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Crystal and Molecular Structure of Organophosphorus Insecticides. 8. Ronnel Oxon

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The crystal and molecular structure of ronnel oxon {*O,O*-dimethyl *O*-2,4,5-trichlorophenyl phosphate, $(\text{H}_3\text{CO})_2\text{P}(\text{O})\text{OC}_6\text{H}_2\text{Cl}_3$, monoclinic, $P2_1/c$, $a = 9.659$ (5), $b = 11.388$ (2), $c = 14.465$ (9) Å, $\beta = 130.09$ (4)°, $Z = 4$, Mo $K\alpha$ radiation} has been determined by three-dimensional x-ray analysis. The structure was solved by direct methods and refined by full-matrix least-squares procedures to a final discrepancy index $R = 0.060$ for 1842 observed reflections ($F_o > 2.5\sigma(F_o)$). The phosphorus-meta hydrogen distance of 5.49 Å is well within the range of literature values cited for the intramolecular site-separation distance for insect acetylcholinesterase (AChE), yet is well outside that for mammalian AChE. CNDO molecular orbital calculations are presented to show the charge density distribution in ronnel oxon.

In the case of acetylcholinesterase (AChE) inhibition, one would ideally like to know the three-dimensional structure of the active sites, or that of a small range of possible low-energy conformations. The complexity of this enzyme virtually prohibits direct elucidation of its structure. However, accurate structural determinations of smaller molecules such as the organophosphorus (OP) and/or carbamate insecticides, which strongly interact with the active site(s) of AChE, would allow not only inferences to be made with regards to the topography of AChE but also yield valuable molecular insight into the insecticides themselves. 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.

The crystal structure investigation of ronnel oxon was undertaken as a part of a study of various organophosphorus (OP) insecticides being carried on at this Laboratory (Baughman and Jacobson, 1975; Gifkins and Jacobson, 1976; Rohrbaugh and Jacobson, 1977; Baughman and Jacobson, 1976; Baughman and Jacobson, 1977; Baughman et al., 1978a,b). [Structural investigations of the carbamates are concurrently being performed (Takusagawa and Jacobson, 1977a,b,c)]. The purpose of such a program is to better understand the relationship between structure and mechanism(s) relative to an insecticide's toxicity/activity. Since ronnel (*O,O*-dimethyl *O*-2,4,5-

trichlorophenyl phosphorothioate, the first reference) is a thiophosphate OP, it is logical to investigate the oxon compound in order to note any conformational similarities and/or dissimilarities which might result as a result of *in vivo* oxidation.

EXPERIMENTAL SECTION

Crystal Data. From a 99+% pure sample of the title compound, a rectangular prismatic crystal with approximate dimensions $0.22 \times 0.16 \times 0.18$ mm was selected and mounted on the end of a glass fiber using Elmer's Glue-All. The crystal was then mounted on a four-circle diffractometer and three ω -oscillation photographs were taken at various χ and ϕ settings and verified that the crystal was indeed single.

From these photographs 15 independent reflections were selected and their coordinates were input into an automatic indexing program (Jacobson, 1976). The reduced cell scalars which resulted indicated monoclinic symmetry, which was confirmed by inspection of ω -oscillation photographs taken about each of the three axes in turn. Only the b axis showed a mirror plane. 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 $\pm 2\theta$ ($45^\circ > |2\theta| > 20^\circ$) measurements of 14 strong independent reflections. At 27 °C using Mo $K\alpha$ ($\lambda = 0.70954$ Å) they are $a = 9.659$ (5), $b = 11.388$ (2), $c = 14.465$ (9) Å, and $\beta = 130.09$ (4)°. The observed density of 1.63 (3) g cm⁻³ determined by the flotation method is in good agreement with the calculated value of 1.668 g cm⁻³ for four molecules with a molecular

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weight of 305.5 g mol⁻¹ in a unit cell having a volume of 1217.25 Å³.

Collection and Reduction of X-Ray Intensity Data.

The data were collected at 27 °C with graphite-monochromated Mo K α 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 2 θ sphere of 50° [(sin θ)/ λ = 0.596 Å⁻¹] in the hkl and $\bar{h}\bar{k}l$ 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 2420 reflections were recorded in this manner. Examination of the data revealed the following systematic absences: $h0l$ when $l = 2n + 1$ and $0k0$ when $k = 2n + 1$. These absences uniquely determine the space group as $P2_1/c$.

