

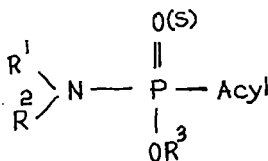
PART - I

ORGANOPHOSPHORUS PESTICIDES:

General Introduction.

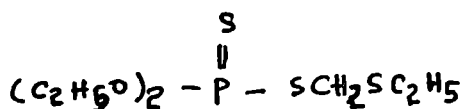
1. Introduction:

One of the most important classes of pesticides is the Organophosphorus compounds. Substances with a great variety of pesticidal properties are found among the Organophosphorus compounds with insecticidal, acaricidal, nematocidal, fungicidal, herbicidal, anthelmintic, insect sterilizing and rodenticidal properties. The development of organophosphorus pesticides resulted from the researches of Professor Schrader ⁽¹⁾ in Germany and Professor Saunders ⁽²⁾ in England, Saunders prepared some nerve poisons, including O,O-diisopropyl phosphorofluoridate (DFP). In 1937, Schrader found a contact insecticidal activity in some Organophosphorus compounds of the general formula:

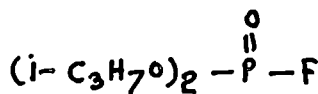


Where R^1 , R^2 and R^3 are alkyl groups, and "acyl" is an inorganic, or organic acid radical such as Cl, F, SCH and CH_3COO . Since

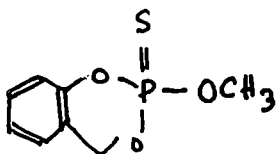
The unique properties of compounds such as Systox have resulted in successful plant systemic insecticides, and this has been still further refined in seed and soil treatments with compounds such as Phorate,



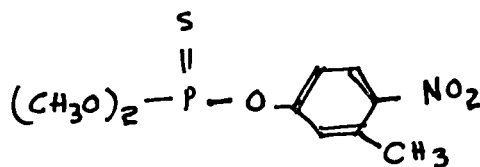
Phorate (Thimet)



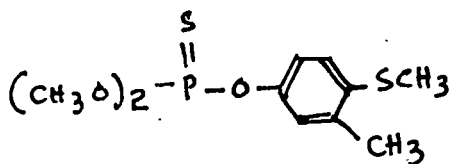
DFP



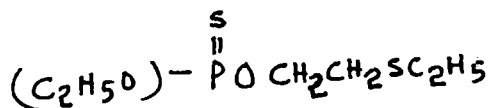
Salithion



Fenitrothion

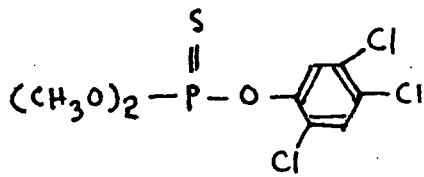


Fenthion

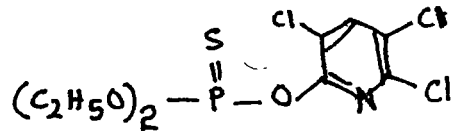


Systox

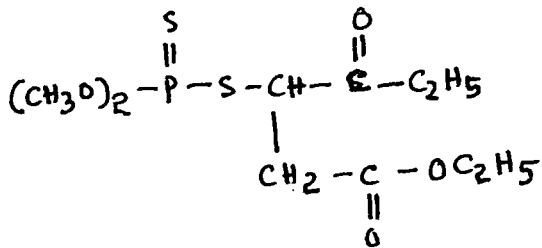
which protects newly developed seedlings from insect attack. Compounds such as Ronnel can be fed to cattle to kill cattle grubs living in the animals' bodies, while others such as Deptrex have pronounced stomach-



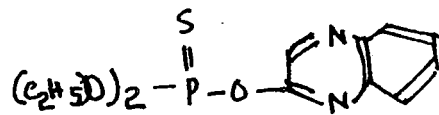
Ronnel



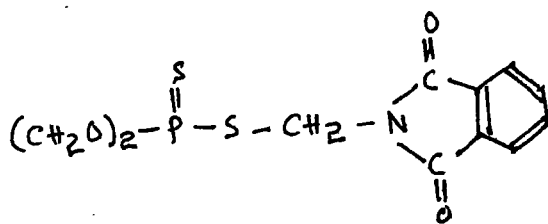
Chloropyrifos



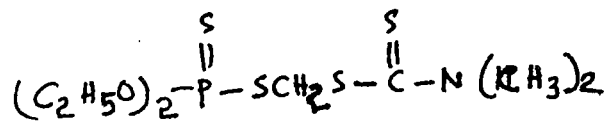
Malathion



Quinalphos

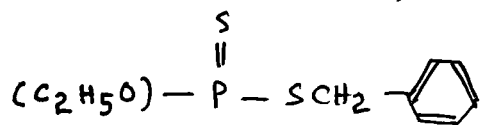


Imidan

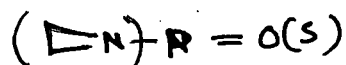


Azothion

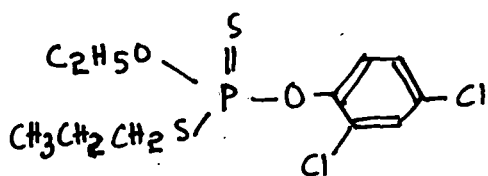
poison action but virtually no contact activity and are especially useful in poison baits. Kitazin has fungicidal activity. Many aziridine derivatives of phosphoric acid are actively studied for insect chemosterilants (tepa, thiotepa).



