Table II. Comparative Results for Zineb Content by the Carbon Disulfide Evolution and Chloramine-T Methods
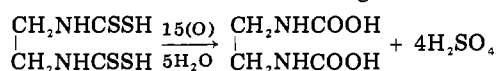
Sample no.	% zineb content	
	CS_2 evolution	Chloramine-T oxidation
1	78.6	78.7
2	79.2	80.2
3	78.0	77.8
4	78.9	78.7
5	78.7	79.2

normality of sodium thiosulfate, and w = weight of formulation taken in milligrams.

RESULTS AND DISCUSSION

To establish the number of equivalents of chloramine-T consumed by 1 mol of zineb, samples of known zinc ethylene bis(dithiocarbamate) content were analyzed. The results are presented in Table I.

From the results given in Table I, it is evident that each mol of zineb requires 30 equiv of chloramine-T. This is in accordance with the following stoichiometric equation:

$$\begin{array}{c} CH_2NHCSSH \\ | \\ CH_2NHCSSH \end{array} \xrightarrow[5H_2O]{15(O)} \begin{array}{c} CH_2NHCOOH \\ | \\ CH_2NHCOOH \end{array} + 4H_2SO_4$$

Therefore, 1 ml of 0.1 N chloramine-T is equivalent to 0.919 mg of zineb. A few comparative results obtained by the carbon disulfide evolution method and the chloramine-T method are presented in Table II.

Clarke et al. (1951) have pointed out that during digestion of zineb with sulfuric acid in the carbon disulfide procedure, the sample may not decompose to yield the expected 2 mol of carbon disulfide and hydrogen sulfide may be evolved if the digestion is carried out at a lower temperature. The formation of a large amount of hydrogen sulfide may lead one to think that the sample has deteriorated. Therefore, the experimental conditions require careful maintenance. Furthermore, the method also requires special apparatus. The chloramine-T oxidation method described above does not require any special apparatus and it is very simple and rapid. It is also accurate as 30 equiv of chloramine-T is consumed per mol of zineb. It is therefore well suited for routine analysis.

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Crystal and Molecular Structure of Organophosphorus Insecticides. 4. Bromophos

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The crystal and molecular structure of bromophos (O-(4-bromo-2,5-dichlorophenyl) O,O-dimethyl phosphorothioate, $(H_3CO)_2P(S)OC_6H_2Cl_2Br$, orthorhombic, $P2_12_12_1$, a = 7.307 (5), b = 27.19 (3), and c = 6.440 (4) Å, Z = 4, Mo Kα radiation) has been determined by three-dimensional x-ray analysis. The structure was solved by conventional Patterson and Fourier techniques to a final discrepancy index R = 0.048 for 1217 observed reflections ($F_o > 2.5\sigma(F_o)$). The structure features an intramolecular hydrogen bond which restricts rotation about the phenolic C–O bond, thus giving a very probable in vivo model. The phosphorus–meta hydrogen distance of 5.52 Å falls well within the range of literature values cited for the intramolecular active site-separation distance for acetylcholinesterase (AChE), yet is well outside that for mammalian AChE.

The crystal-structure investigation of bromophos, a bromine analogue of ronnel, was undertaken as a part of a study of various insecticides being carried on at this laboratory (Gress and Jacobson, 1973; Baughman and Jacobson, 1975; Gifkins and Jacobson, 1976; Rohrbaugh and Jacobson, 1976; Baughman et al., 1976; Takusagawa and Jacobson, 1976). The purpose of such a program is to determine the structural dependence of an insecticide's toxicity/activity and to better understand the mechanism(s) involved.

In the case of acetylcholinesterase (AChE) inhibition, one would ideally like to know the active sites' three-dimensional structure (or that of a small range of possible low-energy conformations). Using organophosphorus (OP)

and/or carbamate insecticides, the problem may be approached indirectly. Such information could lead to the construction of insecticides which would better conform structurally as well as chemically to the most favorable (minimum energy) orientation of AChE.

EXPERIMENTAL SECTION

Crystal Data. A rectangular prismatic crystal (~99% pure) with approximate dimensions 0.15 mm × 0.12 mm × 0.07 mm was selected and mounted on the end of a glass fiber using Elmer's Glue; other glues with an organic solvent base dissolve the OP insecticide crystals. Preliminary oscillation photographs indicated a single crystal with mmm (orthorhombic) symmetry. The crystal was then mounted on a four-circle diffractometer and three ω-oscillation photographs were taken at various χ and φ settings.

