

## **What are Pesticides?**

Pesticides are chemical substances that are meant to kill pests. In general, a pesticide is a chemical or a biological agent such as a virus, bacterium, antimicrobial, or disinfectant that deters, incapacitates, kills, pests.

This use of pesticides is so common that the term pesticide is often treated as synonymous with plant protection product. It is commonly used to eliminate or control a variety of agricultural pests that can damage crops and livestock and reduce farm productivity. The most commonly applied pesticides are insecticides to kill insects, herbicides to kill weeds, rodenticides to kill rodents, and fungicides to control fungi, mold, and mildew.

## **A Brief History**

Pesticides are not recent inventions! Many ancient civilizations used pesticides to protect their crops from insects and pests. Ancient Sumerians used elemental sulfur to protect their crops from insects. Whereas, Medieval farmers experimented with chemicals using arsenic, lead on common crops. The Chinese used arsenic and mercury compounds to control body lice and other pests. While, the Greeks and Romans used oil, ash, sulfur, and other materials to protect themselves, their livestock, and their crops from various pests.

Meanwhile, in the nineteenth century, researchers focused more on natural techniques involving compounds made with the roots of tropical vegetables and chrysanthemums. In 1939, Dichloro-Diphenyl-Trichloroethane (DDT) was discovered, which has become extremely effective and rapidly used as the insecticide in the world. However, twenty years later, due to biological effects and human safety, DDT has been banned in almost 86 countries.

## **Definition of Pesticides**

The Food and Agriculture Organization (FAO) has defined pesticide as:

Any substance or mixture of substances intended for preventing, destroying, or controlling any pest, including vectors of human or animal disease, unwanted species of plants or animals, causing harm during or otherwise interfering with the production, processing, storage, transport, or marketing of food, agricultural commodities, wood and wood products or animal feedstuffs, or substances that may be administered to animals for the control of insects, arachnids, or other pests in or on their bodies.

Chemical or biological substance designed to kill or retard the growth of pests that damage or interfere with the growth of crops, shrubs, trees, timber and other vegetation desired by humans. Practically all chemical pesticides, however, are poisons and pose long-term danger to the environment and humans through their persistence in nature and body tissue. Most of the pesticides are non-specific, and may kill life forms that are harmless or useful.

### **Examples of pesticides**

Examples of pesticides are fungicides, herbicides, and insecticides. Examples of specific synthetic chemical pesticides are glyphosate, Acephate, Deet, Propoxur, Metaldehyde, Boric Acid, Diazinon, Dursban, DDT, Malathion, etc.

### **Types of Pesticides**

There are many different types of pesticides, each is meant to be effective against specific pests. The term "-cide" comes from the Latin word "to kill."

***These are grouped according to the types of pests which they kill:***

Grouped by Types of Pests They Kill

Insecticides – insects

Herbicides – plants

Rodenticides – rodents (rats & mice)

Bactericides – bacteria

Fungicides – fungi

Larvicides – larvae

Algaecides - algae

Antimicrobials - bacteria and viruses

***Based on how biodegradable they are:***

*Biodegradable:*

The biodegradable kind is those which can be broken down by microbes and other living beings into harmless compounds.

*Persistent:*

While the persistent ones are those which may take months or years to break down.

Another way to classify these is to consider those that are chemical forms or are derived from a common source or production method.

### ***Chemically-related pesticides:***

#### *Organophosphate:*

Most organophosphates are insecticides, they affect the nervous system by disrupting the enzyme that regulates a neurotransmitter.

#### *Carbamate:*

Similar to the organophosphorus pesticides, the carbamate pesticides also affect the nervous system by disrupting an enzyme that regulates the neurotransmitter. However, the enzyme effects are usually reversible.

#### *Organochlorine insecticides:*

They were commonly used earlier, but now many countries have been removed Organochlorine insecticides from their market due to their health and environmental effects and their persistence (e.g., DDT, chlordane, and toxaphene).

#### *Pyrethroid:*

These are a synthetic version of pyrethrin, a naturally occurring pesticide, found in chrysanthemums (Flower). They were developed in such a way as to maximise their stability in the environment.

#### *Sulfonylurea herbicides:*

The sulfonylureas herbicides have been commercialized for weed control such as pyriproxyfen-sodium, cyclosulfamuron, bispyribac-sodium, terbacil, sulfometuron-methyl, Sulfosulfuron, rimsulfuron, pyrazosulfuron-ethyl, imazosulfuron, nicosulfuron, oxasulfuron, nicosulfuron, flazasulfuron, primisulfuron-methyl, halosulfuron-methyl, flupyrsulfuron-methyl-sodium, ethoxysulfuron, chlorimuron-ethyl, bensulfuron-methyl, azimsulfuron, and amidosulfuron.

#### *Biopesticides:*

The biopesticides are certain types of pesticides derived from such natural materials as animals, plants, bacteria, and certain minerals.

### **Benefits of Pesticides**

The major advantage of pesticides is that they can save farmers by protecting crops from insects and other pests. However, below are some other primary benefits of it.

1) Controlling pests and plant disease vectors. 2) Controlling human/livestock disease vectors and nuisance organisms. 3) Controlling organisms that harm other human activities and structures.

## **Effects of Pesticides**

The toxic chemicals in these are designed to deliberately release into the environment. Though each pesticide is meant to kill a certain pest, a very large percentage of pesticides reach a destination other than their target. Instead, they enter the air, water, sediments, and even end up in our food.

Pesticides have been linked with human health hazards, from short-term impacts such as headaches and nausea to chronic impacts like cancer, reproductive harm.

The use of these also decreases the general biodiversity in the soil. If there are no chemicals in the soil there is a higher soil quality, and this allows for higher water retention, which is necessary for plants to grow.

### **Top 10 Reasons To Say No To Pesticides:**

#### ***1) Pesticides don't solve pest problems.***

If they did, we wouldn't repeatedly use them, now would we? Americans use more than a billion pounds of pesticides each year to combat pests on farm crops, in homes, places of business, schools, parks, hospitals, and other public places. Instead, it would be wise to change the conditions that make pests thrive.

#### ***2) Pesticides are hazardous to our health.***

Imagine, some people don't believe this! According to the Environmental Protection Agency (who regularly sleeps with all of the pharmaceutical companies), adverse effects of exposure ranges from mild symptoms of dizziness and nausea to serious, long-term neurological, developmental, and reproductive disorders.

For instance, Glyphosate, better known as Roundup, damages genes and causes birth defects. And it's the most widely used herbicide in the United States; we use almost 200 million pounds a year.

#### ***3) Pesticides cause special problems for children.***

Let's remember that for their size, children drink more water and eat more food and than adults, and both of these can be (and often are) contaminated with pesticides. Their play increases their potential exposure. Imagine, for instance, your child playing on turf or on a grassy lawn or park treated with pesticides.

As Dr. Lynn Goldman wrote while she was an assistant administrator at EPA, “As a pediatrician, I know that children can be more vulnerable to environmental contaminants.”

***4) Pesticides contaminate our food.***

Even after peeling and washing fruits and veggies, about 60 percent of our produce still contains more than one pesticide, says the USDA.