The intensity data were corrected for Lorentz and polarization effects and, since $\mu = 9.21$ cm⁻¹, absorption corrections were not made; maximum and minimum transmission factors were 0.863 and 0.817, respectively. The estimated variance in each intensity was calculated by:

$$\sigma^2_I = C_T + 2C_B + (0.03C_T)^2 + (0.03C_B)^2$$

where C_T and C_B represent the total and background counts, 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 data were averaged and 1848 reflections with $|F_o| > 2.5\sigma(F_o)$ were retained for use in subsequent calculations. During later work it was discovered that six large reflections showed appreciable secondary extinction effects. The data were corrected via the approximation $I_o^{corr} = I_o(1 + 2gI_o)$, where an average value for $g = 4.68 \times 10^{-5}$ was determined using the 15 largest I_o 's.

SOLUTION AND REFINEMENT

The program MULTAN (Main et al., 1971) was employed to obtain the phases for the 499 strongest reflections. The resultant E map (Hubbard et al., 1971) using the best figure of merit unambiguously showed the positions of 13 of the 16 total nonhydrogen atoms. All 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 $\omega = 1/\sigma_F^2$. This refinement yielded a conventional discrepancy factor of $R = \Sigma||F_o| - |F_c||/\Sigma|F_o| = 0.153$. At this stage of the refinement all nonhydrogen atoms had been refined using isotropic thermal parameters. The scattering factors were those of Hanson et al., (1960), modified for the real and imaginary parts of anomalous dispersion (Templeton, 1962). The scattering factors for hydrogen were those of Stewart et al. (1965).

Analysis of an electron density difference map did not reveal either the ring or the methyl hydrogens. Consequently, the ring hydrogen atom position was fixed at 0.95 Å from the corresponding carbon (C(3)). Methyl hydrogens were approximated by two sets of half-hydrogens inserted at tetrahedral positions using the precise positions of the corresponding methyl carbon and the methoxy oxygen and rotated 60° relative to one another. The methyl C-H distances were set equal to 1.0 Å; all isotropic

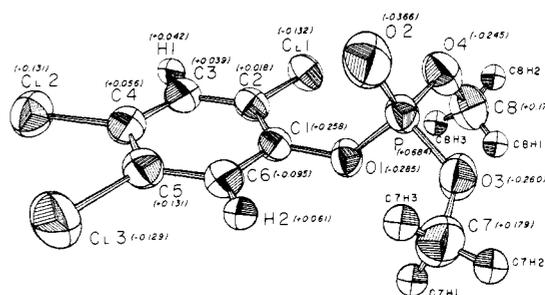


Figure 1. The ronnel oxon molecule showing 50% probability ellipsoids; 30% for hydrogens. The numbers in parenthesis refer to partial charge densities from a CNDO II calculation.

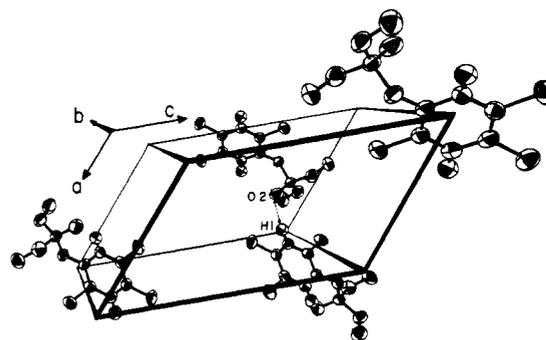


Figure 2. View of a unit cell of ronnel oxon.

hydrogen temperature factors were set equal to 4.5 Å².

Subsequent anisotropic least-squares refinement without varying the hydrogen parameters converged to $R = 0.060$. Since this procedure yielded slightly different nonhydrogen atom 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-square planes are listed in Table IV.

