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## Crystal and Molecular Structure of Organophosphorus Insecticides. 3. Azinphos-methyl

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The crystal and molecular structure of azinphos-methyl (*O,O*-dimethyl *S*-(4-oxo-1,2,3-benzotriazin-3-yl)methyl phosphorodithioate),  $C_{10}H_{12}N_3O_3PS_2$ , has been determined by three-dimensional x-ray analysis. The compound crystallizes in the monoclinic space group  $P2_1/c$  with  $a = 12.084 \pm 0.007$ ,  $b = 15.190 \pm 0.008$ ,  $c = 7.856 \pm 0.003$  Å, and  $\beta = 98.39 \pm 0.03^\circ$  with  $Z = 4$ . Graphite-monochromated Mo  $K\alpha$  radiation ( $\lambda = 0.70954$  Å) was used for measurement of diffraction data at 10 °C. The structure was solved via direct methods and refined by a full-matrix least-squares procedure to a final discrepancy index of  $R = \Sigma ||F_o| - |F_c|| / \Sigma |F_o| = 0.080$ . The phosphorus-(carbonyl carbon) distance corresponding to the anionic-esteratic site separation of acetylcholinesterase is 4.83 (2) Å for azinphos-methyl in the solid state. No appreciable intramolecular interactions which might limit the accommodation of a large range of anionic-esteratic separations were observed.

As discussed by Baughman and Jacobson (1975), accurate three-dimensional structural analyses of organophosphorus insecticides can provide useful information toward the elucidation of bioactive mechanisms. In the first of this series of structural investigations of organophosphorus insecticides, ronnel (*O,O*-dimethyl *O*-2,4,5-trichlorophenyl phosphorothioate) was studied and characterized. From that structural analysis it was found that the distance from the phosphorus to the meta hydrogen on the phenyl ring was 5.51 Å. When the autotoxicosis through inhibition of acetylcholinesterase (AChE) by organophosphorus insecticides is considered, it is interesting to note that the nitrogen to carbonyl carbon atom distance in acetylcholine is estimated at 4.7 Å (Chothia and Pauling, 1969), when the molecule is in a proper conformation to react with bovine erythrocyte AChE. From a series of experiments carried out by Hollingworth et al. (1967), however, it was concluded that the distance between the anionic and esteratic centers of fly head AChE may be as much as 1 Å greater than in the mammalian enzyme. Consequently, the distance between the phosphorus and an electron-deficient site in an effective organophosphorus insecticide would appear to be between approximately 4.7 and 5.7 Å.

The ubiquitous or specific effectiveness of a particular organophosphorus insecticide may depend, then, on its ability to accommodate a range of esteratic-anionic site distances in various AChE enzymes. In some organophosphorus insecticides, the range of phosphorus to positive center distances attainable by the molecule is limited by a single rotational degree of freedom for

phosphorus about the aryl ring system. For example, in ronnel, the phosphorus-meta hydrogen distance is limited by rotation of phosphorus about the C(1)-O(1) bond (Baughman and Jacobson, 1975). This limitation is reflected in a comparison of ronnel's LD<sub>50</sub> for a particular AChE enzyme with the LD<sub>50</sub>'s of other organophosphorus insecticides, assuming that the in vivo transport properties are similar and that the inhibition of AChE is the primary toxic mode.

For ronnel, the LD<sub>50</sub> in female rats is 1740 mg/kg, whereas for azinphos-methyl it is 16 (Pesticides and Toxic Substances Effects Laboratory, 1973). This implies that azinphos-methyl, or more likely its P=O metabolite, is approximately 100 times more efficient than ronnel or its corresponding metabolite in the inhibition of rat AChE. It therefore becomes interesting to investigate the charge separation distance and steric hindrances in azinphos-methyl and to compare them to ronnel. Consequently, a single-crystal x-ray diffraction investigation of azinphos-methyl (*O,O*-dimethyl *S*-(4-oxo-1,2,3-benzotriazin-3-yl)methyl phosphorodithioate) was carried out.