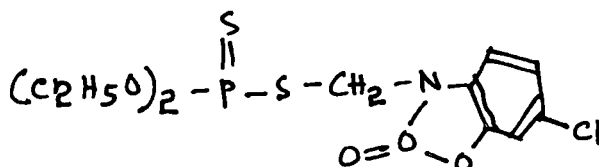
Kitazin



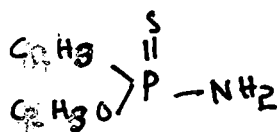
Tepa (P=O) ; Thiotepa (P=S)



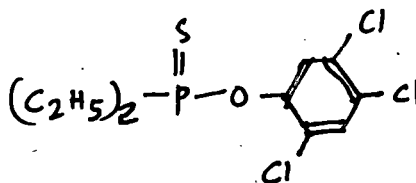
Tokuthion



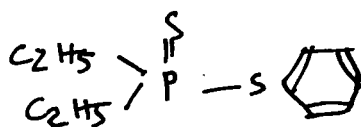
Phosalone



Methamidophos



Aquivitor



Dyfonate

The great advancement in^m agricultural practice, scientific knowledge on the structure-activity relationship, and mode of action of organophosphorus pesticides were achieved by the discovery of Parathion, diethyl p-nitrophenyl phosphorothionate by Schrader in 1944⁽³⁾. Parathion is extremely toxic to mammals as well as to insects. Many less toxic pesticides have been synthesized by slight structural modifications of parathion; for example, chlorthion (in 1952), Fenthion (in 1953), and fenitrothion (in 1959) were discovered.⁽³⁾ Malathion was discovered in 1950, and Demeton in 1951. In 1952, the Perkow reaction was discovered, and many important vinyl phosphate esters have been introduced as practical pesticides; since then several new compounds have been developed and are in commercial use. Common or trade names, chemical structures and other properties of several organophosphorus pesticides have been given in Appendix - 1

The most important advantages of the organophosphorus compounds as pesticides are (i) high pesticidal activity, (ii) broad spectrum of action on pests, (iii) low persistence and breakdown to form products non toxic or slightly^{toxic} to man and animals, (iv) systemic action of a number of compounds, (v) highly selective systemic insecticidal activity, (vi) low dosage of compound per unit of area treated, (vii) rapidity of action on plant pests, (viii) relatively rapid metabolism in vertebrates and absence of accumulation in their bodies, and (ix) also comparatively low chronic toxicity, etc.

The organophosphorus pesticides owe their biological activity to inhibition of enzyme cholinesterase, the role of which is to

hydrolyse choline esters, more precisely acetylcholine. Since this inhibitory action on enzyme activity mainly relates to the pesticidal properties of Organophosphorus compounds, the topic is dealt with, separately, in the following section:

2. Antiesterage activity of Organophosphorus Compounds:

2(a) General:

There are a variety of esterases which hydrolyse carboxylic esters. They may be classified into three groups (A, B and C esterases of A-type, named arylesterase (3.1.1.2) are not inhibited by organophosphates but hydrolyse them. They serve an important role in the detoxication mechanism of organophosphorus pesticides. B esterases are readily inhibited by organophosphates and involve Carboxyesterase (3.1.1.1.) or aliesterase and cholinesterases. C esterases, or acetyl esterases (3.1.1.6), neither hydrolyse organophosphates nor are inhibited by them.

Any of the several enzymes that hydrolyse choline esters is called cholinesterase under class B. The enzyme that particularly hydrolyses its natural substrate, acetyl choline, is called acetylcholinesterase (AChE) and plays an important role in nervous system. It occurs mainly in the erythrocyte of most mammalian nervous tissues central nervous system, ganglia and motor end-plate, and electric organs. Toxic organophosphates and carbamates inhibit this enzyme. Acetylcholinesterase is also called "true cholinesterase" to distinguish it from a similar enzyme, "pseudo cholinesterase" (BuChE), that is found primarily in vertebrate blood serum and some organs, such as the pancreas,

heart and liver. It does not participate in nerve functions and its physiological function is still unknown.

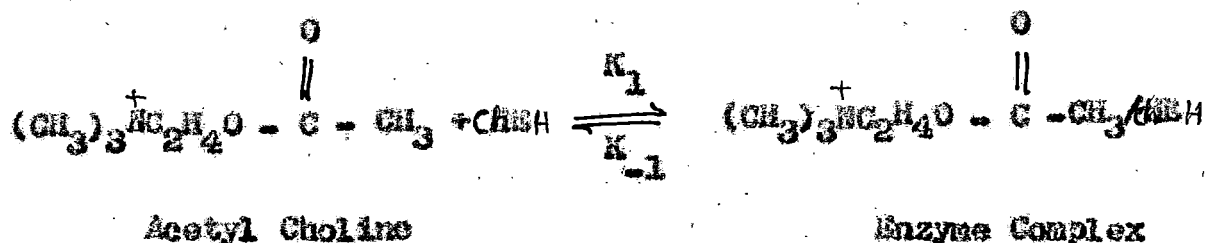
In connection with the mode of action of organophosphorus insecticides, cholinesterases of insects are most interesting to understand. The substrate specificities of the enzyme have been surveyed, using crude homogenates^(4,5), in many species of insects. Brain homogenates of adult insects are generally utilized as enzyme preparations. It may be classified as acetylcholinesterase; it prefers acetyl choline to any other choline esters of homologous higher acids as substrate; the⁽⁴⁾ esterase activity is inhibited by high concentration of acetyl choline. However, the flyhead cholinesterase is distinctly different from mammalian AChE because it hydrolyses butyl choline at about half the rate of acetylcholine, whereas mammalian AChE activity to butyryl choline is very low or nil. Another interesting property of the insect cholinesterase is that it is activated about 60% in the presence of 2 to 3% n-butanol and is protected by the organic solvent from inhibition by organophosphates. Cholinesterase is distributed mainly in the central nervous system of insects, particularly in the membrane.

