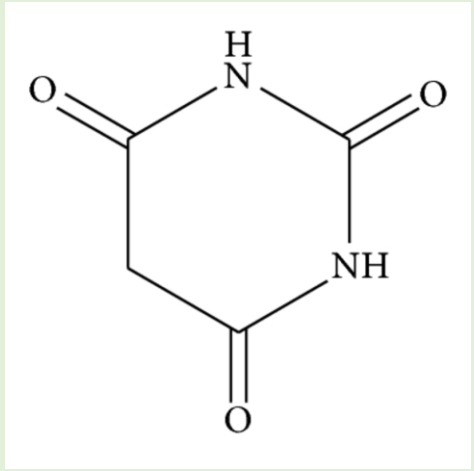
Barbiturate

Barbituric acid, the precursor of barbiturates, was first produced in 1864 by condensation of malonic acid and urea; it had no central nervous system (CNS) effects.

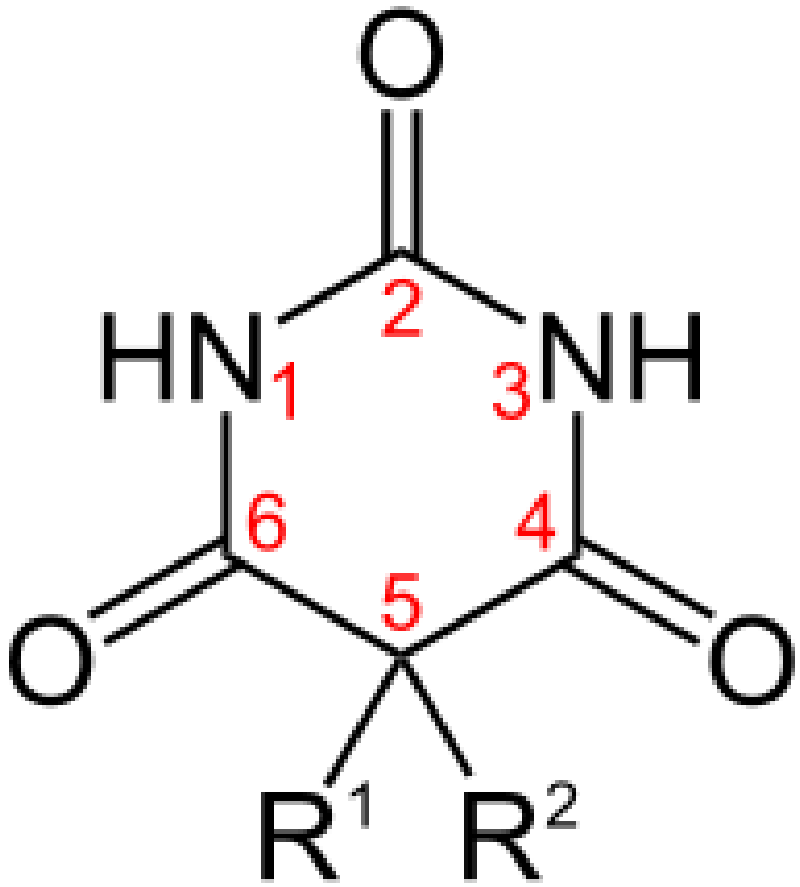


Barbituric acid

Barbiturates were commonly used as sedative-hypnotics in the mid-twentieth century; meantime they were abused by some people as sold on the street.

Use of barbiturates quickly dropped after introduction of benzodiazepines as the safer sedative-hypnotics. However some of the barbiturates are still used as anticonvulsants, sedatives and some as anaesthetics.

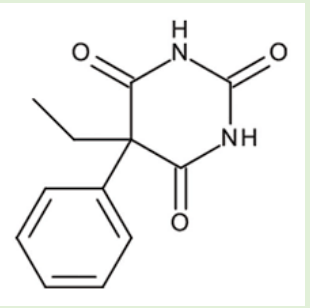
Barbiturate SAR



Barbiturates are classified according to their duration of action.

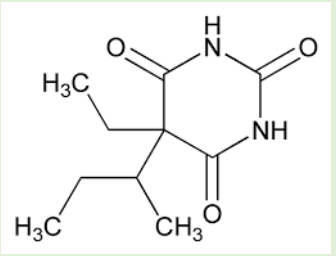
long-acting barbiturates, such **Phenobarbital** (may last for as long as 24 hours) is used in conjunction with other drugs for the treatment of epilepsy, in which their prolonged depressant action helps prevent convulsions.

