GEN. ANAESTHETICS

↳ GAs are the drug which produce reversible loss of sensation and consciousness.

↳ GAs are generally CNS depressant drug, They are generally used during surgical operations.

↳ Basic features of GAs
- → loss of pain / sensation
- → sleep (unconsciousness)
- → Amnesia → "loss of short term memories"
- → Immobility & muscle relaxation
- → Reduce somatic & Atonomic reflexes

STAGES :-

Stage I (Analgesia) : → Patients are conscious and reduction in the perception of painfull stimuli.
→ used in minor surgery

Stage II (Delirium) - Being loss of consciousness & This time Depression produces excitement, involuntary activity, ↑ muscular tone, irregular respiration.

Stage III - (Surgical Anaesthesia) :- unconsciousness
paralysis of reflexes
regular BP & respiration
pupil constriction "stone Eye"

Stage IV (Medullary Paralysis) -
- → Depression of vital centres of medulla & brain stem occur
- → Respiratory & circulatory failure
- → Coma - Death.

CLASSIFICATION

I Inhalation Anaesthetics -

(a) Liquids - (Volatile liquids)

Halogenated - Enflurane, Isoflurane, Halothane
methoxyflurane

Non-Halogenated - Ether

(b) Gas - Cyclopropane, Nitrous oxide (N_2O)

II Intravenous (IV)

(a) Ultra-short acting Barbiturates - Thiopentone
Thiamylal
Methohexital

(b) Dissociative Anaesthetic - Ketamine (Arylcyclohexylamine)

(c) Benzodiazepine - Diazepam, Lorazepam, Midazolam

(d) Narcotic Analgesic - Fentanyl

(e) other - Propofol, Etomidate

Inhalation Anaesthetics

→ Rapid Induction
→ Deep anaesthesia
→ muscle relaxant
→ Safe

Mayer & Overton (1901) - Proposed a theory
Partition Coeff (Lipid/water) & Potency

MAC - Minimal Alveolar Concentration

↳ Lowest conc. of anaesthetic agent in pulmonary alveoli need to produce immobility in response to painful stimulus in 50% individuals.

Med. Chem-I

U5- DRUGS ACTING ON CNS

GENERAL ANESTHETICS

↳ GAs are the drugs which produce reversible loss of sensation and consciousness.

↳ A. Inhaled Anesthetics → Halothane*, Methoxyflurane, Enflurane, Sevoflurane, Desflurane

B) Ultrashort Acting Barbiturates (IV)
Methohexital Sodium, Thiamylal Sod, Thiopental Sod.

C) Dissociative Anesthetics- Ketamine hydrochloride*

MAC %	
Methoxyflurane	0.16
Halothane	0.75
Isoflurane	1.2
~~Seve~~ Enflurane	1.68
Sevoflurane	2
Desflurane	6
N_2O	105

A INHACED ANESTHETICS

① Halothane

$CF_3-CH(Br)-Cl$

(RS) 2-bromo,-2-chloro-1,1,1-trifluoro ethane

$CH_2 \equiv CHCl \xrightarrow[130^\circ C]{3HF} CF_3-CH_2Cl$

trichloro ethylene

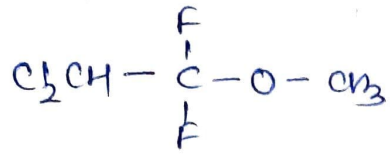
$CF_3-CH_2Cl \xrightarrow{Br_2, 450^\circ C} CF_3-CH(Br)-Cl$

Halothane

MOA - (+) GABA & Glycine action
(-) Cation, NMDA & Cholinergic pathway

USES - # Induction - 2.4% - Smooth & rapid
Maintanance - 0.5 - 1.0%
Used along with O_2 and NM blocker

② Methoxyflurane

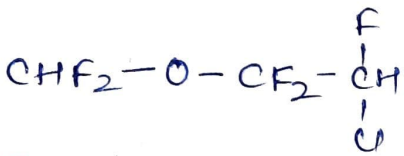


2,2-dichloro-1,1-difluoro ethyl methyl ether

MOA → (+) $GABA_A$ & Glycene receptor
(+) Acetylcholine receptor

Use → # Good analgesiac with GA action
management of pain due to ~~acute~~ acute trauma