2(b) Mechanism of Action of Acetyl Cholinesterase.

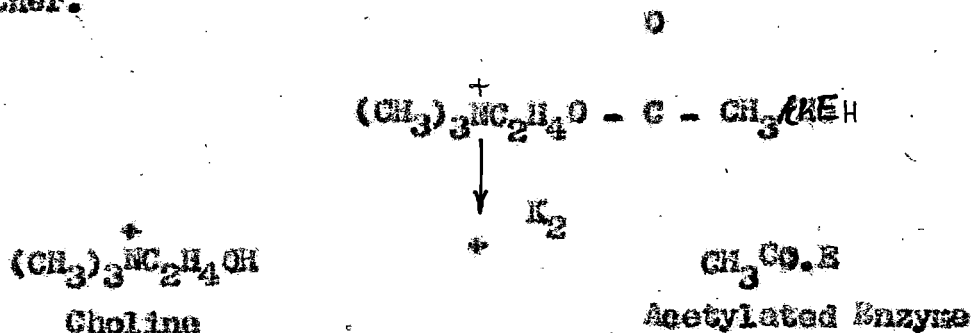
In order to understand the function of acetylcholine and cholinesterase, it is necessary to discuss briefly the physiological processes involved. At myoneural junctions in mammals and in insects, the terminal portion of muscle and the nerve fibre are at a slightly negative potential with respect to the outside. If this gradient is

altered so that the inside becomes less negative, an action potential moves down the nerve; when this potential reaches the nerve ending at the myoneural junction, acetylcholine is released and diffuses through the gap between the nerve and the muscle (the gap is about 100 Å wide) and is absorbed into the muscle ending. This interaction of acetylcholine with the receptor end of the muscle gives rise to an action potential in the muscle that responds by performing work, that is, contracting. After its purpose is accomplished, the acetylcholine is hydrolysed by acetylcholinesterase (Cholinesterase) and the muscle returns to its original state, ready to respond to future stimuli. (6)

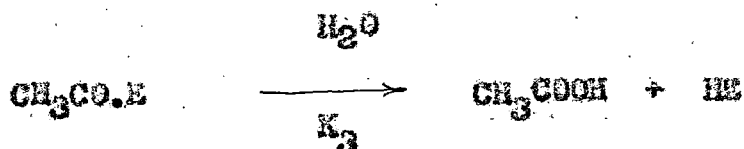
The reaction between acetyl choline (ACH) and cholinesterase (ChE) takes place in three stages and can be represented by the following sequence:



At this stage there is an equilibrium between the enzyme and its substrate on the one hand and the complex of the two on the other.



This complex yields choline and acetylated enzyme in the second stage. The final stage is the deacetylation reaction in which the acetylated enzyme is hydrolysed to give the free enzyme and acetic acid.



The active center of acetylcholinesterase (AChE) is structurally complementary to its substrate acetylcholine. Acetylcholine contains a trimethyl ammonium group with a positive charge on N and an ester linkage. In fact, the catalytic action of acetylcholinesterase is due to the structure of the enzyme protein itself. Folding the protein molecule, certain amino acid residues at distant sites of the chain are brought close to one another to form an active zone. The active zone contains two active sites. One binds the trimethyl ammonium group and is concerned chiefly with specificity (binding site or "anionic site") and the other one, which catalyses the hydrolytic process of the substrate, is relatively 'nonspecific' (esteratic site or catalytic site). (7)

2(b). (1) Binding site:

The substrate specificity of AChE for ester containing a cationic group suggests the presence of an anionic site in the active zone which attracts, binds, and orients the substrate by electrostatic

forces, facilitating the attack of the esteratic site. The methyl groups of acetylcholine may contribute considerably to the binding of the substrate to the enzyme protein in terms of hydrophobic forces between the alkyl groups and non-polar portions of the protein molecule. The nonpolar portions are evidently at the anionic site, so that the anionic site binds the cationic portion ~~part~~ of the substrate by electrostatic and hydrophobic forces ⁽⁷⁾. A weak interaction between the carbonyl group and the esteratic site may also participate in the fixation of the substrate.

AChE also catalyses the hydrolysis of some non-cationic esters, such as phenyl acetate, indoxyl acetate and indophenyl acetate. It appears that these substrates bind with AChE at different sites from that for acetylcholine binding. For example, an alkylating agent MCP (2-chloro-N-(chloro ethyl)-N-methyl-2-phenyl ethylamine) inhibits completely the activity of AChE for acetylcholine, probably due to alkylating the anionic site but, on the contrary, enhances the activity for indophenyl acetate ⁽⁸⁾. This alkylation causes a moderate inhibition for phenyl acetate and indoxyl acetate. These effects are all due to changes in K_2 (acylation process) but not K_m (formation of enzyme-substrate complex). O' Brien proposed, therefore, three different binding sites for AChE: α , β and γ sites ⁽⁹⁾. The α -site corresponds to the anionic site and binds with some alkylating agents such as MCP as well as cationic substances such as acetylcholine, choline etc. These substances are called " α -agents". The β -site is responsible for binding with organophosphates, carbamates, phenyl acetate and indoxyl acetate. It is a hydrophobic portion, and the

interaction with these inhibitors and substrates is weakened by α -agents. The γ -site combines with indophenyl acetate, acetyl fluoride, etc. and is postulated to shift into the vicinity of the esteratic site by the configurational change induced by the action of α -agents.

