Date :

Name of the Experiment : Unit-V UNIT-5

General Anaesthetics

General anaesthetics are CNS depressant drugs that induce absence of perception of all sensations and loss of pain.

* anaesthesia (Greek) – Without perception of insensibility. "lack of feeling"

4 stages of anaesthesia

Stage I :-[Analgesia] - This stage starts with the first inhalation of anaesthetic gas and ends with the onset of consciousness.

Stage II : [Delirium or Excitement] :- This stage begins with loss of consciousness. The inhibitory control of the higher centres is removed, and the sub consciousness emotions take over.

Stage III :- [Surgical Anaesthesia] :- This is the stage of unconsciousness and paralysis of reflexes. In this stage the patient reflects complete tranquility respiration is full and regular, the pulse is slow and the pupils become constricted -All surgical procedures are carried out in this stage.

Stage IV : [Medullary paralysis] :- This stage begins with central respiratory paralysis and ends with cardiac failure and death.

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- General anaesthetics are the agents that produce reversible loss of consciousness throughout the body.
- They depress CNS not selectively but reversible.

Mechanism of Action :-

-> General anaesthetics are thought to be non-spaific in action i.e they donot act on specific receptor site due to the wide structural variation.

-> The anaesthetic drug is thought to act by interrupting the function of central nervous system.

-> Mayer & overtone propsed independently a lipid theory. This theory states that, a direct relationship exist between lipid solubility of an agent and its anaesthetic potency.

-> Acc to this theory, anaesthesia occurs when a sufficient conc of anaesthetic is achieved in lipid bilayer to perturb its structure in such as to render some excitable membrane protein embedded in it.

-> When G.A is dissolved in lipid bilayer and membranes, they cause disordering or ↑ed fluidity of the membrane.

-> This may inactivate the protein essential functioning of CNS or ion channel, which would remain open resulting in Cl^- ion influx leading to synaptic hyper polarization, which ⊗s neuronal function.

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* Ligand-gated ion channels are imp-targets for anaesthetic action.
* Cl^- channels gated by the inhibitory $GABA_A$ receptors are sensitive to clinical concentrations of a wide variety of anaesthetics.
* GA's ↑ the sensitivity of $GABA_A$ receptor GABA, thus enhancing the inhibitory neurotransmission and depressing nervous system activity.

* major targets – Ligand-gated ion channel ✓
* important one – $GABA_A$ receptor gated Cl^- channel

Anaesthesia – is a reversible condition of a comfort, quiescence and physiological stability in a patient before, during and after performance of a procedure.

General anaesthesia – for surgical procedure to render the patient unware/ unresponsive to the painful stimuli.

Local anaesthesia – reversible inhibition impulse generation & propagation in nerves. In sensory nerve, such an effect is desired when painful procedures must be performed.

Surface – Ointment/Jelly/Solutions
infiltration – injection to the LA to produce analgesia over an area.
regional – Spinal, epidural & iv regional anaesthesia

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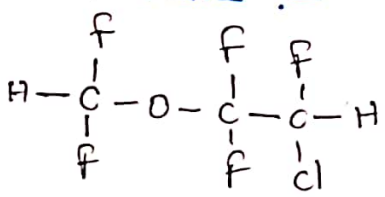
Classification of GA's

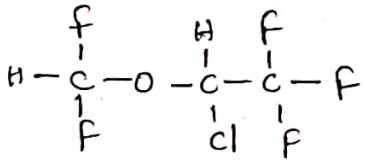
- Inhalational anaesthetics
  - Halothane *(gas).
  - Enflurane (ether)
  - Sevoflurane (")
  - Isoflurane (")
  - Desflurane (")
  - Methoxyflurane (")
- Dissociative anaesthetics
  - *Ketamine hydrochloride
- Ultrashort acting barbiturates
  - * Methohexital sodium
  - Thiamylal sodium
  - Thiopental sodium

1. Enflurane :-



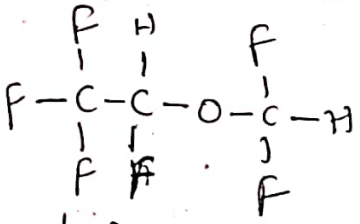
2 chloro-1, 1,2 trifluoro methyl ether

2. Isoflurane :-



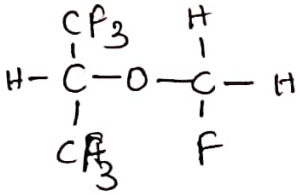
(RS) 1-chloro 2,2,2 trifluoroethyl difluoromethyl ether.

