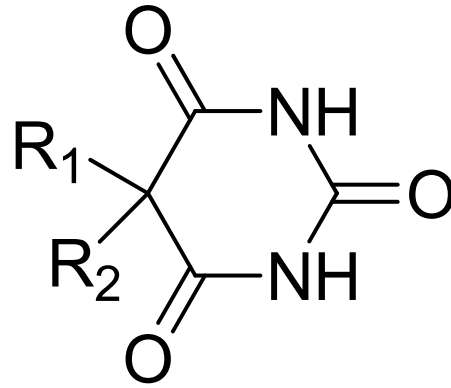


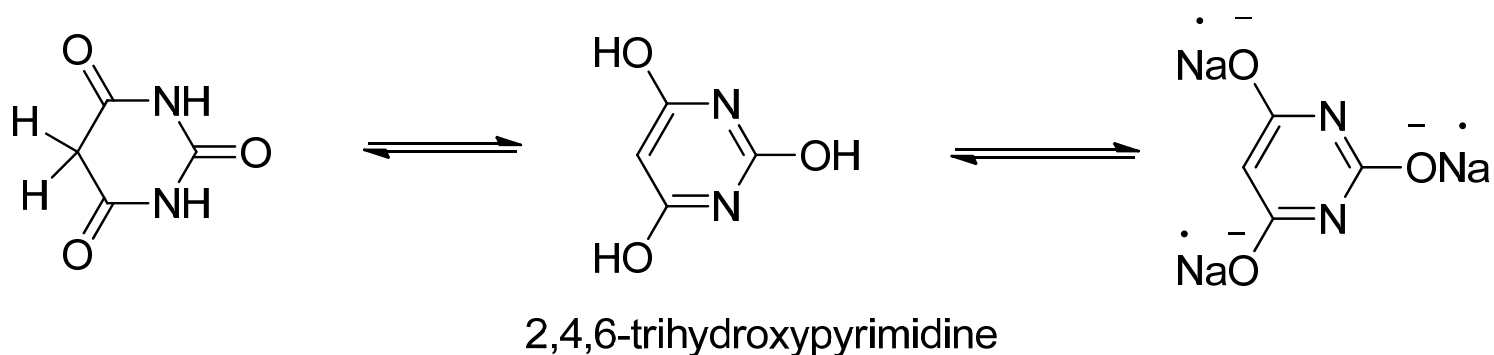
## SAR of barbiturates

Barbiturates are represented by the general structure



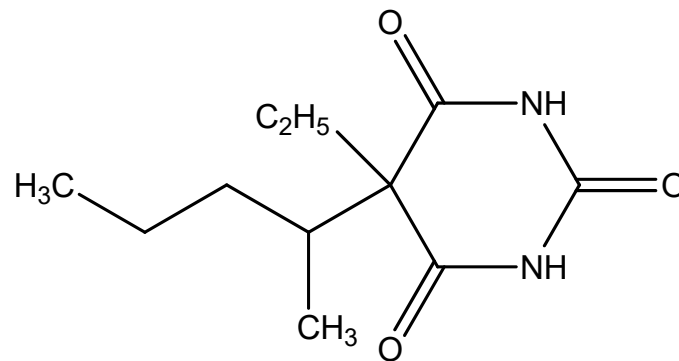
- ❖ Both hydrogen atoms present at the 5<sup>th</sup> position of barbituric acid must be replaced because if hydrogens are present at 5<sup>th</sup> it leads to tautomerisation to highly acidic trihydroxypyrimidine

- ❖ The trihydroxypyrimidine ionizes at physiological pH and can not cross the blood brain barrier (BBB) to show sedative action.



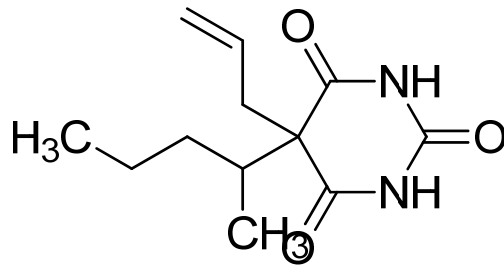
- ❖ The total number of carbon atoms present in the two groups at 5<sup>th</sup> position should not be less than 4 and more than 10 for optimal therapeutic action.

- ❖ There is an inverse correlation exist between the total number of carbon atom at 5<sup>th</sup> position and duration action..
- ❖ The branched chain isomer exhibit greater activity and shorter duration of action e.g. pentobarbital.



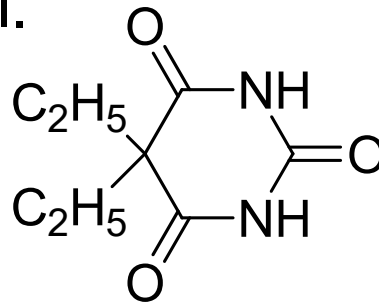
Pentobarbital

- ❖ Presence of double bonds in the alkyl substituents at 5<sup>th</sup> position produce compounds more vulnerable to tissue oxidation hence, they are short acting e.g. secobarbital.

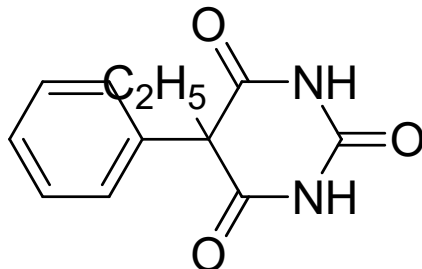


Secobarbital

- ❖ Presence of short chain at 5<sup>th</sup> position resist oxidation and hence possess longer duration of action e.g. barbital.

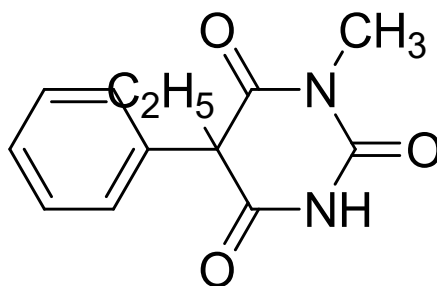


- ❖ Aromatic or alicyclic rings exert greater potency than the corresponding aliphatic group having similar number of carbon atom.



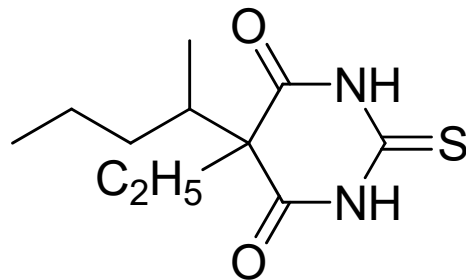
Phenobarbital

- ❖ Methylation of one of the imide hydrogen increases onset of action and reduce duration of action e.g. mephobarbital.



Mephobarbital

- ❖ Replacement of oxygen atom present at 2<sup>nd</sup> position (carbonyl oxygen) by Sulphur atom reduce onset of action and duration of action. E.g. thiopental



- ❖ Inclusion of more Sulphur atom (e.g. 2,4-dithio, 2,4,6-trithio) decreases activity. Similarly introduction of imino group in place of carbonyl group abolish the activity. (2-imino, 4-imino, 2,4-diimino, 2,4,6-triimino).