2(b). (ii) Esteratic site:

The pH-activity curves for cholinesterases are bell-shaped with a maximum at approximately pH 8, and indicate the requirement of basic and acidic groups in the catalytic site of these enzymes because the charge of acetyl choline does not change in this pH range. The decrease in activity at lower pH may be due to inactivation of the basic group by protonation. The activity drop at the higher pH range, on the other hand, is attributed to the deprotonation of the acidic group. According to Krupka, two catalytically active basic groups are involved in AChE: one basic group (B_1) has a pK_a value of about 5.5 and the other (B_2) has a pK_a of 6.3⁽¹⁰⁾. The catalytically active acidic group (AH) has a pK_a value in the range of 9.2 and 10.4^(10,11). Referring to the pK values of functional groups involved in protein, the imidazole group of histidine is most probable as each of the two basic groups B_1 and B_2 . As regards the structure of the active site of cholinesterases, more direct evidence on chemical analysis of components of the enzyme protein has been found. The method involves a specific reaction of the active site of an enzyme followed by the analysis of the groups involved. Cholinesterases, carboxyesterases and so called "serine proteases" such as chymotrypsin and trypsin react

stoichiometrically with organophosphorus esters such as diisopropylphosphorofluoridate (DFP) to form an enzymatically inactive product (12). Furthermore, the substrate prevents the inhibition, indicating that the reaction occurs on a common active site, that is, an esteratic site. All such enzymes inhibited by an organophosphate labelled with ³²P give O-phosphoryl serine after hydrolysis of the protein (13,14). All hydrolases sensitive to organophosphorus inhibitors have a dibasic amino acid (glutamic acid in esterases and aspartic acid in proteases) preceding the phosphorylatable serine, which is followed by alanine (in esterase) or glycine (in proteases). These findings suggest that the hydroxyl group of serine in the amino acid sequence Glu-Ser-Ala or Asp-Ser-Gly plays an important part in the catalytic site of esterases or proteases.

2(c) The Catalytic mechanism.

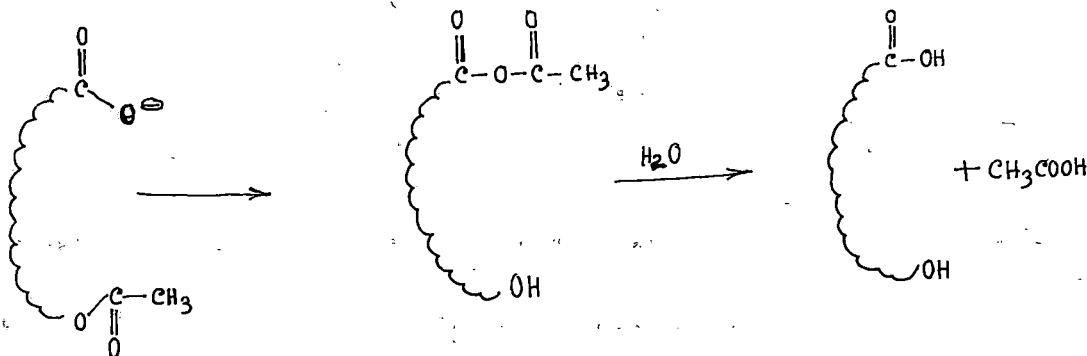
As free serine neither catalyses the hydrolysis of esters nor reacts with organophosphates, the hydroxyl group must be activated by other amino acid groups in the enzyme molecule. However, it looks more probable that the imidazole group of histidine is responsible for the activation of serine-hydroxyl, if its possible participation in catalysis is taken into consideration. The formation of a hydrogen bond between the doubly bonded nitrogen of the unprotonated imidazole ring and the hydroxyl group of serine residue may create a partial negative charge on the oxygen of serine which may attack nucleophilically the

carbonyl of the substrate (or the phosphoryl of inhibitors).



The acylated serine thus formed should be rapidly hydrolysed. Krupka showed that one of the two active basic groups (B_2 , pK_a 5.5) in the catalytic site of acetylcholinesterase functions in acetylation of serine hydroxyl and is located within 5\AA of the anionic site and another basic group (B_1 , pK_a 6.3) functions in deacetylation and is located at 9\AA from the anionic site (10). The higher pK value of B_1 is probably due to the interaction of carboxylic acid near the base (within 5\AA). This imidazole group activates a water molecule to attack the acetyl serine by abstracting a proton in a similar way as the activation of serine-hydroxyl in the step of acetylation. The active zone of the enzyme must have a suitable steric configuration to permit the joint attack of the active groups, which are not adjacent like imidazoles and serine hydroxyl. According to the induced-fit theory proposed by Koshland, it is not a rigid template, but is flexible and inducible by the substrate to align catalytic groups properly (16). The most probable mechanism is presented schematically after Krupka, as shown in the Fig. 1. In this active acidic group AH (pK_a 9.2 - 10.4) appears to be the phenolic hydroxyl group of tyrosine. An

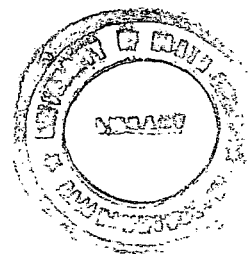
intermolecular carboxylate ion in the sterically proper position relative to the ester bond accelerates the hydrolysis by nucleophilic attack (17) to form an intermediat anhydride, which is then rapidly hydrolysed .



2(d) Inhibition of enzyme activity:

Unlike the reversible inhibition by quaternary ammonium compounds, the inhibition of acetylcholinesterase by organophosphate esters is irreversible and based on phosphorylation of the esteratic site. By an analogy of the enzyme substrate interaction, the model proposed by Krupka may be applied to illustrate schematically the reaction of organophosphorus inhibitors with AChE (Fig. 2). In this scheme, S is the anionic site or the hydrophobic binding site (O' Brien's β -site).