***5) Pesticides are particularly hazardous for farmers, farm workers, and people who live near them.***

There are no comprehensive systems for keeping track of the number and type of pesticide illnesses in the U.S., but research shows that farmers and farmworkers face risks of acute poisoning and long-term illness.

Because agricultural pesticides account for over 75 percent of total U.S. pesticide use, farmers and farmworkers are often exposed to large amounts of pesticides. The EPA has estimated that between 10 and 20 thousand pesticide-related illnesses occur among farmers and farmworkers every year, but the agency believes that these large numbers are actually serious underestimates.

Mothers, meanwhile, who live near farms and are exposed to insecticides are more likely to have children with ADHD.

***6) Pesticides are dangerous to pets.***

Poisoning of pets is common. For example, in 1990 the American Association of Poison Control Centers received over 11,000 calls regarding pesticide-poisoned pets. Only antifreeze causes more pet poisoning deaths than rodent control pesticides and organophosphate insecticides.

Exposure to herbicide-treated lawns and gardens increases the risk of bladder cancer by four to seven times in Scottish Terriers, according to a study by Purdue University veterinary researchers. Since when do canines get cancer?

***7) Pesticides contaminate our water.***

According to a national study, 90 percent of our nation’s urban streams are contaminated with pesticides.

**8) Pesticides are not good for fish and birds.**

When pesticides contaminate water they can be particularly toxic to fish. In addition to fish, other marine or freshwater animals are endangered by pesticide contamination. A pesticide's capacity to harm fish and aquatic animals is largely a function of its (1) toxicity, (2) exposure time, (3) dose rate, and (4) persistence in the environment.

It is clear that some chemicals have the potential to affect entire food chains. Routine environmental use of neonicotinoids, for instance, perpetuates the propensity for runoff, groundwater infiltration, and the cumulative and largely irreversible damage to invertebrates, all of which raise significant environmental concerns.

**9) Pesticide "Health & Safety Testing" is conducted by chemical companies.**

As we mention in *Vanishing of the Bees*, this is a bad case of the fox guarding the hen house. The Environmental Protection Agency does not conduct independent studies. They rely on the chemical companies to do due diligence. And my oh my, what a surprise that they find all the poisons relatively safe. Well, be certain that doesn't mean a thing!

**10) Pesticides just have too many secrets.**

Where are they used? When? How much? What's in them? We almost never have good answers to these questions. But we do know many persist in the environment and that they synergize when combined. And inactive ingredients are really not inactive at all.

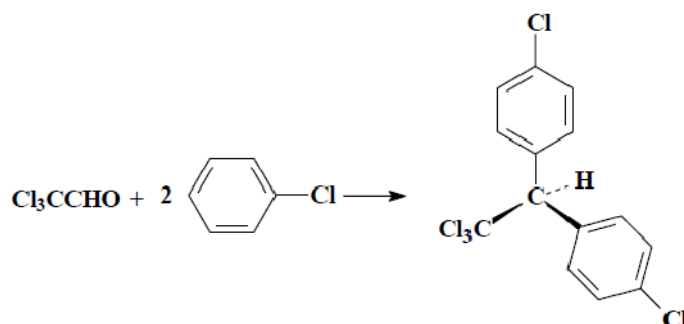
**Synthesis and uses:**

**DDT**

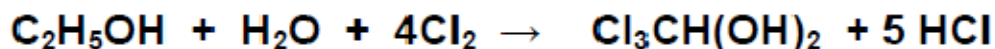
DDT [1,1'-(2,2,2-trichloroethylidene)bis(4-chlorobenzene), 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane] was synthesized for first time in 1874 by Zeidler. It does not occur naturally in the environment, its pesticide properties were recognized in 1939 by Paul Muller. Muller received in 1948 the Nobel Prize for the discovery of DDT insecticide properties. This compound was first used with success in Naples, during World War II, against body louse which is the vector for typhus. After the war, DDT was widely used on a variety of agricultural crops and

for the control of disease vectors as well. Due to its toxicity and non-biodegradability it is now banished from a large number of countries.

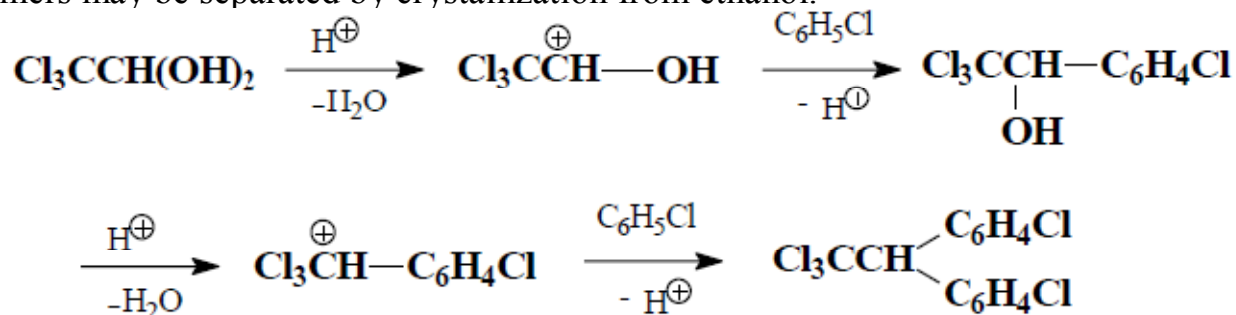
The synthesis of DDT is based on the condensation reaction of chlorobenzene with trichloro-acetaldehyde (chloral) or its hydrate (molar ratio 2/1) in the presence of acid catalyst ( $\text{H}_2\text{SO}_4$  conc. or fumans;  $\text{HSO}_3\text{Cl}$ ). The reaction is an electrophilic substitution (Friedel Crafts alkylation). Unfortunately, beside the p,p'-substituted product there are small amounts of p,o'- and o,o'-isomers.



Industrially, chloral may be manufactured by ethanol chlorination, due to the oxidative properties of  $\text{Cl}_2$ , procedure discovered by Liebig. The reaction is very complex and it is necessary to have a definite ratio between reagents and addition of water for hydrolyzing the possible formed diacetals. The hemiacetal is the only compound giving the corresponding trichloro-derivative. If the water is added at the beginning of the reaction it goes to the expected product:



In the Friedel Crafts reaction, beside the major product, p,p'-isomer (DDT), the o,p-isomer has been identified together with only traces of o,o'-isomer. The isomers may be separated by crystallization from ethanol.