From these photographs 17 independent reflections were

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selected and their coordinates were input into an automatic indexing program (Jacobson, 1974). The reduced cell and reduced cell scalars which resulted from this program indicated orthorhombic symmetry, which was confirmed by inspection of ω-oscillation photographs taken about each of the three axes in turn. All axes showed mirror symmetry. Observed layer line spacings agreed, within experimental error, with those predicted for this cell by the indexing program.

The lattice constants were obtained from a least-squares refinement based on the precise ±2θ (|2θ| > 20°) measurements of 15 strong independent reflections. At 27 °C using Mo Kα (λ 0.70954 Å) they are a = 7.307 (5), b = 27.19 (3), and c = 6.440 (4) Å. The observed density of 1.90 ± 0.02 g cm^{-3} determined by the flotation method is in good agreement with the calculated value of 1.889 g cm^{-3} for four molecules, having a molecular weight of 366.00 g mol^{-1}, in a unit cell with a volume of 1279.56 Å^3.

Collection and Reduction of X-Ray Intensity Data. The data were collected at 27 °C with graphite monochromated Mo Kα radiation on an automated four-circle diffractometer designed and built in the Ames Laboratory and previously described by Rohrbaugh and Jacobson (1974). All data within a 2θ sphere of 45° ((sin θ)/λ = 0.539 Å^{-1}) in the hkl and hk̄l octants were measured, using an ω-stepscan technique.

As a general check on electronic and crystal stability, the intensities of three standard reflections were remeasured every 75 reflections. These standard reflections were not observed to vary significantly throughout the entire period of data collection (∼2 days). Hence, a decomposition correction was unnecessary. A total of 2533 reflections were recorded in this manner. Examination of the data revealed only the following systematic absences: h00 when h = 2n + 1, 0k0 when k = 2n + 1, and 00l when l = 2n + 1. These absences uniquely determine the space group as $P2_12_12_1$.

The intensity data were corrected for Lorentz and polarization effects and, since μ = 40.25 cm^{-1}, absorption corrections were also made; maximum and minimum transmission factors were 0.755 and 0.547, respectively. The estimated variance in each intensity was calculated by:

$$\sigma_I^2 = \{C_T + 2C_B + (0.03C_T)^2 + (0.03C_B)^2 + (0.03C_N)^2\}/A^2$$

where C_T, C_B, and C_N represent the total, background, and net counts, respectively, A is the transmission factor, and the factor 0.03 represents an estimate of nonstatistical errors. The estimated deviations were calculated by the finite difference method (Lawton and Jacobson, 1968). Equivalent data were averaged and 1225 reflections with $F_o > 2.5\sigma(F_o)$ were retained for use in subsequent calculations. During later work it was discovered that eight large reflections suffered from secondary extinction effects; these were eliminated from the final stages of refinement.

Solution and Refinement. The position of the bromine was obtained from an analysis of a standard three-dimensional Patterson function. The remaining atoms were found by successive structure factor (Busing et al., 1962) and electron density map calculations (Hubbard et al., 1971). These atomic positions were subsequently refined by a full-matrix least-squares procedure (Busing et al., 1962) minimizing the function $\Sigma\omega(|F_o| - |F_c|)^2$, where $\omega = 1/\sigma_F^2$, to a conventional discrepancy factor of $R = \Sigma\|F_o| - |F_c\|/|F_o| = 0.058$. At this stage all 16 nonhydrogen atoms had been refined with anisotropic thermal parameters. The scattering factors
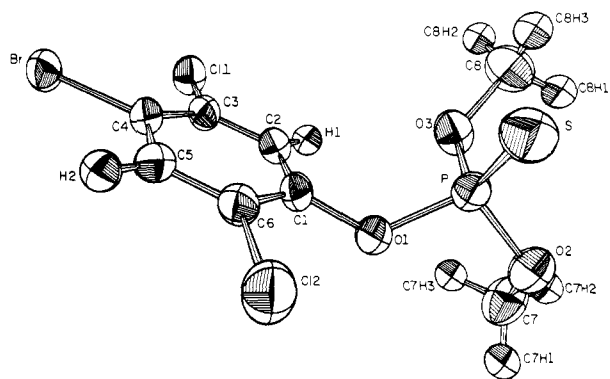

Figure 1. The bromophos molecule showing 50% probability ellipsoids; 30% for hydrogens.

used were those of Hanson et al. (1960), modified for the real and imaginary parts of anomalous dispersion (Templeton, 1962).