3. Desflurane :-



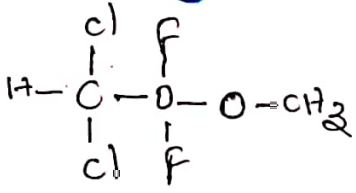
1,2,2,2 tetrafluoro ethyl difluoro methyl ether.

4. Sevoflurane :-



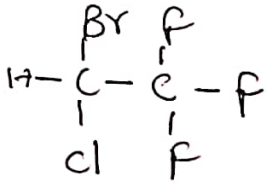
2-fluoromethoxy-1,1,1, 3,3,3- hexafluoropropane.

5. Methoxyflurane



1-Methoxy 2,2 dichloro 1,1 difluoro ethane.

6. Halothane



2-Bromo-2 chloro-1,1,1- trifluoro ethane.

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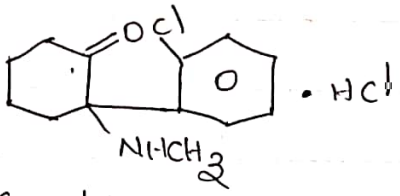
Dissociative anaesthetics :-

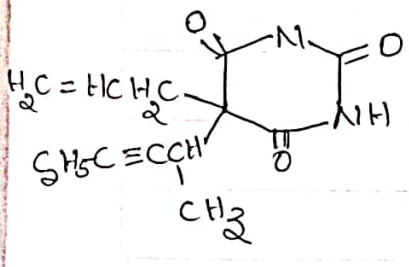
7. Ketamine Hydrochloride :



(±) - 2-(o-chlorophenyl-2-methylamino cyclohexanone hydrochloride.

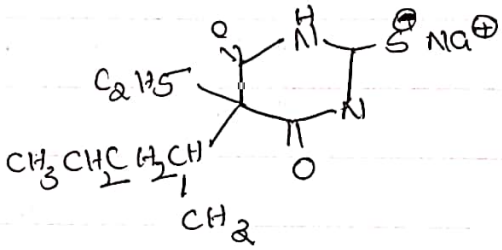
ultrashort acting barbiturates :-

8. Methohexital Sodium



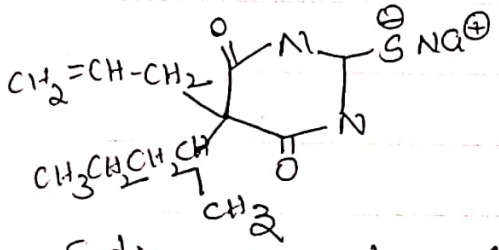
1 methyl-5-(1-methyl-2pentynyl) -5-(2-propenyl) barbituric acid.

9. Thiopental Sodium



5-ethyl-5-(1-methyl butyl -2-thio barbituric acid.

10. Thiamylal Sodium :-



Sodium-5-allyl-5-(1-methyl butyl)-2-thio barbiturate.