The reaction basically corresponds to the acetylation of the site in the normal process for the enzymatic hydrolysis of the true substrate acetylcholine. It may be shown by the following equation and the rate constant K is given as below:



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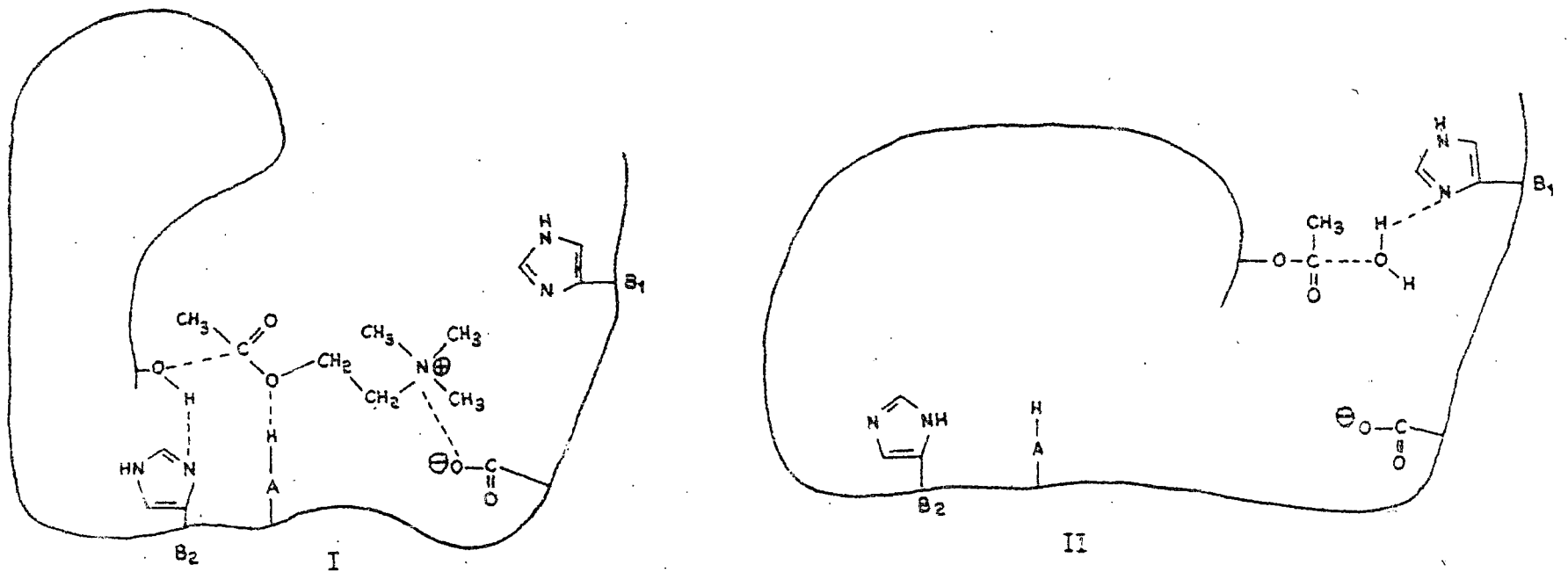


Fig. 1. Schematic Mechanism of action of AChE, after Krupka.
 (I) Enzyme-substrate complex in AChE.
 (II) Deacetylation of acetyl-AChE.

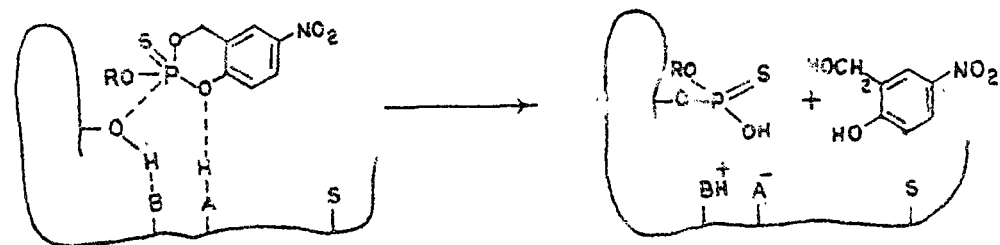


Fig. 2. Schematic mechanism of reaction of organophosphate with AChE.



$$K = \frac{1}{tI} \ln \frac{100}{b}$$

Where K = bimolecular rate constant, t = time in minutes,

I = molar inhibitor concentration and b = percentage residual activity.

Since the concentration of inhibitor (I) is much higher than that of the enzyme (e) in most ordinary experiments and consequently almost constant over the course of reaction, the bimolecular reaction shows first-order Kinetics.

Although the inhibitory potency is more properly expressed by the rate constant K, it is often expressed by the I_{50} value, which is the molar concentration of the inhibitor needed to cause 50% inhibition of the enzyme activity at a fixed time of incubation and is given by the following expression:

$$I_{50} = \frac{0.693}{t K}$$

Correlation between the reactivity of a phosphorus ester and its inhibition of cholinesterase, however, has not always been ideal, and Main⁽¹⁸⁾ introduced a Kinetic treatment for the reaction that takes into account the reversibility of the complex. This reversibility is dependent on the affinity of the inhibiting compound for the active

site of cholinesterase as well as on the rate of phosphorylation (Fig.2). By utilizing different Kinetic methods the values for K_1 (affinity const.), K_p (phosphorylation const.), and K_e (bimolecular inhibition constant) may be determined (19,20,21). Because of the high value of the phosphorylation constant K_p and the relatively high value of the affinity constant $K_1 = K_{-1}/K_1$, the amount of complex present at any given time is extremely small, and this is why the reaction follows first-order Kinetics and is bimolecular. Fukuto (19) has hypothesized that steric factors also play a significant role in the inhibition of the enzyme and possibly the affinity constant K_1 "may be affected by steric interaction between the phosphorus ester and the enzyme."

