

SEDATIVE AND
HYPNOTICS
MOA AND
STRUCTURES

Sedatives and Hypnotics

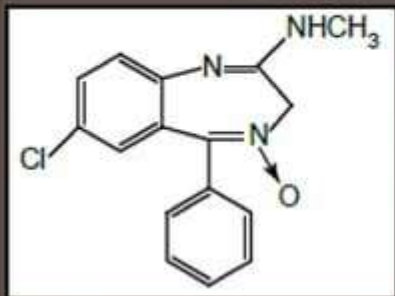
Mode of action: Benzodiazepine receptors are present in the brain and they form a part of **GABA A** receptor's chloride ion channel macromolecular complex.

Binding of benzodiazepines to these receptors produces activation of GABA A receptor and increases chloride conductance by increasing the frequency of **opening chloride ion channel**.

Hyper-polarization—block depolarization- decrease neural excitement

Benzodiazepines

Chlordiazepoxide



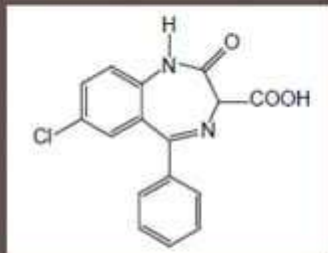
7-Chloro-5-phenyl-2-methylamino-1,4-benzodiazepine-4-oxide

Adverse reactions include **drowsiness, ataxia, confusion**

Used for the relief of anxiety and tension, withdrawal symptoms of acute alcoholism, and also used as **sedative as well as muscle relaxant**.



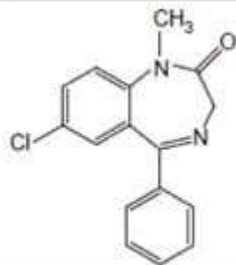
Benzodiazepines Chlorazepate



7-Chloro-2-oxo-5-phenyl-1,4-benzodiazepin-3-carboxylic acid

A water-soluble benzodiazepine derivative effective in the treatment of anxiety. It has also muscle relaxant and anticonvulsant actions.

It is used as a sedative and hypnotic



Benzodiazepines

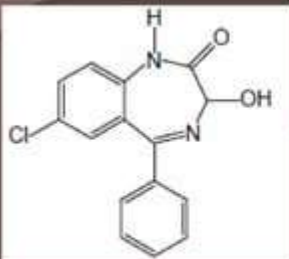
Diazepam*

7-Chloro-1-methyl-5-phenyl-1,4-benzodiazepin-2-one

(Calmpose, Valium)

It is used as a skeletal muscle relaxant, anticonvulsant and antianxiety agent.

Patients on the drug should be cautioned not to drive an automobile or to operate dangerous machinery until a few days after the drug has been discontinued.



Benzodiazepines Oxazepam

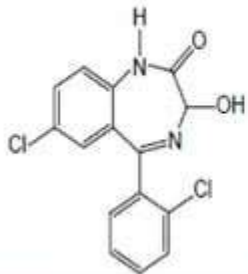
7-Chloro-3-hydroxy-5-phenyl-1,4-benzodiazepin-2-one

It is useful for the control of acute tremulousness, anxiety associated with alcohol withdrawal.

Side effects that have been observed include rashes, nausea, lethargy, oedema etc. More severe reactions include leucopenia and jaundice.

Benzodiazepines **Lorazepam**

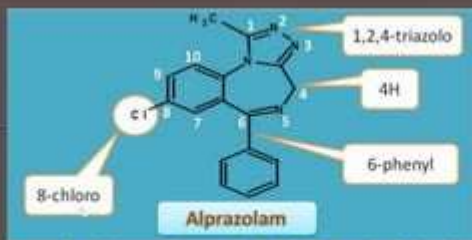
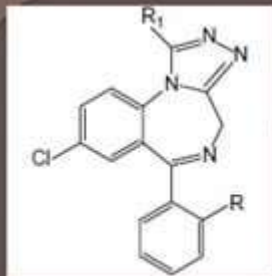
7-Chloro-5-(2-chlorophenyl)-3-hydroxy-1,4-benzodiazepin-2-one



