design, the purpose of exchanging one bioisostere for another is to enhance the desired biological or physical properties of a compound without making significant changes in chemical structure.
- ❖ Bioisosterism is used to **reduce toxicity, change bioavailability, or modify the activity** of the lead compound, and may alter the metabolism of the lead.

Classical bioisosterism was originally formulated by James Moir and refined by Irving Langmuir as a response to the observation that different atoms with the same valence electron structure had similar biological properties.

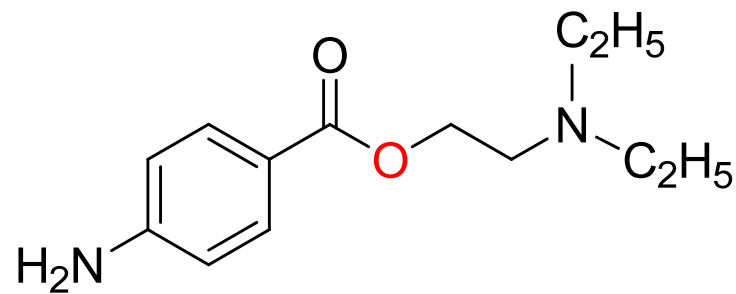
For example



❖ **Procainamide**, an amide, has a longer duration of action than **Procaine**, an ester, because of the bisosteric replacement of the ester oxygen with a nitrogen atom. Procainamide is a classical bioisostere because the valence electron structure of a disubstituted oxygen atom is the same as a trisubstituted nitrogen atom.



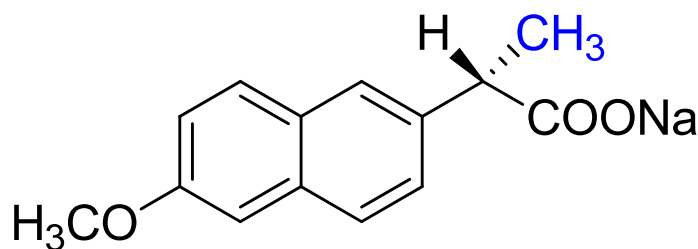
Procainamide



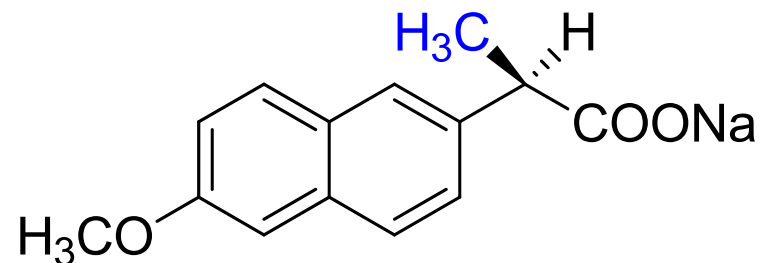
Procaine

Effect of optical isomerism on biological activity

- These compounds essentially possess identical physical as well as chemical characteristics but have different pharmacological activities.
- The difference is due to the interaction of asymmetric carbon atom of the molecule with a stereospecific receptor.
- The enantiomer having **high affinity** for the receptor is called **eutomer**, whereas the one with **low affinity** is called **distomer**.
- e.g. (S) (+)-naproxen sodium exhibits activity as analgesic, antipyretic and anti-inflammatory. However (R) (-)-naproxen sodium is inactive.



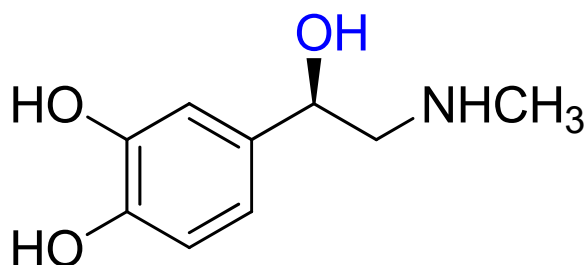
(S) (+)-Naproxen sodium



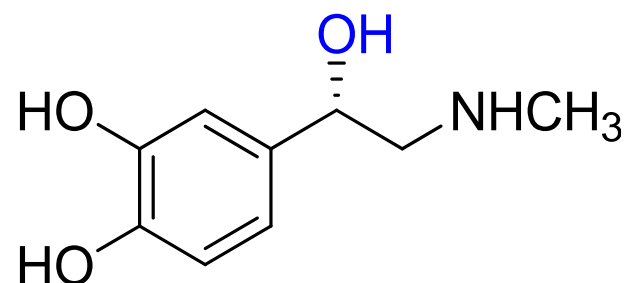
(R) (-)-Naproxen sodium

03-03-2021

- **(-) Epinephrine** is 12-15 times more **active** as vasoconstrictor than **(+) Epinephrine**



(-) epinephrine



(+) epinephrine

- **(-) Isoprenaline** is 800 times more active bronchodilator than **(+) Isoprenaline**.
- **(-) Hyoscyamine** is 15-20 times more active as mydriatic than **(+) Hyoscyamine**.