DESCRIPTION OF STRUCTURE AND DISCUSSION

The phenoxy group in ronnel oxon, shown in Figures 1 and 2 (Johnson, 1971), is essentially planar (cf. Table IV, plane III). For the most part, packing in the ronnel oxon 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 atoms with $\delta(+)$ and $\delta(-)$ charges. The H(1)···O(2) interaction related via the c -glide operation serves as such an example (cf. Figure 2 and Tables II and III), while on the other hand, the O(2)···C(7)H₃ and C(8)H₃···Cl(3) interactions appear to be van der Waals in character (cf. Table II).

The C(1)-O(1) bond in ronnel oxon is significantly ($>10\sigma$) shorter than the two methoxy C-O bonds (cf. Table II), while the P-O(1) bond is the longest of the three P-O bonds, being at least 10σ longer than the other two. These observations, which are in agreement with CNDO II molecular orbital calculations of the Pople and Beveridge (1970) type, are consistent with a bonding formulation in which there is a weak π overlap of the p_z orbital on the oxygen with the ring system which simultaneously weakens the O-P bond. The latter effect should enhance phosphorylation (Clark et al., 1964). Such variations in bond lengths have been noted earlier as the bond lengths corresponding to P-O(1) and C(1)-O(1) in ronnel oxon, ronnel

Table I. Final Atomic Positional^a and Thermal^b Parameters for Ronnel Oxon

| Atom | x | y | z | β_{11} | β_{22} | β_{33} | β_{12} | β_{13} | β_{23} |
|-------|-------------------------|------------|------------|--------------|--------------|--------------|--------------|--------------|--------------|
| Cl(1) | 0.0254 (1) ^c | 0.7603 (1) | 0.5886 (1) | 21.6 (2) | 9.5 (1) | 11.0 (1) | -0.4 (1) | 10.7 (1) | 1.4 (1) |
| Cl(2) | -0.1213 (2) | 0.9231 (1) | 0.1870 (1) | 25.0 (3) | 12.6 (1) | 6.6 (1) | 2.2 (1) | 7.3 (1) | -0.5 (1) |
| Cl(3) | 0.2408 (2) | 1.0730 (1) | 0.3475 (1) | 29.7 (3) | 12.6 (1) | 11.0 (1) | -1.0 (1) | 13.7 (2) | 1.4 (1) |
| P | 0.5180 (1) | 0.8459 (1) | 0.8083 (1) | 15.2 (2) | 7.7 (1) | 7.0 (1) | 1.0 (1) | 5.6 (1) | 0.8 (1) |
| O(1) | 0.3394 (3) | 0.9222 (2) | 0.7150 (2) | 17.3 (5) | 9.0 (2) | 6.8 (2) | 2.3 (3) | 6.4 (3) | 0.7 (2) |
| O(2) | 0.5843 (4) | 0.7909 (3) | 0.7530 (3) | 23.2 (7) | 14.4 (4) | 10.7 (3) | 6.0 (4) | 9.4 (4) | 1.0 (3) |
| O(3) | 0.6430 (4) | 0.9343 (3) | 0.9129 (3) | 22.4 (6) | 11.4 (3) | 8.1 (3) | -2.6 (3) | 6.7 (3) | 0.2 (2) |
| O(4) | 0.4716 (4) | 0.7570 (3) | 0.8646 (3) | 25.6 (7) | 10.0 (3) | 11.7 (3) | 0.9 (4) | 10.1 (4) | 2.6 (2) |
| C(1) | 0.2384 (5) | 0.9169 (3) | 0.5912 (3) | 14.0 (6) | 7.0 (3) | 6.7 (3) | 2.0 (3) | 5.6 (4) | 0.5 (2) |
| C(2) | 0.0840 (5) | 0.8476 (3) | 0.5209 (3) | 15.7 (7) | 7.2 (3) | 8.2 (3) | 1.3 (4) | 7.4 (4) | 0.9 (3) |
| C(3) | -0.0265 (5) | 0.8496 (3) | 0.3963 (3) | 16.2 (7) | 8.2 (3) | 8.1 (3) | 0.5 (4) | 6.8 (4) | -0.4 (3) |
| C(4) | 0.0198 (5) | 0.9196 (3) | 0.3418 (3) | 15.8 (7) | 8.4 (3) | 6.6 (3) | 2.4 (4) | 5.7 (4) | 0.1 (3) |
| C(5) | 0.1774 (5) | 0.9869 (3) | 0.4126 (3) | 18.8 (8) | 8.0 (3) | 8.6 (4) | 1.4 (4) | 8.9 (5) | 0.5 (3) |
| C(6) | 0.2853 (5) | 0.9861 (3) | 0.5375 (3) | 17.2 (7) | 7.5 (3) | 8.0 (3) | -0.3 (4) | 7.8 (4) | -0.1 (3) |
| C(7) | 0.7147 (8) | 1.0349 (5) | 0.8955 (5) | 36 (1) | 12.9 (5) | 11.6 (5) | -7.9 (7) | 12.9 (8) | -1.5 (4) |
| C(8) | 0.4023 (7) | 0.7910 (5) | 0.9248 (5) | 29 (1) | 14.0 (5) | 13.2 (5) | 0.1 (6) | 14.5 (7) | 3.0 (4) |
| H(1) | -0.133 | 0.803 | 0.349 | 4.5 | | | | | |
| H(2) | 0.391 | 1.033 | 0.586 | 4.5 | | | | | |

