Drugs and Pharmaceuticals

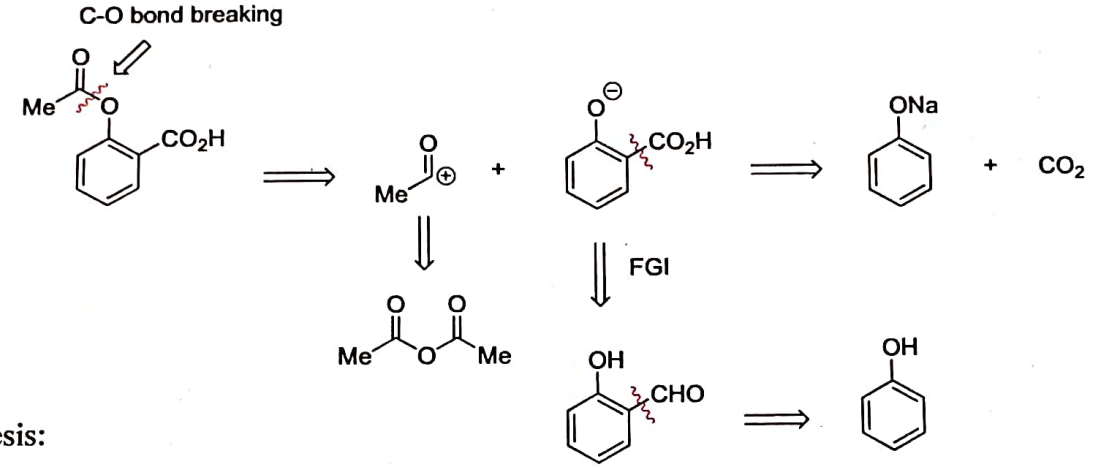
Basic Retro-synthetic approach & Synthesis of Drugs

Analgesic, antipyretic & anti-inflammatory drugs:

Aspirin:

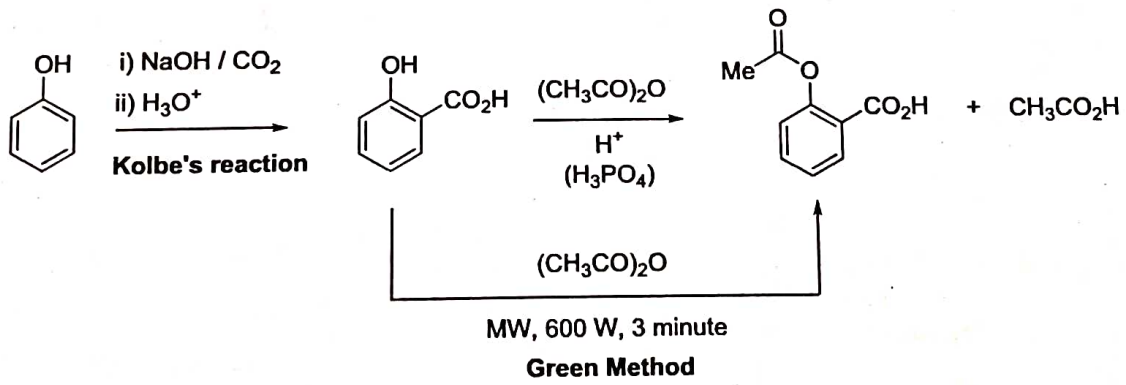
Acetyl salicylic acid, commonly known as **Aspirin**, possesses analgesic, antipyretic & anti-inflammatory properties.

Retro-synthesis:

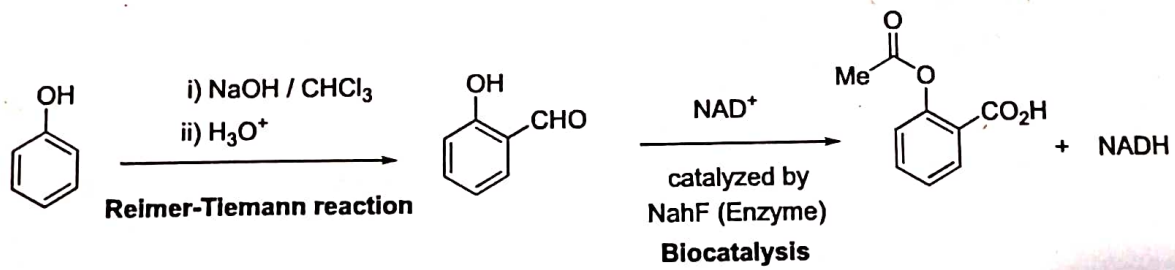


Synthesis:

Method I:



Method II:

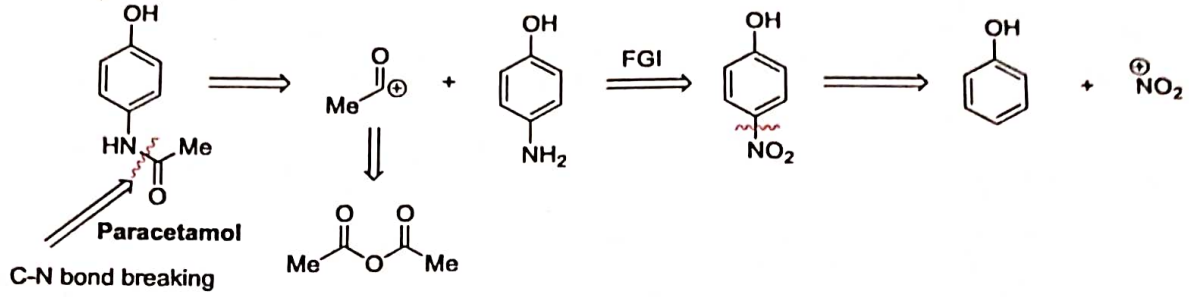


Paracetamol:

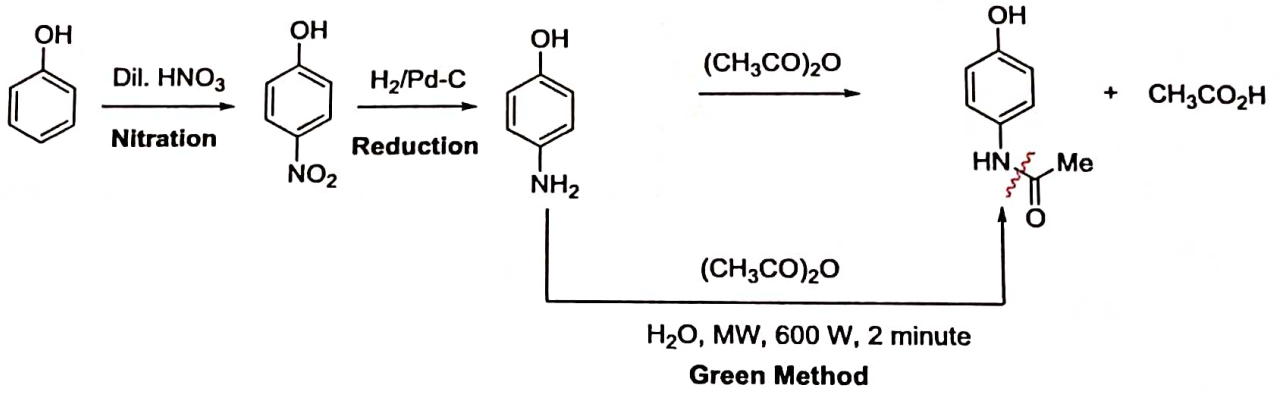
Acetaminophen (or Paracetamol) is a well-known drug that is used to relieve headaches, fever, and aches and pains in joints and muscles. It is also a main ingredient in many cold and flu

medications and prescriptions. It is considered a safe and effective drug when used in the recommended dosages.

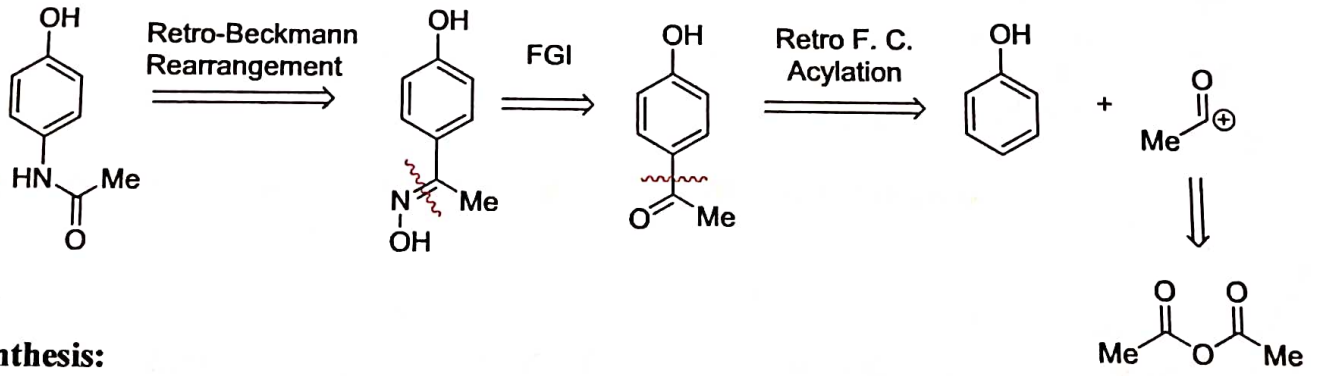
Retro-synthesis I:



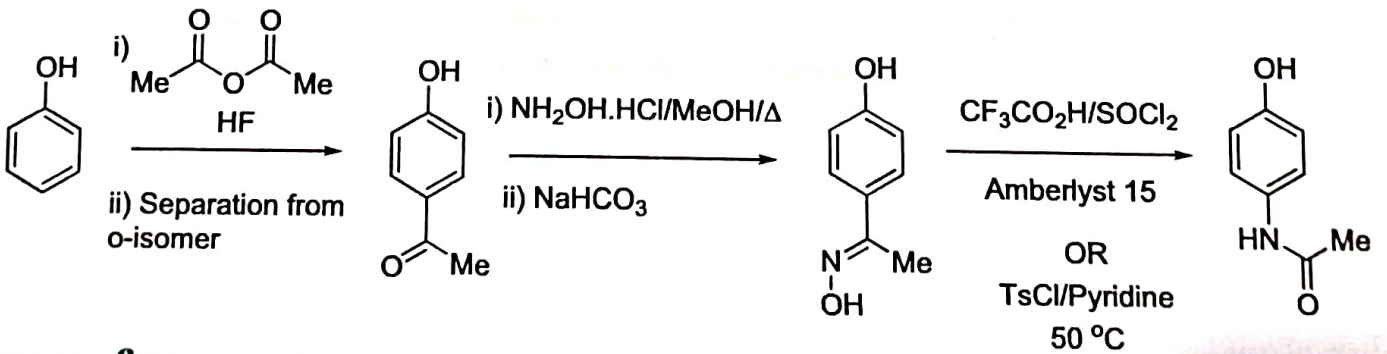
Synthesis:



Retro-synthesis II:

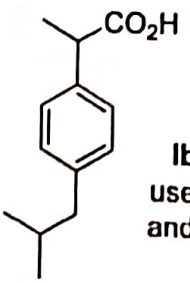


Synthesis:



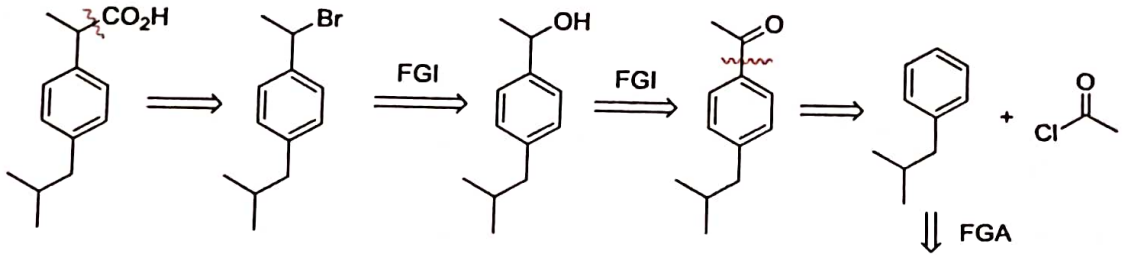
Ibuprofen:

Synthesis of



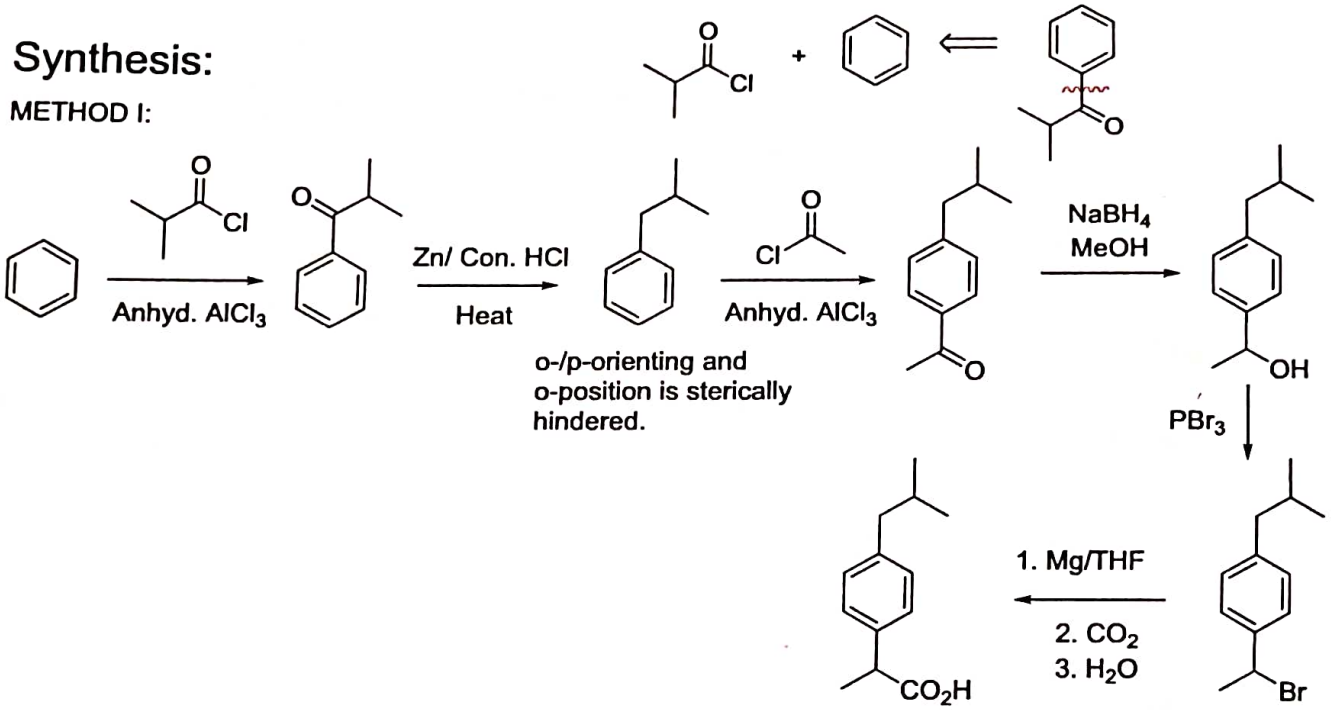
Ibuprofen
used for fever
and relief pain

Retrosynthetic analysis:

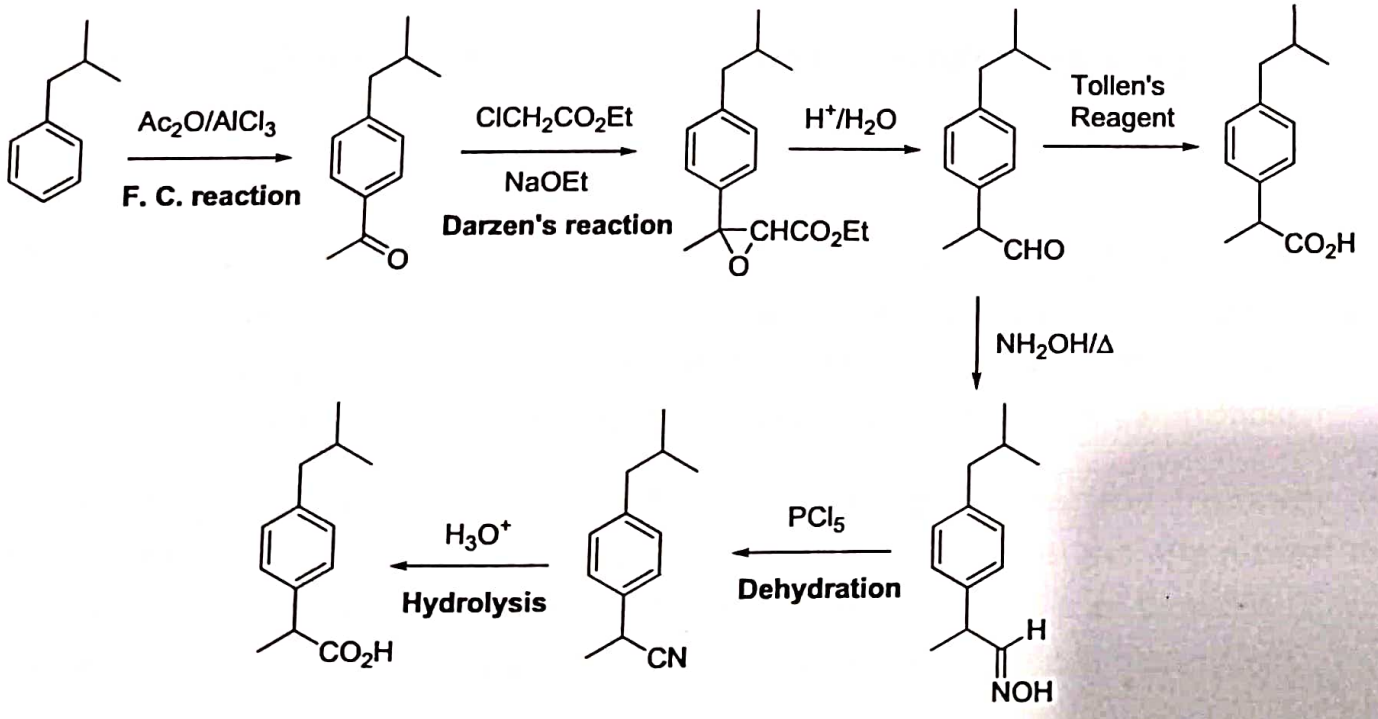


Synthesis:

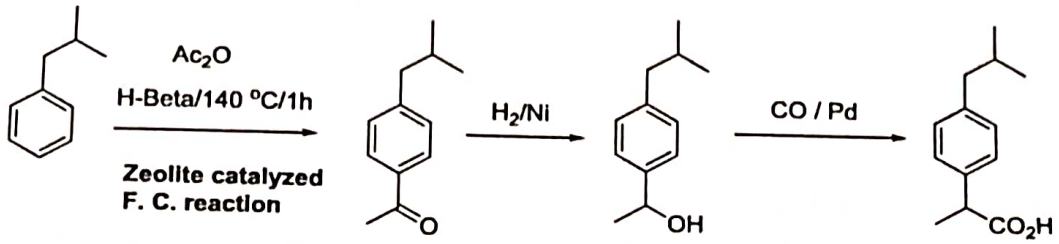
METHOD I:



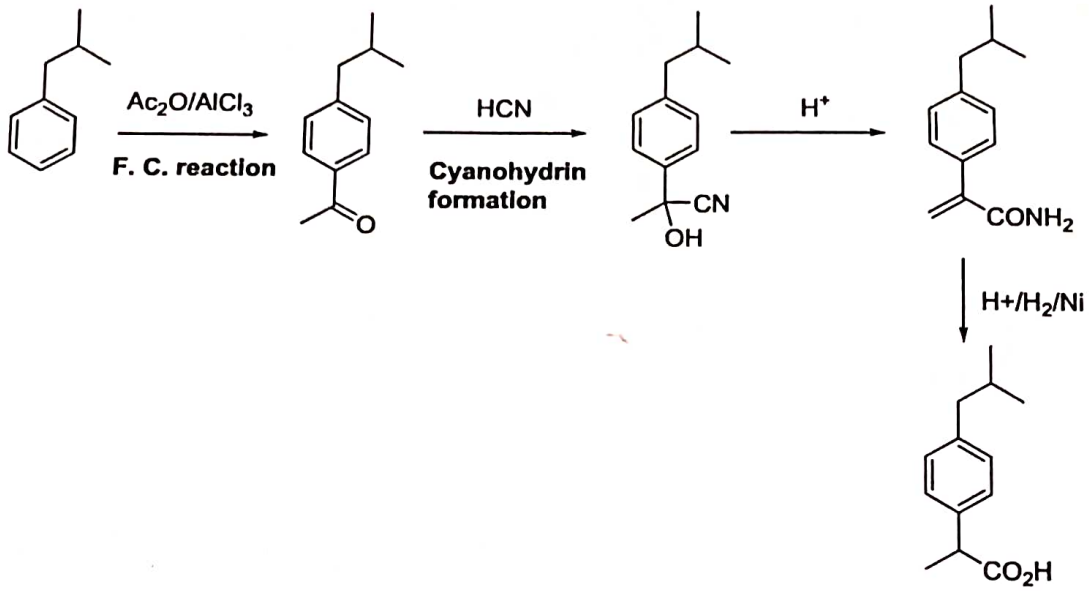
METHOD II: Traditional Synthesis involving less than 40 % atom utilization.



METHOD III: **A Greener Synthesis of Ibuprofen:** Involves more than 80 % atom utilization



METHOD IV: Starting from isobutyl benzene



Medicinal use of Ibuprofen:

It is used to relief pain and to reduce fever. It is a non-steroidal anti-inflammatory drug.

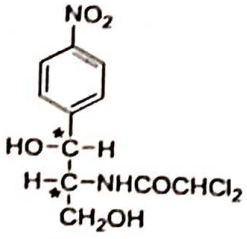
Antibiotics:

Chloramphenicol: It is capable of exerting its effect against viral diseases as well as those due to bacterial invasion and opens up the whole field of the chemotherapy of *virus* and *rickettsial* infections in man including typhus, undulant fever, *Salmonella septicaemia,* whooping cough, gastroenteritis, *lymphogranulomainguinale,* typhoid and paratyphoid.

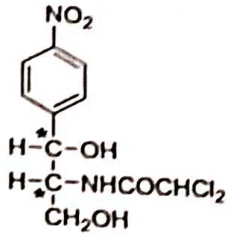
Chloramphenicol is particularly recommended for the management and treatment of serious infections produced by the strains of both Gram-positive and Gram-negative organism thathave developedeventually resistance to either ampicillin or penicillin G, for instance: *H. influenzae, Salmonella typhi, S. pneumoniae, B. fragilis,* and *N. meningitidis.*

Structure Activity Relationship:

Chloramphenicol possesses *two chiral (asymmetric) carbon atoms*as shown below:



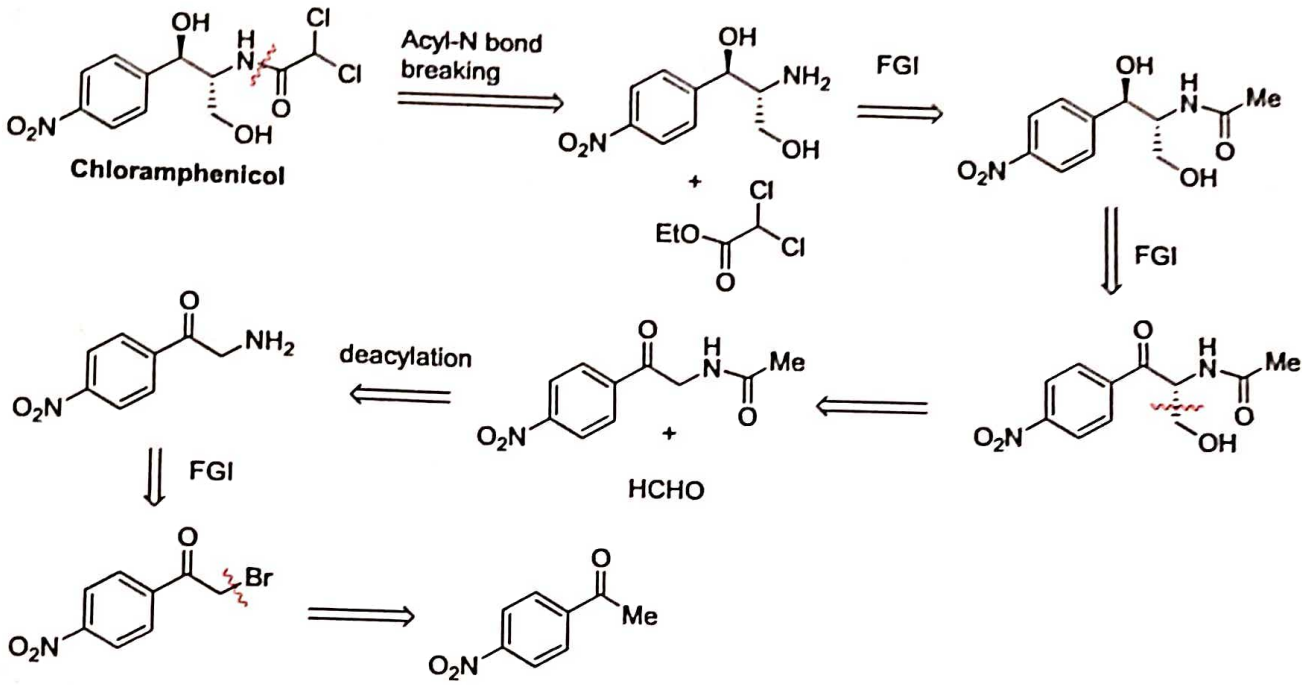
(Threo from)