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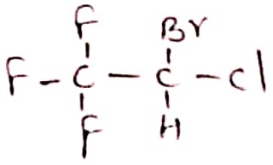
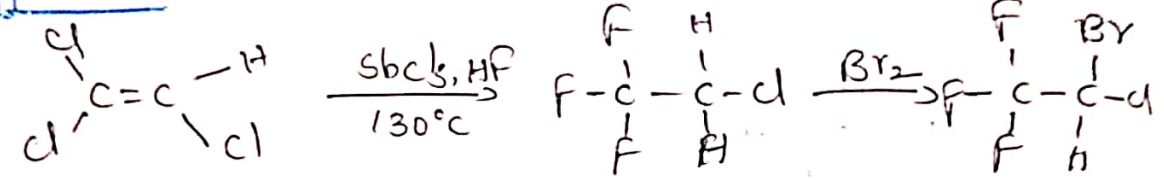
① Halothane : [Flothane]



Synthesis :-



Trichloroethane → Trifluorochloro ethane → Halothane

MOA :- Halothane activates GABA and glycine receptor. It also inhibits Ach & Na^{+2} channels & activates $5HT_3$ & K^+ ion channels.

Uses :- It is a potent, safe & frequently employed general inhalation anaesthetic.

- generally used to start or to maintain anaesthesia.

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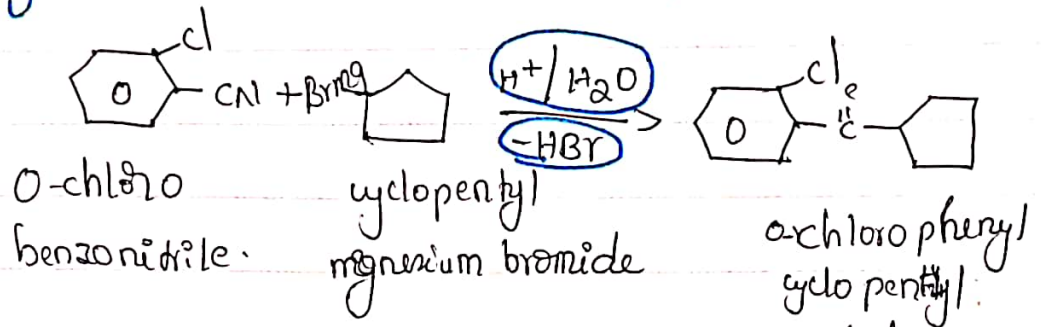
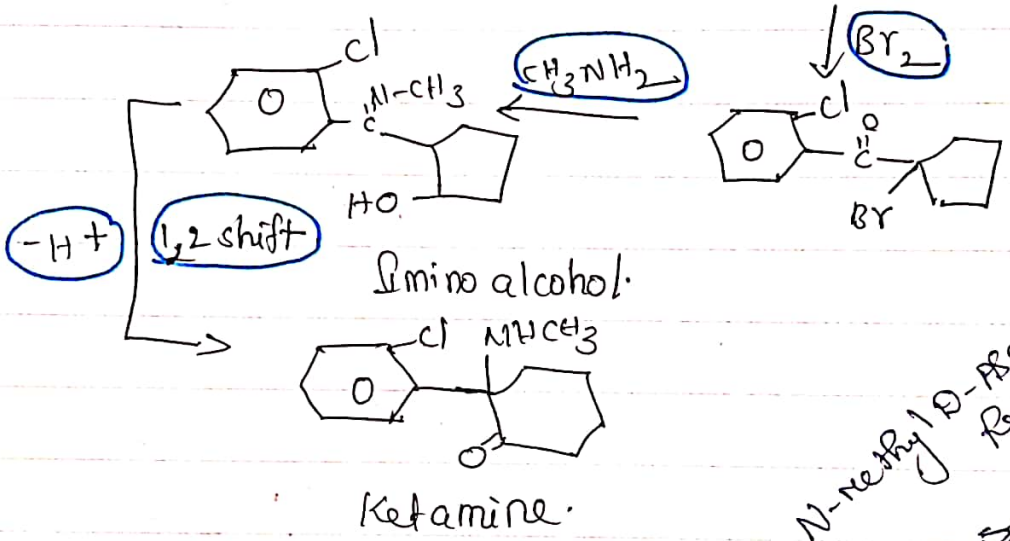
Synthesis:-



O-chloro benzonitrile.

cyclopentyl magnesium bromide

o-chloro phenyl cyclo pentyl ketone.



