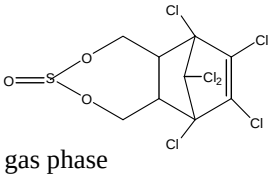
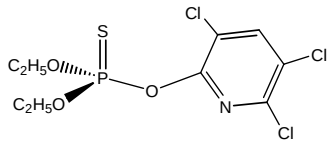
CH3041 Tutorial 9 Answers
Pesticides, Toxic Aromatics & Heavy Metals

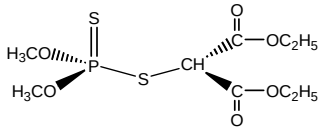
1. Using examples explain why organochlorine insecticides have been phased out and organophosphate and carbamate insecticides brought in.



Organochlorine pesticides include : DDT (p-$ClC_6H_4)_2CHCCl_3$), Lindane (γ - $C_6H_6Cl_6$).
The only one in current permitted use is endosulphan:
The chlorinated insecticides have high K_{OW} values, low rates of biodegradation, low water solubility, low vapour pressure and are non-polar.
This means that when sprayed in the environment they persist and are moved in both the gas phase and liquid phase to regions remote from the site of application. They then concentrate in sediments and enter the biological system where they are concentrated in lipid tissue. This allows for bioaccumulation in an organism and due to the long half life of the OC and it's metabolites each trophic level can accumulate progressively higher levels. BioConcentration Factor for DDT is around 10^5 (water level to a higher predator such as falcons). The high levels obtained in the body of top level organisms interferes with their reproductive functioning and causes increased mortality. For this reason although they are relatively non-toxic to humans and are good insecticides (interfere with the CNS Na/K pump mechanism). Insects also gained an appreciable resistance to most OCs.
Organophosphate pesticides in use include : malathion, chlorpyrifos



Chlorpyrifos

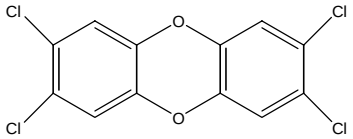


malathion

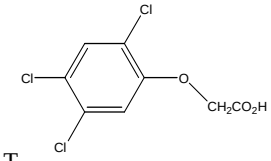
These are sulphonate ester compounds with moderately low mammalian toxicity. They readily biodegrade in the environment. In the case of malathion it is hydrolysed in mammals to generate a non-toxic metabolite (the carboxyl ester linkages are cleavged). The organophosphates are quite polar molecules and will absorb readily on soils and sediments. Combined with the ready biodegradation (high chemical reactivity) they do not enter the food chain. Both OPs and carbamates are Acetylcholinesterase inhibitors - interfere with CNS function. The carbamate insecticides have lower mammalian dermal toxicity than the organophosphates, carbaryl is a commonly used example.

2. Agent Orange, a 1:1 mixture of the herbicidal chemicals 2,4-D and 2,4,5-T, was widely used as a defoliant in the Vietnam war. The class of chemicals called Dioxins were implicated as being responsible
for the after effects of people working with the defoliant. Explain how this could have **formed** and how the **toxicity characteristics** of the defoliant could be **assessed**.

The dioxins are formed by the addition of oxygen in the synthesis of 2,4,5-T and as a side reaction which results from the coupling of two phenoxide ions formed from the phenol starting material (concentration is low < 10ppm). In general the reaction of two chloro-substituted benzene rings in the presence of chlorine and oxygen under high temperature forms a series of substituted dioxin molecules.



2,3,7,8-tetrachlorodibenzodioxin



2,4,5-T

The toxicity characteristics could be assessed by working out the concentrations of each of the dioxin congeners are present (by GC-MS or GC-ECD) and then using the toxic equivalent factor for each dioxin along with the concentration to work out a Toxic Equivalent.

$$TE = (TEF_{congener\ A} \times concentration_{congener\ A}) + (TEF_{congener\ B} \times concentration_{congener\ B}) + ...$$

The toxicity characteristics could also be assessed using Guinea pigs as a test animal

3. **Bioaccumulation** is a common problem with pesticides, toxic aromatic compounds and heavy metals. Using DDT as an example explain what factors are important for a compound to bioaccumulate and explain using Pb as example why this bioaccumulates but **doesn't biomagnify**.