If the acetylcholinesterase is destroyed, is irreversibly bound, or forms a complex from which it is released more slowly than under natural conditions, its substrate, acetylcholine, is not promptly removed from the receptor surface of the muscle. This causes the muscle to remain depolarised longer than usual and gives rise to several action potentials passing through the muscle. The result is a twitching of the muscle leading to tetanus and eventually paralysis of the muscle. Death in mammals occurs as a result of asphyxia caused by the paralysis of respiratory muscles.

3. Chemical Hydrolysis of Organophosphorus Pesticides:

Since most organophosphorus insecticides hydrolyse, their persistence and/or appearance of hydrolysis products may be obtained from Kinetic studies. Hydrolysis rates of these compounds and their metabolites are of interest since chemical hydrolysis determines

whether or not toxic residues will persist.

3(a) Kinetic Equation for Hydrolysis:

The reaction between an organophosphorus esters (A) and water, base or acid (B) obeys second-order kinetics ⁽³⁾.



The rate equation may be represented as:

$$\frac{dx}{dt} = K_2 (a - x) (b - x)$$

where a and b are the initial concentration of reactants A and B respectively, and x is the decrease in concentration after time t. In conditions where one reactant B is in large excess or where the concentration of b is held constant, the reaction may be regarded as pseudo first-order and the above equation reduces to:

$$\frac{dx}{dt} = K_1 (a - x)$$

The half-life (t_{50})- value is given by the equation:

$$t_{50} = \frac{0.693}{K_1}$$

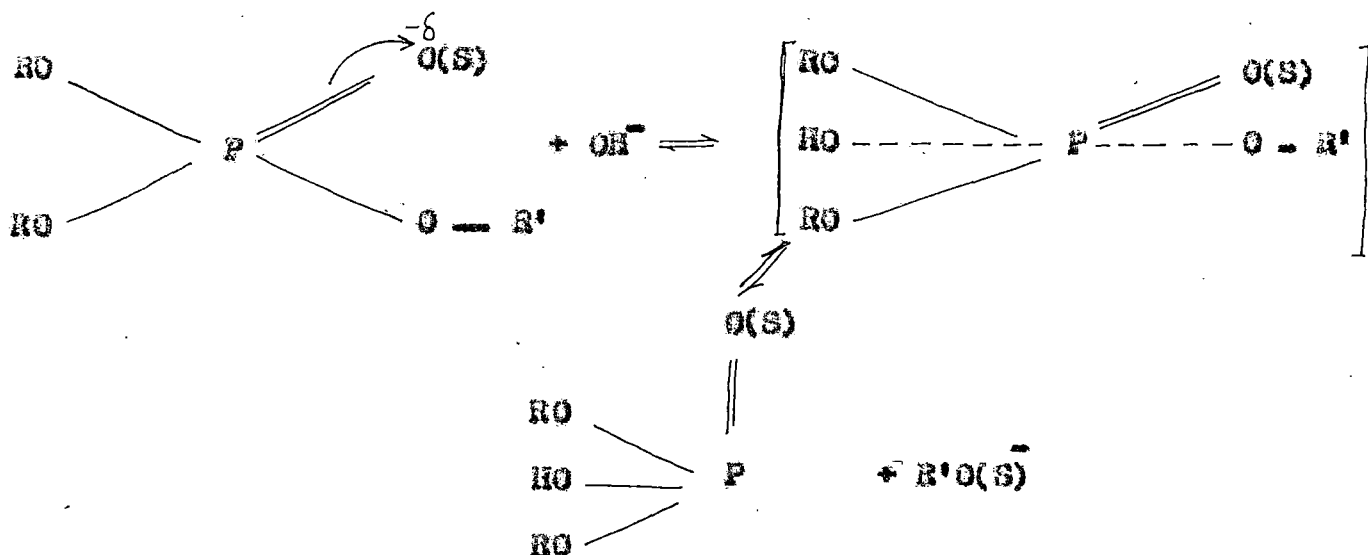
3(b) General Hydrolysis:

Fukuto ⁽²²⁾ stated that tertiary phosphate esters are

Some organophosphorus compounds, however, do not follow this general rule of acidic and basic hydrolysis. Cleavage of the P-O(S) or R'-O(S) bonds depend, in many cases, upon the nature of the R' group.

Where hydrolysis proceeds under catalysis by OH^- , S_N^2 type of reaction occurs (24). That is:

(i) the reaction is a nucleophilic substitution in which the OH^- substitutes for the R' - O group:



(ii) the reaction proceeds by a bimolecular mechanism, and

(iii) no stable intermediate forms as the OH^- approaches the molecule and attacks the P atom which has been made electrophilic by the inductive effects of the = O or = S atom and the R' group.

In all probability, $\text{R}'\text{O}(\text{S})^-$ is released simultaneously as the OH^- attacks the P atom. The reaction depends upon the electron deficiency of the phosphorus atom, which may be affected by the electronic properties of substituents on phosphorus. Thus, the hydrolyzability of

the esters is increased by the presence of electron-withdrawing groups and is decreased by the presence of electron-releasing groups. The electron-withdrawing property of acidic substituents in ordinary phosphorus pesticides increases in the order $OR < OPh < SPh < OP(O)-(OR)_2 < F$. For a series of diethyl substituted phenyl phosphates, paraoxon analogues, a detailed investigation was conducted by Fukuto and Metcalf (25). They found a linear relationship between hydrolyzability as logarithms of hydrolysis constants and Hammett's σ constants of substituents on the phenyl ring. This means that the more electron-attractive the substituent is, the more reactive is the phenyl phosphate. Electron-releasing substituents make the ester less hydrolyzable. Thus, the p-nitro derivative, whose σ constant is + 1.27, is hydrolysed 29 times faster than the non-substituted phenyl phosphate ($\sigma = 0$), and 142 times faster than the m-dimethylamino derivative ($\sigma = -0.211$). A similar relationship was also observed with diethyl-S-(p-substituted) phenyl phosphorothiolates (26).