Phenobarbital



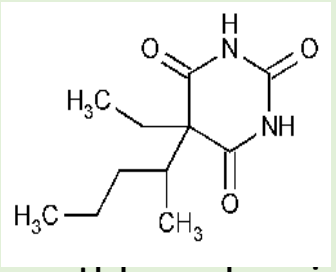
Barbiturates of intermediate duration of action, such **Butabarbital** , act for 6 to 12 hours and are used to relieve insomnia.

butabarbital



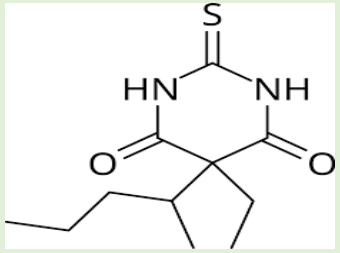
Short-acting barbiturates, such as **Pentobarbital** , are used to overcome difficulty in falling asleep.

pentobarbital

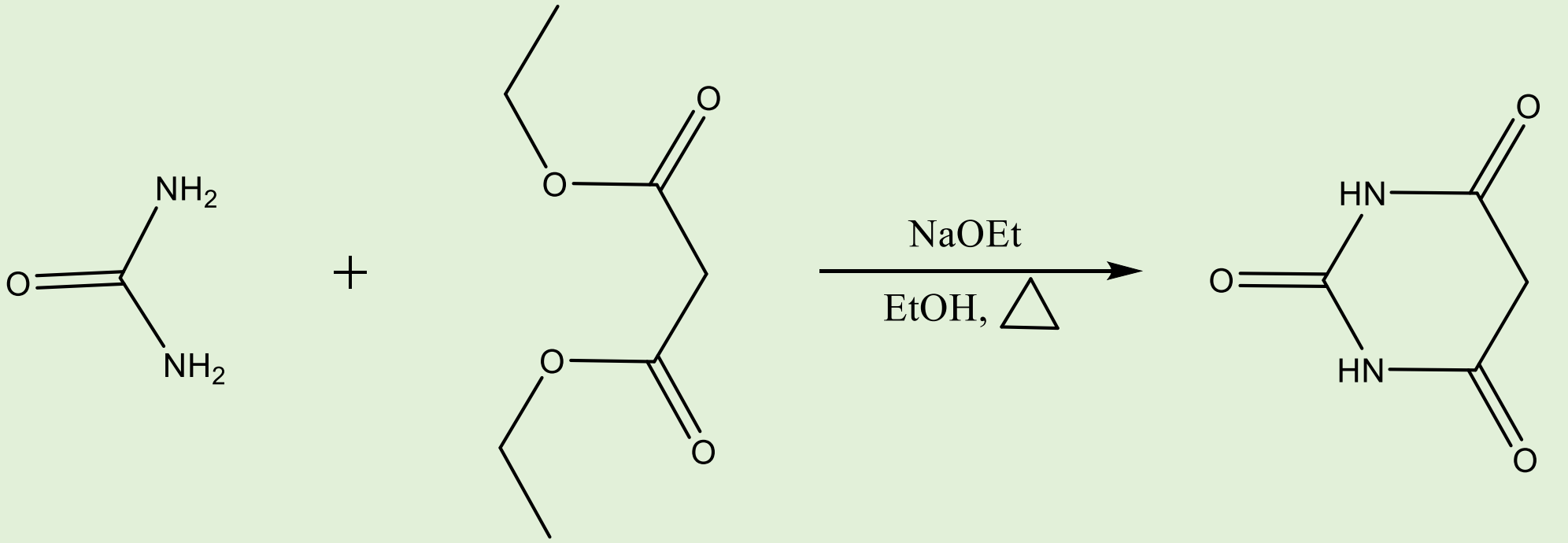


Ultra short-acting barbiturates, such as **Thiopental** , are used intravenously to induce unconsciousness smoothly and rapidly in patients about to undergo surgery, after which gaseous anesthetics are used to maintain the unconscious state.

