Teacher: DR. SUBHANKAR SARDAR

Class : Semester-4

Paper: SEC-2

Topic : Pesticide Chemistry (Part-2)

(Synthesis and technical manufacture and uses of representative pesticides in the following classes: Organochlorines (DDT, Gammexene,); Organophosphates (Malathion, Parathion)

Reference: Wikipedia (Google)

1. https://en.wikipedia.org/wiki/Pesticide
2. https://en.wikipedia.org/wiki/DDT
3. https://en.wikipedia.org/wiki/Lindane
4. https://en.wikipedia.org/wiki/Hexachlorocyclohexane
5. https://en.wikipedia.org/wiki/Malathion
6. https://en.wikipedia.org/wiki/Parathion

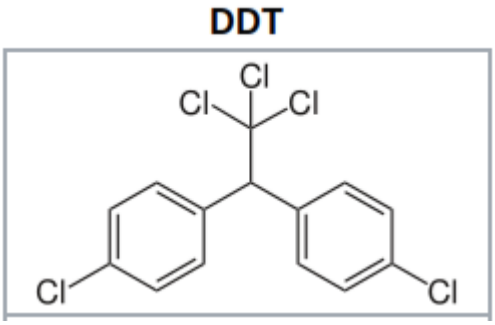
Synthesis and technical manufacture and uses of representative pesticides in the following classes: Organochlorines (DDT, Gammexene,); Organophosphates (Malathion, Parathion)

Definition of organochlorine:

The term organochlorine refers to a wide range of chemicals that contain carbon, chlorine and, sometimes, several other elements. A range of organochlorine compounds have been produced including many herbicides, insecticides, fungicides. The DDT, Gammexene are the examples of organochlorine.

DDT (dichlorodiphenyltrichloroethane)

IUPAC name: 1-chloro-4-[2,2,2-trichloro-1-(4chlorophenyl)ethyl]benzene



The Full form of DDT is Dichloro Diphenyl Trichloroethane. The molecular formula of DDT is $C_{14}H_9Cl$. It is highly hydrophobic and not soluble in water but it is soluble in most of the organic solvents, oils and fats. It is produced artificially by the reaction of chloral (CCl_3CHO) with chlorobenzene (C_6H_5Cl) in the presence of the catalyst sulphuric acid (H_2SO_4).

Uses:

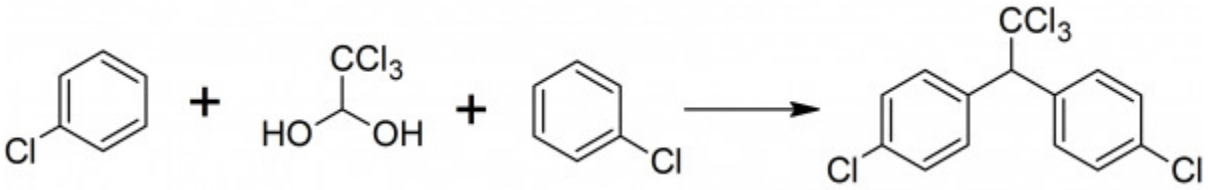
- Malaria remains the primary public health challenge in many countries. DDT was used extensively during World War II to control malaria and typhus among civiliansand troops. DDT was used to control the insect vectors of typhus – nearly eliminating the disease in many parts of Europe. In the South Pacific, it was sprayed aerially for malaria and dengue fever control with spectacular effects. DDT was effective in reducing malaria morbidity and mortality.
- DDT is a tasteless, colorless, crystalline and almost odorless organochloride substance which is famous for its insecticidal properties. Generally, it is used in agriculture and

farming to kill the insects and protect the crops. When it is sprayed on the plants, the insects residing on the plants are exposed with it. It affects the insect's neurons which lead to eventual death. It also puts a very adverse effect on the human life cycle through edible plants. It is poisonous for both humans and animals. It is accumulated in tissues and remains active for many years.

- If we talk about its adverse effect on humans, it would be a very harmful substance for them. It leads to a lot of diseases like diabetes, liver cancer, breast cancer and uncontrolled cell mutation which later leads to tumor and cancer in humans.

