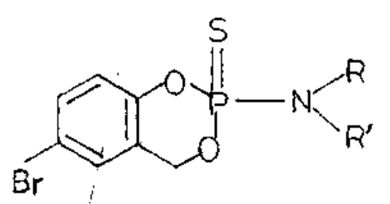
SYNOPSIS

The work embodied in this dissertation is related to the investigation of some bromo 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 reported 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. Investigations 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 (ND-6) 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 (ND-6) is a solid (m.p. 84°C) and has about 1.5 - 2 times greater oral insecticidal activity to <u>Periplaneta americana</u> than salithion and comparable activity to grasshoppers (Oxya nitidula). Moreover, introduction of an amide group in place of an alkyl ester 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 bromo-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-bromo-4H-1,3,2-benzodioxaphosphorin 2-sulphides having general structure



where $-N\begin{matrix} R \\ R^1 \end{matrix}$ = Diisobutylamide

= Dipentylamide

= Dihexylamide

= Dibutylamide

= 2,6-Dimethylmorpholino

= 2-Ethylpiperidine

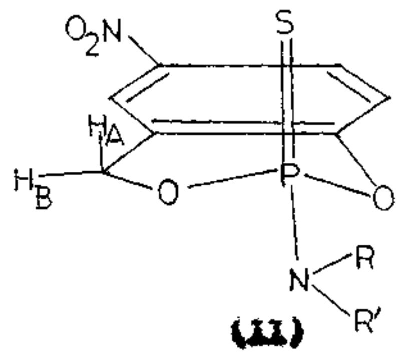
= 4-Benzylpiperidine

= Hexamethylenimide.

CHAPTER 2

It deals with the works related to the synthesis and spectral properties of bromo saligenin cyclic phosphoramidothioates. The structures of these compounds have been established by chemical analysis, UV, IR, Mass, ^{1}H NMR, ^{13}C NMR spectral data. All the compounds show common IR bands : 1010 - 1040 cm^{-1}(s), P-O-C(alkyl); 1235 - 1260 cm^{-1}(s) and 870 - 910 cm^{-1}(s), P-O-C (aryl); 805 - 815 cm^{-1}, P=S(I); 640 - 690 cm^{-1}, P=S(II). In mass spectra all the compounds show molecular ion peaks (M^{+}) and $(M + 2)^{+}$ ion peaks. For the proton noise decoupled ^{13}C spectra of BR-6, BR-12, BR-14 and BR-17 at 100 MHz the saturated carbons 2 and 3 bonds from the phosphorus show splitting due to ^{13}C - ^{31}P spin coupling. The chemical shift values for the CH_2 carbon (C_4) in the dioxaphosphorin ring of BR-6, BR-12, BR-14 and BR-17 are almost the same. ^{13}C chemical shifts are often quite sensitive to conformation, it supports the similarity of the structure. In ^{1}H NMR spectra all of the compounds have signals at δ = 4.65-6.74 ppm for the $-CH_2-$ group protons in the dioxaphosphorin ring.

From the study of the ^{1}H NMR spectral data of some 2-alkoxy/phenoxy/alkylamido-6-nitro-4H-1,3,2-benzodioxaphosphorin 2-sulphides it is fairly evident that the chemical shift difference of the protons H_A and H_B increases in going from 2-alkoxy to 2-alkylamido compounds, and that the 2-substituent at the same time increases in bulk, and probably spends more time in the conformation with the least steric interaction. The structure II appears to explain, to a reasonable extent, the reversal of the expected proton chemical shift order for the quasi axial and quasi equatorial protons, due to the position of the magnetically anisotropic P=S bond relative to the $-CH_2-$group in the dioxaphosphorin ring.



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CHAPTER 3

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

All the compounds have less oral insecticidal activity than salithion against *P. americana*. They are less toxic to male rats than salithion and are not phytotoxic. All the bromo saligenin cyclic phosphoramidothionates show very poor anticholinesterase activity in blow-fly head homogenate and goat whole blood. From the chemical hydrolysis it has been observed that the 6-bromo saligenin cyclic phosphoramidothionates are most stable to alkaline hydrolysis (pH 11.65). These compounds show very good inhibitory effect on the growth of *Helminthosporium oryzae*; compared with that of Hinosan they have greater inhibitory effect.

A good correlation is obtained between the pED_{50} value (for *H. oryzae* at 72 hrs) and the Structural Information Content (SIC) and hydrophobic parameter (log P). The regression equation is

$$pED_{50} = \underset{(\pm 0.336)}{23.422}\ \text{SIC} - \underset{(\pm 0.222)}{27.494}\ (\text{SIC})^2 - \underset{(\pm 0.122)}{0.096}\ \log P + \underset{(\pm 2.362)}{0.486}$$

$n = 13$; $s = 0.14$; $r = 0.94$

$F_{(3,9)}\ \text{cal} = 23.9$ and $F_{(3,9)(0.001)}\ \text{tab} = 13.9$

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 followigg

(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 *H. oryzae* the regression equation involving pED_{50} with SIC, $(\text{SIC})^2$ and log P provides the best fit equation which suggests that stereo-hydrophobic make-up and topology of the bio-active molecule is a major determinant for the bioresponse.

Further studies on antifungal activity of some bromo saligenin cyclic phosphoramidothionates against *Pyricularia oryzae* have been presented.

In Chapter 4 the studies on some 6-nitro/chloro saligenin cyclic phosphoramidothionates having pesticidal activities (including insecticidal activity, acute oral toxicity, anticholinesterase activity, fungicidal activity) have also been presented.

The antifungal activity data justify further examination of these phosphoramidothionates as potential fungicides. However, their application in the field to protect plants from diseases is yet to be studied. In order to find out the chemical structure-biological activity relationship in these compounds we have to synthesize several new compounds in which different group is to be incorporated in different positions of the aromatic ring and to investigate their biological activity.