^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 temperature factors have been set equal to 4.5. Nonhydrogen thermal parameters are ($\times 10^3$). ^c In this and succeeding tables, estimated standard deviations are given in parenthesis for the least significant figures; later tables include the error in the lattice constants. Since the hydrogen parameters were not refined, no standard deviations are given. Positions for the methyl hydrogens are not given as they were approximated.

Table II. Selected Interatomic Distances (Å) for Ronnel Oxon

| Bonding distances | | Interaction | via | Obsd distance | Total van der Waals Distance (Pauling, 1960) |
|-------------------|-----------|------------------------------|---|---------------|--|
| C(1)-C(2) | 1.388 (5) | P ··· H(1) | Intramolecular | 5.487 (5) | (3.1) |
| C(2)-C(3) | 1.382 (5) | P ··· H(2) | Intramolecular | 3.367 (2) | 3.1 |
| C(3)-C(4) | 1.382 (5) | P ··· Cl(1) | Intramolecular | 3.770 (3) | 3.7 |
| C(4)-C(5) | 1.395 (6) | P ··· C(7)H ₃ | Intramolecular | 2.597 (5) | 3.9 ^a |
| C(5)-C(6) | 1.387 (5) | P ··· C(8)H ₃ | Intramolecular | 2.627 (5) | 3.9 ^a |
| C(6)-C(1) | 1.373 (5) | Cl(1) ··· O(1) | Intramolecular | 2.966 (3) | 3.20 |
| C(1)-O(1) | 1.383 (4) | C(7)H ₃ ··· O(1) | Intramolecular | 2.915 (6) | 3.4 ^a |
| C(2)-Cl(1) | 1.726 (4) | C(8)H ₃ ··· Cl(1) | Intramolecular | 3.772 (6) | 3.8 ^a |
| C(3)-H(1) | 0.950 (4) | C(8)H ₃ ··· O(3) | Intramolecular | 2.934 (6) | 3.4 ^a |
| C(4)-Cl(2) | 1.716 (4) | Cl(2) ··· O(3) | -1 cell in x and z | 3.048 (4) | 3.20 |
| C(5)-Cl(3) | 1.723 (4) | Cl(1) ··· C(7)H ₃ | 2 ₁ + 1 cell in x and z - 1 in y | 3.493 (5) | 3.8 |
| C(6)-H(2) | 0.950 (4) | O(2) ··· C(7)H ₃ | 2 ₁ + 1 cell in x and z - 1 in y | 3.669 (7) | 3.4 |
| P-O(1) | 1.599 (3) | O(4) ··· H(2) | 2 ₁ + 1 cell in x and z - 1 in y | 2.749 (3) | 3.0 |
| P=O(2) | 1.450 (3) | O(4) ··· C(6) | 2 ₁ + 1 cell in x and z - 1 in y | 2.572 (5) | 3.1 |
| P-O(3) | 1.552 (3) | Cl(3) ··· C(8)H ₃ | 2 ₁ + 1 cell in x and z - 1 in y | 3.778 (6) | 3.8 |
| P-O(4) | 1.536 (3) | O(2) ··· C(3) | c-glide + 1 cell in y - 1 in x and z | 3.309 (5) | 3.1 ^b |
| O(3)-C(7) | 1.442 (5) | O(2) ··· H(1) | c-glide + 1 cell in y - 1 in x and z | 2.379 (3) | 3.6 |
| O(4)-C(8) | 1.451 (6) | | | | |

^a Assumes linear addition of a "spherical" methyl group van der Waals radius. ^b Bondi, 1964.