Imino alcohol.

Ketamine.

N-methyl D-Aspartate Receptor.

MOA:- It acts as a Selective antagonist of NMDA receptor & glutamate receptor. It also interacts with and inhibits the NMDAR. So it is a uncompetetive antagonist of NMDA receptor. It ⊗s sodium & Ca^{+2} channels.

Uses:- It is an intravenous anaesthetic agent and drug of choice for short surgical operation and mainly used as induction anaesthesia.

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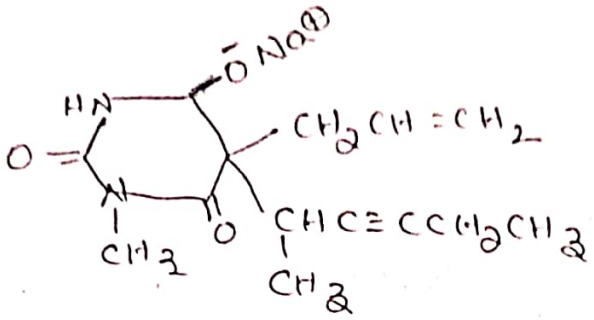
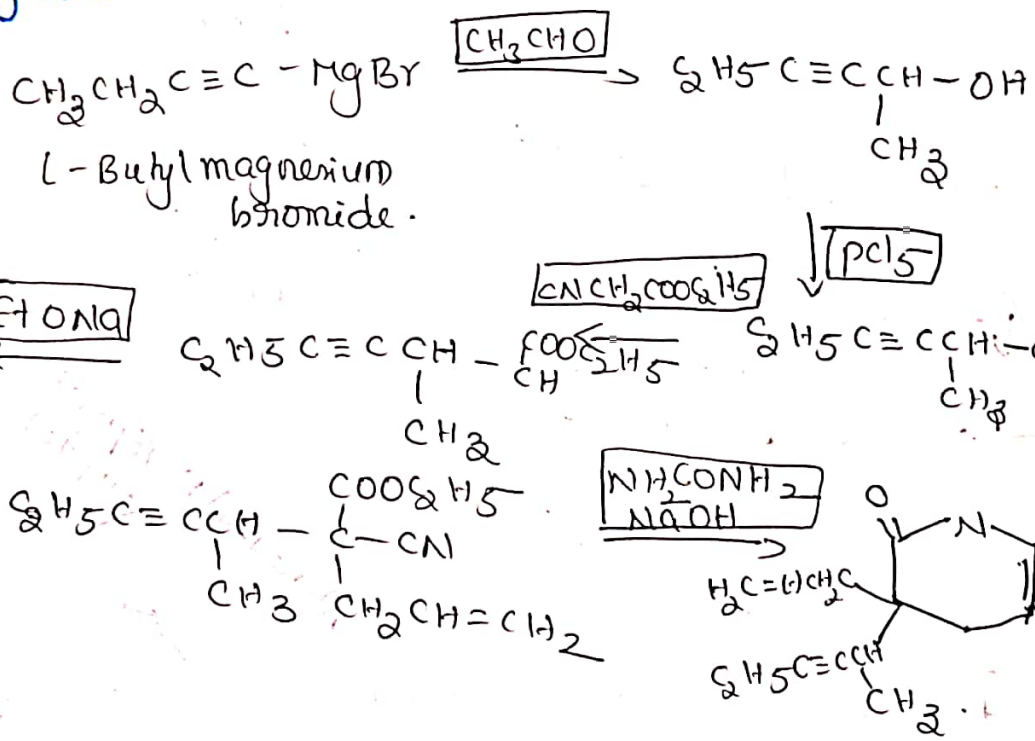


Synthesis:-



MOA:- It binds to a site which is associated with Cl^- ion pores present on the GABA receptors. It opens the Cl^- ions pores and inturn produces inhibitory effect.

Use:- It is useful for short surgical operation such as oral surgery, gynecological investigation, Electro convulsive therapy.