Pure p,p'-DDT (or 4,4'-DDT) is a colorless crystalline or powderlike substance m.p. 109°C, b.p. 185°C at 0.05 mm Hg (decomp.), odourless to slightly fragrant, solubility in water 1.2-5.5 µg/L at 25°C (highly insoluble). Because of its lipophilicity (log Kow = 6.36), it shows bioaccumulation in adipose tissues and also biomagnification. DDT is moderately toxic to human and animals, the LD50 values depending on the testing animals: 113-118 mg/kg (rats), 150-300 mg/kg (mice), 300 mg/kg (rabbits), 500-750 mg/kg (dogs) and >1000 mg/kg (sheeps). It affects neural signal transmission. DDT is less toxic on dermal application than by ingestion. Due to its moderate toxicity it has been classified in the Class II:

Being semi-volatile is expected to be found in the atmosphere (o-isomers are more volatile). By monitoring the DDT presence in the environment, in fact a mixture of compounds is surveyed. Not only the p,p'-isomer (active substance) is comprised, but a whole group of similar compounds. The o,p'-isomer (amount depending on the reaction conditions) and the reaction by-products including the isomers p,p' and o,p' of DDD [1,1-dichloro-2,2-bis(4-chlorophenyl)ethane] are present, together with a degradation product [1,1-dichloro-2,2bis(4-chlorophenyl)ethylene]. DDT and the related compounds are very persistent in the environment, as much as 50% can remain in the soil 10-15 years after the application.

One problem in connection with the DDT complex is the possibility of such compounds to mimic hormones generating the disruption of endocrine system in wildlife and in humans. The chemical properties (low water solubility, high stability and semi-volatility) favour its long range transport so that DDT and its metabolites have been detected even in arctic air, water and organisms.

DDT and the related compounds have been detected in food from all over the world and this route it seems to be the greatest source of exposure for the general population. Thus, DDT has been banned or restricted for a great number of countries. But it is still used to control mosquito vectors of malaria, typhus and other vector borne diseases, in numerous countries.

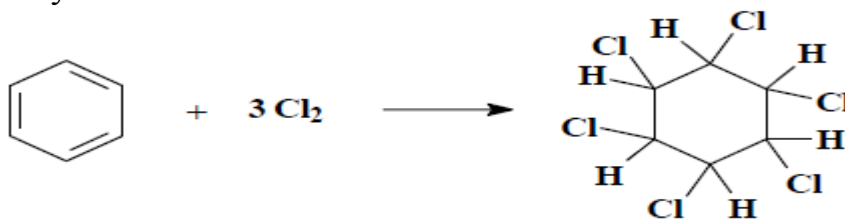


## Hexachlorocyclohexane ( $\gamma$ -HCH, BHC, Lindane, Gammexene)

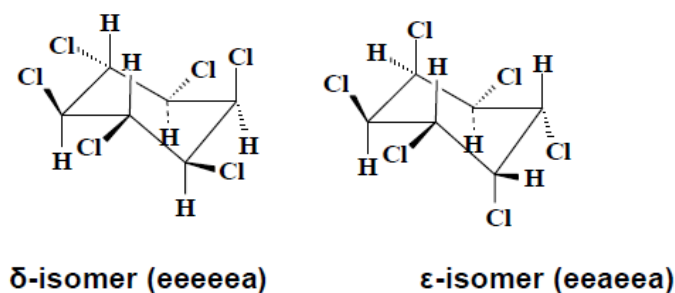
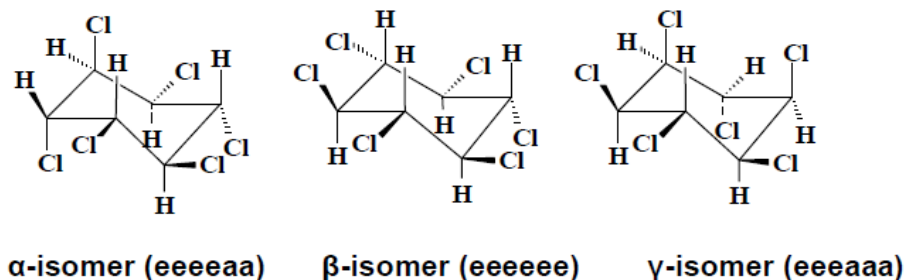
$\gamma$ -Hexachlorocyclohexane ( $\gamma$ -HCH, BHC, Lindane) is one of the best known halogenated organic insecticide that has been used worldwide for agriculture and public health. HCH is degraded rapidly under anaerobic conditions, but it is extremely persistent in upland soil. Because of its high toxicity and persistence in soil, the use of this insecticide has been prohibited in many countries.

The Hexachloro-cyclohexane has a number of possible isomers due to the axial or equatorial (a-e) positions of the chlorine atoms. The first synthesis of HCH was performed in 1825, by Faraday. The identification of all the isomers took 70 years involving many researchers Meunier ( $\alpha$  and  $\beta$ -isomers), Linden and Matthews ( $\gamma$  and  $\delta$ -isomers), Kanner ( $\epsilon$ -isomer) and Kolka ( $\eta$  and  $\theta$ -isomers).

HCH is obtained by the chlorine addition to benzene.



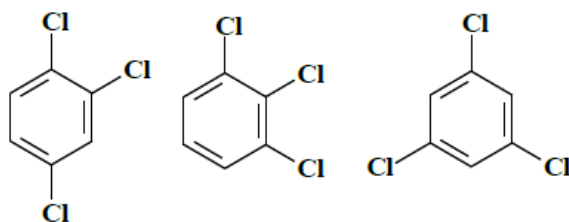
Crude benzene hexachloride consists of: 55-70% of the  $\alpha$ -isomer (e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>a<sub>1</sub>a<sub>1</sub>), m.p. 157<sup>0</sup>C, 10-18% of the  $\gamma$ -isomer (a<sub>1</sub>a<sub>1</sub>a<sub>1</sub>e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>), m.p. 112<sup>0</sup>C, 5-14% of the  $\beta$ -isomer (e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>), m.p. 309<sup>0</sup>C, 6-8% of the  $\delta$ -isomer (e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>a<sub>1</sub>), m.p. 138<sup>0</sup>C, 3-4% of the  $\epsilon$ -isomer (e<sub>1</sub>e<sub>1</sub>a<sub>1</sub>e<sub>1</sub>a<sub>1</sub>e<sub>1</sub>a<sub>1</sub>), m.p. 219<sup>0</sup>C and traces of others [ $\zeta$  (e<sub>1</sub>a<sub>1</sub>e<sub>1</sub>a<sub>1</sub>e<sub>1</sub>a<sub>1</sub>),  $\eta$  (e<sub>1</sub>e<sub>1</sub>a<sub>1</sub>e<sub>1</sub>a<sub>1</sub>e<sub>1</sub>a<sub>1</sub>) and  $\theta$  (e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>a<sub>1</sub>e<sub>1</sub>a<sub>1</sub>e<sub>1</sub>a<sub>1</sub>)]. The isomer having insecticide activity is the  $\gamma$ -isomer (a<sub>1</sub>a<sub>1</sub>a<sub>1</sub>e<sub>1</sub>e<sub>1</sub>e<sub>1</sub>) (see formula below):



Higher chlorinated isomers like: heptachlorocyclohexane and octachlorocyclohexane are present as impurities and contribute to the unpleasant odor of benzene hexachloride. The photo-addition of chlorine to benzene may be performed continuously or discontinuously, with various conversion values (10-50 %). The content in  $\gamma$ -isomer is of 10-15%. Due to the fact that only the  $\gamma$ -isomer is active, efforts have been done to enhance the content in this isomer by stereoselective synthesis. A discontinuous process, using as initiator for free-radicals (Azoisobutyronitrile), was described in a Romanian patent by Nenitzescu and coworkers. A content of 18% in the active isomer was obtained by this procedure. Another procedure giving a high content of the  $\gamma$ -isomer is the ionic addition of chlorine to benzene in dark conditions. The discontinuous procedure led to a content of 15% of the  $\gamma$ -isomer, while the improved continuous process had given 17% of this isomer.