(Baughman and Jacobson, 1975), Coroxon (*O,O*-diethyl *O*-(3-chloro-4-methyl-2-oxo-(2*H*)-1-benzopyran-7-yl) phosphate, Gifkins and Jacobson, 1976), bromophos (*O*-(4-bromo-2,5-dichlorophenyl) *O,O*-dimethyl phosphorothioate, Baughman and Jacobson, 1976), fospirate (dimethyl 3,5,6-trichloro-2-pyridyl phosphate, Baughman and Jacobson, 1977a), crufomate (2-chloro-4-(1,1-dimethylethyl) methyl methylphosphoramidate, Baughman et al., 1977a), and chloropyrifos (*O,O*-diethyl *O*-3,5,6-trichloro-2-pyridyl thiophosphate, Baughman et al., 1978b) are all within 3σ of being identical. The angles of the type S=P-O or O=P-O in these compounds are all greater than the tetrahedral angle of 109.47°. In ronnel oxon the angle between the normal to the ring and the P=O vector is 34.4° which is nearly identical with the angle of 34.8° between the normals to the O(1)-O(3)-O(4) plane and the ring. Comparable angles of 23.7, 38.5, 23.9, 39.6, 19.9, and 23.5° have been observed in ronnel, Coroxon, azinphos-methyl (*O,O*-dimethyl *S*-(4-oxo-1,2,3-benzotriazin-

3-yl)methyl phosphorodithioate, Rohrbaugh et al., 1976), bromophos, fospirate, and amidithion (*O,O*-dimethyl *S*-(*N*-2-methoxyethylcarbonylmethyl) phosphorodithioate, Rohrbaugh and Jacobson, 1977), respectively. The latter case is the most surprising result as amidithion has many more rotational degrees of freedom and consequently is not as rigid as the other compounds.

As a result of Cl(2) and Cl(3) being less than the sum of their van der Waals radii apart, the following angles are significantly ($>3\sigma$) dissimilar: Cl(2)-C(4)-C(5) > Cl(2)-C(4)-C(3) and Cl(3)-C(5)-C(4) > Cl(3)-C(5)-C(6), (cf. Figure 1, Tables II and III). The C(1)-O(1)-P angle is considerably greater than the tetrahedral angle (cf. Table III) yet is identical with the corresponding angle in ronnel. Therefore the *difference* in van der Waals radii of the respective doubly bonded atoms (oxygen vs. sulfur) does not seem to be the major source of this discrepancy. The "p-ring" bonding noted earlier likely serves to modify the hybridization on O(2), through van der Waals interactions

Table III. Bond Angles (Degrees) for Ronnel Oxon

| | |
|------------------------------|-----------|
| C(1)-C(2)-C(3) | 120.6 (3) |
| C(2)-C(3)-C(4) | 119.4 (3) |
| C(3)-C(4)-C(5) | 120.0 (3) |
| C(4)-C(5)-C(6) | 120.1 (3) |
| C(5)-C(6)-C(1) | 119.8 (3) |
| C(6)-C(1)-C(2) | 120.1 (3) |
| O(1)-C(1)-C(2) | 120.2 (3) |
| O(1)-C(1)-C(6) | 119.6 (3) |
| Cl(1)-C(2)-C(1) | 120.1 (3) |
| Cl(1)-C(2)-C(3) | 119.3 (3) |
| H(1)-C(3)-C(2) | 120.4 (4) |
| H(1)-C(3)-C(4) | 120.3 (4) |
| Cl(2)-C(4)-C(3) | 118.7 (3) |
| Cl(2)-C(4)-C(5) | 121.3 (3) |
| Cl(3)-C(5)-C(4) | 121.0 (3) |
| Cl(3)-C(5)-C(6) | 118.8 (3) |
| H(2)-C(6)-C(5) | 120.1 (4) |
| H(2)-C(6)-C(1) | 120.1 (4) |
| C(1)-O(1)-P | 123.2 (2) |
| O(1)-P-O(2) | 112.9 (2) |
| O(1)-P-O(3) | 102.1 (2) |
| O(1)-P-O(4) | 106.3 (2) |
| O(2)-P-O(3) | 118.4 (2) |
| O(2)-P-O(4) | 113.0 (2) |
| O(3)-P-O(4) | 102.7 (2) |
| P-O(3)-C(7) | 120.3 (3) |
| P-O(4)-C(8) | 123.2 (3) |
| P-O(2) ··· H(1) ^a | 128.6 (2) |
| P-O(4) ··· H(2) ^b | 119.7 (2) |