### EXPERIMENTAL SECTION

**Crystal Data.** A sample of the title compound was kindly supplied by P. A. Dahm. A crystal of dimensions  $0.2 \times 0.2 \times 0.3$  mm was mounted on a glass fiber with Duco cement and subsequently attached to a standard goniometer head. From six preliminary  $\omega$ -oscillation photographs taken on an automated four-circle x-ray diffractometer at various  $\chi$  and  $\phi$  settings, 14 independent reflections were selected and their coordinates were input to the automatic indexing program ALICE (Jacobson, 1974).

The resulting reduced cell and reduced cell scalars indicated 2/m (monoclinic) symmetry. A monoclinic crystal system was confirmed by inspection of axial  $\omega$ -

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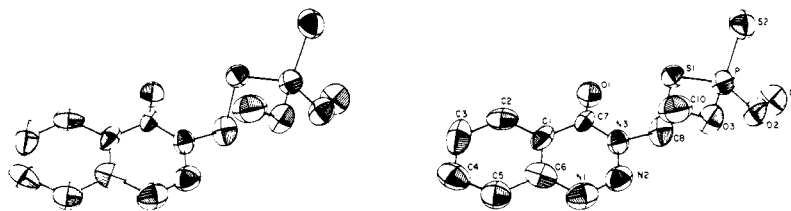


Figure 1. Stereographic view of azinphos-methyl with hydrogen atoms omitted. In this and succeeding drawings 50% probability ellipsoids are depicted.

oscillation photographs, which displayed a mirror plane with respect to the  $b^*$  reciprocal lattice axis. Observed layer line spacings were within experimental error to those predicted for this cell. A least-squares refinement of the lattice constants (Williams, 1964) based on the  $\pm 2\theta$  measurements of 12 strong independent reflections on a previously aligned four-circle diffractometer (Mo  $K\alpha$  graphite monochromated radiation,  $\lambda = 0.70954 \text{ \AA}$ ), at  $10^\circ \text{C}$ , yielded  $a = 12.084 \pm 0.007$ ,  $b = 15.190 \pm 0.008$ ,  $c = 7.856 \pm 0.003 \text{ \AA}$ , and  $\beta = 98.39 \pm 0.03^\circ$ .

**Collection and Reduction of X-ray Intensity Data.** Data were collected at  $10^\circ \text{C}$  by bathing the crystal in a cool nitrogen gas stream and by utilizing an automated four-circle diffractometer both designed and built in this laboratory. The diffractometer is interfaced to a PDP-15 computer in a time-sharing mode and is equipped with a scintillation counter. Graphite monochromated Mo  $K\alpha$  X-radiation was used for data collection.

All data within a  $2\theta$  sphere of  $42^\circ$  ( $(\sin \theta)/\lambda = 0.500 \text{ \AA}^{-1}$ ) in the  $hkl$  and  $\bar{h}kl$  octants were measured via a peak-height data collection mode, using a takeoff angle of  $4.5^\circ$  and yielded 2751 reflections.

As a general check on electronic and crystal stability, the intensities of three standard reflections were remeasured every 50 reflections. These standard reflections were not observed to vary significantly throughout the entire data collection period. Examination of the data revealed systematic absences of  $h0l$  reflections for  $l = 2n + 1$  and  $0k0$  reflections for  $k = 2n + 1$ , thus uniquely defining the space group as  $P2_1/c$ .

The intensity data were corrected for Lorentz and polarization effects and no absorption correction was made—the crystal was nearly cylindrical and the minimum and maximum transmission factors differed by less than 5% ( $\mu R = 0.05$ ). The estimated variance in each intensity was calculated by:

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

where  $C_T$  and  $C_B$  represent the total count and 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). Equivalent zone data were averaged and only those reflections for which  $F_o > 3\sigma_F$  were retained for structural refinement. There were consequently 696 independent reflections used in the subsequent structural analysis.

**Solution and Refinement of Structure.** The program MULTAN (Main et al., 1971) was used to assign phases to the 400 largest  $E$  values. The  $E$  map (Hubbard et al., 1971) resulting from the solution set corresponding to the best figure of merit unambiguously revealed the positions of all 19 nonhydrogen atoms. The remaining atoms were found by successive structure factor (Busing et al., 1962) and electron density map calculations.

