

# E-CONTENT FOR COMPLETE COURSE

## e-book: **MEDICINAL CHEMISTRY** (For B.Pharm 6<sup>th</sup> semester)

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## UNIT- II

### Anticholinergic, Cholinergic, Anticholinesterases

#### Definition of Anticholinergic agents :-

Anticholinergic agent is a substance that blocks the neurotransmitter acetylcholine in the central and peripheral nervous system.

OR

Anticholinergic agents block or interfere with the action of ACh at the postganglionic endings of parasympathetic nerve endings. They block only the muscarinic actions of acetylcholine.

→ They are also called as parasympatholytics, spasmolytics, or cholinergic blocking agents, parasympathetic blockers.

Ex:- Atropine

Definition of cholinergic agents :- The cholinergic drugs are chemicals that

act at the same sites as the neurotransmitter acetylcholine. They are the drugs which stimulate the parasympathetic system & imitate or mimic the action of ACh.

OR

Cholinergic drugs are prescription medications designed to mimic the actions of ACh.

⇒ These drugs are also called as parasympathomimetic or cholinomimetics.

Ex: Neostigmine, Physostigmine, Methacholine, pilocarpine.

Definition of Anticholinesterases :- These are the drugs that inhibit or block the action of acetylcholinesterase.

OR

Anticholinesterase or cholinesterase inhibitors inhibit the enzyme acetylcholinesterase so that it is unable to hydrolyse ACh & thus they preserve ACh at nerve endings.

Ex:- Physostigmine, Neostigmine

Definition of Adrenergic agents :- These are the drugs that produce effects which are similar to the responses from stimulation of adrenergic nerves.

OR

The adrenergic drugs mimic the effects of sympathetic nervous stimulation of organs and structures that contain the adrenergic receptor.

⇒ These are also called as adrenomimetics, sympathomimetic, adrenergic stimulants.

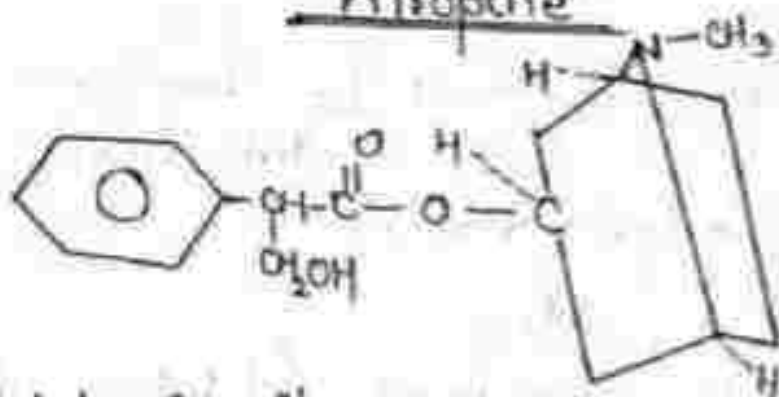
Ex: Adrenaline, Ephedrine etc.

# Synthesis of the Drugs

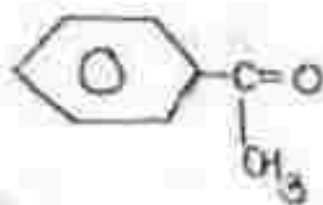
## Anticholinergic Drugs:

### Atropine

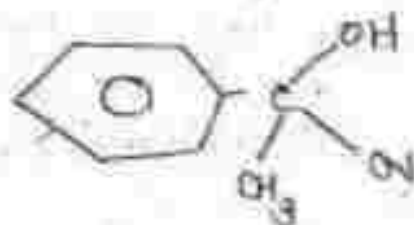
### I Method



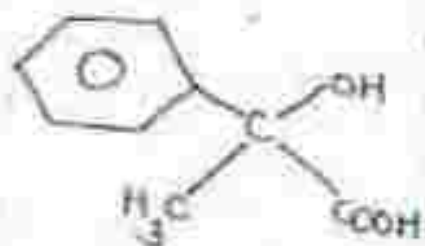
### 1. Synthesis of tropic acid:-



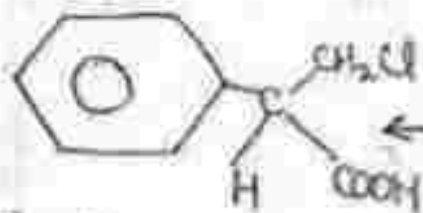
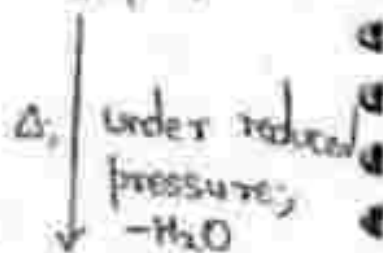
Methyl phenyl ketone



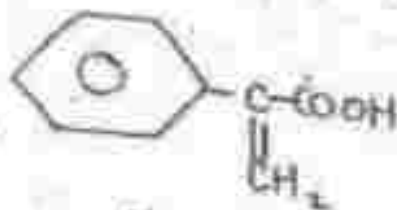
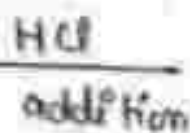
Methyl phenyl nitrile  
or nitrile



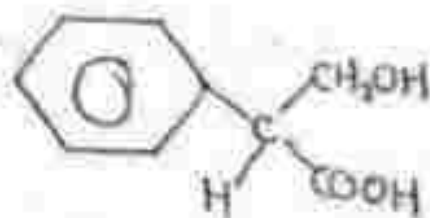
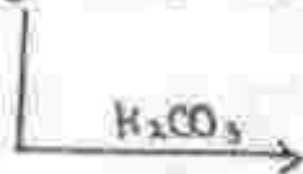
$\alpha$ -Hydroxy- $\alpha$ -phenyl propionic acid



$\alpha$ -chloromethyl- $\alpha$ -phenyl acetic acid

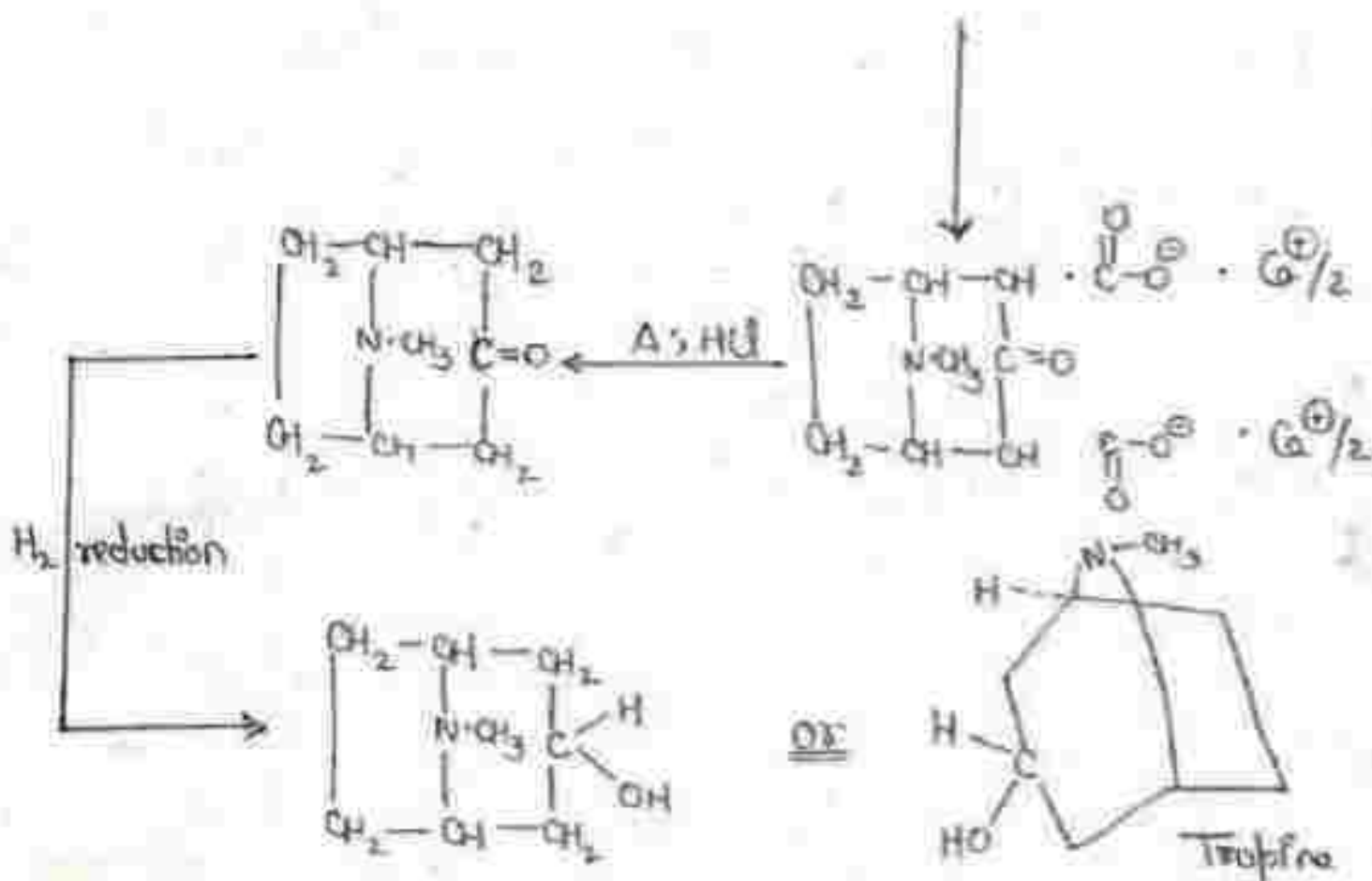
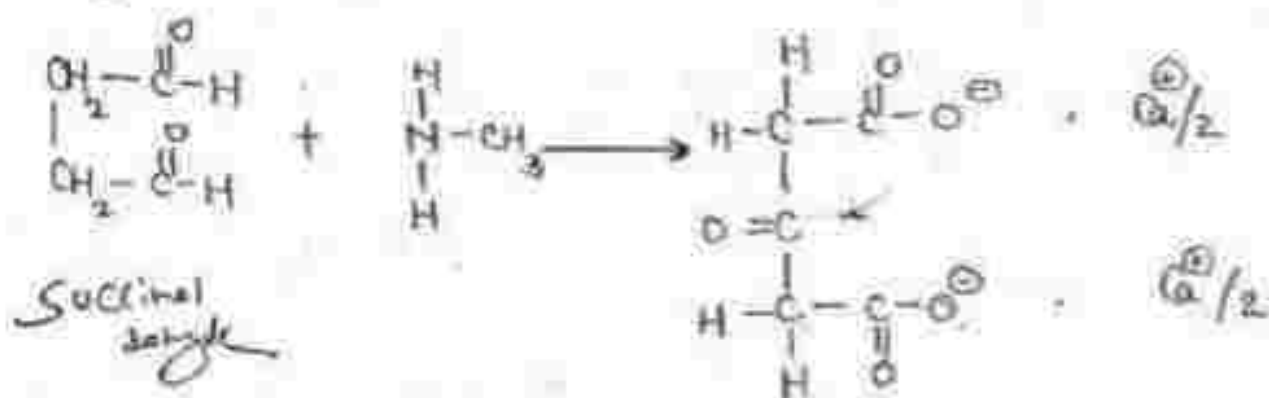


$\alpha$ -methylene- $\alpha$ -phenyl acetic acid

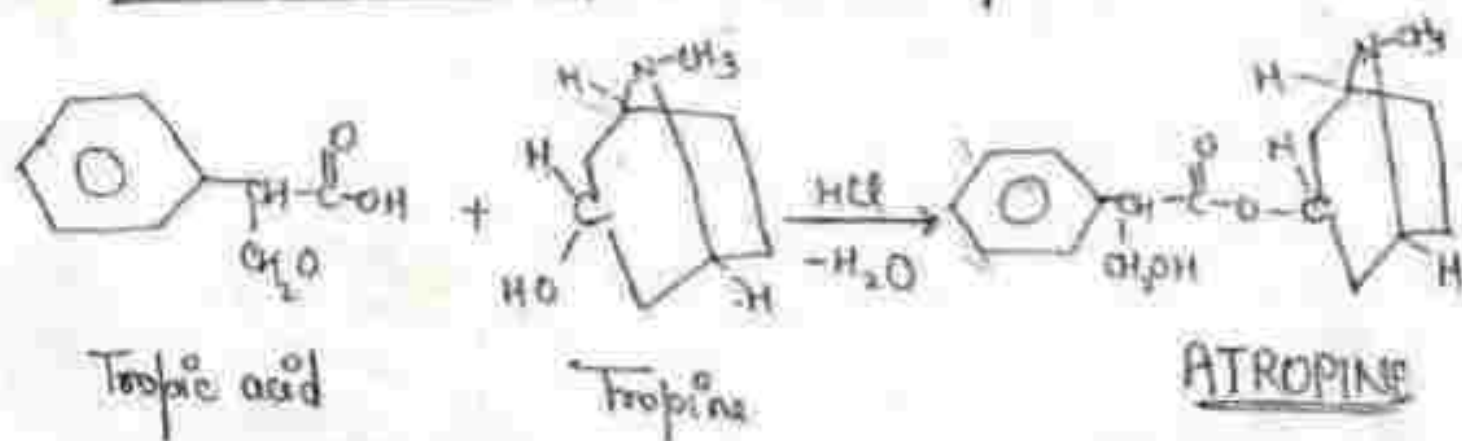


Tropic acid

## 2. Synthesis of Tropicine :-



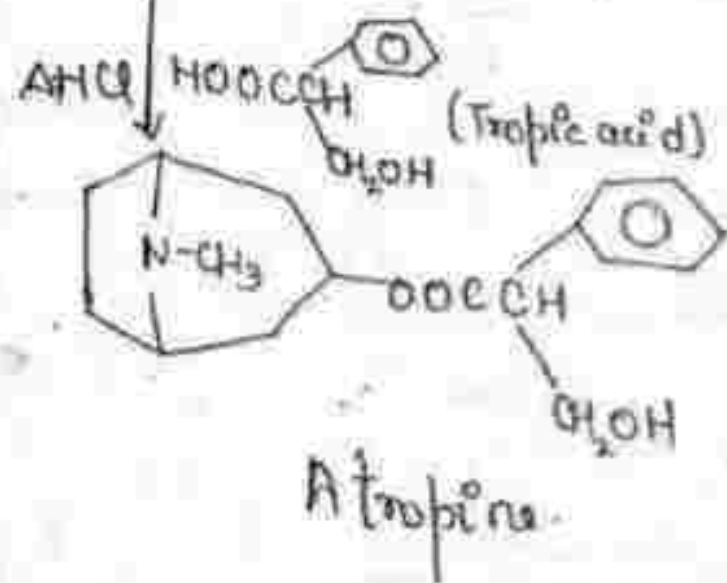
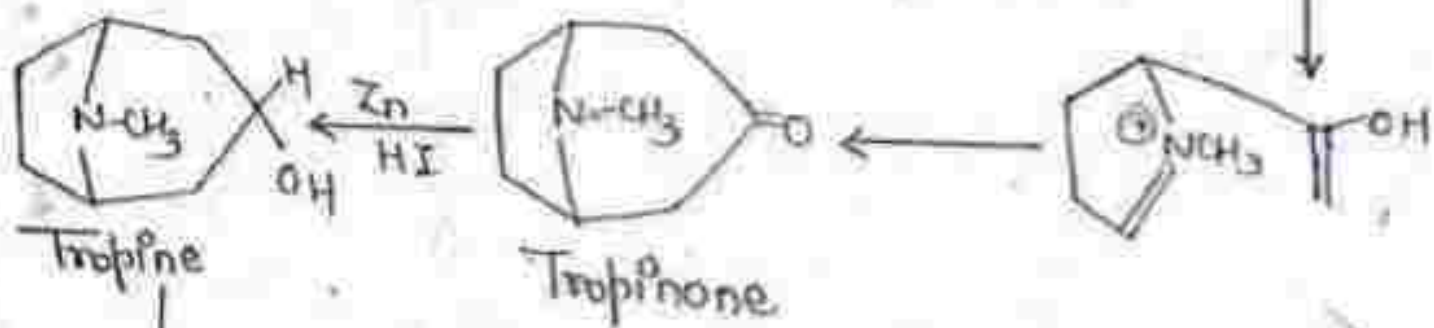
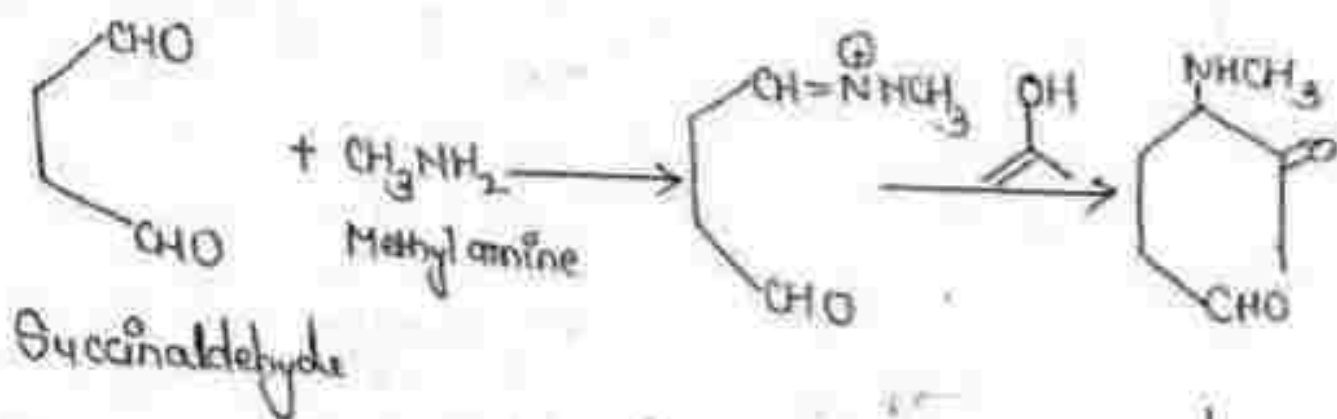
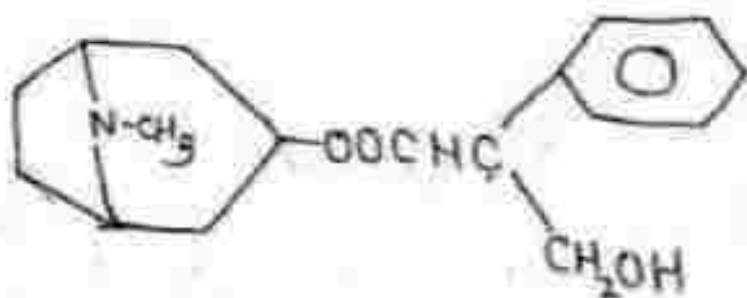
## iii - Condensation of Tropic acid & Tropicine :-



OR

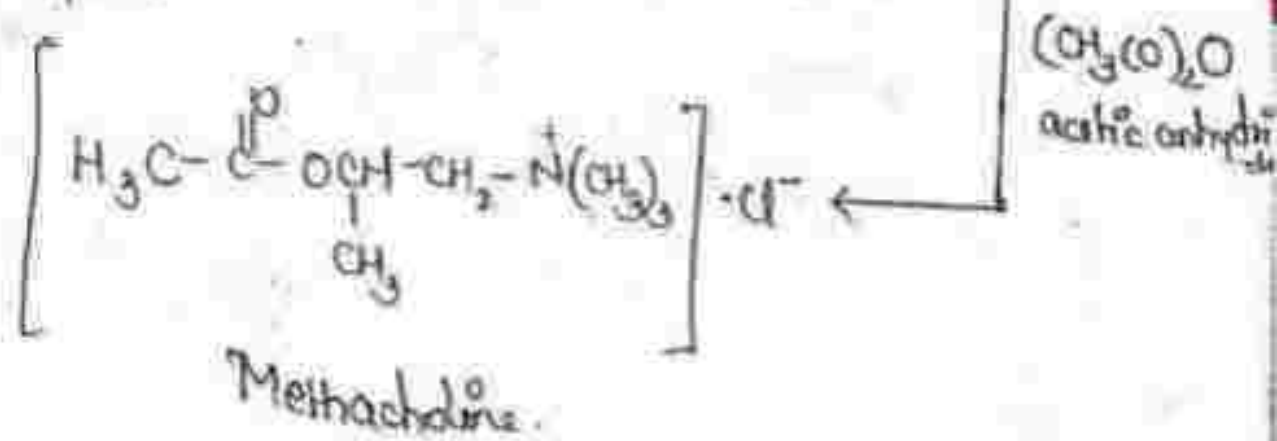
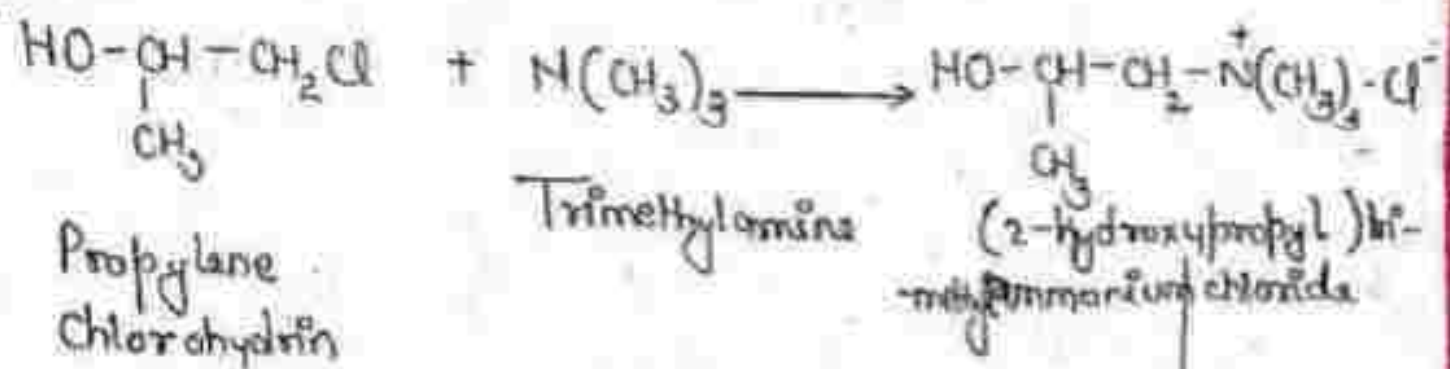
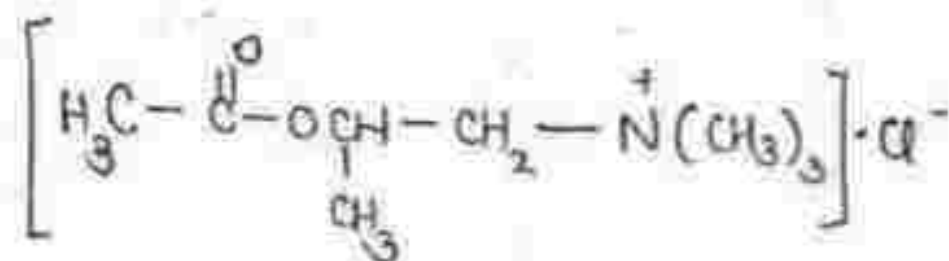
## II Method

### Atropine

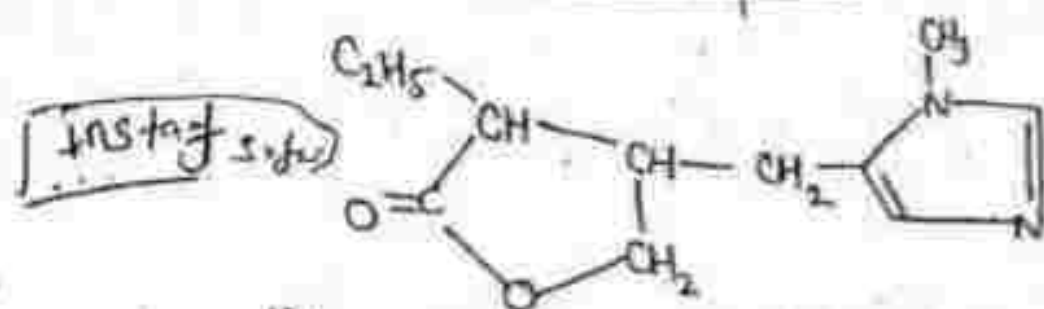


## Cholinergic Drugs:-

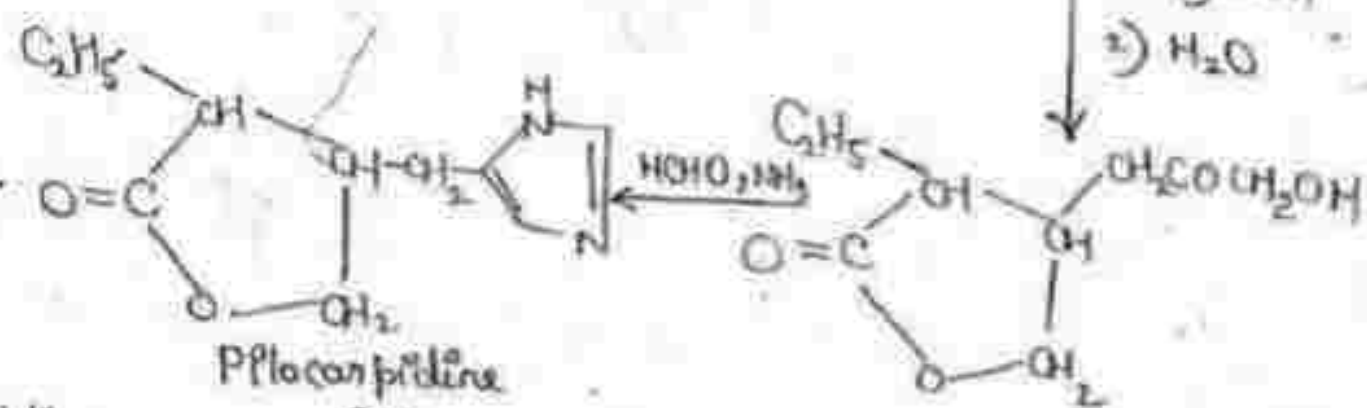
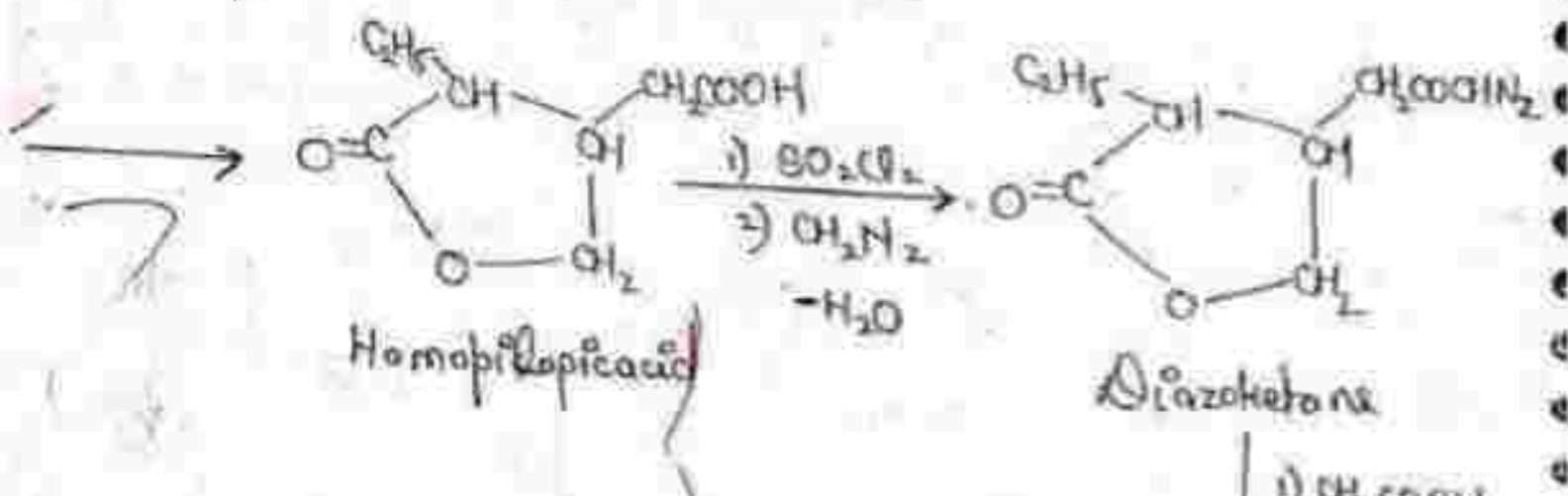
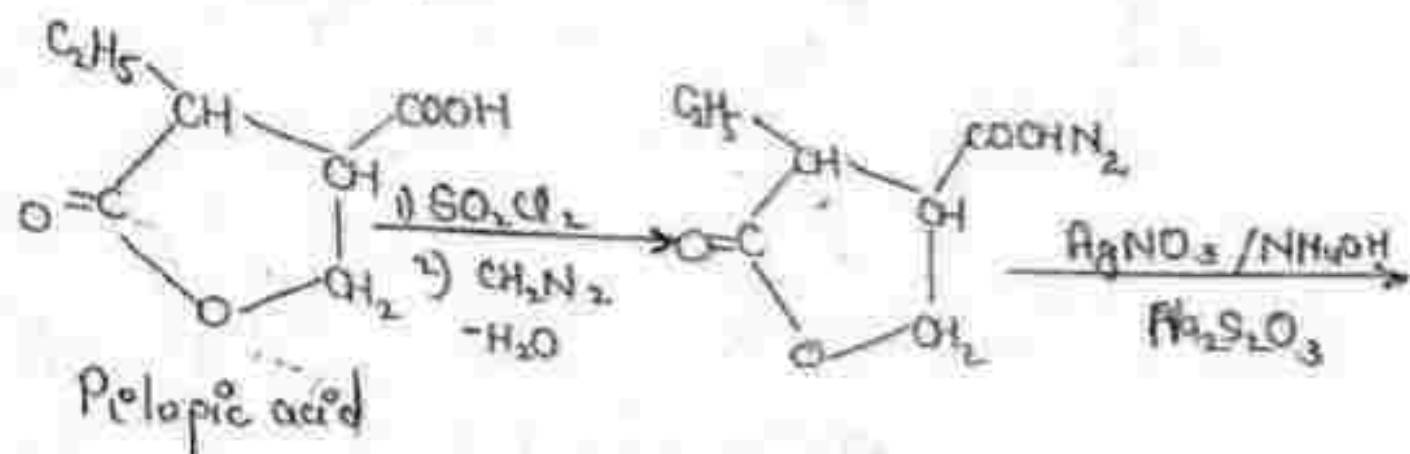
### Methacholine



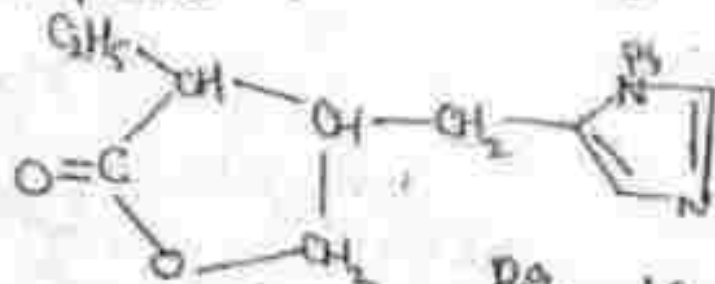
# Pilocarpine



17.

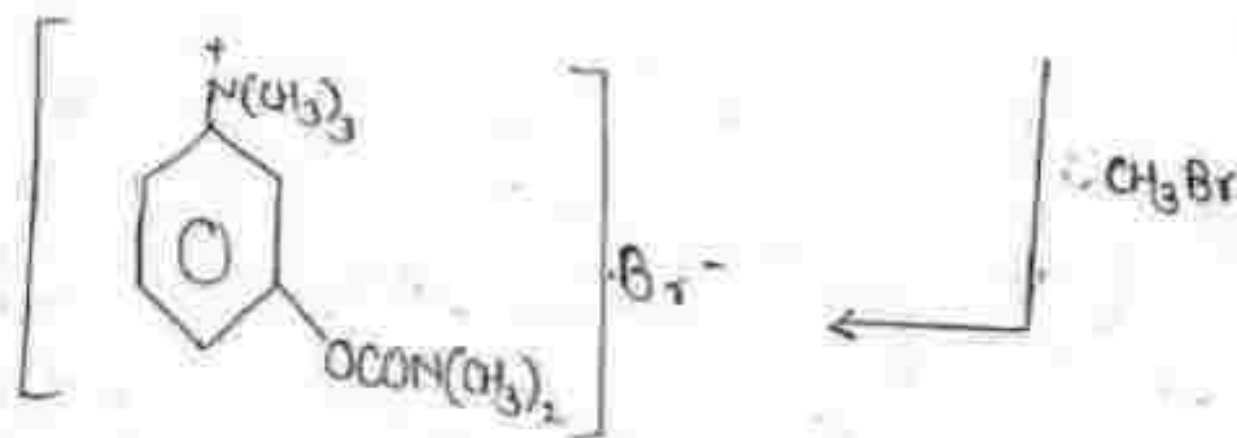
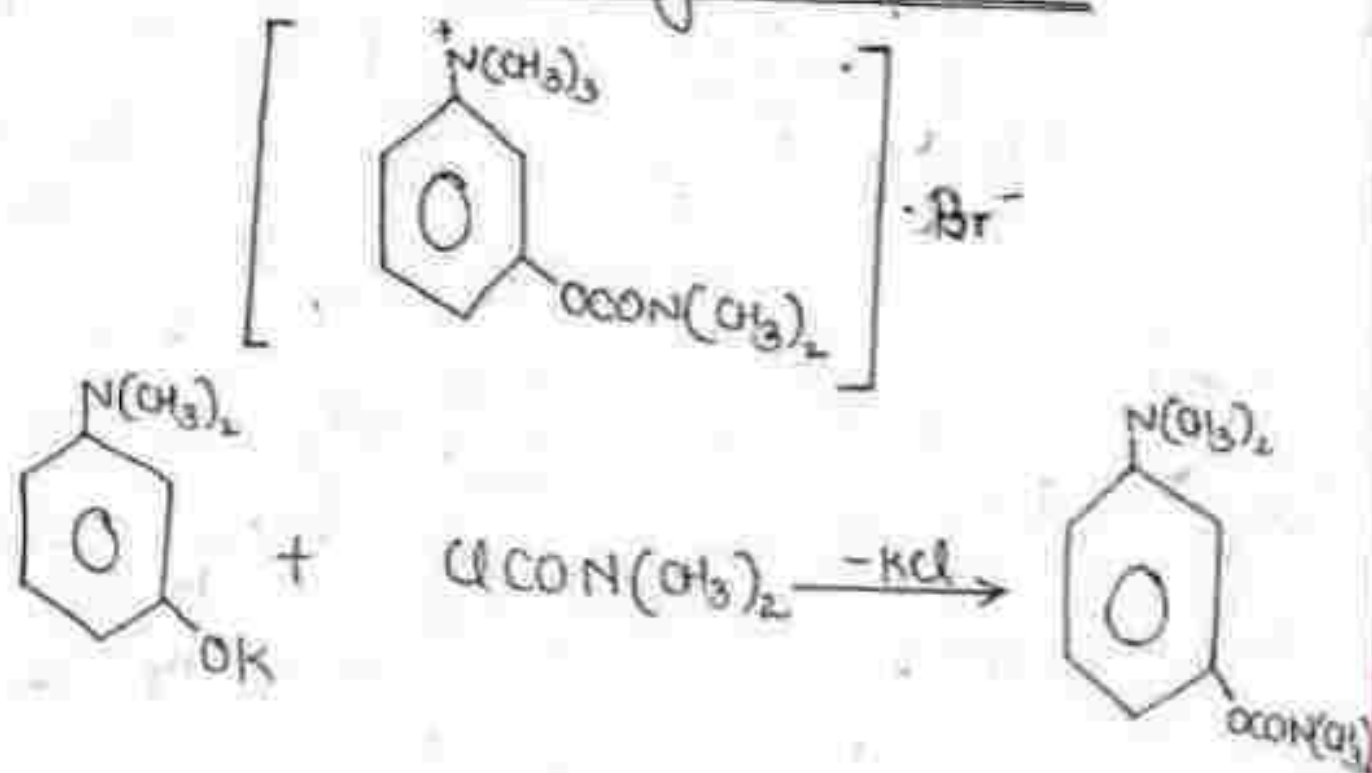


Methylation



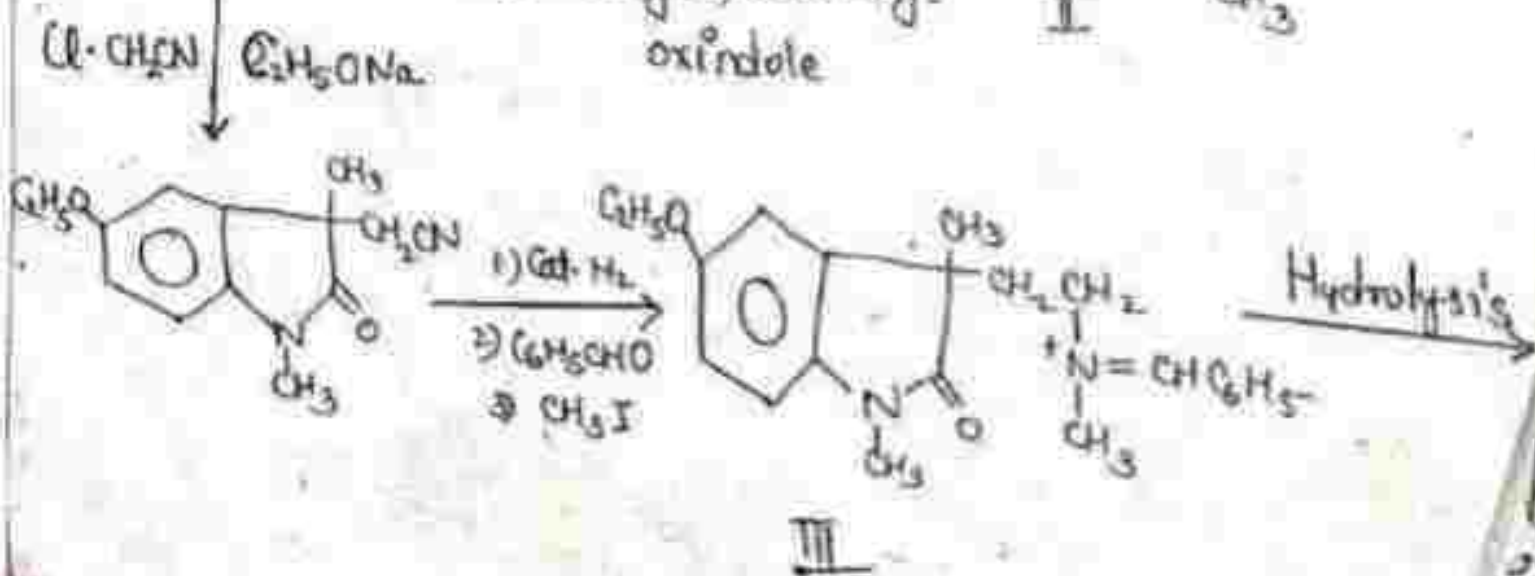
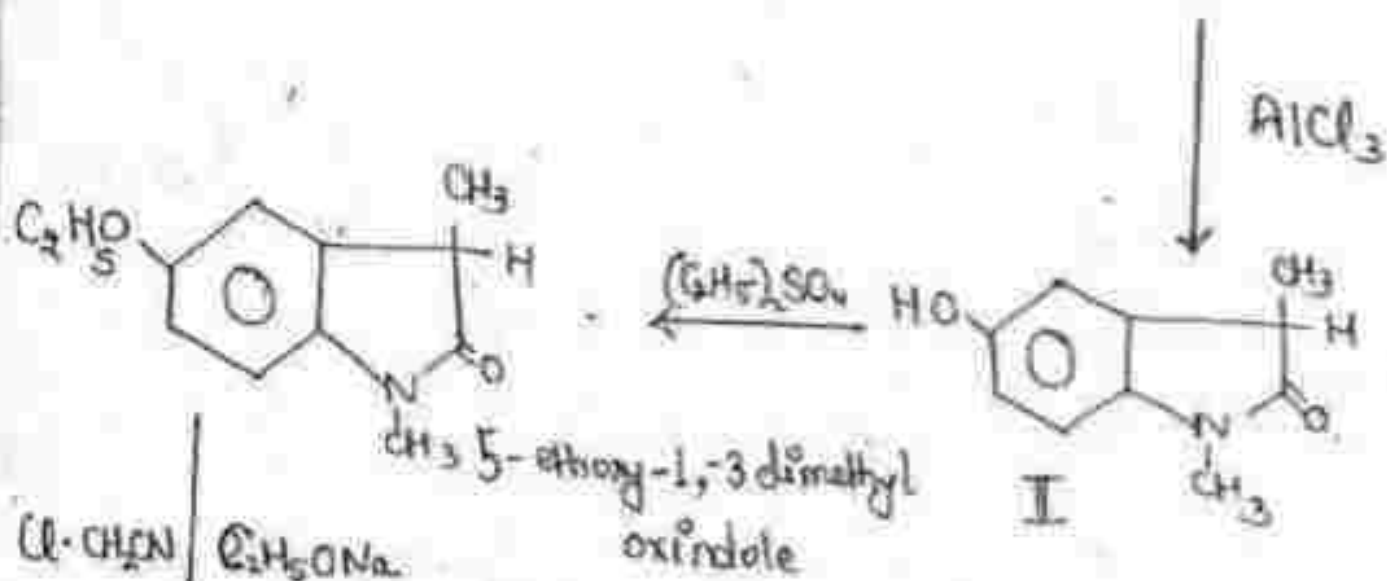
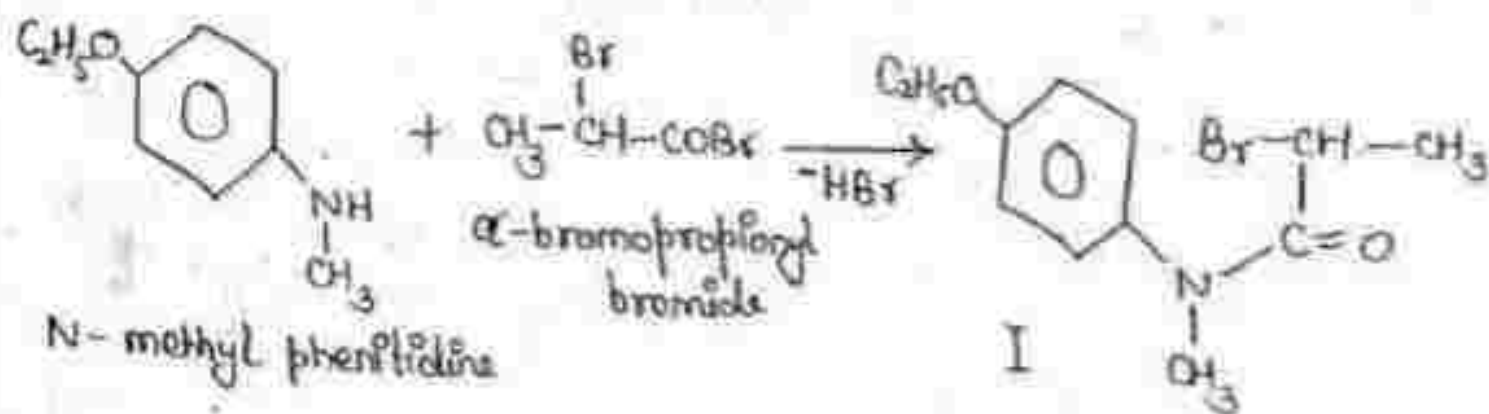
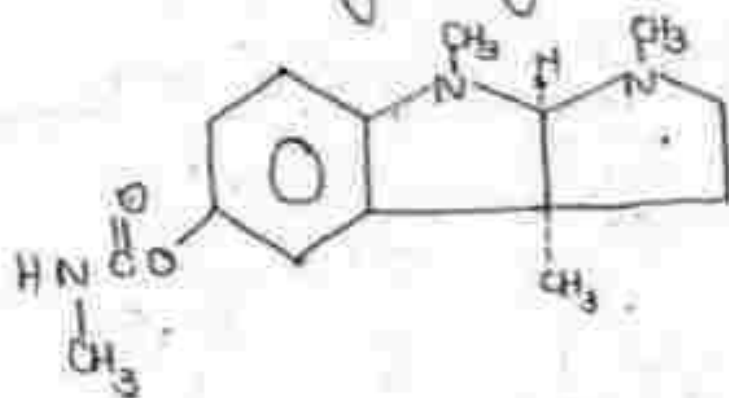
# Anticholinesterases