In general, organophosphorus pesticides have bonds connecting phosphorus with hetero atoms such as oxygen, nitrogen, sulphur, and halogens, which all possess the lone pair of electrons. Such a lone pair of electrons can be donated into the vacant 3d orbitals of the phosphorus atom. By virtue of this $p\pi - d\pi$ contribution, the bondings are fortified, the electron density of phosphorus increases, and consequently, the phosphorus compounds become less susceptible to the attack of nucleophiles. Electron-withdrawing groups make the bond deficient in π -electrons and the compounds more reactive.

Certain classes of organophosphorus compounds are much more reactive than expected from pK values or electron attractivity of

the acidic groups. These include phosphorothiolates, phosphoramidates, enol phosphates, and cyclic phosphates. Steric factors, activation, and other factors should also be considered.

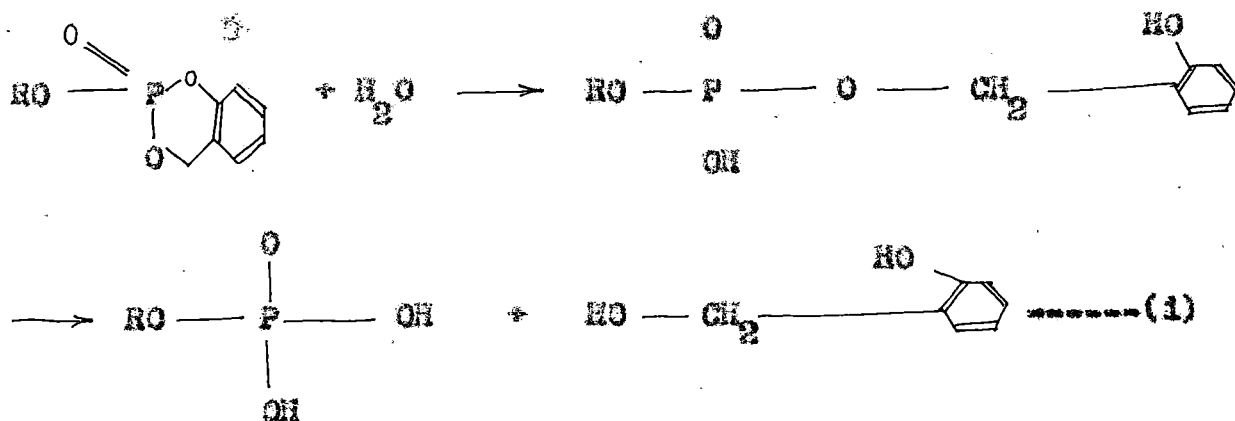
The hydrolyzability of phosphorus esters is also subject to the influence of nonacidic groups. Alkyl groups have an inductive effect to release electrons. The effect overlaps with the $p\pi - d\pi$ contribution of lone pair electrons on the oxygen to the ester group and increases in the order ; methyl < ethyl < propyl. Thus methyl esters are generally more unstable than corresponding ethyl and higher alkyl esters; demeton-S-methyl and parathion-methyl are hydrolysed 2 and 5 times faster, respectively, than the corresponding ethyl homologues.

Moreover, the methyl ester group is susceptible to dealkylation reactions. Because phosphorus acids are such strong acids that their anions can serve as good leaving groups, phosphorus ester have alkylating properties. The important role of the alkylation reaction by phosphate ester may be recognized in the biogenesis of isoprenoids ⁽²⁷⁾. With organophosphorus pesticides, the alkylation reaction is significant ⁽²⁸⁾ in chemical and biochemical degradations. In the course of hydrolysis, the methyl esters often yield dealkylated products, besides the normal hydrolysis product by the cleavage of a bond connected to the most acidic group. The dealkylation reaction takes place much more readily in a methyl ester bond than in an ethyl ester bond. When the reaction was carried out with equimolar KOH (0.025M) in 95% ethanol for 20 hrs. at room temperature, parathion yielded 11% of the dealkylated product, whereas a much higher percentage (46%) of degradation at the

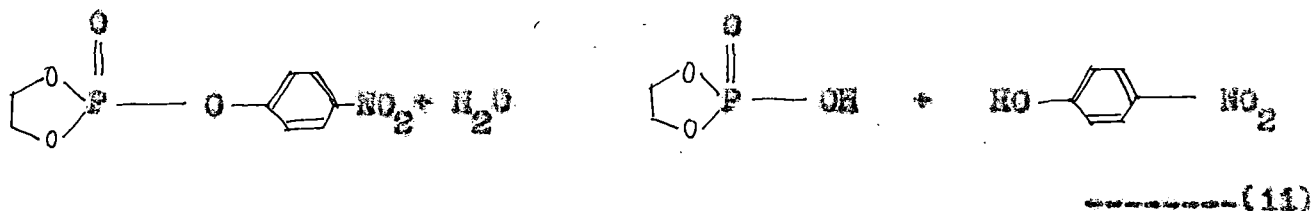
alkyl phosphate bond was observed with parathion-methyl (29). When the concentration of KOH is increased or the concentration of ethanol is decreased, normal hydrolysis is more prevalent than dealkylation. This suggests that the hydroxide ion attacks phosphorus to cause hydrolysis, and alcohol attacks the methyl group preferably to cause dealkylation.

