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Crystal and Molecular Structure of Organophosphorus Insecticides. 9. Stirofos

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The crystal and molecular structure of stirofos (2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate), $(H_3CO)_2PO_2C_8H_3Cl_4$, has been determined by three-dimensional X-ray analysis. The compound crystallizes in the triclinic space group $P\bar{1}$: $a = 14.023$ (4), $b = 15.088$ (5), $c = 6.930$ (2) Å, $\alpha = 93.94$ (2), $\beta = 90.29$ (4), and $\gamma = 98.97$ (4)°. The structure was solved via direct methods and refined to a final residual of $R = 0.123$. The two molecules per asymmetric unit assume nearly identical configurations with the orientation of the phosphate group relative to the planar organic moiety differing markedly from previous studies of organophosphorus insecticides. The average angle between the P=O bond and the normal to the plane of the ring system was 85.8° compared to 23.7° for ronnel, 38.4° for coroxon, 23.9° for azinphos-methyl, and 23.5° for amidithion. In addition, the partial charge on phosphorus (via a CNDO II molecular orbital calculation) differed considerably from previous studies, i.e., stirofos, +1.385 e; amidithion, +1.063 e; and azinphos-methyl, +1.041 e.

Previous crystal structure analyses of organophosphorus insecticides have attempted to outline possible structural and electronic features of insecticide molecules which may be important factors when considering their toxicity (Baughman and Jacobson, 1975; Gifkins and Jacobson, 1976; Rohrbaugh et al., 1976; Rohrbaugh and Jacobson, 1977). As has been discussed, the ubiquitous or specific effectiveness of a particular insecticide may depend on its ability to accommodate a range of esteratic-anionic site separations in various acetylcholinesterase (AChE) enzymes. In addition, the effectiveness may be related to the relative charge densities on the corresponding sites of the insecticide that could be involved in enzyme binding (Rohrbaugh and Jacobson, 1977). Finally, gross topographical features of the insecticide molecules may also be important in regulating toxicity.

It is of interest to compare such molecular features among insecticides exhibiting varying degrees of toxic effectiveness. Since our previous studies have included azinphos-methyl ($LD_{50} = 16$ mg/kg) and amidithion ($LD_{50} = 420$ mg/kg), we decided to carry out a crystal structural investigation of stirofos, 2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate. It has an LD_{50} of 4000
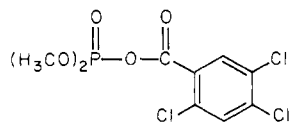
mg/kg (Pesticides and Toxic Substances Effects Labo-

ratory, 1973) and its structure determination should provide parameters useful for comparison to its more toxic counterparts.

EXPERIMENTAL SECTION

Crystal Data. A sample of stirofos was kindly supplied by the Pesticides and Toxic Substances Effects Laboratory, U.S. EPA, Research Triangle Park, N.C. A nearly spherical crystal of radius 0.18 mm was mounted on a glass fiber with Duco cement and subsequently attached to a standard goniometer head. From five preliminary ω-oscillation photographs taken on an automated four-circle X-ray diffractometer at various χ and ϕ settings, only seven reflections of significant intensity were observed and their coordinates were input to the automatic indexing program ALICE (Jacobson, 1976). In spite of the crystal's poor diffraction characteristics, these seven reflections yielded a good cell, and intensity data were subsequently collected using this crystal.

The resulting reduced cell and reduced cell scalars indicated a triclinic crystal system. Inspection of the axial ω-oscillation photographs verified, within experimental error, the layer line spacings predicted for this cell by the automatic indexing program. A least-squares refinement of the lattice constants (Takusagawa, 1975) based on the $\pm 2\theta$ measurements of 13 moderately strong independent reflections on a previously aligned four-circle diffractometer (Mo Kα graphite monochromated X-radiation, $\lambda = 0.70954$ Å) yielded $a = 14.023$ (4), $b = 15.088$ (5), $c = 6.930$ (2) Å, $\alpha = 93.94$ (2), $\beta = 90.29$ (4), and $\gamma = 98.97$ (4)°.

Collection and Reduction of X-Ray Intensity Data. Data were collected at room temperature on an automated four-circle diffractometer designed and built in this lab-

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oratory and previously described by Rohrbaugh and Jacobson (1974).