In addition to positional parameters for all atoms, the anisotropic thermal parameters for all nonhydrogen 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  $\omega = 1/\sigma_F^2$ , to a conventional discrepancy factor of  $R = \Sigma ||F_o| - |F_c|| / \Sigma |F_o| = 0.091$ . Analysis of the weights ( $\omega$ ) was performed via a requirement that  $\omega(|F_o| - |F_c|)^2$  should be a constant function of  $|F_o|$  and  $(\sin \theta)/\lambda$  (Cruickshank and Pilling, 1961). Accordingly, analysis of the weighting scheme indicated that the reflections at very low as well as very 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  $R = 0.080$ . The scattering factors used were those of Hanson et al. (1960), modified for the real and imaginary parts of anomalous dispersion (Templeton, 1962).

The final positional and thermal parameters are listed in Table I. The standard deviations were calculated from the inverse matrix of the final least-squares cycle.

**Description and Discussion.** A stereographic view of azinphos-methyl depicting 50% probability ellipsoids is provided in Figure 1 (Johnson, 1971). Selected interatomic distances and angles (Busing et al., 1964) are listed in Tables II and III, respectively. Intramolecular bond distances and angles are in good agreement with those reported previously in the literature.

When considering the proposal of Clark et al. (1964) relating effectiveness in phosphorylation to weakness of P-(aryl-group 6A element) bonds, azinphos-methyl should pose no problem to phosphorylation, since a phosphorus-sulfur bond is certainly a weaker bond than an analogous P-O bond commonly found in organophosphorus insecticides. Consequently, the inhibition of AChE by azinphos-methyl oxon should not be hindered by any significant barrier to phosphorylation. Distortion of tetrahedral geometry about phosphorus is observed in this compound as in others previously reported (Gifkins and Jacobson, 1976). The (methoxy oxygen)-phosphorus-(methoxy oxygen) angle, in particular, is nearly  $4^\circ$  smaller than that reported for ronnel (Baughman and Jacobson, 1975), i.e.  $94.3 (7)$  to  $98.0 (3)^\circ$ , respectively.

The planarity of the ring system is quite striking, as can be seen in the tabulation of atom deviations from the least-squares plane (Table IV). The greatest deviation from planarity is  $\sim 0.03 \text{ \AA}$ , which is negligible when considering thermal motion and standard deviations.

Packing forces do not appear to dictate coordination geometry about the phosphorus atom to any great extent, but torsion angles do appear to be affected by intermolecular steric repulsion effects of the methoxy groups (cf. Figure 2). Torsion angles about specific bonds are listed in Table V.

C(7) appears to be the likely atom on which an electron-deficient site may reside. The P-C(7) distance in the solid state for azinphos-methyl is  $4.83 (2) \text{ \AA}$ . The corresponding distance for ronnel is  $5.51 \text{ \AA}$ . From solid state considerations alone, the phosphorus-(partially positive center) distance in ronnel is  $0.7 \text{ \AA}$  longer than the corresponding distance for azinphos-methyl. It is suggested by Hollingworth et al. (1967) that the distance between