It is used as sedative and hypnotic

It has much more polarity than diazepam

duration of action is short



Benzodiazepines

Alprazolam

R = H, R1 = CH₃

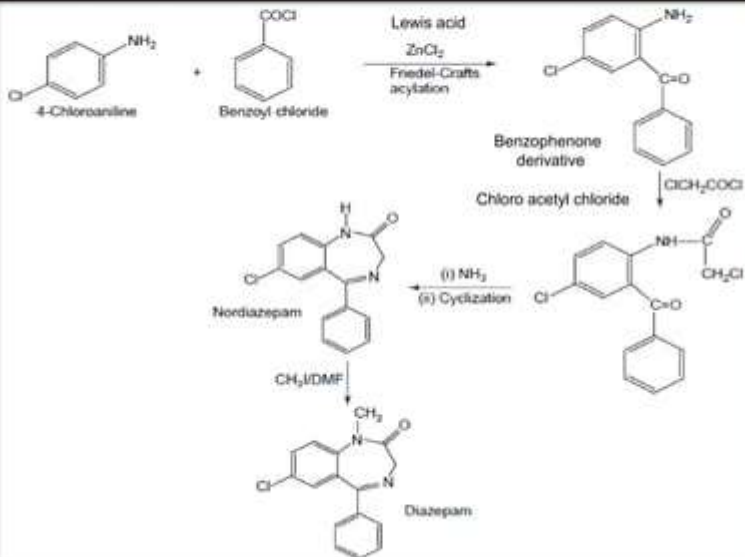
8-chloro-1-methyl-6-phenyl-4H-triazolo benzodiazepine

Metabolism of Alprazolam: The methyl group of this drug is metabolized by oxidation reaction to methyl alcohol and conjugation reaction takes place.

It is useful in the short-term management of insomnia

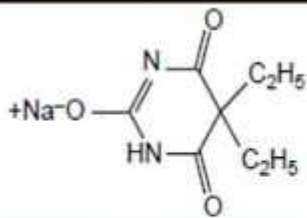
The duration of action is short and the drug is a highly potent anxiolytic

Diazepam Synthesis



BARBITURATES

Barbiturates are derivatives of barbituric acid. Their hypnotic activity is conferred by the replacement of H-atom attached to the C-5 position by aryl or alkyl radicals.