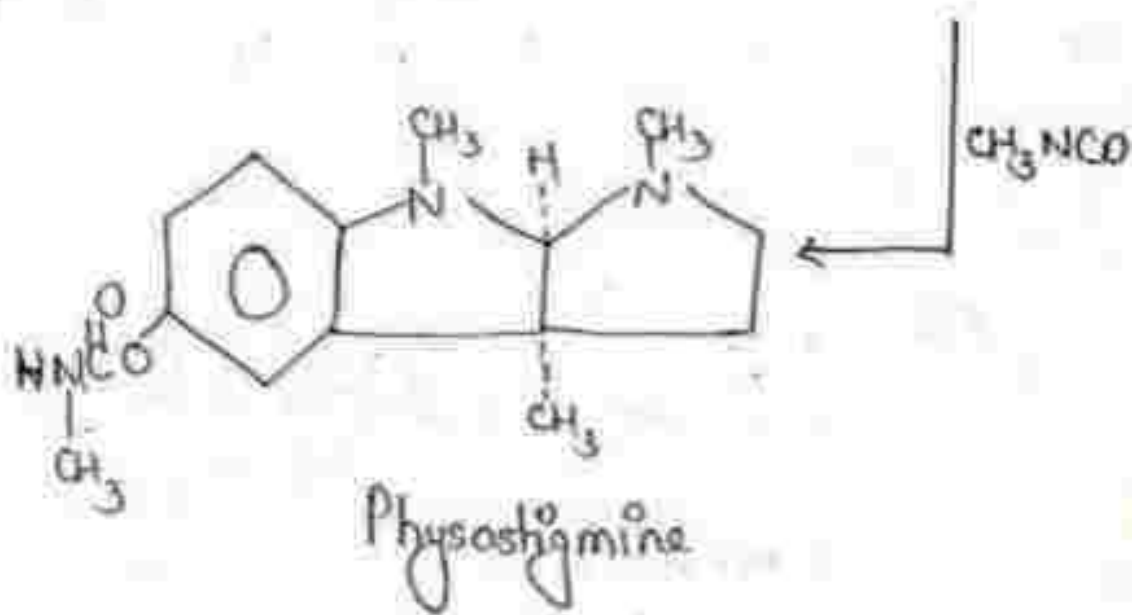
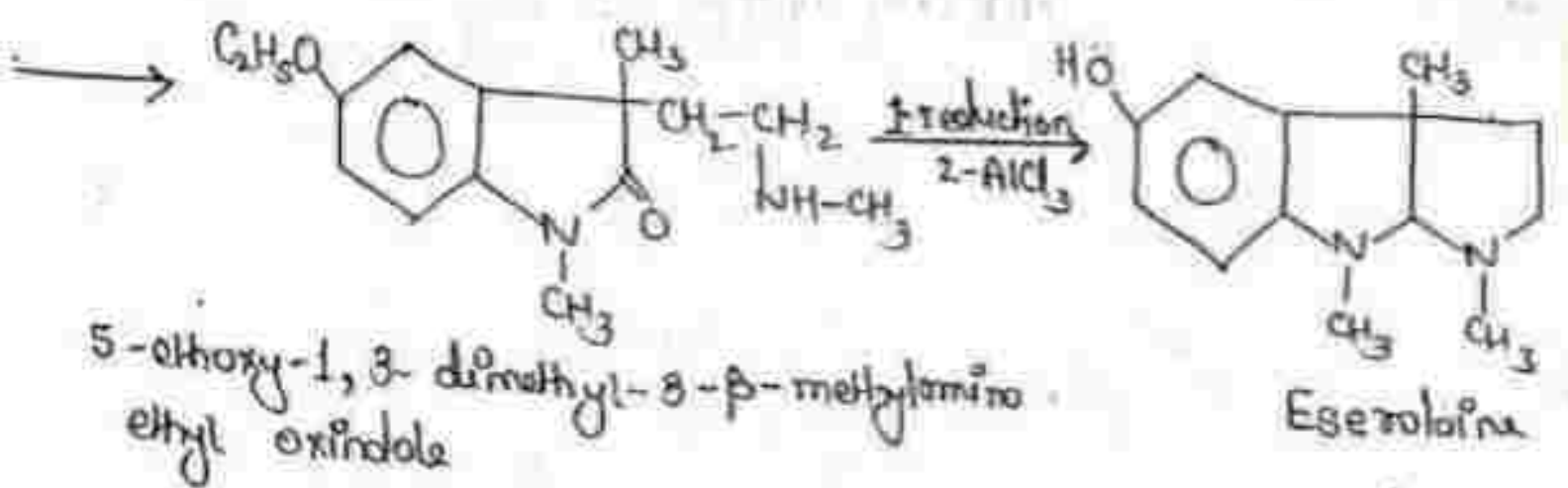
## Neostigmine Bromide



Neostigmine bromide

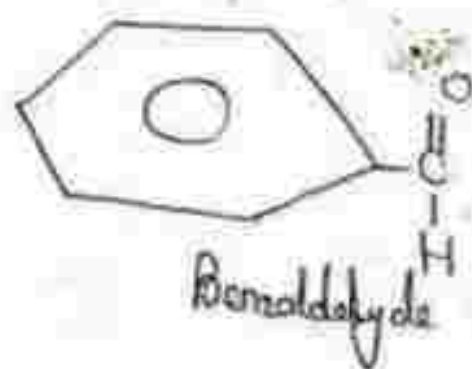
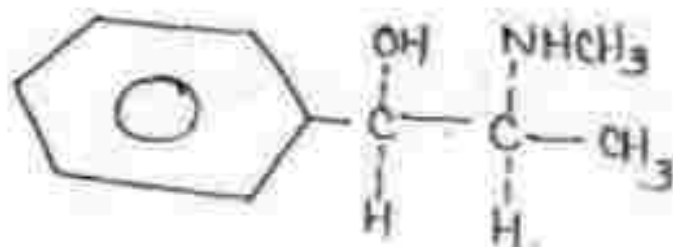
# Physostigmine



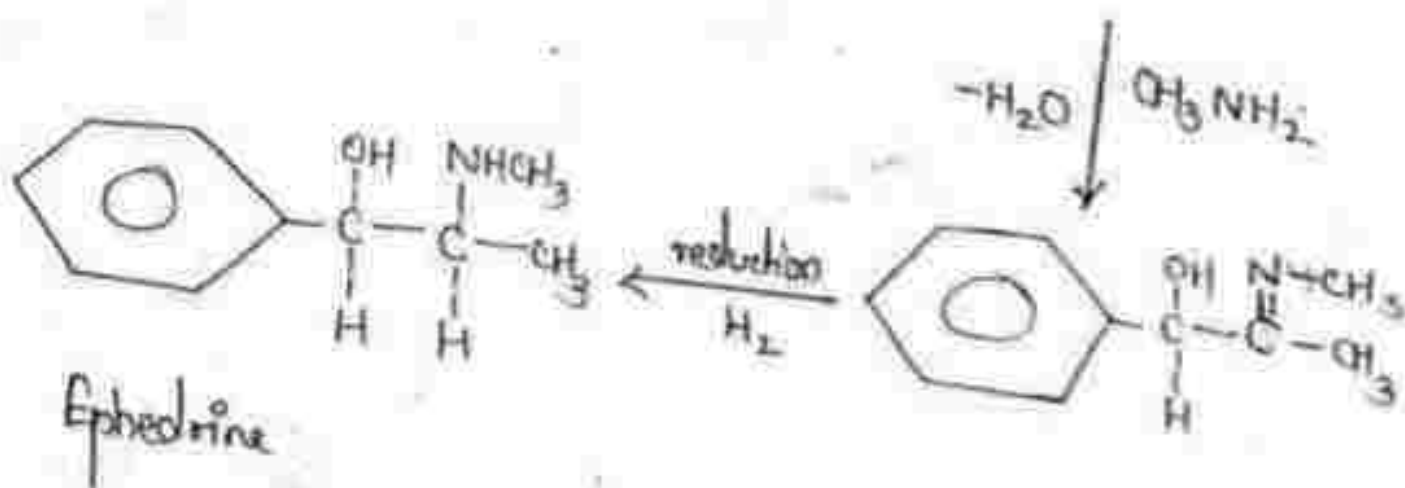
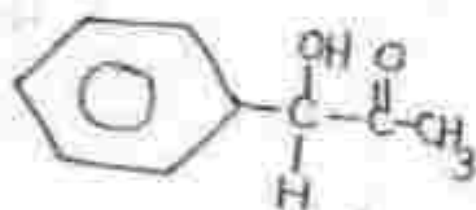


# Adrenergic Drug

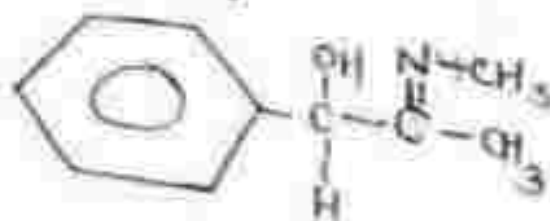
## Ephedrine



Fermentation  
Molasses

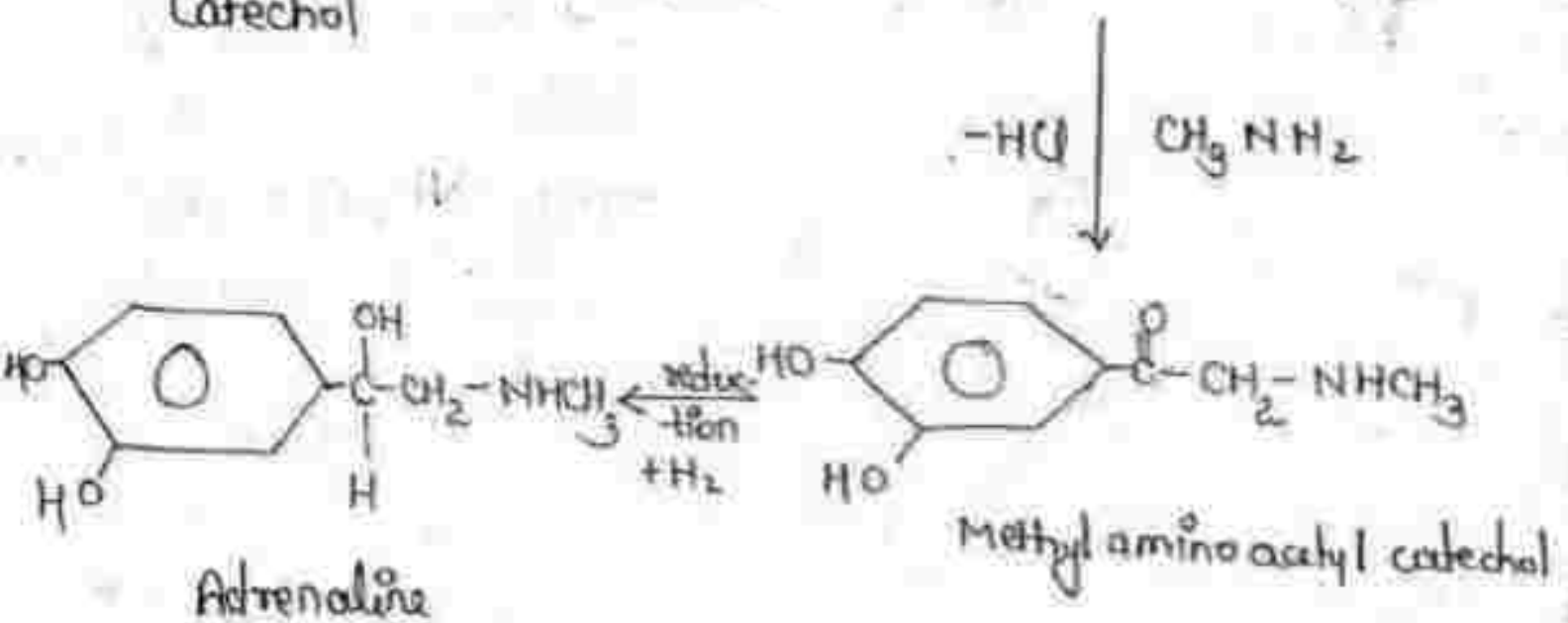
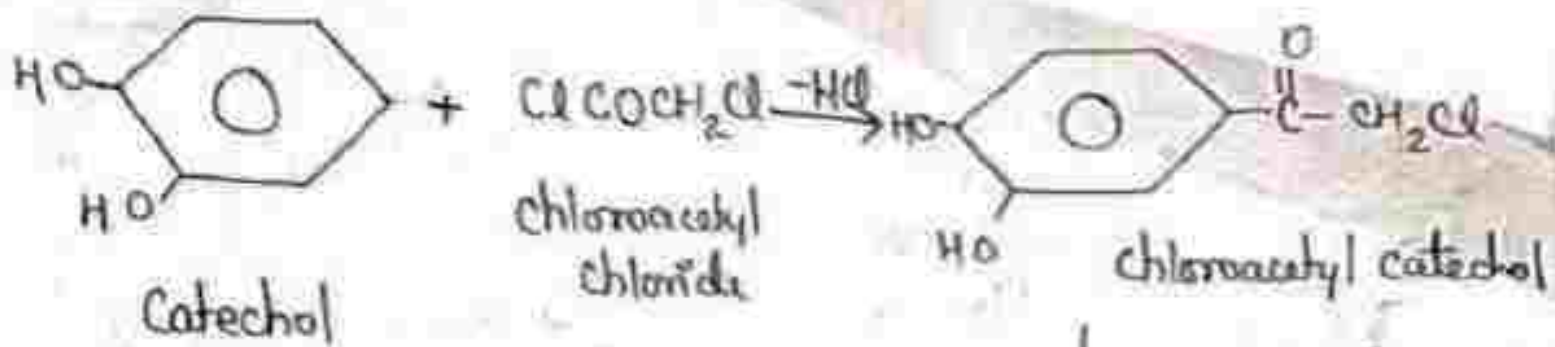
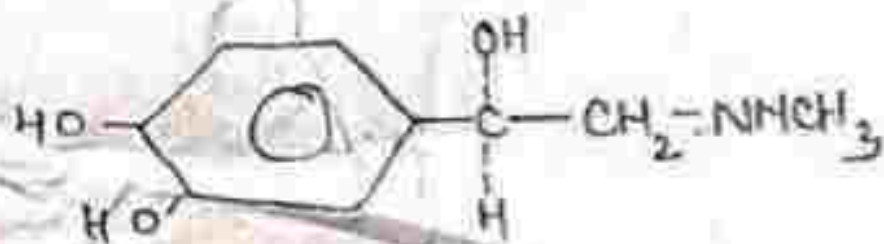


reduction  
H<sub>2</sub>

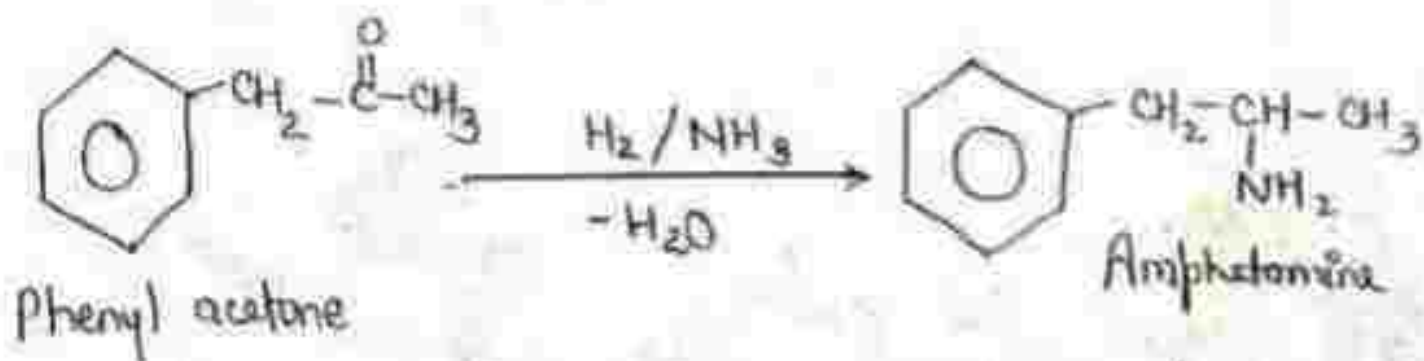
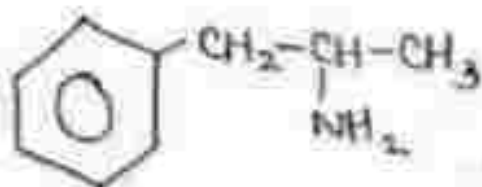


-H<sub>2</sub>O / CH<sub>3</sub>NH<sub>2</sub>

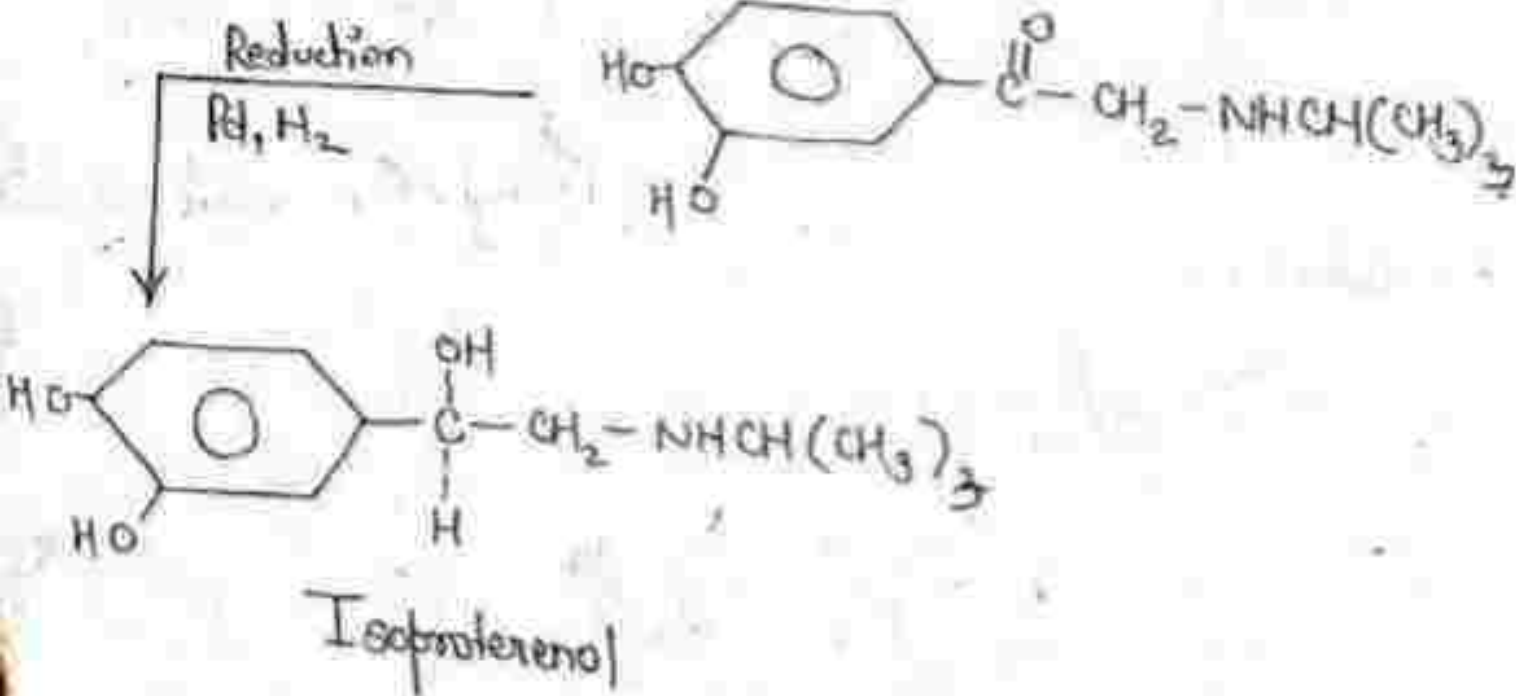
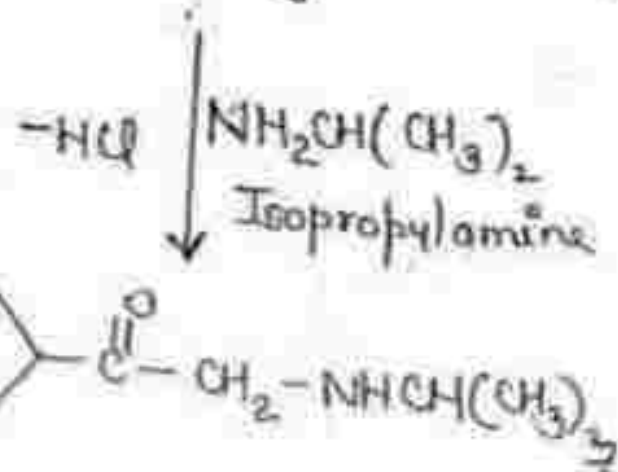
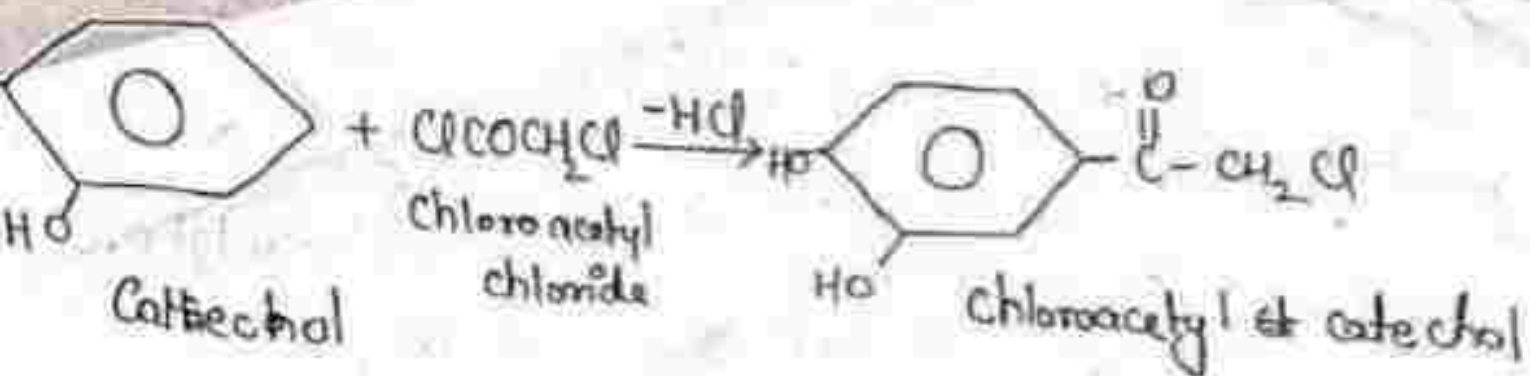
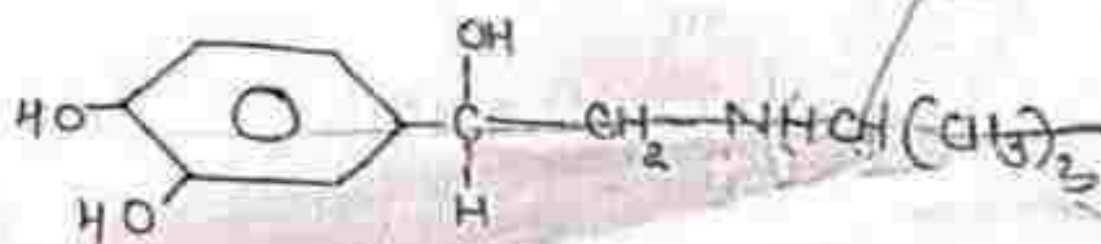
## Adrenaline



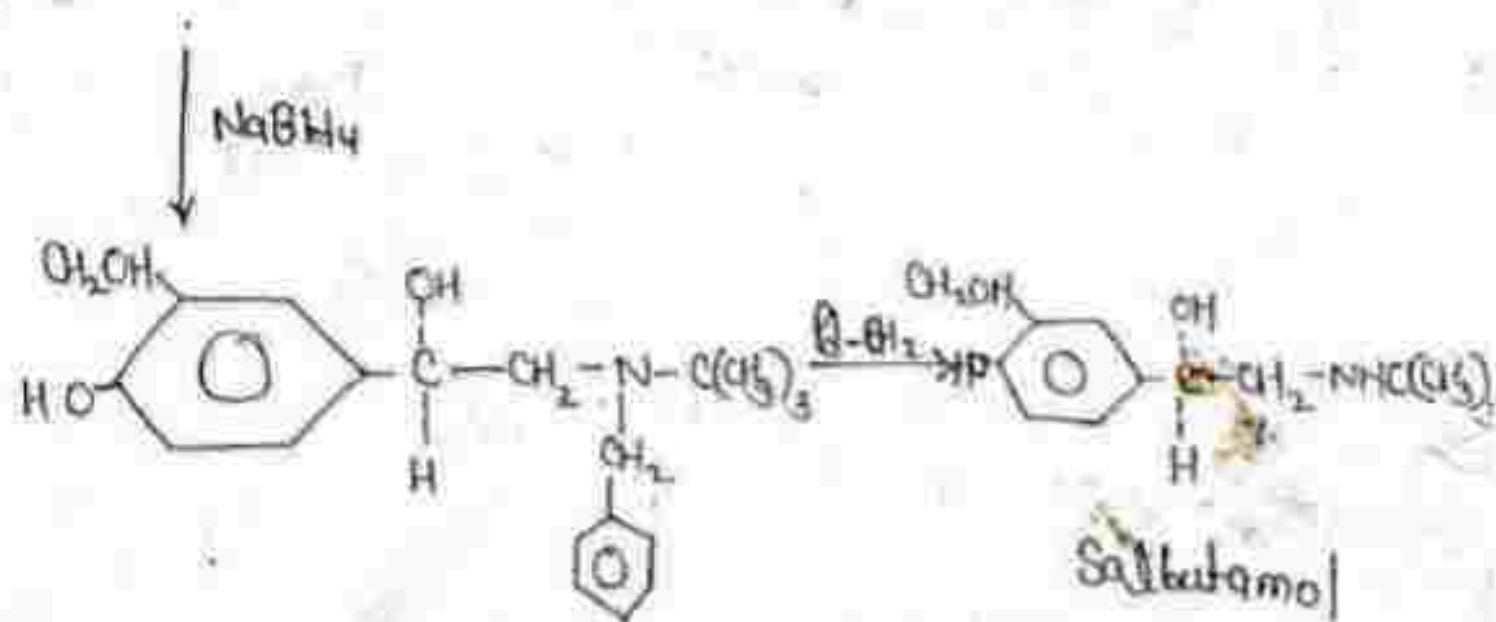
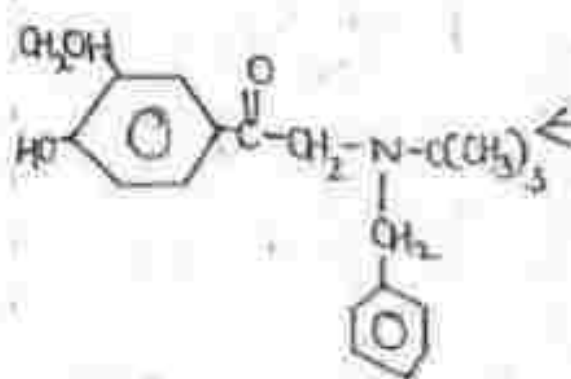
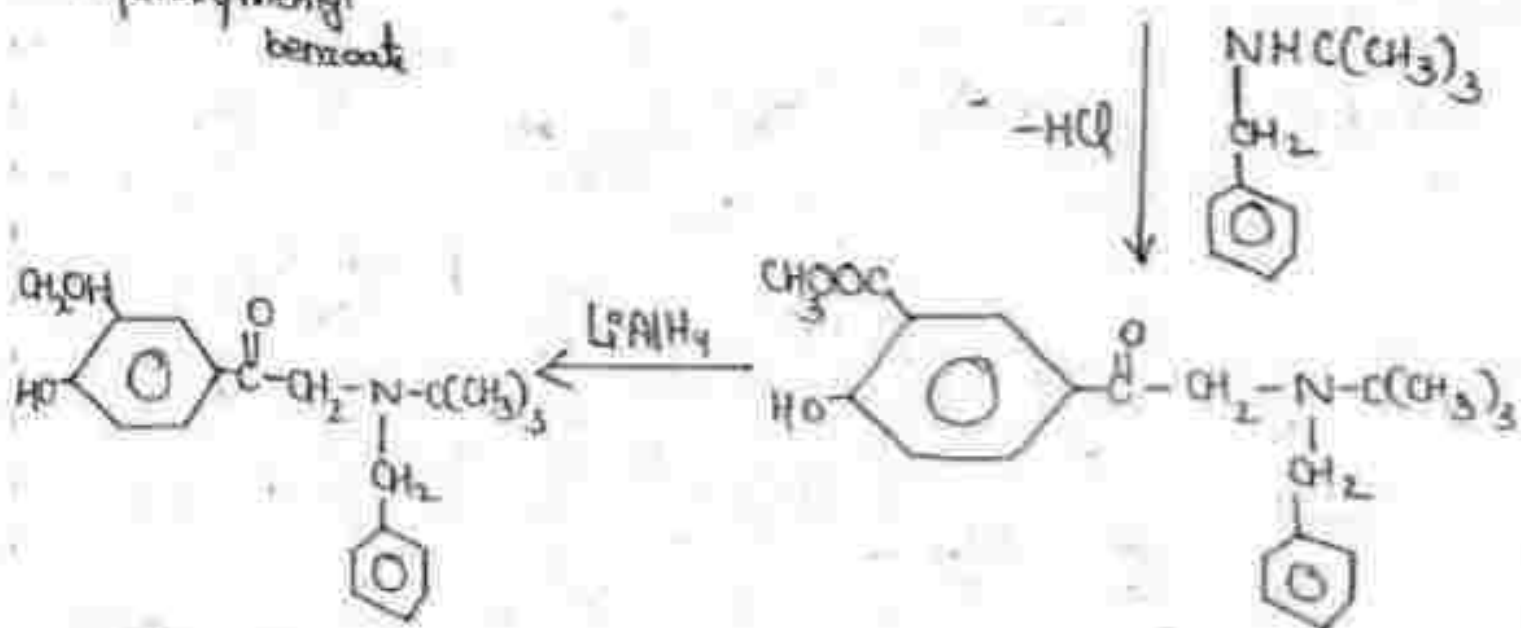
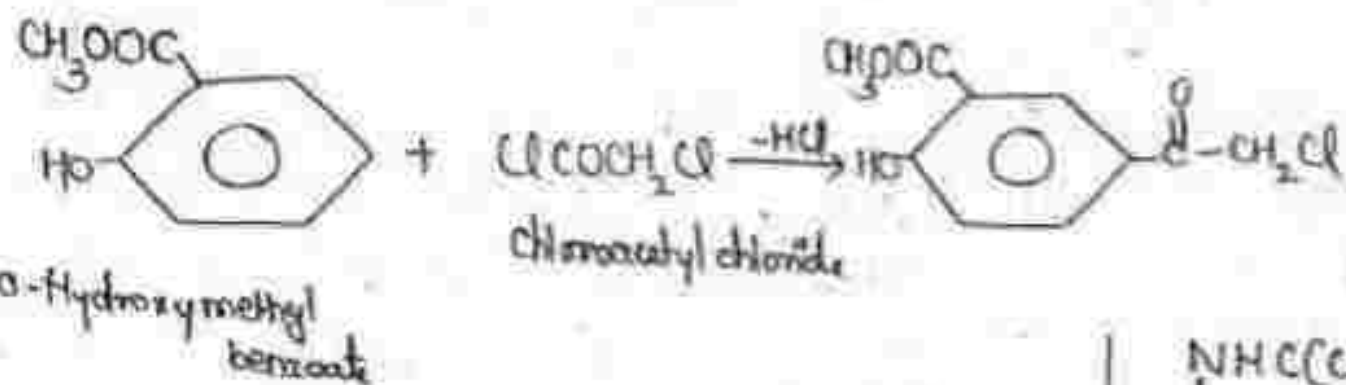
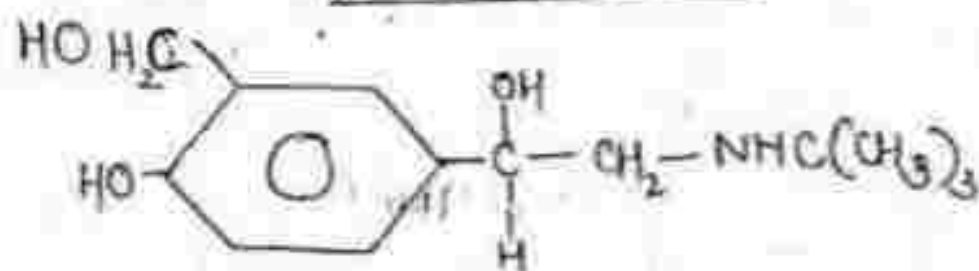
## Amphetamine



# Isoproterenol

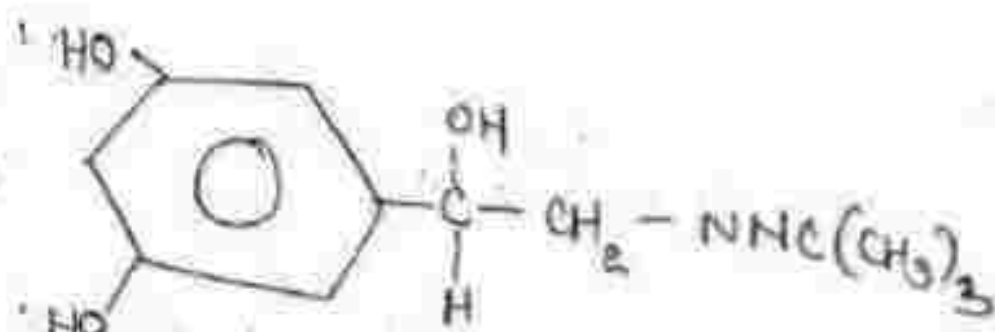
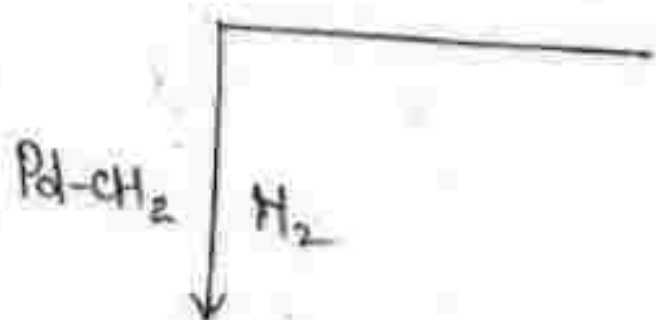
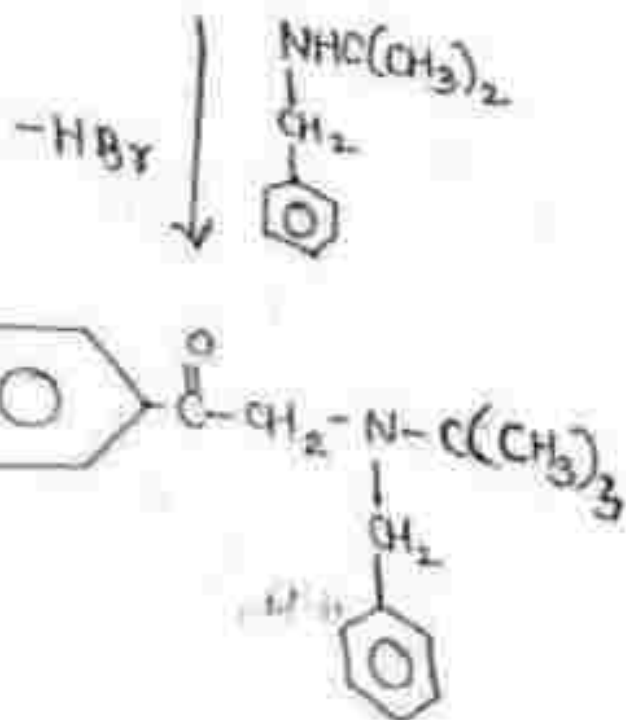
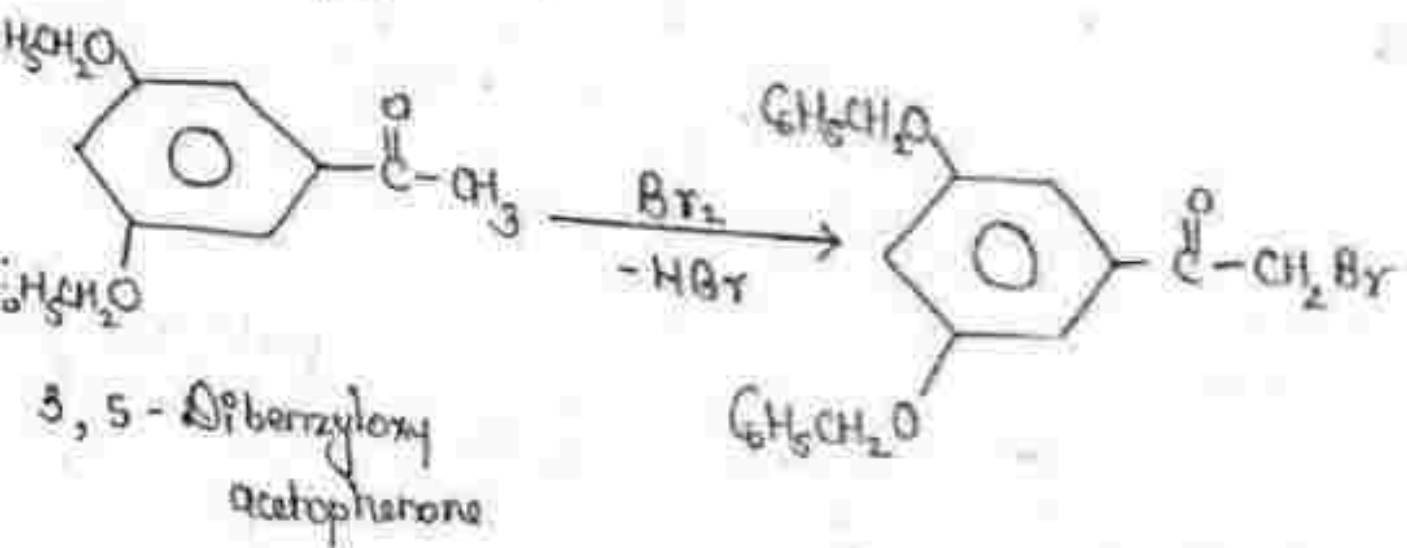
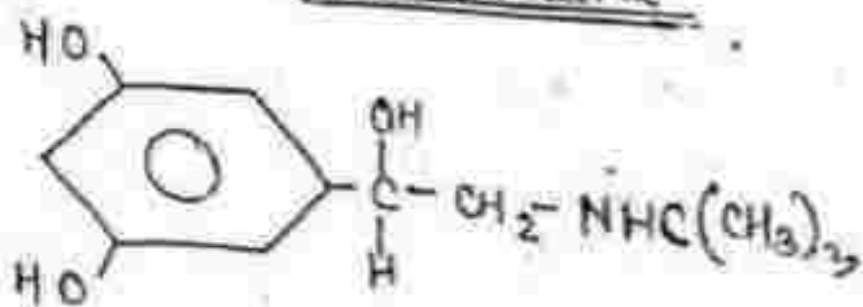


# Salbutamol



Salbutamol

# Terbutaline



Terbutaline

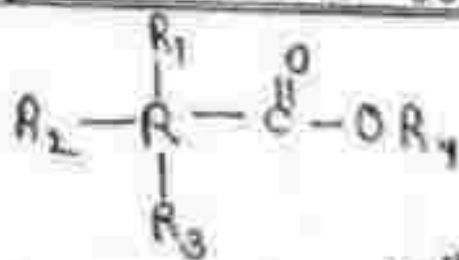
# Classification of Anticholinergic Drugs:-

## Anticholinergic Drugs

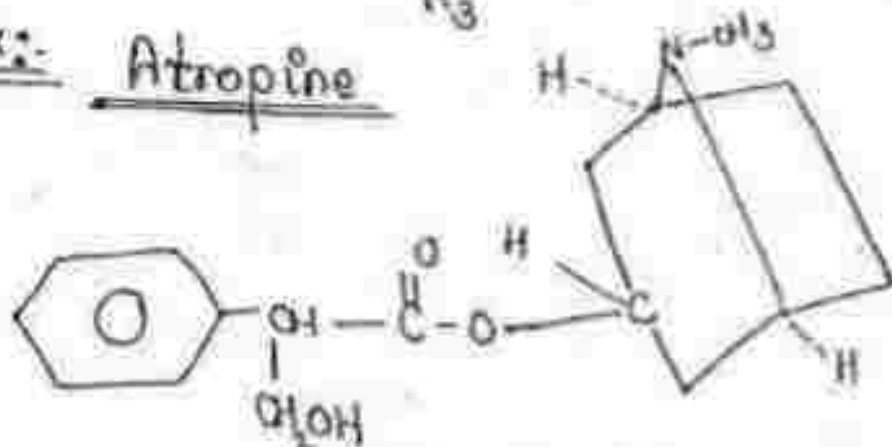
They may be classified on the basis of their chemical structures under the following heads:-

- i- Aminoalcohol Esters
- ii- Aminoalcohol Ethers
- iii- Aminoalcohol Carbamates
- iv- Aminoalcohols
- v- Aminoamides
- vi- Diamines
- vii- Miscellaneous Amines

### i. - Aminoalcohol Esters



Ex:- Atropine

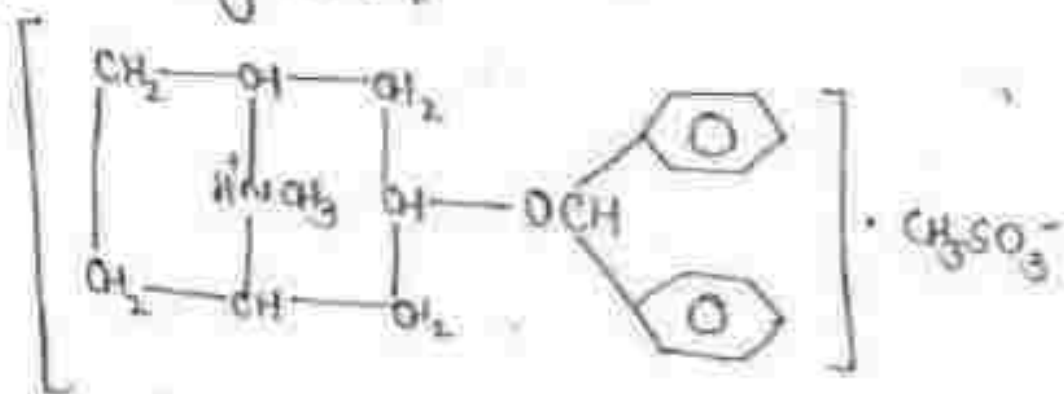


## ii- Aminoalcohol Ethers

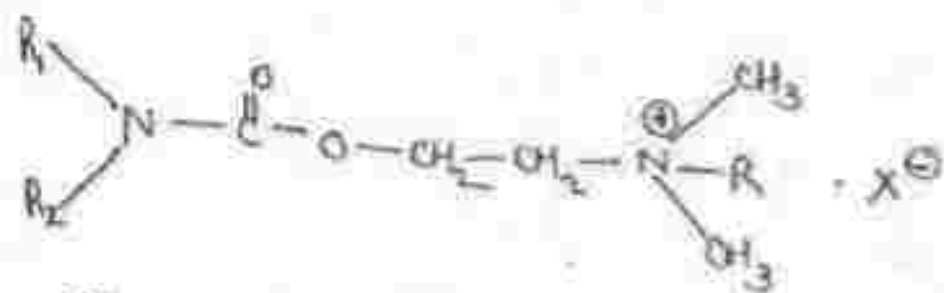
Aminoalcohol Ethers have been more widely employed as anti-parkinsonism agents rather than as usual anti-muscarinic drugs.

Ex: Benztropine mesylate, chlorphenoxamine hydrochloride, orphenadrine citrate.

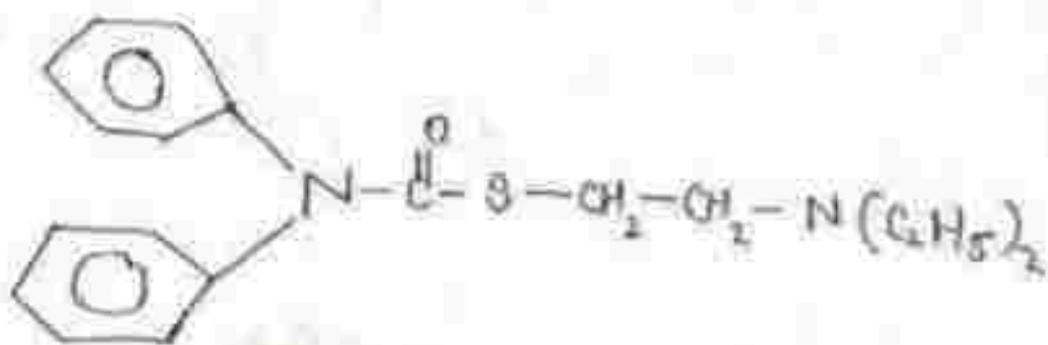
Benztropine mesylate :-



## iii- Aminoalcohol carbamates :-



Ex: Phencarbitamide :-

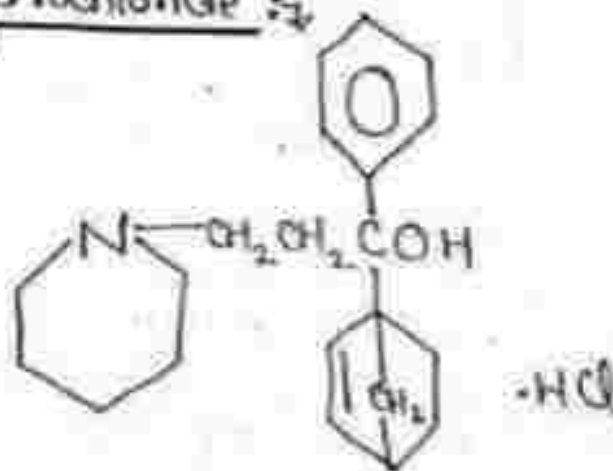


#### iv - Aminoalcohols

These compounds have gained their prominence as antiparkinsonism agents.

Ex: Biperiden hydrochloride, procyclidine hydrochloride etc.