Table I. Final Atom Positional<sup>a</sup> and Thermal<sup>b</sup> Parameters

Atom	x	y	z	$\beta_{11}$	$\beta_{22}$	$\beta_{33}$	$\beta_{12}$	$\beta_{13}$	$\beta_{23}$
S(1)	8 051 (4) <sup>c</sup>	7947 (3)	831 (6)	87 (4)	43 (2)	198 (9)	-4 (3)	17 (5)	-6 (4)
S(2)	5 952 (5)	8680 (4)	2537 (6)	92 (5)	84 (4)	210 (11)	11 (4)	32 (6)	13 (5)
P	7 135 (4)	9043 (3)	1350 (6)	77 (4)	51 (3)	166 (9)	-6 (3)	-5 (5)	1 (5)
O(1)	10 226 (11)	6905 (9)	915 (17)	101 (13)	41 (7)	290 (32)	-10 (8)	-19 (15)	-15 (11)
O(2)	6 825 (10)	9572 (8)	-390 (14)	115 (14)	66 (7)	172 (25)	2 (8)	-18 (15)	15 (12)
O(3)	7 981 (10)	9754 (7)	2201 (14)	108 (13)	45 (7)	186 (27)	2 (7)	-13 (15)	-5 (10)
N(1)	11 623 (17)	9271 (11)	2472 (22)	117 (19)	43 (11)	260 (40)	-2 (12)	61 (23)	-11 (15)
N(2)	10 702 (16)	9220 (11)	1529 (21)	103 (17)	59 (11)	184 (30)	-6 (12)	27 (19)	18 (15)
N(3)	10 259 (14)	8382 (10)	1030 (18)	70 (13)	49 (11)	162 (27)	1 (10)	3 (15)	-9 (13)
C(1)	11 752 (16)	7659 (13)	2655 (20)	95 (19)	47 (12)	142 (32)	12 (13)	31 (22)	29 (16)
C(2)	12 341 (19)	6885 (15)	3306 (23)	103 (22)	65 (14)	173 (37)	-13 (14)	75 (25)	-1 (18)
C(3)	13 358 (20)	6987 (19)	4384 (25)	100 (22)	94 (19)	197 (42)	43 (18)	22 (25)	27 (22)
C(4)	13 787 (19)	7839 (18)	4808 (23)	76 (19)	75 (16)	199 (38)	-16 (16)	44 (20)	-21 (23)
C(5)	13 198 (19)	8557 (16)	4159 (29)	97 (23)	48 (12)	267 (46)	-11 (14)	-3 (28)	-10 (21)
C(6)	12 183 (17)	8492 (14)	3083 (23)	89 (20)	54 (14)	162 (35)	-15 (13)	56 (23)	-47 (18)
C(7)	10 690 (16)	7567 (14)	1432 (20)	73 (17)	40 (11)	123 (32)	26 (12)	61 (20)	26 (16)
C(8)	9 181 (20)	8471 (17)	-207 (23)	115 (23)	83 (16)	93 (40)	7 (13)	-10 (23)	-4 (17)
C(9)	6 134 (42)	9204 (28)	-1887 (52)	152 (39)	85 (31)	243 (58)	-5 (23)	-6 (37)	-20 (32)
C(10)	8 555 (23)	9646 (19)	3987 (32)	120 (26)	73 (17)	243 (61)	-23 (18)	14 (29)	27 (23)
H(1)	185 (16)	637 (12)	312 (21)						
H(2)	377 (15)	638 (12)	439 (20)						
H(3)	471 (15)	792 (11)	488 (19)						
H(4)	351 (15)	911 (14)	467 (22)						
H(5)	925 (24)	819 (15)	1109 (30)						
H(6)	918 (13)	823 (10)	873 (20)						
H(7)	585 (33)	888 (25)	-148 (49)						
H(8)	629 (13)	815 (11)	-204 (20)						
H(9)	514 (14)	904 (11)	-128 (19)						
H(10)	890 (18)	926 (14)	408 (29)						
H(11)	782 (16)	937 (12)	480 (23)						
H(12)	930 (14)	1022 (11)	430 (19)						

<sup>a</sup> The positional parameters for all nonhydrogen atoms are presented in fractional unit cell coordinates ( $\times 10^4$ ). Positional parameters for hydrogen atoms are ( $\times 10^3$ ). <sup>b</sup> The  $\beta_{ij}$  are defined by:  $T = \exp[-(h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + 2hk\beta_{12} + 2hl\beta_{13} + 2kl\beta_{23})]$  and are ( $\times 10^4$ ). An isotropic thermal parameter of 2.5 was assigned for all hydrogen atoms. <sup>c</sup> In this and succeeding tables, estimated standard deviations are given in parentheses for the least significant figures.

Table II. Selected Interatomic Distances (Å) for Azinphos-methyl

P-S(1)	2.071 (7)
P-S(2)	1.898 (7)
P-O(2)	1.580 (12)
P-O(3)	1.565 (12)
S(1)-C(8)	1.863 (28)
O(1)-C(7)	1.191 (20)
O(2)-C(9)	1.448 (30)
O(3)-C(10)	1.478 (26)
N(1)-N(2)	1.243 (20)
N(1)-C(6)	1.408 (25)
N(2)-N(3)	1.410 (22)
N(3)-C(7)	1.360 (21)
N(3)-C(8)	1.510 (28)
C(1)-C(2)	1.426 (26)
C(1)-C(6)	1.388 (25)
C(1)-C(7)	1.490 (24)
C(2)-C(3)	1.393 (28)
C(3)-C(4)	1.412 (31)
C(4)-C(5)	1.357 (28)
C(5)-C(6)	1.385 (27)