Synthesis:

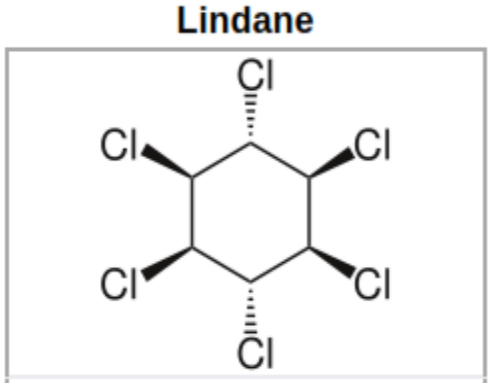
Preparation of DDT (dichlorodiphenyltrichloroethane)



To a three-neck round-bottom flask fitted with a mechanical stirrer and a thermometer 350 g of 95 % sulfuric acid, 50 g of oleum (20 % of free sulfur trioxide), 45 g monochlorobenzene, and 34 g chloral hydrate were added. The mixture is stirred rapidly and at the end of an hour the DDT separates as a fine granular solid. During the reaction the temperature rises to 45°C. For the completion of the reaction the stirring is continued for an additional half hour. The reaction mixture is poured with stirring into two liters of a 1:1 mixture of ice and water and the solid product which separates is collected on a funnel with suction and washed with cold water. To remove an excess of inorganic acid, the crude DDT is transferred to a beaker containing 500 ml. of boiling water. The mixture is stirred well and allowed to cool, whereupon the washed reaction product solidifies. This process is repeated few times and finally order to completely remove the last traces of acid a little sodium bicarbonate is added to the last wash water. The crystals of DDT is filtered and dried yielding 50 g of crude DDT, which corresponds to over 70 % of the theoretical with melting point 90°C. DDT could be

purified by crystallizing from ethyl or propyl alcohol yield product with melting point 108°C. The pure product separates as fine colorless needles that have a slight odor of fresh apples.

Gammexene



Lindane, also known as gamma-hexachlorocyclohexane (γ-HCH), gammaxene, Gammallin and sometimes incorrectly called benzene hexachloride (BHC), is an organochlorine chemical and an isomer of hexachlorocyclohexane that has been used both as an agricultural insecticide and as a pharmaceutical treatment for lice and scabies. The chemical was originally synthesised in 1825 by Faraday. It is named after the Dutch chemist Teunis van der Linden (1884–1965), the first to isolate and describe γ-hexachlorcyclohexane in 1912. Lindane is a neurotoxin that interferes with GABA neurotransmitter function by interacting with the GABA receptor-chloride channel complex at the picrotoxin binding site. In humans, gammaxene affects the nervous system, liver, and kidneys, and may well be a carcinogen. Whether gammaxene is an endocrine disruptor is unclear.

Uses:

- Gammaxene has been used to control a wide variety of insect pests in agricultural, public health, and medicinal applications. It is available as a suspension, emulsifiable concentrate, fumigant, seed treatment, wettable and dustable powder, and ultra-low-volume (ULV) liquid. Lindane is a well-known and extensively studied pesticide that is generally considered safe when used as directed.

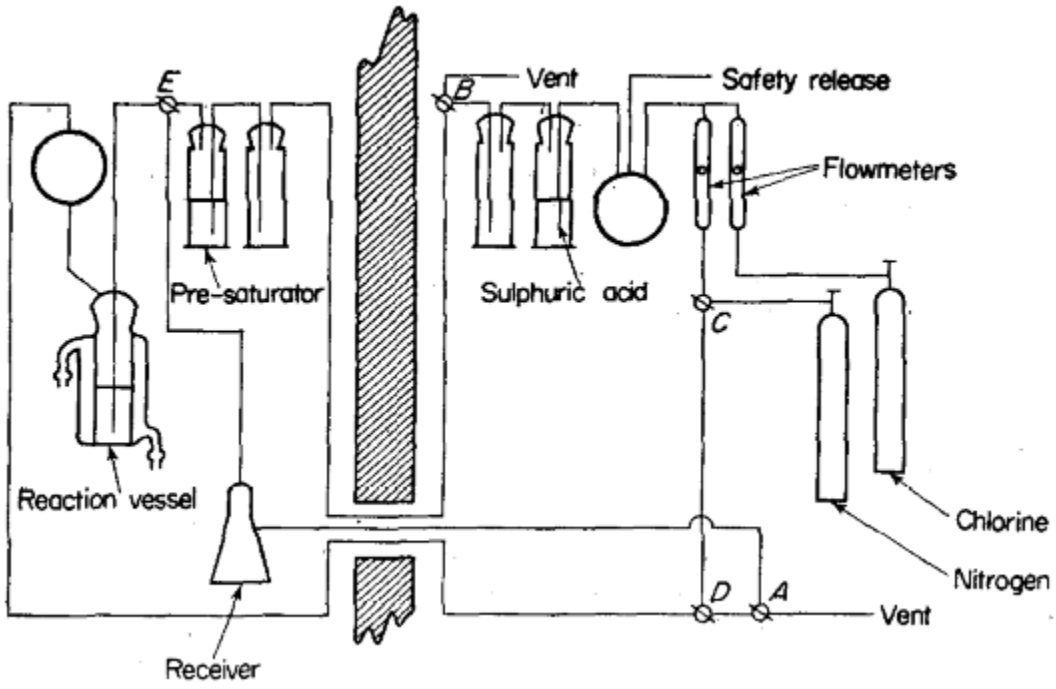
- **Pharmaceutical uses:** Lindane medications continue to be available in the US, though since 1995, they have been designated "second-line" treatments, meaning they should be prescribed when other "first-line" treatments have failed or cannot be used.