③ Enflurane

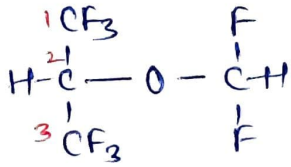


2-chloro-1,1,2-trifluoro ethyl difluoro ~~me~~methyl ether

MOA → (+) GABA action

Uses → GA but no longer use now

④ Sevoflurane

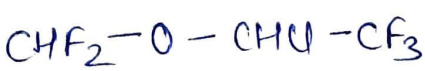


1,1,1,3,3,3-hexafluoro-2-fluoro methoxy propane

MOA → (+) GABA action

Use → GA - Induction & maintenance
Good muscle relaxant

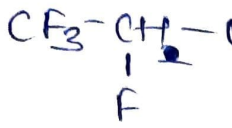
⑤ Isoflurane



1-chloro-2,2,2-trifluoro-ethyl difluoro methyl ether

↳ Good Analgesia & muscle relaxant
↳ ~~PAG~~ GAs
↳ (+) Glycene & GABA and (+) ATPase

⑥ Desflurane

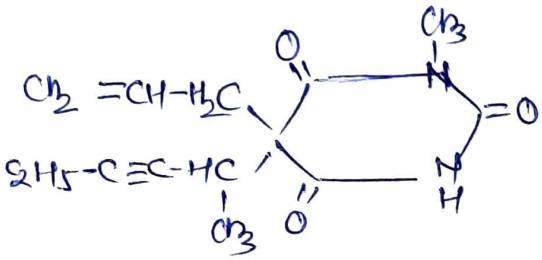


1,2,2,2-tetrafluoro ethyl difluoromethyl ether

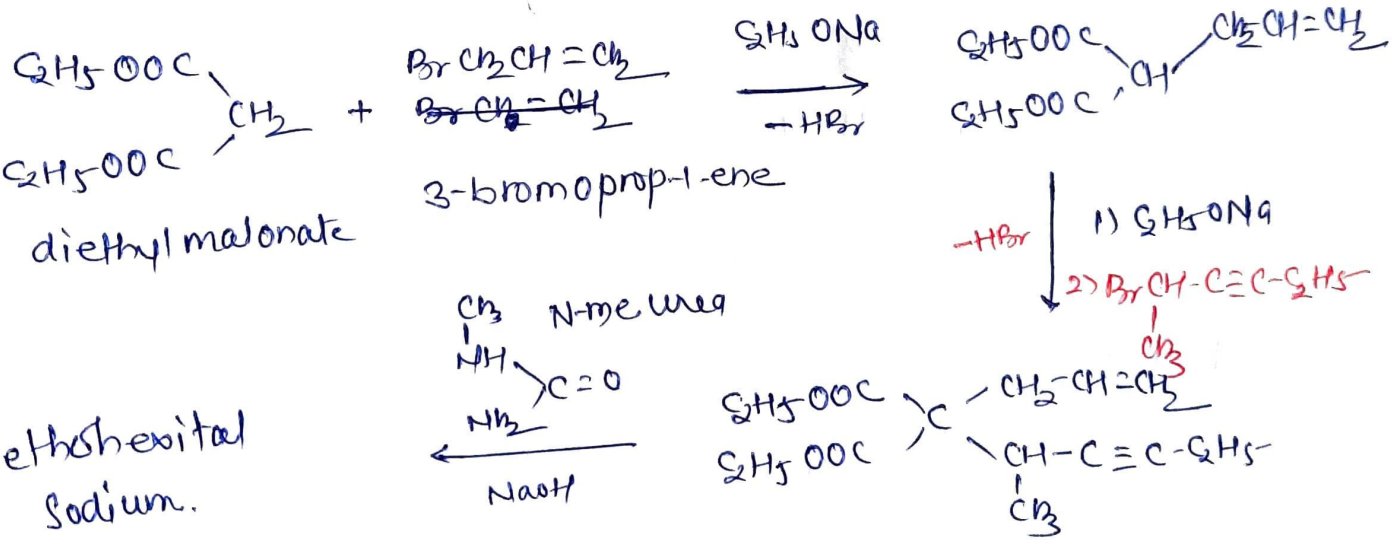
↳ Good Analgesic, GA.