Ring hydrogen atom positions were fixed at 0.95 Å from the corresponding carbons. Analysis of an electron density difference map (Hubbard et al., 1971) did not reveal the individual methyl hydrogen positions. Consequently, approximate tetrahedral positions were inferred from the precise corresponding methoxy oxygen and carbon positions. The methyl C–H distances were set equal to 1.0 Å; all isotropic hydrogen temperature factors were set equal to 4.5 Å^2.

Subsequent least-squares refinement without varying the hydrogen parameters converged to R = 0.048. Since this procedure yielded slightly different carbon and oxygen positions, all of the hydrogen positions were recalculated. Further refinement cycles did not significantly alter any atomic parameters and the discrepancy factor did not change.

The final positional and thermal parameters are listed in Table I. Standard deviations were calculated from the inverse matrix of the final least-squares cycle. Bond lengths and angles are listed in Table II and Table III, respectively (Busing et al., 1964). Dihedral angles and least-squares planes are listed in Table IV.

DESCRIPTION OF STRUCTURE AND DISCUSSION

The phenoxy group in bromophos shown in Figures 1 and 2 (Johnson, 1971) is, as expected, essentially planar (cf. Table IV, plane II). The phosphorus is, as with ronnel (Baughman and Jacobson, 1975), tilted toward the H(1) side of a plane perpendicular to the ring and coincident with the C(1)–O(1) bond while the sulfur is twisted away from the C(1)–O(1)–P plane toward the Cl(2) side of the ring (cf. Table IV, Figures 1 and 3). However, unlike ronnel, in bromophos the distance between H(1) and O(3) (2.61 Å) is indicative of a possible hydrogen bond between the aromatic C(2) atom and the O(3) atom (cf. Table II and Figure 3). Both the P–O(3)–H(1) angle of 100.5° and the C(8)–O(3)–H(1) angle of 130.0° would direct H(1) approximately toward a lone pair lobe on O(3), assuming sp^3 hybridization, thus strengthening a hydrogen bond argument (cf. Table III). The P, O(3), H(1), and C(1) atoms form a near planar grouping (cf. Table IV, plane III).

For the most part, packing in the bromophos crystal can be regarded as either weakly coulombic or van der Waals in nature. The former is a manifestation of the charge density distribution within each individual molecule and hence corroborates one's "chemical intuition" of the δ(+) and δ(−) atoms.

Referring to Figure 2 and Table II, interactions such as the following appear to be van der Waals in character:

Table I. Final Atomic Positional[a] and Thermal[b] Parameters for Bromophos

	Fractional coordinates			Atomic temperature factors					
Atom	X	Y	Z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Br	0.2355 (1)[c]	0.18887 (2)	0.0773 (1)	17.2 (1)	0.90 (1)	28.3 (2)	-0.40 (3)	-3.1 (2)	-0.46 (4)
Cl(1)	0.4044 (3)	0.22662 (8)	0.5173 (4)	23.6 (5)	1.13 (3)	26.0 (6)	-0.1 (1)	-5.8 (5)	1.1 (1)
Cl(2)	0.1954 (3)	0.38363 (8)	-0.1393 (4)	25.1 (5)	1.16 (3)	28.8 (7)	-0.4 (1)	-10.0 (5)	0.9 (1)
S	0.6600 (3)	0.43542 (9)	0.0094 (4)	21.7 (5)	1.37 (3)	19.1 (6)	-0.3 (1)	3.4 (5)	-0.0 (1)
P	0.5392 (2)	0.43276 (7)	0.2688 (3)	13.9 (4)	0.80 (2)	17.4 (5)	-0.03 (9)	-1.0 (4)	-0.0 (1)
O(1)	0.3488 (7)	0.4032 (1)	0.2780 (9)	14 (1)	0.92 (7)	24 (1)	-0.0 (2)	-0 (1)	-1.3 (3)
O(2)	0.4753 (8)	0.4838 (2)	0.3467 (9)	20 (1)	0.92 (7)	20 (1)	0.0 (2)	-0 (1)	-0.3 (2)
O(3)	0.6430 (8)	0.4064 (2)	0.451 (1)	17 (1)	1.35 (9)	23 (1)	-0.7 (2)	-4 (1)	1.8 (3)
C(1)	0.332 (1)	0.3536 (2)	0.227 (1)	12 (1)	0.87 (9)	23 (2)	-0.7 (3)	2 (1)	-0.0 (4)
C(2)	0.383 (1)	0.3189 (2)	0.373 (1)	12 (1)	1.0 (1)	22 (2)	-0.4 (3)	-0 (1)	-0.4 (4)
C(3)	0.350 (1)	0.2693 (2)	0.329 (1)	13 (1)	1.0 (1)	20 (2)	0.0 (3)	-3 (1)	-0.2 (4)
C(4)	0.279 (1)	0.2554 (2)	0.143 (1)	12 (1)	0.9 (1)	20 (2)	-0.3 (3)	0 (1)	-0.5 (4)
C(5)	0.231 (1)	0.2911 (3)	-0.004 (1)	14 (1)	1.0 (1)	19 (1)	0.4 (3)	-1 (1)	-0.4 (4)
C(6)	0.258 (1)	0.3398 (2)	0.040 (1)	13 (1)	0.9 (1)	21 (2)	0.0 (3)	-3 (1)	0.2 (4)
C(7)	0.384 (1)	0.4901 (3)	0.546 (1)	30 (2)	1.0 (1)	28 (3)	0.3 (5)	5 (2)	-1.3 (5)
C(8)	0.837 (1)	0.4125 (4)	0.478 (1)	15 (1)	1.8 (1)	34 (3)	-0.4 (4)	-7 (2)	-0.4 (7)
H(1)	0.4380	0.3285	0.5008	45					
H(2)	0.1808	0.2815	-0.1337	45					
C(7)H(1)	0.2671	0.5083	0.5258	45					
C(7)H(2)	0.4660	0.5093	0.6413	45					
C(7)H(3)	0.3589	0.4571	0.6083	45					
C(8)H(1)	0.8625	0.4449	0.5473	45					
C(8)H(2)	0.8859	0.3853	0.5678	45					
C(8)H(3)	0.8996	0.4116	0.3406	45					

