Synopsis

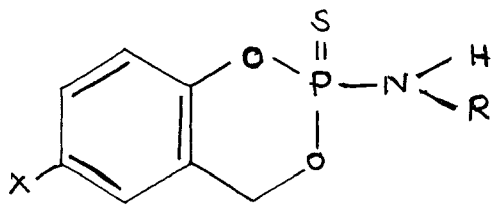
SYNOPSIS

The work embodied in this dissertation is related to the investigation of some 6-bromo/chloro/nitro saligenin cyclic phosphoramidothionates with reference to their synthesis, chemical, biochemical, insecticidal, fungicidal and other toxicological properties besides structure elucidations by chemical analysis and spectroscopic methods.

In Chapter 1 of this dissertation, a brief introduction to saligenin cyclic phosphates and related compounds have been presented (Part I).

Aims and objectives of the present investigation have been presented in Part II (Chapter 1).

Chapter 2 of this dissertation is related to the investigation on some 2-alkylamido-6-bromo/chloro/nitro-4H-1,3,2-benzodioxaphosphorin-2-sulphides having the general structure A,



[A]

where X = Br/Cl/NO_2 and the alkylamido group is iso-propylamido, sec-butylamido, furfurylamido, where X = Br/Cl and iso-propylamido, sec-butylamido when X = NO_2.

The experimental part on the biological and hydrolytic properties are shown in the Appendix - I.

The above mentioned 2-alkylamido-6-bromo/chloro/nitro-4H-1,3,2-benzodioxaphosphorin-2-sulphides have been prepared by the reaction of the corresponding phosphoramidodichloridothionate with 5-bromo/chloro/nitro saligenin at low temperature (0-5°C) in presence of potassium carbonate as dehydrogen chloride agent.

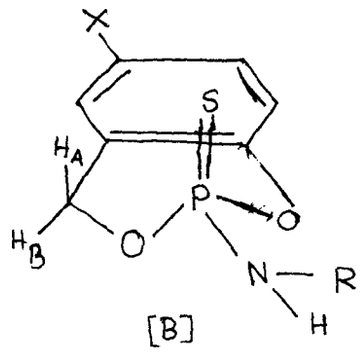
The structures of these cyclic phospheramidothionates have been established by chemical analysis UV, IR, Mass and ^{1}H NMR spectral data.

All compounds show characteristic IR bands for P-O-C (alkyl), P-O-C (aryl), P=S, N-H str. etc.

In mass spectra, they show peaks due to parent molecular ion (M^+) and $(M- SH)^+$ ions. For 6-bromo saligenin cyclic phosphoramidothionates M^+ and $(M + 2)^+$ ion peaks are of almost equal intensi All the bromine containing fragments also show $(fragment +2)^+$ ion peaks. For 6-chloro compounds $(M + 2)^+$ ion peaks are approximately one-third in intensity of the M^+ ion peaks. $(Fragment +2)^+$ ion peaks are also nearly one-third in intensity of the fragment ion peaks.

From the ^{1}H NMR spectral data of the 2-alkylamido-6-bromo/chloro/nitro-4H-1,3,2-benzodioxaphosphorin-2-sulphides it is evident that the 2-substituent spends more time in the conformation with least steric interactions. Several plot expansions of some of the phosphoramidothionates suggest that the molecules are probably in one conformation. A Dreiding model of the molecules seems to have a stable conformation in which one of the methylene

proton (H_A) is quasi-axial and the other (H_B) is quasi-equatorial (structure B).



[B]

All the phosphoramidothionates are almost non-insecticidal against cockroach (P. americana (Linn)), blow-fly (C. megacephala) and grasshopper [O. nitidula (Walker)]. They are less toxic to white albino rats than salithion and are not phytotoxic to wheat seed (Triticum spp.) upto 500 ppm.

All the compounds show very poor anticholinesterase activity in blow-fly head homogenate (BFAChE) and in goat whole blood (AChE)

The rate of hydrolysis of the compounds is influenced by the nature of the substituent at the 6-position of the benzodioxaphosphorin ring. 6-chloro and 6-bromo compounds are more resistant to alkaline hydrolysis than that of 6-nitro compounds.

QSAR study further show that the bulkiness of the exocyclic alkylamido group plays a very important role in alkaline hydrolysi

The compounds show good inhibitory effect on the growth of Helminthosporium oryzae; compared with that of edifenphos they have greater inhibitory effect.

From QSAR study it is found that the antifungal activity of the compounds are correlated with the structural information content (SIC) and hydrophobic parameter (π). The regression equation is :

$$pED_{50} = -13.463\ SIC + 17.539\pi - 4.5498\ \pi^2 - 3.4541$$
$$(\pm 7.5769)\quad (\pm 11.090)\quad (\pm 2.8288)\quad (\pm 10.080)$$

$n = 8,\ r = 0.8172,\ s = 0.3685,$

Cal $F_{3,4} = 7.4290$, Theo $F_{3,4(0.05)} = 6.6$

Here 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 we can suggest the following:

(i) None of the steric, hydrophobic parameter alone can account for the antifungal activity.

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

(iii) For H. oryzae the regression equation involving pED_{50} with SIC, π and π^2 provides the best statistically significant equation which suggests that stereo-hydrophobic make-up and topology of the bioactive molecule are the major determinants for the antifungal activity.

Some of the compounds have also been tested for antifungal activity against Pyricularia oryzae. The compounds show very good inhibitory effect on the growth of the fungus P. oryzae and their effects are much greater than that of edifenphos.

In Chapter 3, further studies on synthesis, biological properties and chemical hydrolysis of some 6-nitro/chloro/bromo saligenin cyclic phosphoramidothionates have been presented. The

The biological activities and other data justify further examination of these compounds as potential fungicides. Whether the use of these cyclic phosphorus compounds will protect plants from disease in the field remains 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 groups are to be incorporated in different positi of the aromatic ring, and to investigate their biological activit Besides, structure elucidations in regard to the conformation of the dioxaphosphorin ring from temperature dependent ^{1}H, ^{31}P as wel as ^{13}C NMR spectra, and X-ray crystal structure would clarify the chemical structure - esterase inhibition mechanism so that their selectivity of action can be known, thereby helping us to design selective and biodegradable pesticides.