thiopental



Barbituric acid synthesis

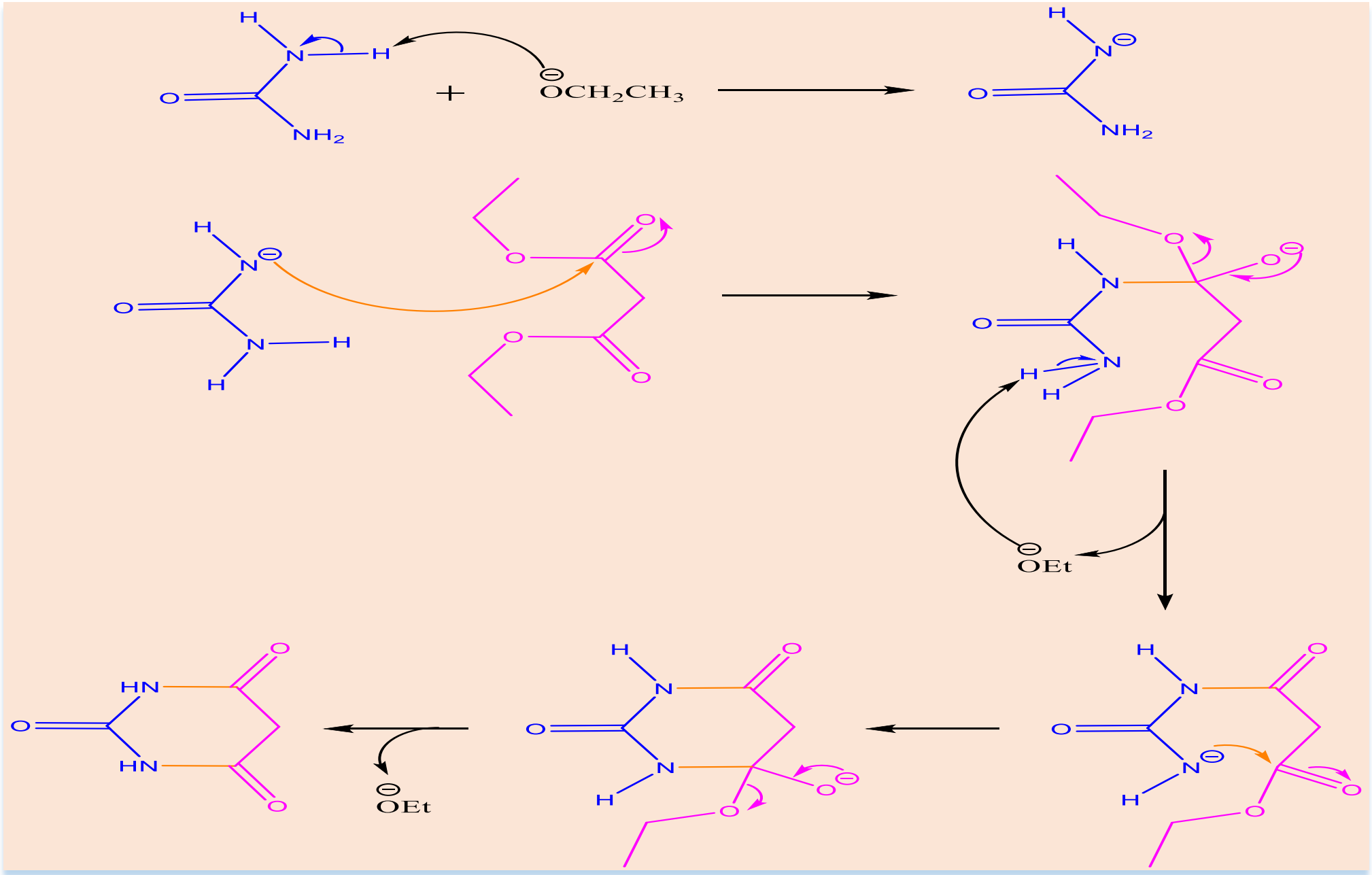


Urea

Diethyl malonate

Barbituric acid

Mechanism of reaction



Procedure

1. In a round-bottomed flask fitted with a reflux condenser protected by a calcium chloride tube, finely cut sodium is dissolved in 250 cc. of absolute alcohol.