Human and animal health effects:

- **Dermal Exposure.** Dermal exposure is an important consideration when evaluating lindane toxicity because of lindane's therapeutic use as a scabicide in creams and lotions. Animal studies substantiate the acute effects of lindane following dermal exposure. Younger animals were more sensitive to the compound than their older counterparts.
- **Oral Exposure.** The clearest evidence of lindane toxicity comes from experimental and observational studies following oral exposure. Animal studies show neurologic and reproductive effects following acute exposure.
- Acute lindane decreased the motor activity, whereas the repeated dosing increased it.

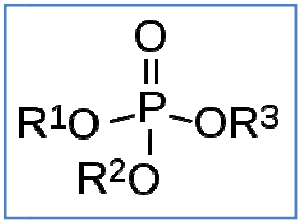
Synthesis: Benzene hexachloride (BHC), any of several stereoisomers of 1,2,3,4,5,6-hexachlorocyclohexane formed by the light-induced addition of chlorine to benzene. The chemical addition of chlorine to benzene produces a mixture of several stereoisomers of 1,2,3,4,5,6-hexachlorocyclohexane. The γ-isomer, which makes up 20–25 percent of this mixture, is more soluble than the other isomers in certain solvents and can be separated from them. Gammexane is prepared by radiation from cobalt-60 has shown that the Gammexane content of the crude material is independent of dose rate, benzene concentration and duration of the chlorination process. Small increases in the Gammexane content can be effected by low temperature chlorination. When compared with the conventional photo-initiated reaction the radiation method exhibits a marginal improvement in Gammexane content but the efficiency of energy utilization is similar.

Procedure: Benzene or a mixture of benzene and carbon tetrachloride was added to the reaction vessel and chlorine passed for 1 hr to de-aerate and saturate the hydrocarbon. This 1 hr time is found to be the optimum period. The vessel was then irradiated for a given time, usually 15 min, and finally most of the excess chlorine was removed by the passage of nitrogen. During the reaction the apply of cooling water was adjusted periodically to maintain an even temperature. The product was then discharged into a receiver and isolated .

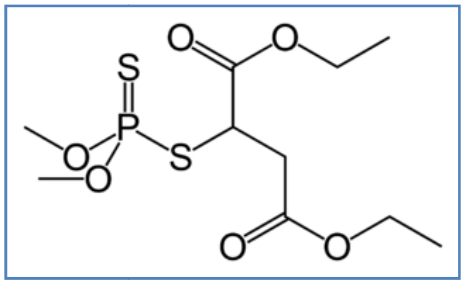


Organophosphates (Malathion, Parathion)

Organophosphates (also known as **phosphate esters**, or **OPEs**) are a class of organophosphorus compounds with the general structure $O=P(OR)_3$. They can be considered as esters of phosphoric acid. Like most functional groups organophosphates occur in a diverse range of forms, with important examples including key biomolecules such as DNA, RNA and ATP, as well as many insecticides, herbicides, nerve agents and flame retardants.



Malathion:



Malathion is an organophosphate insecticide which acts as an acetylcholinesterase inhibitor.

Uses:

Malathion is a pesticide that is widely used in agriculture, residential landscaping, public recreation areas, and in public health pest control programs such as mosquito eradication. In the US, it is the most commonly used organophosphate insecticide.

A malathion mixture with corn syrup was used in the 1980s in Australia and California to combat the Mediterranean fruit fly. In Canada and the US, malathion was sprayed in many cities to combat west Nile virus. Malathion was used over the last couple of decades on a regular basis during summer months to kill mosquitoes, but homeowners were allowed to exempt their properties if they chose. Today, Winnipeg is the only major city in Canada with an ongoing malathion adult-mosquito-control program.

Medical use:

Malathion in low doses (0.5% preparations) is used as a treatment for:

- Head lice and body lice. Malathion is approved by the US Food and Drug Administration for treatment of pediculosis. It is claimed to effectively kill both the eggs and the adult lice, but in fact has been shown in UK studies to be only 36% effective on head lice, and less so on their eggs. This low efficiency was noted when malathion was applied to lice found on schoolchildren in the Bristol area in the UK, and it is assumed to be caused by the lice having developed resistance against malathion.
- Scabies and itch

Mechanism of action:

Malathion is an acetylcholinesterase inhibitor, a diverse family of chemicals. Upon uptake into the target organism, it binds irreversibly to several random serine residues on the cholinesterase enzyme. The resultant phosphoester group is strongly bound to the cholinesterase, and irreversibly deactivates the enzyme which leads to rapid build-up of acetylcholine at the synapse.