The active isomer may be isolated from the synthetic mixture by different procedures: 1) selective crystallization of crude HCH ; 2) extraction with selected solvents like methanol; 3) treatment of the crude HCH with methanol or acetic acid, in which the  $\alpha$  and  $\beta$ -isomers are almost insoluble, followed by chromatographic separation or fractional crystallization.

The commercial product (Lindane) contains minimum of 99.9% (by wt) of the  $\gamma$ -isomer. The rest consists of a mixture of the other isomers of HCH. The pure  $\gamma$ -isomer has an aromatic odor and is very stable to the action of: heat, light and oxidation agents. It is soluble in organic solvents and partially soluble in water (7.3 mg/L). The alkaline conditions lead to the decomposition by elimination reaction giving as main product the 1,2,4-trichlorobenzene together with 1,2,3- and 1,3,5-isomers.



The elimination reaction is favored by the antiperiplanar positions of the H and Cl atoms. Such eliminations are not possible in isomers like  $\alpha$  and  $\beta$  making these isomers stable to alkaline treatment. Lindane could also be degraded by

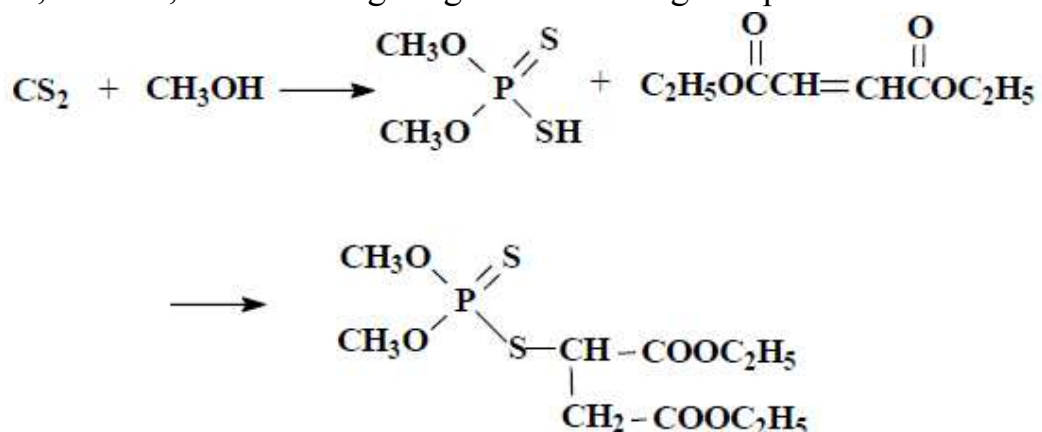
microorganisms. The cyanobacteria *Anabeana* sp. PCC7120 and *Nostoc ellipsosporum* metabolize Lindane. A mixture of 1,2,4- and 1,2,3-trichlorobenzenes is produced. The main product is 1,2,4-trichlorobenzene.

The mechanism of action of Lindane is unknown but its toxicity suggests an interaction with the lipoprotein structure of insect nerves leading to distortion in the nerve impulse transmission. The  $\gamma$ -isomer is the most efficient being 500-1000 times as active as  $\alpha$ -isomer and 5000-10000 as active as  $\delta$ -isomer.

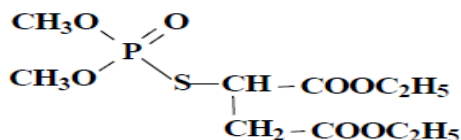
The  $\beta$  and  $\epsilon$ -isomers are almost nontoxic. The LD50 values for rat are 88.91 mg/kg (oral) and 900-1000mg/kg (dermal). Poisoning with hexachlorocyclohexane has the following symptoms: 1) Hypersensitivity to stimulation, sensation of prickling, tingling or creeping on skin; 2) Headache, dizziness, nausea, vomiting, incoordination, tremor, mental confusion, hyperexcitability; 3) In severe cases: convulsions, seizures, coma and respiratory depression. Lindane and other hexachlorocyclohexane isomers are reasonably anticipated to be human carcinogens based on sufficient evidence of carcinogenicity in experimental animals. When administered in the diet, technical-grade  $\alpha$  and  $\beta$ -Hexachlorocyclohexane and Lindane induced liver tumors in mice; the technical-grade material also produced lymphoreticular neoplasms in mice.

### Malathion

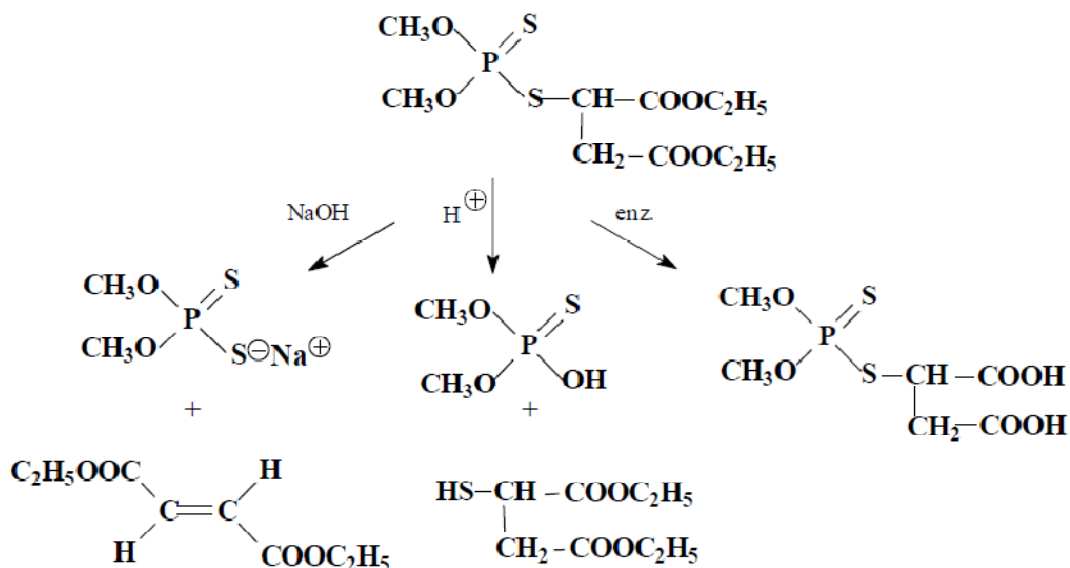
Malathion [[S-[1,2-bis(etoxy-carbonyl)ethyl] O,O-dimethyl phosphorodithioate, or diethyl[(dimethoxyphosphinothioyl)thio]butanedioate] was firstly manufactured in 1950 (American Cyanamid) and since then it has been used to kill insects on many types of crops. It is industrially produced by the reaction of  $P_2S_5$  with methanol in toluene as solvent. The dimethyl phosphorodithioic acid is isolated and then reacts with either diethyl fumarate or diethyl maleate. The crude material is stripped of solvent, washed, and filtered giving the technical grade product



It may be also synthesized starting from dimethyl phosphorodithioic acid or its sodium salt by treatment with diethyl maleate or chlorosuccinic ester, respectively: Pure Malathion is a colourless liquid, m.p. 2.90C, b.p. 156-1570C at 0.7 mm Hg. It has 145 mg/L water solubility at 200C, partition coefficient noctanol/ water 2.36 (2.89) (log P), vapour pressure 5.03 mm Hg at 250C. The technical grade product (90%) is yellow to deep brown with garlic like odour. The mammalian metabolism modifies this compound by oxidative and hydrolytic reactions. The oxidative transformation replace the P=S with P=O, giving Malaoxon [(dimethoxyphosphinyl)thio]-diethylester, which is more toxic (rat oral LD50 158 mg/kg ) than Malathion.