[a] The positional parameters for all atoms are represented in fractional unit cell coordinates. [b] The β_{ij} are defined by: $T = \exp\{-(h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + 2hk\beta_{12} + 2hl\beta_{13} + 2kl\beta_{23})\}$. If only the β_{11} column is listed, this corresponds to an isotropic temperature factor. All hydrogen isotropic β's have been set equal to 4.5. Nonhydrogen thermal parameters are $\times 10^3$. All hydrogen thermal parameters are $\times 10$. [c] In this and succeeding tables estimated standard deviations are given in parentheses for the least significant figures and include the error in the lattice constants. Since the hydrogens were not refined, no standard deviations are given.

Table II. Selected Interatomic Distances (Å) for Bromophos

			Nonbonding distances		
Bonding distances			Via	Obsd distance	Total van der Waals distance (Pauling, 1960)
C(1)-C(2)	1.38 (1)	Cl(1)···H(2)	1 cell in z	3.155 (4)	3.0
C(2)-C(3)	1.40 (1)	Cl(2)···H(1)	1 cell in z	3.280 (4)	3.0
C(3)-C(4)	1.36 (1)	Cl(2)···C(7)H₃	1 cell in z	3.79 (1)	3.8[a]
C(4)-C(5)	1.40 (1)	S···C(7)H₃	1 cell in z	3.90 (1)	3.85[a]
C(5)-C(6)	1.37 (1)	S···C(8)H₃	1 cell in z	3.71 (1)	3.85[a]
C(6)-C(1)	1.38 (1)	Cl(2)···C(8)H₃	1 cell in z and x	3.68 (1)	3.8[a]
C(1)-O(1)	1.391 (9)	Br···S	2_1 (-x direction)	3.467 (4)	3.80
C(2)-H(1)	0.950 (9)	Br···H(2)	2_1 (-x direction)	3.371 (3)	3.15
C(3)-Cl(1)	1.724 (9)	Cl(1)···H(2)	2_1 (-x direction)	3.200 (4)	3.0
C(4)-Br	1.887 (8)	C(7)H₃···Cl(2)	2_1 (z direction)	3.68 (1)	3.80
C(5)-H(2)	0.950 (9)	C(7)H₃···O(1)	2_1 (z direction)	3.68 (1)	3.40
C(6)-Cl(2)	1.724 (9)	C(7)H₃···O(2)	2_1 (z direction)	3.34 (1)	3.40
P-O(1)	1.607 (6)	C(7)H₃···C(7)H₃	2_1 (z direction)	3.82 (1)	4.00
P=S	1.892 (4)	S···Cl(2)	Intramolecular	3.798 (5)	3.65
P-O(2)	1.547 (6)	S···C(8)H₃	Intramolecular	3.35 (1)	3.85[a]
P-O(3)	1.571 (7)	O(3)···H(1)	Intramolecular	2.613 (6)	2.6
O(2)-C(7)	1.46 (1)	P···Cl(2)	Intramolecular	3.875 (4)	3.7
O(3)-C(8)	1.44 (1)	S···O(1)	Intramolecular	2.989 (6)	3.25
		S···O(2)	Intramolecular	2.877 (7)	3.25
		S···O(3)	Intramolecular	2.957 (8)	3.25
		Br···Cl(1)	Intramolecular	3.259 (4)	3.75
		O(1)···O(2)	Intramolecular	2.416 (8)	2.80
		O(2)···O(3)	Intramolecular	2.524 (9)	2.80
		O(3)···O(1)	Intramolecular	2.424 (9)	2.80
		O(1)···C(7)H₃	Intramolecular	2.94 (1)	3.4[a]
		O(3)···C(7)H₃	Intramolecular	3.02 (1)	3.4[a]
		O(1)···C(8)H₃	Intramolecular	3.81 (1)	3.4[a]
		O(2)···C(8)H₃	Intramolecular	3.39 (1)	3.4[a]
		C(7)H₃···C(8)H₃	Intramolecular	3.95 (2)	4.0[a]
		P···H(1)	Intramolecular	3.285 (3)	(3.1)
		P···H(2)	Intramolecular	5.520 (4)	(3.1)