All data within a 2θ sphere of $45°$ [$(\sin \theta)/\lambda = 0.539$ Å^{-1}] in the hkl, $\bar{h}kl$, $h\bar{k}l$, and $\bar{h}\bar{k}l$ octants were measured via an ω-scan data collection technique. There were 3429 reflections measured yielding 1689 independent observed ($|F_o|>3\sigma_{F_o}$) reflections which were used in subsequent calculations. The relatively rapid decrease in intensity with $\sin \theta/\lambda$ and the relatively small number of observed reflections indicated that some disordering in the solid state might be a strong possibility.

As a general check on electronic and crystal stability, the intensities of six standard reflections were remeasured every 75 reflections. These standard reflections were not observed to vary significantly throughout the entire data collection period. The intensity data were corrected for Lorentz–polarization effects, and since the minimum and maximum transmission factors differed by less than 5% for a nearly spherical crystal with $\mu R = 0.16$, no absorption correction was made.

The estimated variance in each intensity was calculated by

$$\sigma_I^2 = C_T + K_t C_B + (0.03C_T)^2 + (0.03C_B)^2$$

where C_T, K_t, and C_B represent the total count, a counting time factor, and the background count, respectively, and the factor 0.03 represents an estimate of nonstatistical errors. The estimated deviations in the structure factors were calculated by the finite-difference method (Lawton and Jacobson, 1968).

SOLUTION AND REFINEMENT OF THE STRUCTURE

Based on examination of the Howells, Phillips, and Rogers (1950) statistical test for a center of symmetry, the space group was assumed to be $P\bar{1}$. From the volume of the cell (1445 Å^3) it was apparent that there were four molecules per cell, i.e., two molecules per asymmetric unit. A direct methods computer program package written by Dr. F. Takusagawa (1975), formerly of this laboratory, was employed in the solution of the structure. The E map (Hubbard et al., 1971) resulting from the solution set of 418 large $|E|$'s unambiguously revealed the positions of 11 atoms in molecule A and 16 atoms in molecule B. The remaining atoms were found by successive structure factor (Busing et al., 1962) and electron density map calculations. The positions of the vinyl and phenyl hydrogen atoms were obtained from difference electron density map calculations. The methyl hydrogen positions were approximated by two sets of methyl hydrogens for each methyl carbon atom. The sets were displaced by $60°$ and were each assigned half-multiplicity.

In addition to positional parameters for all atoms, the anisotropic thermal parameters for all non-hydrogen atoms were refined by a full-matrix least-squares procedure (Busing et al., 1962), minimizing the function $\Sigma\omega(|F_o| - |F_c|)^2$, where $\omega = 1/\sigma^2_{F_o}$, to a conventional residual of $R = \Sigma||F_o| - |F_c||/\Sigma|F_o| = 0.138$. Disorder of some of the atoms in one phosphate group, P(A), was evident. In order to partially account for this disorder, extra atoms were included around the phosphorus and occupancy factors of less than unity utilized. Analysis of the weights (ω) was performed via a requirement that $(|F_o| - |F_c|)^2$ should be a constant function of $|F_o|$ and $(\sin \theta)/\lambda$ (Cruickshank and Pillings, 1961). Such analysis indicated that reflections at high $(\sin \theta)/\lambda$ values were somewhat overweighted, and the weights were subsequently adjusted. No extinction effects were noted. Successive iterations of refinement produced convergence to $R = 0.123$. The rather high R value is a direct result of the disordering. The rapid fall-off

Table I. Final Non-Hydrogen Atom Positional Parameters ($\times 10^4$) and Multiplicities

