SYNOPSIS

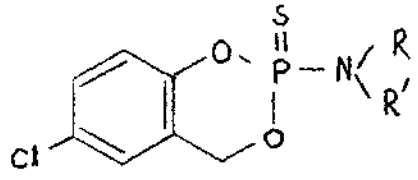
The work embodied in this dissertation is related to the investigation of some chloro saligenin cyclic phosphoramidothionates with reference to their synthesis, spectral properties, chemical, biochemical, insecticidal, fungicidal and other toxicological properties.

CHAPTER 1

A general introduction of some organophosphorus pesticides has been presented. It has been presented to a short review describing the chemical, biochemical, insecticidal, fungicidal and other toxicological properties of saligenin cyclic phosphorus compounds with special emphasis on salithion (2-methoxy-4H-1, 3, 2-benzodioxaphosphorin 2-sulphide) discovered in 1963 by Prof. Eto, Prof. Oshima and their co-workers. Investigation have revealed that the biological activities of these compounds are greatly influenced by the exocyclic substituents on the phosphorus atom.

It was reported by Prof. Eto and his co-workers that 2-methoxy-6-nitro-4H-1, 3, 2-benzodioxaphosphorin 2-sulphide (BD-8) was obtained as a paste after purification through silicic acid column chromatography and found to have about sixty times less insecticidal activity compared with salithion. However, it has been observed in this Laboratory that the methoxy compound

(ED-8) is a solid (m.p.84°c) and has about 1.5-2 times greater oral insecticidal activity to Periplaneta americana than salithion and comparable activity to grasshoppers (Oxya nitigula). Moreover, introduction of an amide group in place of an alkylester group often gives organophosphorus esters fungicidal, nematocidal and other biological activities. There are many examples in literature which show that some phosphoramidothionates, phosphoramides or phosphonamides in which the phosphorus atom is attached directly to the nitrogen atom of an amine or a hetero-cyclic compound such as phthalimide, imidazole or triazole, have very good fungicidal activity. These observation prompted us to undertake a systematic work on chloro-saligenin cyclic phosphoramidothionates. The work embodied in Chapter 2 and Chapter 3 of this dissertation is related to the investigation of some 2-alkylamido-6-chloro-4H-1, 3, 2-benzodioxaphosphorin 2-sulphides having general structure.



where  = Diisobutylamido

= Dipropylamido

= Dibutylamido

= 2, 6-Dimethylmorpholino

= 2-Ethylpiperidino

= 4-Benzylpiperidino

= Hexamethyleniminido.

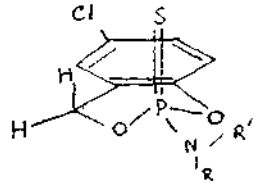
CHAPTER 2

It deals with the works related to the synthesis and spectral properties of chloro saligenin cyclic phosphoramidothionates. The structures of these compounds have been established by chemical analysis, UV, IR, Mass, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral data.

All compounds show common IR bands : 1000-1020 cm^{-1}(s), P-O-C (alkyl); 1235-1260 cm^{-1}(s) and 880-910 cm^{-1}(s), P-O-C (aryl); 800-830 cm^{-1}, P=S(I); 630-670 cm^{-1}(s), P=S(II). In mass spectra all compounds show molecular ion peaks (M^{+}) and $(M+2)^{+}$ ion peaks. In ^{1}H NMR spectra all of the compounds have signals at δ = 4.75-5.75 ppm for the $-CH_2-$protons in the dioxaphosphorin ring.

From the ^{13}C NMR spectral study of CL-6, CL-12, CL-14 and CL-17 it has been observed that the coupling (due to 31 P) to the CH_2 Carbon C_4 in the dioxaphosphorin ring changes only from 5.18 H_Z in CL-12, 5.30 Hz in CL-14, 5.33 Hz in CL-6 and 5.50 Hz in CL-17. This probably means that the conformation is almost the same and this is in accord with the small difference in ^{13}C chemical shifts, 66.45 ppm, 66.47 ppm, 66.35 ppm and 66.20 ppm respectively.

From ^{31}P NMR spectral studies it is fairly evident that the compounds are stable in one conformation.



CHAPTER 3

It deals with the works related to the biological activities and chemical hydrolysis of some 2-alkylamido-6-chloro-4H-1, 3, 2-benzodioxaphosphorin 2-sulphides.

All the compounds have less oral insecticidal activity than salithion against *P. americana* and *Chrysomaya megacephala* except CL-12 compound (2-N, N-2, 6 Dimethylmorpholino-6-chloro-4H-1, 3, 2-benzodioxaphorin 2-sulphide) which has similar activity to salithion against *P. americana*. They are less toxic to male rats than salithion and are not phytotoxic. All the chlorosaligenin cyclic phosphoramidothionates show very poor antichlolinesterase activity in blow-fly head homogenate and goat whole blood. From the chemical hydrolysis it has been observed that the 6-chloro saligenin cyclic phosphoramidothionates are . stable to alkaline hydrolysis (pH 11.85). These compounds show very good inhibitory effect on the growth of *Pyricularia oryzae*: compared with that of Kinosan they have greater inhibitory effect.

A good correlation is obtained between the pI_{50} value (for *P. oryzae* at 72 hrs) and the Structural Information Content (ΔIC) and hydrophobic constant (π). The regression equation is

$$pI_{50} = -0.167\pi - 8.318\,\Delta IC + 10.464$$
$$(\pm 0.070) \quad (\pm 2.260) \quad (\pm 1.431)$$

$n=12,\ r=0.78,\ s=0.19$

$F_{2,9}$ (Cal) = 6.98

$F_{0.05}$ (tab) = 4.30

where n is the number of compounds, s is the standard deviation, r is the correlation coefficient, F is the statistical measure of the significance of correlation.

From the above equation it can be suggested the following

(i) None of the steric, hydrophobic parameters alone can account for the biological (antifungal) response.

(ii) A combination of two or more parameters is always necessary indicating the involvement of more than one factor for the biological activity.

(iii) For *F. oxysp.* the regression equation involving pED_{50} with π and σI provides the best fit equation which suggests that steric-hydrophobic make up and topology of the bio-active molecule is a major determinant for the bioresponse.

The antifungal activity data justify further examination of these phosphoramidothioates as potential fungicides. However, their practical use in the field to protect plants from diseases is yet to be studied.

Further studies on biological activities of some 6-nitro/bromo saligenin cyclic phosphoramidothionates have also been presented.