anionic and esteratic sites of insect AChE may be as much as 1 Å greater than in mammalian enzymes. Thus, it would appear that azinphos-methyl oxon would be a more effective AChE inhibitor than the corresponding analogue of ronnel for the mammalian enzymes, based on the work of Chothia and Pauling (1969) and Hollingworth et al. (1967) mentioned previously. Indeed, such an assumption is substantiated when a comparison of the LD<sub>50</sub>'s in female rats for azinphos-methyl and ronnel is made, i.e. LD<sub>50</sub> (azinphos-methyl) = 16 mg/kg, LD<sub>50</sub> (ronnel) = 1740.

It is evident that rotation about the N(3)-C(8) and C(8)-S(1) bonds of azinphos-methyl provides considerable

Table III. Bond Angles (deg) for Azinphos-methyl

P-S(1)-C(8)	100.9 (8)	C(6)-C(1)-C(2)	120.8 (18)
S(1)-P-S(2)	109.0 (3)	C(7)-C(1)-C(2)	119.3 (18)
S(1)-P-O(2)	107.7 (6)	C(7)-C(1)-C(6)	119.8 (18)
S(1)-P-O(3)	107.7 (5)	C(1)-C(2)-C(3)	118.3 (22)
S(2)-P-O(2)	118.1 (6)	C(2)-C(3)-C(4)	120.3 (22)
S(2)-P-O(3)	118.7 (5)	C(3)-C(4)-C(5)	119.4 (19)
O(2)-P-O(3)	94.3 (7)	C(4)-C(5)-C(6)	122.6 (20)
P-O(2)-C(9)	122.6 (20)	C(5)-C(6)-C(1)	118.6 (21)
P-O(3)-C(10)	120.9 (12)	C(5)-C(6)-N(1)	119.0 (19)
C(6)-N(1)-N(2)	119.5 (16)	C(1)-C(6)-N(1)	122.4 (16)
N(1)-N(2)-N(3)	119.4 (15)	O(1)-C(7)-C(1)	128.0 (16)
N(2)-N(3)-C(7)	129.6 (15)	N(3)-C(7)-O(1)	122.8 (17)
N(2)-N(3)-C(8)	110.7 (15)	N(3)-C(7)-C(1)	109.1 (18)
C(7)-N(3)-C(8)	119.6 (20)	S(1)-C(8)-N(3)	107.3 (13)

flexibility for the phosphorus to C(7) distance, since there are no intramolecular restrictive interactions. Azinphos-methyl oxon, therefore, is not exclusively an insect AChE inhibitor, since free rotation in vivo about the N(3)-C(8) and C(8)-S(1) bonds enables the molecule to accommodate a large range of anionic-esteratic site separations. Ronnel, on the other hand, has only a single rotational flexibility for altering the phosphorus-meta hydrogen separation about the C(1)-O(1) bond, and intramolecular repulsion effects limit the molecule in achieving separations which are more efficient for blocking of mammalian AChE (Baughman and Jacobson, 1975).

The structure of azinphos-methyl therefore suggests that the additional rotational flexibility of phosphorus relative to the positive site of the aryl ring system broadens the specificity of the insecticide. It appears that in the design of organophosphorus insecticides one should consider the range of phosphorus-(partially positive center) distances attainable as a criterion for specificity. In addition, it seems suggestive from this work that similar organo-

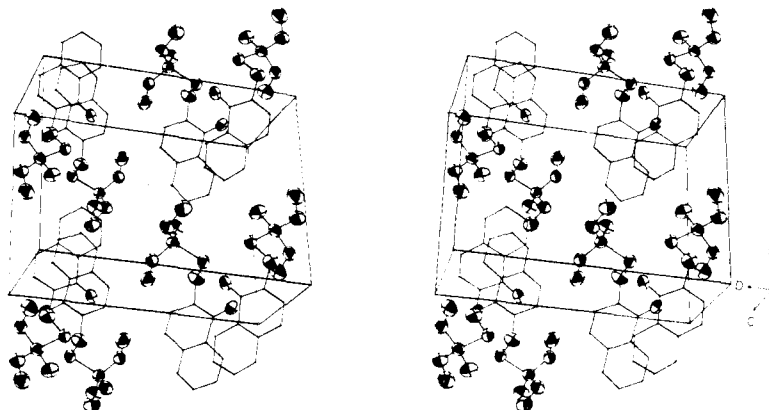


Figure 2. Unit cell stereograph of azinphos-methyl.