2. To this solution 80 g. (0.5 mole, 76 ml) of diethyl malonate is added.

3. Followed by 30 g. (0.5 mole) of dry urea dissolved in 250 cc. of hot (70°) absolute alcohol.

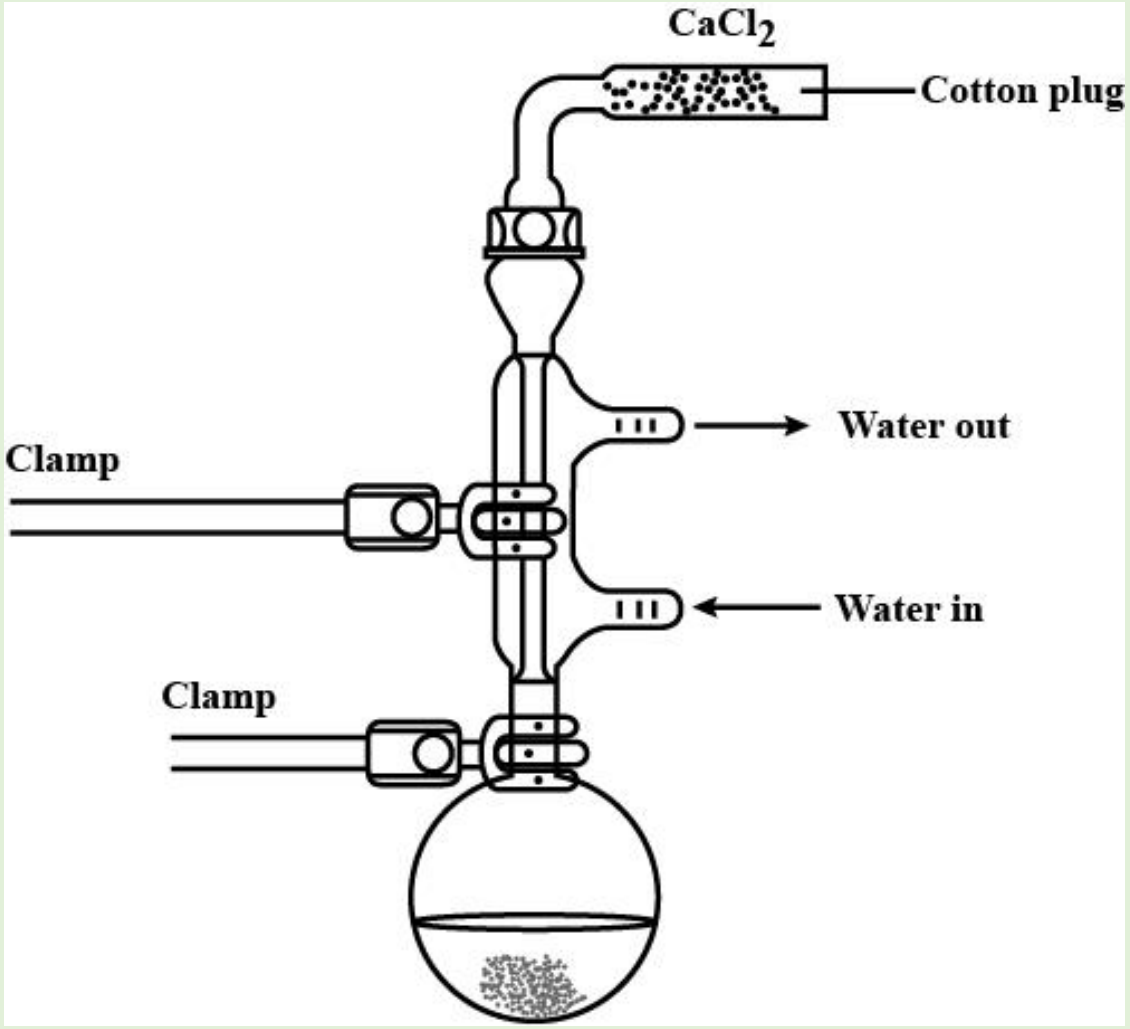
4. After being well shaken the mixture is refluxed for seven hours on an oil bath heated to 110°. A white solid separates rapidly.

5. After the reaction is completed, 500 cc. of hot (50°) water is added and then enough hydrochloric acid to make the solution acidic (about 45 cc.).

6. The resulting clear solution is filtered and cooled in an ice bath overnight.

7. The white product is collected on a Büchner funnel, washed with 50 cc. of cold water, and then dried in an oven at 105–110° for three to four hours.

8. The yield of barbituric acid is 46–50 g. (72–78 per cent of the theoretical amount).


$CaCl_2$
Cotton plug
Water out
Clamp
Water in
Clamp

Calculation

Moles (Urea) = Moles (Barbituric acid)

Wt / M.Wt (Urea) = Wt / M.Wt (Barbituric acid)

30 g / **60.06** g/mol g mol-1 = **Theoretical Wt** / **128.09** g/mol g mol-1

% yield = Practical Wt / Theoretical Wt

Home work

1- Why is the reaction of urea with diethylmalonate considered as a condensation reaction?

2- Explain how the sodium ethoxide was obtained in procedure for synthesis of barbituric acid ?

3- In the procedure, hydrochloric acid was added to make the solution acidic, explain why ?

4- Draw the mechanism of reaction for synthesis of thiopental ?

5- Why the barbituric acid is considered as an acid ?