[a] Assumes linear addition of methyl van der Waals radius.

Cl(2)···C(8)H₃, Cl(2)···C(7)H₃, S···C(8)H₃, C(7)H₃···{Cl(2), O(1), and O(2)}, etc. The latter interaction causes the C(7) methyl groups to be skewed into an orientation unlike that of the C(8) methyl groups (cf. Figures 1 and 2). Owing to differences in electronegativity, the S···C(8)H₃ interaction is a result of the O(3)···C(2) intramolecular hydrogen bond.
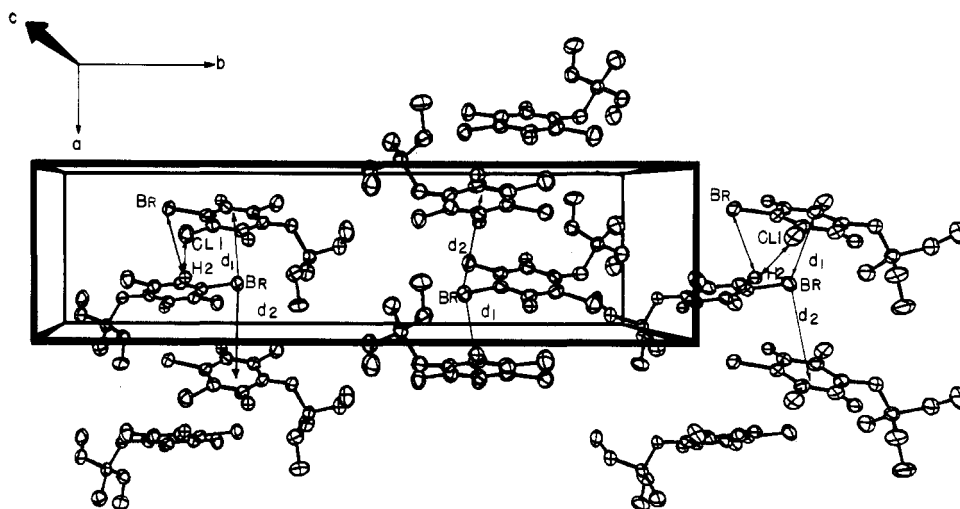
Figure 2. View of three adjacent unit cells illustrating packing in the *a* and *b* directions.

Table III. Bond Angles (Degrees) for Bromophos

C(1)-C(2)-C(3)	118.3 (8)
C(2)-C(3)-C(4)	120.8 (8)
C(3)-C(4)-C(5)	120.2 (8)
C(4)-C(5)-C(6)	119.2 (8)
C(5)-C(6)-C(1)	120.3 (8)
C(6)-C(1)-C(2)	121.1 (7)
O(1)-C(1)-C(2)	118.7 (8)
O(1)-C(1)-C(6)	120.1 (8)
H(1)-C(2)-C(1)	120.9 (8)
H(1)-C(2)-C(3)	120.8 (9)
Cl(1)-C(3)-C(2)	117.8 (7)
Cl(1)-C(3)-C(4)	121.4 (6)
Br-C(4)-C(3)	122.1 (7)
Br-C(4)-C(5)	117.7 (7)
H(2)-C(5)-C(4)	120.4 (8)
H(2)-C(5)-C(6)	120.4 (9)
Cl(2)-C(6)-C(5)	119.1 (7)
Cl(2)-C(6)-C(1)	120.5 (6)
C(1)-O(1)-P	123.2 (5)
S-P-O(1)	117.1 (3)
S-P-O(2)	113.2 (3)
S-P-O(3)	117.0 (3)
O(1)-P-O(2)	100.0 (3)
O(2)-P-O(3)	108.1 (4)
O(1)-P-O(3)	99.4 (3)
P-O(2)-C(7)	122.0 (5)
P-O(3)-C(8)	121.1 (7)
P-O(3)-H(1)	100.5 (3)
C(8)-O(3)· · ·H(1) Intramol.	130.0 (6)
C(4)-Br· · ·H(2) Intermol.	65.3 (2)
C(3)-Cl(1)· · ·H(2) Intermol.	93.8 (3)
C(6)-Cl(2)· · ·H(1) Intermol.	90.9 (3)

