B.Sc Sem – IV
Chemistry Honours
Paper : SEC – 2
Pharmaceutical Chemistry

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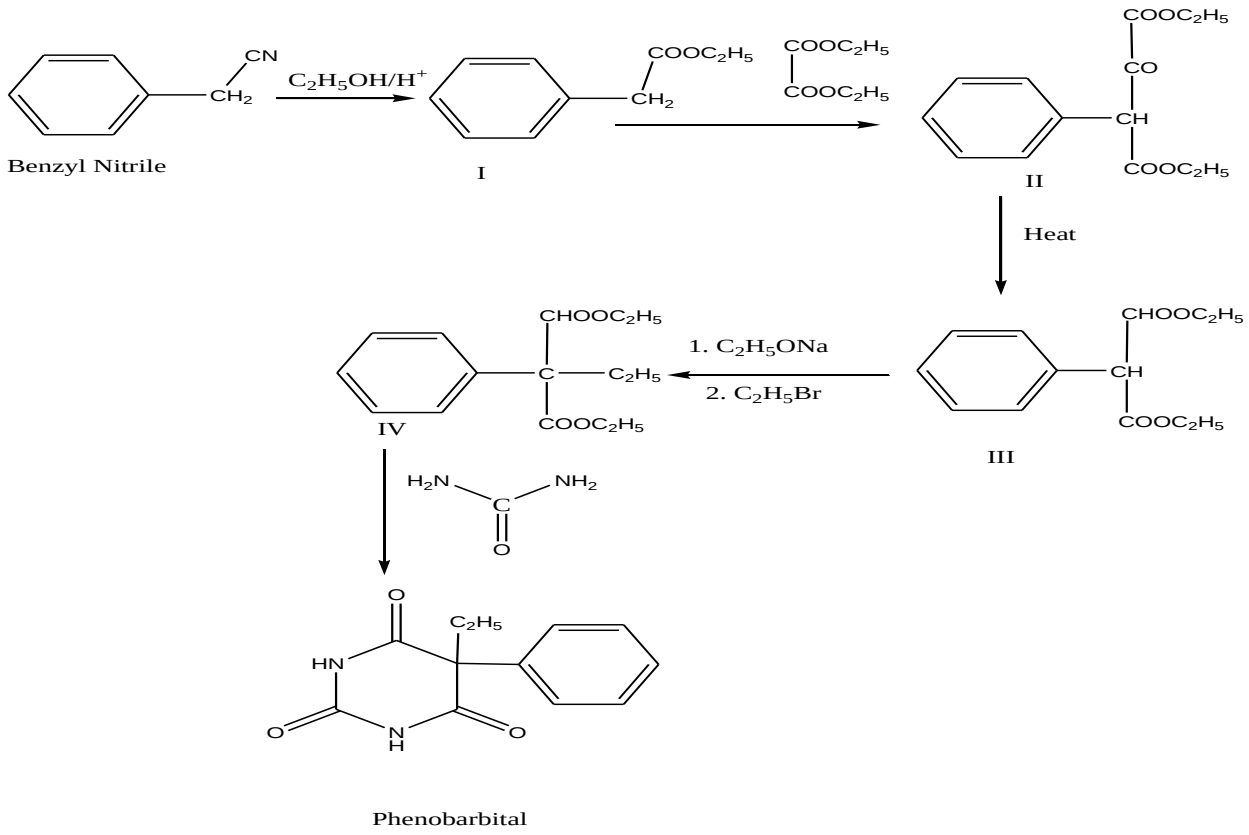
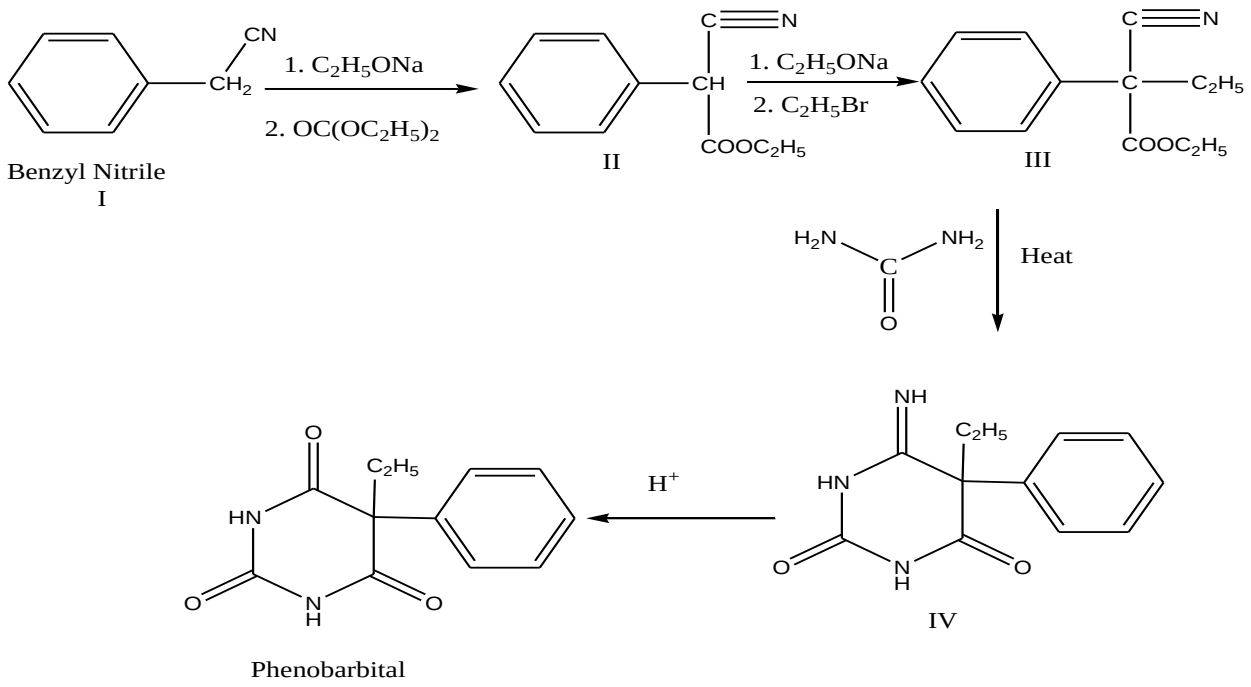
Phenobarbital