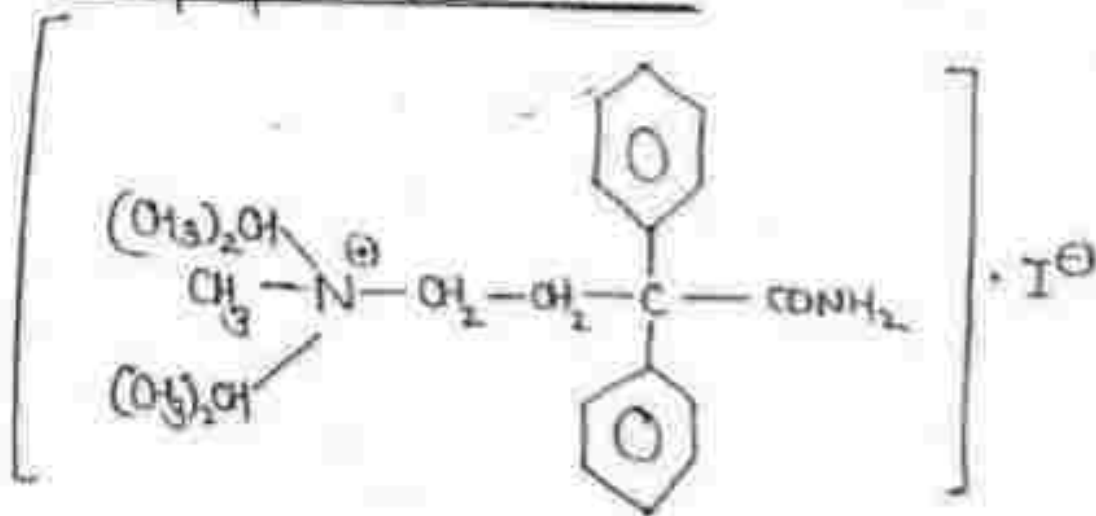
Biperiden Hydrochloride :-



#### v - Aminoamides

The aminoamides differs from their aminoalcohols whereby the polar hydroxyl group in the latter is replaced by the corresponding polar amide function.

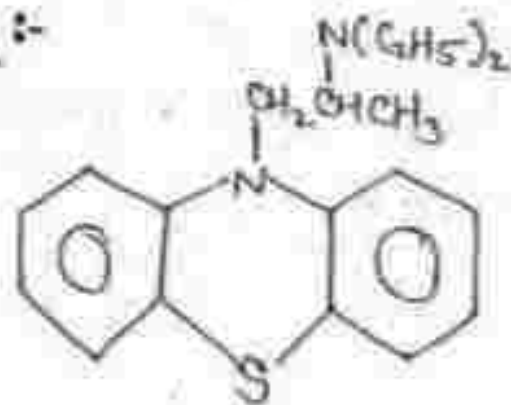
Ex:- Isopropamide Iodide.



## Vi- Diamines

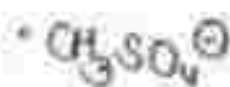
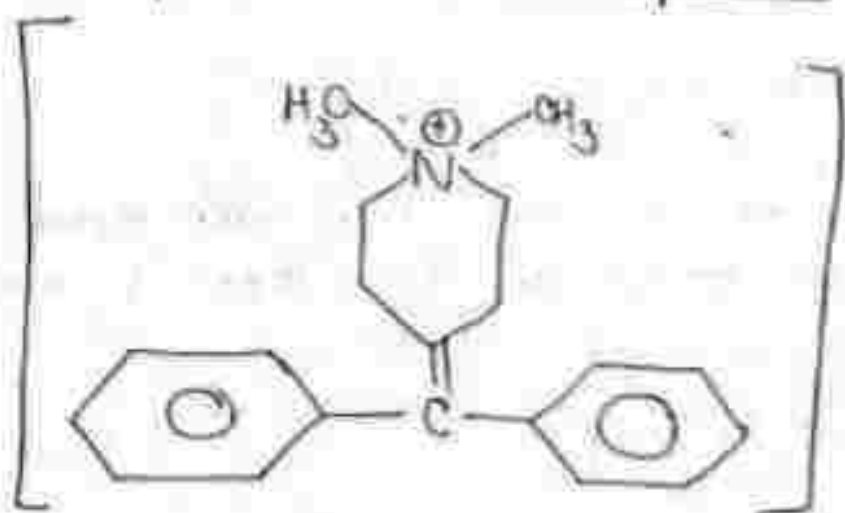
Ex:- Diathazine, ethopropazine hydrochloride::

Ethopropazine :-



## Vii- Miscellaneous Amine

Ex:- Diphenhydramethyl Methsulphate



# CLASSIFICATION OF CHOLINERGIC DRUGS

## Cholinergic Drugs

Acetylcholine and related choline esters

Cholinomimetic alkaloids

Acetylcholine

Metacholine

Carbamylcholine or carbaryl

Bethanechol

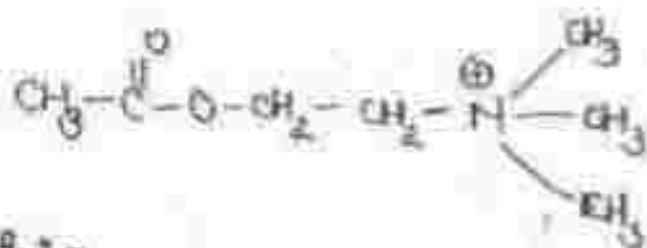
Atropine

Muscarine

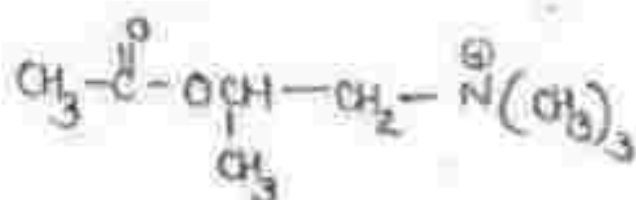
Arecholine

i) Acetylcholine & related choline esters:-

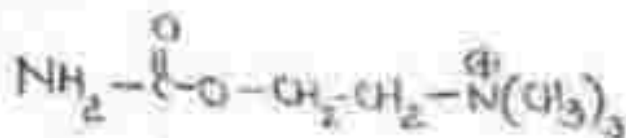
Ex: Acetylcholine :  $\rightarrow$



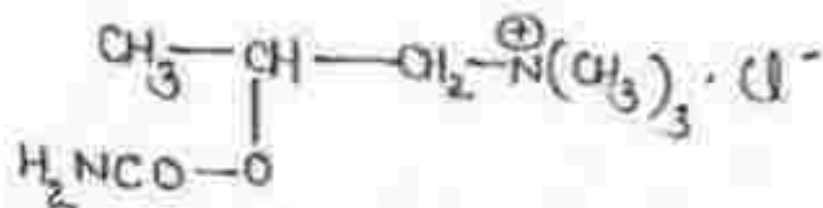
Metacholine :  $\rightarrow$



Carbamylcholine :  $\rightarrow$

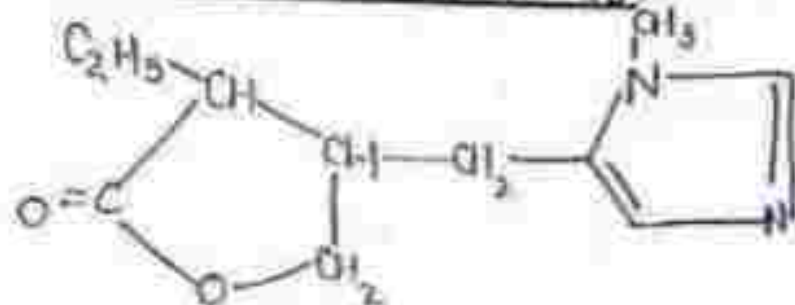


Bethane chol :-

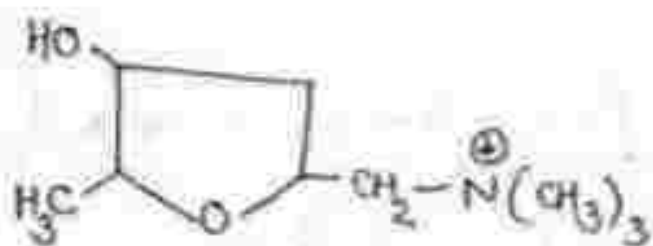


ii Cholinomimetic alkaloids

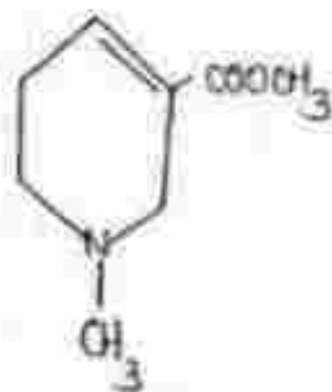
i- Pilocarpine :-



ii- Muscarine :-



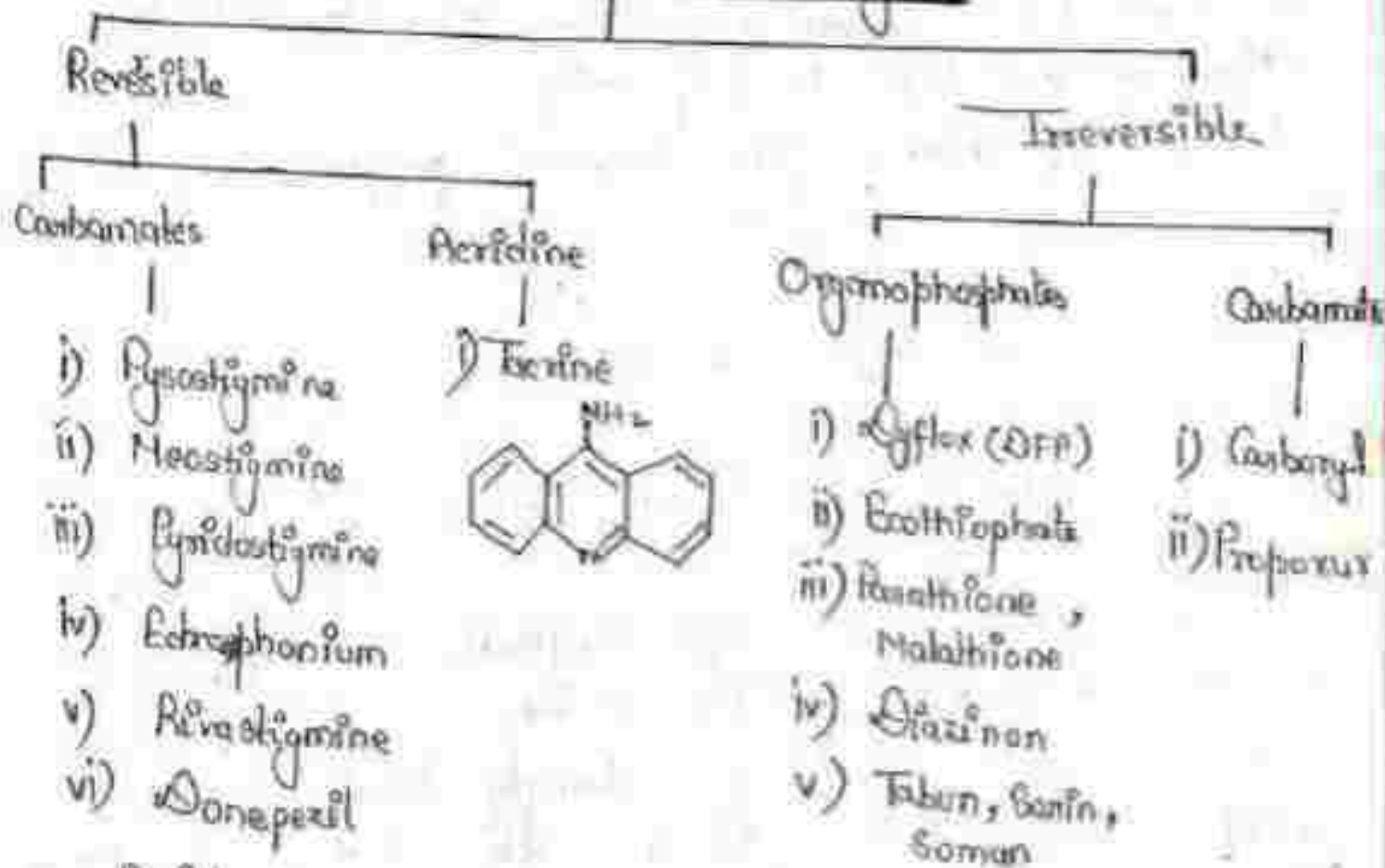
iii- Arecholine :-



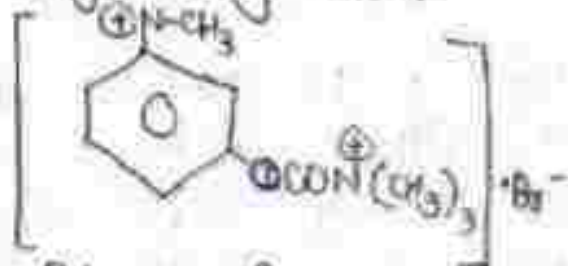
# CLASSIFICATION OF ANTICHOLINESTERASES

Anticholinesterase drugs fall into three main groups according to the nature of their interaction with the active site, which determine their duration of action.

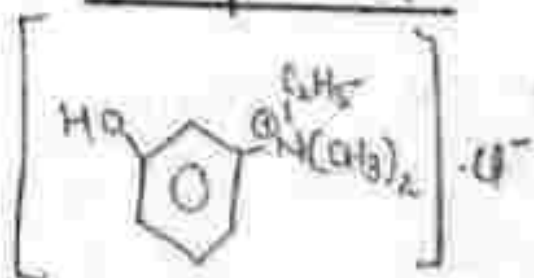
## Anticholinesterase Agents



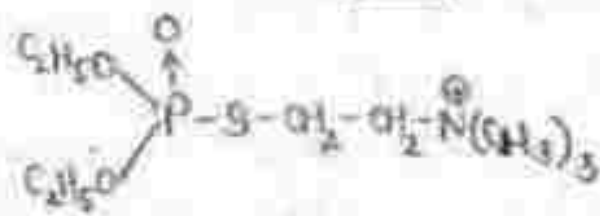
### Pyridostigmine



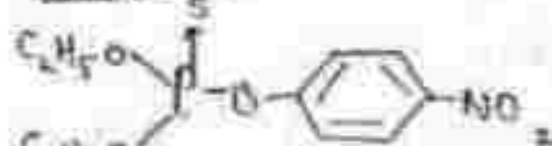
### Edrophonium



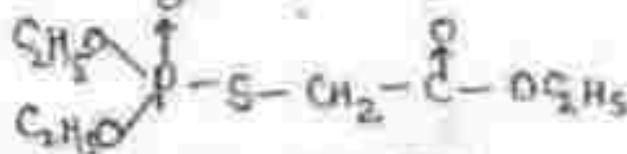
### Ecothiophate



### Parathion



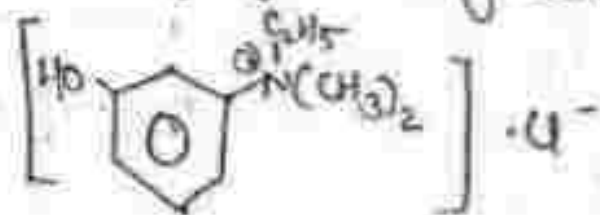
### Malathion



x Based on duration of action.

- 1) Short-acting anticholinesterases:- Edrophonium salts are quaternary ammonium compounds that bind to the anionic sites of the enzyme only.
- The ionic bond formed is readily reversible and the action of the drug is very brief.
- It is used mainly for diagnostic purposes.

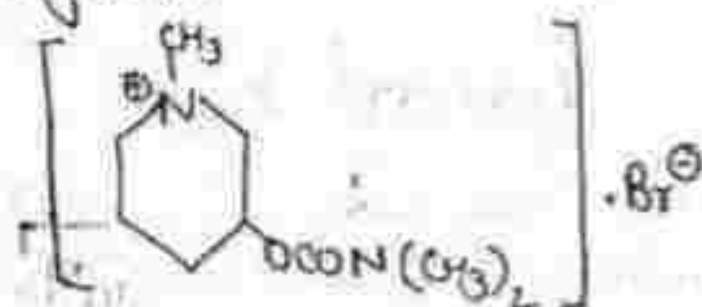
Ex:



- 2) Medium duration anticholinesterases:- Neostigmine, pyridostigmine, and physostigmine, which are quaternary ammonium compounds and a naturally occurring tertiary amine.
- These drugs all possess strongly basic groups, which bind to the anionic site, but are carbamyl, as opposed to acetyl esters.
- Transfer of the carbamyl group to the Serine-OH of the esteratic site occurs as with acetylcholine, but the carbamylated enzyme is very much slower to hydrolyse, taking min. rather than milliseconds.
- The slow recovery of the carbamylated enzyme means that the action of these drugs is quite long lasting.

Ex:-

Pyridostigmine:-



3- Irreversible anticholinesterases:

# Classification of Adrenergic drugs.

## Adrenergic drugs

Phenylethanolamine derivative

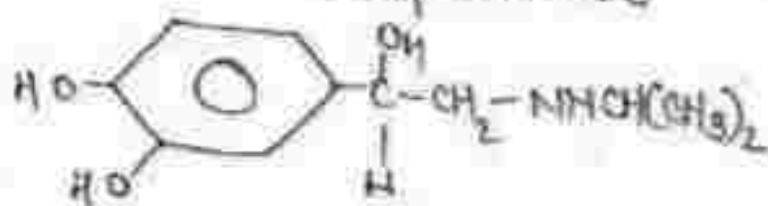
- Isoproterenol
- - Salbutamol
- Adrenaline
- Ephedrine

Imidazoline derivative

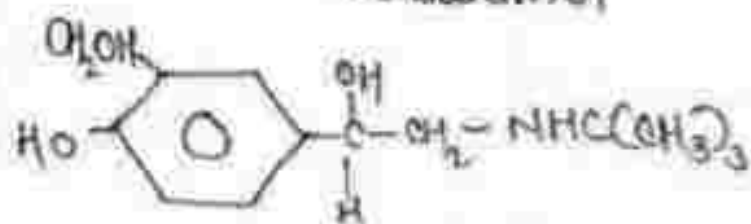
- Xylometazoline
- Oxymetazoline
- Naphazoline

## Structures:

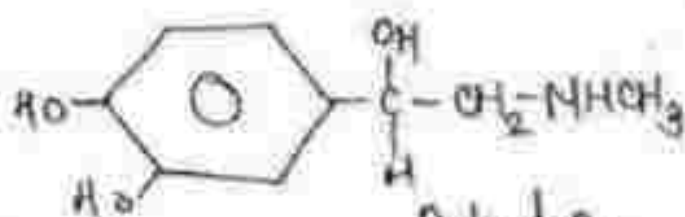
Isoproterenol



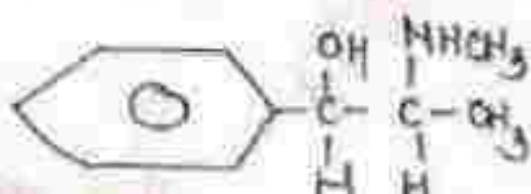
Salbutamol



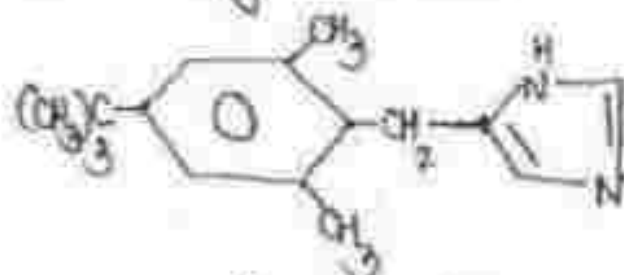
Adrenaline



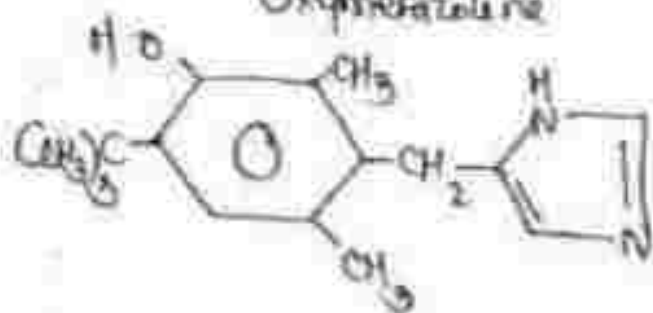
Ephedrine



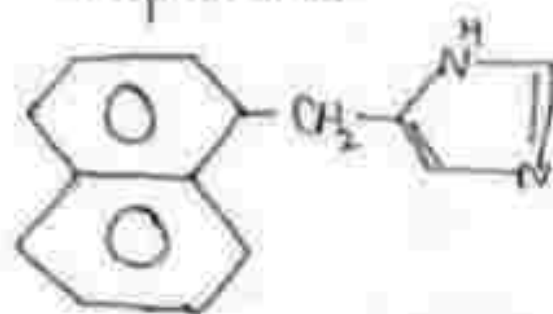
Xylometazoline



Oxymetazoline



Naphazoline



## Mode of Action

### Anticholinesterase

Neostigmine / Physostigmine.

↓  
Act on the AChE enzyme

↓  
Causes Reversible Inhibition of cholinesterase enzyme

↓  
Inhibits metabolism or hydrolysis of ACh

↓  
Accumulation of ACh at nerve ending causes response.

### Anticholinergic drug

Atropine

↓  
Act on muscarinic receptors

↓  
Competitively block the receptors

↓  
Prevents the access of ACh to the receptors

↓  
response.

Anticholinergic  
Adrenergic drugs

Ephedrine / Amphetamine

↓  
Act on adrenergic receptors

↓  
Stimulate the receptor

↓  
↑ release of nor-adrenaline  
to post synaptic  $\alpha$  &  $\beta$  receptors

↓  
response.

Adrenaline / Isoprenaline

↓  
Activate  $\beta_1$  &  $\beta_2$  receptors

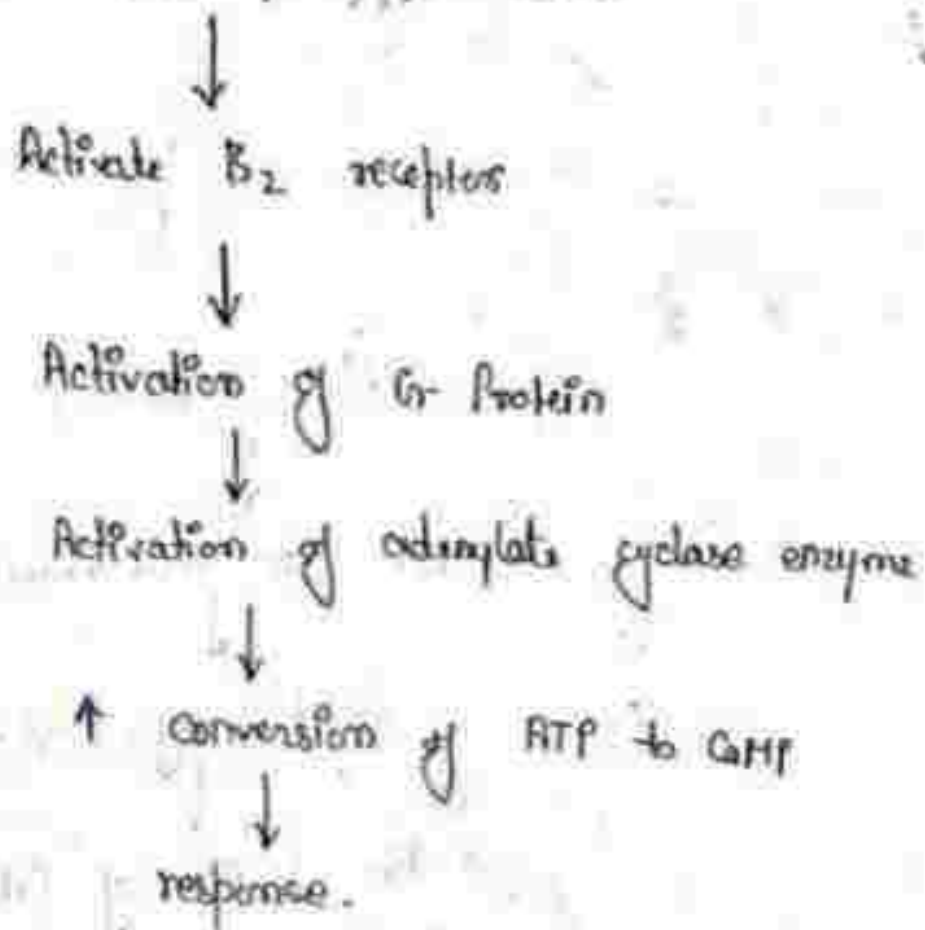
↓  
Activation of G-protein

↓  
Activation of adenylyl cyclase enzyme

↓  
↑ conversion of ATP to GMP

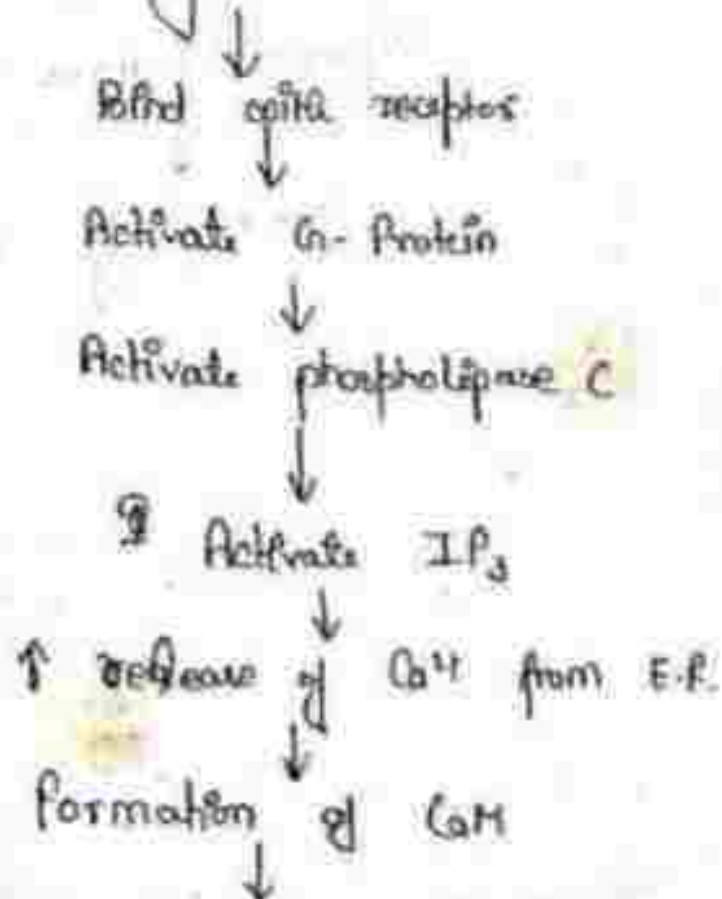
↓  
response.

## Salbutamol / Terbutaline



## Cholinergic drugs (ACh, neostigmine)

Agonist



↓  
Activate  $\text{Ca}^{2+}$  dependent protein  
kinase  
↓  
response.

① Pilocarpine

↓  
Acts on muscarinic receptors  $\text{M}_3$

↓  
Contraction of constrictor pupillae

↓  
The portion of iris occupying the  
iridocorneal angle is withdrawn

↓  
free flow & drainage of  
aqueous humour is restored

↓  
recovery of glaucoma.

# UNIT-VI

## Psychopharmacological Agents

Drugs  
System

acting on the Central Nervous

### General Definitions

**General anaesthetics :-** General anaesthetics are the CNS depressant drugs that induce the absence of perception of all sensation & loss of pain.

**Local anaesthetics :-** Local anaesthetics act by blocking both the sensory & motor nerve conduction to produce temporary loss of sensation to the restricted area of the body without a loss of consciousness.

**Sedatives :-** A sedative drug is a drug which decreases the activity and excitement of the patient and calm the anxiety by producing a mild depression of CNS, without causing unconsciousness or sleep.

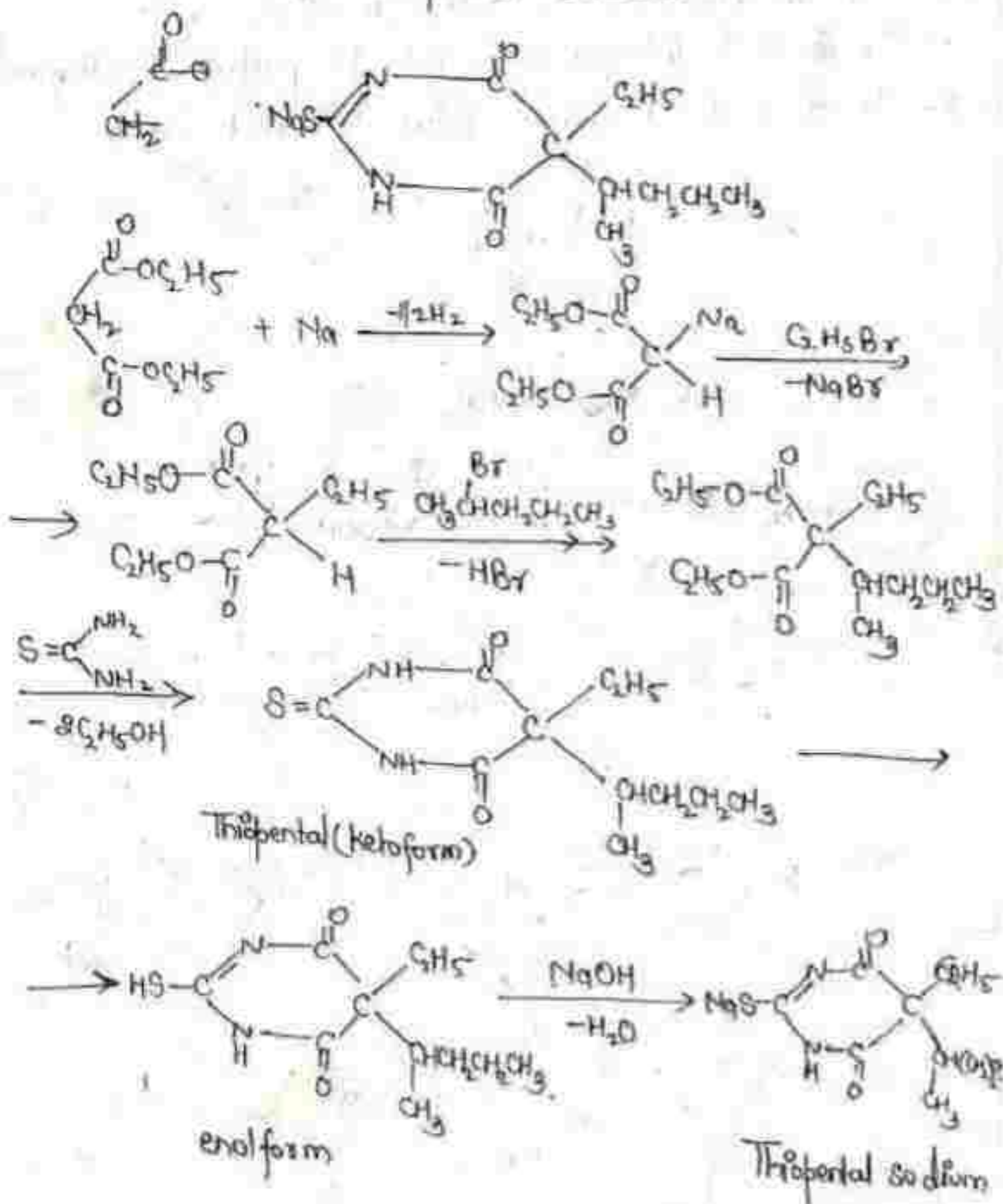
**Hypnotic drug :-** These are the drugs which produces unconsciousness, compelling the patient to sleep by depressing the CNS, particularly reticular activity which characterises wakefulness.

**Opioid analgesics :-**

# Synthesis of Drugs

## General Anesthetics

### Thiopental Sodium



Uses :- Uses :- 1. Thiopental is used in the induction phase of general anaesthesia.

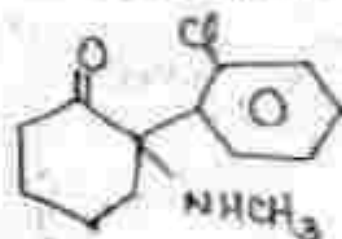
2- In veterinary medicine, it is used to anaesthise the animals.

3- It is also used to induce medical coma.

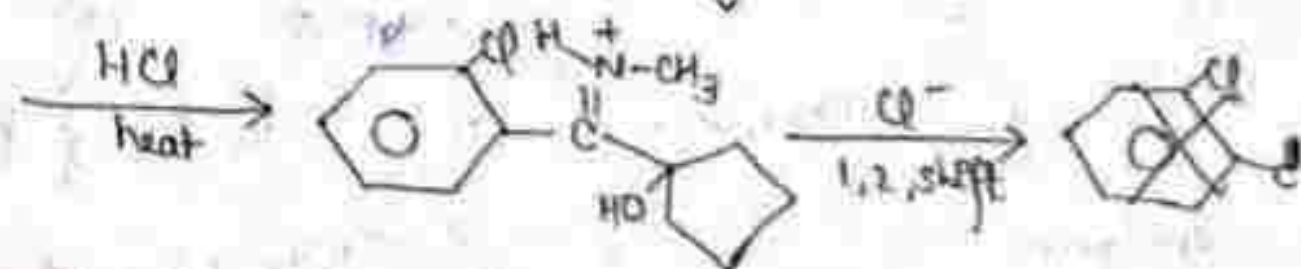
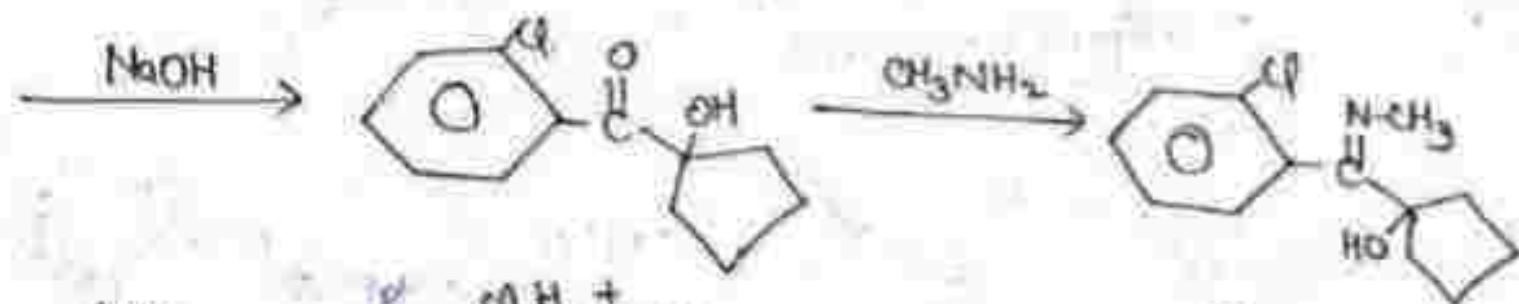
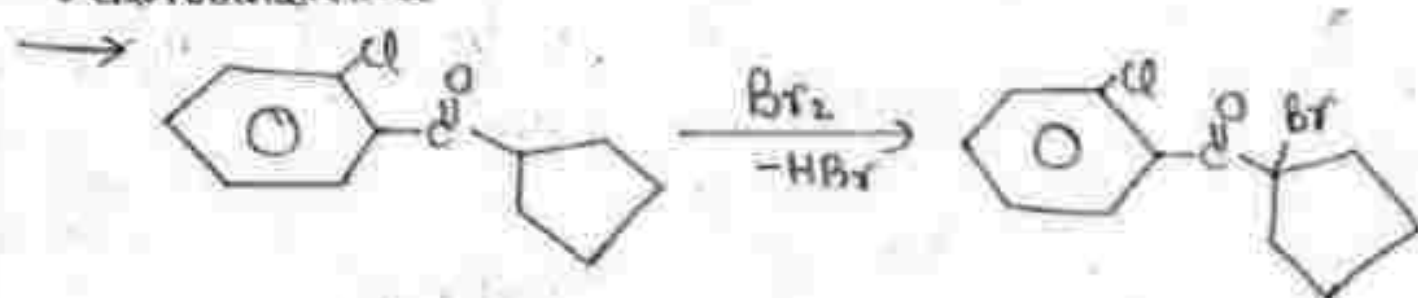
4- It is used Intravenously for the purpose of euthanasia.

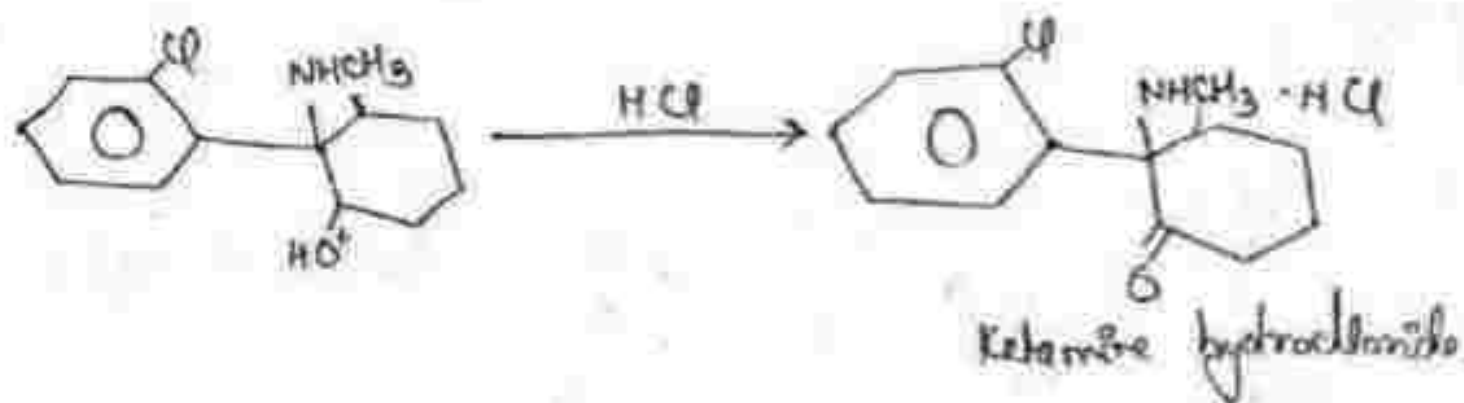
5- It is used in some places as truth serum.

## ketamine



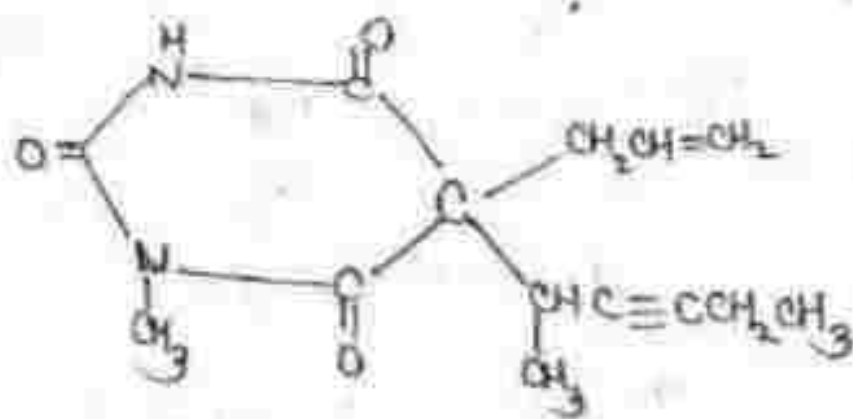
o-chlorobenzonitrile





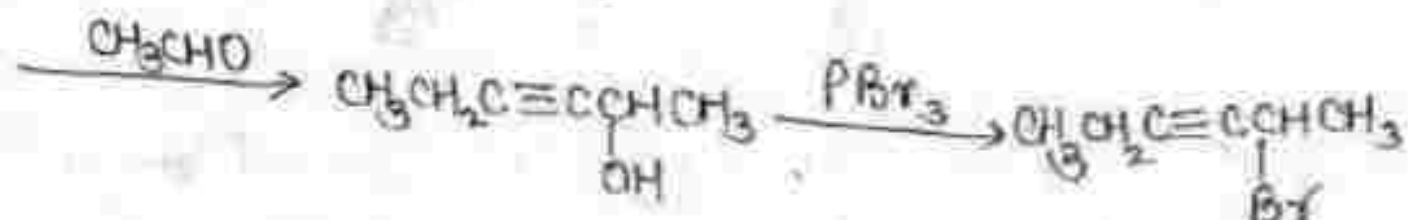
- Uses:-
- 1- It is ~~the~~ a rapid acting general anaesthetic.
  - 2- It is used for surgical operations of short duration.
  - 3- It is used in paediatric anaesthesia.
  - 4- In emergency of surgery in field conditions in war zones.
  - 5- Asthmatics or patients with chronic airway obstructive airway disease.

### Methohexital

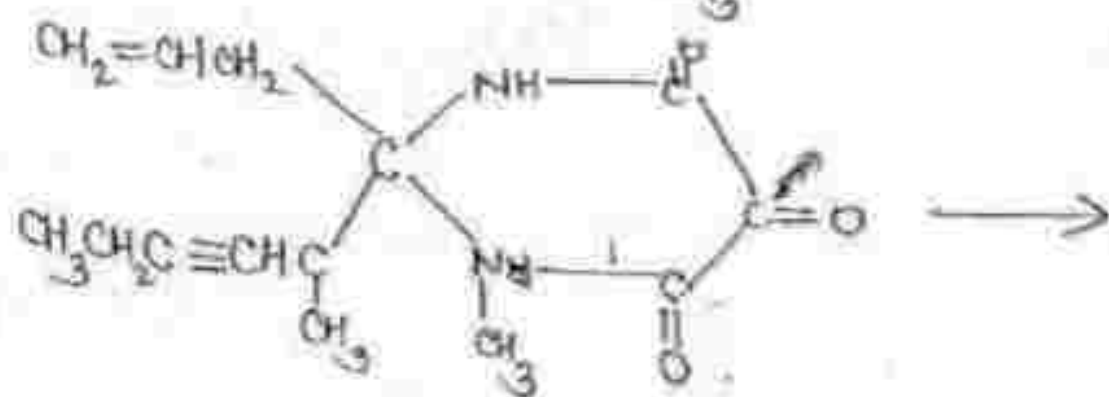
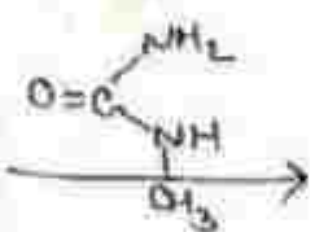
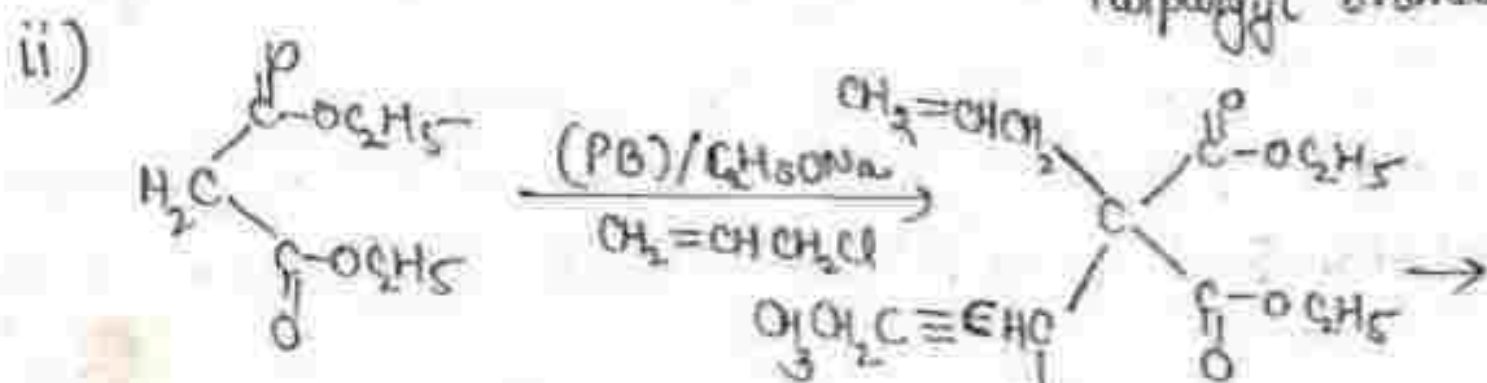


- Uses:-
- 1- for induction of anaesthesia through the intravenous administration.
  - 2- The onset of action is rapid.
  - 3- Useful for short surgical operation.