B. Ultrashort Acting GA

① Methohexital Sodium



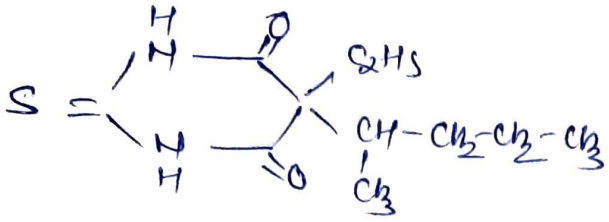
5-allyl-5-(1-methyl-2-pentynyl) barbiturate



MOA – (+) $GABA_AR$

Use – # For Induction of anesthesia
Induce sleep for surgery in dental procedure
~~Antiepily~~ Antiepileptic

② Thiopental Sodium

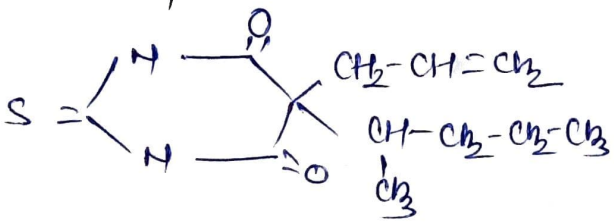


5-Ethyl-5-(1-methyl butyl)
-2-thio barbiturate

MOA - + GABAAR

Uses - # Induce Anesthesia
Hypnotic
Antiepilepsy

③ Thiamylal Sodium

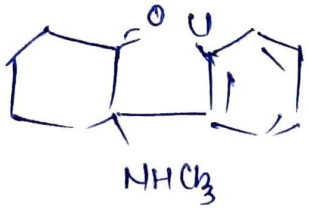


5-(allyl)-5-(1-methyl butyl)
-2-thio barbiturate

Use : Similar as Thiopentone

C. Dissociative Anaesthetic

① Ketamine

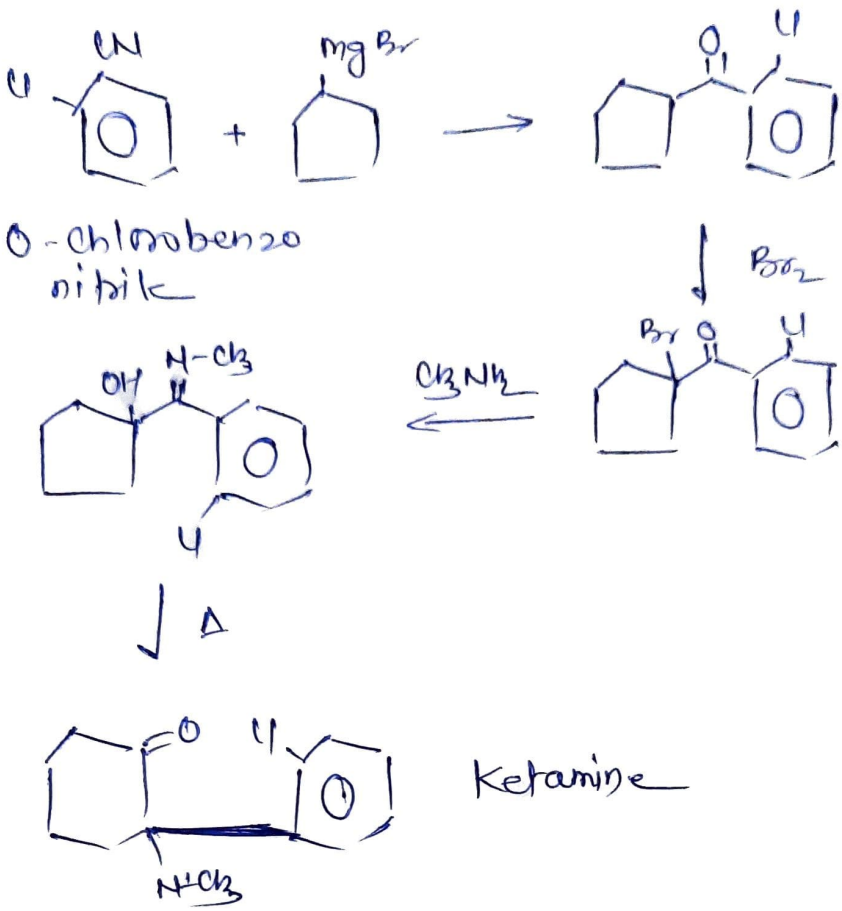


2-(2-Chlorophenyl) 2-(methyl amino)
Cyclohexanone

MOA - NMDA Receptor blocker
- Associated with catalepsy, catatonia, analgesia amnesia

Use - # Induction & maintenance of anesthesia
management of pain
anti depressant

Synthesis -


CN
Cl
MgBr
O
Cl
O-chlorobenzonitrile
Br_2
Br
O
Cl
CH_3NH_2
OH
N-CH_3
Cl
Δ
O
Cl
N^+CH_3
Ketamine