atom	multi-plicity	x	y	z
Cl(1A)	1.0	667 (5)^a	9114 (4)	7008 (10)
Cl(2A)	1.0	1200 (5)	7400 (4)	612 (8)
Cl(3A)	1.0	1116 (5)	3952 (4)	1828 (9)
Cl(4A)	1.0	1296 (5)	4446 (4)	6358 (9)
P(A)	1.0	3156 (4)	8391 (4)	5473 (10)
O(1A)	0.601	3112 (20)	7934 (20)	7406 (36)
O(2A)	1.0	2126 (9)	8381 (9)	4560 (19)
OMe(1A)	0.644	3552 (16)	9418 (16)	5560 (35)
OMe(2A)	0.568	3730 (17)	7929 (19)	3955 (46)
O(1A')	0.486	3330 (22)	7572 (24)	6053 (47)
OMe(1A')	0.351	3235 (31)	9148 (34)	7299 (74)
OMe(2A')	0.426	3883 (26)	8854 (25)	3892 (51)
CMe(1A)	0.895	3299 (30)	10045 (27)	6989 (60)
CMe(2A)	1.020	3895 (27)	8287 (23)	2048 (39)
C(1A)	1.0	609 (16)	8003 (15)	6011 (27)
C(2A)	1.0	1382 (15)	7784 (15)	4977 (24)
C(3A)	1.0	1274 (12)	6867 (13)	4211 (25)
C(4A)	1.0	1241 (12)	6576 (13)	2225 (27)
C(5A)	1.0	1160 (14)	5713 (15)	1529 (33)
C(6A)	1.0	1198 (16)	5026 (14)	2687 (30)
C(7A)	1.0	1259 (13)	5271 (14)	4761 (30)
C(8A)	1.0	1337 (15)	6191 (13)	5479 (34)
Cl(1B)	1.0	5663 (5)	9021 (5)	7398 (11)
Cl(2B)	1.0	6257 (5)	7292 (5)	13297 (9)
Cl(3B)	1.0	6424 (5)	3894 (4)	10945 (9)
Cl(4B)	1.0	6231 (5)	4364 (4)	6549 (9)
P(B)	1.0	8123 (4)	8374 (4)	8927 (9)
O(1B)	1.0	8124 (12)	7990 (11)	6955 (19)
O(2B)	1.0	7031 (9)	8299 (9)	9768 (18)
OMe(1B)	1.0	8681 (12)	7870 (12)	10355 (27)
OMe(2B)	1.0	8536 (10)	9378 (9)	9420 (21)
CMe(1B)	1.0	8815 (27)	8153 (26)	12504 (39)
CMe(2B)	1.0	8290 (26)	10039 (26)	8076 (58)
C(1B)	1.0	5571 (19)	7917 (16)	8027 (32)
C(2B)	1.0	6252 (15)	7688 (13)	9004 (27)
C(3B)	1.0	6311 (13)	6749 (14)	9511 (30)
C(4B)	1.0	6331 (16)	6493 (15)	11416 (28)
C(5B)	1.0	6315 (15)	5631 (13)	11886 (30)
C(6B)	1.0	6329 (15)	5006 (15)	10375 (38)
C(7B)	1.0	6253 (15)	5188 (17)	8394 (36)
C(8B)	1.0	6241 (17)	6063 (17)	8000 (38)

^{a} In this and succeeding tables, estimated standard deviations are given in parentheses for the least significant figures. Multiplicities differing from 1.0 were refined; equivalent atoms were refined independently such that the sum of their multiplicities were not constrained to total 1.0.

in intensities with $\sin \theta/\lambda$ is also a manifestation of this disorder. In fact, if only data with $2\theta < 30°$ are included in the refinement, convergence with $R = 0.088$ is obtained. The scattering factors used for non-hydrogen atoms were those of Hanson et al. (1960), modified for the real and imaginary parts of anomalous dispersion (Templeton, 1962). The hydrogen scattering factors were those of Stewart et al. (1965).

The final positional parameters are listed in Table I. The standard deviations were calculated from the inverse matrix of the final least-squares cycle. In addition, the multiplicities (occupancy factors) for atoms in the disordered phosphate group of molecule (A) are given in this table.

DESCRIPTION AND DISCUSSION

Selected interatomic distances and angles (Busing et al., 1964) are listed in Tables II and III, respectively, and they are in favorable agreement with insecticides we have previously reported. The presence of two molecules in the asymmetric unit affords an excellent opportunity to evaluate the effects of packing forces on the configurations found for the molecule. As has already been noted, packing forces are different enough to allow disordering