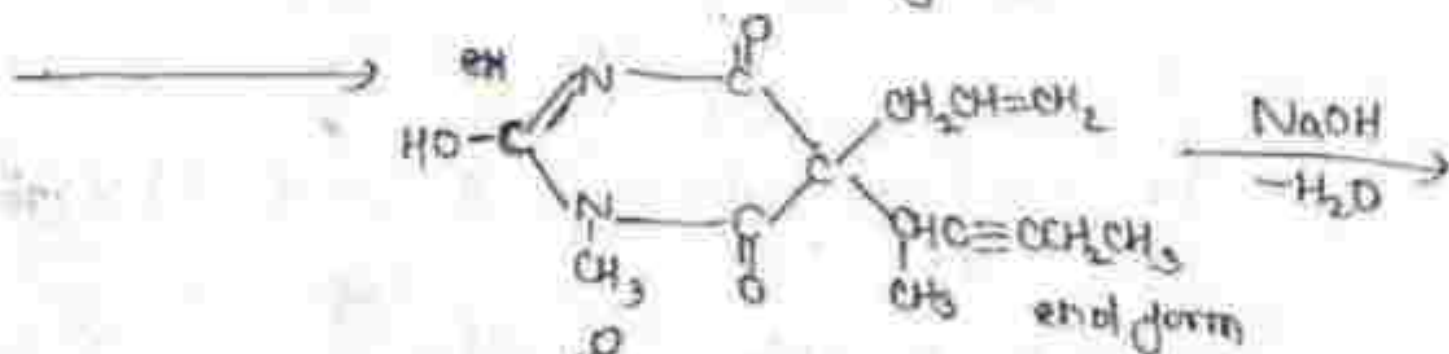
# Synthesis:-



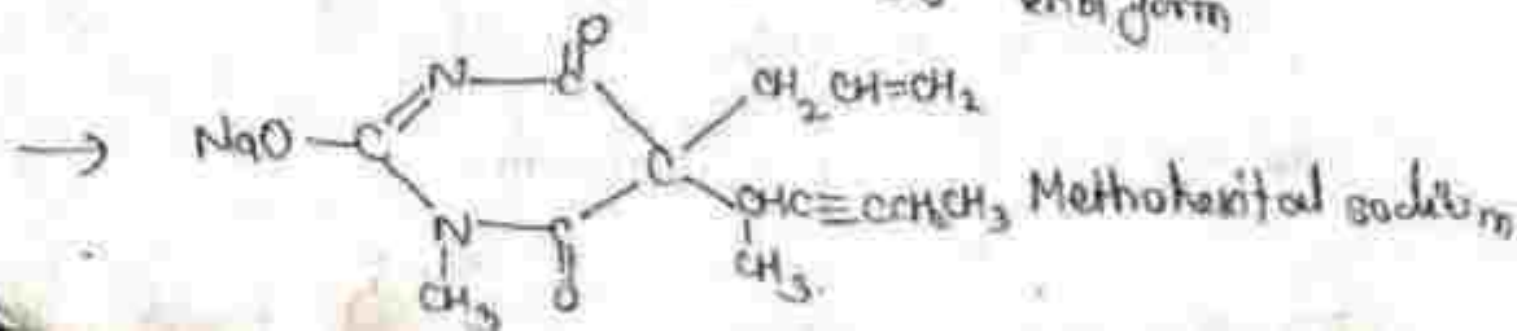
Pentapargyl bromide



methoxal (keto form)

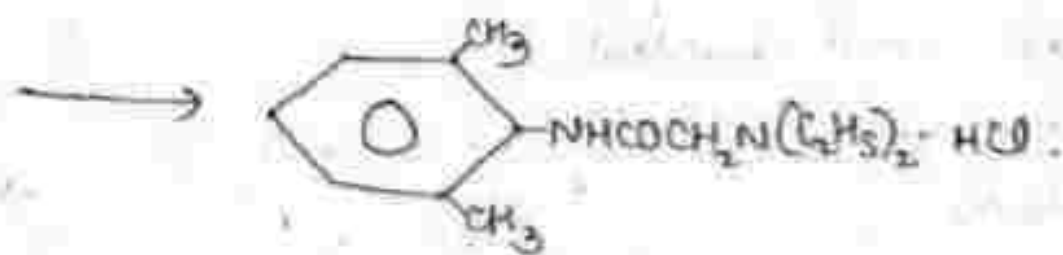
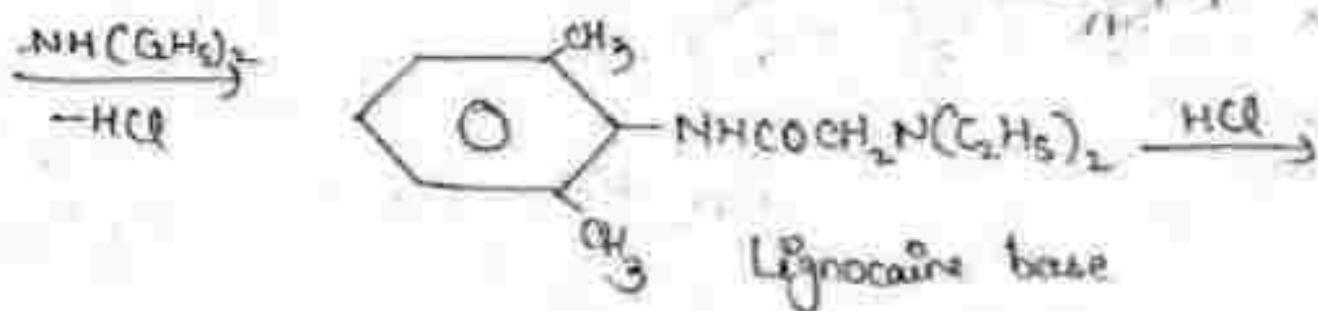
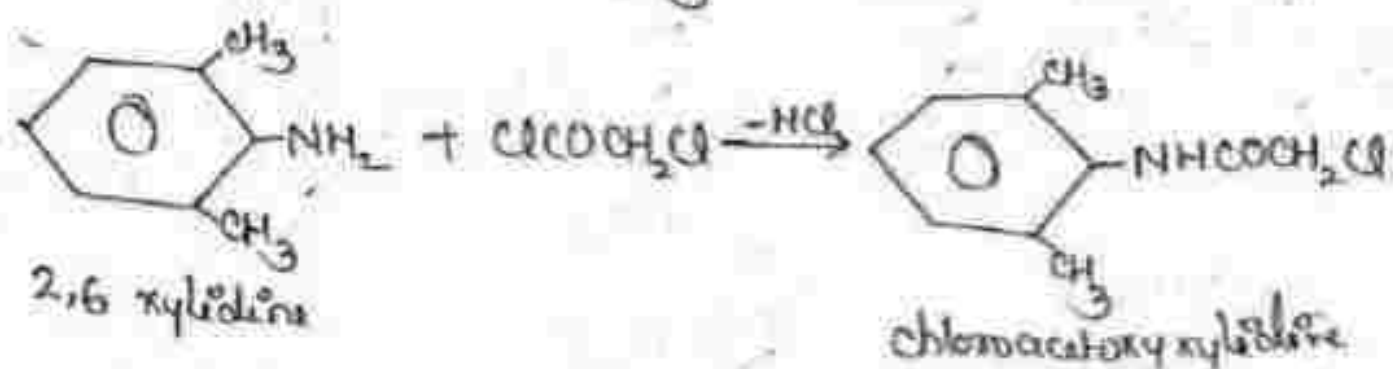
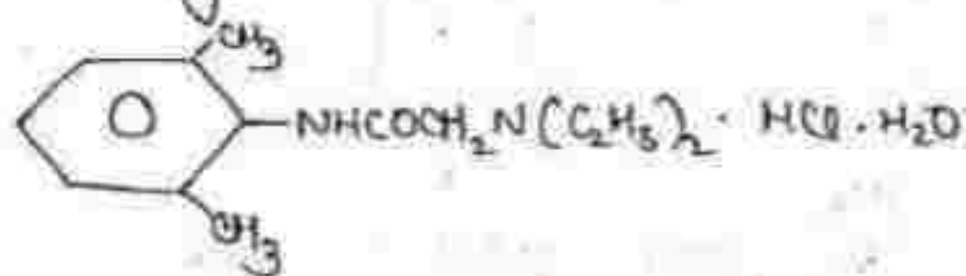


enol form



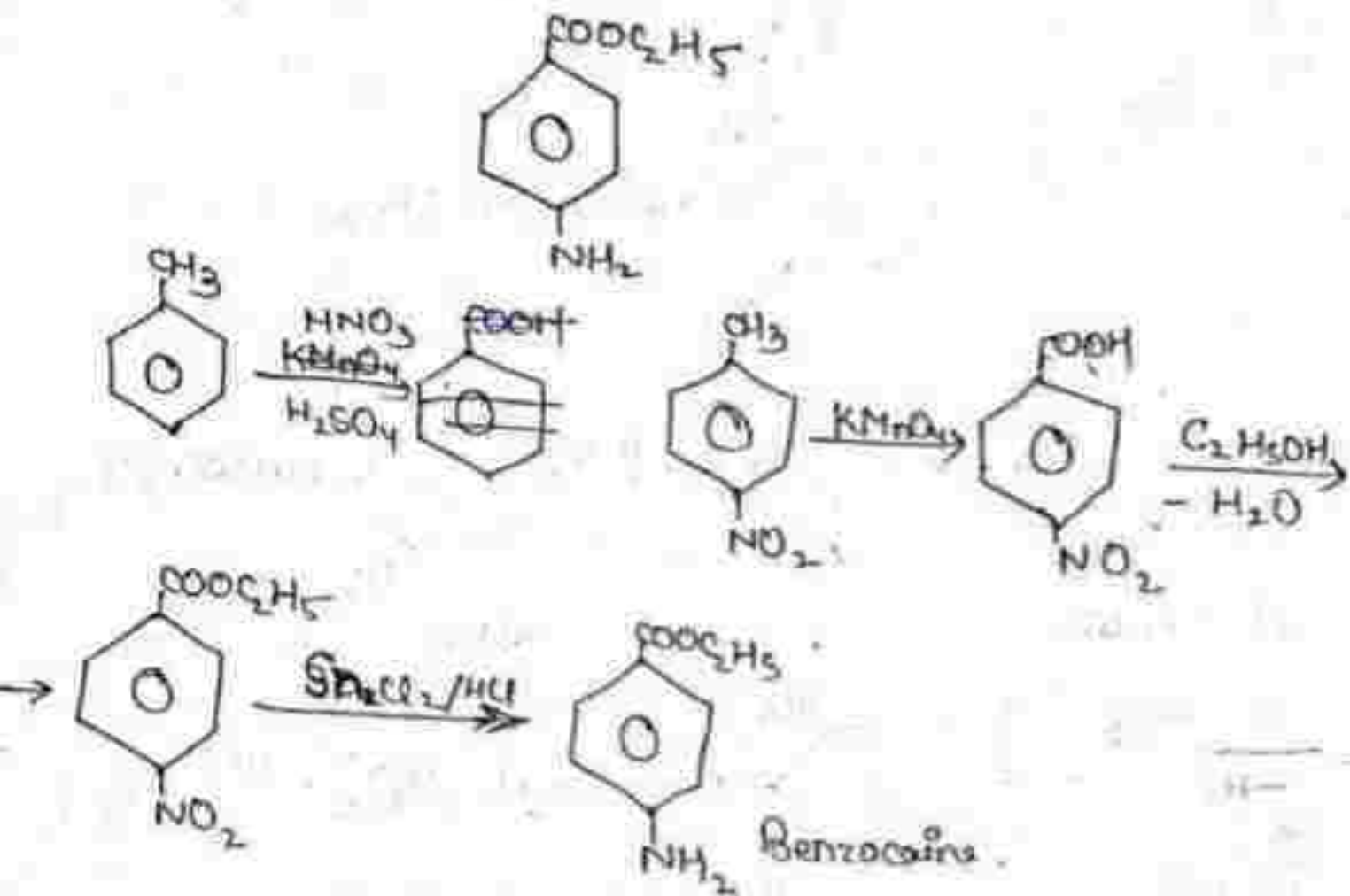
# Local Anaesthetics

## Lignocaine



- Uses:
- 1- Used as local anaesthetic agent.
  - 2- Used in treatment of ventricular arrhythmias.
  - 3- It has also been efficient in refractory cases of status epilepticus.

# Benzocaine



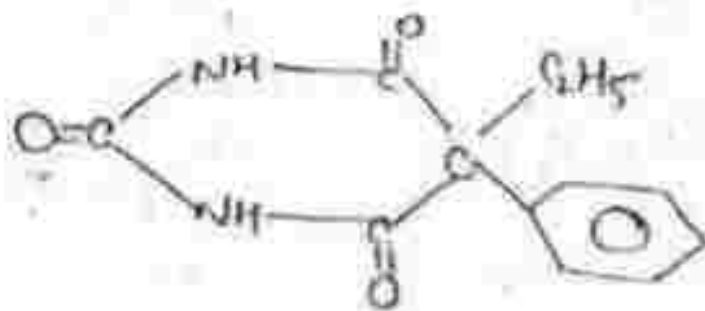
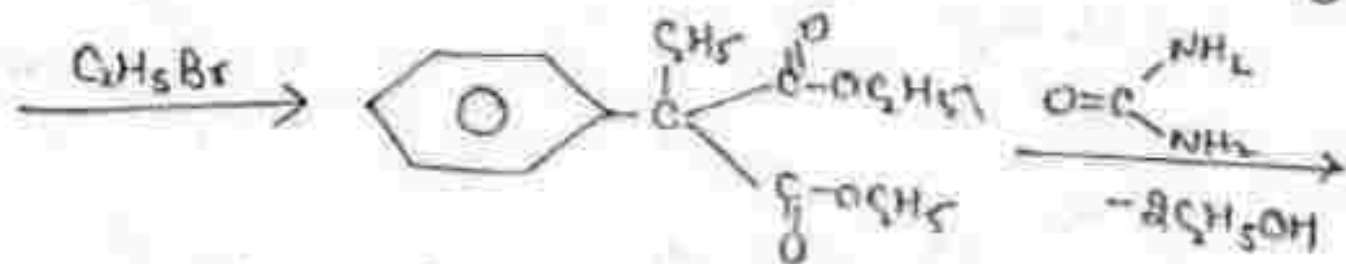
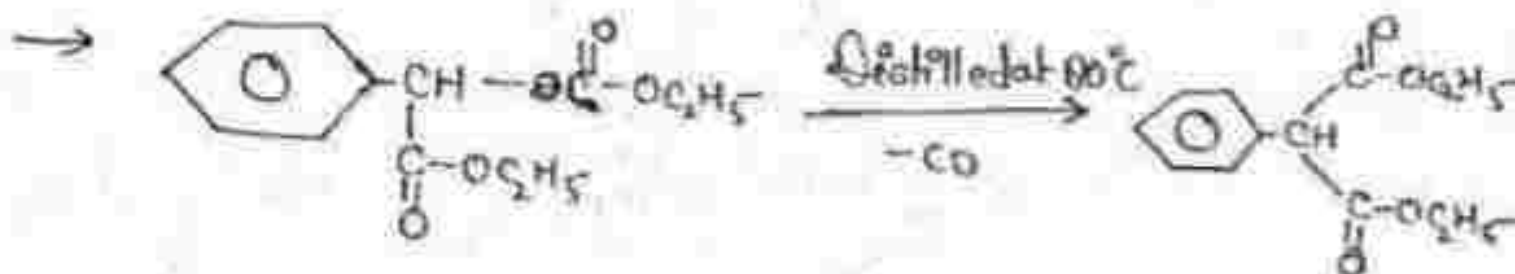
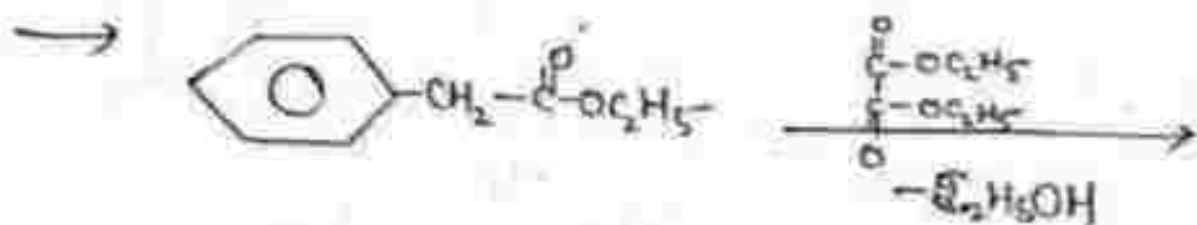
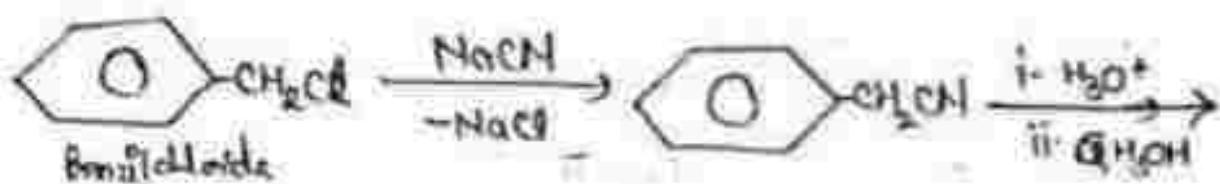
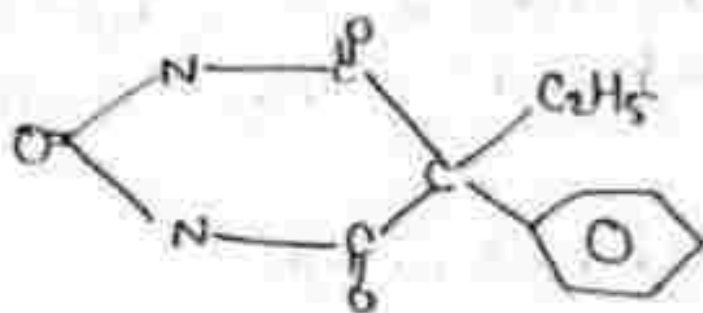
Uses :- ① Used as local anaesthetics.

② It can be applied directly to wounds & ulcerated surfaces.



# Hypnotics & Sedatives

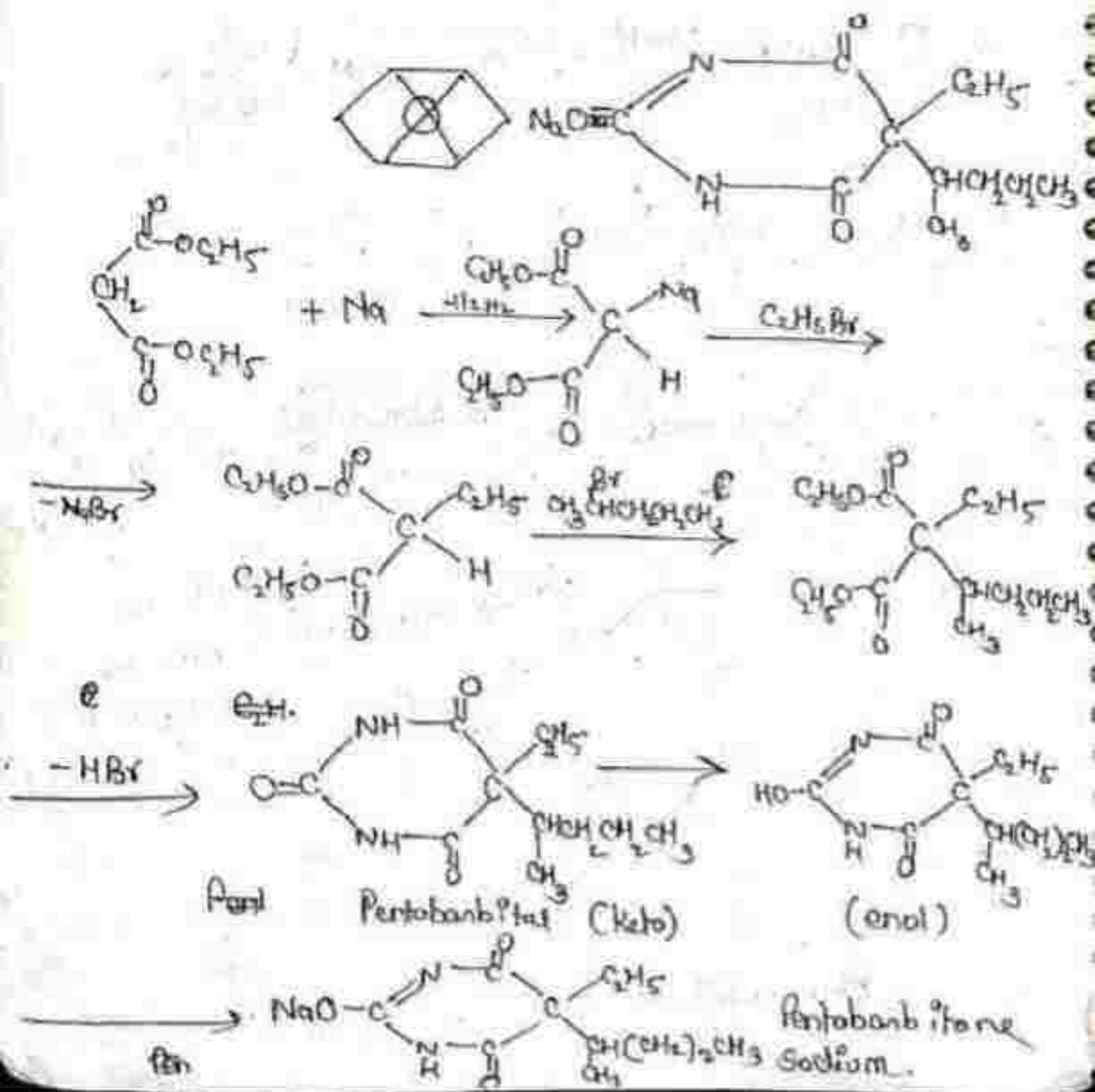
## Phenobarbitalone



Phenobarbitalone

- Uses:-
- 1- Used as sedative & hypnotic.
  - 2- Used as antiepileptic drug.
  - 3- Used in nervous & related tension states.
  - 4- Used in symptomatic therapy of epilepsy.

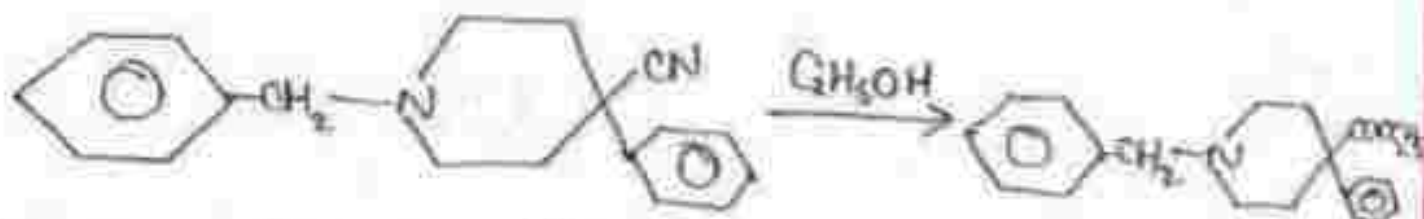
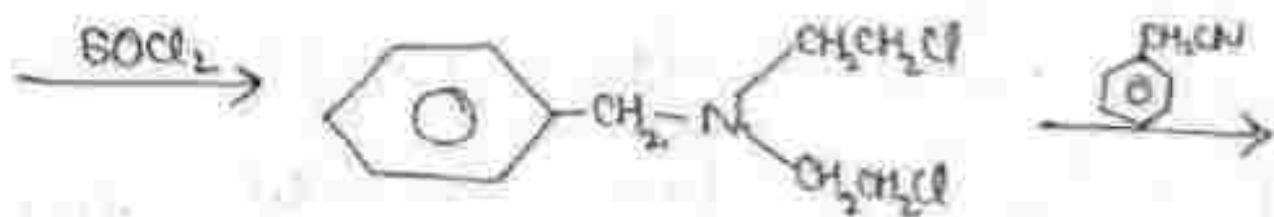
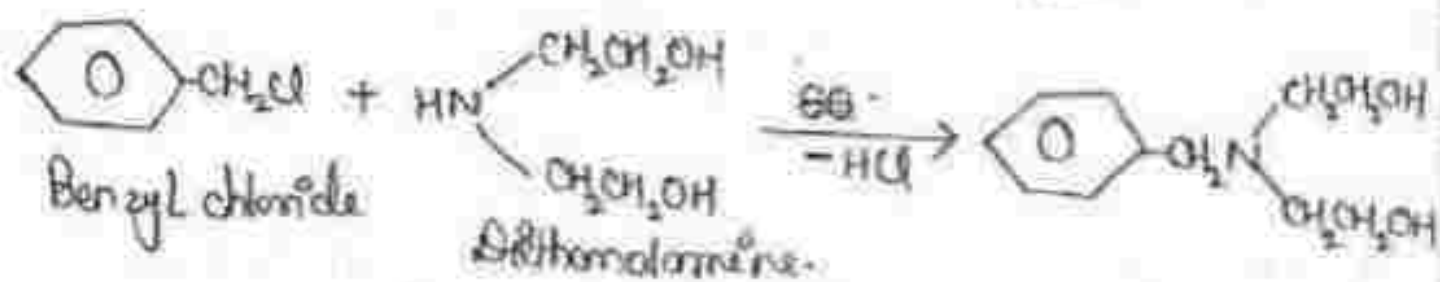
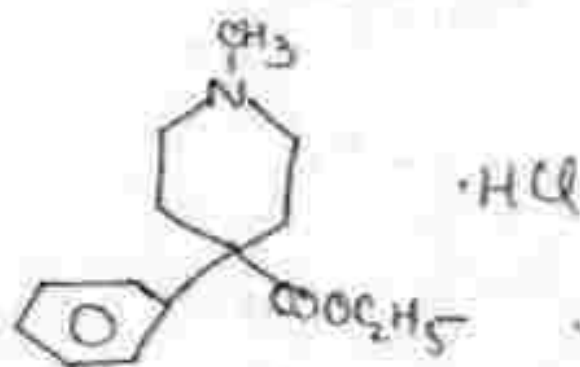
## Pentobarbitone



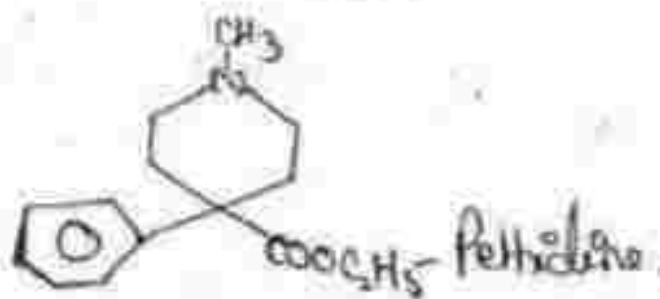
- Uses = 1- In treatment of ~~ins~~ insomnia.  
 2- As a basal anesthetic  
 3- In atychnia poisoning.

## Opioid Analgesics.

Pethidine



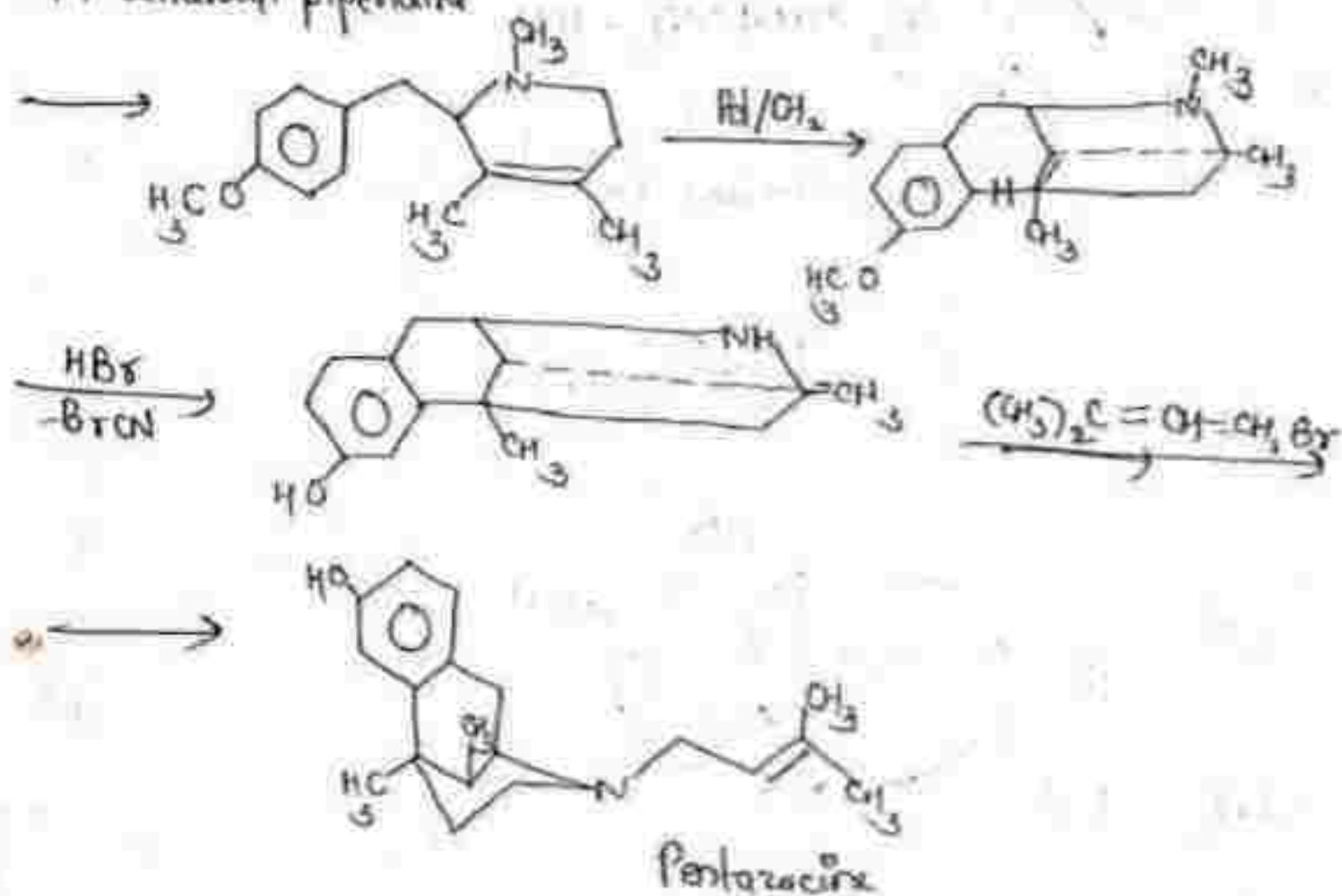
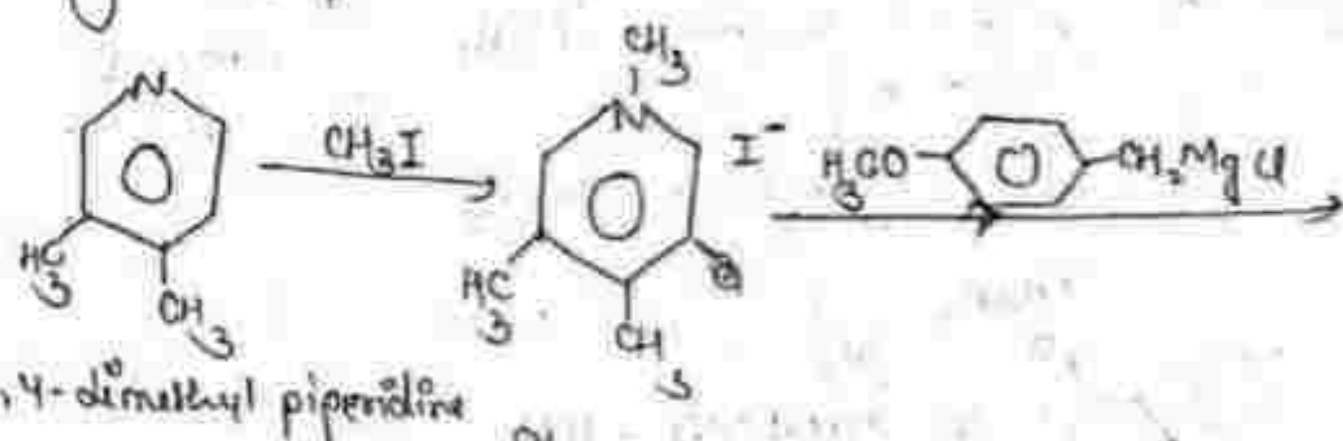
- 1)  $\text{H}_2/\text{Pd}$
- 2)  $\text{HCHO}$
- 3) Catalytic hydrogenation
- 4)  $\text{HCl}$







Synthesis :-



Mode of action :-

Thiopental / Methohexital / Phenobarbital / Pentobarbital



act on chloride ion channel of GABA receptor



↑ opening of time of  $Cl^-$  channel



↑ intracellular conc. of  $Cl^-$  ion



Loss of consciousness / sedation



Anaesthesia

Benzocaine

Lignocaine



Act on  $Na^+$  channel of GABA receptor



Block the channel by acting at inactivation gate i.e. H gate



↓ conductance of  $Na^+$  ion.

↓  
loss of sensation

↓  
Anaesthesia

Pethidine / methadone

Pentazocine

Pethidine / methadone

↓  
Stimulate Act the  $\mu$ -opioid receptor in CNS.

↓  
mimic the action of  
endogenous opioids met-enkephalin  
& leu-enkephalin

↓  
↓ activity of the enzyme adenylylase  
cycase in certain brain  
areas.

↓  
Impaired synthesis of cyclic-AMP.

↓  
It Enhances the activity  
neurons involved in modulation  
of pain impulses.

↓  
Opioid induced analgesia.

Pentazocine



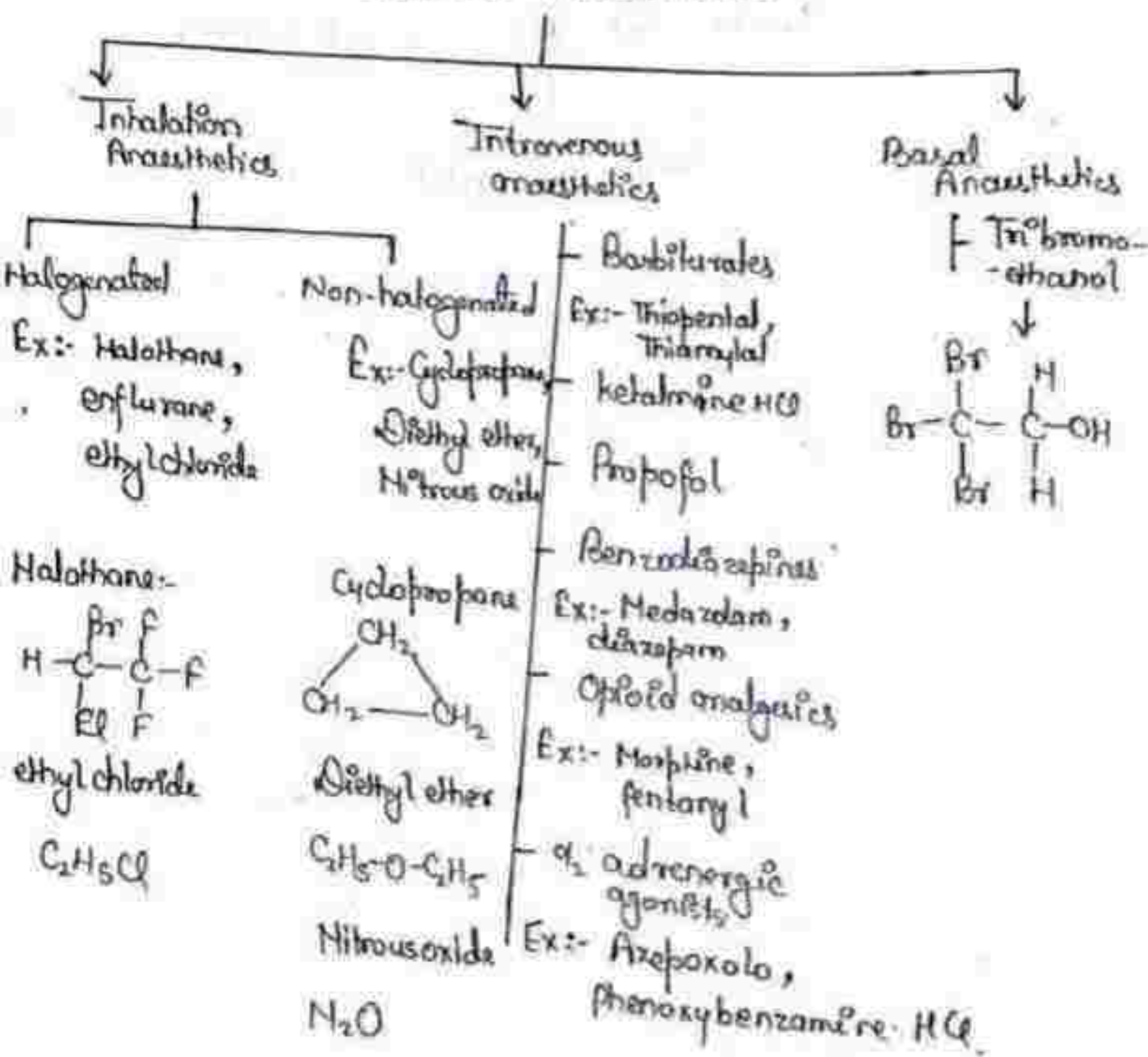
Stimulate Act the  $\mu$ -opioid receptor



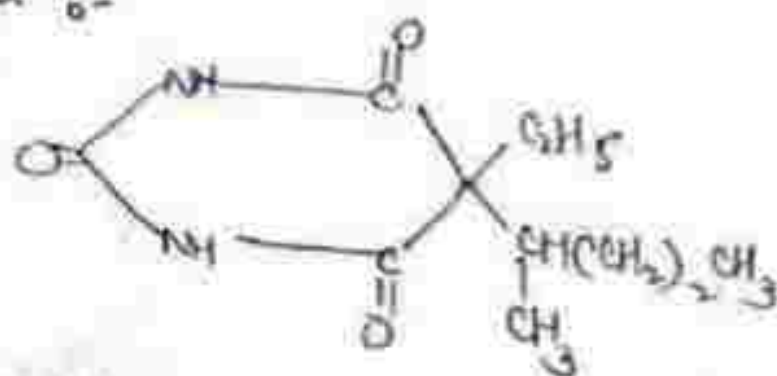
(Same as pethidine & methadone)

# Classification.

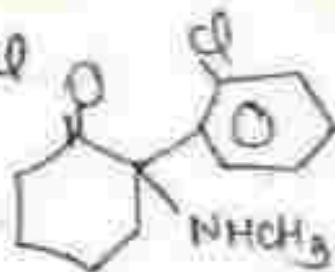
## General Anaesthetics



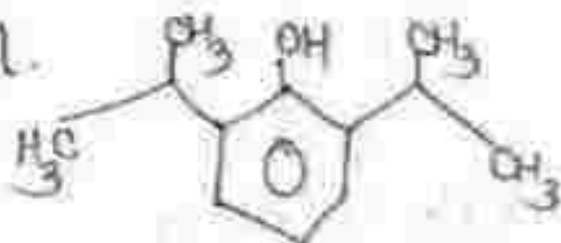
Thiopental :-



2- Ketamine HCl

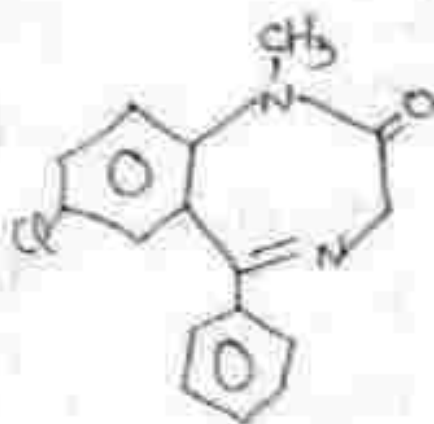


3- Propofol



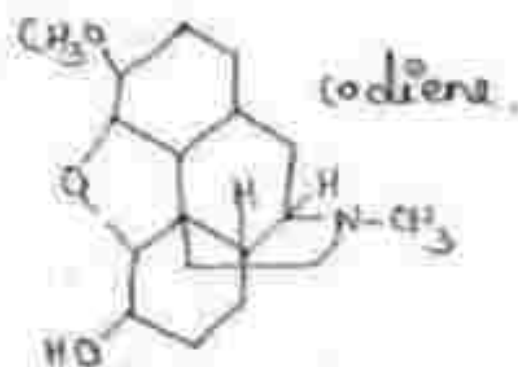
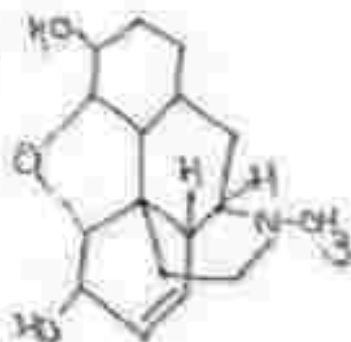
4- Benzodiazepines