Table IV. Atomic Displacements from the Least-Squares Plane<sup>a</sup> Describing the Ring System; Plane Defined by Atoms [O(1), N(1), N(2), N(3), C(1), C(2), C(3), C(4), C(5), C(6), C(7), and C(8)]:  $-0.61582X - 0.00129Y + 0.78789Z + 6.95512 = 0$

Atom	Deviation from planarity, Å
O(1)	-0.027
N(1)	-0.008
N(2)	0.034
N(3)	0.024
C(1)	0.024
C(2)	0.032
C(3)	0.011
C(4)	-0.020
C(5)	-0.026
C(6)	-0.006
C(7)	-0.021
C(8)	-0.018

<sup>a</sup> Plane is defined as  $c_1X + c_2Y + c_3Z - d = 0$ , where  $X$ ,  $Y$ , and  $Z$  are Cartesian coordinates related to the monoclinic  $x$ ,  $y$ ,  $z$  coordinates by the transformation:  $a, 0, c \cos \beta; 0, b, 0; 0, 0, c \sin \beta$ .

Table V. Torsion Angles

Plane A	Plane B	Bond of rotation	Torsion angle ( $\angle AB$ ), deg
S(1)-P-S(2)	C(8)-S(1)-P	S(1)-P	177.8
N(3)-C(8)-S(1)	C(8)-S(1)-P	C(8)-S(1)	107.5
N(2)-N(3)-C(8)	N(3)-C(8)-S(1)	N(3)-C(8)	117.4
Least-squares plane for ring	N(3)-C(8)-S(1)	N(3)-C(8)	64.0

phosphorus insecticides with an additional bound atom between phosphorus and the aryl ring are less specific to insects and, consequently, may not be desirable models for insecticide development.

It is interesting to note that the phosphinate analogue of azinphos-methyl has an LD<sub>50</sub> for rats which is significantly larger, i.e. 1000 mg/kg (Eto, 1974). This implies that accommodation of the AChE enzyme is not dictated solely by phosphorous-(partially positive center) separations, but may also involve a subtle charge density effect about the phosphorus, consequently easing or hindering phosphorylation or enzyme binding.

Results of a CNDO II molecular orbital calculation (Segal, 1970) for both azinphos-methyl and its phosphinate analogue support the intuitive conjecture that the charge on the phosphorus atom should differ slightly in these two compounds (cf. Figure 3). A charge density calculation for azinphos-methyl was made based on the positional

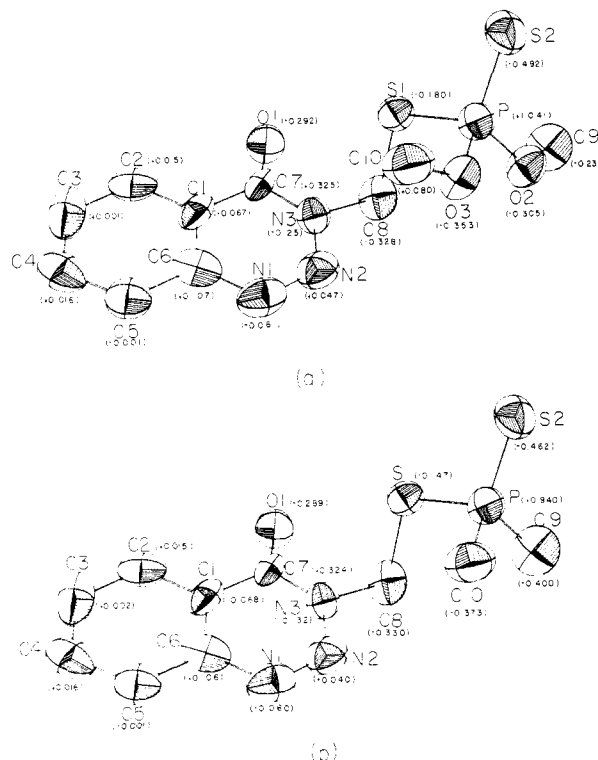


Figure 3. Partial charge densities obtained from CNDO II molecular orbital calculations for (a) azinphos-methyl and (b) its phosphinate analogue.