Packing, as shown in Figure 2, is also facilitated by the interactions of the $\delta(-)$ bromine with the $\delta(+)$ ring centers above and below each bromine, $d_1 = 3.57$ and $d_2 = 4.49$ Å, which may be compared to the van der Waals radii sum of 3.65 Å (Pauling, 1960). This discrepancy in d_1 and d_2 is primarily due to the intrusion of thiophosphate groups. The Br···H(2) distance of 3.37 Å (Table II) and the C(4)-Br···H(2) angle of only 65° (Table III) indicate that only a very weak intermolecular hydrogen bond is likely.

A very interesting mode of packing takes place in the *c* direction. Due to the fact that each chlorine and ring hydrogen has a para counterpart, the molecules advantageously utilize this arrangement by forming hydrogen bonds in a dovetail fashion (cf. Figure 3 and Tables II and III). Since the rings in the *c* direction are all related by a simple translation, they are all parallel. However, they are not coplanar, each being 23° from the *b*–*c* plane (cf. Figures 2 and 3).
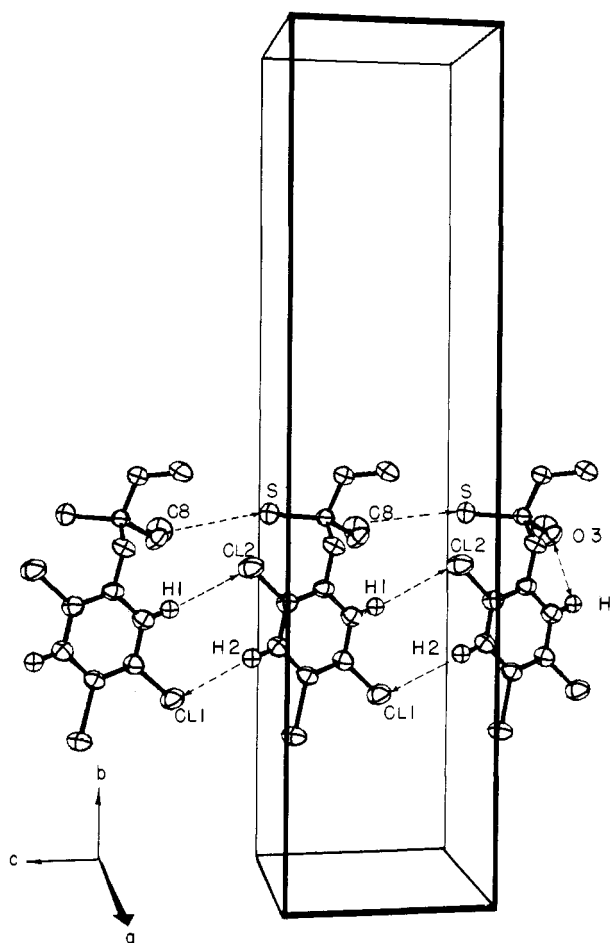
Figure 3. Dovetail packing in the *c* direction.

As with ronnel (Baughman and Jacobson, 1975) and Coroxon (Gifkins and Jacobson, 1976) angles of the type X=P—O (X = S or O) are all greater than the tetrahedral angle of 109.47°. Nontetrahedral angles are to be expected due to the different hybridization involved with the doubly bonded sulfur. The discrepancy also is due to the larger van der Waals radius of the doubly bonded sulfur vs. the singly bonded oxygens. Presumably similar factors are responsible for the distorted PO_4 subunits in coroxon and H_3PO_4 (Furberg, 1955). The increase ($\sim 4°$) in the S–P–O(3) angle compared to the S–P–O(2) angle in bromophos can be attributed to both the increased sulfur–C(8)