Ex: Diazepam



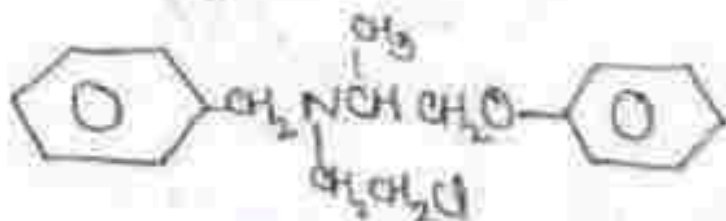
5- Opioid analgesics:-

Ex:- Morphine



6-  $\alpha_2$ -adrenergic agonist

Ex: Phenoxybenzamine HCl

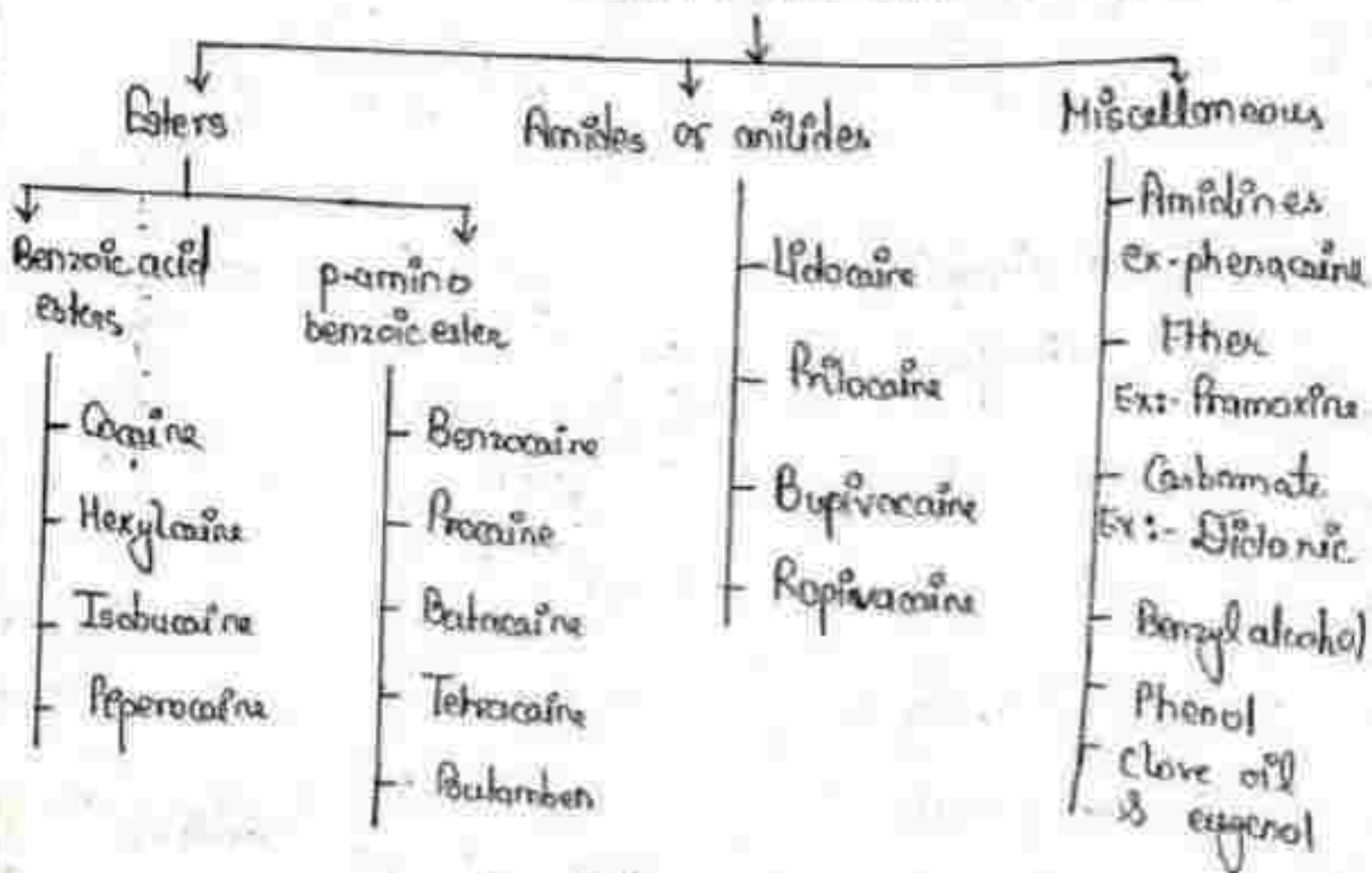


# LOCAL ANAESTHETICS

## Classification

### 1- Benzoic acid derivatives:-

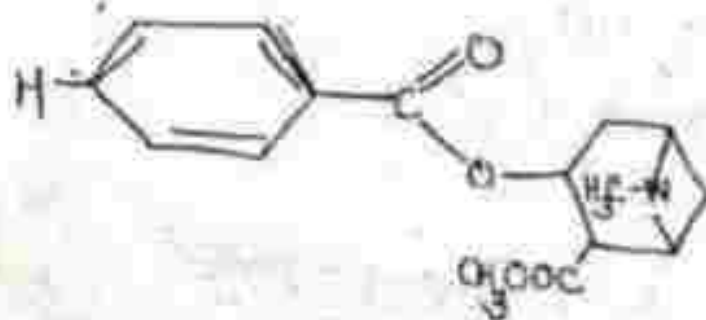
#### Local Anaesthetics



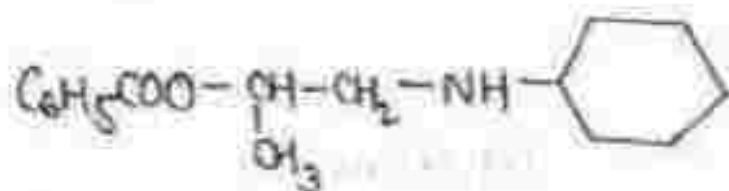
### 1- Esters

#### i- Benzoic acid esters-

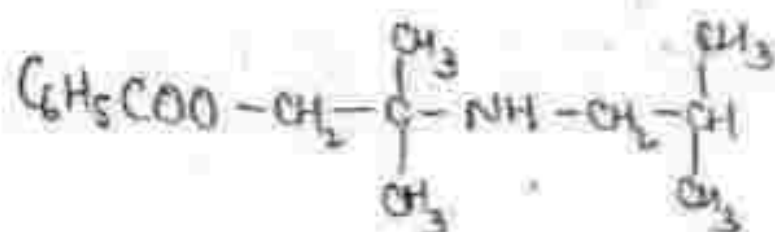
#### a- Cocaine



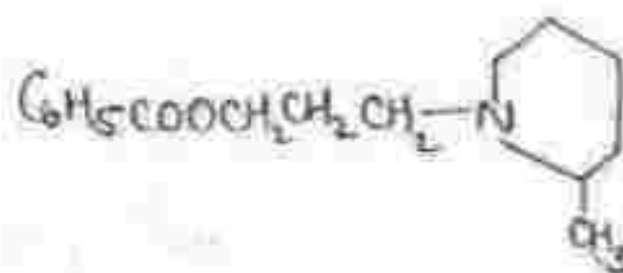
b- Meprobamate



c- Isobutylmeprobamate

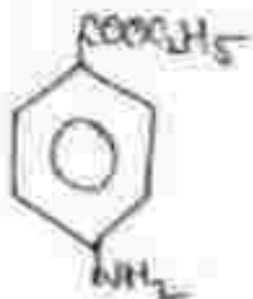


d- Piperazine



e- ii- p- amino benzoic acid ester

g- Benzocaine



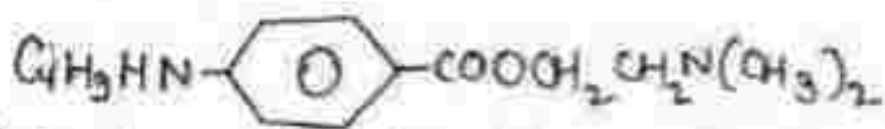
h- Procaine



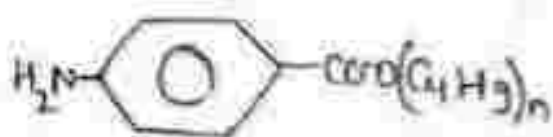
c- Butocaine



d- Tetracaine

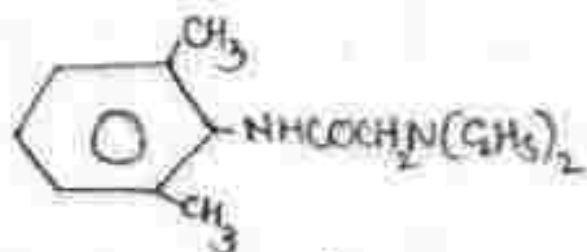


e- Butamben

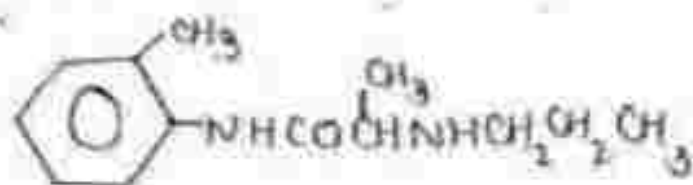


## 2. Amides or amides

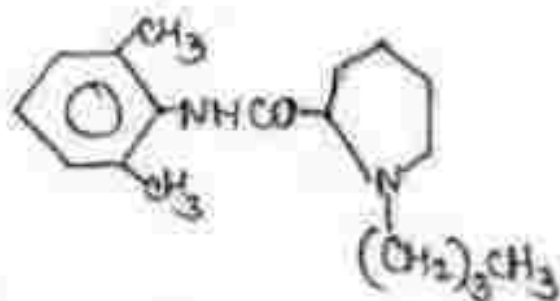
i- Lidocaine



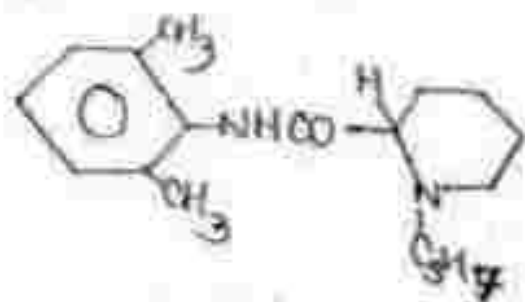
ii- Prilocaine



iii- Bupivacaine



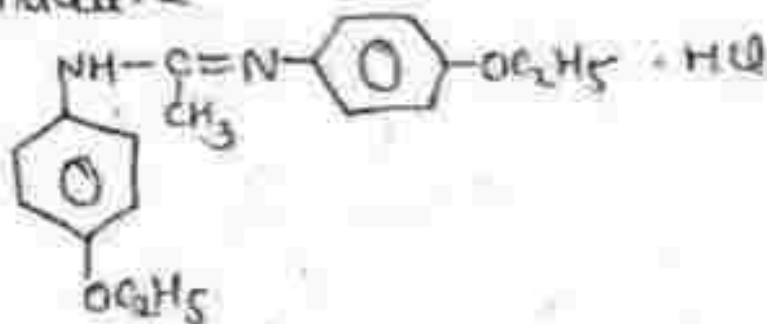
iv- Ropivacaine



## 3. Miscellaneous

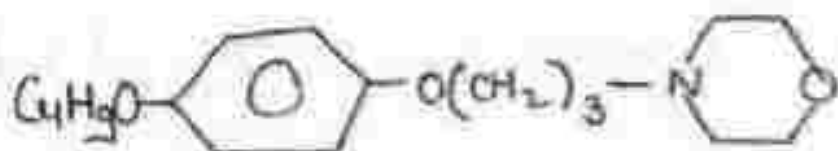
i- Amidine

Ex:- Atenolol



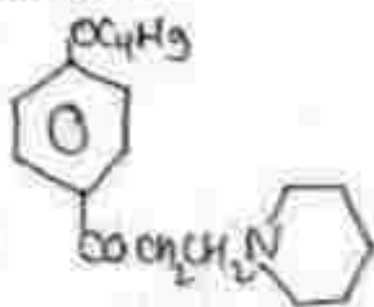
ii- Ether

Ex:- Piroxone



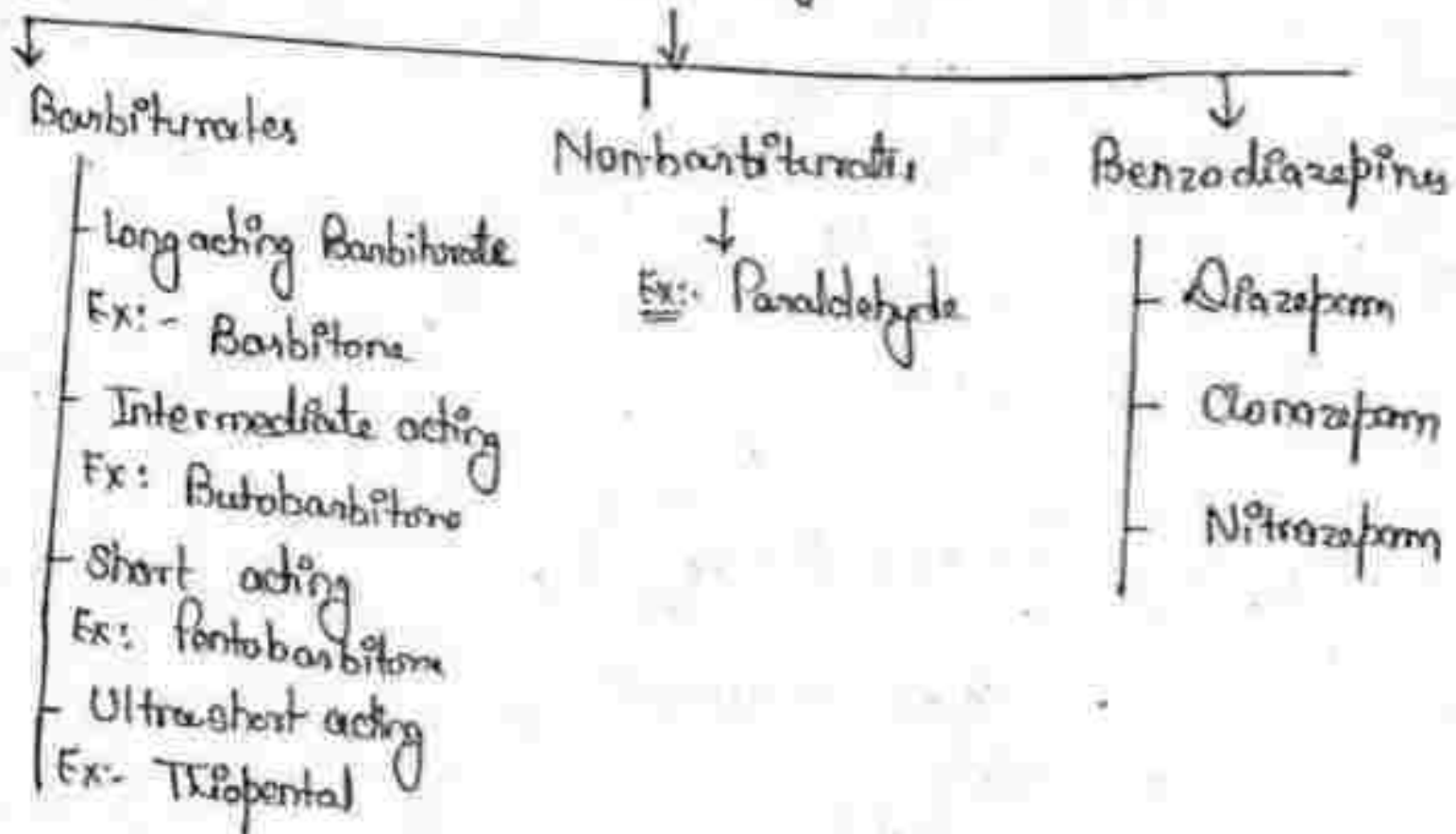
iii- Carbamate

Ex:- Diclone



# Classification.

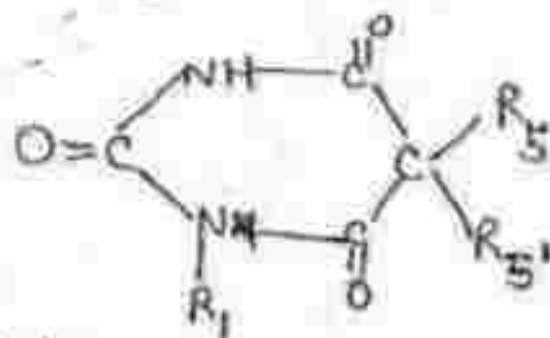
## Sedative and Hypnotics



### 1- Barbiturates

In general, the barbiturates exert a significant depressant action on the cerebrospinal axis.

The relative degrees of depression, sedation, hypnosis, or anaesthesia are dependent on the nature of barbiturates, its dose & route of administration.

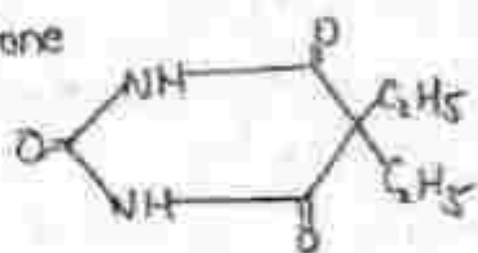


Classification :-

1) Long acting barbiturates :- Onset of action is visible after 1 hour.

- ⇒ Duration of action last for 6-10 hrs.
- ⇒ Largely excreted by the kidney.

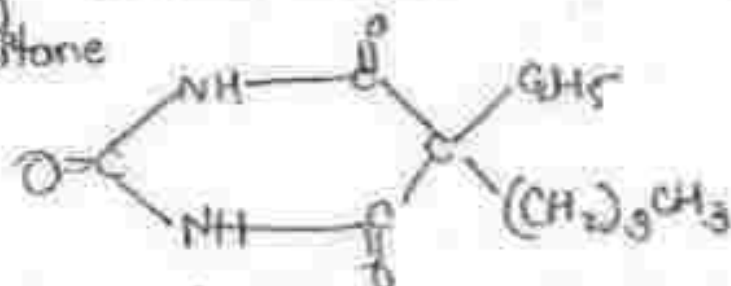
Ex:- barbitone



② Intermediate acting barbiturates :- Onset of action is 30 min.

- ⇒ Duration of action → 2-6 hrs.

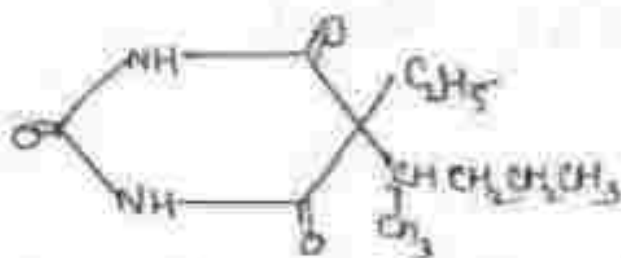
Ex: Butobarbitone



3- Short acting barbiturates :- Onset of action falls within 15 min.

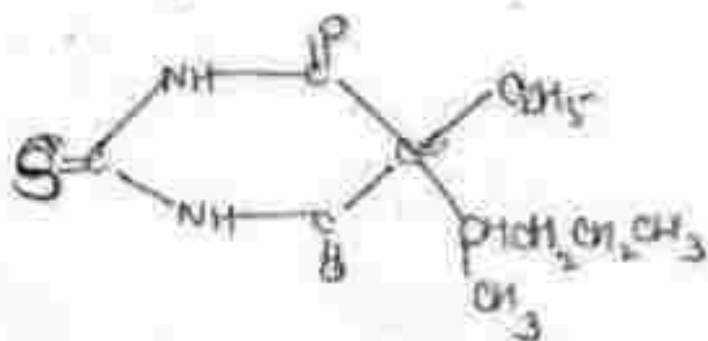
Duration of action → 1-2 hrs.

Ex: Pentobarbitone



4- Ultra-short acting barbiturates :- Onset of action is visible within few sec.

Ex: Thiopental sodium

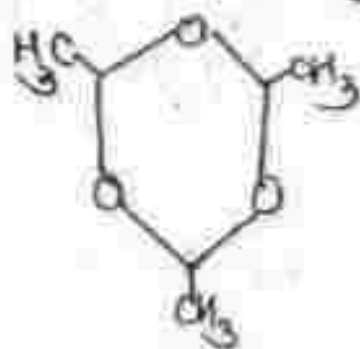


### 2. Non-barbiturates

There are a no. of compounds which do not possess the malonyl urea or barbiturate structure but exhibit marked hypnotic - sedative activity very similar to that of barbiturates.

⇒ They are habit forming like barbiturates

Ex:



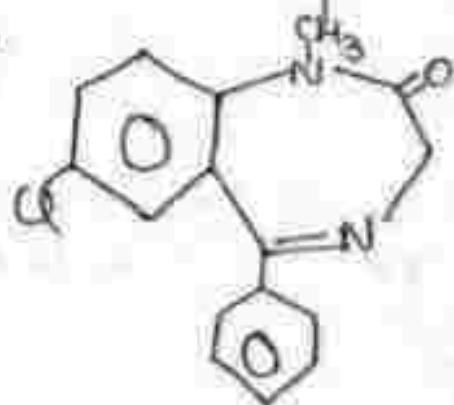
Pentaldehyde.

### 3. Benzodiazepines

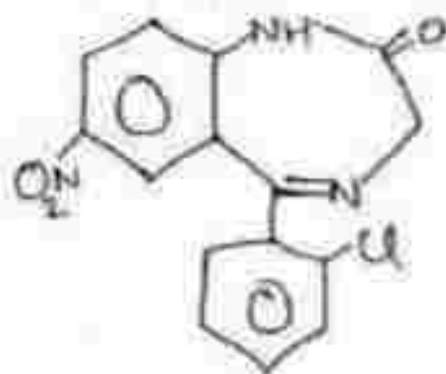
⇒ All benzodiazepines exhibit ~~hyp~~ hypnotic action to more or less extent with varying degree of metabolism in liver.

⇒ Hence only those benzodiazepines which are quickly metabolised & excreted, can be used as hypnotics in clinical practice.

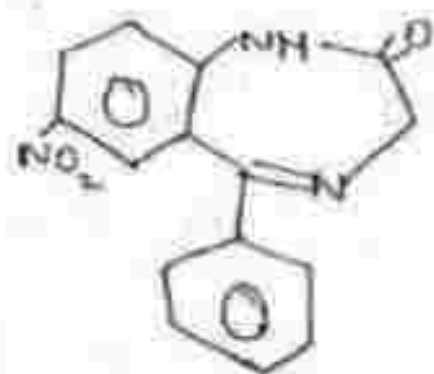
Ex:



Diazepam



Clonazepam

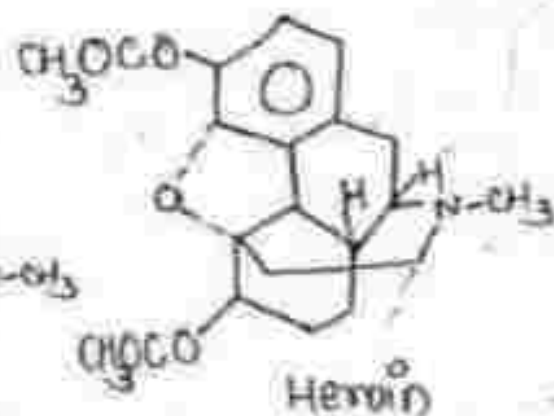
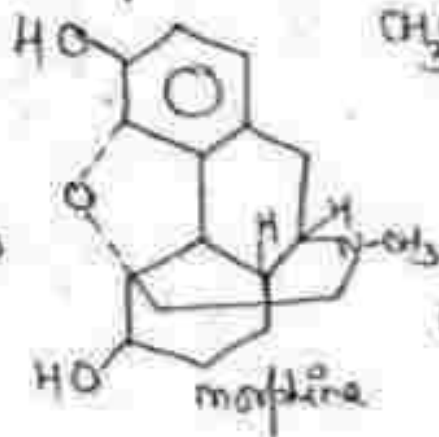
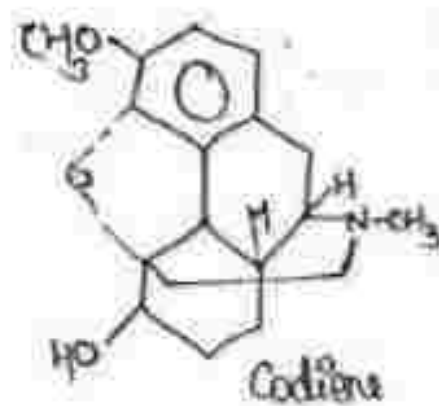


Nitrazepam

# Classification Opioid analgesics

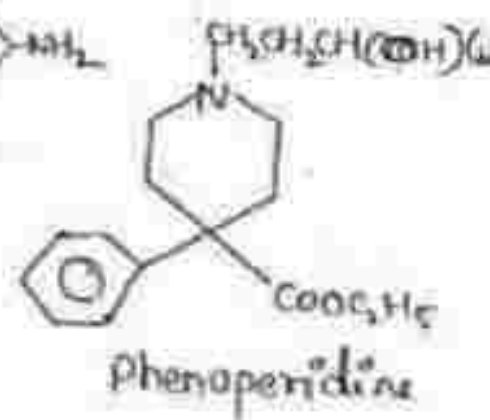
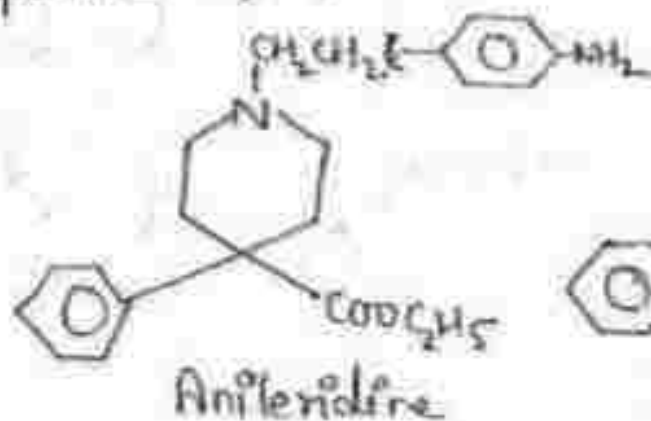
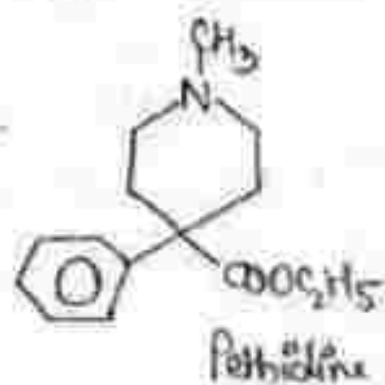
1- Morphine & related opioids:-

Ex:- Codeine, Morphine, Heroin



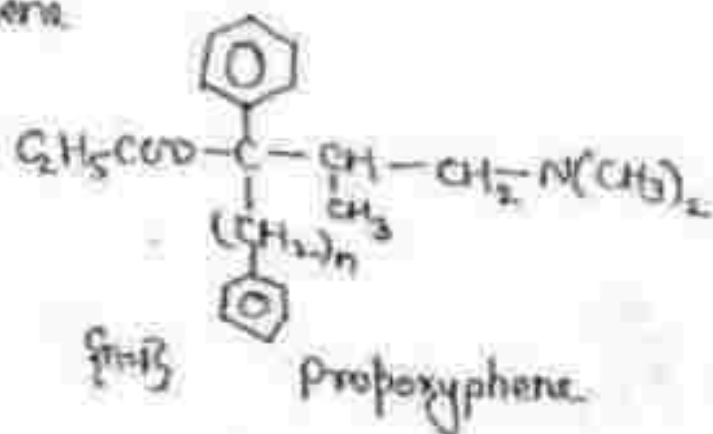
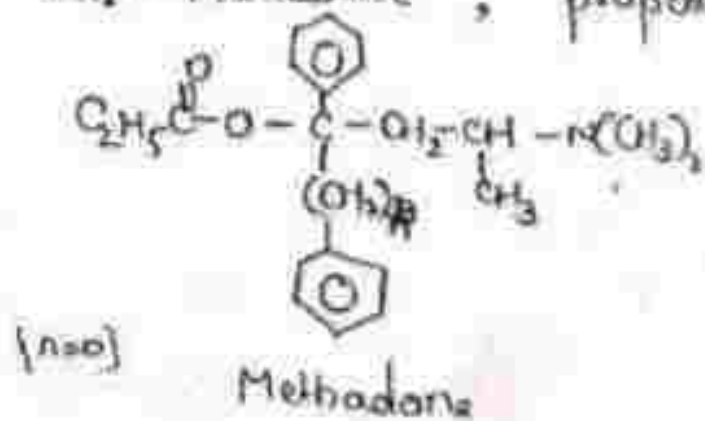
2- Meperidine and congeners:-

Ex:- Pethidine (meperidine HCl), Anileridine, Phenoperidine



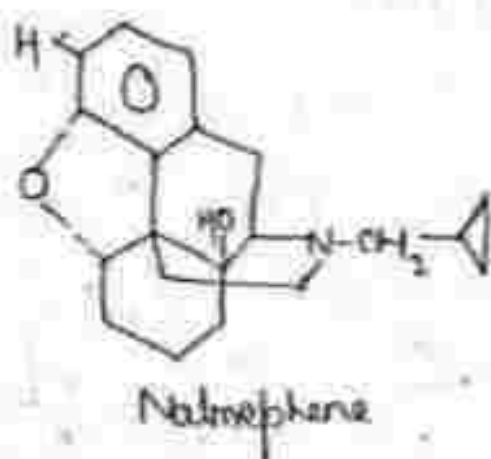
3- Methadone and congeners

Ex:- Methadone, propoxyphene



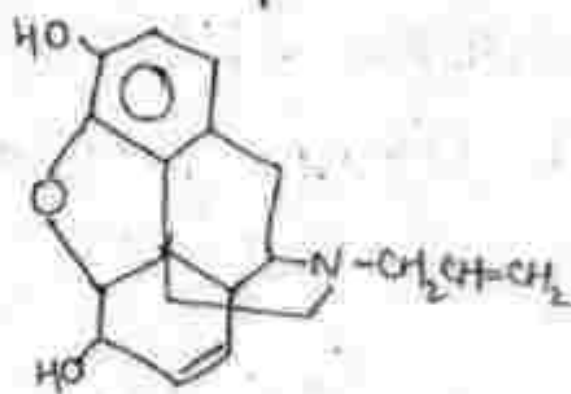
#### 4- Opioid antagonists :-

Ex: Naloxone, Nalmefene



#### 5- Mixed agonist-antagonist :-

Ex: Nalbuphine, Pentazocine



# UNIT-IV

## Definitions

### Antitussives

Antitussives are the agents that are employed in the symptomatic control of cough by way of depressing the cough centre situated in medulla. These are also known as anodynes, cough suppressants & centrally acting antitussives.

Ex:- Codeine, dextromethorphan

Coughing:- Coughing is a protective reflex which may be initiated by irritation in the pharynx or in the deepest level of the respiratory tract.

### Anticonvulsants

Epilepsy:- Epilepsy is a chronic CNS disorder in which a brief episode of seizure appears with or without loss of consciousness.

Anticonvulsant drugs:- It is also called as 'anti-epileptic drugs' which suppress the rapid & excessive firing of neurones that start a seizure.

or

## Antiparkinsonian Drug.

Parkinson's Disease:- It is a progressive neurologic disease in which the balance b/w Dopamine (an inhibitory neurotransmitter) and Ach (excitatory neurotransmitter) is greatly disturbed due to depletion of dopamine.

Antiparkinson Drugs:- These are the drugs which are used in the treatment of Parkinson disease to maintain the balance between the Dopamine and Ach neurotransmitter either by increasing the level of dopamine or by decreasing the conc. of Ach in brain.

## CNS Stimulants

~~Centr~~ CNS stimulants are drugs that produce generalized stimulation of the brain or spinal cord which may lead to convulsion.

or

Those drug subs. that most specifically afford an enhancement in excitability either very much with the different portions of brain or spinal cord.

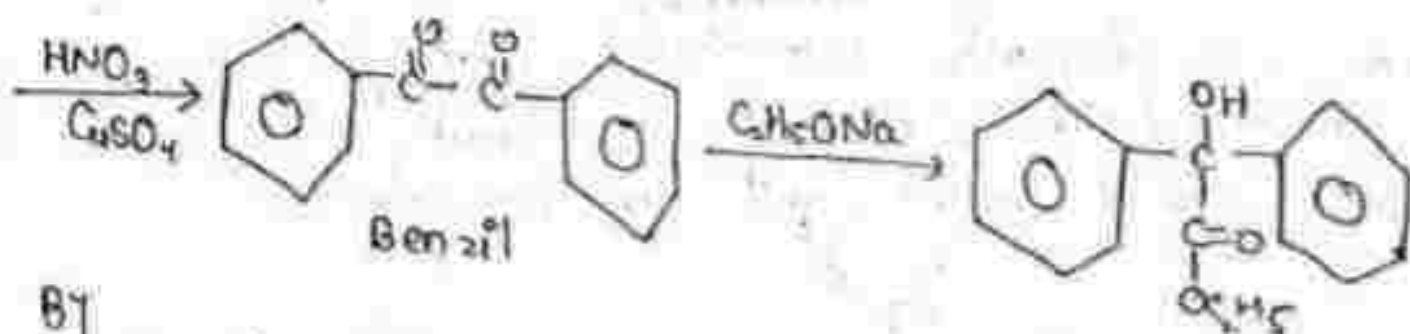
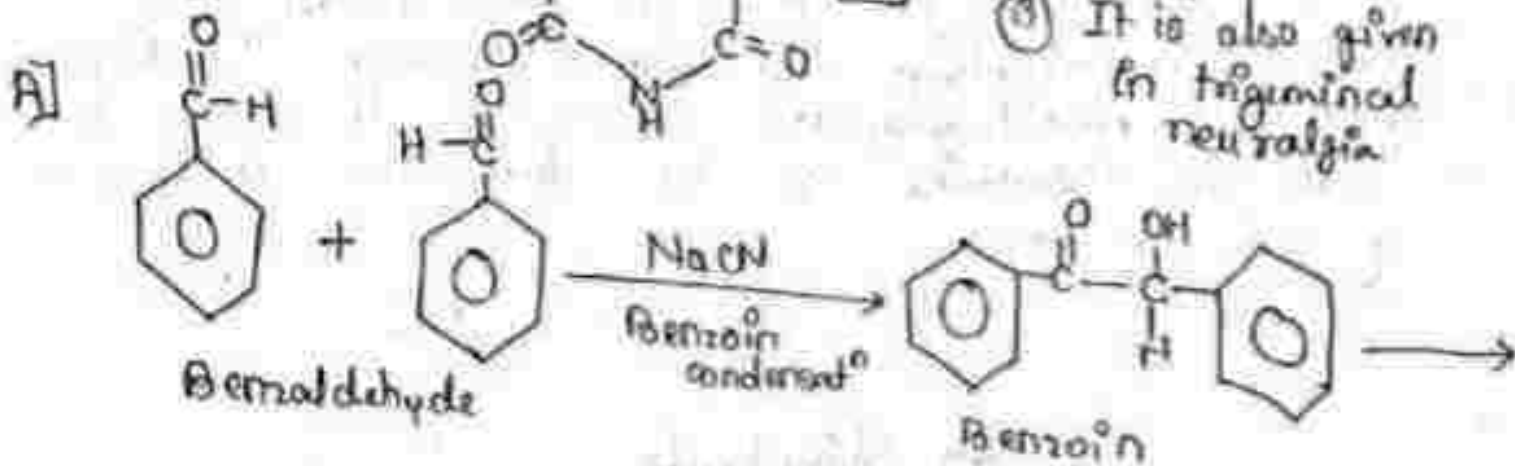
# Synthesis of Drugs

## Anticonvulsants

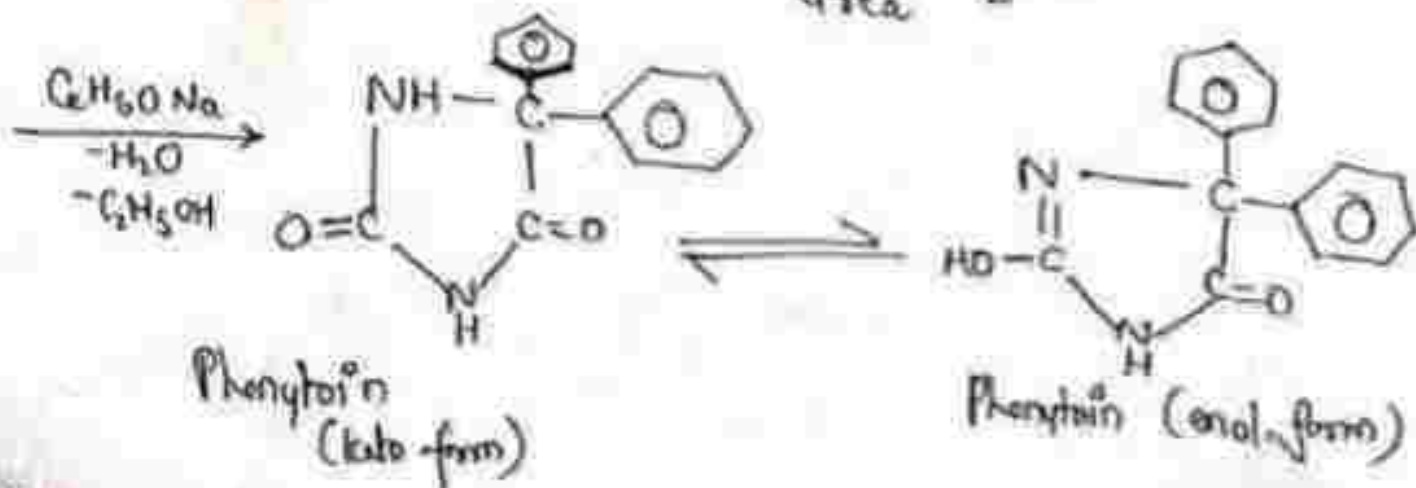
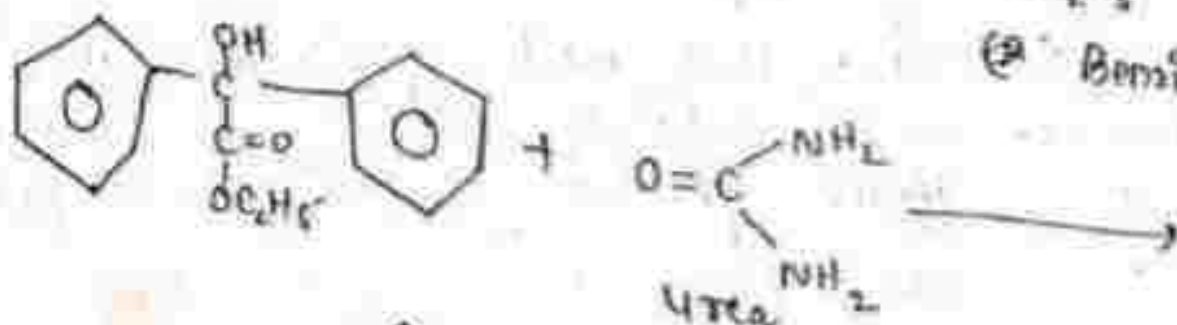
## Uses

### 1. Phenytoin

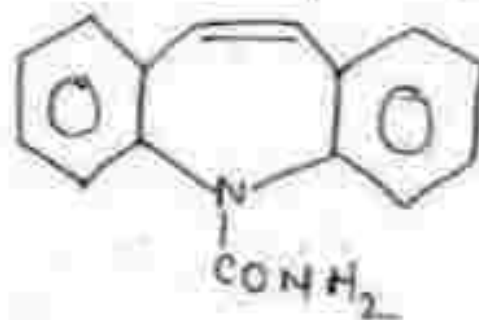
- ① Used in grandmal type of epilepsy
- ② Useful in cardiac arrhythmias
- ③ It is also given in trigeminal neuralgia



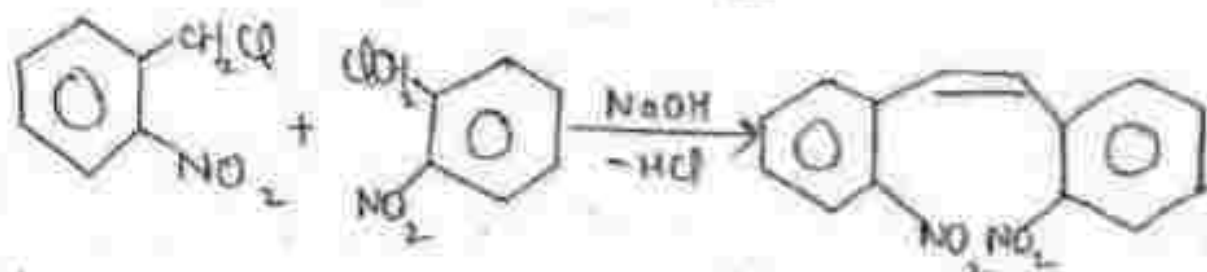
② Benzilic acid ester



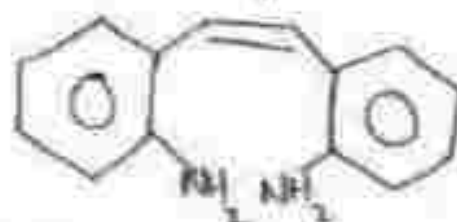
# Carbamazepine



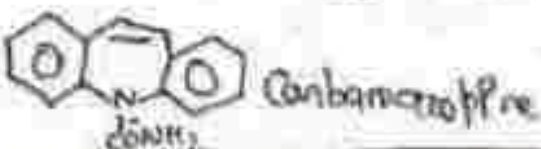
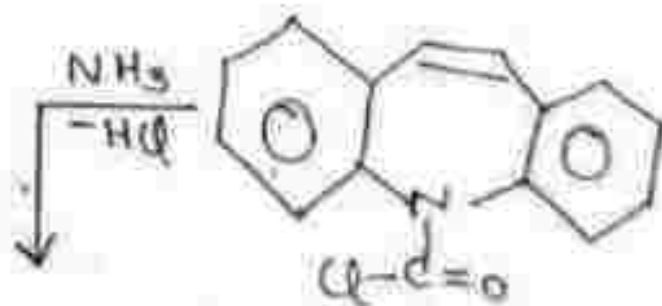
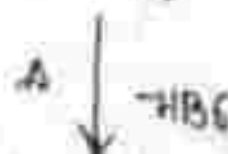
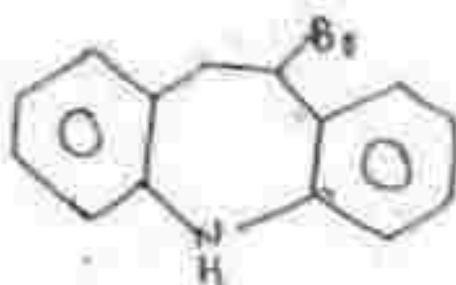
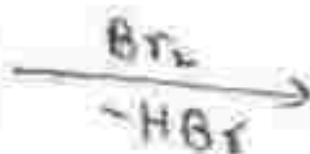
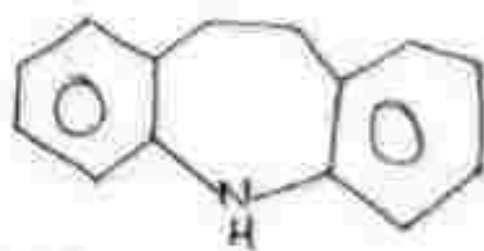
- Uses
- ① Used in grand mal epilepsy & psychomotor
  - ② Effective against temporal lobe & generalised convulsions.



2-chloromethyl nitrobenzene



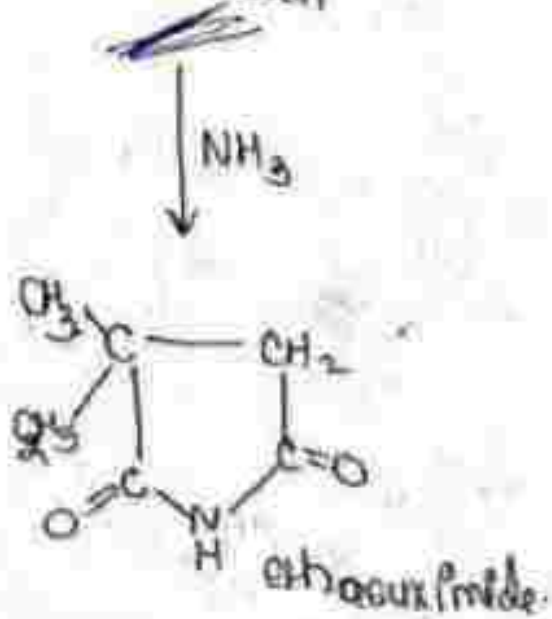
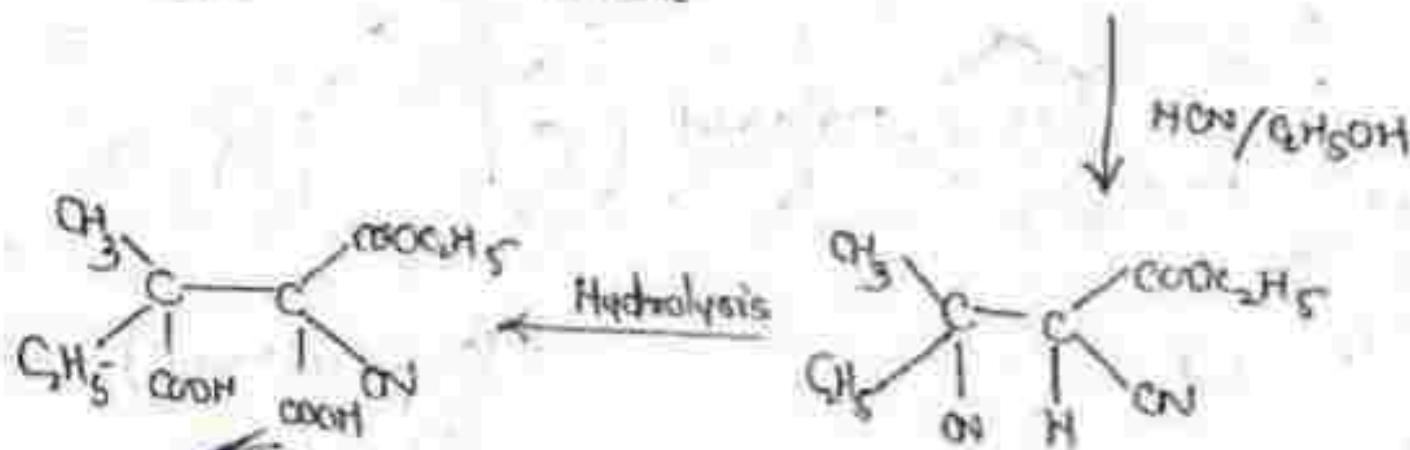
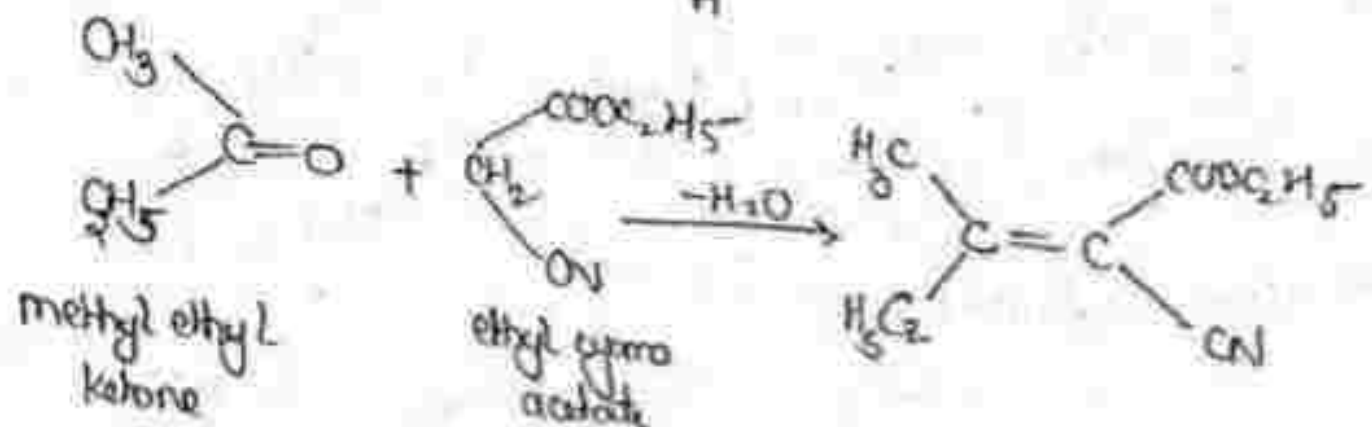
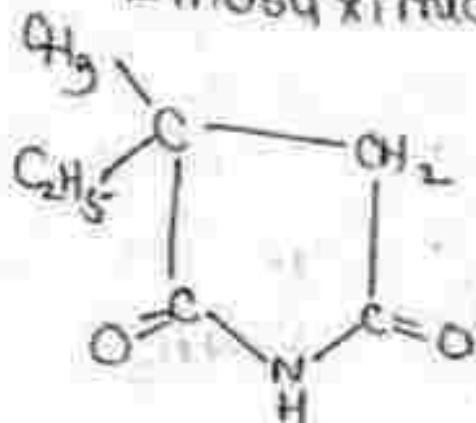
2-(o-aminostyryl)-aniline



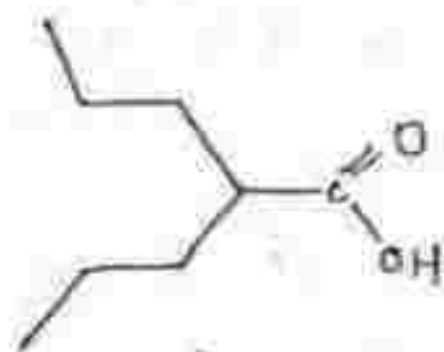
Carbamazepine

# Ethosuximide

Uses  
Used for petit-  
mal seizures.