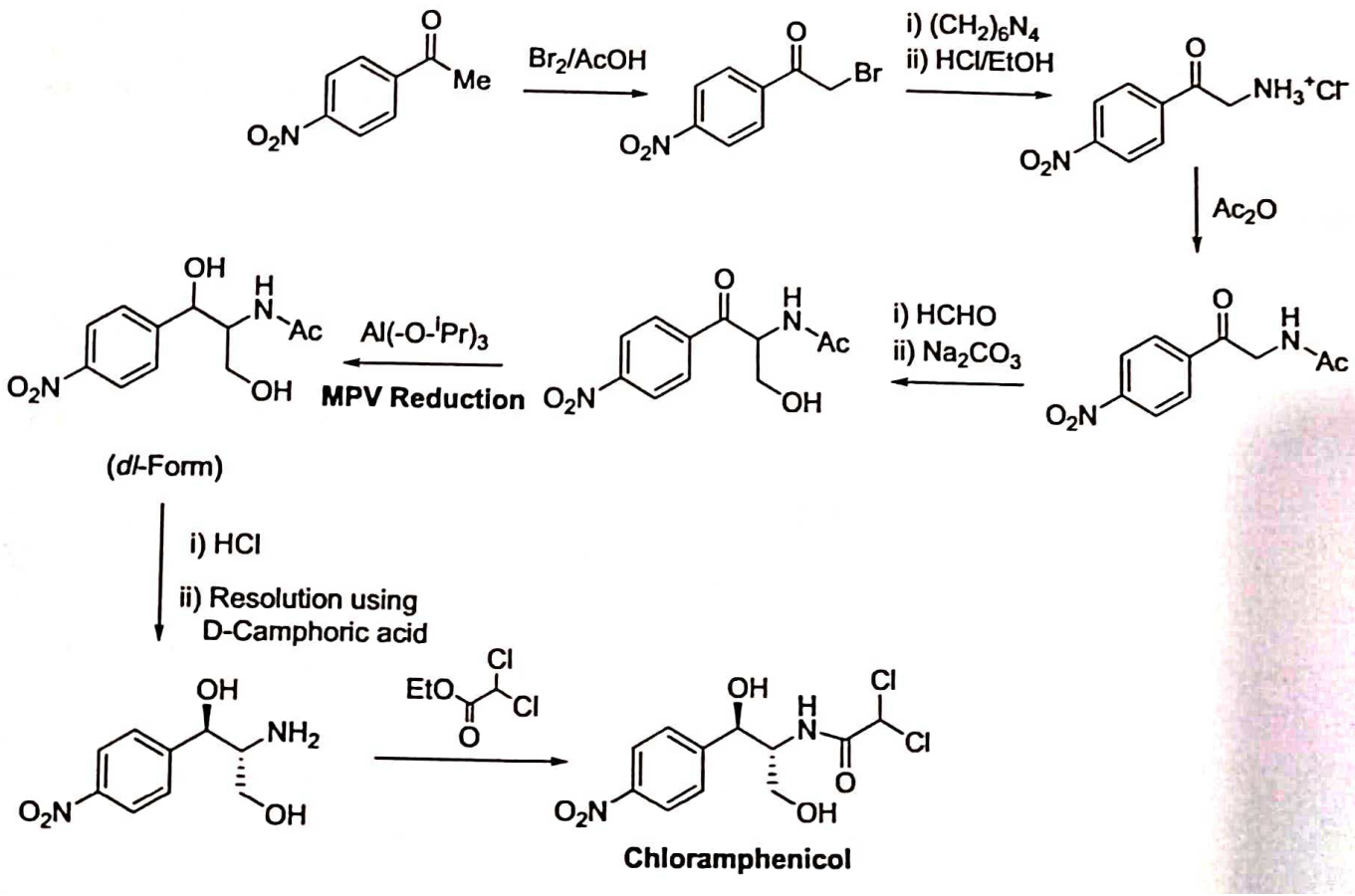
(Erythro form)

It has been observed that the biological activity resides almost exclusively in the **'D-Threoisomer'** whereas the **L-*Threo***, and **D- and L-*Erythro*isomers** are virtually inactive.

Retro-Synthesis:

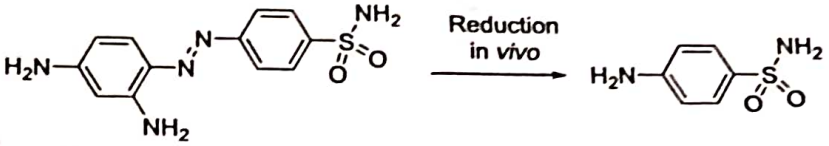


Synthesis:



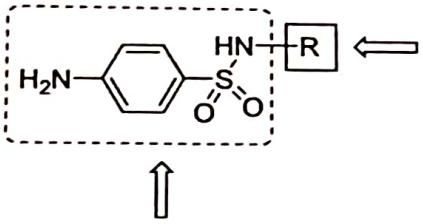
Anti-bacterial & Anti-fungal Drugs:

A. Sulpha Drugs: Since some dyestuffs selectively stained micro-organisms and shows the anti-bacterial activity. **Prontosil red** was active against a Streptococcus infection in mice and a Staphylococcus infection in rabbits. The compound was rapidly tested in humans where it was shown to control septicaemia in children including Domagk's daughter. It had a significant effect on infant mortality. It was seen that the active compound was a bio-transformation product, **sulfanilamide**. However, although this was used as an anti-bacterial agent, it was accompanied by a side effect. The amino group was acetylated in man and the acetate crystallized out in the kidneys. A series of structural modifications were then made to overcome this problem.



Prontosil Red (Inactive) — **Sulfanilamide (Active Drug)**

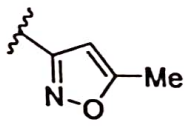
Basic Structure of Sulfonamide Drugs

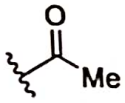


Chemical modification of this part of the molecule changes activitty and modifies pharmacological properties.

This part is responsible for antibacterial and antifungal activity. This Part of the molecule cannot be modified chemically without loss of antibacterial activity.

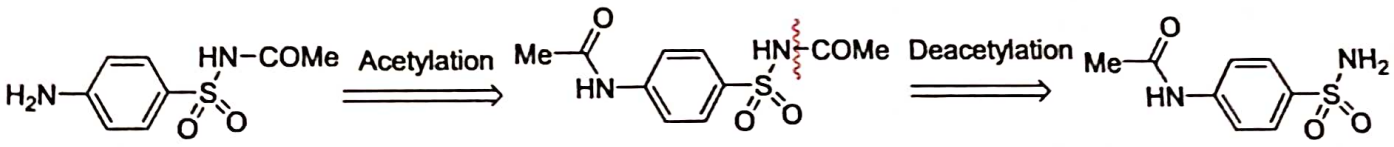
When,

R =  ⟹ **Sulphamethoxazole**

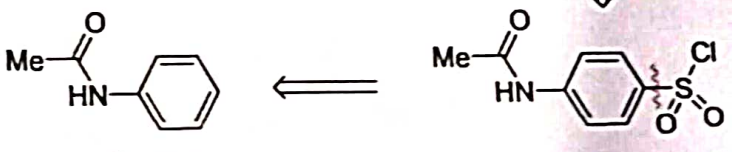
R =  ⟹ **Sulphacetamide**

Sulphacetamide:

Retro-synthesis:

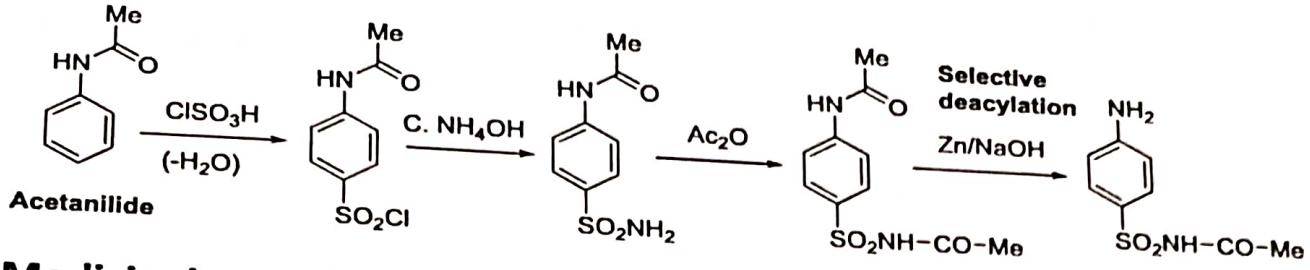


Sulphacetamide



Acetanilide

Synthesis:

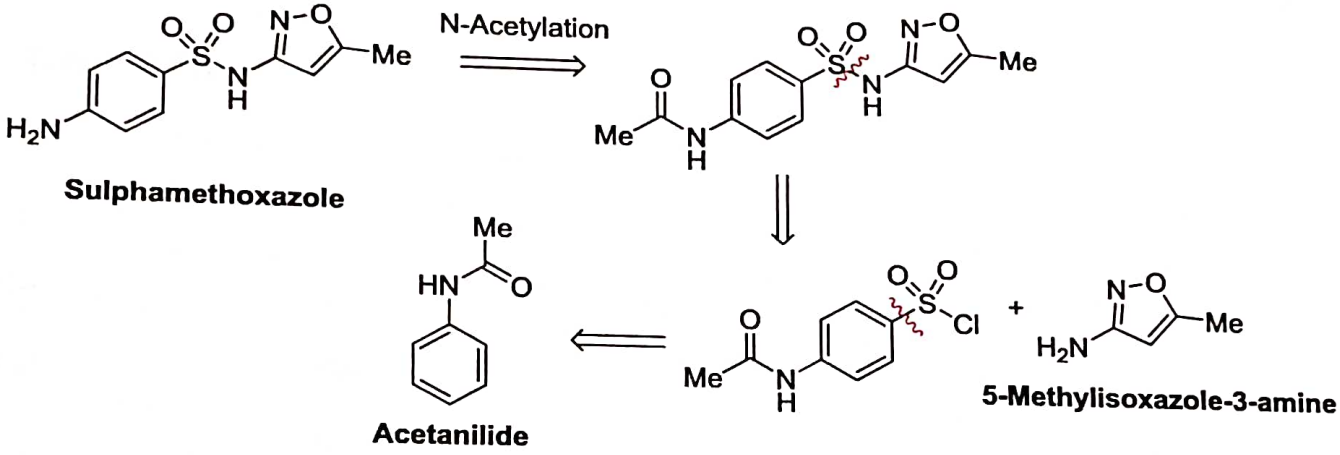


Medicinal use of Sulphacetamide:

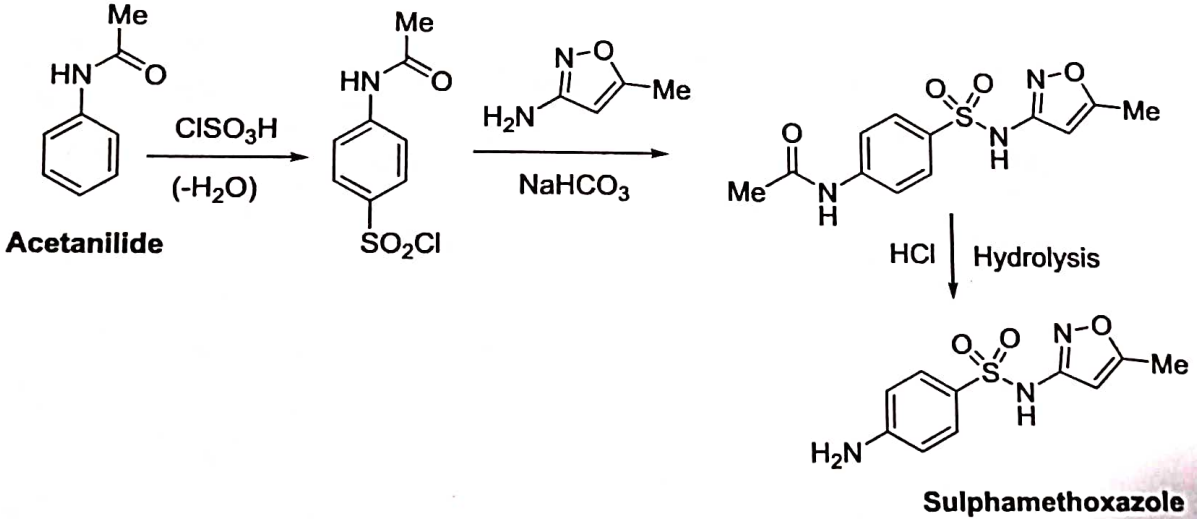
It is chiefly employed by local application in injuries or infections of the eyes. It is also used in the *treatment of acute conjunctivitis and in the prophylaxis of ocular infections after injuries or burns.*

Sulphamethoxazole:

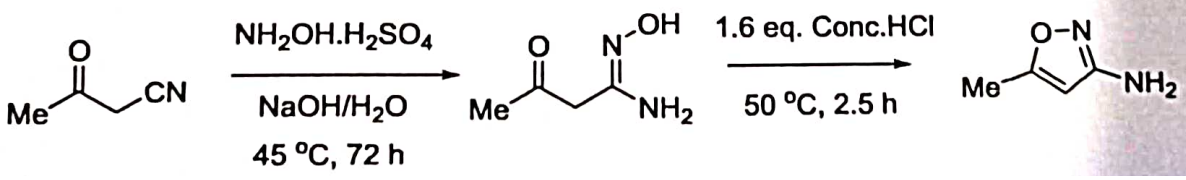
Retro-synthesis:



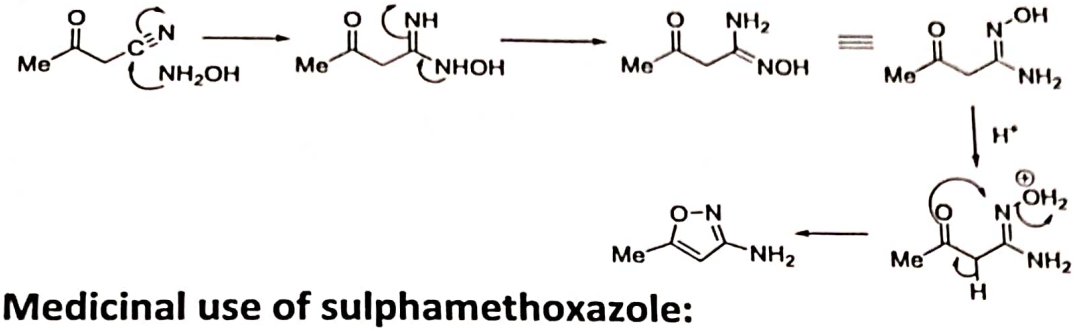
Synthesis:



Synthesis of 5-Methylisoxazole-3-amine:



Mechanism:



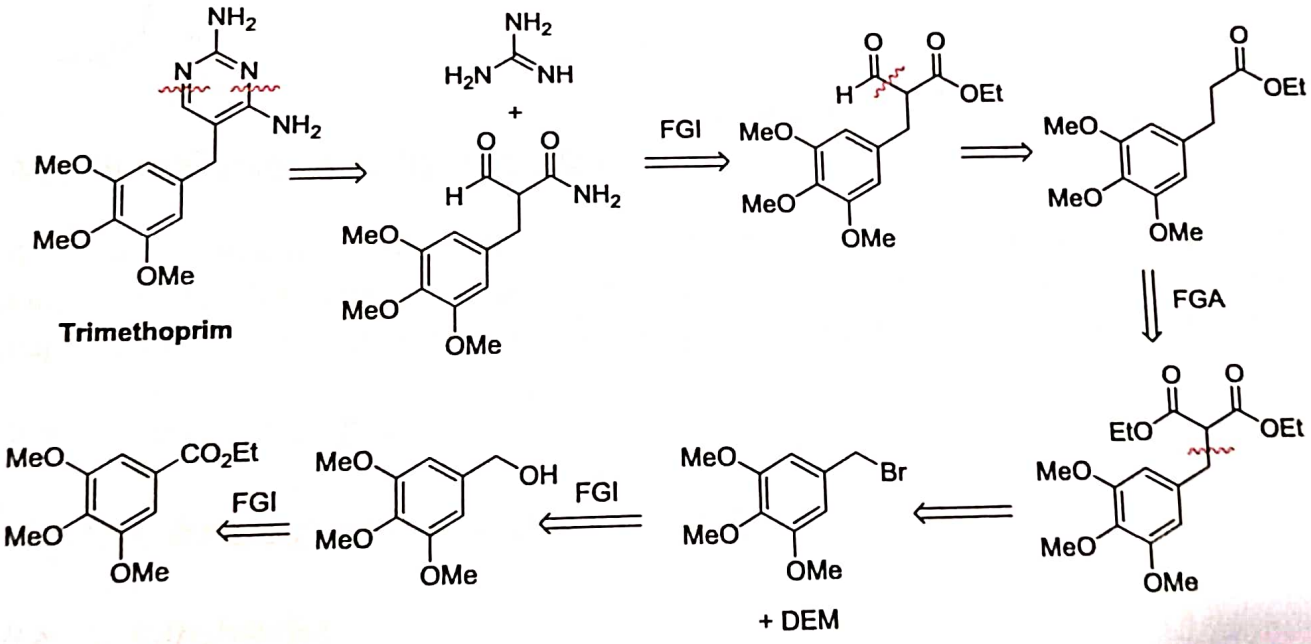
Medicinal use of sulphamethoxazole:

Combined with phenazopyridine, it is used to treat urinary tract infections and to reduce pain associated with it. Combined with trimethoprim, it is used to treat urinary tract infections and ear infections, bronchitis, gonorrhoea etc.

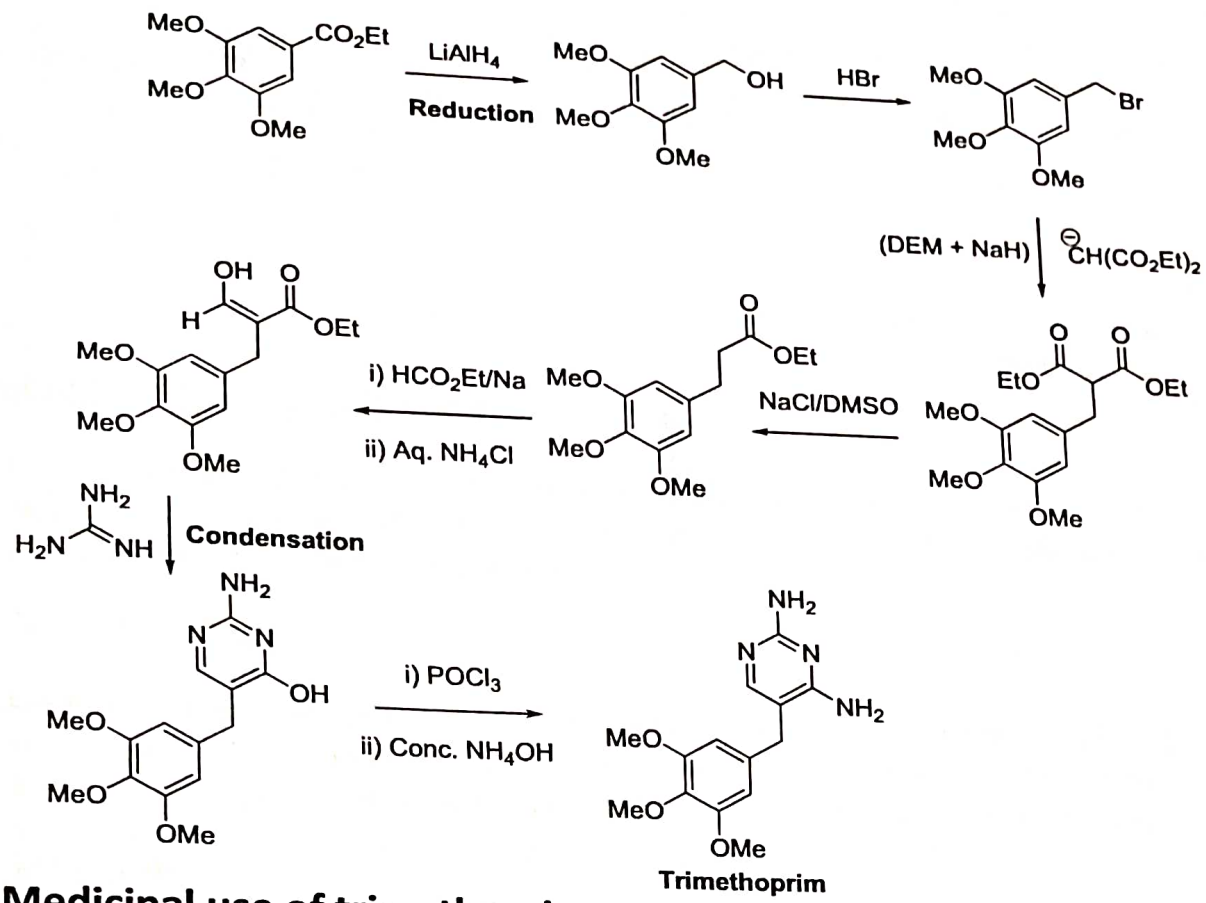
B. Pyrimidine Analogue:

Trimethoprim:

Retro-synthesis:



Synthesis:



Trimethoprim

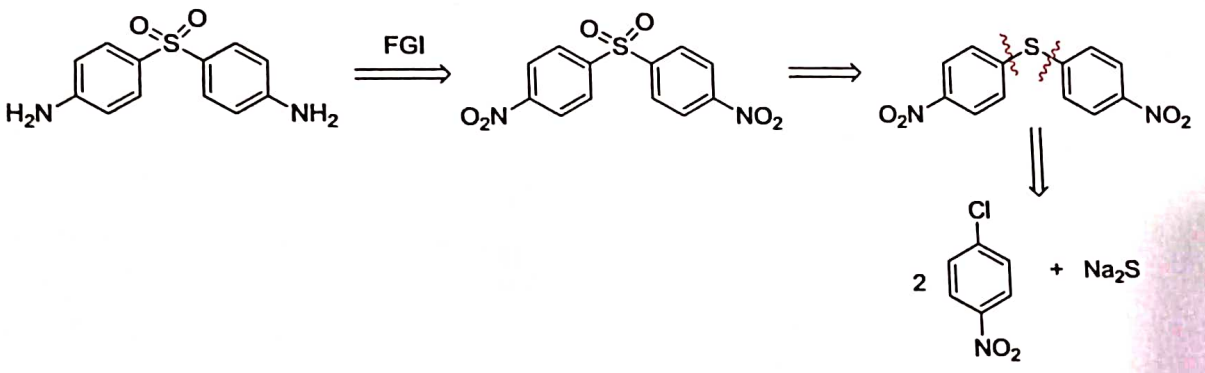
Medicinal use of trimethoprim:

It has been employed in conjunction with sulfametopyrazine in the treatment of chloroquine-resistant malaria but unfortunately could not attain wide acceptance. *It is used in conjunction* with sulphonamides *in the treatment of bacterial infections viz.,* trimethoprim with sulphamethoxazole.

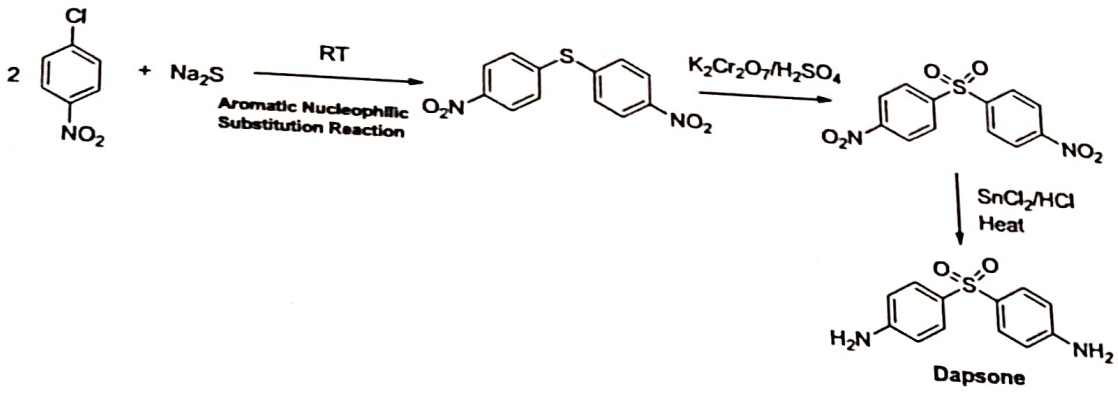
Anti-laprosy Drugs:

Sulfone Analogue: Dapsone:

Retro-synthesis:



Synthesis:



Medicinal use of Dapsone:

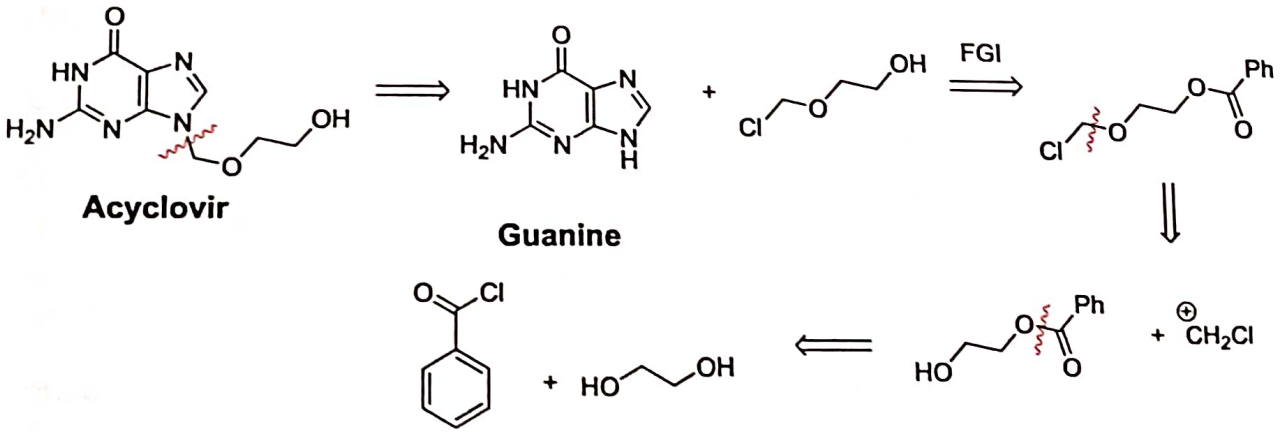
It is employed profusely in the treatment of both *lepromatous* and *tuberculoid* types of leprosy. Dapsone in conjunction with other agents has also been effectively used in the treatment of malaria due to chloroquine resistant *P. falciparum*.

Anti-viral Drugs:

Anti-viral drugs exert their effect against DNA viruses either by interfering with their replication due to its similarity of structure to the nucleotide structures in natural DNA virus or by interfering with the nucleic acid replication of the virus, specifically inhibiting the early steps in DNA synthesis.

Acyclovir:

Retro-synthesis:



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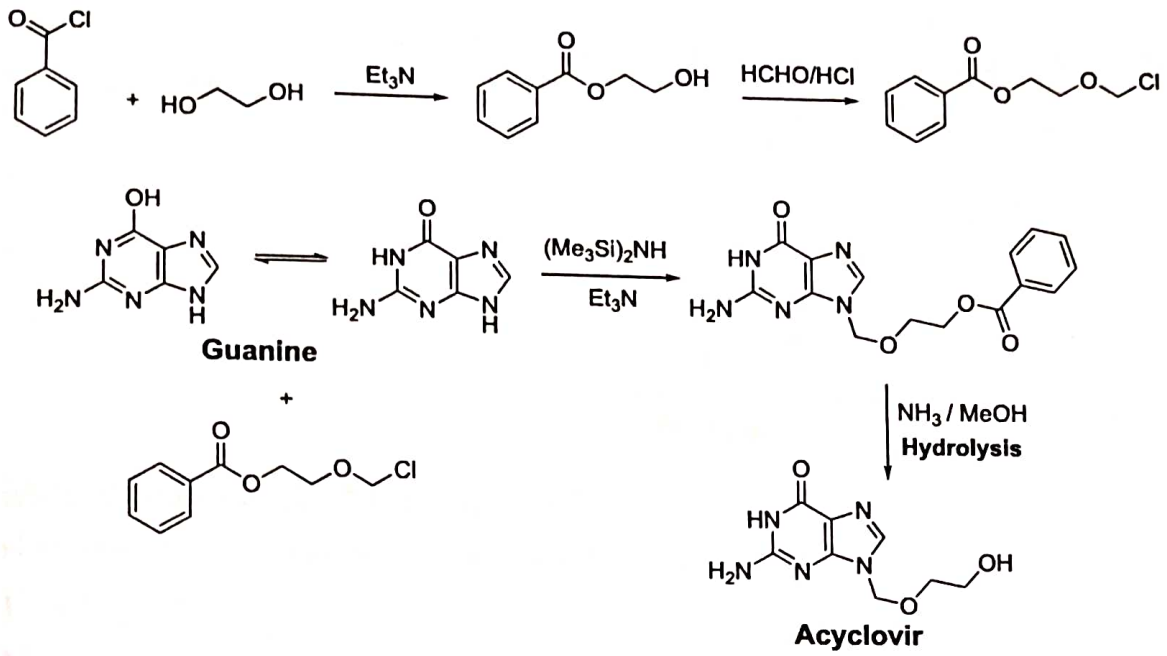