Sodium-5,5'-diethylbarbiturate

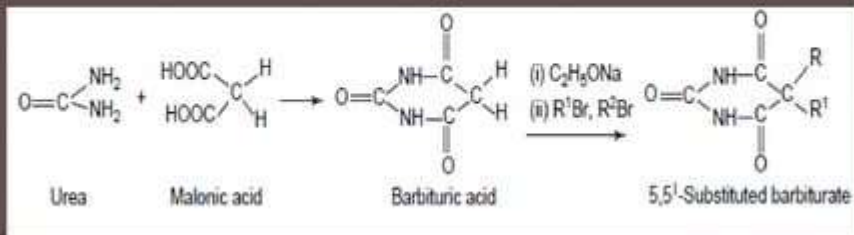
Barbiturates - Barbital*

**Barbitone sodium
(Barbital sodium)**

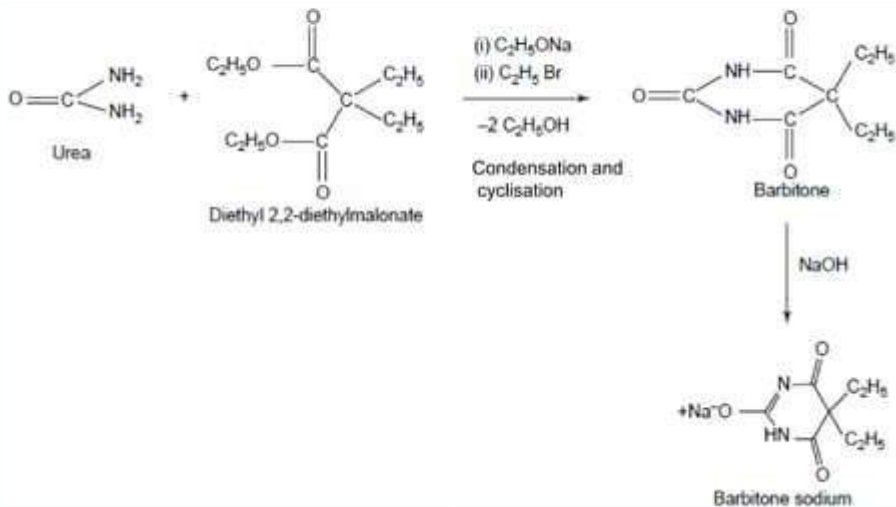
Barbitone sodium forms water-soluble salts with sodium hydroxide.

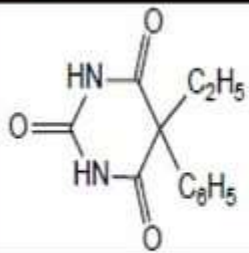
It is a powerful hypnotic drug and used in the treatment of epileptic seizures.

Pyrimidine 2,4,6 trione



Synthesis of Barbitol sodium





Phenobarbital/Phenobarbitone

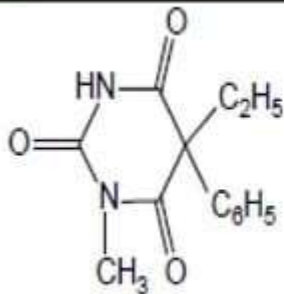
5-Ethyl-5-phenyl barbituric acid

Phenobarbital sodium is a hygroscopic substance.

It is used as sedative, hypnotic and antiepileptic (**drug of choice in the treatment of grandmal and petitmal epilepsy**)

An overdose of it can result in coma, severe respiratory depression, hypotension leading to cardiovascular collapse, and renal failure.

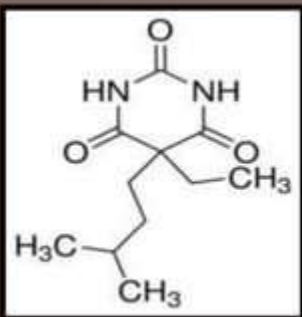
Methyl phenobarbitone/ Mephobarbital



5-Ethyl-1-methyl-5-phenyl barbituric acid

Mephobarbitone is a strong sedative with anticonvulsant action, mild hypnotic.

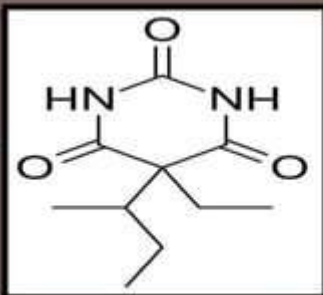
used for the relief of anxiety, tension and apprehension, and is an antiepileptic in the management of generalized tonic-clonic and absence seizures.



Amylobarbitone/ Amobarbital

5-ethyl-5-(3-methylbutyl)-barbituric acid

- A barbiturate with hypnotic and sedative properties (but not antianxiety).
- Adverse effects are mainly a consequence of dose-related CNS depression and the risk of dependence with continued use is high.