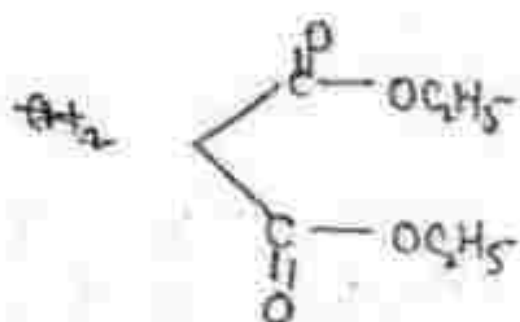


# Valproic acid

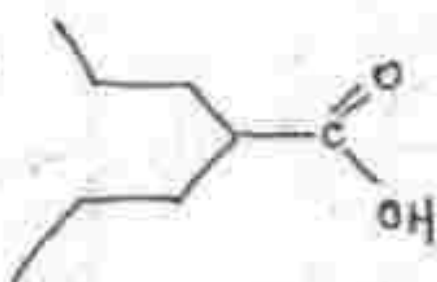
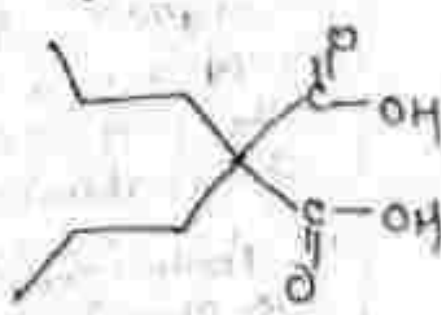
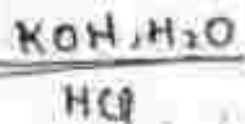
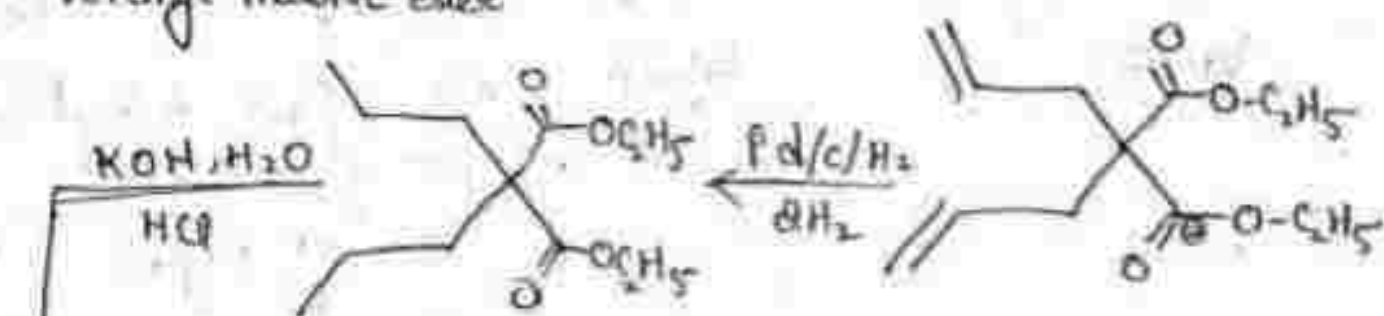
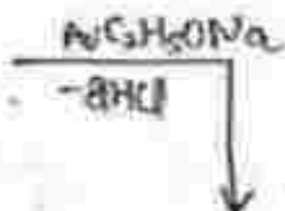
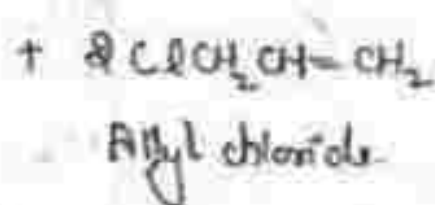


Use

Used for the treatment of myoclonic & tonic-clonic seizures



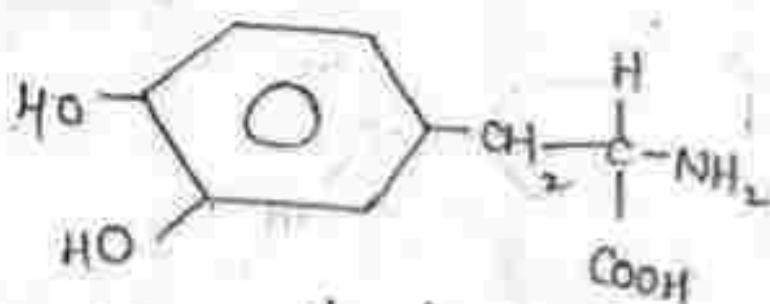
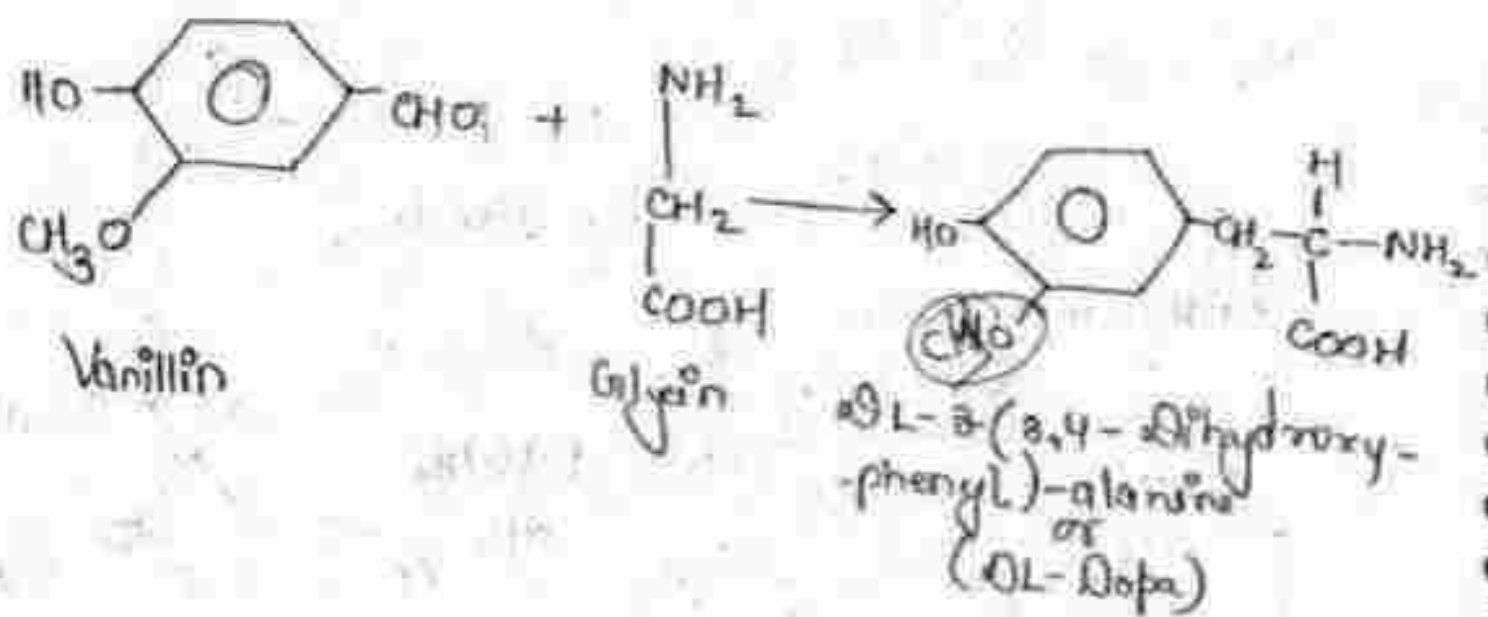
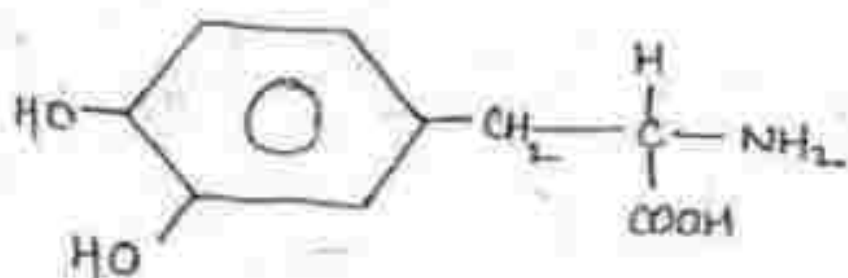
Diethyl malonic ester



Valproic acid

# Antiparkinsonism Drugs.

## 1. Levodopa



Levodopa

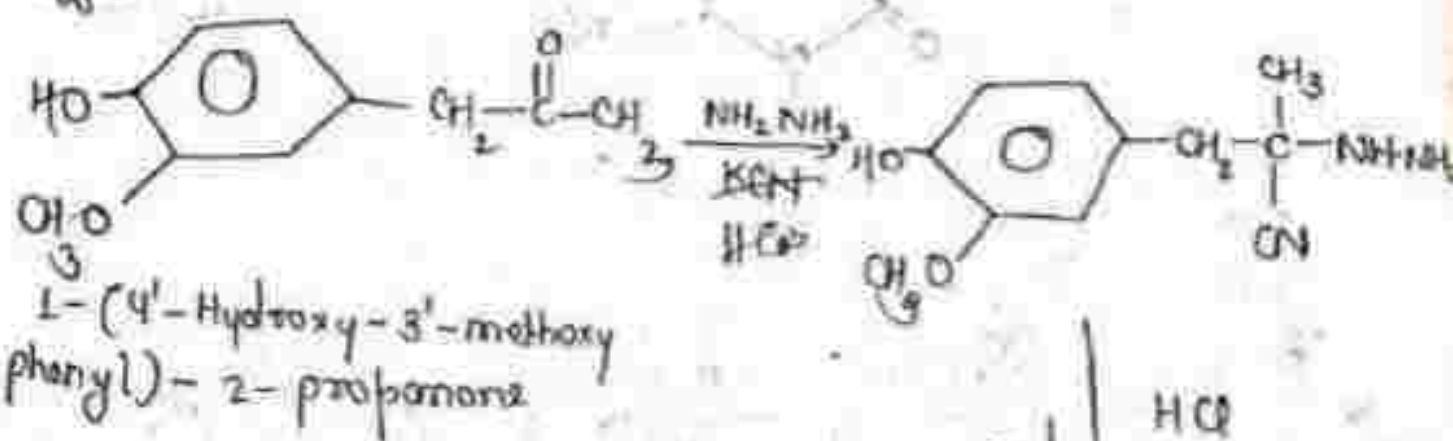
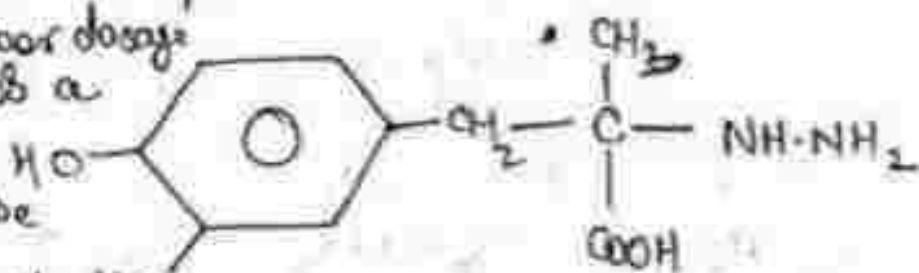
- i- Conversion to L-3-acetyl-3-methoxy-4-acetyl-phenylalanine
- ii- Resolution by α-phenylethylamine
- iii- Hydrolysis with aqueous NaOH

Use

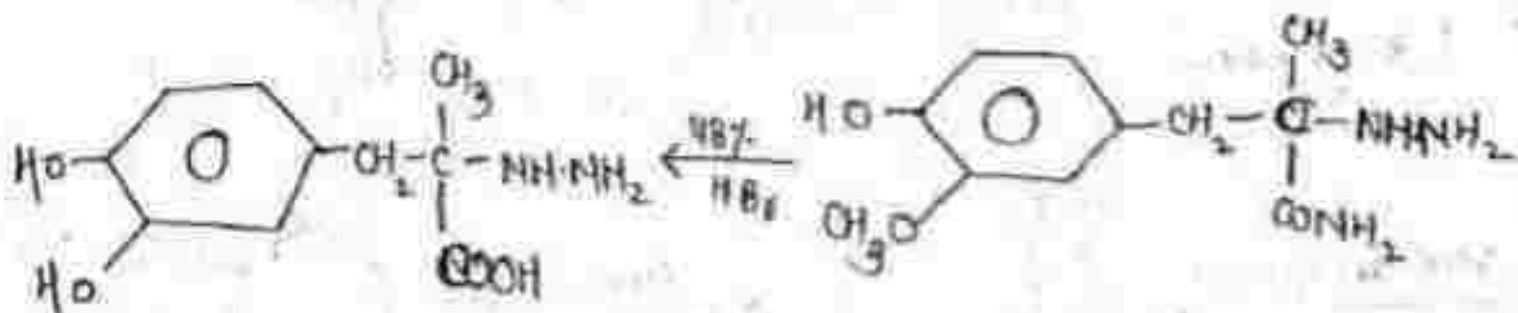
## 2- Carbidopa

E.

Carbidopa with levodopa enable a lower dosage of levodopa is a more rapid response to be obtained & to decrease side effect.



Cold  
HCl  
Glc



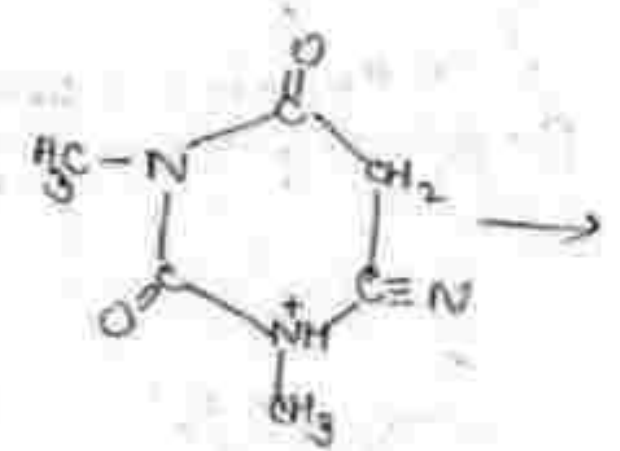
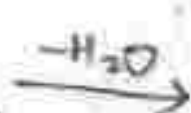
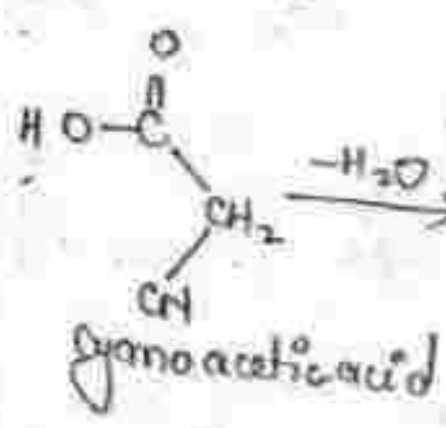
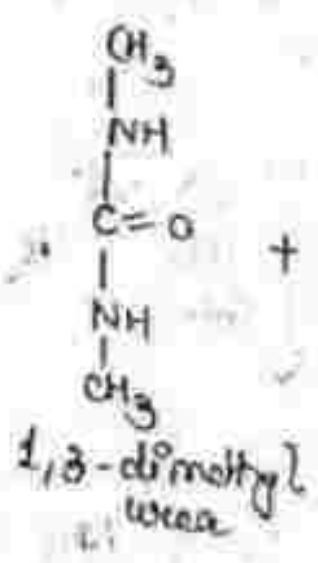
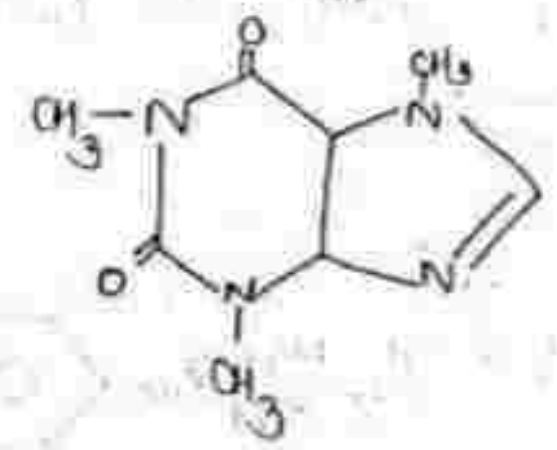
Carbidopa

# CNS stimulants

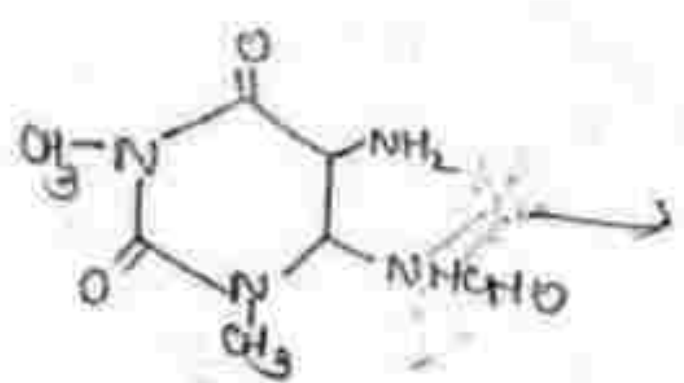
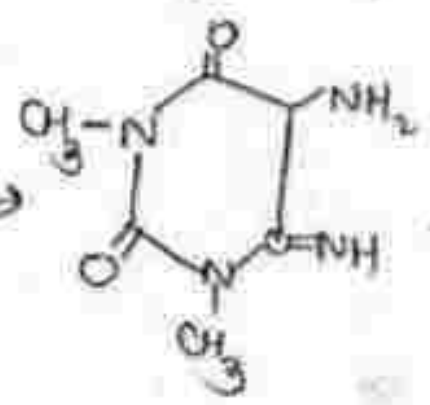
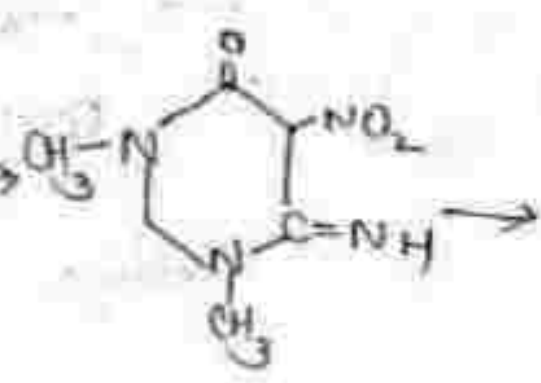
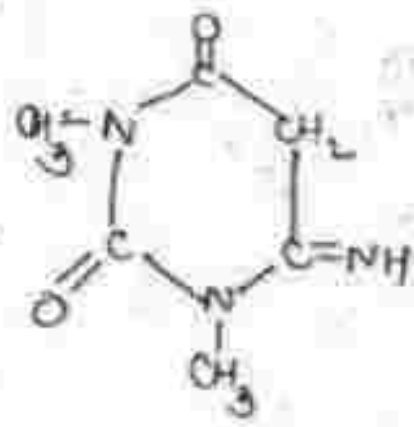
## Uses

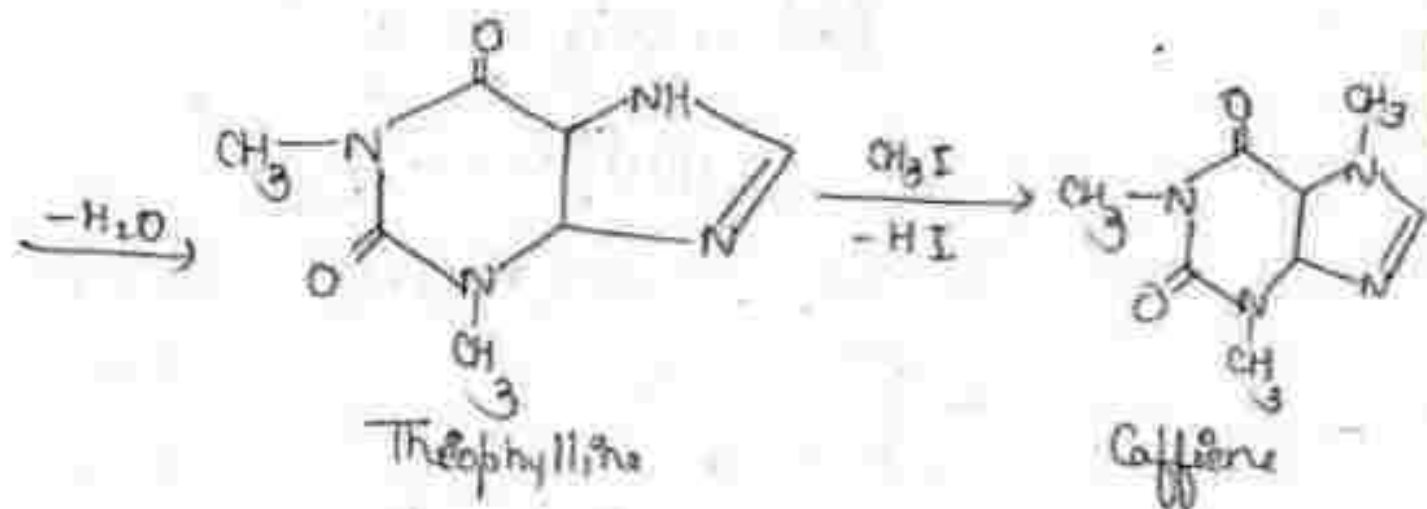
### 1. Caffeine

- ① Helps in stimulation of respiratory centres
- ② It is used as diuretic

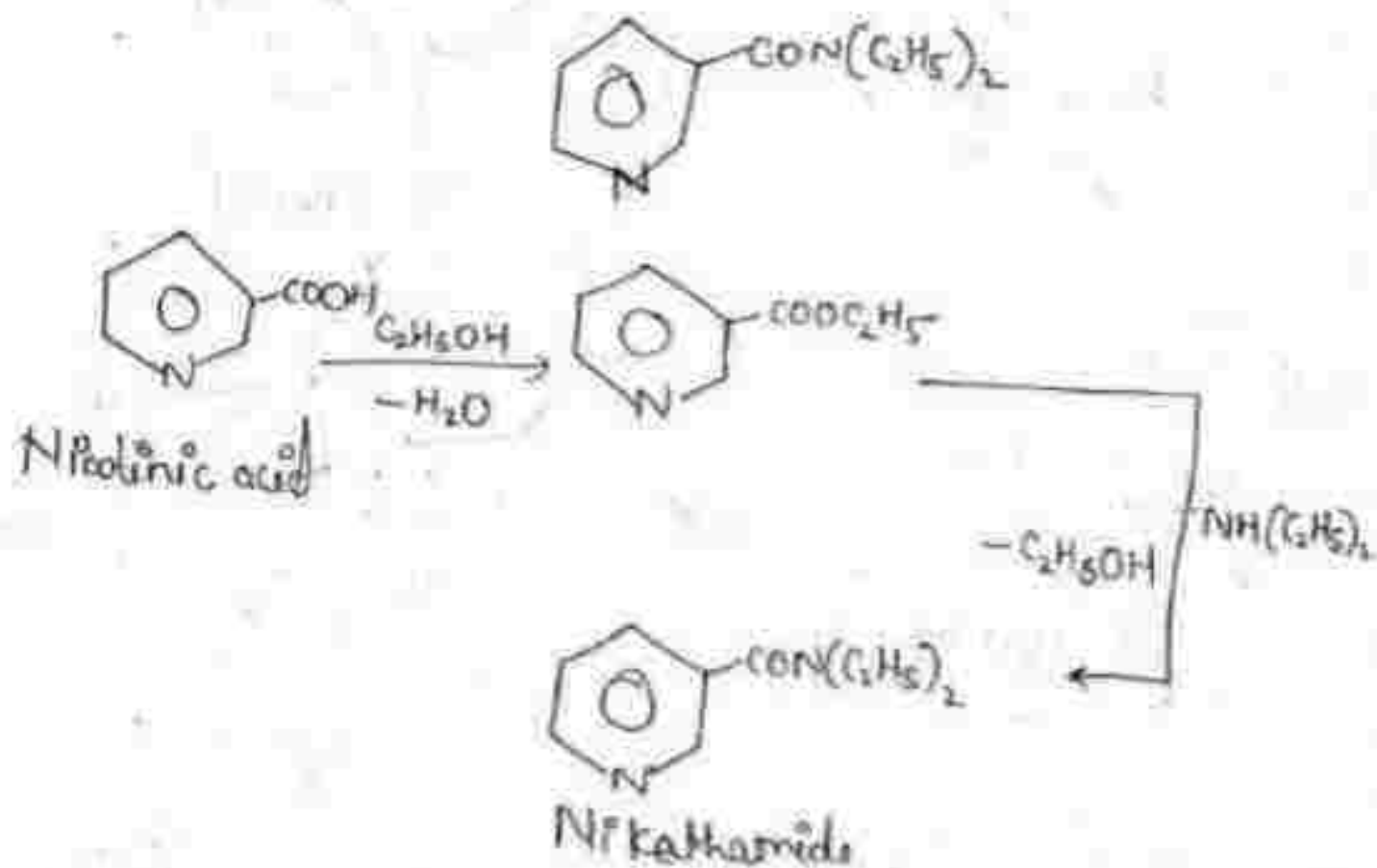


rearrangement





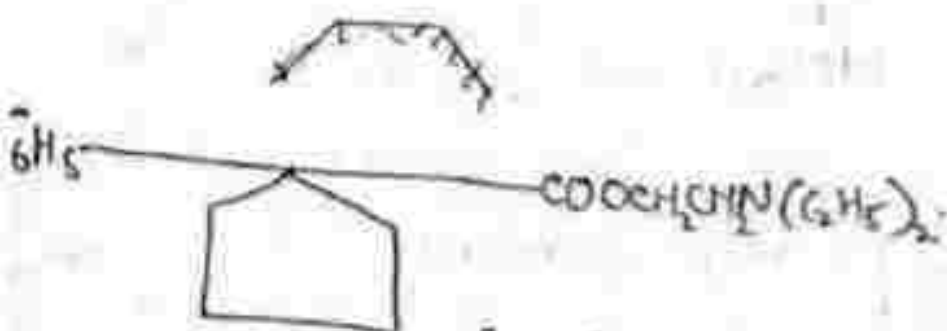
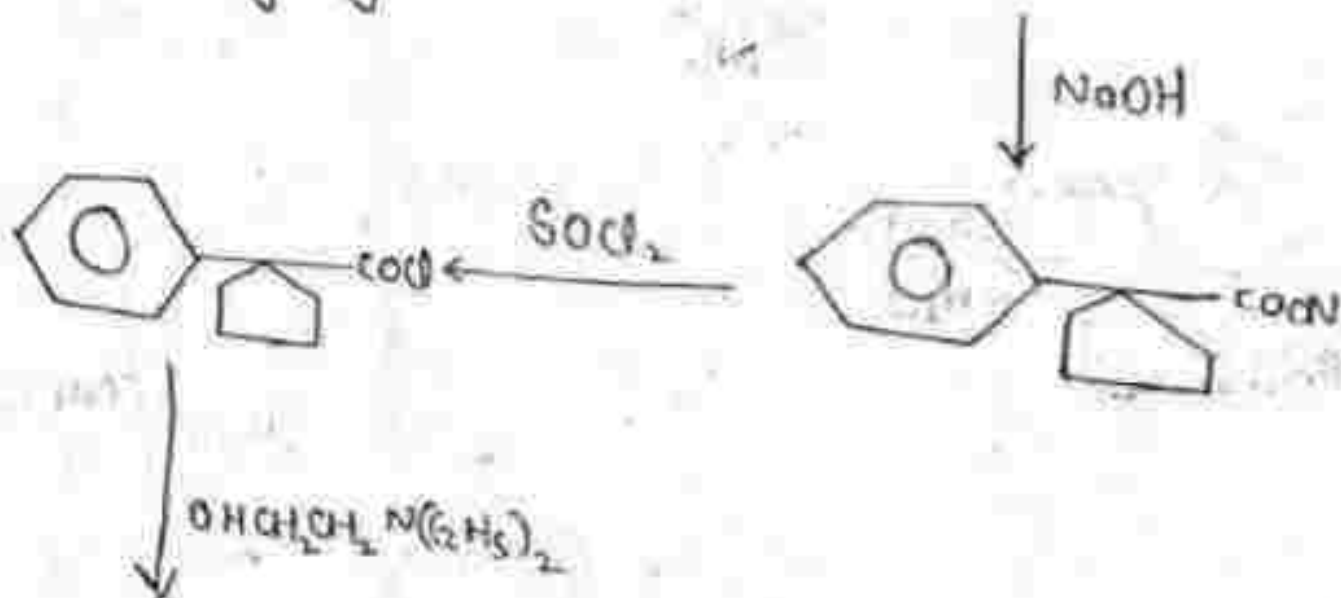
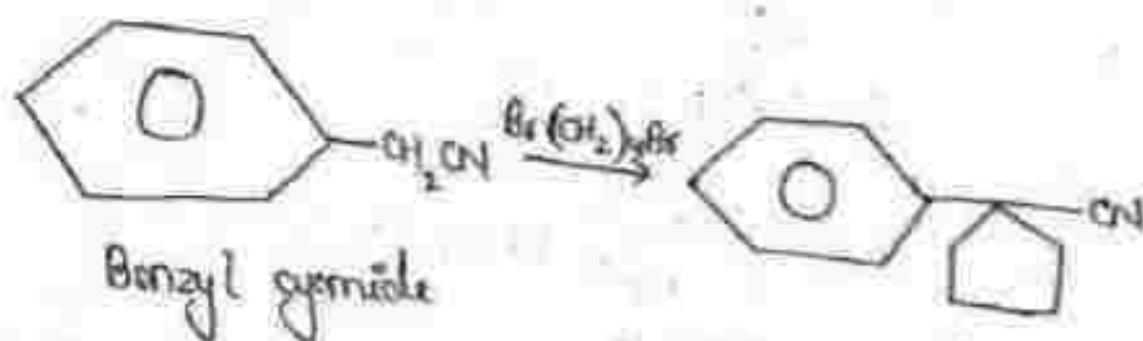
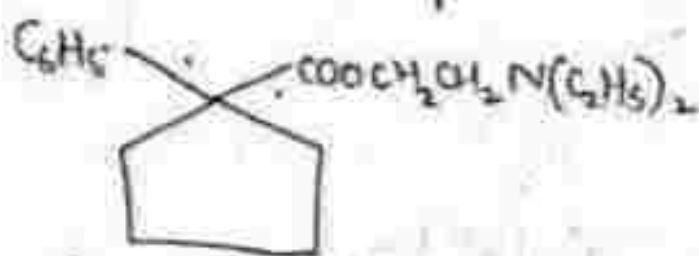
## 2. Nikethamide



Use :- Used as respiratory stimulant.

# Antitussives

## 1. Cloquiphon

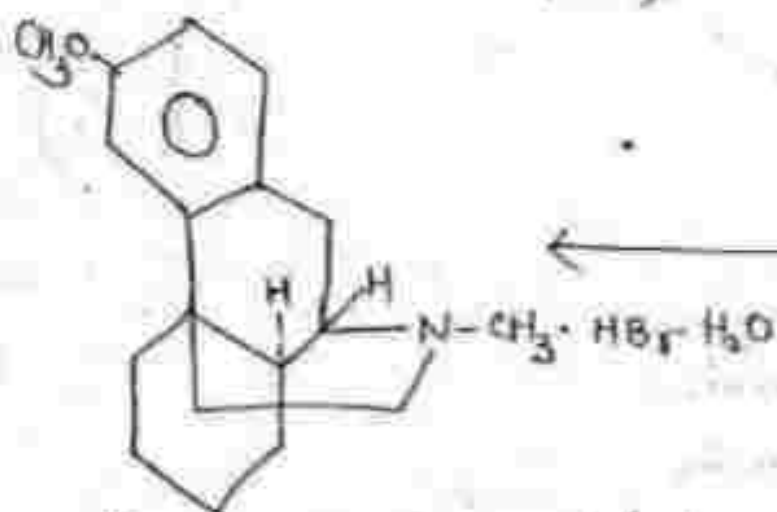
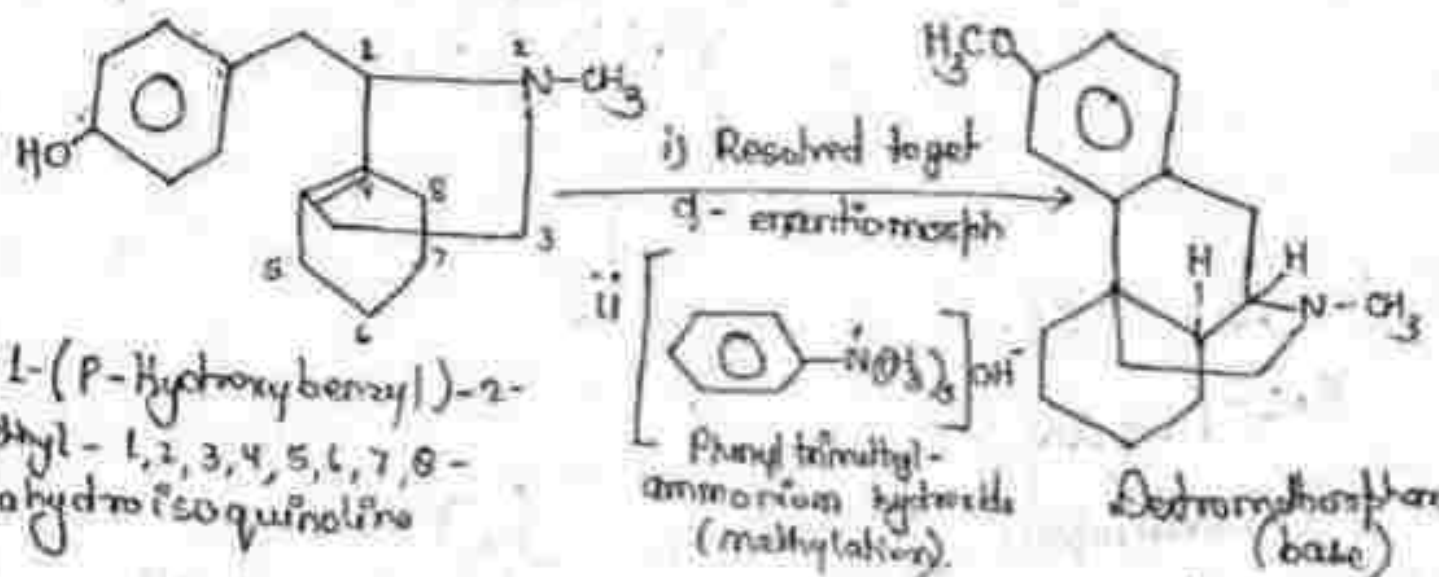
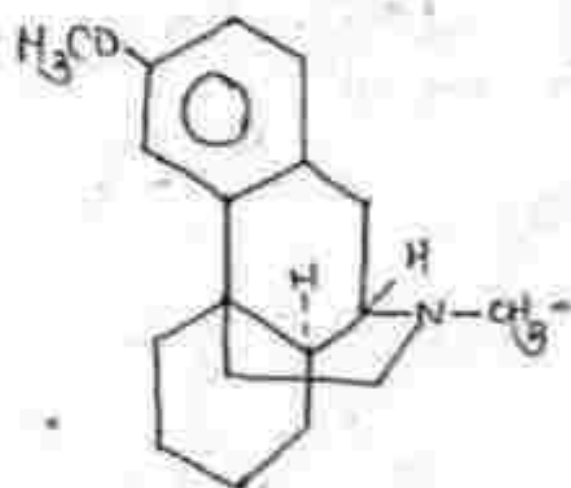


## Cloquiphon

### Uses

- ① Used in respiratory disease
- ② " " treatment of organophosphorus poisoning
- ③ as cough suppressant.

## 2. Dextromethorphan



Dextromethorphan Hydrobromide

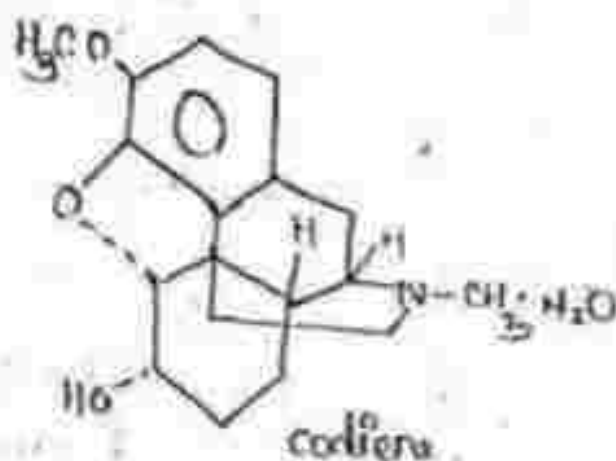
# Classifications

## Antitussives

It may be classified as:-

i - Opioid :-

Ex:- Codeine



ii - Nonopioid :-

Ex:- i Noscipine

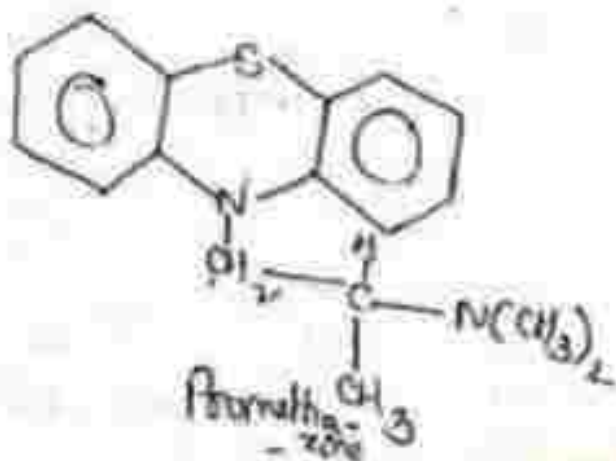
ii - Dextromethorphan

iii - Caramphen



iii - Ant<sup>o</sup> Histamine

ex:- Promethazine

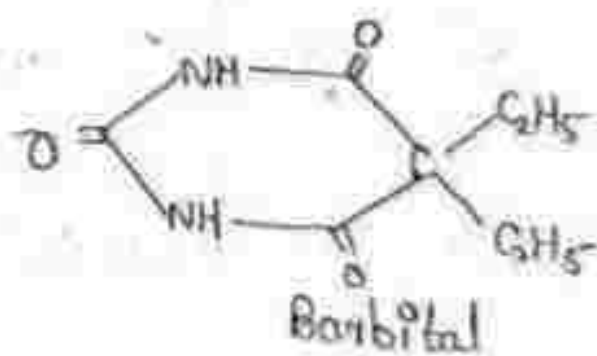


# Anticonvulsants

Classification based on chemical class:-

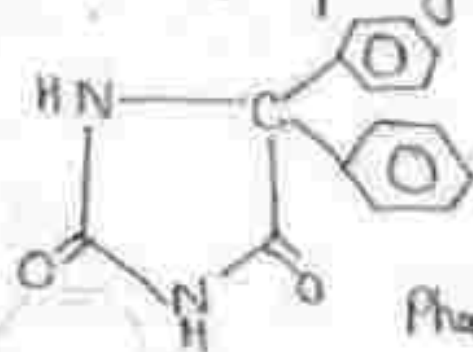
i- Barbiturates :-

Ex:- i Barbital, ii- phenobarbital, Methobarbital etc.  
H Phenobarbital



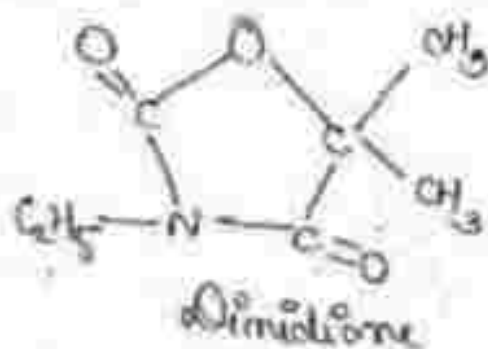
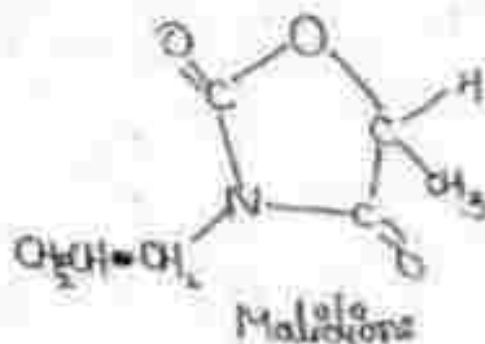
ii- Hydantoins

Ex: Phenytoin, ethotoin, mephentyoin



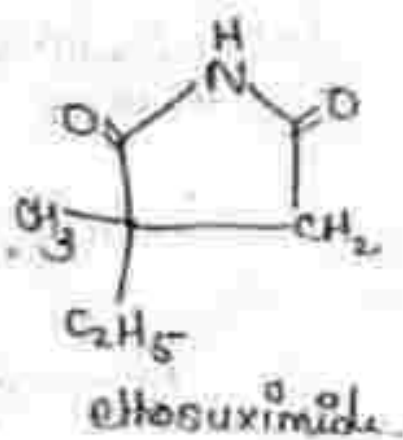
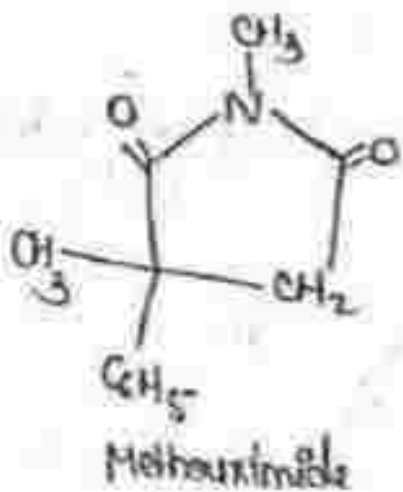
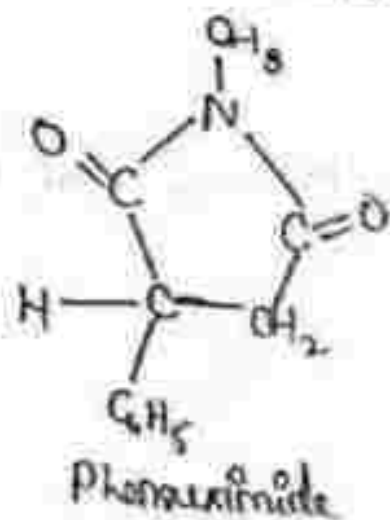
iii- Oxazolidinedione

Ex: Trimethadione, paramethadione, phenylethylhydantoin, malidione, Dimidione.



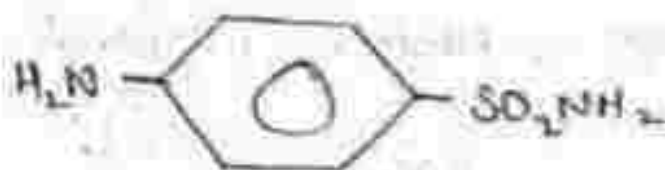
#### 4- Succinimides

Ex:- Phorbuximide, Methauximide, Ethosuximide



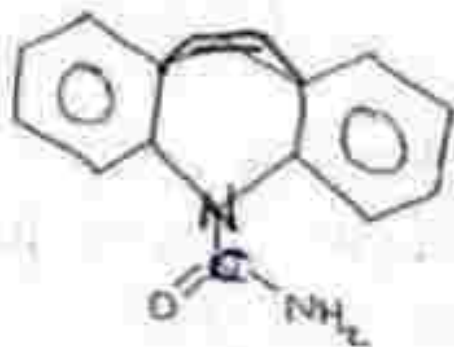
#### 5- Sulphonamides:-

Ex:- Sulphanilamide



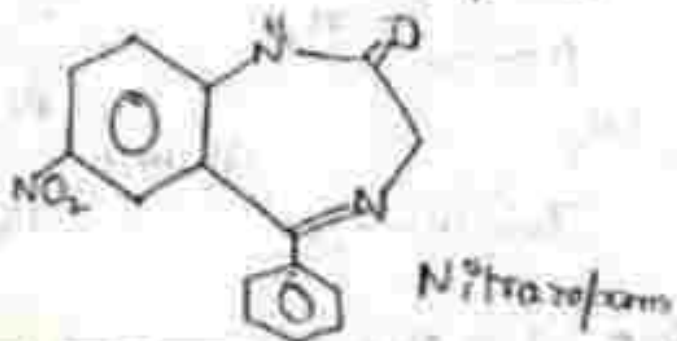
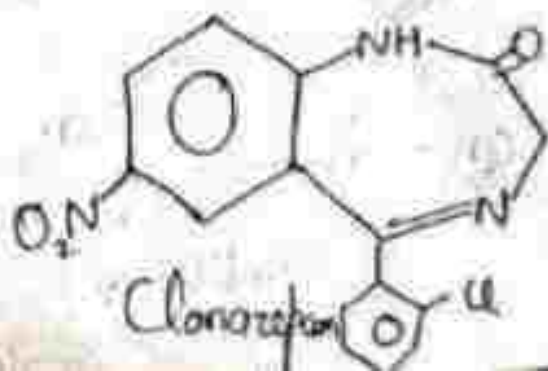
#### 6- Iminostilbines:-

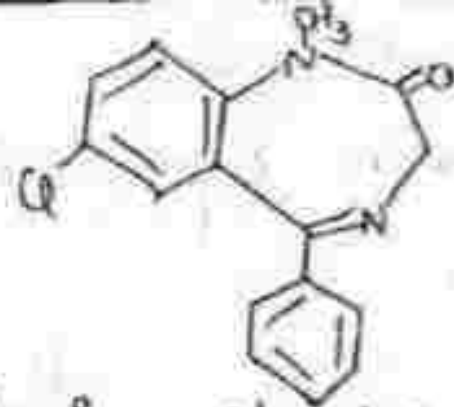
Ex:- Carbamazepine



#### 7 Benzodiazepines

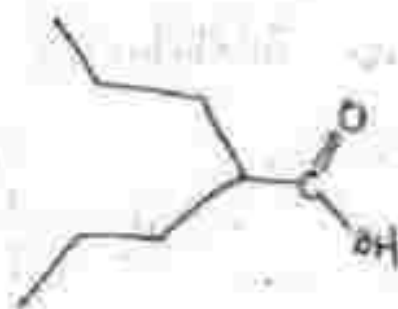
Ex:- Clonazepam, diazepam, clonazepam, nitrazepam



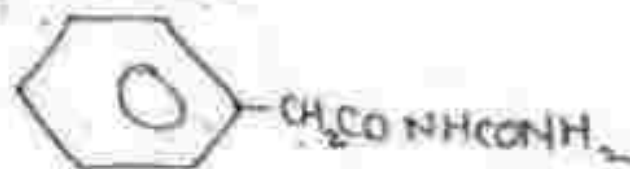


Diazepam

8- Valproic acid derivatives  
Ex:- Valproic acid



9- Miscellaneous  $\rightarrow$  Semicarbazones :-  
Ex: Phenacetimide



\*B]. Based on their mechanism of Action :-

1- Enhancement of  $\text{Na}^+$  channel inactivation :-

Ex:- Phenytoin, Carbamazepine, Lamotrigine & Valproate

2- Enhancement of GABA synaptic transmission :-

i- Agents acting on the GABA/ $\text{Cl}^-$  pore complex ex:- Flunitrazepam

ii- Agents that potentiate GABA :-

a- GABA transaminase inhibitors :-  $\text{b}^+$  Vigabatrin

b- GABA reuptake inhibitors :- tiagabine

iii- Agents that bind to benzodiazepine receptors :- Clobazam, flumazenil

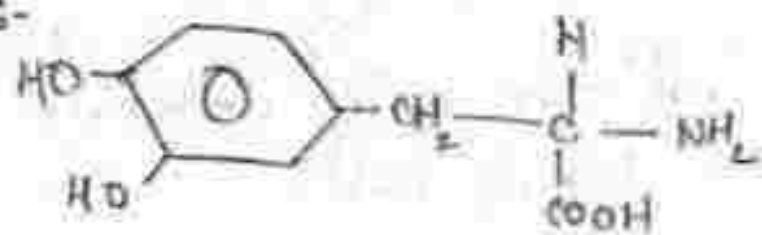
iv- " " " " barbiturate "  $\delta$ -Phenobarbital, mephobarbital

## Antiparkinsonism

I- Drugs affecting Brain Dopaminergic System:-

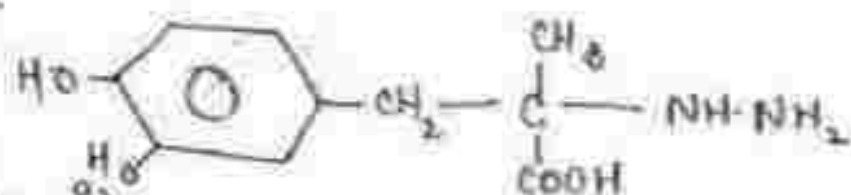
i- Dopamine precursors.