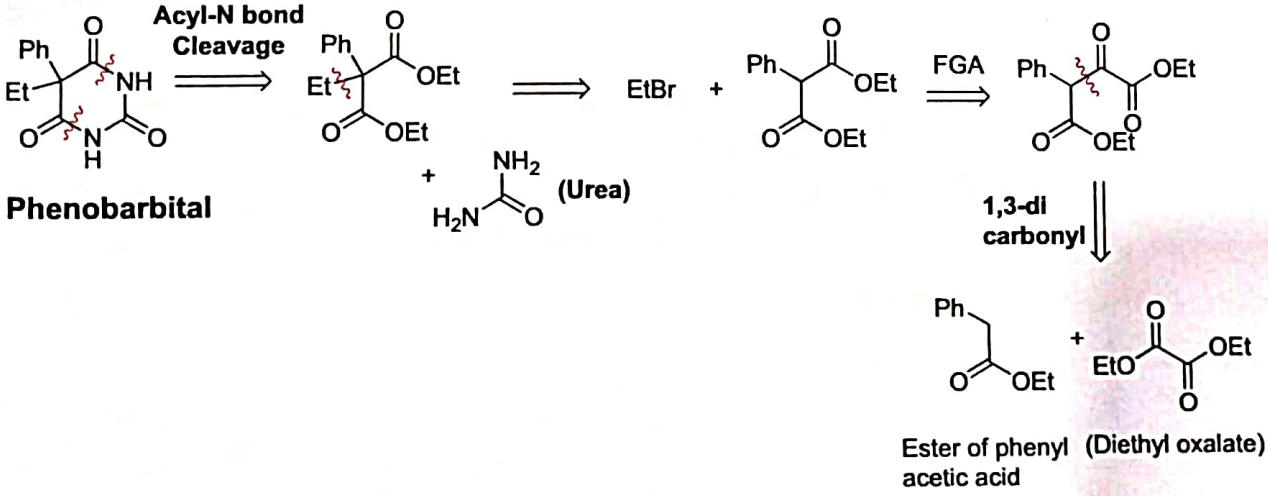
Medicinal use of Acyclovir:

Acyclovir was the first effective antiviral drug. It is effective against a number of herpes viruses, notably simplex, varicella-zoster (shingles), varicella (chickenpox) and Epstein-Barr virus (glandular fever).

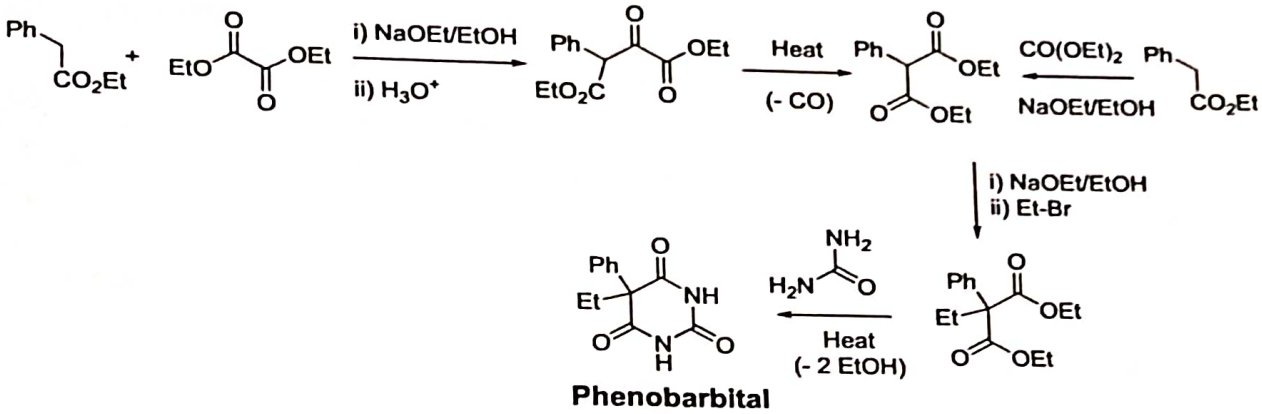
Central Nervous system Drug:

Phenobarbital:

Retro-synthesis:



Synthesis:



Phenobarbital

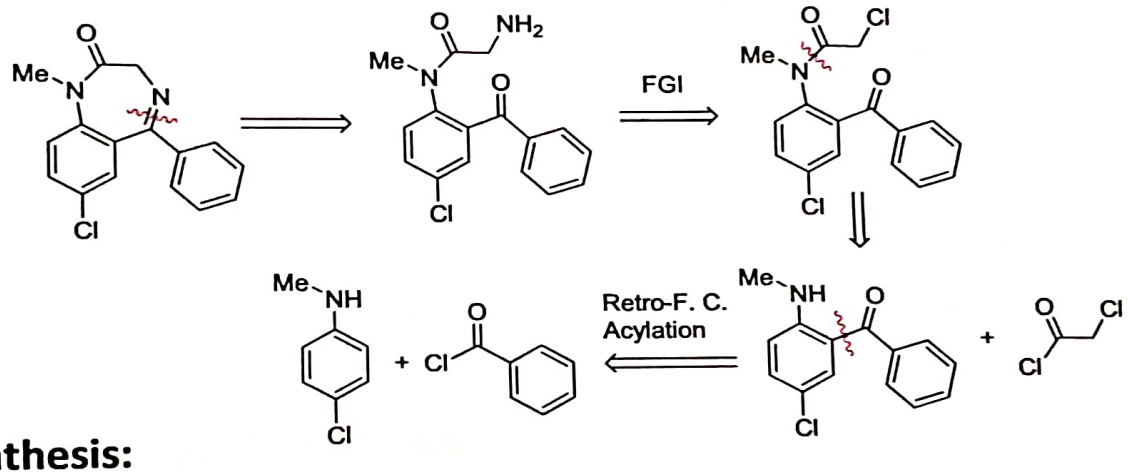
Medicinal use of Phenobarbital:

Phenobarbital is used as both sedative and hypnotic.

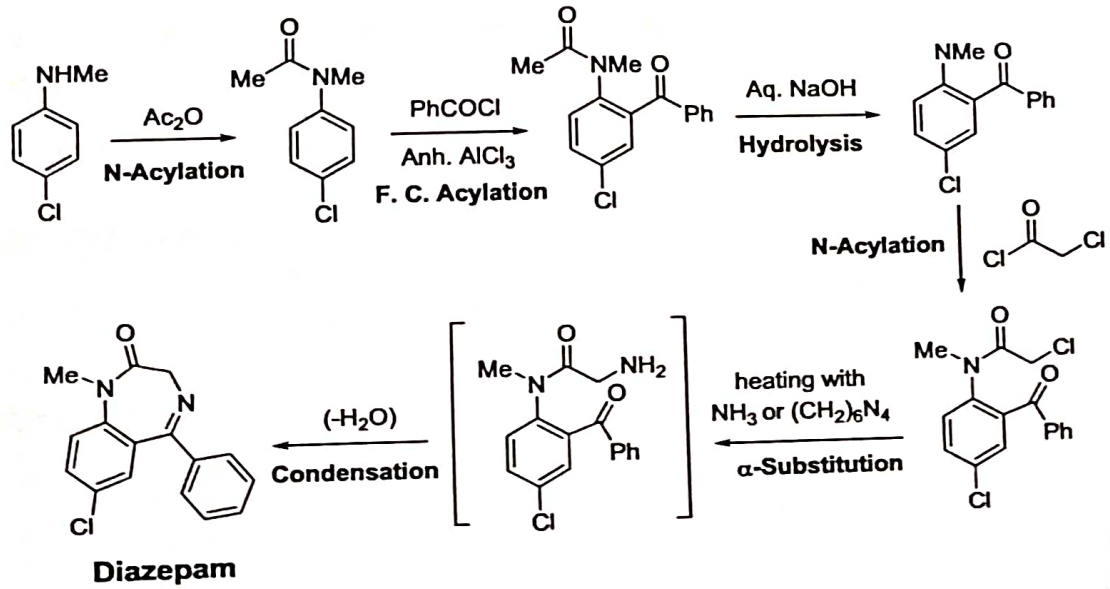
Diazepam:

Method I:

Retro-synthesis:



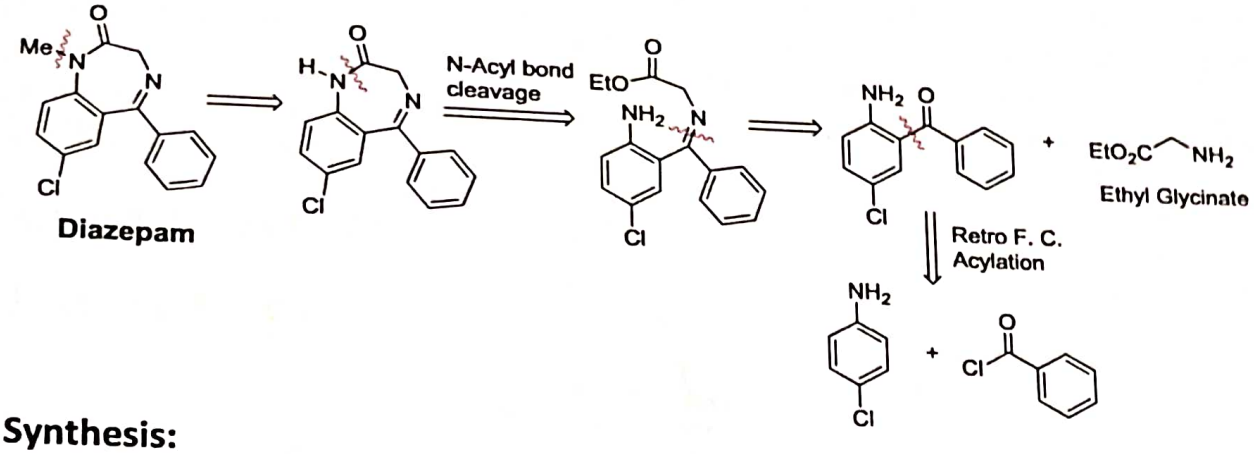
Synthesis:



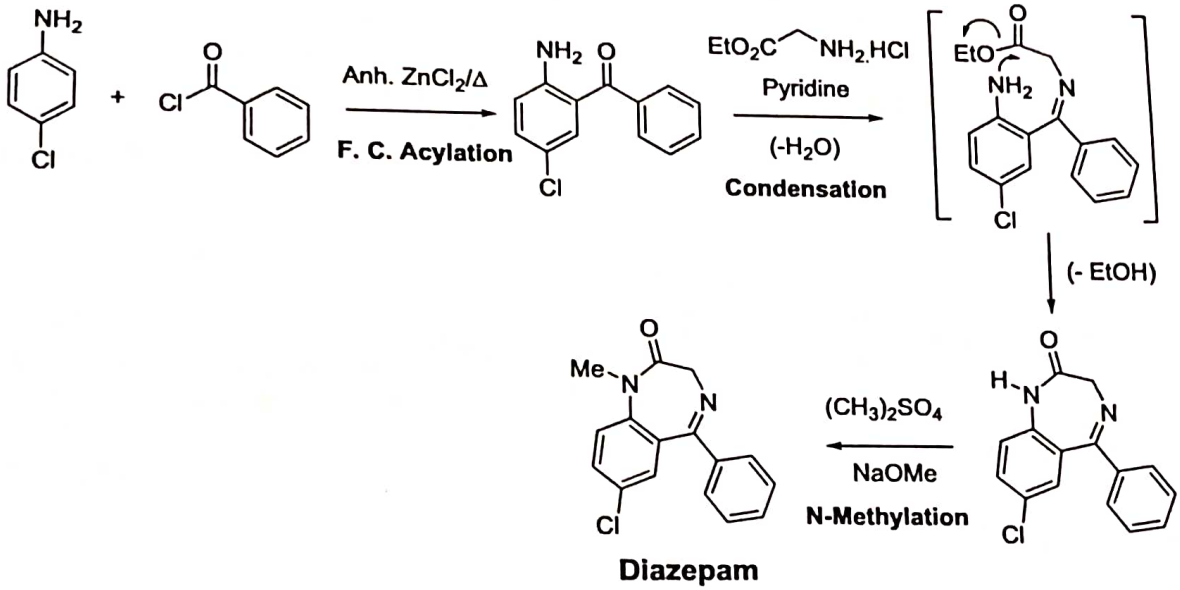
Diazepam

Method II:

Retro-synthesis



Synthesis:



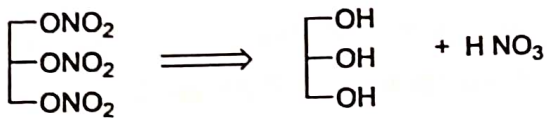
Medicinal use of Diazepam:

It is used as an anti-anxiety and anti-tension drug.

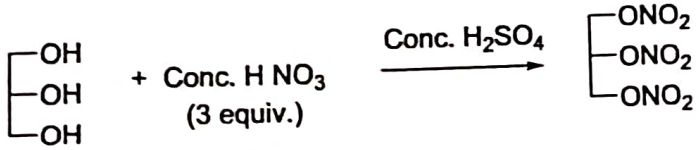
Cardiovascular Drug:

Glyceryl trinitrate:

Retro-synthesis:



Synthesis:

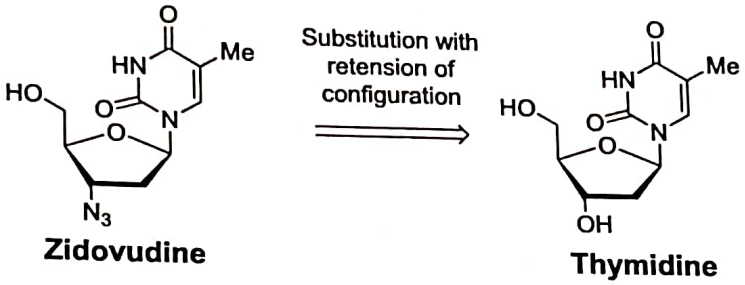


Medicinal use of Glyceryl trinitrate:

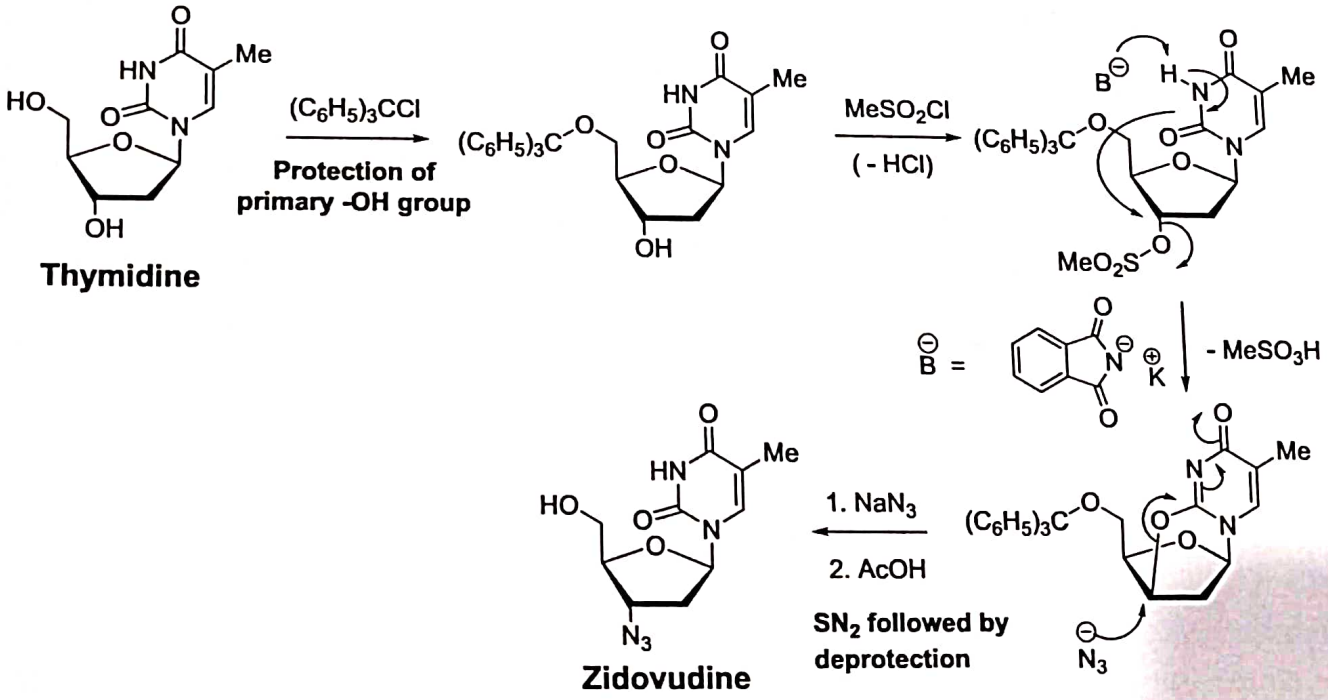
In medicine, Trinitrate (also called nitroglycerin) is used for angina, a painful symptom of ischemic heart disease caused by inadequate flow of blood and oxygen to the heart caused due to the narrowing of blood vessels that carries blood to the heart muscle and as a potent antihypertensive agent. Nitroglycerin corrects the imbalance between the flow of oxygen and blood to the heart.

Zidovudine (AZT):

Retro-synthesis:



Synthesis:



Medicinal use of Zidovudine:

Zidovudine or AZT is an analog of thymidine that possesses antiviral activity. It is active against the retroviruses that cause AIDS (HIV virus) and certain types of leukaemia.