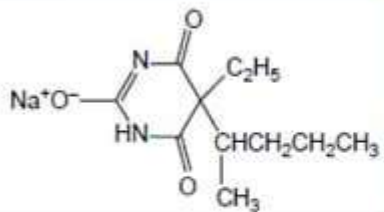


Butisol or secbutobarbitone

/Butabarbital

5-butan-2-yl-5-ethyl-barbituric acid

- Butabarbital is a fast onset barbiturate with short duration of action
- **Treats severe insomnia and pre-operative anxiety**
- Butabarbital has been detected in multiple biofluids, such as urine and blood. It is a potentially **toxic compound**.
- Butabarbital is less commonly used ----- benzodiazepines are preferred



Pentobarbital

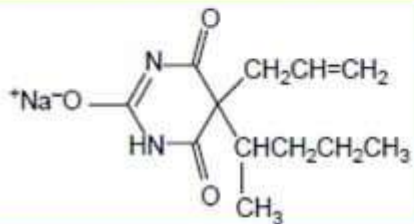
Sodium-5-ethyl-5-(1-methylbutyl) barbiturate

It is used as a sedative or hypnotic for the short-term management of insomnia and is a preanaesthetic medication, used in the treatment of strychnine poisoning.

Administered intravenously, for the control of certain convulsive syndromes.

This barbiturate reduces cerebral blood flow and, thereby, decrease oedema and intracranial pressure.

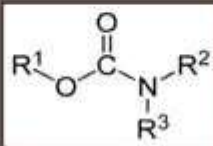
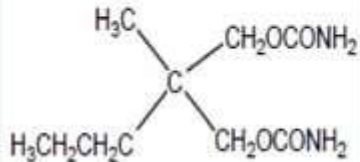
Quinobarbitone sodium /Secobarbital



Sodium-5-allyl-5-(1-methylbutyl) barbiturate

It is used in status epilepticus and in toxic reactions to strychnine and as local anaesthetic.

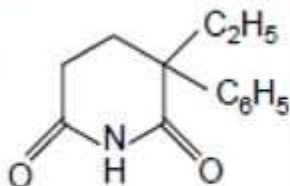
Acyclic hypnotics containing nitrogen – Miscellaneous-Meprobamate



2-Methyl-2-propyl-1,3-propanediol dicarbamate

It is used in the treatment of anxiety disorders. It is also a centrally acting skeletal muscle relaxant.

The agents in this group find use in a number of conditions, such as strains and sprains that may produce acute muscle spasm.



Glutethamide

3-Ethyl-3-phenyl piperidine-2,6-dione

It is used as a hypnotic drug to induce sleep without depressing respiration.

Over dosage is less likely to depress respiration

Adverse reactions include a generalized rash, rarely nausea

Some of these side effects may be due to the anticholinergic activity of this drug.

Alcohols and Aldehydes-Miscellaneous- Ethchlorvynol

The 4 Stages of Sleep



NREM Stage 1

- transitional period between wakefulness and sleep
- lasts around 5 to 10 minutes



NREM Stage 2

- muscle relax
- blood pressure and breathing rate drop
- deepest sleep occurs



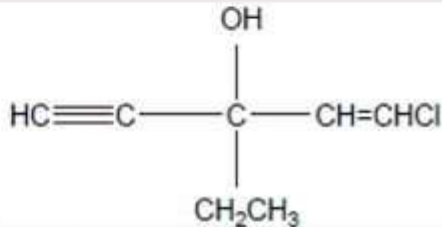
NREM Stage 3

- body temperature drops and heart rate begins to slow
- brain begins to produce sleep spindles
- lasts approximately 20 minutes



REM Sleep

- brain becomes more active
- body becomes relaxed and immobilized
- dreams occur
- eyes move rapidly



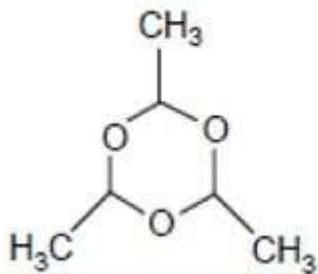
1-Chloro-3-ethyl-1-penten-4-yn-3-ol

It also possesses muscle relaxant and anticonvulsant properties

Adverse effects include suppression of REM sleep, ataxia, and hypotension. [Hypnogram](#)

Alcohols and Aldehydes

- Miscellaneous- Paraldehyde



2, 4, 6-Trimethyl-1,3,5-trioxane

It is exclusively used in the management of hospitalized patients undergoing alcohol withdrawal.