DDT is a typical organochlorine pesticide molecule it has a high K_{OW} value, low rate of biodegradation, low water solubility and low vapour pressure. Because DDT is lipophilic and hydrophobic it is easily incorporated into biomass where it concentrates in the fatty tissue of organisms. Due to the long half life and non-polar nature of the organochlorine it is not readily excreted and the material bioaccumulates in an organism which has ingested the material. The metabolite DDE is even more stable and the Total DDT is found and analysed for in each organism. At each trophic level there is an increase in the concentration of Total DDT found in the organism which is referred to as biomagnification (each higher trophic level organism preys on many lower trophic level organisms, the sum of the Total DDT in all the lower trophic level organisms which have been consumed by one high trophic level organism is concentrated into this organism).
Pb is a toxic heavy metal which is accumulated by the body primarily in the bones (90%). It is able to be excreted slowly from the body (t½ 20y) which means that the loads do not increase indefinitely and once and input stops they can be lowered again. The bioavailable form of Pb is generally Pb^{2+}, Pb metal has a low vapour pressure and is generally oxidised readily, Pb does not biomethylate in the environment.
As the Pb levels in the soft tissue are quite low and bones are not generally consumed Pb does not biomagnify.

4. Explain the use of **SAR analysis** to predict activity and toxicity characteristics using a class of pesticides as an example.

Structure Activity Relationship analysis is used to predict the bioactivity of a chemical based on the structural similarities between the molecule of interest and related molecules whose activities are known. A set of physical data such as planarity, size, polarity, K_{OW}, presence of a particular functional group at a position in the molecule etc. that correlates with the activity may be used to predict the activity of molecules with only this physical data at hand.
In the case of pesticides design of a new pesticide is often based on keeping the core of the molecule constant while changing the peripheral groups. Using the organophosphate pesticides are an example:
The phosphothionate ester compound parathion was found to be an effective insecticide which functioned as a acetylcholinesterase inhibitor. Unfortunately, the compound also worked in this manner with mammals and as a result has a particularly low LD_{50} for humans (around 2mg child). Many subsequent phosphothionate insecticides have been designed which keep the core $P(=S)(OR)_3$ type of structure but change the nature of the R groups considerably. In parathion there are two Me R groups and one para-nitrophenyl group. Chlorpyrifos changes to two Et R groups and a 2,3,5-tri-chloropyrazine ring which retains good insecticidal properties but has acceptable mammalian toxicity (it has however caused some fish kills). Malathion replaces the phenyl ring by a diester group which has significant susceptibility to hydrolysis by mammalian enzymes but not be insects, as a result it is a widely used effective insecticide. In each instance the basic structure of the molecules has been retained while the toxicity has been varied so that is effective for insects but not for mammals by altering only certain elements of the structure of the molecule.

5. Lead does not biomethylate in the environment while mercury does. Both metals are regarded as priority pollutants which must carefully monitored. Explain why **biomethylation is a problem** and why **Pb** is a highly toxic metal despite the fact that it **does not biomethylate**.

Biomethylation is the process whereby a metal ion is transformed into an organometallic compound containing methyl groups bound to the metal. The classic example of biomethylation is mercury and the most famous cases of mercury poisoning have involved organomercury species. In particular Minamata disease was attributed to the conversion of pollutant Hg(II) in sediments to $MeHg^+$ by microorganisms. The organomercurial is lipophilic and is able to cross the blood-brain barrier where it acts as a central nervous system poison. $HgMe^+$ is a cumulative poison which bioaccumulates in fatty tissue and clearance from the body is relatively slow. It achieves very high bioconcentration factors (BCF 50000) and this makes Hg a very problematic metal.
The element Pb is generally found in the environment as the aqueous ions Pb(II) which is readily dispersed in the aquatic realms. The micro-organisms responsible for the biomethylation of Hg are unable to methylate Pb. Inorganic mercury Hg(II) is not lipophilic and when ingested is trapped by the kidneys. Pb(II) in contrast is stored in the bones. Both the metals Pb and Hg therefore bioaccumulate and are also

able to eliminated from the body by the protein metallothionen but once the protein capacity has been exceeded then they accumulate in the target organs. In the base of Pb(II) once it has accumulated in the bones the half-life for release is very long ($t_{1/2}$ 20y). Both metals are inherently toxic as they bind strongly to biomolecules and the presence of these metals above certain threshold levels in the blood plasma will mark the onset of toxic effects which range from CNS damage (Hg, Pb), impaired blood synthesis (Pb) and destruction of the kidneys (Hg).