Table II.   Interatomic Distances (A) for Stirofos

<div align="center">molecule A</div>

Cl(1A)-C(1A)	1.76 (2)		OMe(1A')-CMe(1A)	1.37 (6)
Cl(2A)-C(4A)	1.74 (2)		OMe(2A)-CMe(2A)	1.47 (4)
Cl(3A)-C(6A)	1.67 (2)		OM(2A')-CMe(2A)	1.49 (4)
Cl(4A)-C(7A)	1.73 (2)		O(2A)-C(2A)	1.31 (2)
P(A)-O(1A)	1.55 (2)		C(1A)-C(2A)	1.37 (3)
P(A)-O(1A')	1.38 (3)		C(2A)-C(3A)	1.43 (3)
P(A)-O(2A)	1.57 (1)		C(3A)-C(4A)	1.41 (2)
P(A)-OMe(1A)	1.56 (2)		C(3A)-C(8A)	1.40 (3)
P(A)-OMe(1A')	1.64 (5)		C(4A)-C(5A)	1.34 (2)
P(A)-OMe(2A)	1.52 (2)		C(5A)-C(6A)	1.36 (3)
P(A)-OMe(2A')	1.62 (4)		C(6A)-C(7A)	1.46 (3)
OMe(1A)-CMe(1A)	1.41 (4)		C(7A)-C(8A)	1.43 (3)

<div align="center">molecule B</div>

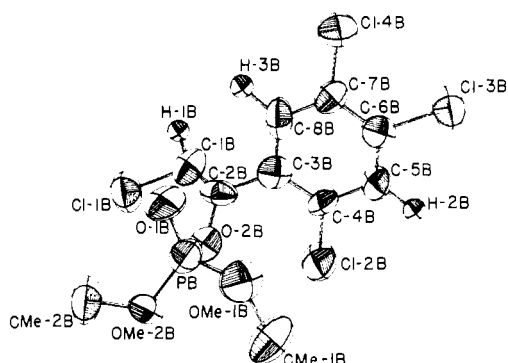|				
Cl(1B)-C(1B)	1.74 (2)		O(2B)-C(2B)	1.39 (2)
Cl(2B)-C(4B)	1.73 (2)		C(1B)-C(2B)	1.27 (3)
Cl(3B)-C(6B)	1.77 (2)		C(2B)-C(3B)	1.50 (3)
Cl(4B)-C(7B)	1.72 (3)		C(3B)-C(4B)	1.40 (3)
P(B)-O(1B)	1.45 (1)		C(3B)-C(8B)	1.41 (3)
P(B)-O(2B)	1.63 (1)		C(4B)-C(5B)	1.36 (3)
P(B)-OMe(1B)	1.56 (2)		C(5B)-C(6B)	1.36 (3)
P(B)-OMe(2B)	1.55 (1)		C(6B)-C(7B)	1.42 (3)
OMe(1B)-CMe(1B)	1.52 (3)		C(7B)-C(8B)	1.37 (3)
OMe(2B)-CMe(2B)	1.49 (3)			

Figure 1. View of stirofos molecule B with methyl hydrogen atoms omitted. In this and succeeding drawings, 50% probability ellipsoids are depicted.

of one phosphate group but not the other. However, examination of Tables II and III shows that distances and angles in molecule A agree with those found for molecule B to 5σ or better. Also the corresponding dihedral angles between various planes in both molecules agree to within 3.4° implying that the equilibrium molecular configuration is relatively unperturbed by solid state effects. Since molecule B was less affected by disorder, it will be used as representative of the molecular configuration for the majority of the discussion. A view of the stirofos molecule B depicting 50% probability ellipsoids (Johnson, 1971) is provided in Figure 1, and a unit cell stereograph containing both molecules A and B is provided in Figure 2.
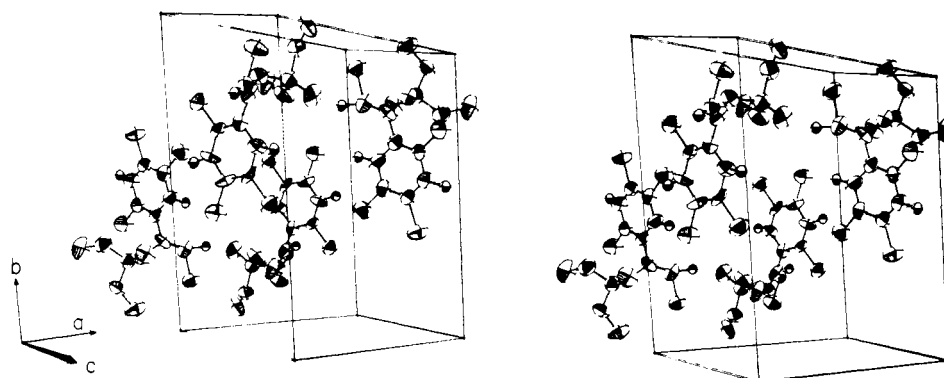
The geometry about the phosphorus atom appears to be somewhat distorted from tetrahedral as has been observed in prior crystal structure analyses of organophosphorus insecticides (Baughman and Jacobson, 1975; Gifkins and Jacobson, 1976; Rohrbaugh et al., 1976; Rohrbaugh and Jacobson, 1977). In particular, the angles involving the doubly bonded oxygen (O(1)) with the methoxy oxygens (OMe(1) and OMe(2)) are approximately 3 to 10° greater than tetrahedral (cf. Table III), with corresponding reduction in the other angles.