Synthesis. Barbiturate drugs are obtained via condensation reactions between a derivative of diethyl malonate and urea in the presence of a strong base. The **synthesis of phenobarbital** uses this common approach as well but differs in the way in which this malonate derivative is obtained.

The first method for synthesizing phenobarbital begins with benzyl nitril, which is transformed into the ethyl ester derivative through acidic ethanolysis. Acylation of the benzyl position with diethyl oxalate produces the compound identified in II , which splits off carbon monoxide when heated and forms α-phenyl-malonic-acid diethyl ester(III). Subsequent deprotonization at the benzyl position with sodium ethanolate and the chemical reaction with ethyl bromide produces α-ethyl-α-phenyl-malonic-acid diethyl ester(IV). The last step is a condensation reaction with urea, through which the desired phenobarbital is produced



The second method also begins with benzyl nitrile as the reactant. In the first step, the benzyl position is deprotonized with sodium ethanolate and then the chemical reaction with diethyl carbonate. Proceeding from the resulting compound, alkylation is then performed with ethyl bromide at the benzyl position, producing the compound shown in III. the chemical reaction with urea produces the 4-imin derivative of phenobarbital. Subsequent acidic hydrolysis produces the desired phenobarbital.



Uses : Phenobarbital belongs to the group of barbituric acids, which are characterized by their sedative and anesthetic effects. That is why phenobarbital was used as sleep-inducing drug/sleeping pill in the past. But it is no longer approved for use because of its addictive potential and adverse side-effects. Today it is administered primarily in preparation for anesthesia and as an anticonvulsant. It is also frequently used in the treatment of canine epilepsy Phenobarbital acts on GABAA receptors in the central nervous system. GABA receptors inhibit nerve-impulse conduction. In the thalamus gamma, aminobutyric acid is responsible for inducing or prolonging sleep. That also explains the use of phenobarbital as a sleep-inducing drug and a narcotic. It activates the ligand-controlled GABA receptors by bounding the domains and opening a chloride-ion channel. In most neurons the concentration of chloride-ions is kept at a low level and chloride-ions flow into the cell along this concentration-gradient. The resultant flow blocks depolarization, which is imperative for action-potential triggering. Thus the excitability of nerve cells is reduced. Epilepsy is a chronic dysfunction of the CNS. This connection affects signal transmission. In the brain ,hyper-excitable neurons self-discharge in different directions at the same time. These discharges disperse/spread and then lead to convulsive seizures. Today we understand that Phenobarbital works against this type of convulsion, reducing the hyper--excitability of neurons by activating the GABAA-receptors.

What is the mechanism of action of phenobarbital?

Phenobarbital's mechanism of action increases the amount of time chloride channels are open, which in turn depresses the central nervous system. This **action** occurs by acting on GABA-A receptor subunits.

What class of drug is phenobarbital?

Phenobarbital belongs to a class of drugs known as **barbiturate** anticonvulsants/hypnotics. It works by controlling the abnormal electrical activity in the brain that occurs during a seizure.

What is the antidote for phenobarbital?

Treating **Phenobarbital** Overdose

Treatment may require that the individual be kept under observation for a period of time. In some cases, the only care needed may be monitoring of vital signs. If opioids were involved in the overdose the patient may be given naloxone, an **antidote** that reverses the effects of opioids.

Thank You