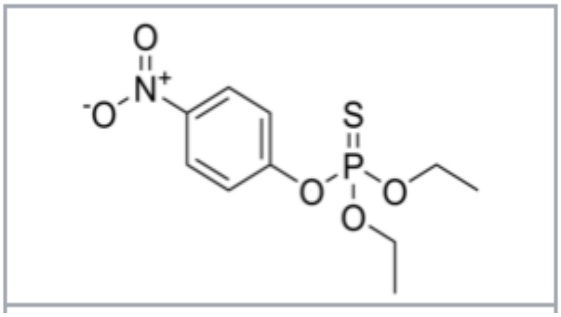
Synthesis:

Malathion is produced by the addition of dimethyl dithiophosphoric acid to diethyl maleate or diethyl fumarate. The compound is chiral but is used as a racemate.

The organophosphorus insecticide, S-1,2-di(ethoxycarbonyl)ethyl O,O-dimethyl phosphorodithioate (common chemical name: malathion), is commercially produced in the United States and abroad. Malathion is not known to occur as a natural substance. It is produced commercially by the reaction of phosphorus pentasulfide (P_2S_5) with methanol in toluene solvent to produce an intermediate, dimethylphosphorodithioic acid (DMPDT), and a byproduct, hydrogen sulfide (H_2S). The DMPDT intermediate is isolated and then reacted with either diethylfumarate or diethylmaleate. The crude material is then stripped of solvent, washed, and filtered to produce technical-grade malathion.

Parathion

Parathion



Parathion, also called parathion-ethyl or diethyl parathion and locally known as "Folidol", is an organophosphate insecticide and acaricide. It is highly toxic to non-target organisms, including humans, so its use has been banned or restricted in most countries. The basic structure is shared by parathion methyl.

When pure, parathion is a white crystalline solid. It is commonly distributed as a brown liquid that smells of rotting eggs or garlic. The insecticide is somewhat stable, although it darkens when exposed to sunlight.

Synthesis:

Parathion is synthesized from diethyl dithiophosphoric acid $(C_2H_5O)_2PS_2H$ by chlorination to generate diethylthiophosphoryl chloride ($(C_2H_5O)_2P(S)Cl$), and then the chloride is treated with sodium 4-nitrophenolate (the sodium salt of 4-nitrophenol).

$$2\ (C_2H_5O)_2P(S)SH + 3\ Cl_2 \rightarrow 2\ (C_2H_5O)_2P(S)Cl + S_2Cl_2 + 2\ HCl$$

$$(C_2H_5O)_2P(S)Cl + NaOC_6H_4NO_2 \rightarrow (C_2H_5O)_2P(S)OC_6H_4NO_2 + NaCl$$

Uses:

As a pesticide, parathion is generally applied by spraying. It is often applied to cotton, rice and fruit trees. The usual concentrations of ready-to-use solutions are 0.05 to 0.1%. The chemical is banned for use on many food crops.

Insecticidal activity

Parathion acts on the enzyme acetylcholinesterase indirectly. After an insect (or a human) ingests parathion, an oxidase replaces the double bonded sulfur with oxygen to give paraoxon.

$$(C_2H_5O)_2P(S)OC_6H_4NO_2 + 1/2\ O_2 \rightarrow (C_2H_5O)_2P(O)OC_6H_4NO_2 + S$$

The phosphate ester is more reactive in organisms than the phosphorothiolate ester, as the phosphorus atoms become much more electropositive.[6]

Safety

Parathion is a cholinesterase inhibitor. It generally disrupts the nervous system by inhibiting acetylcholinesterase. It is absorbed via skin, mucous membranes, and orally. Absorbed parathion is rapidly metabolized to paraoxon, as described in Insecticidal activity. Paraoxon exposure can result in headaches, convulsions, poor vision, vomiting, abdominal pain, severe diarrhea, unconsciousness, tremor, dyspnea, and finally lung-edema as well as respiratory arrest. Symptoms of poisoning are known to last for extended periods, sometimes months. The most common and very specific antidote is atropine, in doses of up to 100 mg daily. Because atropine may also be toxic, it is recommended that small frequently repeated doses be used in treatment. If human poisoning is detected early and the treatment is prompt (atropine and artificial respiration), fatalities are infrequent. Insufficient oxygen will lead to cerebral hypoxia and permanent brain damage. Peripheral neuropathy including paralysis is noticed as late sequelae after recovery from acute intoxication. Parathion and related

organophosphorus pesticides are used in hundreds of thousands of poisonings annually, especially suicides.

It is known as "Schwiegermuttergift" (mother-in-law poison) in Germany. For this reason, most formulations contain a blue dye providing warning.