parameters obtained from the structural study, and a similar calculation was performed for the phosphinate analogue based on the assumption that the structural parameters should not differ significantly from those obtained for azinphos-methyl. The substitution of methyl carbon atoms in the methoxy oxygen positions of azinphos-methyl at phosphorus-carbon distances of  $\sim 1.56$  Å yields the results shown in Figure 3. In general, the phosphorus-carbon distances should be somewhat longer, and a CNDO II calculation with the methyl groups radially displaced such that the P-C distance is  $\sim 1.74$  Å yields an even lower value for the positive charge on phosphorus (+0.853), leaving all other atomic charges essentially unchanged. The numbers associated with the partial charge densities in Figure 3 are not intended to represent the absolute charge on each atom, since the CNDO II calculation is an approximation of physical reality. Comparisons, however, should be valid since the same approximations are applied to both molecules.

From these calculations, it can be seen that the partial charge density on the phosphorus atom is significantly

different in these two molecules, whereas the charge on C(7) remains essentially invariant. Since the toxicity of the phosphinate analogue to mammals is significantly lower than that of azinphos-methyl and since the structural parameters of the two compounds would appear to be similar, it seems logical to suspect a charge density dependence in the toxic mechanism.

These results, consequently, provide impetus for future calculations of charge densities in other series of organophosphorus insecticides. In addition to the possibility of charge density effects in AChE inhibition, intramolecular restrictions or freedoms may also contribute to the inhibition, and x-ray diffraction analyses of organophosphorus insecticides can provide valuable information to elucidate the mechanisms of acetylcholinesterase inhibition in both mammals and insects.

**Supplementary Material Available:** A listing of the observed and calculated structure factor amplitudes (4 pages). Ordering information is given on any current masthead page.

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## Acid Dissociation Constants of Arsenic Acid, Methylarsonic Acid (MAA), Dimethylarsinic Acid (Cacodylic Acid), and *N*-(Phosphonomethyl)glycine (Glyphosate)

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Acid dissociation constants have been measured for arsenic acid ( $\text{H}_3\text{AsO}_4$ ), methylarsonic acid ( $\text{CH}_3\text{AsO}_3\text{H}_2$ ; MAA), dimethylarsinic acid [ $(\text{CH}_3)_2\text{AsO}_2\text{H}$ ; cacodylic acid], and *N*-(phosphonomethyl)glycine ( $\text{HO}_2\text{CCH}_2\text{NHCH}_2\text{PO}_3\text{H}_2$ ; glyphosate). A recently devised mathematical technique for  $\text{p}K$  and end point determinations which corrects for strong acid or base impurities was modified and used to analyze automatic titrator titration curves and correct  $\text{p}K$  values to zero ionic strength. Thermodynamic  $\text{p}K$  values =  $-\log (a_{\text{HA}}/a_{\text{AH}})$  at 25 °C are:  $\text{H}_3\text{AsO}_4$ ,  $\text{p}K_2 = 7.089 \pm 0.01$ ; MAA,  $\text{p}K_1 = 4.114 \pm 0.01$ ,  $\text{p}K_2 = 9.148 \pm 0.01$ ; cacodylic acid,  $\text{p}K_1 = 6.288 \pm 0.01$ ; glyphosate,  $\text{p}K_1 = 2.32 \pm 0.03$ ,  $\text{p}K_2 = 5.86 \pm 0.03$ ,  $\text{p}K_3 = 10.86 \pm 0.03$ .

Dimethylarsinic acid (cacodylic acid; hydroxydimethylarsine oxide) and methylarsonic acid (methane-

arsonic acid; MAA) and its sodium salts (MSMA and DSMA) are extensively used as postemergence herbicides applied to the foliage of weeds. Lead and calcium salts of arsenic acid were formerly used in large quantities as insecticides and are still used to a limited extent, and *N*-(phosphonomethyl)glycine (glyphosate) is a new broad-spectrum, translocatable herbicide with potential uses in agronomic crops. These materials differ from many

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