Five membered cyclic phosphate neutral esters are too unstable to be utilised as pesticides (30). This is attributable to the extraordinary enhancement of the reactivity due to the strain in the five-membered ring (31,32). Though six-membered cyclic esters derived from alkanediols are not so very reactive, those derived from *o*-hydroxybenzyl alcohol (Saligenin) are considerably reactive, and methyl Saligenin cyclic phosphorothionate (2-methoxy-4H-1,3,2-benzodioxaphosphorin-2-sulphide) has been actually utilized as an insecticide, named Salithion, in Japan since 1963 (33). The hydrolysis rate of Salithion-*O*-analogue is much faster than that of paraoxon (34). The acidity of Saligenin ($pK_a = 9.92$) is almost the same as that of phenol, and much weaker than that of *p*-nitrophenol ($pK_a = 7.14$). Diethyl phenyl phosphate is only 1/300 as reactive as the *p*-nitro substituted analogue, paraoxon. Thus, the high reactivity of the Saligenin cyclic phosphate is much greater than expected. Strain in the ring appears to be not so much; the endocyclic O-P-O angle of Salithion (104°) is in the range of the angle of acyclic phosphate esters (102° to 108°) (3). Five-membered cyclic phosphates have a strained O-P-O angle of 98° to 99° (35). The reactivity of Saligenin cyclic phosphate is also affected by the exocyclic substituent on phosphorus by virtue of their electronic characteristics. The relative reaction rate decreases in the following order : $RS \approx Ar > Ar - O > H > RO > NHAr > NH_2 > NR_2$.

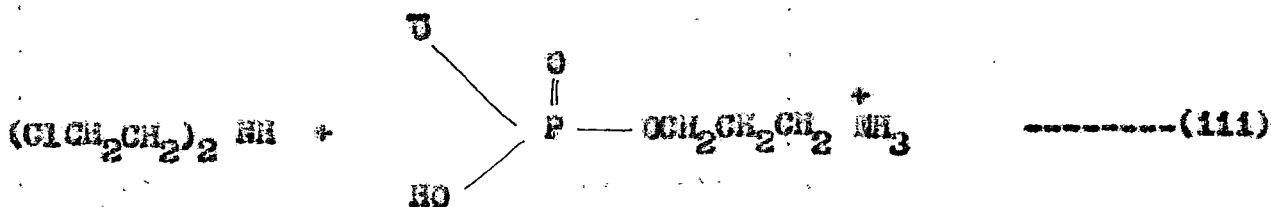
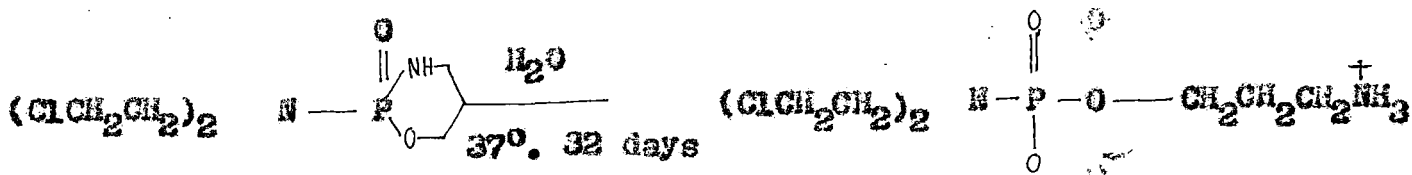
The hydrolysis of the cyclic esters proceeds by opening of the heterocyclic P-O-C (aryl) bond at the first step and is followed by the liberation of Saligenin. [Eqn. (i)]



The cleavage of the exocyclic ester bond does not take place by alkaline hydrolysis, though it does in dealkylation. This is the case even in the derivatives of a stronger acid such as p-cyanophenol ($\text{pK}_a = 7.95$). On the contrary, in the ethylene cyclic phosphate of p-nitrophenol, the hydrolysis of the exocyclic ester occurs preferably prior to ring opening ⁽³⁰⁾. [Eqn. (ii)]



Cyclophosphamide is gradually hydrolysed in water at both the endo- and exo-cyclic phosphoramidate linkages without the cleavage of the ester bond ⁽³¹⁾. [Eqn. (iii)]



The first-order half-lives of some common organophosphorus pesticides including some metabolites are listed in Table-I (36). Very good discussions on chemical structure and hydrolyzability of various organophosphorus pesticides are given by Eto (3) and Faust (36).

Half-lives of some Organophosphorus Pesticides in Ethanol (Tem. 70°C,
pH 6.0 Buffer Solution (1:4))

Compound	Half-life hours	Compound	Half-life hours
Thimet oxon	0.50	Demeton-s	18.0
Dichlorvos	1.35	Morphothion	18.4
Thimet	1.75	Baytex	22.4
Trichlorphon	3.2	Vamidothion	25.4
Mecarbaz	5.9	Menazon	27.6
Malaoxon	7.0	Paraaxon	28.0
Demeton-β-methyl	7.6	Thionazin	29.2
Malathion	7.8	Di sulfoton	32.0
Thionazin-oxon	8.2	Diazinon	37.0
Parathion Methyl	8.4	Ethion	37.5
Fenchlorphos	10.4	Parathion	43.0
Azinphosmethyl	10.4	Phenkapton	92.0
Sumithion	11.2	Chlorfenvinphos	93.0
Dimethoate	12.0	Carbophenothion	110.0
Thiometon	17.0	Dimefox	212.0
Methyl oxy-demeton	17.1		

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