As discussed in the study of amidithion (Rohrbaugh and Jacobson, 1977), the orientation of the planar segment of the organic moiety relative to the phosphate group may be an important topographical feature of organophosphorus insecticides. If one calculates the angle between the normal to the plane of the ring system and the P=O bond, the values obtained for stirofos in the solid state configuration are 85.7° for molecule A and 85.8° for molecule B. These results are in poor agreement with 23.7° for ronnel (Baughman and Jacobson, 1975), 38.4° for coroxon (Gifkins and Jacobson, 1976), 23.9° for azinphos-methyl (Rohrbaugh et al., 1976), and 23.5° for amidithion (Rohrbaugh and Jacobson, 1977). Since both molecule A and molecule B assume essentially the same configuration, it would appear that this is the preferred orientation for stiorfos and possibly reflects the configuration of the molecule in vivo as well. It is tempting to speculate that this apparent deviation in the orientation of the ring system relative to the phosphate group from those of previous studies is correlated to the considerably

Figure 2. Unit cell sterograph of stirofos.

Crystal and Molecular Structure of Stirofos

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Table III. Bond Angles (Degrees) for Stirofos

molecule A

O(1A)-P(A)-O(2A)	112 (1)	P(A)-OMe(2A')-CMe(2A)	113 (3)
O(1A)-P(A)-OMe(1A)	117 (1)	Cl(1A)-C(1A)-H(1A)	91 (11)
O(1A)-P(A)-OMe(1A')	70 (2)	Cl(1A)-C(1A)-C(2A)	118 (2)
O(1A)-P(A)-OMe(2A)	112 (2)	O(2A)-C(2A)-C(1A)	123 (2)
O(1A)-P(A)-OMe(2A')	144 (2)	C(1A)-C(2A)-C(3A)	115 (2)
O(1A')-P(A)-O(2A)	115 (1)	C(2A)-C(3A)-C(4A)	126 (2)
O(1A')-P(A)-OMe(1A)	144 (2)	C(2A)-C(3A)-C(8A)	119 (2)
O(1A')-P(A)-OMe(1A')	111 (2)	Cl(2A)-C(4A)-C(3A)	116 (1)
O(1A')-P(A)-OMe(2A)	69 (2)	Cl(2A)-C(4A)-C(5A)	119 (2)
O(1A')-P(A)-OMe(2A')	116 (2)	C(3A)-C(4A)-C(5A)	125 (2)
O(2A)-P(A)-OMe(1A)	100 (1)	H(2A)-C(5A)-C(4A)	126 (8)
O(2A)-P(A)-OMe(1A')	105 (2)	H(2A)-C(5A)-C(6A)	109 (8)
O(2A)-P(A)-OMe(2A)	106 (1)	C(4A)-C(5A)-C(6A)	123 (2)
O(2A)-P(A)-OMe(2A')	104 (1)	Cl(3A)-C(6A)-C(5A)	123 (2)
OMe(1A)-P(A)-OMe(2A)	107 (2)	Cl(3A)-C(6A)-C(7A)	121 (2)
OMe(1A)-P(A)-OMe(2A')	57 (1)	C(5A)-C(6A)-C(7A)	116 (2)
OMe(1A')-P(A)-OMe(2A)	145 (2)	Cl(4A)-C(7A)-C(6A)	120 (2)
OMe(1A')-P(A)-OMe(2A')	104 (2)	Cl(4A)-C(7A)-C(8A)	120 (2)
P(A)-O(2A)-C(2A)	122 (1)	C(6A)-C(7A)-C(8A)	121 (2)
P(A)-OMe(1A)-CMe(1A)	124 (2)	H(3A)-C(8A)-C(3A)	130 (10)
P(A)-OMe(1A')-CMe(1A)	121 (4)	H(3A)-C(8A)-C(7A)	103 (10)
P(A)-OMe(2A)-CMe(2A)	121 (2)	C(3A)-C(8A)-C(7A)	121 (2)