^a Through 2₁ + 1 cell in *x* and *z* - 1 in *y*. ^b Through *c*-glide + 1 cell in *y* - 1 in *x* and *z*.

with the ring are not completely negligible.

In contrast to ronnel, the O-Me vectors in ronnel oxon are approximately pointed in the *opposite* direction as the P-O(2) vector. The actual direction may be a function of crystal packing as intermolecular interactions involving methyl groups exist in both compounds. Yet the sets of methyl groups in both compounds basically tend to align in a pairwise unidirectional fashion, probably due to the lone pair repulsions of the methoxy oxygens and the double bonded moiety.

As with ronnel, bromophos, crufomate, and fospirate, the phosphorus in ronnel oxon is opposite the Cl(1) side of a plane which is perpendicular to the ring and contains the C(1)-O(1) bond. The position of the phosphorus appears to be dictated by the van der Waals interactions of the phosphorus with H(2) and/or Cl(1) (cf. Table II), thus restricting rotation about the C(1)-O(1) bond to quite a small range of angles. Furthermore, the phosphorus is nearly symmetrically placed with respect to the ring, being 3.52 and 3.41 Å away from C(2) and C(6), respectively, and having a C(2)-C(1)-O(1)-P torsional angle of ~98° (cf. Table IV).

On the basis of a restricted phosphorus position, comparison of some intramolecular distances with literature site-separation distances for AChE should give some insight into the toxicity/activity of ronnel oxon. In addition to being "distance compatible", the two atoms involved must both have a net δ(+) charge to be in agreement with the AChE model of Krupka (1964). (Only two atoms are being considered here in accordance with the presence of two residues in the active site of AChE. Analysis of the steric interactions of the remaining parts of both molecules, without knowing more about the structure of AChE, would be futile.)

Using a CNDO II calculation (after Pople and Beveridge, 1970) approximate values for the charge density distribution in ronnel oxon can be computed; results are shown in parenthesis in Figure 1. Examination of this figure

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

| Torsional angle | |
|------------------|---------|
| P-O(1)-C(1)-C(2) | 97.98 |
| O(2)-P-O(1)-C(1) | 12.51 |
| O(1)-P-O(3)-C(7) | -68.70 |
| O(1)-P-O(4)-C(8) | -55.38 |
| O(2)-P-O(3)-C(7) | 55.92 |
| O(2)-P-O(4)-C(8) | -179.80 |

| Atom | Distance from plane, Å |
|--|------------------------|
| Plane (I) ^a defined by C(1), O(1), P, and O(2): (0.56915)X + (0.81552)Y + (0.10483)Z - (7.41029) = 0 | |
| C(1) | -0.033 |
| O(1) | 0.059 |
| P | -0.054 |
| O(2) | 0.028 |
| C(4) | -0.177 |
| Cl(2) | -0.279 |
| Plane (II) ^a defined by C(8), O(4), P, and O(2): (0.49175)X + (0.06157)Y + (0.86855)Z - (7.11910) = 0 | |
| C(8) | -0.001 |
| O(4) | 0.001 |
| P | 0.001 |
| O(2) | -0.001 |

Plane (III)^a defined by all 12 phenoxy group members: (-0.65204)X + (0.75669)Y - (0.04737)Z - (9.69391) = 0

| | |
|-------|--------|
| C(1) | -0.013 |
| C(2) | -0.028 |
| C(3) | -0.006 |
| C(4) | 0.003 |
| C(5) | -0.017 |
| C(6) | -0.010 |
| O(1) | 0.083 |
| Cl(1) | -0.036 |
| H(1) | 0.000 |
| Cl(2) | 0.062 |
| Cl(3) | -0.036 |
| H(2) | -0.003 |