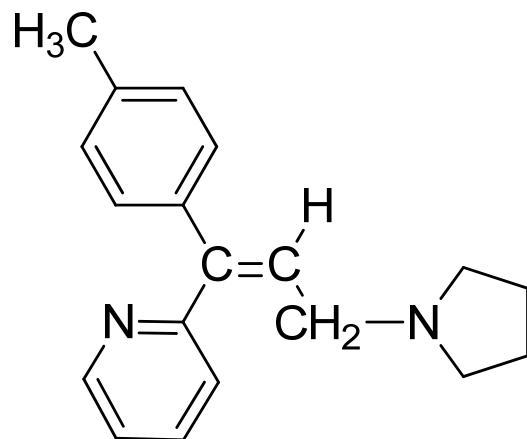
Effect of Geometrical isomerism on biological activity

❖ Geometrical isomerism result due to restricted rotation along the double bond.

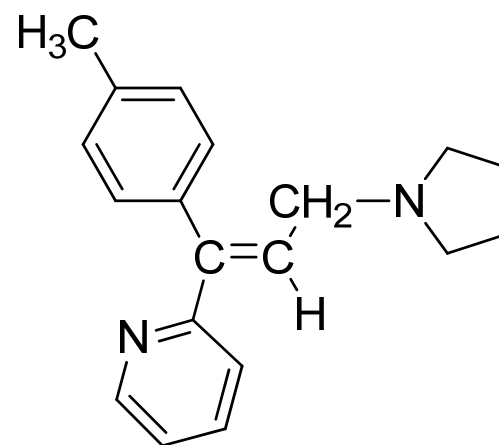
❖ Geometrical isomers are of two types Cis- /Z-isomer and Trans- /E –isomer:

e.g. (E)-tripolidine aromatic rings are located on the opposite side of the double bond, shows potent antihistaminic actions.

However in in (Z)-Tripolidine the two heterocyclic aromatic rings are strategically located on the same side of the double bond and is found to be inactive.



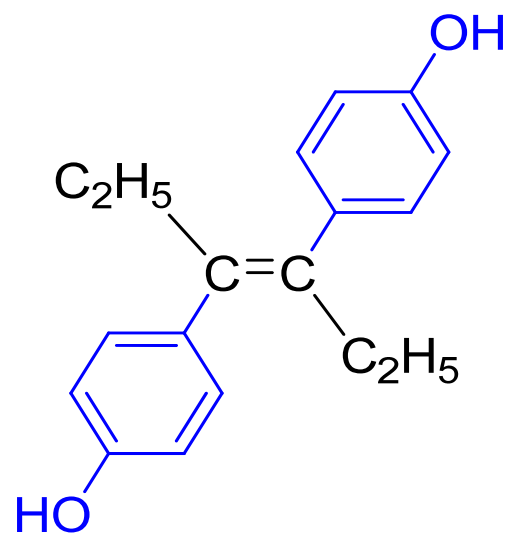
(Z)-Tripolidine



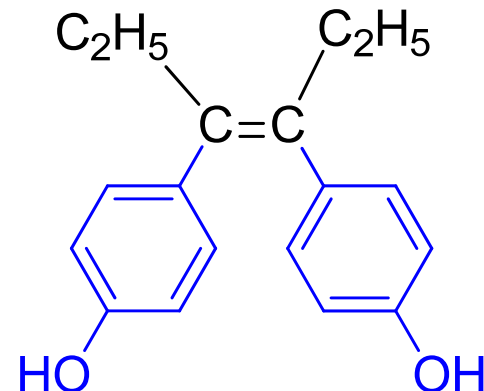
(E)-Tripolidine

03-03-2021

- ❖ In trans-diethyl stilbesterol, the presence of two phenolic hydroxy functions in **opposite side** lead to oestrogenic activity. However cis-diethyl stilbesterol having two phenolic hydroxyl groups in **same side** is inactive.



**Trans-diethyl
stilbesterol**



**Cis-diethyl
stilbesterol**