molecule B

O(1B)-P(B)-O(2B)	112 (1)	Cl(2B)-C(4B)-C(3B)	119 (2)
O(1B)-P(B)-OMe(1B)	112 (1)	Cl(2B)-C(4B)-C(5B)	117 (2)
O(1B)-P(B)-OMe(2B)	120 (1)	C(3B)-C(4B)-C(5B)	124 (2)
O(2B)-P(B)-OMe(1B)	105 (1)	H(2B)-C(5B)-C(4B)	120 (8)
O(2B)-P(B)-OMe(2B)	102 (1)	H(2B)-C(5B)-C(6B)	121 (8)
OMe(1B)-P(B)-OMe(2B)	104 (1)	C(4B)-C(5B)-C(6B)	116 (2)
P(B)-O(2B)-C(2B)	124 (1)	Cl(3B)-C(6B)-C(5B)	117 (2)
P(B)-OMe(1B)-CMe(1B)	123 (2)	Cl(3B)-C(6B)-C(7B)	119 (2)
P(B)-OMe(2B)-CMe(2B)	117 (2)	C(5B)-C(6B)-C(7B)	124 (2)
Cl(1B)-C(1B)-H(1B)	93 (9)	Cl(4B)-C(7B)-C(6B)	122 (2)
Cl(1B)-C(1B)-C(2B)	119 (2)	Cl(4B)-C(7B)-C(8B)	121 (2)
O(2B)-C(2B)-C(1B)	123 (2)	C(6B)-C(7B)-C(8B)	117 (2)
C(1B)-C(2B)-C(3B)	125 (2)	H(3B)-C(8B)-C(3B)	134 (10)
C(2B)-C(3B)-C(4B)	124 (2)	H(3B)-C(8B)-C(7B)	104 (10)
C(2B)-C(3B)-C(8B)	118 (2)	C(3B)-C(8B)-C(7B)	121 (2)

torsional angles

atom				bond	angle (degrees)
P(A)	O(2A)	C(2A)	C(3A)	O(2A)-C(2A)	74.6
P(B)	O(2B)	C(2B)	C(3B)	O(2B)-C(2B)	73.4
O(1A)	P(A)	O(2A)	C(2A)	P(A)-O(2A)	23.5
O(1B)	P(B)	O(2B)	C(2B)	P(B)-O(2B)	20.9

lower toxicity of stirofos in mammalian systems (LD_{50} = 4000 mg/kg) than the other insecticides mentioned above. The low toxicity could be viewed, in part at least, as due to an inability of this insecticide molecule to accommodate a topographical feature of mammalian AChE enzymes.

In considering autotoxicosis through inhibition of acetylcholinesterase (AChE) by organophosphorus insecticides, it is useful to recall that the nitrogen to carbonyl carbon distance in acetylcholine is estimated at 4.7 Å (Chothia and Pauling, 1969), when the molecule is in a proper configuration to react with bovine erythrocyte AChE. Experiments carried out by Hollingworth et al. (1967) indicated, however, that the distance between the anionic and esteratic centers of fly head AChE may be as much as 1 Å greater than that in the mammalian enzyme. Results of a CNDO II molecular orbital calculation (Segal, 1970) on stirofos indicate that in addition to the phosphorus, there are three probable positive centers that could be involved in enzyme binding (cf. Table IV). They are C(4), C(6), and C(7), and the corresponding distances to the phosphorus are, respectively, 4.1, 5.6, and 5.0 Å for molecule A, and 4.0, 5.5, and 5.1 Å for molecule B. It appears that the P–C(4) separations are too small to permit C(4) to be an efficient binding site. C(6) and C(7), however, are far enough away from the phosphorus atom to render them likely candidates for binding to insect and