Ex: Levodopa :-



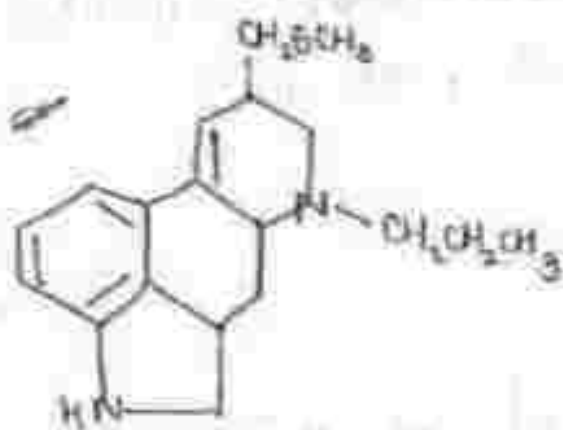
ii- Peripheral Decarboxylase Inhibitors :-

Ex: Carbidopa :-



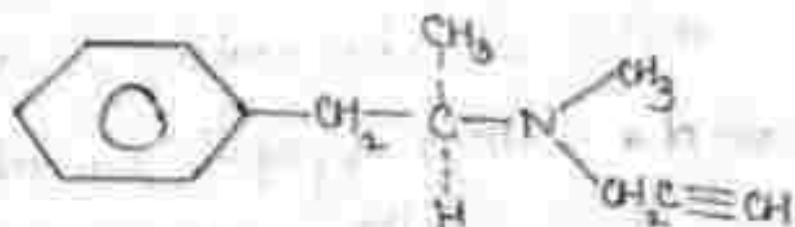
iii- Dopaminergic agonist :-

Ex: Pergolide



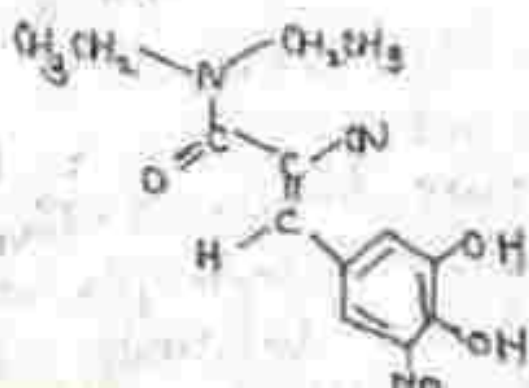
iv- MAO-B Inhibitors

Ex: Selegiline

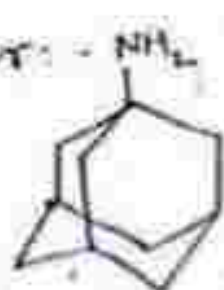


v- COMT Inhibitor

Ex: Entacapone



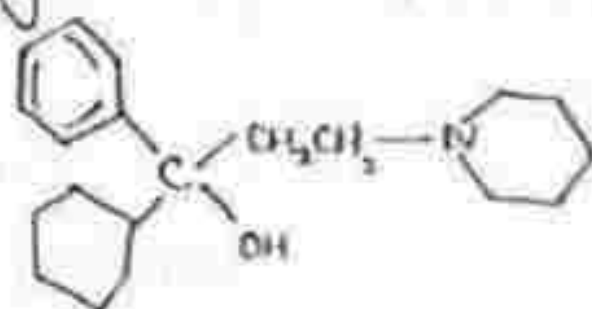
vi - Dopamine facilitator: -  $\text{NH}_2$   
Ex: Amantadine



2- Drugs affecting Brain cholinergic system.

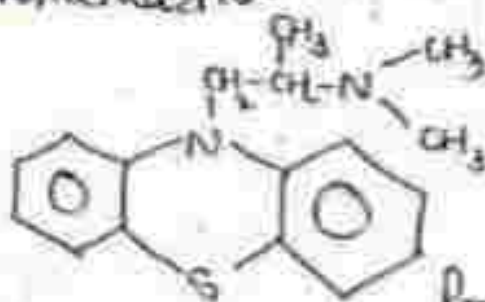
i - Central Anticholinergics:

Ex: - Benzhexol



ii - Antihistaminics:-

Ex: - Orphenadrine, Promethazine



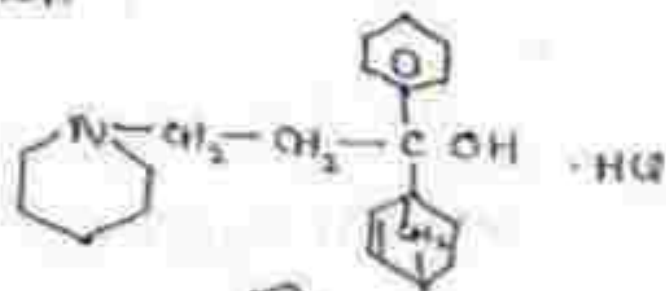
Promethazine

OR

Classification

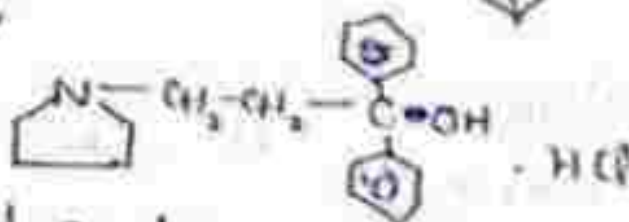
① Piperidine analogues

Ex: - Piperiden HCl



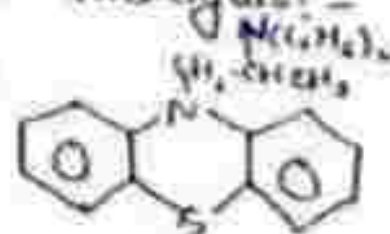
② Pyrrolidine analogues

Ex: - Procyclidine HCl



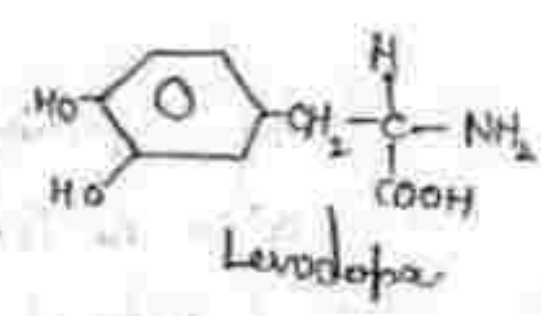
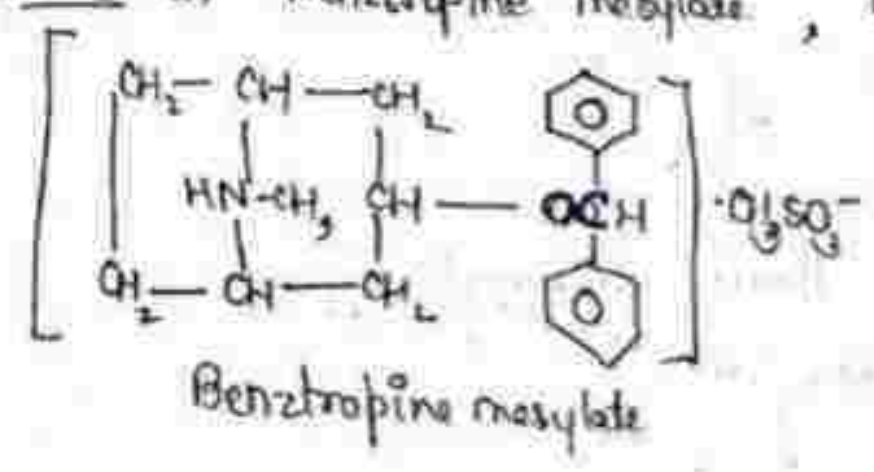
③ Phenothiazine derivative analogues:-

Ex: - Ethopropazine HCl



④ Miscellaneous

Ex: Benztropine mesylate, Levodopa



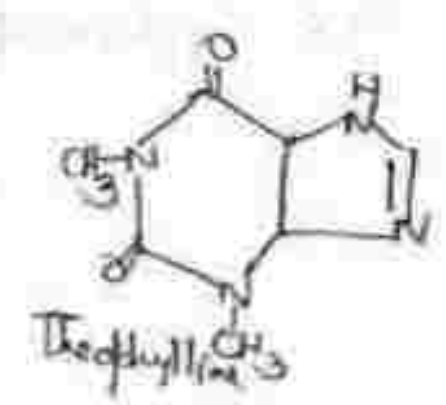
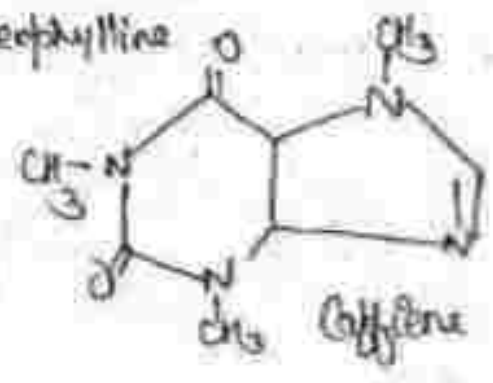
10-11

CNS Stimulants

Classification

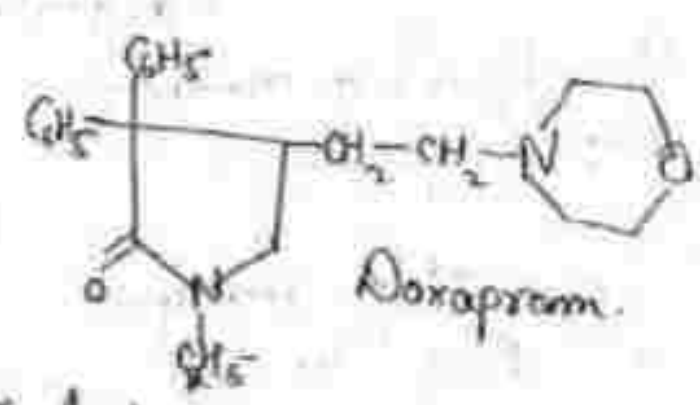
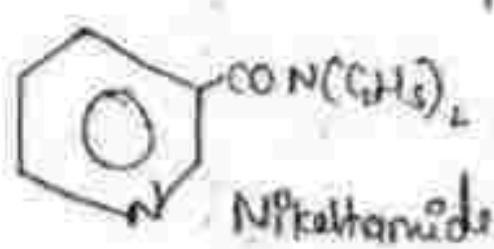
1- Xanthine Derivatives

Ex: Caffeine, theophylline



2) Analeptics:

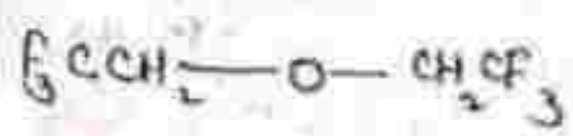
Ex: Nikethamide, Doxapram



③ Miscellaneous

Ex: Fluorethyl

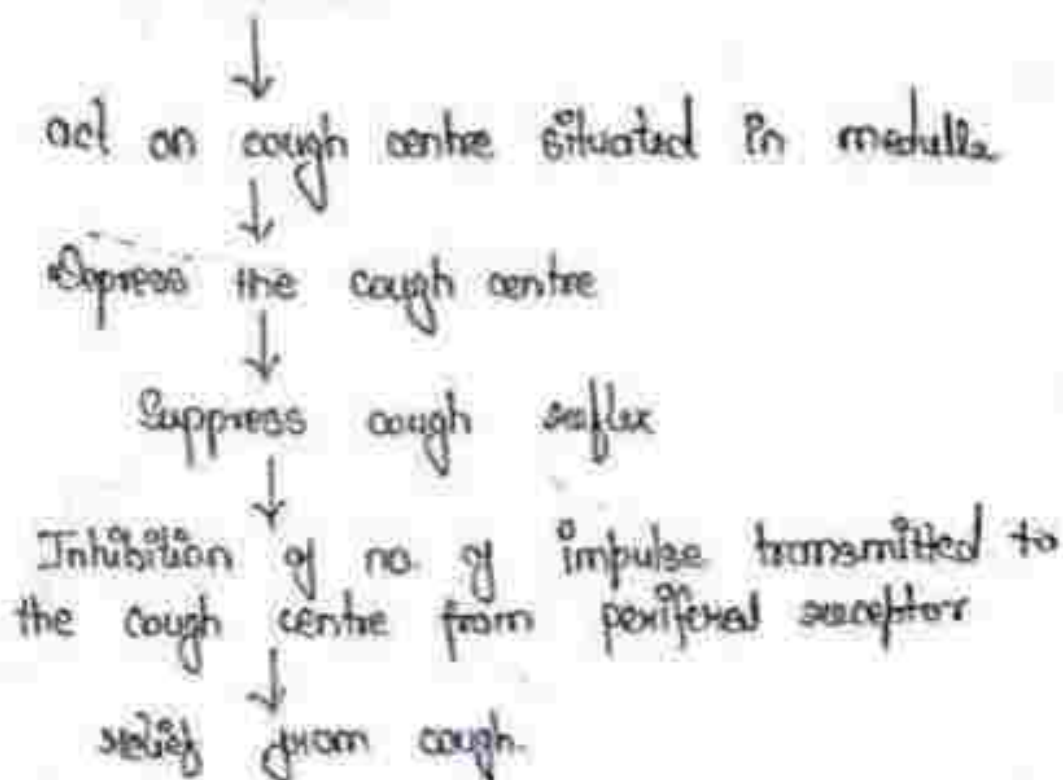
CNS stimulants:-



## Mode of Action

### Antitussives Drugs

Antitussives



1. Cramiphen      +      Caramiphen      2. dextromethorphan

## Mode of Action Anticonvulsants

① Drugs (acetazolamide)

↓  
Promote elimination of  
excess  $\text{CO}_2$  from brain  
& blood circulation

↓  
Stimulates nerve  
functioning

↓  
recovery

② Drugs (phenobarbital, diphenyl  
hydantoin)

↓  
↑ level of GABA in brain

↓  
Causes non-specific  
depression of CNS function

↓  
Control release of  
neurotransmitter

↓  
recovery

③ \* Drugs (valproic acid)

↓  
Act on Glutamic acid the  
enzyme GABA transaminase  
& semialdehyde dehydrogenase  
responsible for metabolism  
of GABA

↓  
Inhibit the enzyme responsible  
for metabolism of GABA

↓  
↑ the activity of Glutamic acid  
decarboxylase (GAD) responsible  
for GABA synthesis

↓  
↑ GABA synthesis

↓  
↑ GABA level in brain → recovery

④ \* Drugs (Phenytoin,  
Carbamazepine)

↓  
Act on voltage-gated  
 $\text{Na}^+$  channel

↓  
Block the  $\text{Na}^+$  channel

↓  
Inhibit the influx of  
 $\text{Na}^+$  channel

↓  
↓ the intracellular  $\text{Na}^+$  ions

↓  
Prevents depolarisation

↓  
↓ electrical excitability

↓  
recovery

## ⑥ Drugs (Ethosuximide)

↓  
Act on T-type calcium channel.

↓  
Block the channel

↓  
reduces the low-threshold  $Ca^{2+}$  currents in T-type  $Ca^{2+}$  channels the thalamic neurons.

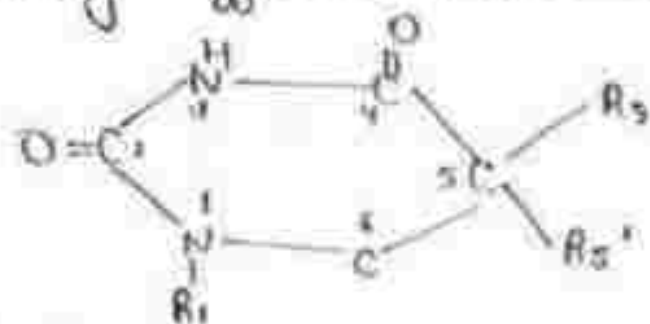
↓  
Prevents generation of the absence seizures.

## SAR of Anticonvulsant drugs

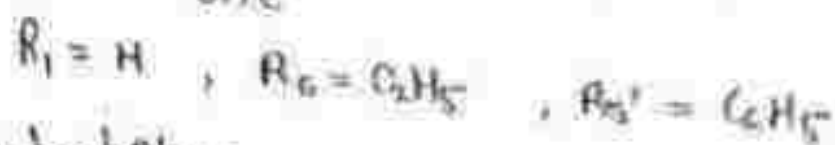
### 1- Anticonvulsant barbiturates

- ⇒ Barbiturates as a class of drugs mostly possess sedative and hypnotic properties. Suprisingly only a few of them really show anticonvulsant characteristics.
- ⇒ The most commonly employed anticonvulsants are:- phenobarbital, mephobarbital & methobarbital. of which phenobarbital is the drug of choice & is used in all the three type of epileptic seizures i.e., grandmal, petitmal & psychomotor.
- ⇒ Mephobarbital loses N-methyl group through metabolism & gets readily converted to phenobarbital.
- ⇒ Methobarbital is mostly demethylated to barbital in vivo.
- ⇒ Also it possesses more sedating property than phenobarbital, it could be safely recommended for grand mal seizures.

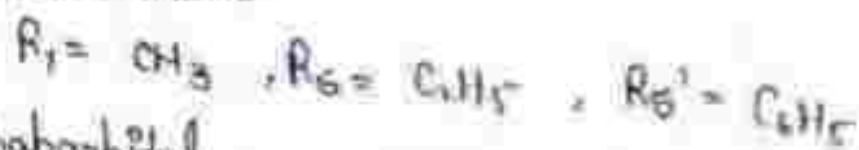
The clinically effective anticonvulsant barbiturates are :-



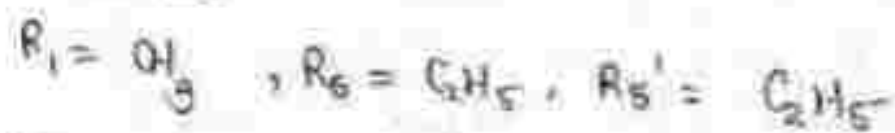
Ex: ① Phenobarbitone



② Mephobarbitone



③ Methobarbital



SAR :-

→ The drug should have the following properties :-

- ① Lipid solubility
- ② Acidic nature.

Substitution at C<sub>5</sub> :-

- 1- When any one of the substituent is phenyl at C<sub>5</sub> , then optimal activity is observed.

Ex:- Methobarbital is less active than phenobarbital & mephobarbital.

- 2- If both the substituents are phenyl at 5<sup>th</sup> C<sub>5</sub> position then , ↓ activity.

Ex:- The 5,5 - diphenyl derivative has less activity than phenobarbitone.

- 3- One alkyl substitution at 1 C<sub>5</sub> & C<sub>6</sub> → ↓ activity.

- 4- The presence of triple or double bond i.e., unsaturation at C<sub>5</sub> → ↓ activity.

## Substitution at $C_1$ & $C_2$

⇒ Alkyl substitution at  $C_1$  &  $C_2$  position  $\rightarrow$  ↓ activity.

## Substitution at $C_2$ :-

⇒ Replacement of 'O' by 'Na' or 'S'  $\rightarrow$  ↑ activity.

⇒ 'Na' gives more activity than 'S'.

## 2. Hydantoins

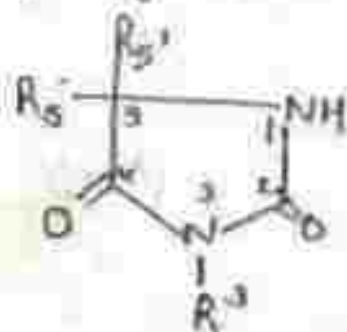
⇒ The concept that antiepileptics need not impair consciousness is emerged with the discovery of the most extensively used antiepileptic agent phenytoin in 1938.

⇒ It is a non-sedative structural relative of phenobarbital.

⇒ Since then, many hydantoins were synthesized and were evaluated for their antiepileptic activity.

⇒ The hydantoins are most effective against grand mal while they remain ineffective against partial activity. The clinically used hydantoins are:- Phenyloethylhydantoin, phenytoin, mephentyoin, Ethotoin.

SAR



Hydantoin

	$R_3$	$R_4$	$R_5'$
Phenyloethyl hydantoin	H	$C_6H_5$	$C_6H_5$
phenytoin	H	$C_6H_5$	$C_6H_5$
Mephentyoin	$CH_3$	$C_6H_5$	$C_6H_5$
Ethotoin	$C_2H_5$	H	$C_6H_5$

Substitution at 5<sup>th</sup> position:-

- ⇒ One phenyl ring is essential is at 5<sup>th</sup> position for activity.
- ⇒ If both the substituents at 5<sup>th</sup> position are phenyl or aromatic ring substituents → ↑ activity.

Ex:- Phenytoin is more active than Mephenytoin.

- ⇒ Alkyl substitution at position 5 may contribute to sedation i.e., ↓ activity.

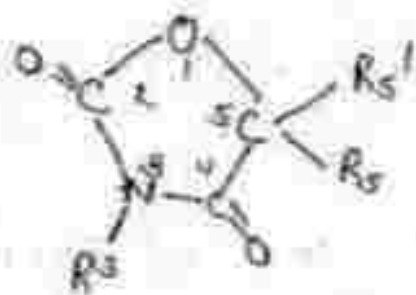
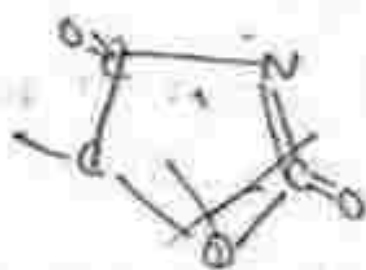
Substitution at 3<sup>rd</sup> position:-

- ⇒ If any substituent is present at 1 or 3 position, it will affect the activity. It will either increase or decrease the activity depending upon substitution.

### 3. Oxazolidinediones

- ⇒ The oxazolidine 2,4-diones were originally developed as hypnotics or analgesics but were introduced into anticonvulsant therapy b/w 1946-1948.
- ⇒ These compounds are isosterically related to the hydantoins differing only in that an 'o' atom is replaced by NH group.
- ⇒ Trimethadione, paramethadione & Mephadione are the clinically used drugs from this class.
- ⇒ The oxazolidinediones are effective in the treatment of partial seizures but if used alone, are ineffective against other types of epilepsy.

## SAR



Ex:

	$R_3$	$R_5$	$R_{5'}$
Trimethadione	$\text{CH}_3$	$\text{CH}_3$	$\text{CH}_3$
Paramethadione	$\text{CH}_3$	$\text{CH}_3$	$\text{CH}_3$
Malidione	$\text{CH}_2\text{CH}=\text{CH}_2$	$\text{CH}_3$	$\text{H}$
Dimedione	$\text{C}_2\text{H}_5$	$\text{CH}_3$	$\text{CH}_3$
5,5 - Diphenylloxazolidine 2,4-dione	$\text{H}$	$\text{C}_6\text{H}_5$	$\text{C}_6\text{H}_5$

① The lower alkyl substituents on  $\text{C}_5$  tend towards antipetimal activity while aryl substituents towards antigrandmal activity.

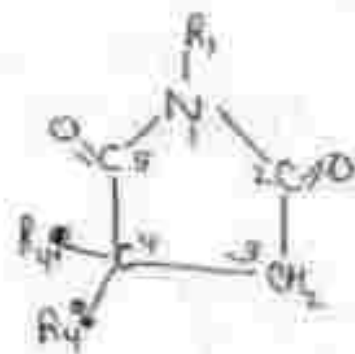
Ex: Malidione & dimedione are active against petitmal & epilepsy while 5,5-diphenylloxazolidine 2,4-dione is active against grandmal epilepsy.

② N-alkyl substitution does not affect activity.

## 4. Succinimide

- ⇒ Though less potent, succinimides have enjoyed more success over oxazolidinones since they possess less significant side effects.
- ⇒ These drugs are moderately effective against a petimal seizures but remain ineffective against grandmal.
- ⇒ The first drug from this series, Phensuximide introduced in 1953 is the weakest & now rarely used.
- ⇒ It is followed by methsuximide (1958) and ethosuximide (1960).

### SAR:-



### ④ Ex:

	$R_1$	$R_{4''}$	$R_{4'}$	$R_4$
Phensuximide	$\text{C}_6\text{H}_5$	H	$\text{CH}_3$	$\text{CH}_3$
Methsuximide	$\text{CH}_3$	$\text{C}_6\text{H}_5$	$\text{CH}_3$	$\text{CH}_3$
Ethosuximide		$\text{CH}_3$	$\text{CH}_3$	H

Substitution at 4<sup>th</sup> position:-

- ⇒ There must be one phenyl ring at  $C_4$  for activity.

Ex:- Methsuximide & Phensuximide are more active than ethosuximide.

Subst

- ⇒ If both the substituents at  $C_4$  are alkyl group then  $\rightarrow$  ↓ activity.

Substitution at 1<sup>st</sup> position:-

⇒ N-methylation decreases the activity.

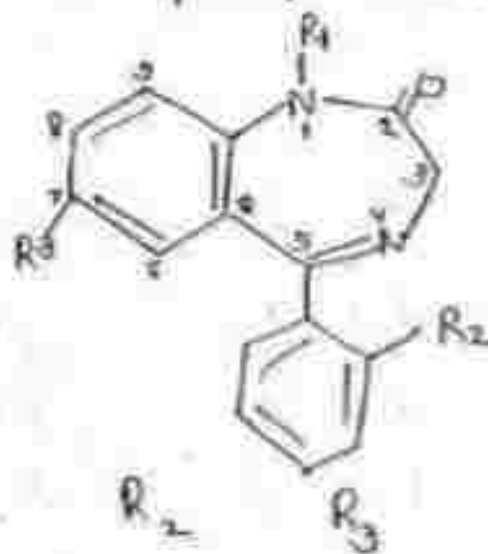
## 5. Benzodiazepines

⇒ Benzodiazepines were discovered by Leo Sternbach in 1956 at Roche Laboratories.

⇒ The benzodiazepines started their career primarily as sedative-anxiolytic drugs but established themselves also as effective antiepileptic drugs in recent yrs.

⇒ Chlordiazepoxide was the first clinically used (1960) antiepileptic agent from this class, followed by oxazepam, nitrazepam, diazepam & clonazepam.

SAR



	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>
Nitrazepam	H	H	NO <sub>2</sub>
Clonazepam	H	H	NO <sub>2</sub>
Diazepam	CH <sub>3</sub>	H	H

① A phenyl group at 5<sup>th</sup> position is necessary for activity. But only halogen substituents are allowed in the ortho position.

② The  $e^-$  withdrawing group or atom at  $\gamma^{\text{th}}$  position  $\uparrow$  the activity while  $e^-$  donating substituents at 1, 8 or 9 position  $\downarrow$  it.

③ The  $e^-$  withdrawing group at ortho or diaortho position at 5-phenyl  $\uparrow$  the activity while any substituent at meta or para position at 5-phenyl  $\downarrow$  the activity.

④ Methyl substitution at 1<sup>st</sup> position  $\uparrow$  the activity.

Toumann Goodmann common formula for anticonvulsant

# Mode of Action of Antiparkinsonism

• Drugs (when given with levodopa)

↓  
Act on COMT enzyme  
(Catechol-O-methyl transferase)

↓  
Inhibit metabolism of dopamine

↓  
Increase the plasma conc.  
and duration of action of levodopa  
↓  
recovery

## Mode of action of Levodopa & Carbidopa

Levodopa

↓  
Passes BBB

↓  
Decarboxylated to  
DA (dopamine)

↓  
↑ formation of DA  
in motor regulatory  
area of CNS

↓  
restores depleted DA  
level

↓  
Improve symptoms of  
parkinsonism

Carbidopa

↓  
Inhibit the enzyme dopa  
decarboxylase

↓  
Retard the peripheral break-  
down of L-Dopa

↓  
Allow a greater fraction  
of L-Dopa to cross BBB

↓  
Produce higher DA level in  
central motor regulatory area

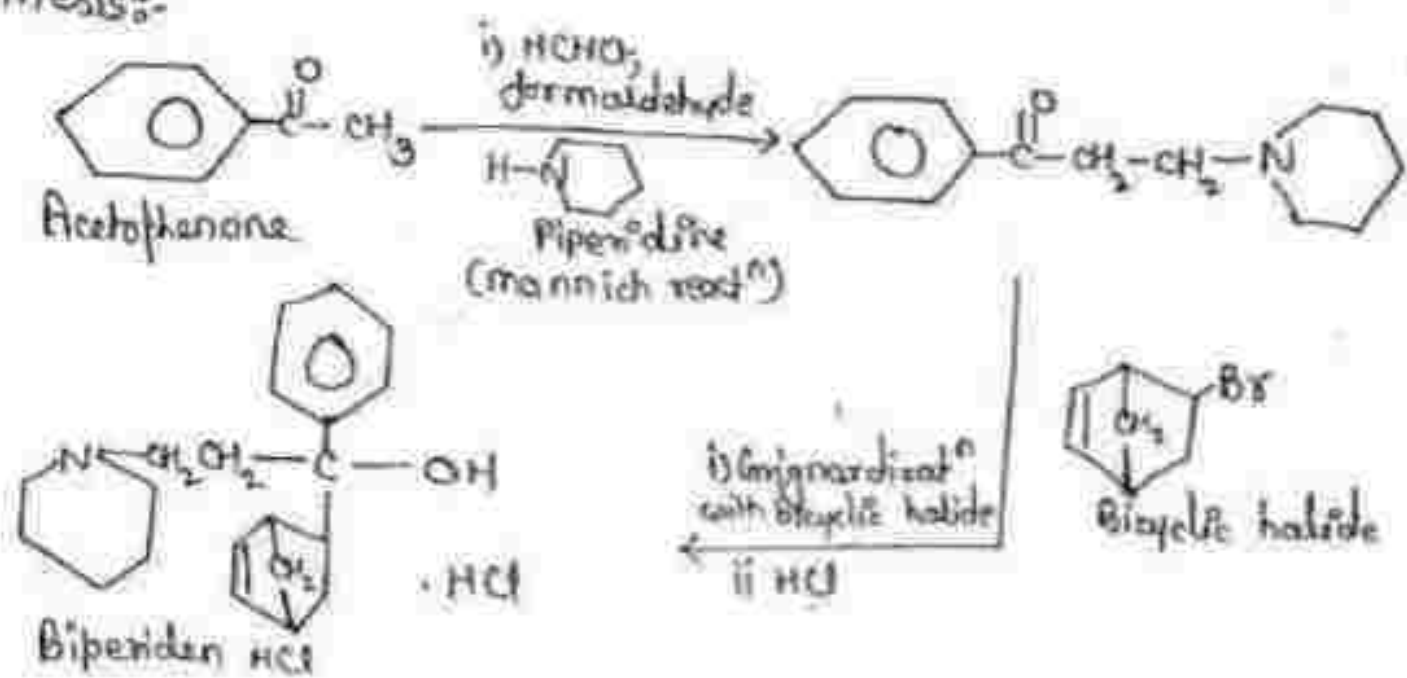
↓  
Improve symptoms of  
parkinsonism

Q = Discuss two classes of agents used to treat parkinsonism

Ans = 1- Piperidine analogues:- A few structural analogues of piperidine proved to be potent antiparkinsonism agents. Ex:- of this group:- Biperiden HCl, Gyrmine HCl & Trihexyphenidyl HCl.

Ex: Biperiden hydrochloride:-

Synthesis:-



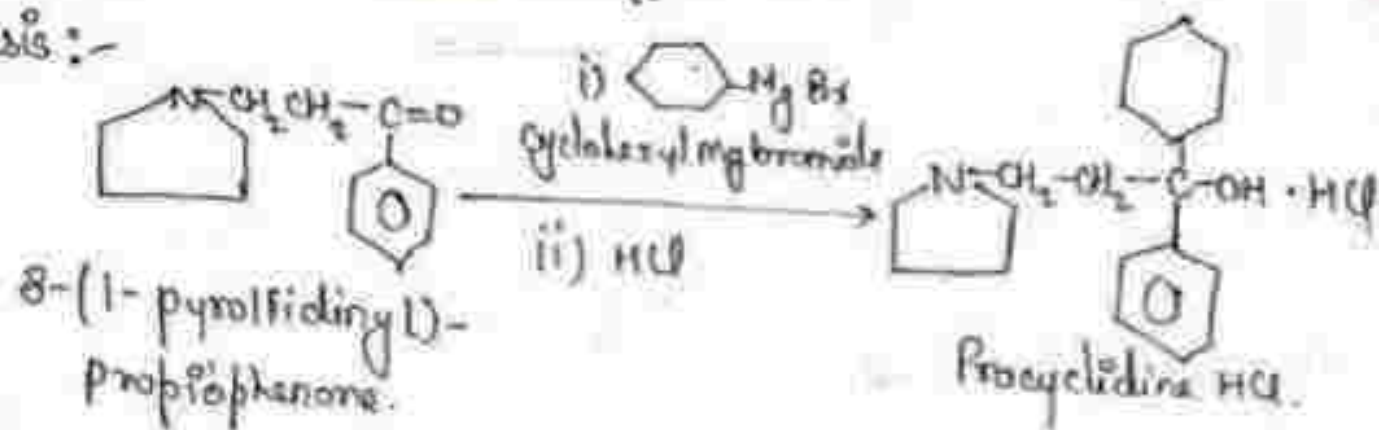
Uses:- Biperiden is used in treatment of parkinsonism, muscle rigidity, akinesia & tremor.

- 1) It is also employed in acute crises due to acetylcholinesterase inhibitors.
- 2) It is also used in lowering spasticity in pyramidal tract disorders.

2- Pyrrolidine Analogue:- The introduction of a 5-membered heterocyclic ring i.e., pyrrolidine instead of the 6-membered piperidine ring also gave rise to important antiparkinsonism agent.

Ex: Amantadine HCl.

Synthesis:-



Use:- for the treatment of postencephalitic parkinsonism.  
 Also used to

## Mechanism of Action

CNS Stimulants  
Drugs

act on  
receptor

↓  
ACh, Glycine or adenosine

↓  
Causes antagonism at receptor

↓  
Increase neuronal excitation / increase excitatory time duration

↓  
Stimulation occurs.

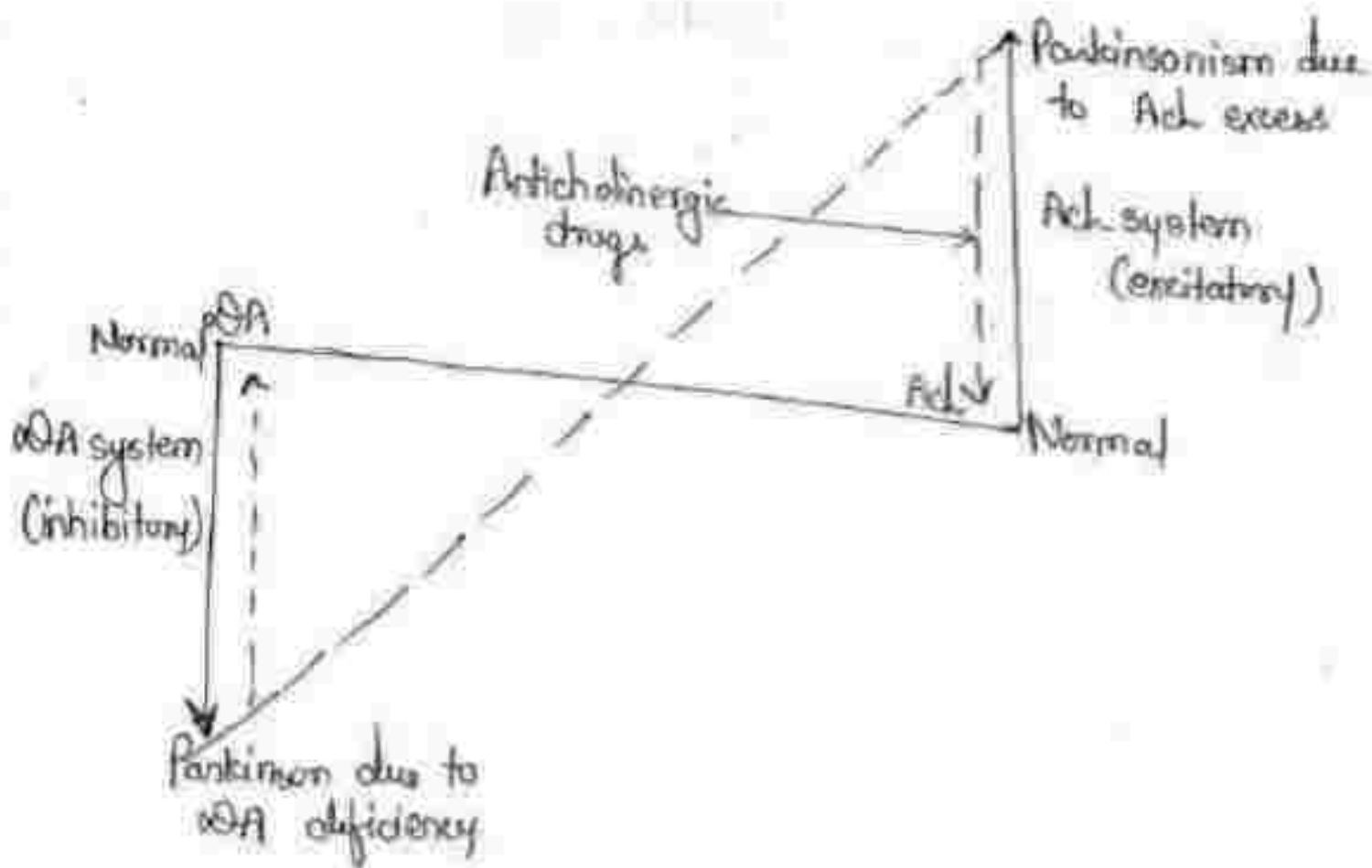


Fig. A diagrammatic representation b/w DA & ACh acting as antagonistic neurotransmitter.

## Mode of Action.

Nikethamide

↓  
act on chemoreceptor in carotid artery

↓  
stimulate chemoreceptors

↓  
stimulate respiratory centre in brain stem.

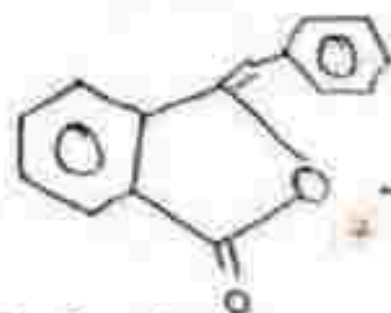
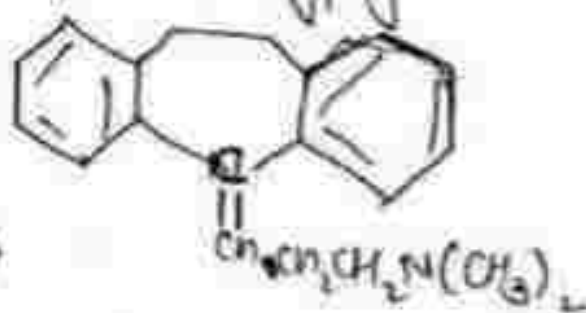
Caffeine



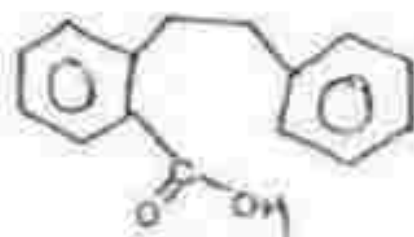
Unit - 11th

Neuroleptics

Amitriptyline

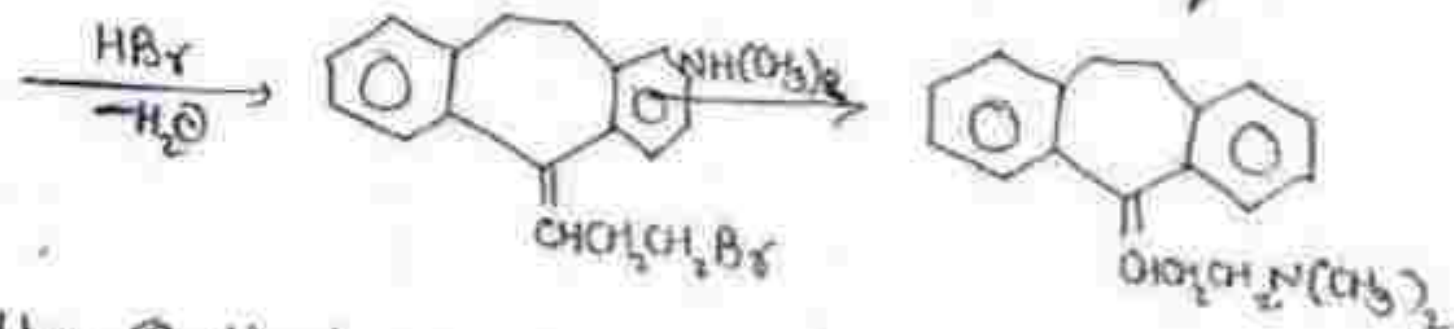
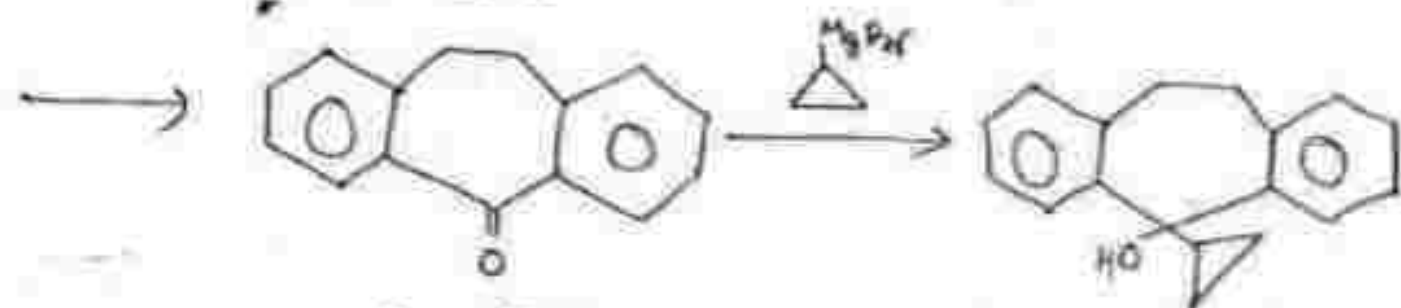


HI/Pd



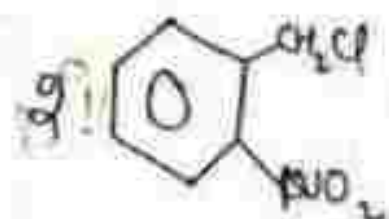
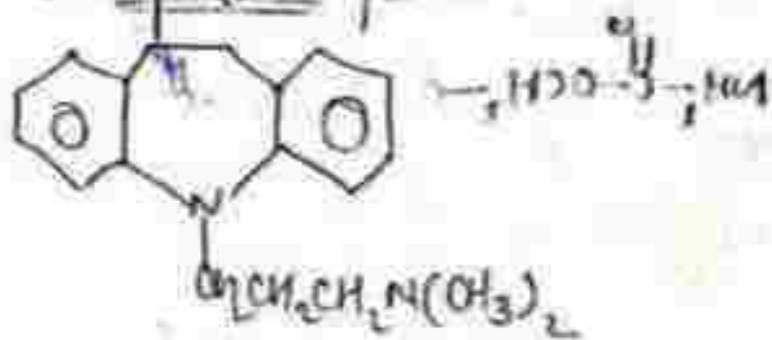
PPA

3-Benzilidene phthalide



Uses ① Used in anxiety.  
② " " depression.

# Impipramine

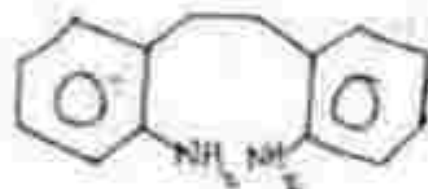


2-chloromethyl nitrobenzene

$\text{SO}_2/\text{HCl}$



amylalcohol



$-\text{NH}_3$



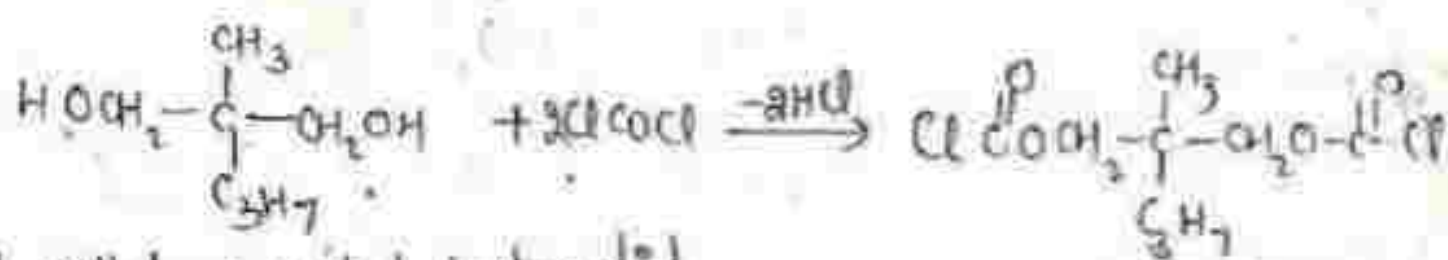
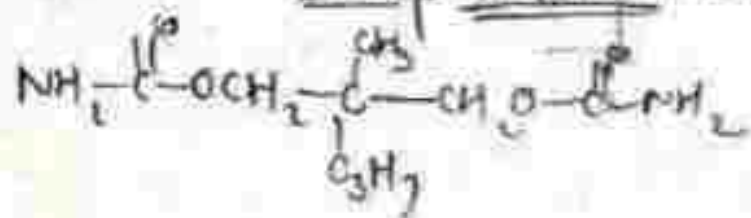
$\text{ClCH}_2\text{CH}_2\text{CH}_2\text{N}(\text{CH}_3)_2$



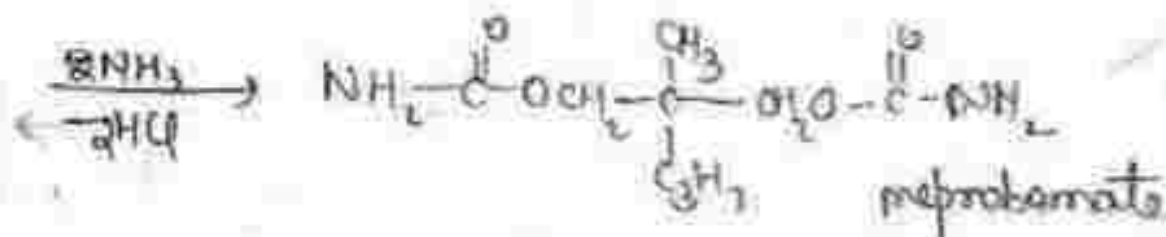
Imipramine

- Uses:
- ① Useful in treatment of depression.
  - ② In psychosis treatment.