The hydrolysis of one of the two carboxylic ester linkages ( $\alpha$  or  $\beta$ ) by Carboxylesterases ( $\alpha/\beta$  0.07-5.0) is responsible for the low acute toxicity to mammals. Multiple forms of Carboxylesterases are widely distributed in mammalian tissues. Even the brain tissue has a detectable level of activity of this enzyme, as observed in female mice. By nonenzymatic hydrolysis, dimethyl esters of phosphordithioic, phosphorothioic and phosphoric acids have been obtained. The hydrolysis of Malathion gives different products according the pH values. At low pH, acid phosphorothioic and mercaptosuccinic diethylester are obtained. In alkaline conditions the products are: phosphorodithioic acid and fumaric diethylester. The hydrolytic transformations of Malathion in different conditions are represented below:

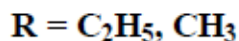
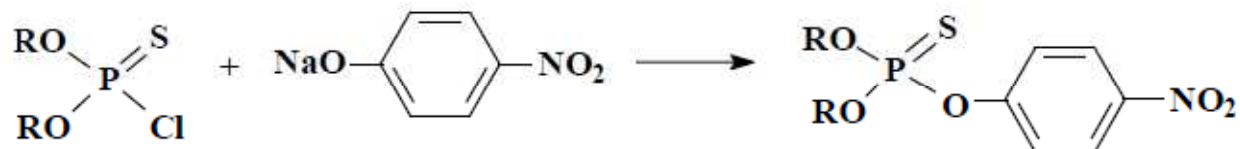


**Hydrolytic transformations of Malathion**

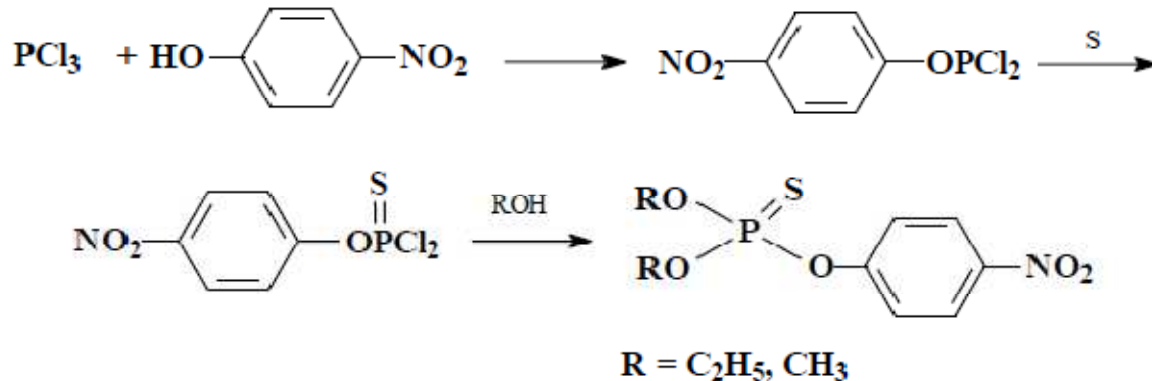
Malathion is not very toxic for mammals [oral LD50 190 mg/kg (mouse) and 290 mg/kg (rat)] and could be used as veterinary ectoparasiticide (WHO/EPA Class III). Experimental work showed a higher toxicity to younger animals due to a lower rate of detoxification. Exposure to high amounts (air, water, or food) may cause difficulty in breathing, chest tightness, vomiting, cramps, diarrhea, watery eyes, blurred vision, salivation, sweating, headaches, dizziness, loss of consciousness and finally death. Almost all of the systemic effects observed after exposure to this insecticide are due to the action of one of its active metabolites (e.g. Malaoxon) on the nervous system. There are no evidences that Malathion causes cancer. It is toxic to fish [LC50 carp (48 hr) 9.8-10.4 mg/L] and it bioaccumulates. Hormonal effects have been also observed in fish. The pure compound is less toxic than the technical grade compound. Further studies demonstrated that the impurities from the technical product inhibit the activity of Malathion-Carboxylesterases, which detoxify Malathion, as well as of Cholinesterase, thereby increasing the toxicity. The impact of on acute toxicity was evidenced in a rat in which the esterase hydrolyzing the carboxylic ester part was artificially suppressed (oral LD50 7.5 mg/kg) in comparison with the situation when the same enzyme is fully active (oral LD50 10,000 mg/kg). Released on in air it is transformed by indirect photolysis to the oxygen analog. Hydrolysis is considered to be the predominant degradation process in water, occurring more rapidly in alkaline conditions. In soil and sediments, the major degradation process of Malathion is a microbially mediated biodegradation by enzyme-catalyzed hydrolysis.

### Parathion

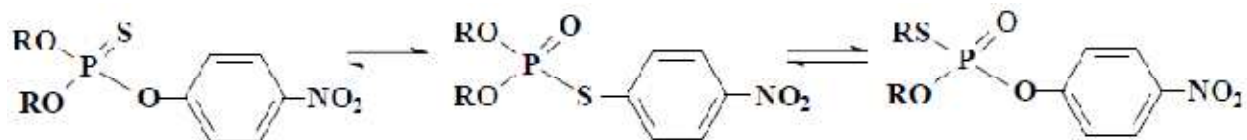
Parathion (R = C<sub>2</sub>H<sub>5</sub>), O,O-diethyl-O-(4-nitrophenyl) phosphorothioate; and Methyl-Parathion (R = CH<sub>3</sub>), [O,O-dimethyl-O-(4-nitrophenyl) phosphorothioate; are among the best known insecticides with such structure. The synthesis of these compounds was performed by treatment of the diethyl (dimethyl) - phosphorothioic chloride with pNO<sub>2</sub>-phenoxide:



Another synthesis started from  $\text{PCl}_3$  and  $\text{pNO}_2$ -phenol. The obtained compound was treated first with S and then with ethanol (methanol)