Table IV. Partial Charge Densities Obtained from a CNDO II Molecular Orbital Calculation

atom	partial charge (e)	atom	partial charge (e)
Cl(1B)	-0.166	C(1B)	+0.011
Cl(2B)	-0.133	C(2B)	+0.188
Cl(3B)	-0.145	C(3B)	-0.007
Cl(4B)	-0.113	C(4B)	+0.132
P(B)	+1.385	C(5B)	-0.016
O(1B)	-0.496	C(6B)	+0.127
O(2B)	-0.407	C(7B)	+0.103
OMe(1B)	-0.350	C(8B)	-0.007
OMe(2B)	-0.367	H(1B)	+0.041
CMe(1B)	-0.148	H(2B)	+0.036
CMe(2B)	-0.081	H(3B)	+0.034

mammalian AChE enzymes, respectively.

Secondary candidates for enzyme binding are H(1), H(2), and H(3) (cf. Table IV). The corresponding phosphorus–hydrogen distances are, respectively, 4.5, 6.0, and 4.2 Å for molecule A and 4.6, 6.1, and 4.2 Å for molecule B. The P–H(3) distances appear to be too short to enable efficient enzyme binding, but H(1) and H(2) could accommodate mammalian and insect AChE enzymes, respectively. Consequently, it is difficult to explain the low mammalian toxicity of stirofos based on positive center

separation arguments. The molecule seems to possess a number of positive centers that could accommodate the anionic-esteratic separation requirements of both mammalian and insect AChE enzymes.

As discussed previously (Rohrbaugh et al., 1976), there may exist a relationship between insecticide effectiveness and the partial charge density on the phosphorus atom. The charge on the phosphorus of amidithion (Rohrbaugh and Jacobson, 1977) is +1.063 e and that of the phosphorus of azinphos-methyl (Rohrbaugh et al., 1976) is +1.041 e. These two values are not significantly different. It was noted, however, that the charge on phosphorus for the phosphinate analogue of azinphos-methyl differs by 0.1 e (Rohrbaugh et al., 1976). The phosphinate analogue of azinphosmethyl has an LD_{50} for rats two orders of magnitude larger than azinphos-methyl, i.e., LD_{50} (azinphos-methyl) = 16, LD_{50} (phosphinate analogue) $\approx$ 1000 mg/kg. For stirofos (LD_{50} = 4000 mg/kg), the partial charge on phosphorus is found to be +1.385 e (cf. Table IV). It is readily apparent that this value is significantly different from the values obtained for either azinphos-methyl or amidithion. If there exists an optimum charge on phosphorus for which enzyme binding or phosphorylation is enhanced, it would appear to be close to the value found for azinphos-methyl. It could then be hypothesized that any deviation from some "optimum" value for the charge on phosphorus would decrease the effectiveness of the insecticide. In order to substantiate or refute this hypothesis, however, further data on additional insecticides are required.

SUMMARY

The main structural features of organophosphorus insecticides conjectured to be important in determining enzyme binding effectiveness are positive center separations, partial charge on the phosphorus atom, and gross topographical features, particularly, the orientation of the planar organic moiety relative to the P=O bond. The latter two features are outgrowths of the structural studies carried out in this series of reports.

It is difficult to rank the molecular structural features in order of importance. An attempt has been made, however, to establish these molecular parameters as elements of toxic effectiveness. When considering the studies of azinphosmethyl, amidithion, and stirofos, in particular, it should be noted that these compounds represent insecticides of vastly different levels of effectiveness. Azinphos-methyl is roughly 25 times more toxic to mammals than is amidithion, and the primary difference in molecular parameters is the range of positive center separations available to these molecules. Azinphos-methyl is 60 times more effective than its phosphinate analogue which presumably has a very similar molecular structure. The primary difference between these molecules appears to be the partial charge on phosphorus. Finally, azinphos-methyl is nearly 400 times more toxic than stirofos, and these two molecules differ both in partial charge on the phosphorus atom and in the orientation of the planar organic moiety relative to the P=O bond.

It is apparent that further studies of insecticides are necessary to accumulate such correlation data, so that a better understanding of the relationship of structural parameters to toxic effectiveness can be obtained.

Supplementary Material Available: A listing of the observed and calculated structure factor amplitudes, the final hydrogen atom positional parameters, and the final non-hydrogen thermal parameters. (11 pages). Ordering information is given on any current masthead page.

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