Table IV. Dihedral Angles (Degrees) and Least-Squares Planes

Plane (I)[b] defined by C(1) to C(6): $(0.91687)X + (-0.05745)Y + (-0.39503)Z - (1.10472) = 0$

Atom	Distance from plane, Å
C(1)	-0.0059
C(2)	0.0129
C(3)	-0.0119
C(4)	0.0036
C(5)	0.0038
C(6)	-0.0025

Plane (II)[b] defined by all 12 phenoxy group members: $(0.91791)X + (-0.05270)Y + (-0.39327)Z - (1.13354) = 0$

Atom	Distance from plane, Å
C(1)	0.0161
C(2)	0.0324
C(3)	0.0005
C(4)	0.0116
C(5)	0.0143
C(6)	0.0150
O(1)	-0.0757

Atom	Distance from plane, Å
H(1)	0.0645
Cl(1)	-0.0564
Br	-0.0199
H(2)	0.0161
Cl(2)	-0.0183
O(2)	0.4834
O(3)	1.4541

Plane (III)[b] defined by C(1), H(1), O(3), and P: $(0.67286)X + (-0.48031)Y + (-0.56264)Z - (-3.87615) = 0$

Atom	Distance from plane, Å
C(1)	0.0722
H(1)	-0.0743
O(3)	0.0968
P	0.0947
C(2)	0.2422

Plane (IV)[b] defined by C(1), O(1), S, and P: $(0.68424)X + (-0.50462)Y + (0.52647)Z + (-2.55342) = 0$

Atom	Distance from plane, Å
C(1)	0.1424
O(1)	-0.2873
S	-0.0839
P	0.2288
C(5)	-0.2941

Planes defined by:	Dihedral angle[a]
C(1)-C(2)-C(6); C(1)-O(1)-P	78.4 (6) (toward H(1))
C(1)-C(2)-C(6); O(1)-P-S	113.4 (7) (away from ring and toward Cl(2))
C(1)-O(1)-P; O(1)-P-S	59.4 (7) (toward Cl(2))
C(1)-C(3)-C(5); O(1)-O(2)-O(3)	39.6 (4) (O(3) fragment above ϕ plane)

[a] Angles correspond to proper orientation shown in Figures 1–3 (and calculated intramolecular distances) so that the phosphorus is tilted toward the H(1) side of the ring and the sulfur is directed away from H(1). [b] Planes are defined as $c_1X + c_2Y + c_3Z - d = 0$, where X, Y and Z are cartesian coordinates which are related to the triclinic cell coordinates (x, y, z) by the transformations: $X = xa \sin\gamma + zc\{(\cos\beta - \cos\alpha\cos\gamma)/\sin\gamma\} = xa$, $Y = xa\cos\gamma + yb + zc\cos\alpha = yb$, and $Z = zc\{(1 - \cos^2\alpha - \cos^2\beta - \cos^2\gamma + 2\cos\alpha\cos\beta\cos\gamma)^{1/2}/\sin\gamma\} = zc$.

methyl group interaction and the hydrogen bond (cf. Figure 2 and Tables II and III).

The C(1)–O(1) bond is significantly ($\sim 5\sigma$) shorter than the two methoxy C–O bonds (cf. Table I). This indicates a stronger C(1)–O(1) bond, possibly due to a weak p → "ring" overlap. The P–O(1) bond is the longest of the three P–O bonds being $\gtrsim 5\sigma$ longer than the other two P–O bonds. Hence, the P–O(1) bond lengthening parallels the shortening of the C(1)–O(1) bond (cf. Table II), enhancing phosphorylation (Clark et al., 1964). The corresponding P–O and C–O bond lengths for bromophos, ronnel, and coroxon are all within 3σ of being identical.

Molecular orbital calculations are needed to arrive at quantitative electron distributions and hence a numerical representation of the $\delta(+)$ and $\delta(-)$ regions. Since many of these types of calculations are much more useful when used to diagnose trends in similar compounds, an MO calculation on bromophos is planned along with MO calculations on other OP insecticides. These results will be presented in a future paper. This information along with the accurate distances and angles afforded by x-ray crystallography will give an uncustomary microscopic view of the molecule in question.

Alternatively, as noted earlier, the utilization of the $\delta(+)$ and $\delta(-)$ charges in the crystalline packing of bromophos gives one an excellent *indirect* insight into the probable use of these same $\delta(+)$ and $\delta(-)$ charges in the overall process of AChE inhibition. Charge distribution, as manifested in Hammett σ values, is known to be a major contributor to the inhibition of AChE by OP insecticides (Fukuto and Metcalf, 1956).