^a Planes are defined by $c_1X + c_2Y + c_3Z - d = 0$, where *X*, *Y*, and *Z* are Cartesian coordinates which are related to the triclinic cell coordinates (*x*, *y*, *z*) by the transformations: $x = xa \sin \gamma + zc \{(\cos \beta - \cos \alpha \cos \gamma)/\sin \gamma\} = xa + zc \cos \beta$, $y = xa \cos \gamma + yb + zc \cos \alpha = yb$, $z = zc \{1 - \cos^2 \alpha - \cos^2 \beta - \cos^2 \gamma + 2 \cos \alpha \cos \beta \cos \gamma\}^{1/2}/\sin \gamma = zc \sin \beta$.

shows that P···H(1) (5.49 Å), P···C(3) (4.78 Å), P···C(4) (5.25 Å), and P···C(5) (4.68 Å) are the most important pairs in this regard. These distances fall outside of or just border the mammalian AChE site-separation range of 4.3-4.7 Å (Hollingworth et al., 1967, O'Brien, 1963) and yet are close to or within range for insect AChE given by Hollingworth et al. (1967) of 5.0-5.5 Å and O'Brien (1963) of 4.5-5.9 Å. It is even conceivable that "C(5)-C(4)-C(3)-H(1)" might correspond to a region of δ(+) charge having P···δ(+) distances of from 4.68 to 5.49 Å. Considering charge, distance, steric factors, and overall reactivity, P···H(1) may be slightly favored as the reactive species toward insect AChE in ronnel oxon. The P···C(5) pair, due to its shorter distance, may play a more important role in mammalian toxicity, unless significant conformational alterations in AChE or ronnel oxon accompany any *in vivo* free energy changes.

It should be noted that even rotations about the C(1)-O(1) bond of ±40°, which may possibly be achieved *in vivo*, would correspond to a maximum change in the P-H(1) distance, for example, of only ±0.03 Å which is not likely to be critical with respect to the distances in AChE and to the I₅₀ of the insecticide as pertains to the con-

formation which AChE or ronnel oxon might have to distort in order to react. However, such a rotation would cause the phosphorus to be in a slightly different position relative to the other ring substituents. This may be partially responsible, then, for changes in I_{50} and/or LD_{50} values as a result of subtle steric influences of the insecticide AChE. In this regard it would be quite interesting to compare the toxicities of the pure *d* and *l* forms of ronnel oxon; a 1:1 racemic mixture is present in a centrosymmetric space group. But, in order to make better comparisons and predictions, many heretofore unreported insect and mammalian I_{50} and LD_{50} values will need to be investigated and tabulated. In addition CNDO calculations will need to be performed to obtain a better idea of the charge distribution and potential energy barriers which may be necessary to overcome in adduct formation.

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Supplementary Material Available: A listing of the observed and calculated structure factor amplitudes (9 pages). Ordering information is given on any current masthead page.

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Lipid Distribution in Flue-Cured Tobacco Plants

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The increasing use of reconstituted tobacco sheet in cigarette manufacture and the reported relationship between tumorigenicity of smoke and lipid content of cigarettes has generated interest in lipid analysis of tobacco plant parts used in the manufacture of sheet. We analyzed various plant parts of three varieties of flue-cured tobacco and reported data for hexane extractables, total solanesol, neophytadiene, hydrocarbon waxes, total major fatty acids, and total sterols. Total lipid content was highest in strip, followed by whole leaf, stem, and stalk in decreasing order. Solanesol, the major lipid, was present only in whole leaf and strip. Concentrations of the other lipids generally followed the same decreasing order as seen for the total lipids.

The amount of reconstituted tobacco sheet used in the manufacture of commercial cigarettes has increased from

about 15% in 1964 to the present level of 30% in some blends (Wynder and Hoffmann, 1967; DeJong et al., 1975). The increase has been due to the monetary savings made possible by the manufacture of sheet from the normally discarded stems and fines. Alterations in smoke composition related to the increased stem content of cigarettes

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