The technical Parathion is a yellow to deep brown liquid, m.p.  $6^\circ\text{C}$ , b.p.  $160^\circ\text{C}$  at 1 mm Hg, practically insoluble in water, with a solubility of 12.4 mg/L at  $25^\circ\text{C}$ , soluble in: alcohols, animal and vegetable oils, aromatic hydrocarbons, esters, ethers, n-hexane, dichloromethane, etc., Pow 3.83 (log P) at  $25^\circ\text{C}$ , vapour pressure  $4 \times 10^{-5}$  mm Hg at  $20^\circ\text{C}$ . Methyl-Parathion is a crystalline solid, m.p.  $36^\circ\text{C}$ , water solubility 55 mg/L at  $25^\circ\text{C}$ , highly soluble in organic solvents, vapour pressure  $9.7 \times 10^{-4}$  mm Hg at  $20^\circ\text{C}$ . Parathion hydrolyzes slowly at pH 7 or below. It is stable at normal temperatures. At temperatures above  $120^\circ\text{C}$ , decomposes and may develop enough pressure to cause explosions. Thermal decomposition releases toxic gases such as  $(\text{C}_2\text{H}_5)_2\text{S}$ ,  $\text{SO}_2$ ,  $\text{CO}$ ,  $\text{CO}_2$ ,  $\text{P}_2\text{O}_5$ , and nitrogen oxides. Both compounds are easily hydrolyzed. In water, Parathion will usually disappear within a week, being subject to degradation by microorganisms and chemical hydrolysis. The half-life for photo-degradation in water is 1-10 days. An alkaline pH leads to an increasing rate of breakdown. A photochemical thione-thiol transformation was evidenced:



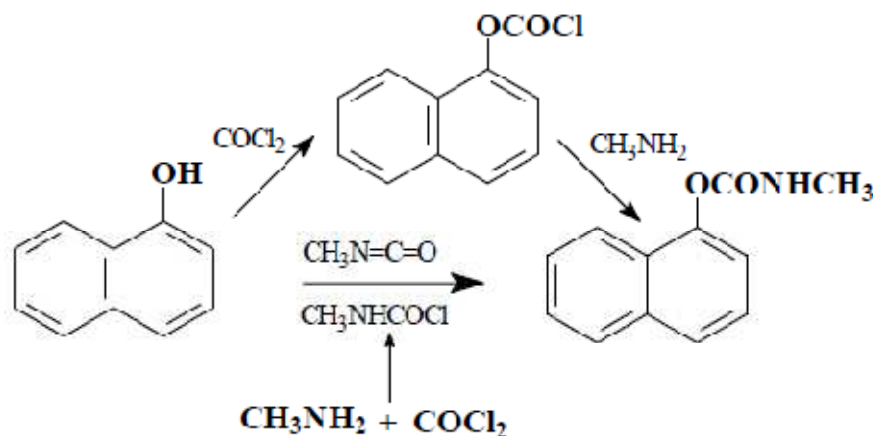
Parathion is a broad spectrum pesticide used to control many insects and mites. It has a wide range of applications on different crops and against a great number of insect species. It has non-systemic, contact, stomach and even fumigant actions. Its application is restrained by its high toxicity. In the agricultural areas of many countries is an increasing concern regarding soil contamination due to the widespread use of OP compounds. Commercial Parathion being largely used in



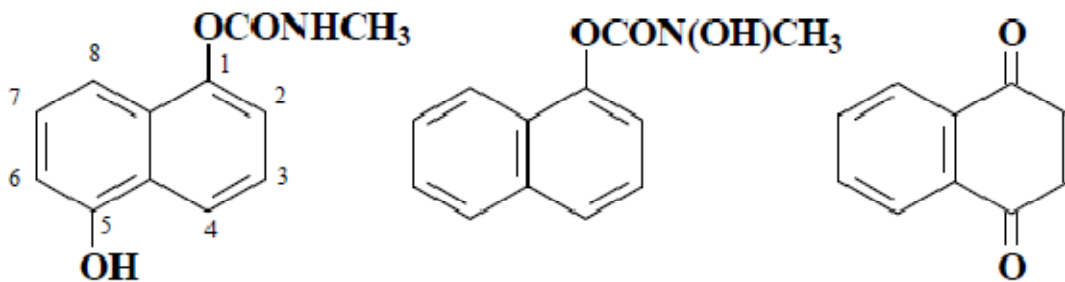
Latin America, there is a deep concern for the environment and the public health. For measurement of the chemical environmental pollution earthworms have been used as biomarkers. The study of the effects on earthworms evidenced the high toxicity of this pesticide. According to experimental data, Parathion is highly toxic by all routes of exposure. Human fatalities may be caused by ingestion, dermal adsorption, and inhalation of it. The oral LD50 is 2- 30 mg/kg (rats), 5-25 mg/kg (mice) and 3-5 mg/kg (dogs). Also toxic to the fetus it does not cause birth defects. Parathion is extremely toxic to birds like: mallards, pigeons, quails, sparrows and grouse and less toxic to pheasants. It is moderately toxic to fish and aquatic invertebrates (like crayfish, snails and worms), with a LC50 (96 hr) golden orfe, largemouth bass, rainbow trout 0.19-1.5 mg/L. Its high toxicity is mostly due to the metabolic transformation into Paraoxon. Another metabolite is the amino-derivative, obtained by the NO<sub>2</sub> group reduction. Methyl-Parathion is also a wide spectrum insecticide having contact and stomach action. It is largely used in agriculture, horticulture and veterinary medicine. Methyl-parathion is considered dangerous because of its high toxicity and classified in Class I (EPA) and Class Ia (WHO) with an oral LD50 14 mg/kg (rats). This insecticide presents no reproductive effects, no mutagenic response and no carcinogenic effects. In anaerobic sediments NO<sub>2</sub> is reduced to NH<sub>2</sub>. It is metabolized by oxidation to Methyl-Paraoxon and by hydrolysis to a mixture of Phosphorothioates, Phosphates and 4-NO<sub>2</sub>-phenol.

### Carbaryl

The best known insecticide belonging to this group is Carbaryl (1-naphthyl-N-methyl carbamate). It has been synthesized by the general procedures previously described, from 1-naphthol on treatment with COCl<sub>2</sub>, N-methylamine or with methyl-isocyanate.



Carbaryl is a crystalline solid, m.p. 142°C, has a low vapour pressure (1.17 x 10<sup>-6</sup> mm Hg at 25°C) and it does not volatilize into the air. It has a relatively low water solubility (40 ppm at 30°C), being more soluble in organic solvents (methanol 7960 ppm, methylene chloride 242600 ppm), with a partition coefficient n-octanol/water (log P) 2.36 at 25°C. It is a broad-spectrum insecticide used in agriculture for many crops due to its lower toxicity and rapid detoxification in mammals. The oral LD50 for rats is 850 mg/kg (males) and 500 mg/kg (females). It is also not very toxic for birds, mallard duck LD50 (oral, acute) > 2179 mg/kg, pheasants LD50 (oral, acute) > 2000 mg/kg, pigeons LD50 (oral, acute) 1000-3000 mg/kg. The insecticide is toxic for fish according to experimental data, channel catfish (96 hrs) LC50 15.8 ppm, asellus (96 hrs) LC50 280 ppb, daphnia magna (48 hrs) LC50 18.6 ppb. It is decomposed in the environment. In air it reacts with OH radicals. In water the compound is hydrolyzed easily in alkaline conditions, the half life at 25°C being 10-17 days at pH 7 and 3 h at pH 9, respectively. In acidic water Carbaryl is rather stable (half life > 1500 days, at 270C) [18]. In the environment it degrades faster due to the presence of microorganisms. The half life values in rivers and springs are 23-28 h. The degradation products are: methylamine, 1-naphthol, and CO<sub>2</sub>. In water, under light, Carbaryl gives also photolytic transformations leading to 1-naphthol, turned into 2-hydroxy-1,4-naphtho-quinone in basic conditions. Carbaryl is not persistent in soil being degraded by water light and microorganisms. Some bacteria may use it as source of carbon (Pseudomonas) via salicylic aldehyde. The degradation occurs faster in aerobic soil than in anaerobic conditions. The products in anaerobic soil are 1-naphthol (major product) together with 5-hydroxy-1-naphthyl N-methylcarbamate, 1-naphthyl-(Nhydroxymethyl) carbamate and 1,4-naphthoquinone.