However, one must be concerned not only with *amounts* of charge but also the relative *locations* of the charges. The restriction of the rotation about the C(1)–O(1) bond allows bromophos (and conceivably bromophos oxon) less flexibility in reacting with the AChE active site(s) and is manifested in the mammalian LD_{50} value of 3750–6100 mg kg^{-1} (Eto, 1974), which is at least 2–3 times greater than for most OP insecticides. Consistent with this, the P···H(2) intramolecular distance of 5.52 Å and the P···H(1) intramolecular distance of 3.29 Å fall well outside of the mammalian AChE site-separation distance range of 4.3–4.7 Å (Hollingworth et al., 1967; O'Brien, 1963), yet the P···H(2) distance of 5.52 Å is well within the 5.0–5.5 Å (Hollingworth et al., 1967) and 4.5–5.9 Å (O'Brien, 1963) ranges quoted for insect AChE. The observed disparity in insect vs. mammalian LD_{50} values typical of many OP insecticides (White-Stevens, 1971) appears to be attributable, in part, to the inherently small selective range of favorable intramolecular P···"$\delta(+)$" distances (P···"meta $\delta(+)$" when phenyl groups are involved). Restriction of the P···H(2) distance in bromophos serves to further limit any inhibition reaction. Presumably bromophos oxon which is present in vivo has a conformation similar to that of bromophos. In addition, the conformation of bromophos will be intimately responsible for the oxon's formation. A restricted phosphorus–meta hydrogen distance has already been observed in the phosphate ruelene (Baughman et al., 1976).

Accordingly, selective design of an OP (or carbamate) system should be possible. This design should contain an immobile phosphorus (or carbonyl carbon) and a $\delta(+)$ function (-H, -N(CH$_3$)$_3^+$, etc.), enhanced by judiciously selected electron-withdrawing substituents, at a distance chosen to fully utilize the AChE site disparity. Investigations of hydrogen bond restricted phosphorus atoms in the *oxon* compounds will be included in future work, as will MO calculations.

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Captan Hydrolysis

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Captan [N-(trichloromethylthio)-4-cyclohexene-1,2-dicarboximide] undergoes hydrolysis readily in water with a maximum half-life of 710 min. Over the pH range 2–6, the reaction is pH independent and the pseudo-first-order rate constant is $(1.8 \pm 0.1) \times 10^{-5}$ s^{-1}. Above pH 7 the reaction is pH dependent and the second-order rate constant for alkaline hydrolysis is $(5.7 \pm 0.4) \times 10^{2}$ M^{-1} s^{-1}. The products are 4-cyclohexene-1,2-dicarboximide, carbon dioxide, hydrochloric acid, and sulfur. Folpet [N-(trichloromethylthio)phthalimide] and captafol [N-(1,1,2,2-tetrachloroethylthio)-4-cyclohexene-1,2-dicarboximide] hydrolyze at pH 7 with rates similar to that of captan. It is very likely that hydrolysis will be an important degradative pathway for these fungicides in the aquatic environment.

Captan [N-(trichloromethylthio)-4-cyclohexene-1,2-dicarboximide] is a widely used surface fungicide (18 million lb, 1971) (U.S. Environmental Protection Agency, 1972) for control of scabs, blotches, rots, mildew, and other diseases on fruits, vegetables, and flowers. It is also used in general purpose pesticide mixes. With widespread usage, therefore, captan may be expected to have an impact on the aquatic environment.

A few studies are reported in the literature concerning the effects of the fungicide on aquatic life. One of the most recent reports (Hermanutz et al., 1973) presents data on the toxic effects of captan on survival, growth, and reproduction of fathead minnows. They also investigated the survival of blue gills and brook trout in the presence of captan breakdown products.

The literature contains several reports concerning the hydrolysis of sulfenimide fungicides, but the available data are inconsistent and are not helpful in delineating the degradative pathway in water. Kinetics and products of the hydrolysis of captan are reported and compared with those of folpet [N-(trichloromethylthio)phthalimide] and captafol [N-(1,1,2,2-tetrachloroethylthio)-4-cyclohexene-1,2-dicarboximide]. In addition, hydrolysis data are compared with some of the findings of biologists concerned with the reaction of captan with thiols.

EXPERIMENTAL SECTION

Equipment. All melting points (mp) were obtained on a Fisher Johns melting point apparatus and are uncorrected. Infrared spectra (ir) were obtained with a Perkin-Elmer 621 grating infrared spectrophotometer, and ultraviolet spectra were recorded on a Perkin-Elmer 602

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