## Meprobamate Antidepressant

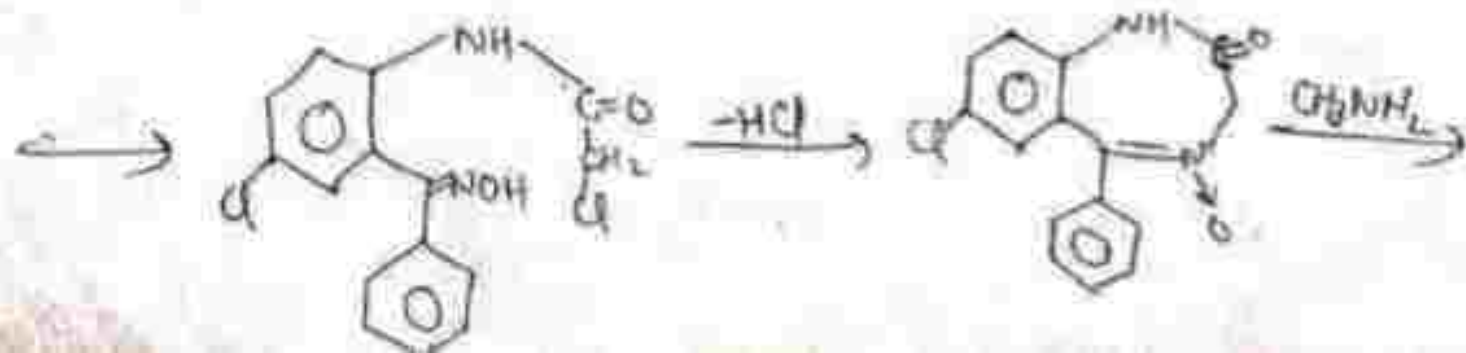
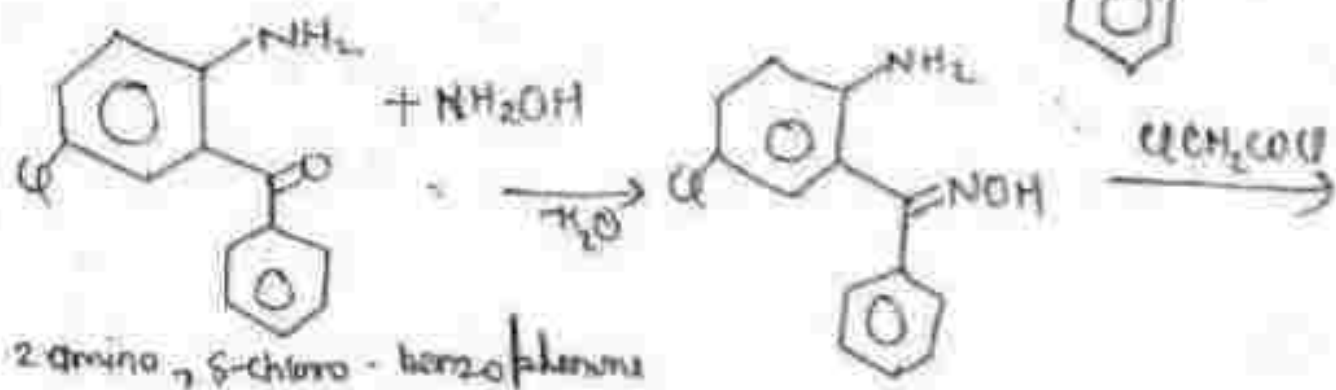
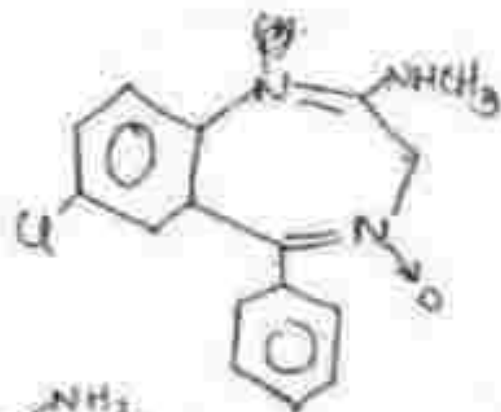


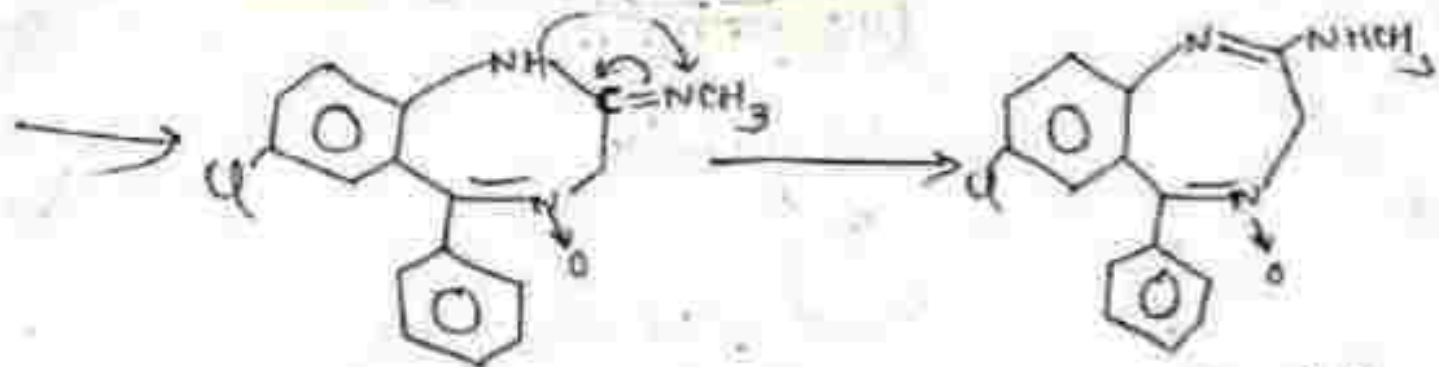
2-methyl - 2-propyl propanediol



Use:- 1- Act as anticonvulsant & muscle relaxant.  
2- Used as mild tranquilizer in anxiety & tension.

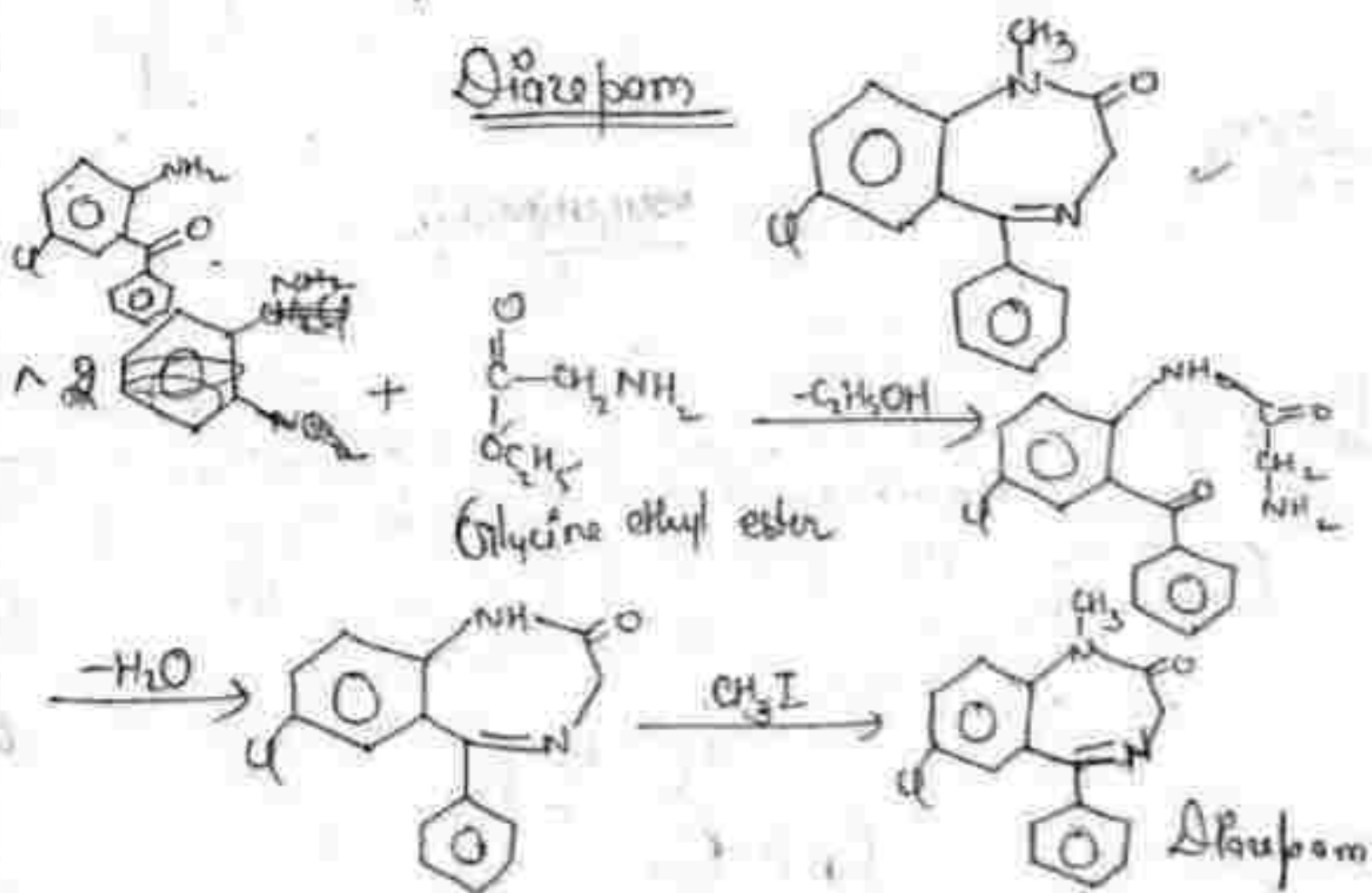
## Chlordiazepoxide





- Uses:-
- ① In treatment of anxiety disorder & insomnia
  - ② Used in muscle spasm in alcohol withdrawal syndrome.
  - ③ for premedication.

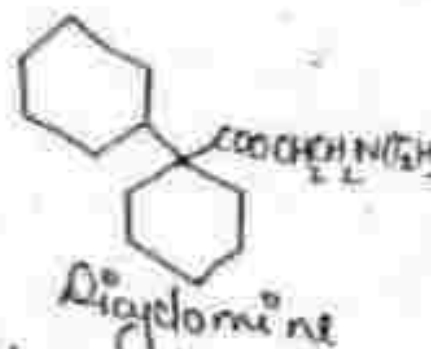
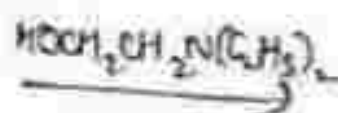
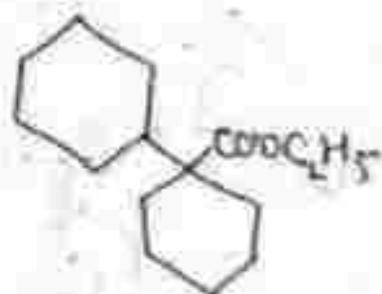
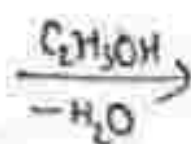
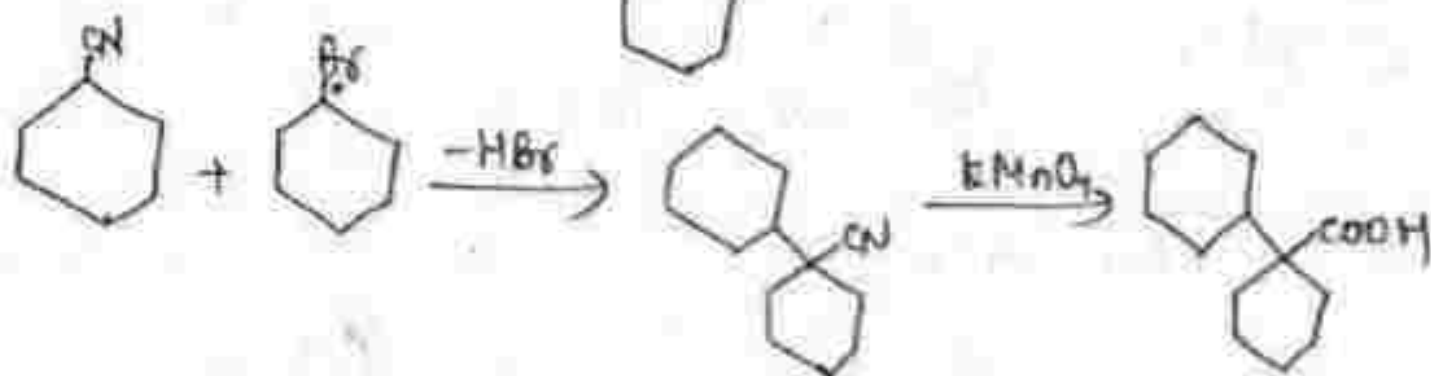
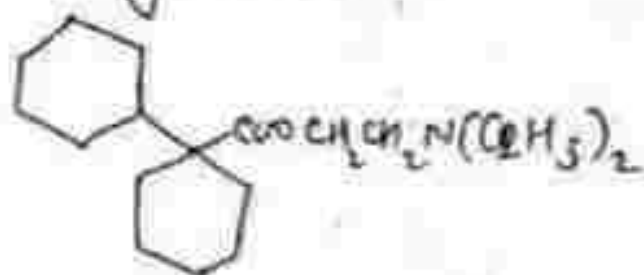
### Diazepam



- Uses:-
- ① To control anxiety & tension states
  - ② Helpful In withdrawal syndrome of in alcohol
  - ③ Used in certain types of epilepsy.

## Antispasmodic

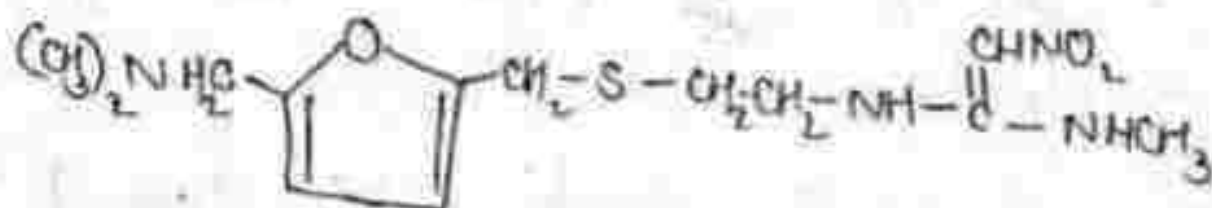
### Dicyclomine

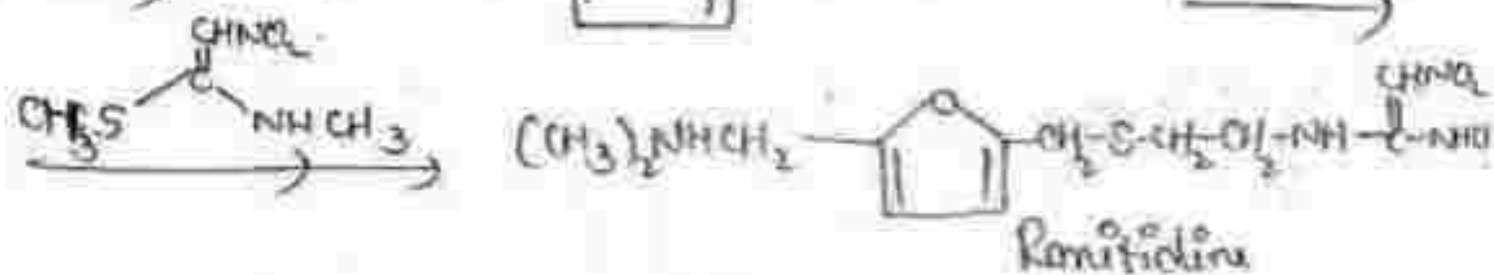
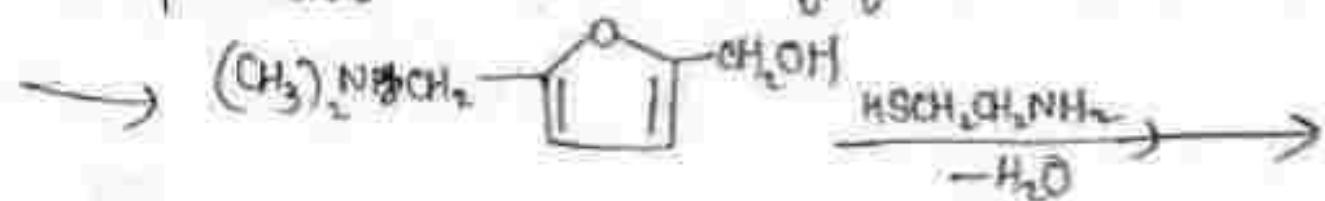
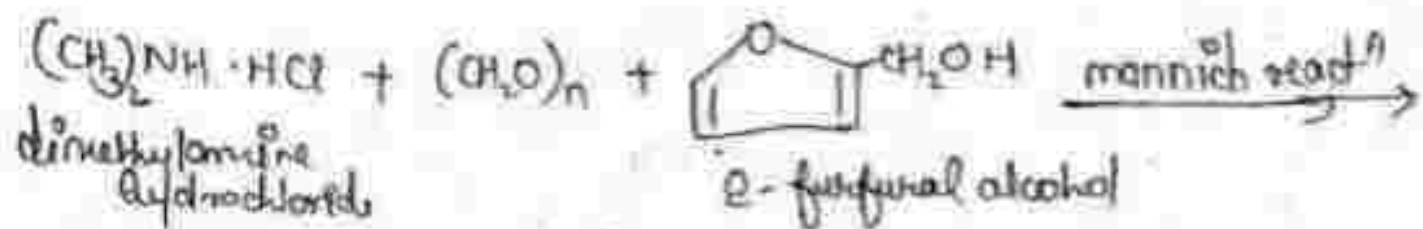


- Uses:
- ① Acts as antimuscarinic & antispasmodic agent.
  - ② In treatment of irritable colon, spastic colitis, mucus colitis, spastic constipation, dystonia.
  - ③ In diagnosis of peptic ulcer.

## Ant ulcer drug

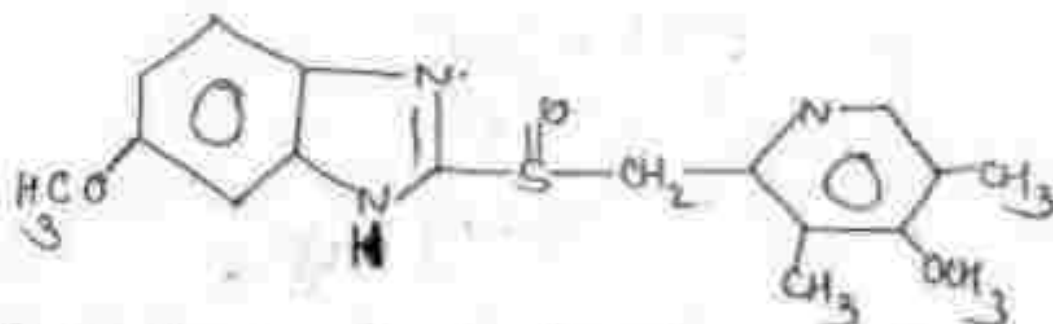
### Ranitidine



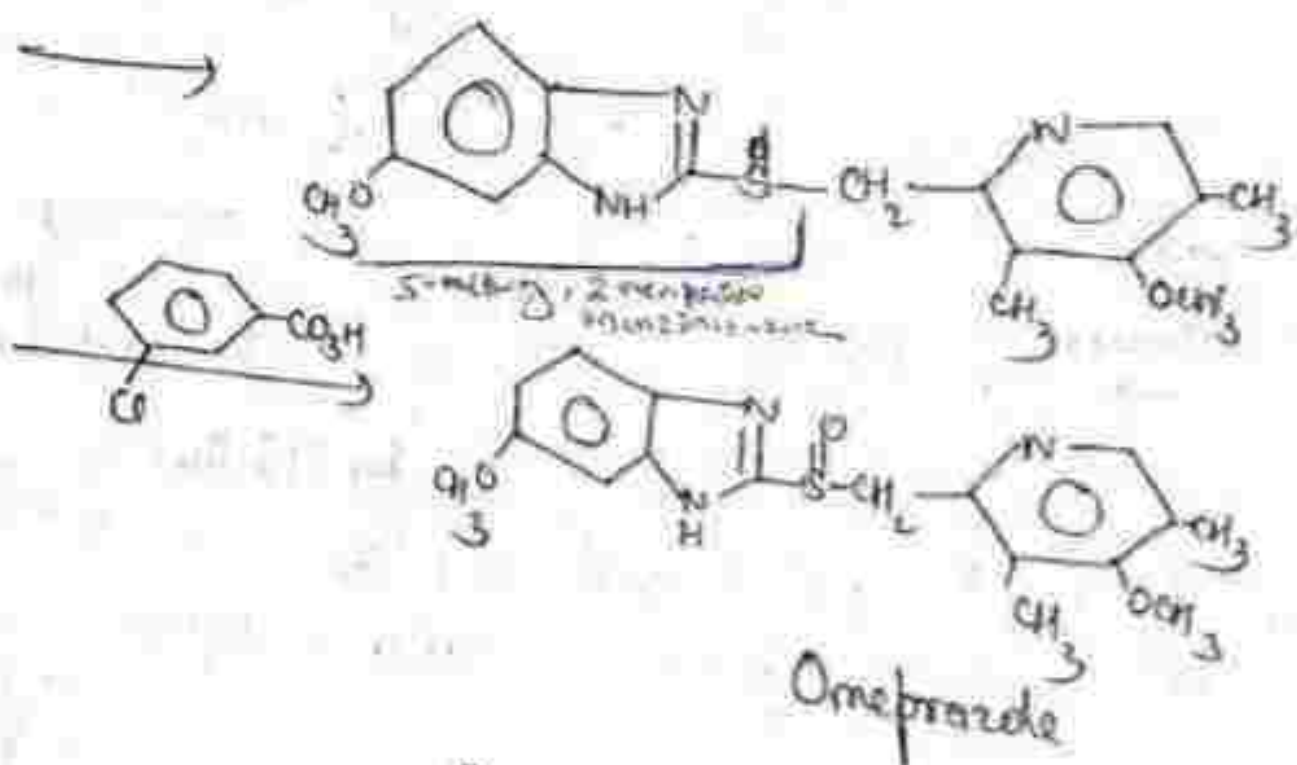
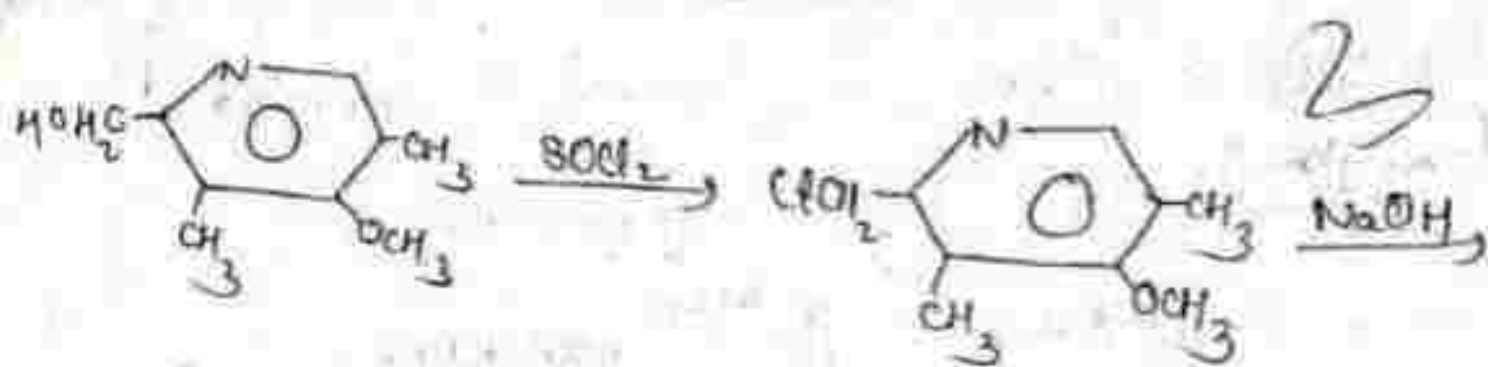


- Uses:-
- ① Inhibits gastric acid secretion.
  - ② Used in gastric & duodenal ulcer.

## Omeprazole

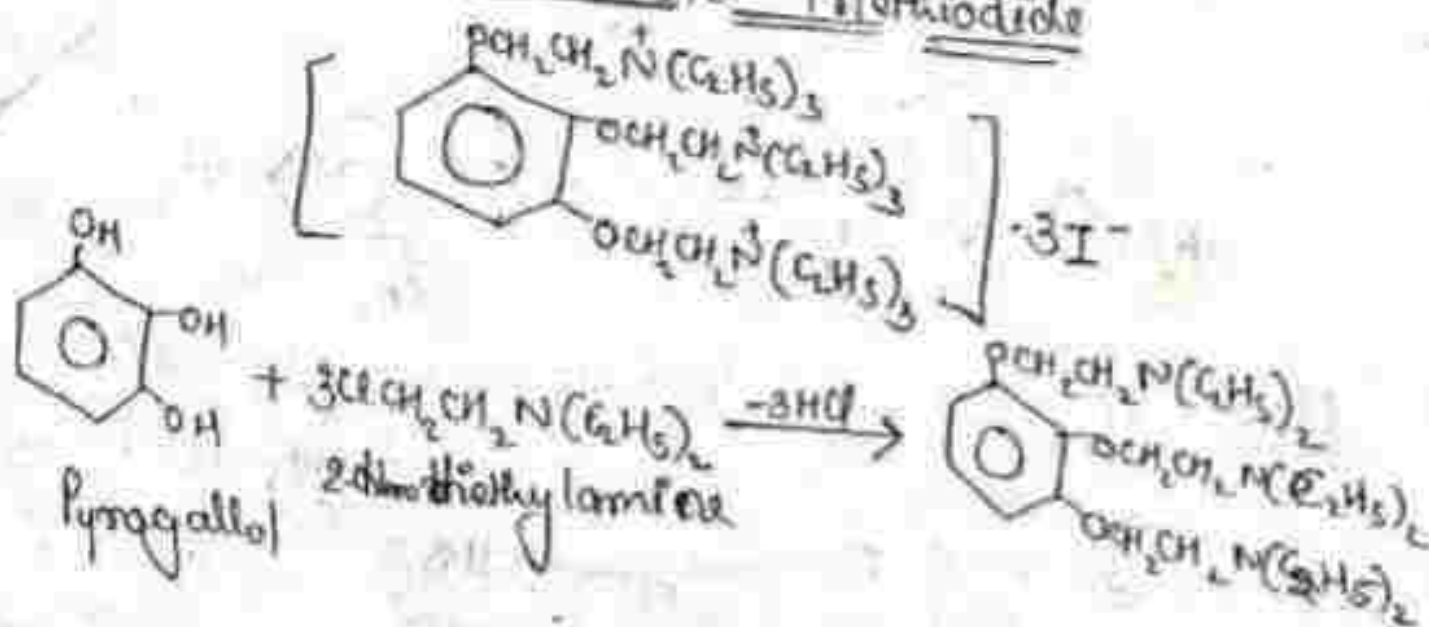


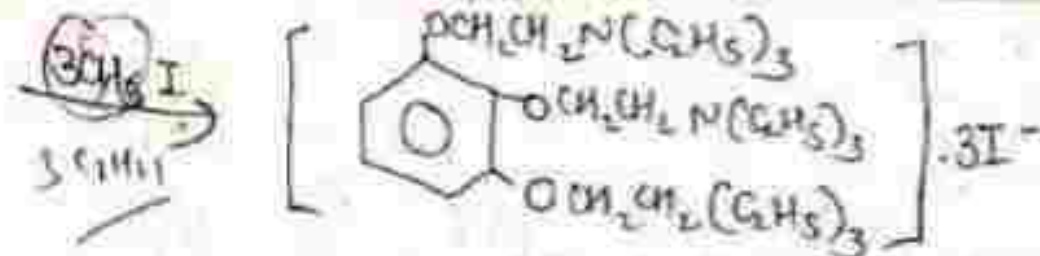
- Uses:-
- ① Used in treatment of peptic ulcer.
  - ② " " " " dyspepsia, aspiration syndrome
  - ③ Used in Zollinger-Ellison syndrome.



## Per Neuromuscular blocking Drugs

### Gallamine Triethiodide

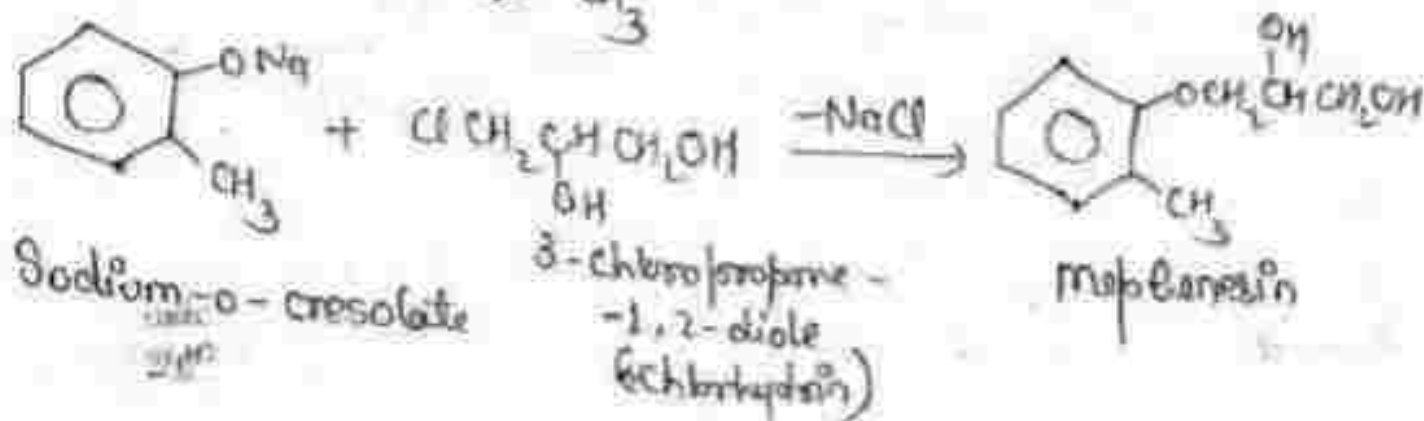
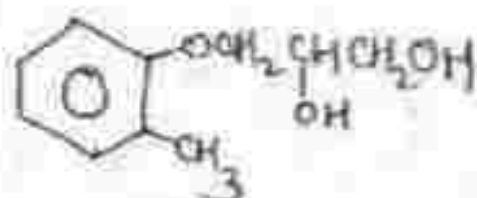




Gallamine triethiodide.

- Uses: -
- ① As a muscle relaxant.
  - ② In  $\uparrow$  To reduce painful spasm of tetanus.
  - ③ In orthopedic operation.
  - ④ In diagnosis of myasthenia gravis.

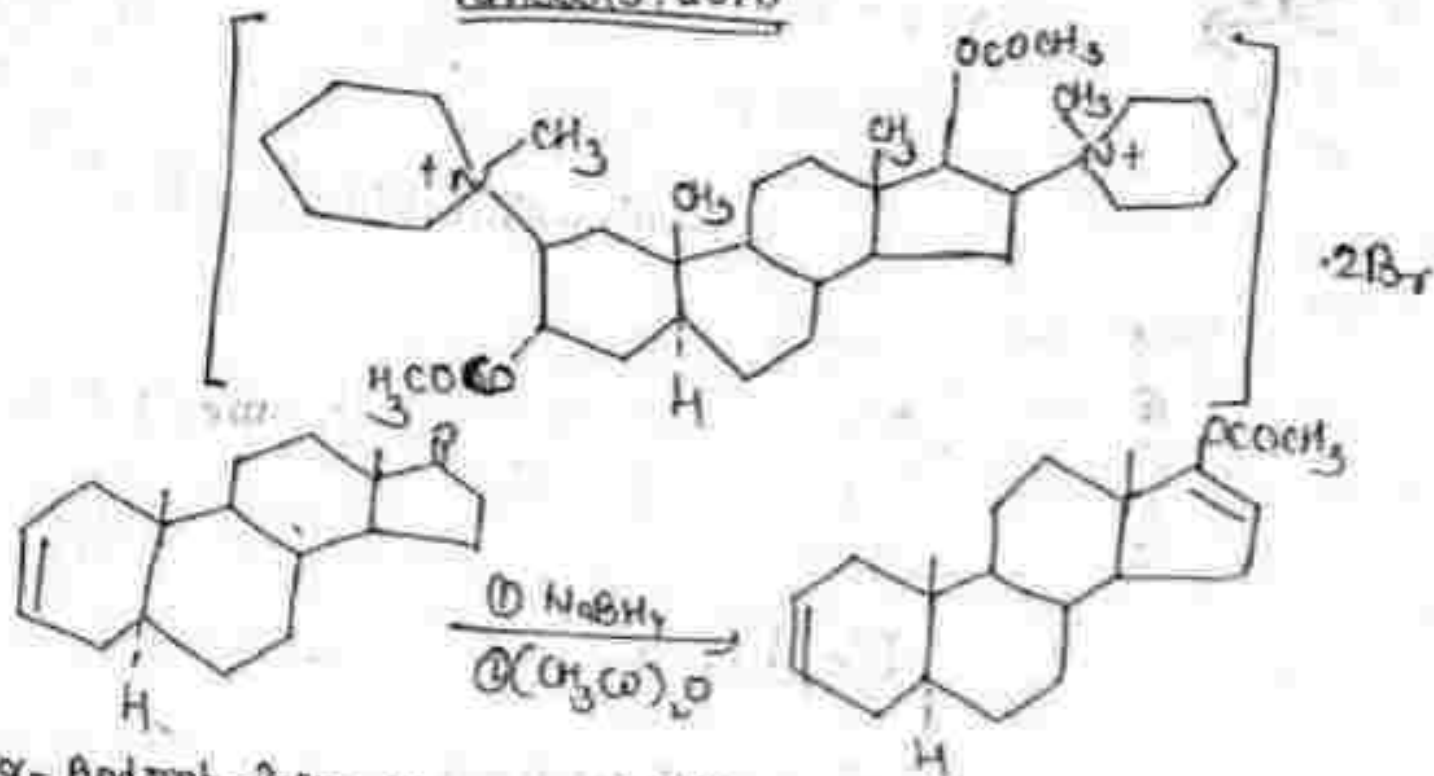
### Mephensin



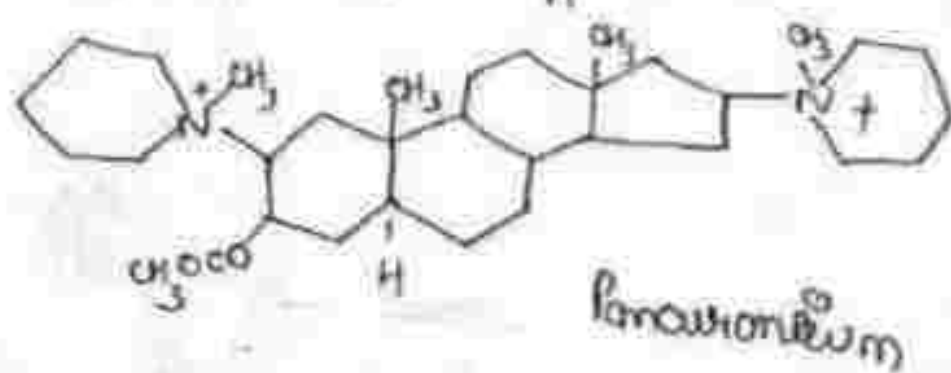
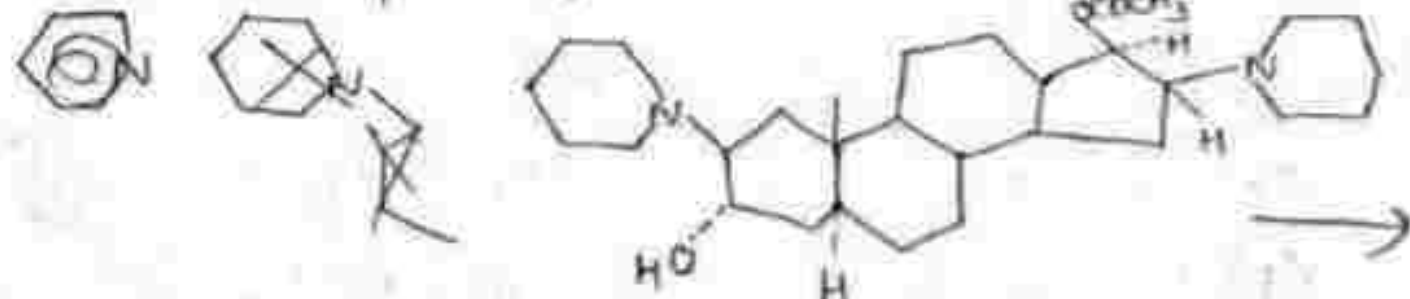
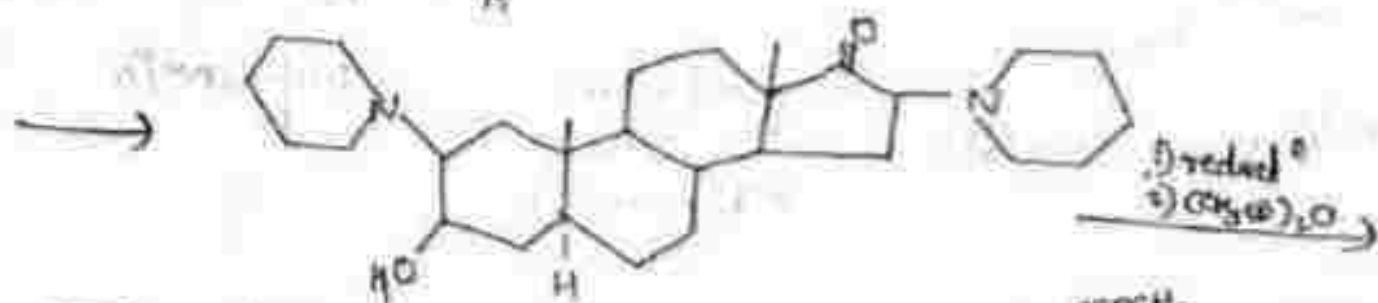
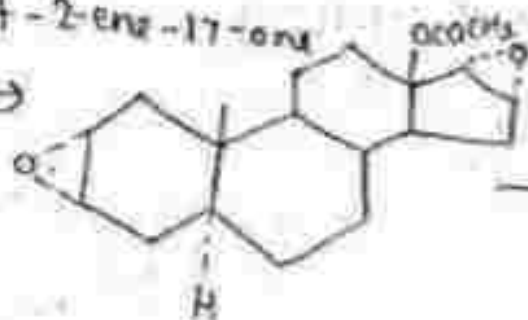
- Uses: -
- ① As a muscle relaxant
  - ② In treatment of anxiety & tension
  - ③ In parkinsonism, chorea, atetosis



# Ротенонийум



5 $\alpha$ -Androst-2-en-17-one



# Uses As a muscle relaxant:

## Neuroleptics

Imipramine / Amitriptyline

↓  
Block amine pump on presynaptic nerve ending

↓  
Inhibit neuronal reuptake of nor-adrenaline & serotonin as central neurotransmitters.

↓  
↑ conc. & persistence of these neurotransmitters in synaptic cleft.

↓  
↑ neuronal transmission.

↓  
recovery from the symptoms of psychoses.

## Mechanism of Action of drugs.

### Antihistamine

① Ranitidine

↓  
Act on  $H_2$  receptors

↓  
block the  $H_2$  receptors

↓  
Inhibit the interaction of histamine with  $H_2$  receptors

↓  
Inhibit gastric acid secretion elicited by histamine

↓  
Improve symptoms of ulcer.

② Omeprazole

↓  
act on proton pump

↓  
block the proton pump

↓  
Inhibition of the  $H^+ / K^+$  ATPase in gastric parietal cell.

↓  
suppress gastric acid secretion

↓  
↓ gastric acidity.

### Antispasmodic

Dicyclanil

↓  
Act on muscarinic receptors on smooth muscle.

↓  
block the receptor for Ach on smooth muscle.

↓  
↓ effect of Ach released from nerves

↓  
block the nerve impulses at the site of parasympathetic ganglia.

↓  
response.

### Antidepressant

① chlorazepate

↓  
bind to benzodiazepine receptor in limbic & cortical areas of CNS

↓  
↑ GABA's inhibitory effect

↓  
block cortical & limbic arousal

↓  
keeps mild emotional behavior.

② Diazepam

↓  
bind to benzodiazepine receptor that are associated with the receptor for GABA

↓  
↑ in GABA induced  $Cl^-$  conductance

↓  
hyperpolarisation of cell & synaptic transmission → response

### Neuromuscular blocking agent

① Pancuronium / Galantamine triethiodide

↓  
Act on the nicotinic cholinergic receptor

↓  
compete with Ach for the receptor & non-competitively block the receptor site.

↓  
Ach is prevented from combining with the nicotinic cholinergic receptor.

↓  
Ach fails. Depolarisation is prevented

↓  
muscle relaxation occurs.

Morphine (centrally acting muscle relaxant)

↓  
Act on interneuronal spinal neurons

↓  
depress polysynaptic pathway.

↓  
depress interneuronal transmission

↓  
controls muscle tone.

## Narcotic analgesics

These comprise a group of both naturally occurring & synthetic agents which interact with specific opioid receptor sites in CNS to relieve pain in conscious person.

### Classification ① Narcotic Agonist Analgesics

(A) Phenanthrenes  $\Rightarrow$  i) Naturally occurring opiate alkaloids.  
Ex: Morphine, codeine.

(B) ii) Semisynthetic derivatives of morphine (Ex: hydromorphone, oxycodone).

(C) iii) Semisynthetic derivatives of codeine  
Ex: hydrocodone, oxycodone.

(D) Methadones - Ex: Methadone propoxyphene.

(E) Morphinans Ex: Levorphanol

(F) Phenyl piperidines (Ex: Pethidine, fentanyl).

② Non-narcotic agonist-antagonist Analgesics.

A. Phenanthrenes (Buprenorphine, nalbuphine)

B. Morphinans (butorphanol)

C. Benzomorphanes (Phenazocine, pentazocine).

### Effects

CNS :- Analgesia, sedation.

CVS :- ~~HR~~  $\downarrow$  BP

GI :- stomal motility  $\downarrow$  peristalsis.

Smooth muscle:  $\uparrow$  tone of non-vascular smooth muscle.

Eye :- miosis

Urinary system: Urinary tract spasm

# Neuromuscular blocking agents

Peripherally acting

~~Neuro~~ Classified:-

① Nondepolarising blockers:- These agents competitively block the receptor site & ACh fails to reach the nicotinic cholinergic receptor.  
→ The postsynaptic membrane is maintained in hyperpolarised state & no stimulat<sup>n</sup> or depolarisat<sup>n</sup> occurs.  
Ex:  $\alpha$ -Tubocurarine, pancuronium, gallamine.

② ~~Non~~ Depolarising:- These agents depolarise the postsynaptic membrane & maintain it in refractory state.  
→ Unlike curare, there are initial muscle contract<sup>n</sup> referred to as fasciculat<sup>n</sup>.

Ex: Succinylcholine, decamethonium.

B. Succinyl CoA

- Dicholine ester of succinic acid
- resembles decamethonium in being a long, slender flexible bis-quaternary +vely charged molecule.
- Equivalent to 2 ACh molecules joined back to back.
- Rapid onset of act<sup>n</sup> (1 min) & short durat<sup>n</sup> of act<sup>n</sup> (5 min) bc it is rapidly hydrolysed by plasma ChE.

Centrally acting

- ①
- ②
- ③
- ④

⑤ Direct action  
① Dantrolene  
② Quinine.

## Antianxiety Drugs.

- ② These drugs used to relieve stress, tension & anxiety.

Anxiety :- feeling of apprehension, uncertainty & fear.

Classification :-

- ① Benzodiazepines :- Diazepam, Clonazepam, Chlordiazepoxide, Alprazolam, midazolam, Haloperidol, Lorazepam.
- ② Carbamates :- Meprobamate.
- ③ Miscellaneous :- Hydroxyzine, buspirone, propranolol, Clonidine.

Ph. Act<sup>n</sup> :- ① Antianxiety effect  $\rightarrow$  meprobamate.

② Anticonvulsant effect  $\rightarrow$  Diazepam, lorazepam, nitrazepam.

③ Hypnotic effect.

④ CVS  $\rightarrow$   $\downarrow$  BP

⑤ Analgesic effect.

## Antidepressants

### ① Tricyclic antidepressants

i- Ambenzapines Exo = Imipramine

ii- Sibenzocycloheptanes Exo Amitriptyline

### ② Monoamine oxidase ~~and~~ Inhibitors (MAOI) Exo - Phenelzine.

### ③ Atypical antidepressants:-

Exo:- Fluoxetine, maprotiline, trazadone.

Mechanistically they can be classified as:-

#### ① Norepinephrine:- reuptake inhibitor.

i) Tertiary amine tricyclic Exo - Amitriptyline

ii) Sec. " " Exo - Amoxapine

#### ② Serotonine:- reuptake inhibitor

Exo fluoxetine, Desferaline.

③ MAOI  $\Rightarrow$  Exo - Phenelzine.

④ Atypical antidepressant Exo - trazadone.