A complex study of <sup>14</sup>C Carbaryl decomposition was done by Murthy and coworkers. More CO<sub>2</sub> resulted from the compound in moist soil than in flooded soil, together with 5-hydroxy-Carbaryl and 4- and 5-hydroxy-Carbaryl,

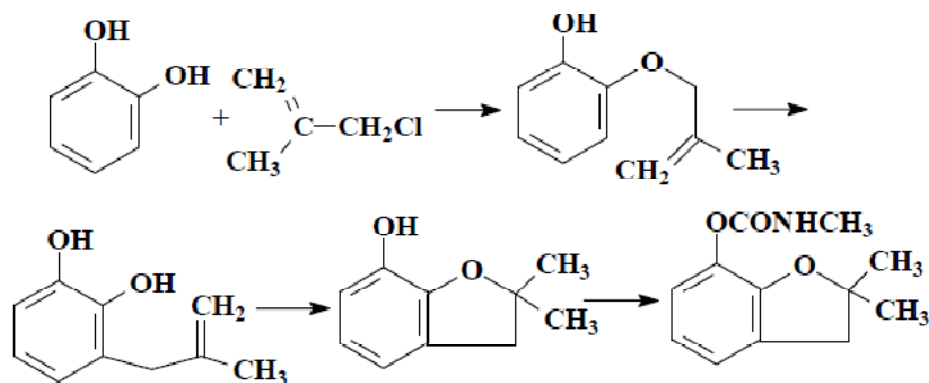


respectively. It is also easily metabolized by various animals the metabolites being excreted like glucuronides or sulfates. The identified metabolites are: 1-naphthyl (N-hydroxymethyl) carbamate, 4-hydroxy-1-naphthyl- and 5-hydroxy-1-naphthyl-N-methyl-carbamate and 5,6-dihydroxy-1-naphthyl-N-methylcarbamate. Carbaryl is highly toxic to honey bees. Plants metabolism is similar to that of animals. A number of metabolites obtained by hydrolytic and oxidative reactions have been identified for  $^{14}\text{C}$  Carbaryl (hydroxylated compounds like: 4-hydroxy-, 5-hydroxy-, 6-hydroxy-, 5,6-dihydroxy- and N-hydroxymethyl- derivatives, together with 1-naphthol).

### 6.3.1.3. Benzoannelated heterocycles

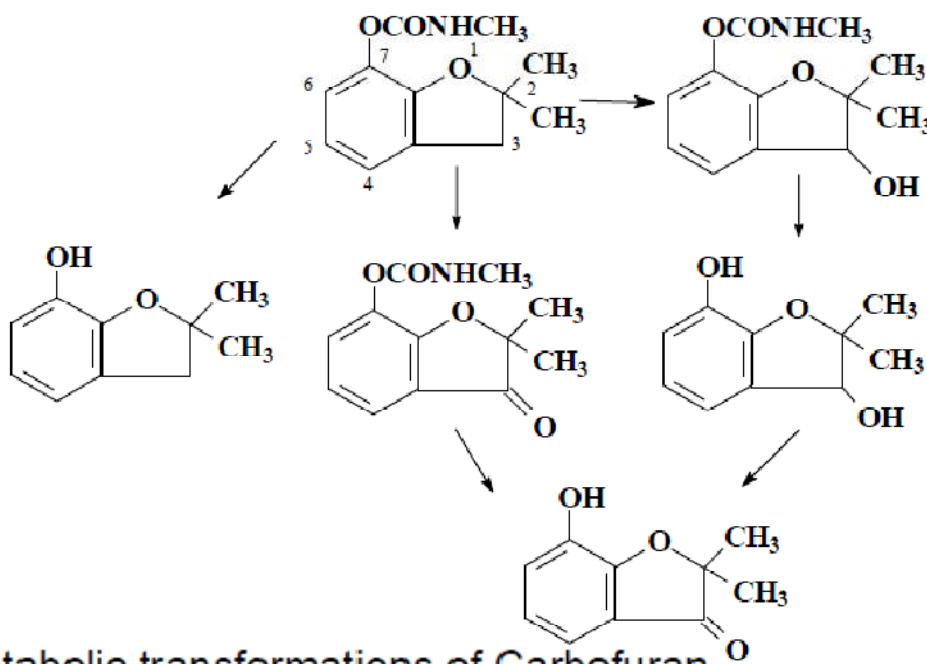
#### Carbofuran

Another well known Carbamate is Carbofuran (2,3-dihydro-2,2-dimethyl-7-benzofuranyl N-methylcarbamate). It was prepared by the following reaction sequence



The ether obtained by a phenol treatment with methylchloride gave, by a Claisen rearrangement, the alkyl derivative which turned by cyclization into the furan derivative. Carbofuran is obtained from this intermediate by treatment with  $\text{CH}_3\text{NCO}$ . Carbofuran is a broad-spectrum insecticide with first applications for eradication of pests on corn and rice and expanded later on crops like fruits (bananas, pumpkins, cucumbers, watermelons, cantaloupes, etc.) and grapes. It is a white crystalline solid with a slight phenolic odor, with m.p.  $153-4^\circ\text{C}$ , vapour pressure  $3.4 \times 10^{-6}$  mm Hg at  $25^\circ\text{C}$ , a water solubility 0.7 g/L and with a partition coefficient n-octanol/water 2.32 (log P) at  $25^\circ\text{C}$ . Carbofuran is highly toxic by inhalation and ingestion and moderately toxic by dermal absorption. The toxicity of Carbofuran was determined in several species. The values for the oral LD50

depend on the species: 6.4 to 14.1 mg/kg for rats, 18.5 mg/kg for dogs, and 25 to 38.9 mg/kg for chickens. Mice are less sensitive with an oral LD50 250-500 mg/kg.. Variations of sensitivity in different species reflect most probably the differences in metabolic deactivation of insecticide to its less toxic metabolic products. The lethal accidents are due to the direct inhibition of Acetylcholinesterase, the signs of poisoning appearing within minutes as Carbofuran acts on the enzyme. The environmental fate of the insecticide depends on the conditions. In soil the persistence depends on of the organic content, moisture and pH. Microbial degradation is very rapid. Sunlight exposure speeds up the degradation. Photolysis and photooxidation via OH radicals are the major pathway for the degradation in water, the half life values are 5.1 weeks at pH 7.0 and 1.2 h at pH 10.0. Carbofuran is also very mobile and it rapidly leaches from most soils. The half life in the body is from 6 to 12 hours. It does not accumulate in tissue. The compound is transformed by hydrolytic or oxidative enzymatic reactions:



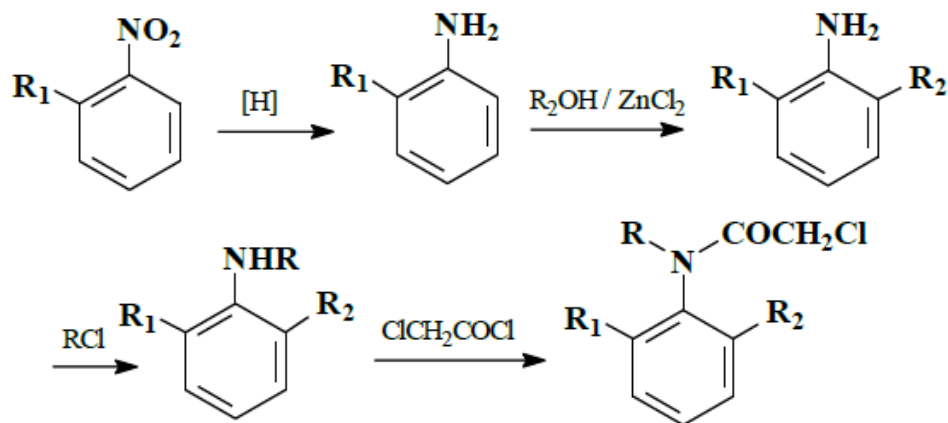
Metabolic transformations of Carbofuran

This pesticide is highly toxic to birds. Birds are accidentally poisoned by direct spraying, ingestion of granules, contaminated drinking water or consumption of contaminated prey. It seems that Carbofuran has been responsible for more deaths of bird than any other insecticide. The LD50 values are 0.238 mg/kg in fulvous ducks, 0.48-0.51 mg/kg in mallard ducks and 4.15 mg/kg in pheasants. There is

little evidence for cumulative or chronic toxicity of Carbofuran to the major organs. This is most probably due to its limited duration, consequence of the rapid metabolism. Complex studies indicate that Carbofuran is not teratogenic or mutagenic.

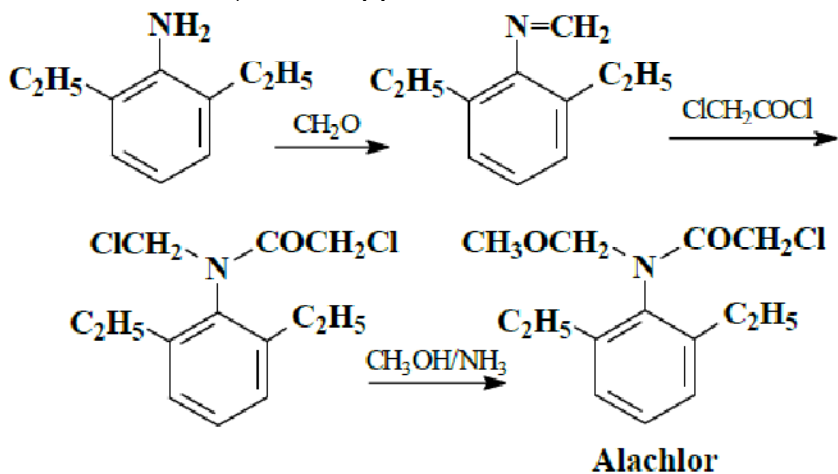
### Alachlor and Butachlor

Herbicides are used for controlling annual grasses and broadleaf weeds, in a large number of crops, like: corn, dry beans, sunflowers, and soybeans. The absorption in broadleaf species is by roots, while in grass species by shoots. These compounds interfere within normal cell development, leading to abnormal seedling. The compounds belonging to this group are aniline derivatives. They are prepared by a general multi-step method, having as key intermediate the corresponding 2,6-dialkylaniline



The best known products are:

- **Alachlor** [R =  $-\text{CH}_2\text{OCH}_3$ ,  $\text{R}_1 = \text{R}_2 = \text{C}_2\text{H}_5$ , 2-chloro-N-(2,6-diethylphenyl)-N-(methoxymethyl)acetamide] which stops root elongation by interfering with the plant ability to produce protein. It has been synthesized by the method described below but also by other approaches

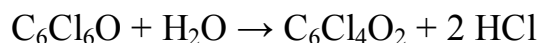
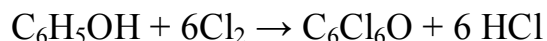


Alachlor is a slightly toxic compound, with an oral LD50 for rats of 930- 1350 mg/kg. It is suppose to have carcinogenic effects.

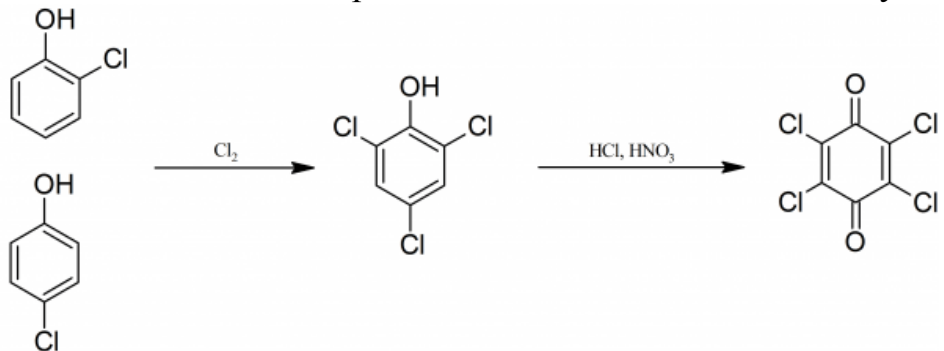
- **Butachlor** [R = -CH<sub>2</sub>OC<sub>4</sub>H<sub>9</sub>, R<sub>1</sub> = R<sub>2</sub> = C<sub>2</sub>H<sub>5</sub>, N-(butoxymethyl)-2-chloro-N-(2,6-diethylphenyl)acetamide] is an homologue of Alachlor having similar effects on weeds. It has a lower solubility than Alachlor due to the longer aliphatic chain in R.

### Chloranil

Chloranil is a quinone with the molecular formula C<sub>6</sub>Cl<sub>4</sub>O<sub>2</sub>. Also known as tetrachloro-1,4-benzoquinone, it is a yellow solid. Like the parent benzoquinone. Chloranil is produced by chlorination of phenol to give hexachlorocyclohexa-2,5-dien-1-one ("hexachlorophenol"). Hydrolysis of the dichloromethylene group in this dienone gives chloranil. Mol wt. 245.88, Toxicity: Oral rat LD50: 4000 mg/kg, physical state: yellow to greenish crystalline powder, melting point: 291°C boiling point: Sublimes, specific gravity: 1.97 solubility in water: Insoluble



Another method: All chloro derivatives of phenol are converted to chloranil by the bellow procedure.



Chloranil is used as a fungicide. It is used as an oxidizing agent in the organic synthesis especially for dye intermediates and vulcanization agent.